UCL Multimorbidity Project

"Socioeconomic inequalities in health expectancy with and without multiple morbidities"

Dr Madhavi Bajekal

REVES Conference, Vienna, 9th June 2016

NHS National Institute for Health Research
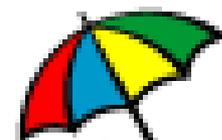
Legal & General

Collaboration for Leadership in Applied Health Research and Care
— **North Thames**

Project essentials

- **Research Team (co-authors)**:
    1. **Dr Madhavi Bajekal (Principal Investigator),** Senior Fellow, DAHR UCL
    2. **Mei Sum Chan**, Research Assistant, DAHR UCL
    3. **Dr Melvyn Jones**, Senior Lecturer, Dept of Primary Care UCL
    4. **Dr Ardo van den Hout**, Lecturer, Dept of Statistical Science UCL
    5. **Dr Spiros Denaxas**; Senior Lecturer, Farr UCL
    6. **Dr Mar Pujades**, University Academic Fellow, MRC Medical Bioinformatics Centre, Leeds

- **Funding**: CLAHRC matched funding by Legal & General Assurance Society (2 WTE L&G, 6 P/T UCL). Lead sponsor – Joseph Lu

- **Timeline**: Jan 2015 to Dec 2017 (3y)

- **Advisory Board**: Carol Jagger (chair), Chris Salisbury, Fiona Matthews, Brian Ridsdale, José Iparraguirre

Overview

1. Project aims and objectives

2. Understanding the dataset pre-analysis – selected analyses

3. MSM model specification

4. Provisional results

5. Next steps
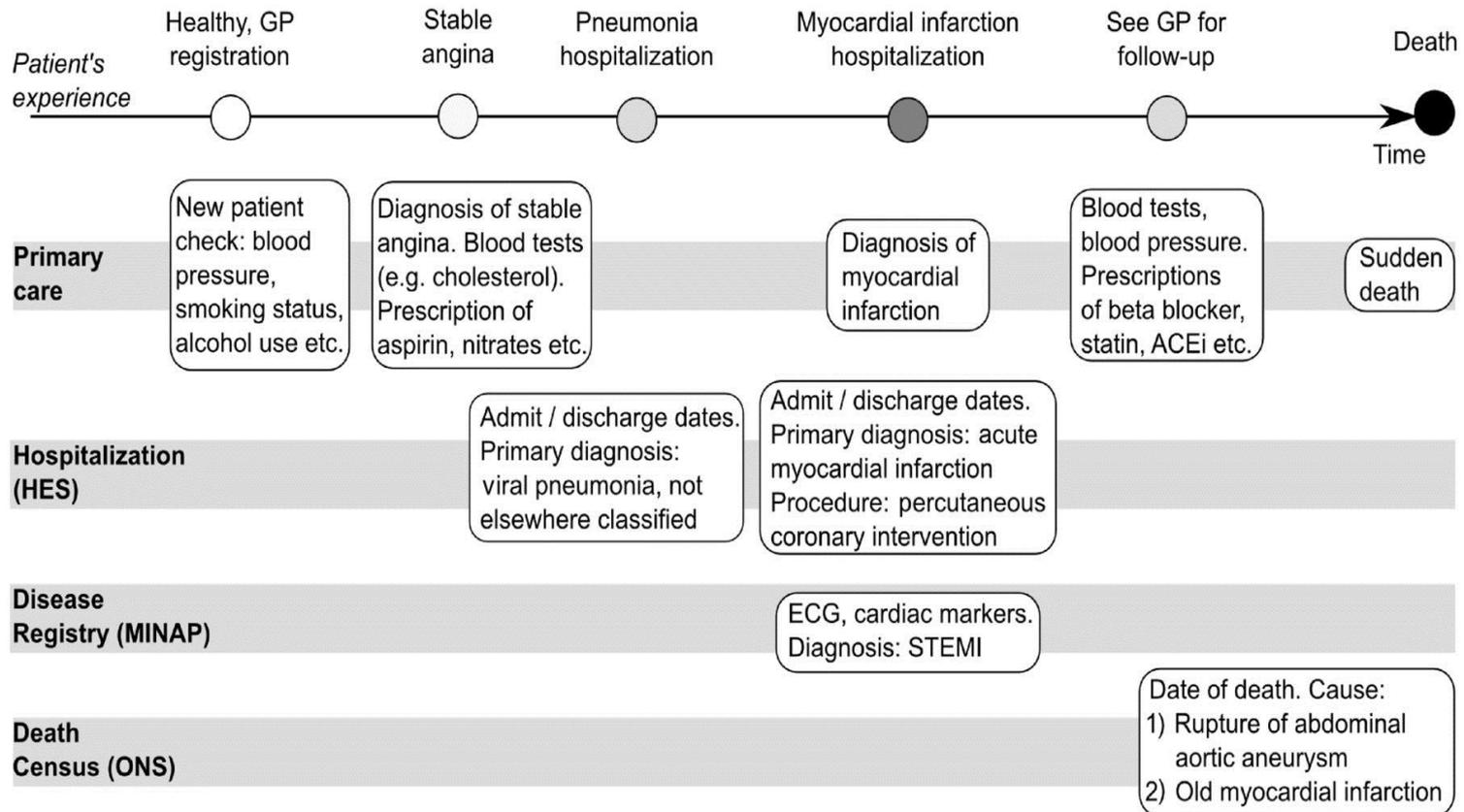
# Multimorbidity and socioeconomic disadvantage at older ages

- <u>What is Multimorbidity</u> (MM)?
  - " the co-occurence of two or more <u>chronic conditions</u> within one person *without specifying an index condition*"
  - A chronic condition/disease is a "health problem that requires *management <u>over a period of years</u> or decades*" (WHO)

- <u>We know</u> that the level of deprivation affects:
  - The age of onset of MM, and the number of conditions
  - Disease combinations –physical and mental health more common in deprived than in affluent at ages <55

- <u>What we don't know:</u>
  - Do older poor become morbid earlier in the life course and hence die younger? Or do they acquire more lethal diseases?
  - For similar disease combinations, is disease progression and survival different in deprived and advantaged groups?

Project Aims

- Two approaches to investigate the impact of socioeconomic inequalities:

  - ***Disease-count based approach***: estimate the differential rates of transition between health states and partition total life expectancy into years with and without disease (0,1,2,3+ diseases).

  - ***Disease cluster-based approach***: What are the common disease clusters? For patients with the same combination of diseases, does the mortality risk vary by socioeconomic deprivation?

'Big Data': linked Electronic Health Records _CPRD

Notes: ECG = Electrocardiography, STEMI = ST-segment elevation Myocardial Infarction, ACEI = Angiotensin-converting-enzyme Inhibitor.

Spiros C Denaxas et al. Int. J. Epidemiol. 2012;ije.dys188

Dataset

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Cohort specification

Inclusion criteria

- **Open cohort design**, with patients becoming cohort members on the earliest date that all three of the following criteria were fulfilled, which was designated the 'index date':

  1. Registered in linked practices and with a valid postcode of residence (to allocate patient to deprivation quintile of their small area of residence)

  2. UTS (up to (quality) standards) practice for at least 1 year

  3. All patients aged 45 and over on Jan 1st 2001 and patients in participating practices who turn 45 between **1st Jan 2001 and 25th March 2010**, irrespective of initial health status.

Follow up period – (from Jan 2001) to March 2010

- Patients' follow-up censored at the earliest date of death, deregistration from the practice, last data collection for the patient's practice, or the overall study end date.

1.3 million patients with 12 million consultations relating to 30 chronic diseases

Data

Challenge – which diseases?

- **Considerable methodological, conceptual and clinical challenges**
  - **No clear break point, no consensus**

- **Conflicting views on how to define multi-morbidity**
  - **(health conditions-eg pain; syndromes-eg sensory deficits)**

- **Always easier to justify adding a disease**
  - **Low prevalence but serious disease like MND**

- **Each disease requires 10-20 hours to produce a final, approved code list (Read code + ICD10)**

Which diseases?

Disease Prevalence ↑

Hypertension*
Obesity*
Diabetes
COPD
Asthma
High cholesterol*
Cancer (malignant)
CHD (angina, heart attack)
Depression
Osteoarthritis
Stroke
Thyroid disorder
Renal failure (CKD)
Anxiety
Osteoporosis
Dementia
Rheumatic Arthritis
Heart Failure
Chronic back pain
Other arthritis

Listing long-term conditions based on prevalence/frequency

➤ **Selecting TOP 5 – misses out Cancer**

➤ **Selecting Top 10 – misses out a MM patient with hypertension, kidney failure, heart failure and osteoporosis**

➤ **Selecting Top 20 – misses out patients with diseases like Parkinson's or liver disease**

• Risk factors* or chronic diseases?

* hypertension, hyperlipidaemia, hyper cholesterol

From: Mercer S, Salisbury C, Fortin M: **ABC of Multimorbidity**, Wiley 2014.

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List of diseases in-scope (30)

Asthma or COPD or bronchiectasis	Dementia or Alzheimer's	Osteoporosis
Atrial Fibrillation	Diverticulitis of intestine	Osteoarthritis (active Rx) or Chronic severe back pain
Anxiety	Epilepsy	Peripheral Arterial Disease
Alcohol problems	Glaucoma	Parkinson's disease
Coronary Heart Disease	Hypothyroidism	Psychoactive substance misuse
Chronic Kidney Disease (CKD 4,5)	Heart Failure	Prostate disorders
Cancer (in last 5 years)	Inflammatory Bowel Disease	Psoriasis
Chronic liver disease	Learning Disabilities	Rheumatoid Arthritis
Depression (ever + SSRI last year)	Multiple Sclerosis	Stroke or TIA
Diabetes	Motor Neurone Disease	Severe Mental Illness

Which Diseases?
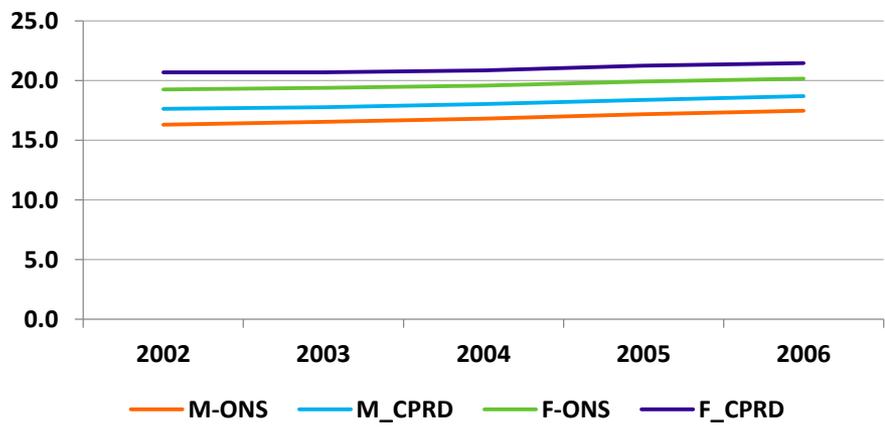
Understanding the dataset pre-modelling

How representative is the CPRD?
LE@65 comparison England vs CPRD
(3 year moving averages, citing middle year, 2002 to 2006)
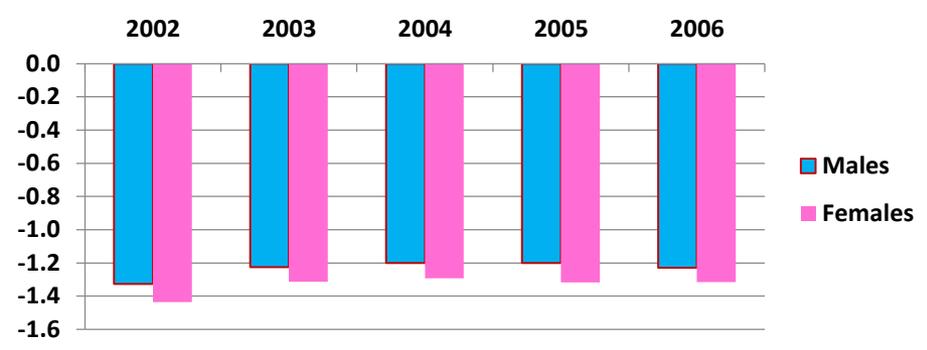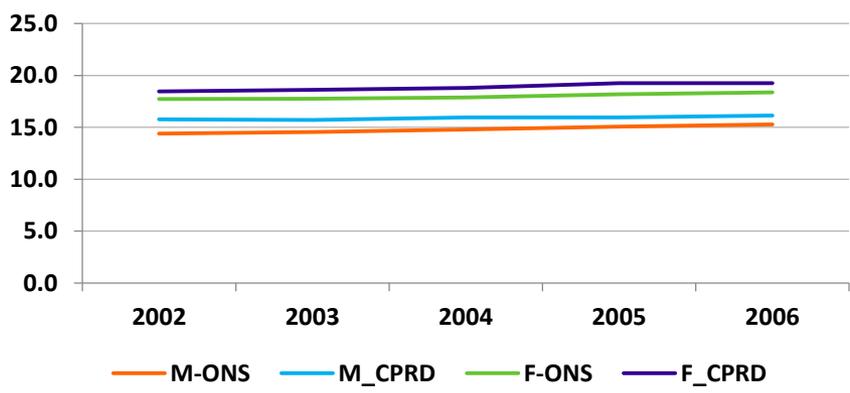
All England
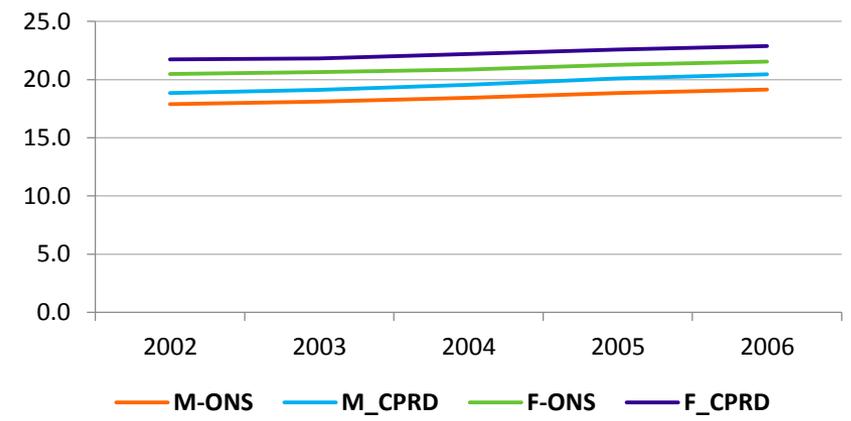
Difference *ONS minus CPRD, Eng*

Most Deprived Q5

Least deprived Q1

External validation
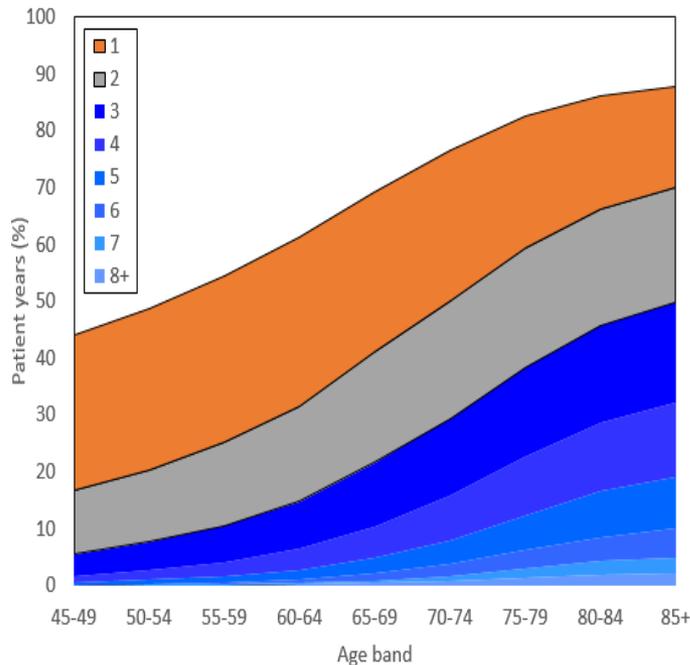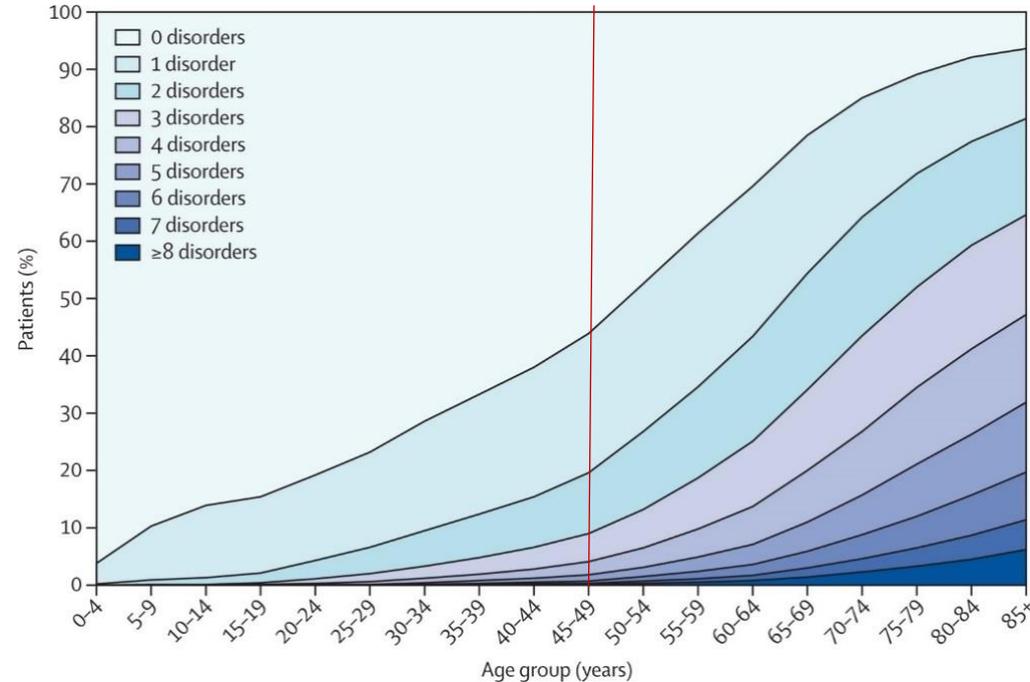
Morbidity prevalence for ages 45-85+, persons

England CPRD 2007
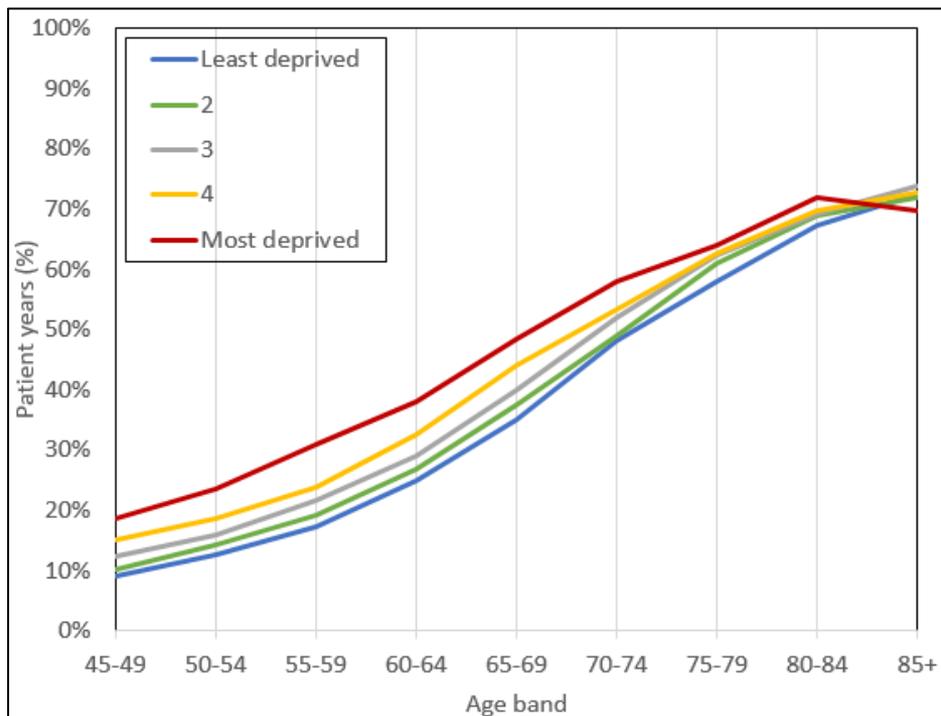
Scotland CPRD, 2007 (Barnett et al)
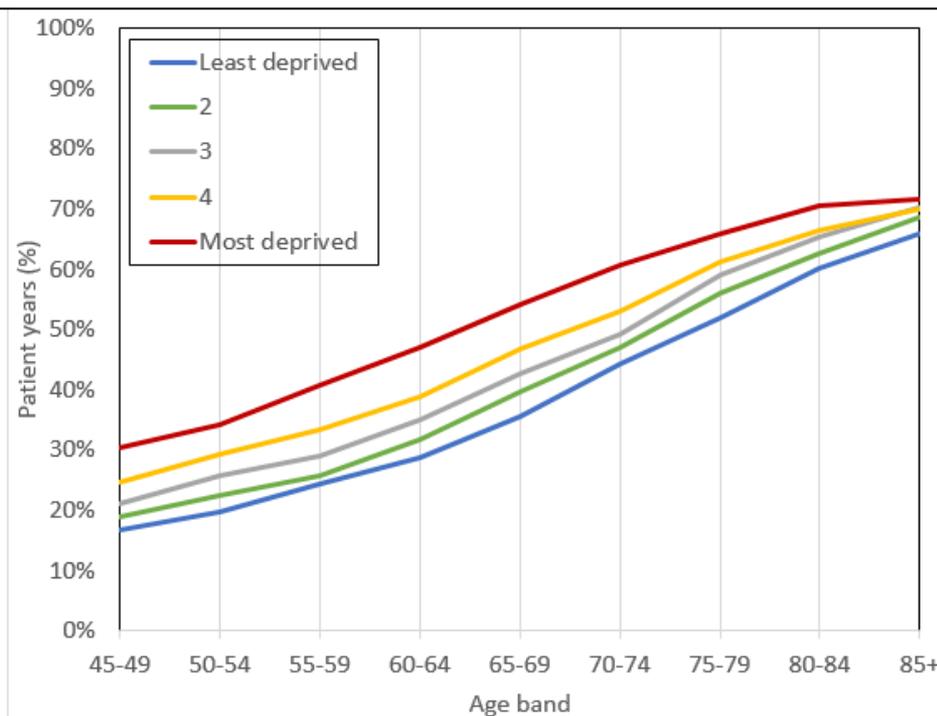
- **The distribution of disease counts by age is broadly similar between the 2 studies**

- **Barnett et al MM prevalence are higher, possibly because of including 40 vs our 30 chronic diseases and Scottish vs English data**

- **Its worth noting that even in the 85+ age band, >10% of patients have none of 30 chronic diseases, and just 70% would be considered MM (compared to 80% in Scotland)**

External validation

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Prevalence of multimorbidity by deprivation quintiles (2+ diseases)

Males
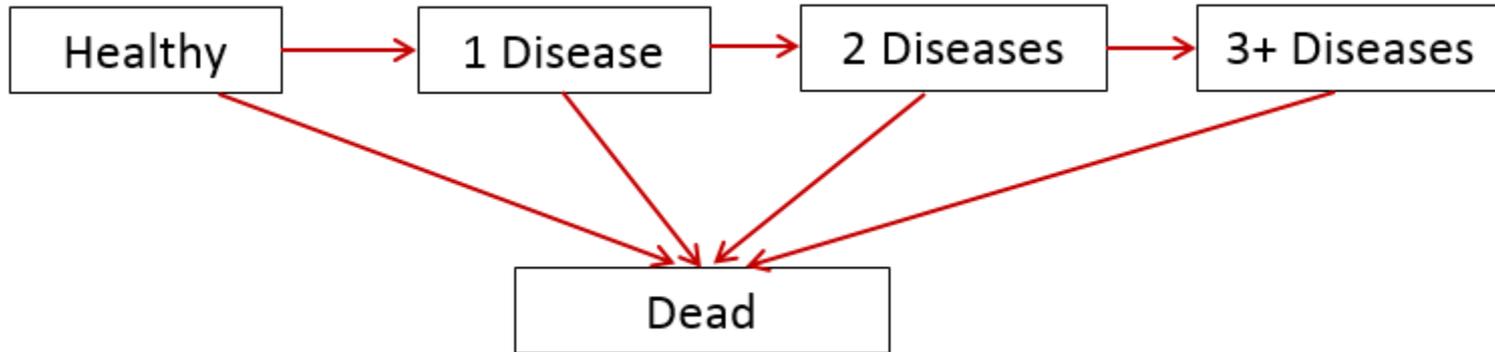
Females

- **Clear social gradient in the prevalence of MM, with differentials narrowing with advancing age**

- **Age-related increase in MM steeper for men than for women**

MSM Model Specification

Model structure

- **Progressive model, i.e. no recovery; state 5 is absorbing (death)**

- **Individuals transition to next state at the time of new diagnosis, or death.**

- **In this way, all transition times are taken to be known (no interval censoring). Eg the '1 disease' state is defined as having one of the selected diseases, and the age of entry in this state is estimated by the age at diagnosis as recorded in the data.**

Analysis of movers and stayers in CPRD data

- Significant proportions of the 1.3m patients have moved between each state, during the study period of up to 9¼ years

- 60% of all patients are stayers

- The MSM transition rates are largely informed by the remaining 40%

|		Final state					
		Healthy	**1 disease**	**2 diseases**	**3+ diseases**	**Dead**	**Total**
Initial state	**Healthy**	446,180	112,283	41,541	25,583	37,449	663,036
	1 disease	-	191,216	67,112	51,596	37,634	347,558
	2 diseases	-	-	73,597	58,828	28,412	160,837
	3+ diseases	-	-	-	81,772	38,587	120,359
	Dead	-	-	-	-	-	-
	Total	446,180	303,499	182,250	217,779	142,089	1,291,790

Key:
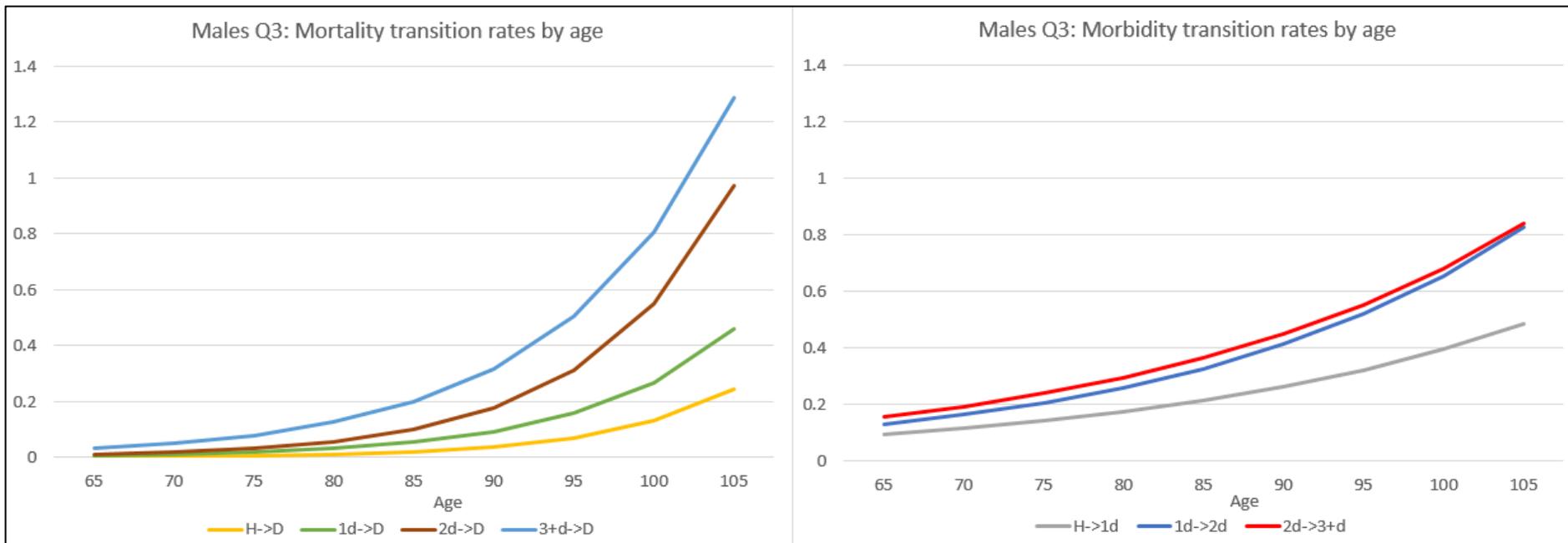
Stayers

Model inputs

- Input data split by: **Sex**, **IMD quintiles** and **Smoker status** – **2 x 5 x 3 = 30** separate models

- Current model covariates:
  - **Age** – time-dependent, continuous (65+)

- Smoker status is recorded at baseline – fixed, 3 categories (current-, ex- and never-smokers)

- Timescale: **Age** (from 65 onwards)

- Sample size: Random sample of **3,600-10,000** patients per model

- In each random sample of patients, we check for:
  - Sufficient transitions between each pair of states
  - Occurrence of only 1-step, progressive transitions to living states
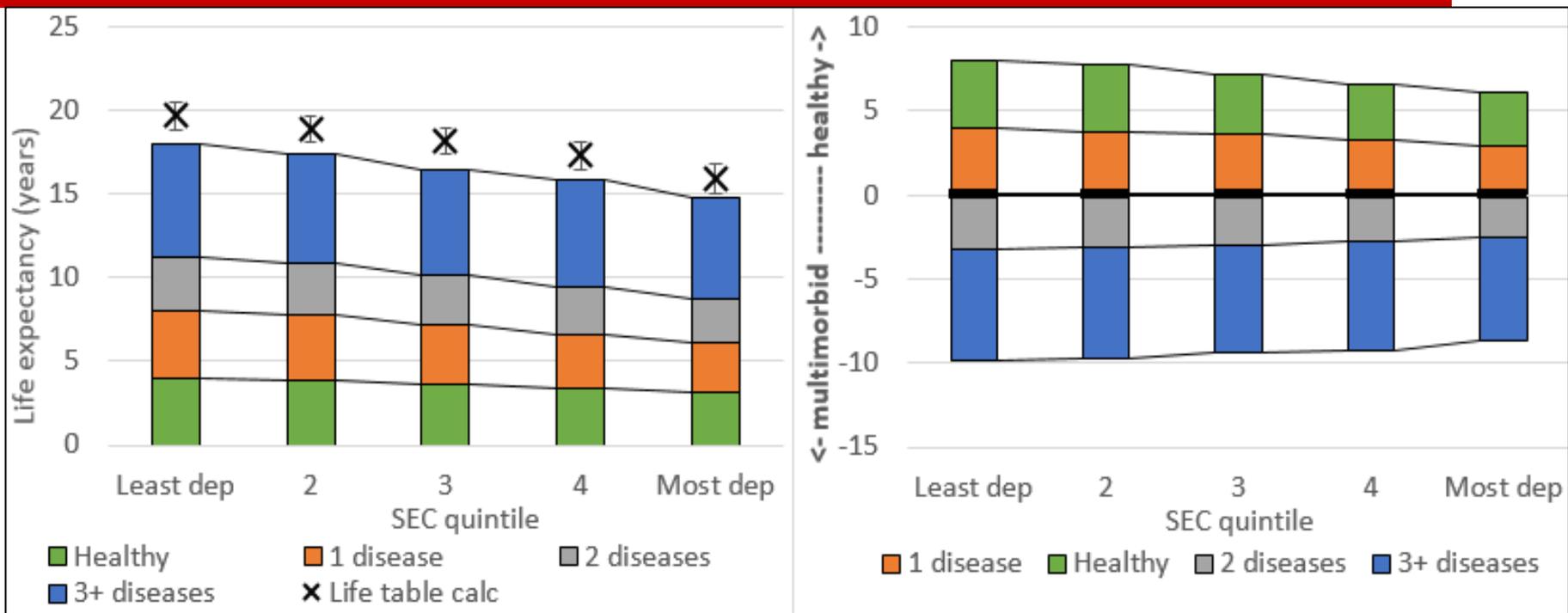
Provisional Results

Analysis of transition rates – model parameters by age. Males Q3

Males Q3: Mortality transition rates by age

Males Q3: Morbidity transition rates by age
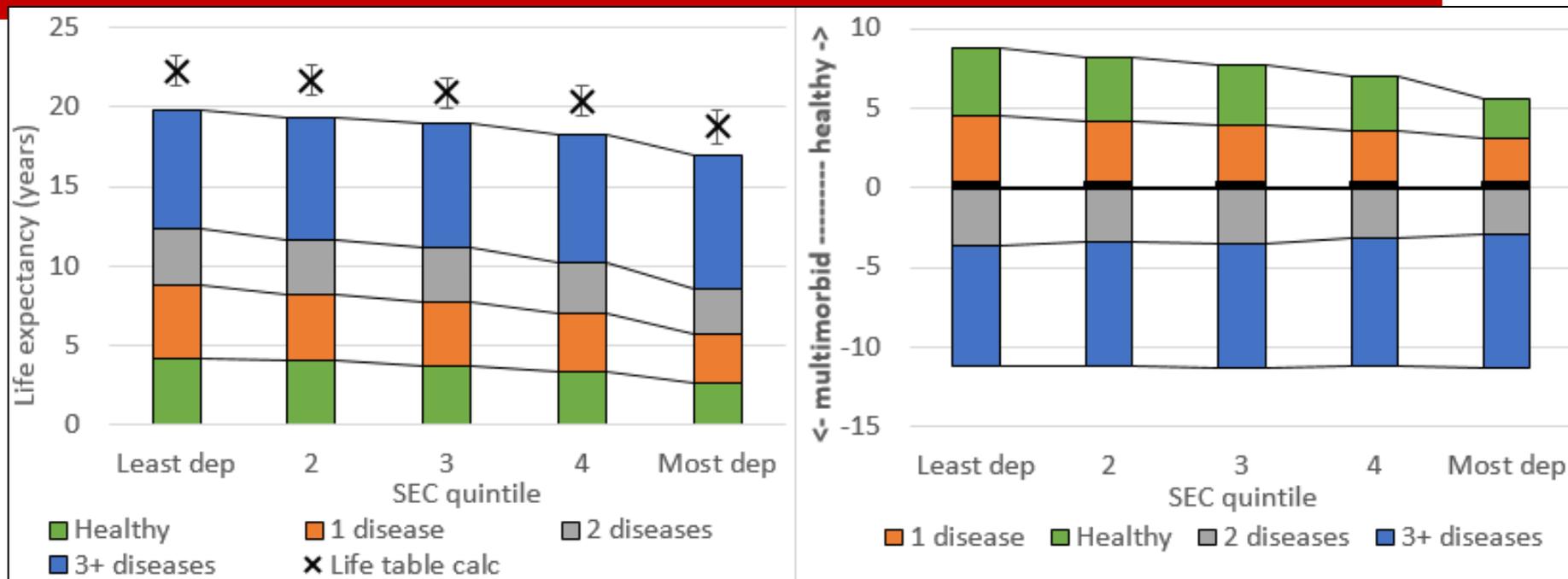
- **Mortality risk increases with age: and is lowest for those with no chronic disease and becomes progressively higher with each additional disease acquired**

- **Rate of transition from healthy to 1d (disease) are lowest for all groups; transitions from 1d to 2d and 2d to3+d are higher (in this example v similar)**

- **Similar patterns are seen across SEC quintiles for males and females**

Provisional results
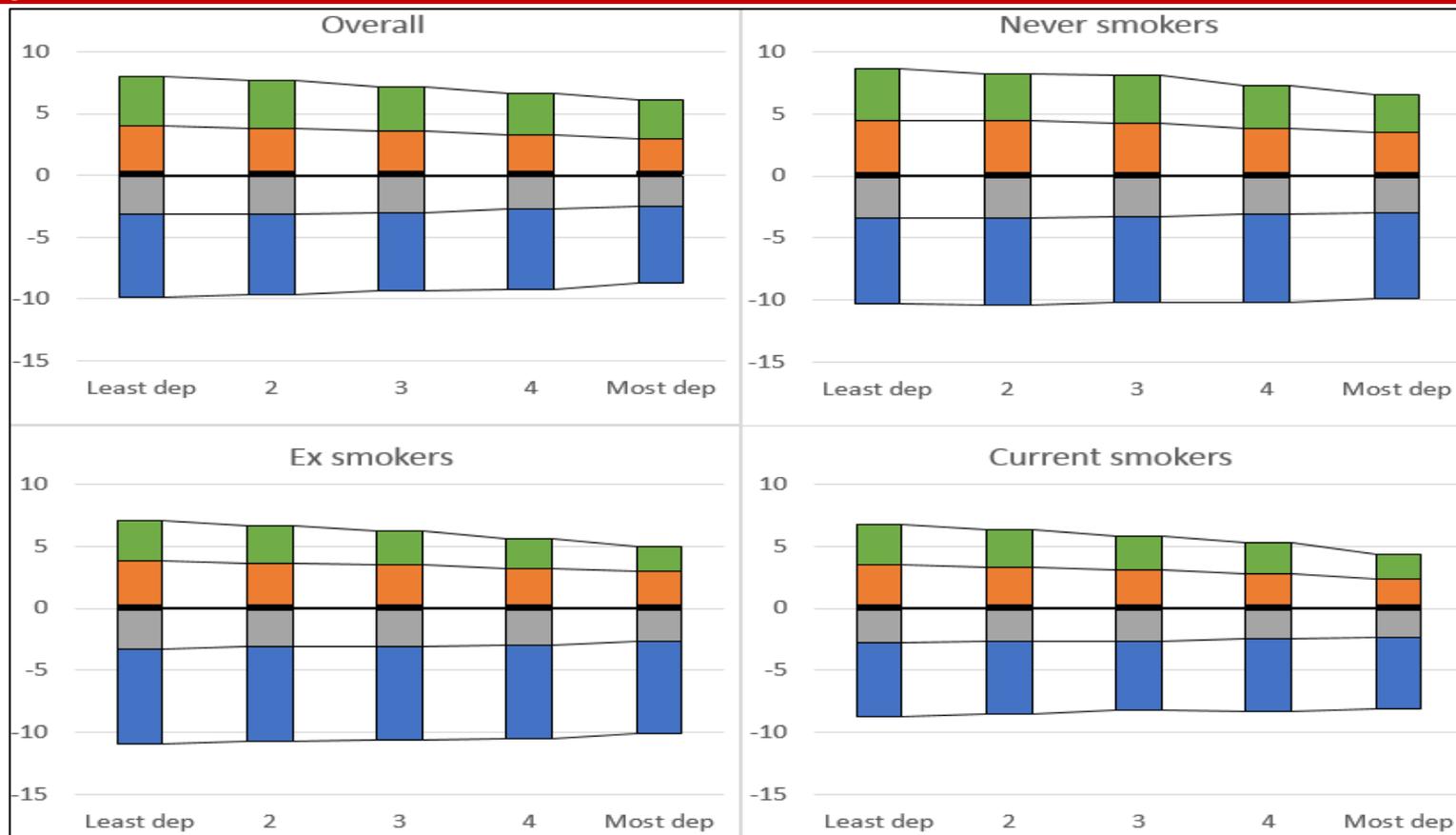
- **Modelled LEs are lower than life table LE for CPRD by about 1.5 years.**

- **Social gradient in total LE as expected– 3.1y diff between most-least deprived quintile**

- **But: when separated into years spent with MM (2+ diseases), most deprived males have the shortest 'healthy' life years and die earlier after developing MM.**

Basic model – Females LE@65 by IMD
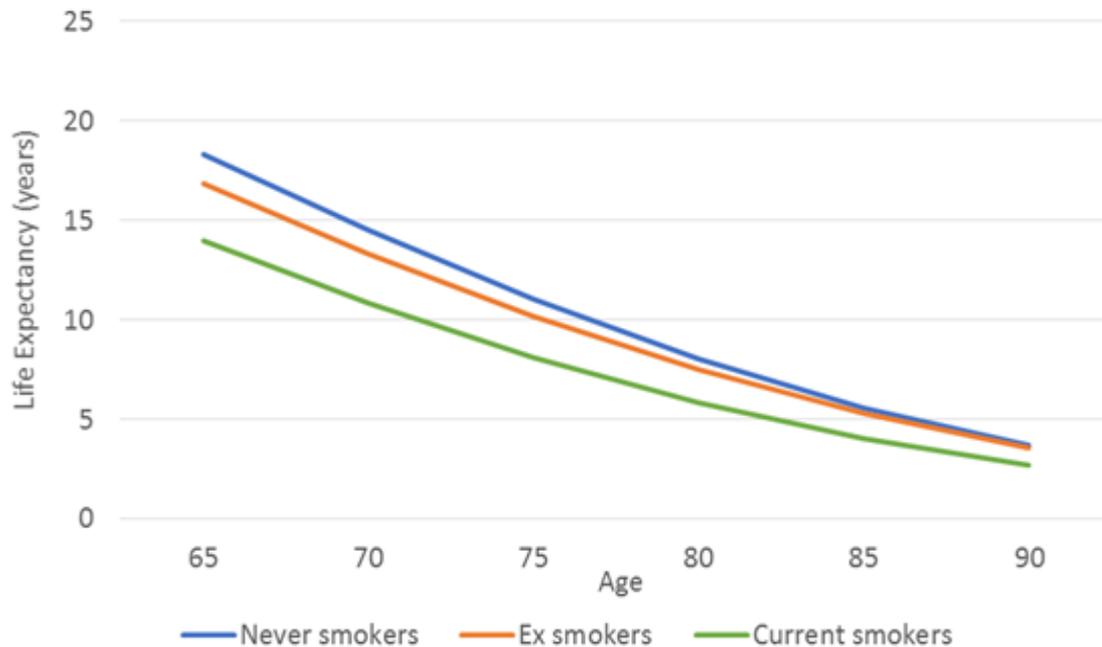
- **LEs are lower than life table LE for CPRD by about 2 years. (X)**
- **Social gradient in total LE is shallower than for men (2.2y diff)**
- **Unlike for males, time spent with MM (2+ diseases) is similar across all quintiles**
- **Differences in 'healthy' LE contribute most to the social gradient in LE for women**

Males LE@65 – Time spent with/out MM by IMD and smoker status

- **Years spent without MM: most for never-smokers; similar for ex- and current smokers**
- **Years spent with MM: similar for never- and ex-smokers; and fewest for current smokers**
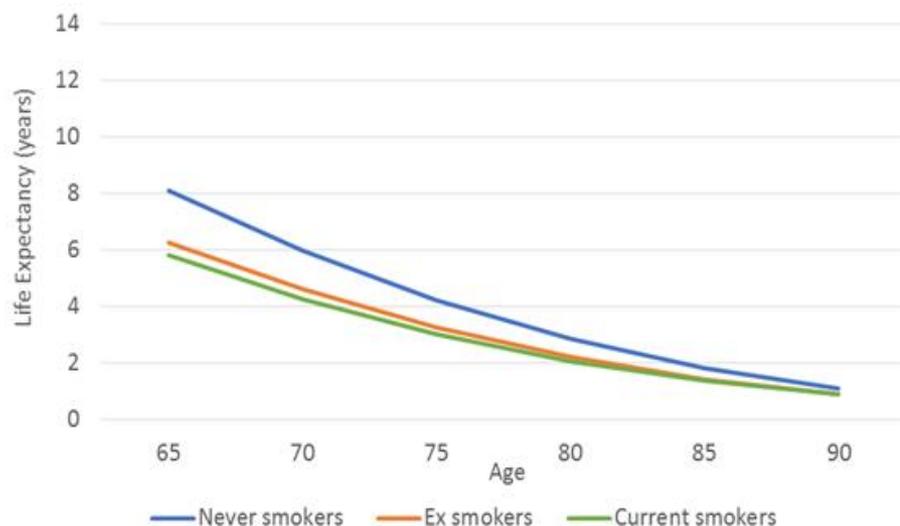
Males, Q3 – Total LE by age and smoker status
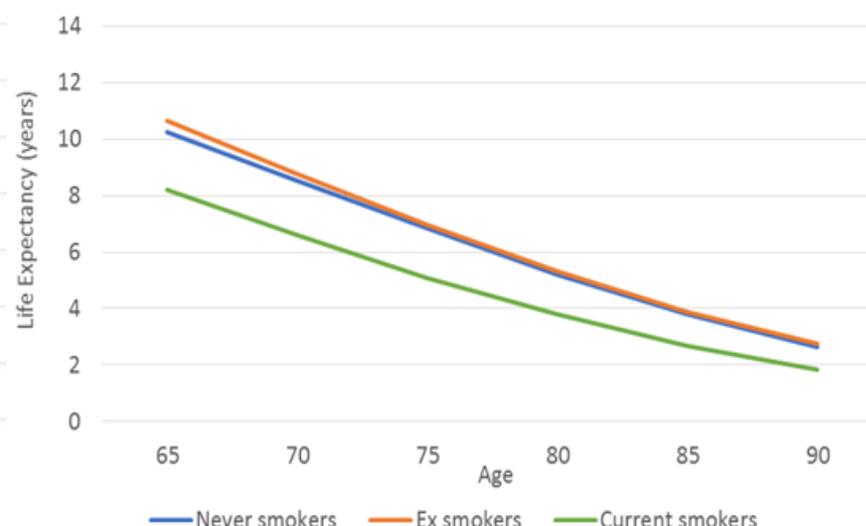
- **LE for never-smokers > ex-smokers> current smokers, and converges with age.**

- **At age 65, the LE gap between never-smokers and those who'd quit is 1.5 years and those who smoke is 4.3y * (all in Q3)**

- For both sexes and all SEC quintiles, the pattern across ages is broadly similar as above

- * This compares to a difference of 2.3 years @50 attributable to deaths from smoking using cause-of -death elimination analysis for E&W (*Kelly, Preston, 2016*)

Males Q3 – Time spent with/out MM by age and smoker status

Time spent *without* multimorbidity

Time spent *with* multimorbidity:

- **Never-smokers spend more years of life *without* multimorbidity (or 'healthy') than either ex- or current smokers**

- **Never- and ex-smokers spend more years of life *with* multimorbidity than current-smokers.**

- **Hence, current smokers have lowest LE because they spend least time healthy and die quicker once they become multimorbid.**

- **This pattern is similar for both sexes and across SEC quintiles**

Provisional results

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Summary of key messages and issues

- Modelling Issue:
    - Model-based LEs are consistently lower than direct life table estimates for all categories by gender, IMD and smoker status.

Additional insights made possible by using a multi-state model

- **The 'gap' in LE between most and least deprived has 2 components:**
    - the onset of MM is at an earlier age for the most deprived
    - and thereafter, progression to death is quicker for most- than for least-deprived.

- **Do IMD differences in smoking explain this?** *Yes and no.*
    - **For the same smoking status, people in deprived areas live shorter lives than those living in affluent areas – eg even for non-smokers, LE of most deprived was the lowest.**
    - **But the age of onset of MM is delayed for non-smokers; whereas it is earlier, and at similar ages, for ex- and current smokers.**
    - **Once MM sets in, non- and ex-smokers live the same number of years before death; current smokers with MM die sooner.**

Next Steps

- **Use MSM modelling to move from a count-based approach to a disease-based approach**

    - To assess where in the disease process the socioeconomic inequalities in life expectancy arise for patients who have a similar combination of diseases (*earlier age at onset, or faster progression to death once diseases diagnosed?*)

- **Methodological challenges ahead**

    - Explore alternative MSM specifications, to further reduce the modelled-life table LE discrepancy

    - Disease clusters – clinically determined or statistical – how to operationalise in a MSM framework?

Questions and comments?

Thank you for your attention

- Multimorbidity Project Contact:
  - m.bajekal@ucl.ac.uk

- CLAHRC – North Thames contact sites
  - Website: http://www.clahrc-norththames.nihr.ac.uk/health-inequalities-multiple-morbidities/
  - Email: clahrc.norththames@ucl.ac.uk
  - Twitter: @CLAHRC_N_Thames

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- The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

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Email:
clahrc.norththames@ucl.ac.uk

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