Supplementary Information for

Identifying profiles, trajectories, burden, social and biological factors in 3.3 million individuals with multimorbidity in England

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S1 Note 1: Identification of multimorbidity profiles

S1.1 Threshold selection for merging clusters

To merge identified clusters across different age bands into unified multimorbidity profiles, we determined thresholds for hierarchical clustering using the following criteria:

- Clusters from the same age band were not merged.
- Only clusters from adjacent age bands were eligible for merging, ensuring multimorbidity profiles do not span non-consecutive age groups.

Using these criteria, we identified the merging threshold as the smallest hierarchical clustering distance that met both conditions.

S1.2 Multimorbidity profile naming convention

When naming multimorbidity profiles, we consider several key clinically meaningful factors:

- **Common conditions reflecting population characteristics.** Highly prevalent conditions such as depression or hypertension, though often not profile-specific, characterise substantial proportions of cluster populations and thus are relevant for clinical context.
- **Clinically significant rare conditions.** Conditions with a lower prevalence within a profile, but significant clinical implications or distinctive diagnostic value, were considered as important differentiators.
- **Within-age-band differentiation.** Conditions or body systems uniquely prevalent within certain profiles relative to others of the same age group were emphasised, clarifying between-profile distinctions and improving clinical interpretability.

Consequently, we defined the following guidelines for the naming of multimorbidity profiles:

- **Conditions with 100% prevalence.** Conditions universally present within a profile were always included in the profile name (e.g., Anxiety or Depression in names of M1, M3, F1, F3, and F5).
- **Complex profiles.** Profiles characterised by an average of more than four conditions per individual were labelled with the suffix "Complex".
- **Condition inclusion criteria.**
  - Profile names included up to three specific conditions or body systems, except for profiles designated as "Complex".
  - Conditions included in names must meet at least one of the following criteria:
    - Within-profile prevalence greater than 40% (e.g., conditions included in names of M10 and F2), or
    - Substantially higher within-profile prevalence relative to other profiles in the same age band (e.g., Cancer in names of M5 and F13, Cancer and Diabetes in the name of M8).
- **Use of system-level naming.**
  - When multiple conditions from the same physiological system were present, the system name was used (e.g., Cardiovascular, Cardiometabolic, Renal, Respiratory, and Musculoskeletal systems in the name of F15).
  - If one condition within a system demonstrated a significantly higher prevalence compared to others, the system was explicitly labelled as "xx-predominant" (e.g., Osteoporosis-predominant in the name of F13).
- **Ordering of conditions and systems.** Conditions and systems were listed in descending order of prevalence within the profile.

Supplementary Figures

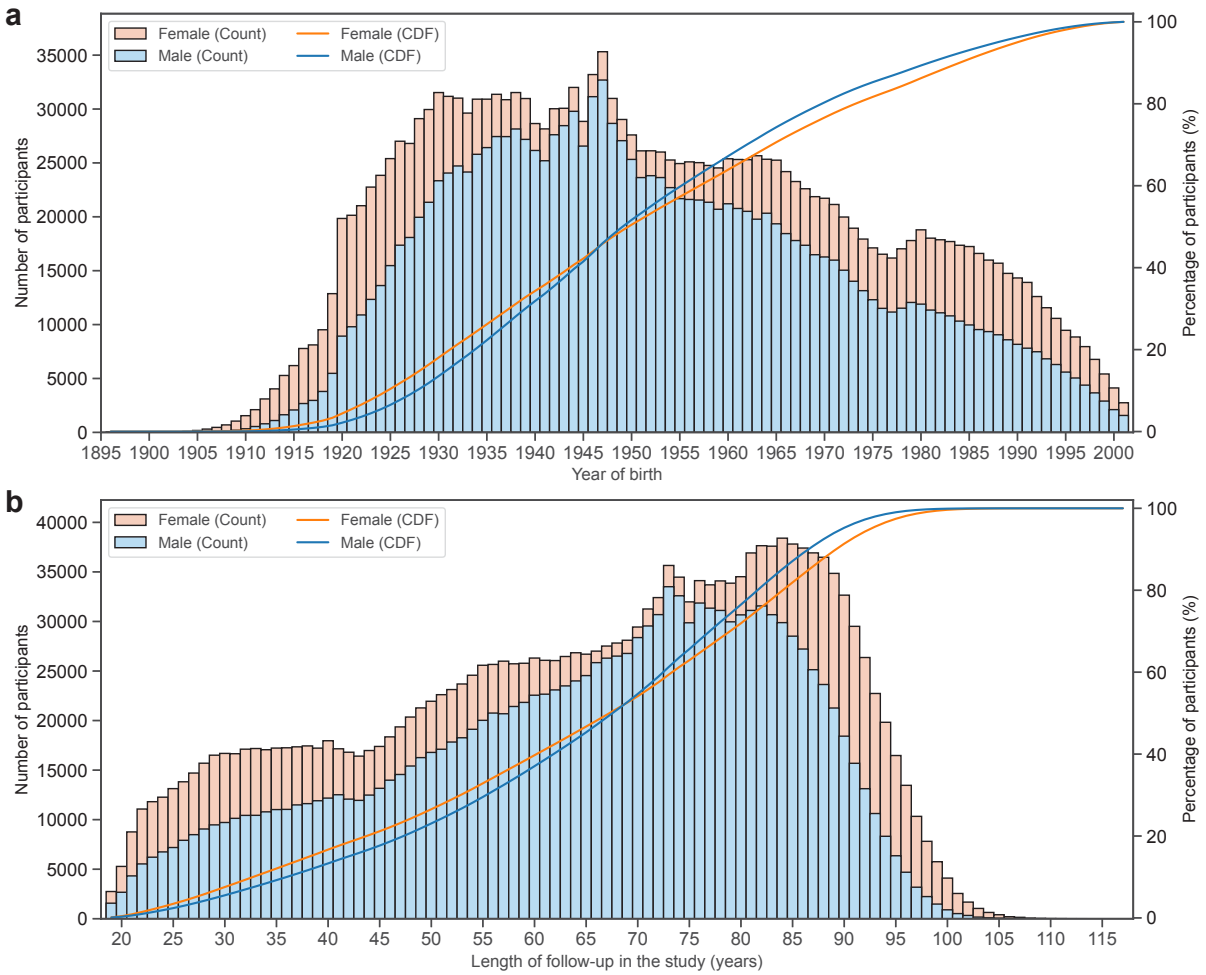


Figure S1: Participant birth year and follow-up duration. a, Distribution of participants by year of birth and sex. **b,** Length of follow-up in the study (years), stratified by sex. The stacked bars represent the absolute counts of participants, while the lines indicate the cumulative percentages.

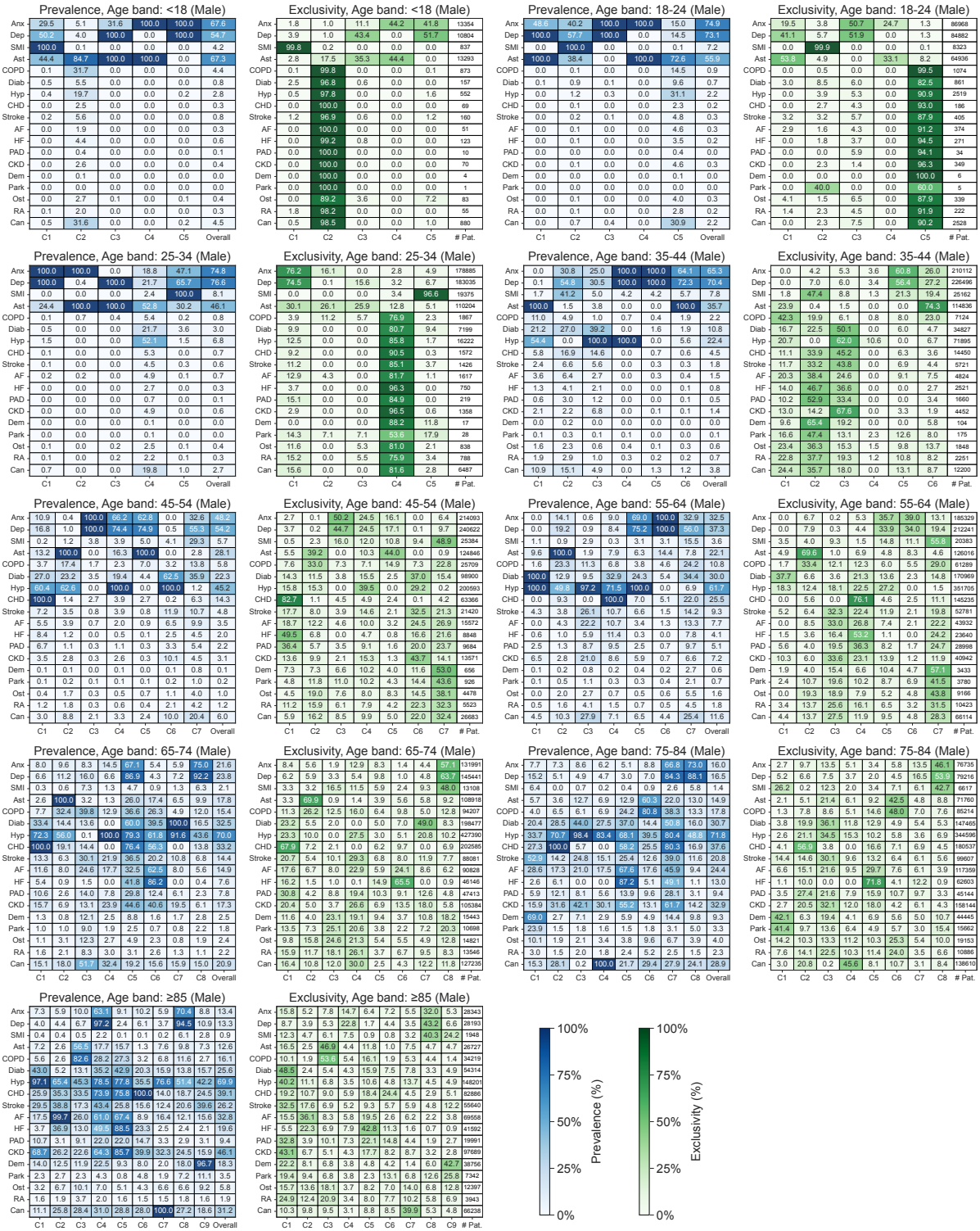


Figure S2: Condition prevalence and exclusivity for clusters in different age bands for males. Condition abbreviations: anxiety (Anx), depression (Dep), serious mental illness (SMI), asthma (Ast), chronic obstructive pulmonary disease (COPD), diabetes (Diab), hypertension (Hyp), coronary heart disease (CHD), stroke or transient ischaemic attack (Stroke), atrial fibrillation (AF), heart failure (HF), peripheral arterial disease (PAD), chronic kidney disease (CKD), osteoporosis (Ost), rheumatoid arthritis (RA), cancer excluding non-melanoma skin cancers (Can).

Figure S3: Condition prevalence and exclusivity for clusters in different age bands for females. Condition abbreviations: anxiety (Anx), depression (Dep), serious mental illness (SMI), asthma (Ast), chronic obstructive pulmonary disease (COPD), diabetes (Diab), hypertension (Hyp), coronary heart disease (CHD), stroke or transient ischaemic attack (Stroke), atrial fibrillation (AF), heart failure (HF), peripheral arterial disease (PAD), chronic kidney disease (CKD), osteoporosis (Ost), rheumatoid arthritis (RA), cancer excluding non-melanoma skin cancers (Can).

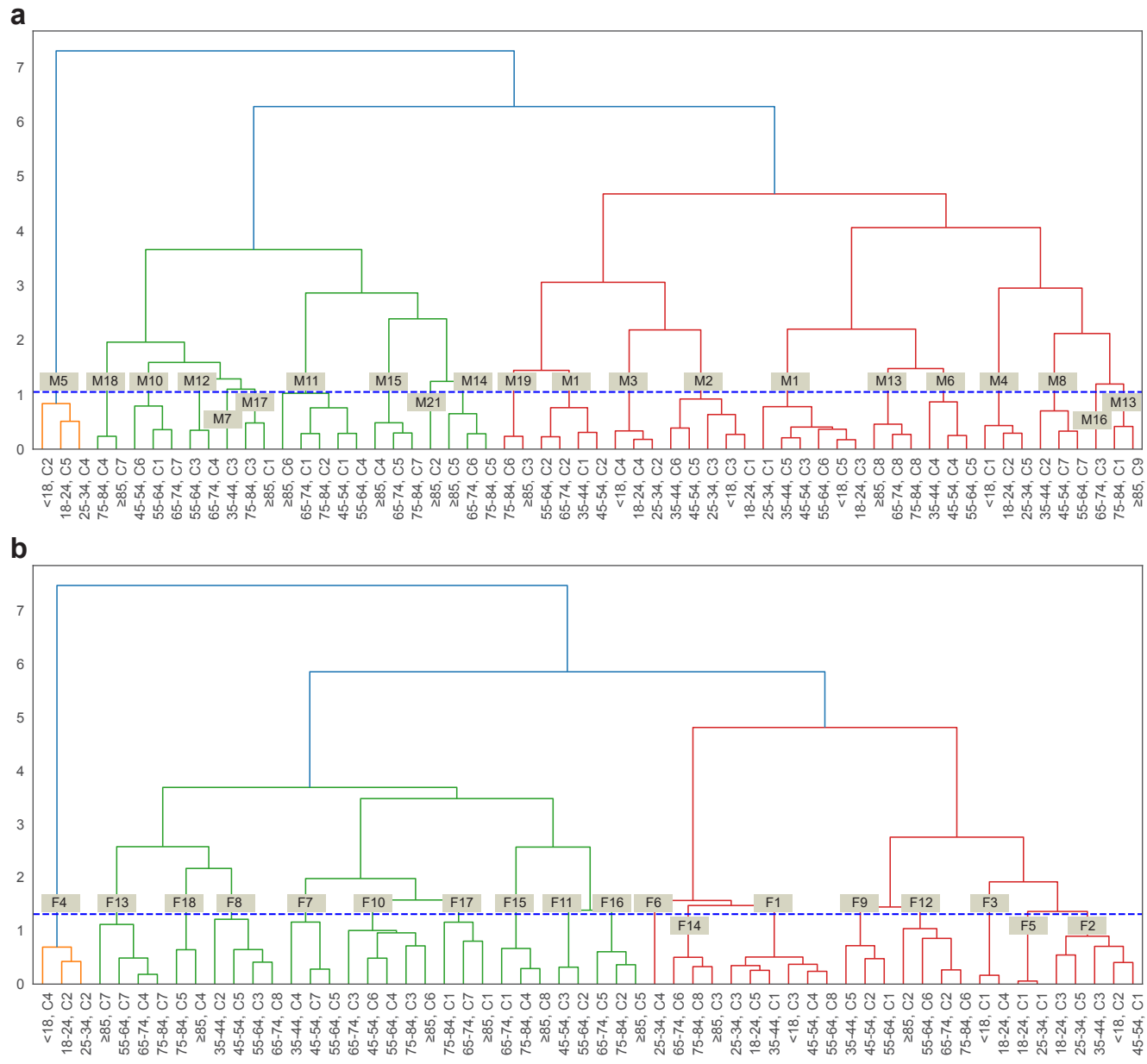


Figure S4: The cluster merging process for multimorbidity profiles. a, Clusters merged from different age bands for males. **b,** Clusters merged from different age bands for females. The blue dashed lines indicate the threshold to stop the merging process, determined by the rules in Note S1.1.

a

	Anx	Dep	SMI	Ast	COPD	Diab	Hyp	CHD	Stroke	AF	HF	PAD	CKD	Dem	Park	Ost	RA	Can
M1	100.00	100.00	2.37	8.84	1.19	2.13	0.44	1.54	0.51	0.47	0.01	0.18	0.20	0.04	0.08	0.22	0.21	1.68
M2	51.65	82.04	3.66	100.00	2.68	1.97	2.32	0.97	0.34	0.42	0.07	0.10	0.12	0.02	0.03	0.33	0.22	1.15
M3	100.00	0.21	0.00	100.00	0.37	0.00	0.00	0.00	0.00	0.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
M4	44.53	62.88	100.00	33.09	0.18	2.69	1.37	0.04	0.24	0.08	0.02	0.00	0.06	0.01	0.03	0.08	0.12	0.88
M5	16.99	18.90	1.80	59.11	9.16	18.12	45.48	4.52	4.68	4.65	2.99	0.62	4.66	0.07	0.05	2.85	2.32	22.91
M6	69.10	75.90	3.50	10.35	3.04	21.14	100.00	5.39	5.16	2.63	0.36	1.79	4.26	0.23	0.23	0.47	0.62	4.88
M7	25.05	30.49	4.98	3.82	0.97	39.17	100.00	14.64	5.62	2.67	2.07	1.25	6.75	0.04	0.05	0.63	0.98	4.92
M8	32.39	55.54	24.64	5.07	17.29	33.39	3.86	16.36	11.65	10.89	6.09	7.14	5.12	1.64	1.42	4.41	4.08	21.88
M9	8.29	10.79	0.95	100.00	23.59	16.46	54.91	10.43	4.38	5.31	1.05	1.62	4.03	0.34	0.55	2.25	1.83	12.52
M10	2.61	3.30	1.97	5.66	3.46	90.02	96.31	0.04	9.18	5.29	0.83	4.33	13.19	0.82	0.45	0.63	1.31	11.01
M11	8.54	7.94	0.21	5.46	6.48	30.68	68.48	100.00	12.18	11.86	8.35	10.38	17.32	1.53	1.03	1.23	1.48	15.28
M12	9.55	4.59	1.86	1.52	12.31	3.41	99.01	0.00	23.40	19.28	2.15	8.12	22.86	1.90	1.61	2.67	3.39	30.79
M13	74.07	91.13	6.12	10.83	12.33	16.12	45.77	15.12	9.30	7.23	0.79	2.56	9.97	6.10	3.40	2.88	1.28	18.70
M14	5.95	3.33	0.52	14.87	25.48	38.93	67.85	60.92	23.77	65.88	87.11	14.91	56.16	5.14	1.10	3.56	2.32	21.08
M15	66.28	87.58	3.43	22.99	35.87	52.06	79.61	77.53	38.72	42.77	46.04	27.79	54.87	13.43	3.01	5.96	2.66	24.71
M16	8.32	16.01	7.29	3.20	39.84	13.58	0.05	14.40	30.13	24.57	1.48	14.04	13.10	12.06	9.05	12.29	8.26	51.70
M17	8.16	4.63	0.58	10.86	5.92	43.68	97.95	12.52	26.39	19.82	1.26	8.96	51.01	9.45	1.95	2.47	1.88	3.89
M18	6.11	4.41	0.22	7.08	6.85	24.11	81.44	4.13	14.34	17.21	0.75	4.94	30.74	2.64	1.67	4.33	1.70	100.00
M19	9.17	6.90	0.81	59.10	81.37	14.01	41.30	27.93	14.07	20.15	7.49	9.42	16.03	7.03	1.91	9.74	4.72	29.09
M20	8.12	13.55	4.99	6.32	3.52	18.58	36.98	26.19	47.72	23.54	2.38	4.80	15.91	79.73	18.94	9.74	2.48	16.60
M21	5.92	4.37	0.37	2.65	2.57	5.20	65.39	35.32	38.83	99.71	36.92	3.10	26.20	12.51	2.74	6.72	1.94	25.82

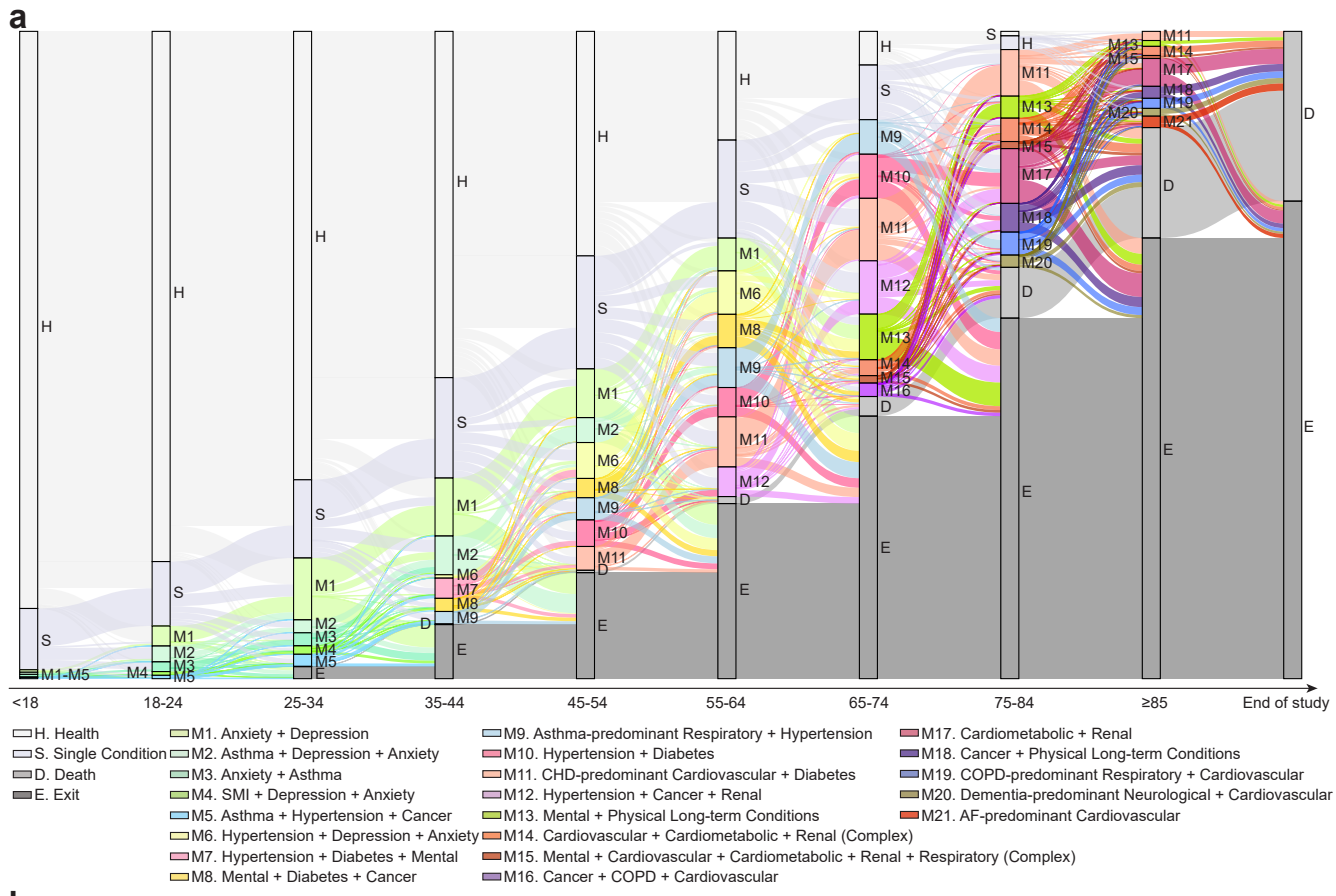
M1. Anxiety + Depression
M2. Asthma + Depression + Anxiety
M3. Anxiety + Asthma
M4. SMI + Depression + Anxiety
M5. Asthma + Hypertension + Cancer
M6. Hypertension + Depression + Anxiety
M7. Hypertension + Diabetes + Mental
M8. Mental + Diabetes + Cancer
M9. Asthma-predominant Respiratory + Hypertension
M10. Hypertension + Diabetes
M11. CHD-predominant Cardiovascular + Diabetes
M12. Hypertension + Cancer + Renal
M13. Mental + Physical Long-term Conditions
M14. Cardiovascular + Cardiometabolic + Renal (Complex)
M15. Mental + Cardiovascular + Cardiometabolic + Renal + Respiratory (Complex)
M16. Cancer + COPD + Cardiovascular
M17. Cardiometabolic + Renal
M18. Cancer + Physical Long-term Conditions
M19. COPD-predominant Respiratory + Cardiovascular
M20. Dementia-predominant Neurological + Cardiovascular
M21. AF-predominant Cardiovascular

b

	Anx	Dep	SMI	Ast	COPD	Diab	Hyp	CHD	Stroke	AF	HF	PAD	CKD	Dem	Park	Ost	RA	Can
F1	100.00	100.00	1.94	2.19	0.83	1.26	1.52	0.47	0.40	0.18	0.02	0.08	0.39	0.05	0.05	1.02	0.51	2.66
F2	74.41	81.43	2.10	99.96	1.90	1.89	0.02	0.24	0.34	0.13	0.03	0.05	0.29	0.01	0.02	0.29	0.40	1.21
F3	100.00	0.00	0.00	100.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
F4	24.71	43.91	29.10	48.60	3.96	12.88	31.18	1.27	3.48	1.14	1.38	0.54	2.67	0.06	0.06	3.59	5.60	17.43
F5	0.00	100.00	0.00	100.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
F6	100.00	100.00	79.98	27.26	0.92	19.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
F7	57.53	71.65	2.97	22.57	2.76	17.81	100.00	3.93	3.50	1.03	0.14	0.65	5.49	0.16	0.12	1.19	1.77	6.81
F8	32.26	57.52	19.68	1.16	13.51	17.87	0.08	7.16	8.91	4.42	1.08	1.85	9.65	3.46	1.79	7.41	9.59	43.36
F9	34.85	30.92	3.43	100.00	22.87	14.99	3.35	3.45	3.22	1.75	0.34	0.71	3.87	0.23	0.24	5.94	5.84	20.29
F10	8.25	6.17	1.58	12.14	3.67	49.38	98.58	16.48	12.60	6.26	0.29	3.84	36.09	5.49	0.70	3.18	3.30	11.52
F11	28.73	41.83	1.92	28.05	19.77	36.35	40.11	70.92	20.28	18.09	20.54	13.63	15.05	0.82	0.26	4.91	4.17	5.77
F12	11.22	13.03	0.42	99.22	27.04	11.14	65.31	10.46	5.05	5.56	2.24	1.41	11.95	2.72	0.51	16.52	3.73	14.48
F13	14.32	14.20	0.68	5.70	9.52	3.30	51.10	10.88	10.84	7.49	0.95	2.51	13.93	3.53	2.24	94.87	9.83	25.81
F14	84.51	96.31	5.55	13.13	9.63	10.55	47.90	8.36	7.63	4.72	0.49	1.26	15.33	8.02	2.01	13.83	2.26	14.78
F15	73.80	93.13	3.67	34.27	31.27	46.01	84.54	57.33	33.00	38.05	33.42	15.70	58.75	14.30	1.81	24.24	4.27	20.83
F16	8.02	5.44	0.42	12.58	14.47	29.53	66.53	55.92	27.13	55.59	50.22	10.83	48.70	6.71	0.78	14.08	4.03	14.66
F17	16.58	14.76	1.05	4.46	6.48	5.06	97.28	15.06	14.42	11.44	0.01	2.95	24.65	1.88	1.34	9.78	4.47	40.79
F18	12.63	17.24	4.69	6.38	3.95	11.38	54.31	14.94	30.75	14.11	0.88	1.99	28.36	97.62	5.17	23.94	2.84	13.20

F1. Anxiety + Depression
F2. Asthma + Depression + Anxiety
F3. Anxiety + Asthma
F4. Mental + Asthma + Hypertension
F5. Depression + Asthma
F6. Anxiety + Depression + SMI
F7. Hypertension + Depression + Anxiety
F8. Mental + Cancer + Diabetes
F9. Asthma-predominant Respiratory + Mental
F10. Cardiometabolic + Renal
F11. CHD-predominant Cardiovascular + Diabetes + Mental
F12. Asthma-predominant Respiratory + Hypertension
F13. Osteoporosis-predominant Musculoskeletal + Hypertension + Cancer
F14. Mental + Physical Long-term Conditions
F15. Mental + Cardiovascular + Cardiometabolic + Renal + Respiratory + Musculoskeletal (Complex)
F16. Cardiovascular + Cardiometabolic + Renal (Complex)
F17. Hypertension + Cancer + Renal
F18. Dementia-predominant Neurological + Cardiovascular + Musculoskeletal

Figure S5: Condition prevalence for each multimorbidity profile. a, Males. **b,** Females. Condition abbreviations: anxiety (Anx), depression (Dep), serious mental illness (SMI), asthma (Ast), chronic obstructive pulmonary disease (COPD), diabetes (Diab), hypertension (Hyp), coronary heart disease (CHD), stroke or transient ischaemic attack (Stroke), atrial fibrillation (AF), heart failure (HF), peripheral arterial disease (PAD), chronic kidney disease (CKD), osteoporosis (Ost), rheumatoid arthritis (RA), cancer excluding non-melanoma skin cancers (Can).



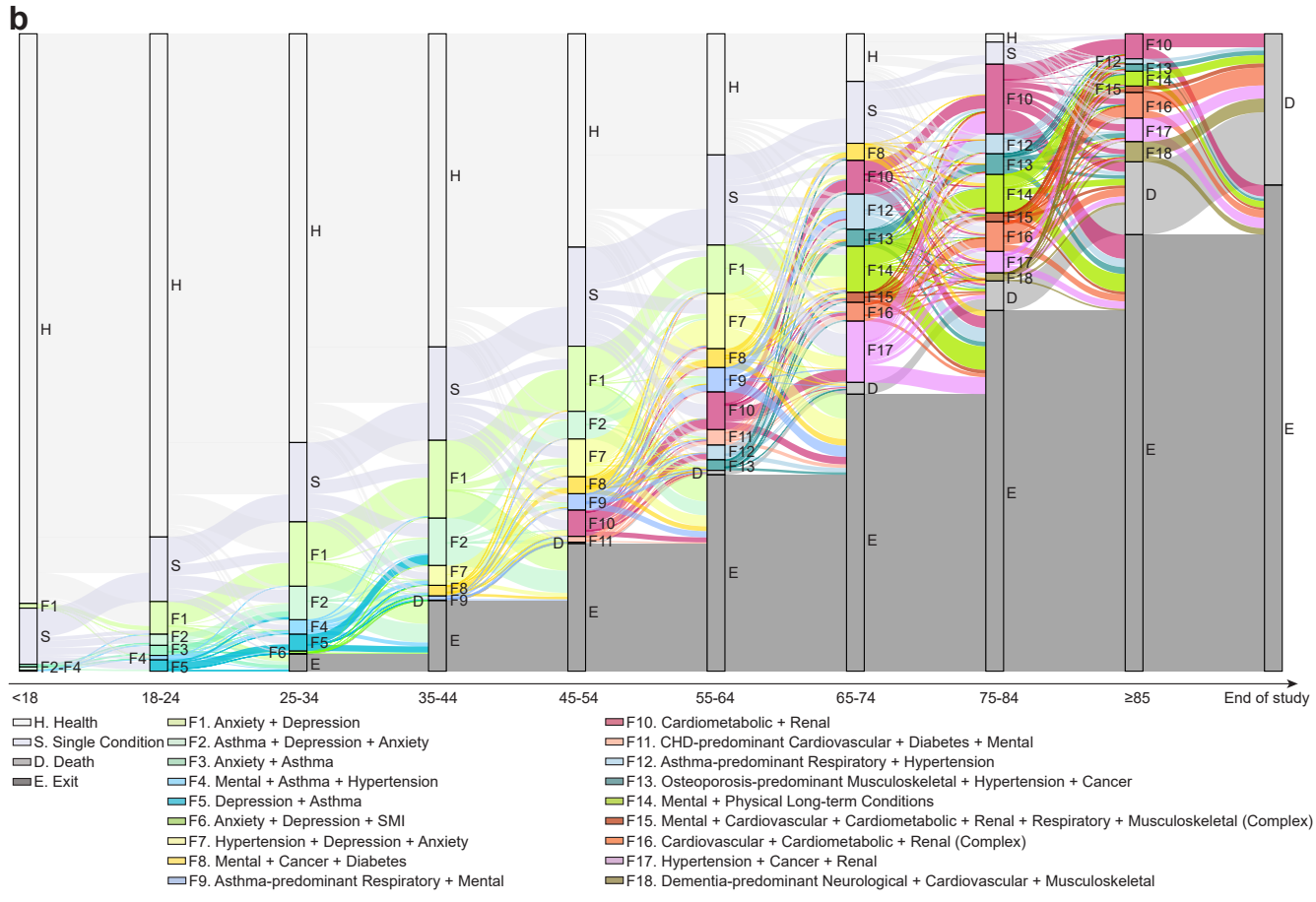


Figure S6: The Complete multimorbidity trajectories over the life course. a, Males. **b,** Females. The Sankey diagrams illustrate transitions of the 3.3 million individuals in the primary study cohort between multimorbidity profiles across different age bands, including transitions from individuals with no or single conditions into multimorbidity profiles. The colour coding follows the same scheme as in Fig. 3.

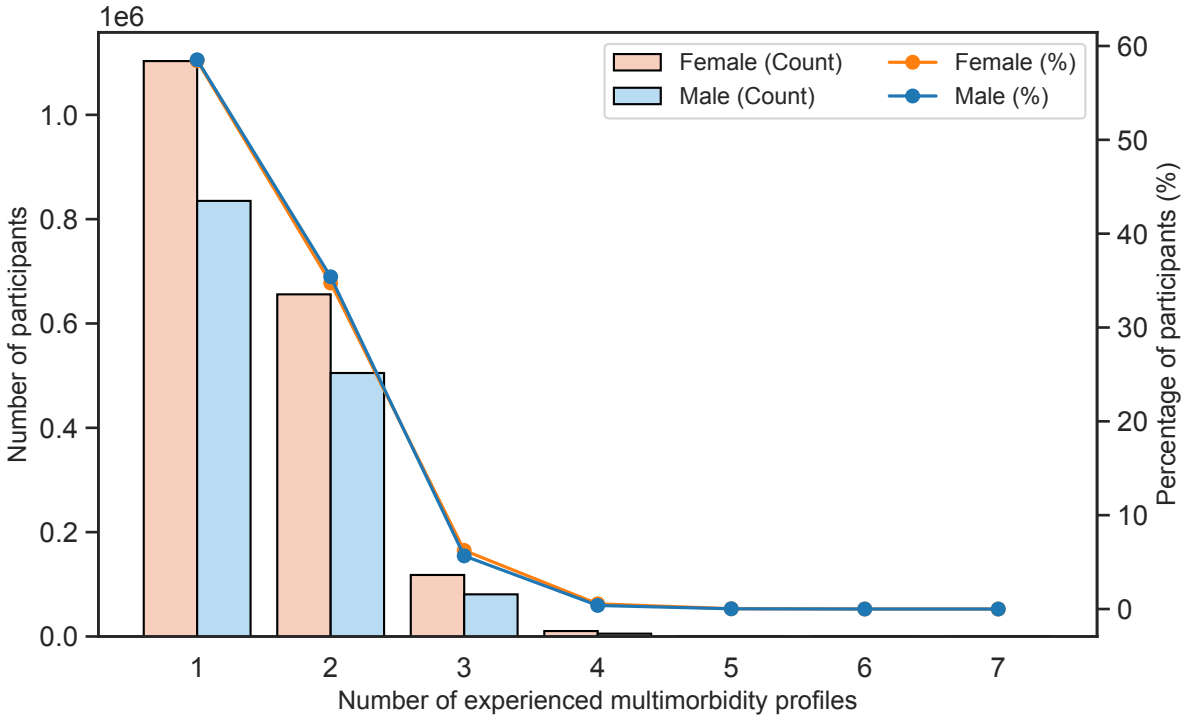


Figure S7: Distribution of Individuals by Number of Experienced Multimorbidity Profiles. This figure illustrates the distribution of individuals based on the number of multimorbidity profiles experienced, derived from the multimorbidity trajectories shown in Fig. 3. The bars represent the number of individuals in each group, stratified by sex, whereas the overlaid lines depict the corresponding percentages of the 3.3 million primary study cohort.

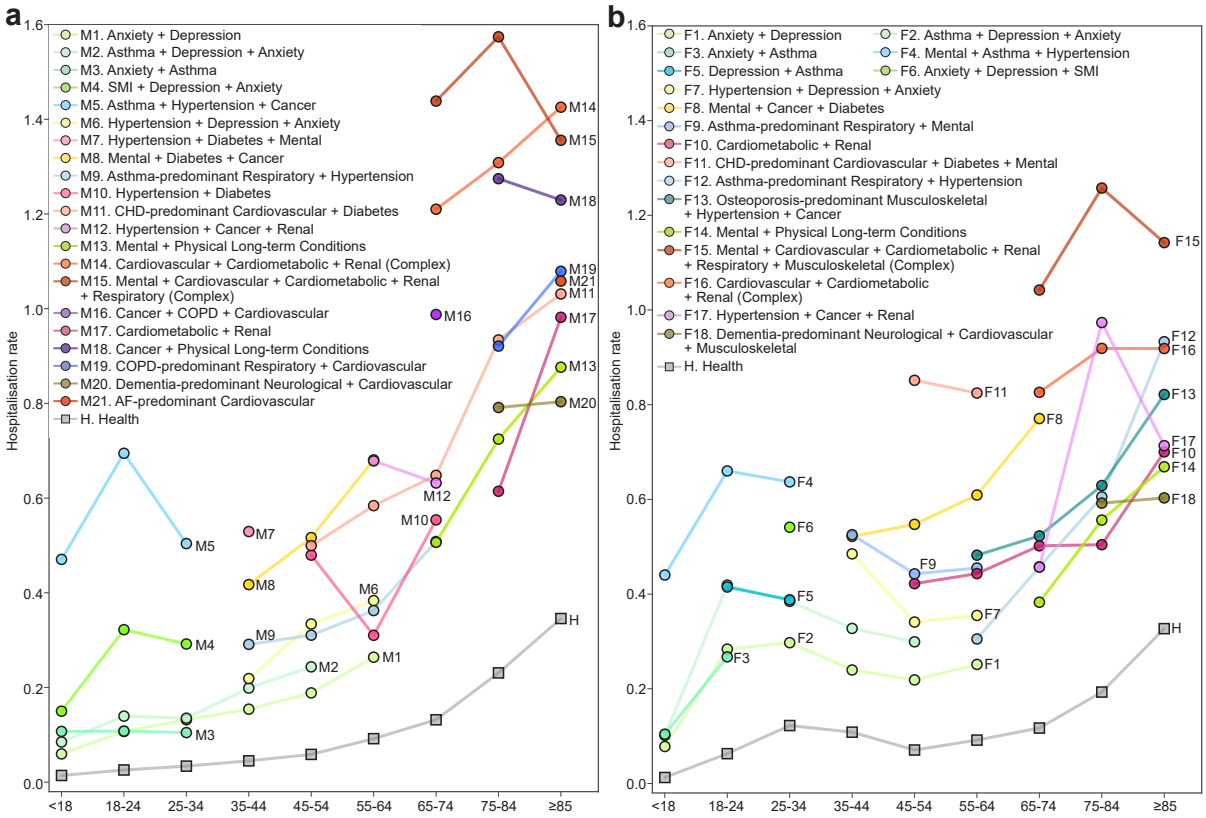


Figure S8: Multimorbidity burden in terms of hospitalisation prevalence over the life course. a, b, Hospitalisation prevalence across multimorbidity profiles and age bands in males and females, respectively. Each line represents a multimorbidity profile, with values calculated within profile-specific cohorts and age bands. Hospitalisation prevalence was defined as the proportion of individuals experiencing at least one hospitalisation within the corresponding profile and age band. The healthy cohort is shown in grey for comparison. The colour coding follows the same scheme as in Fig. 3.

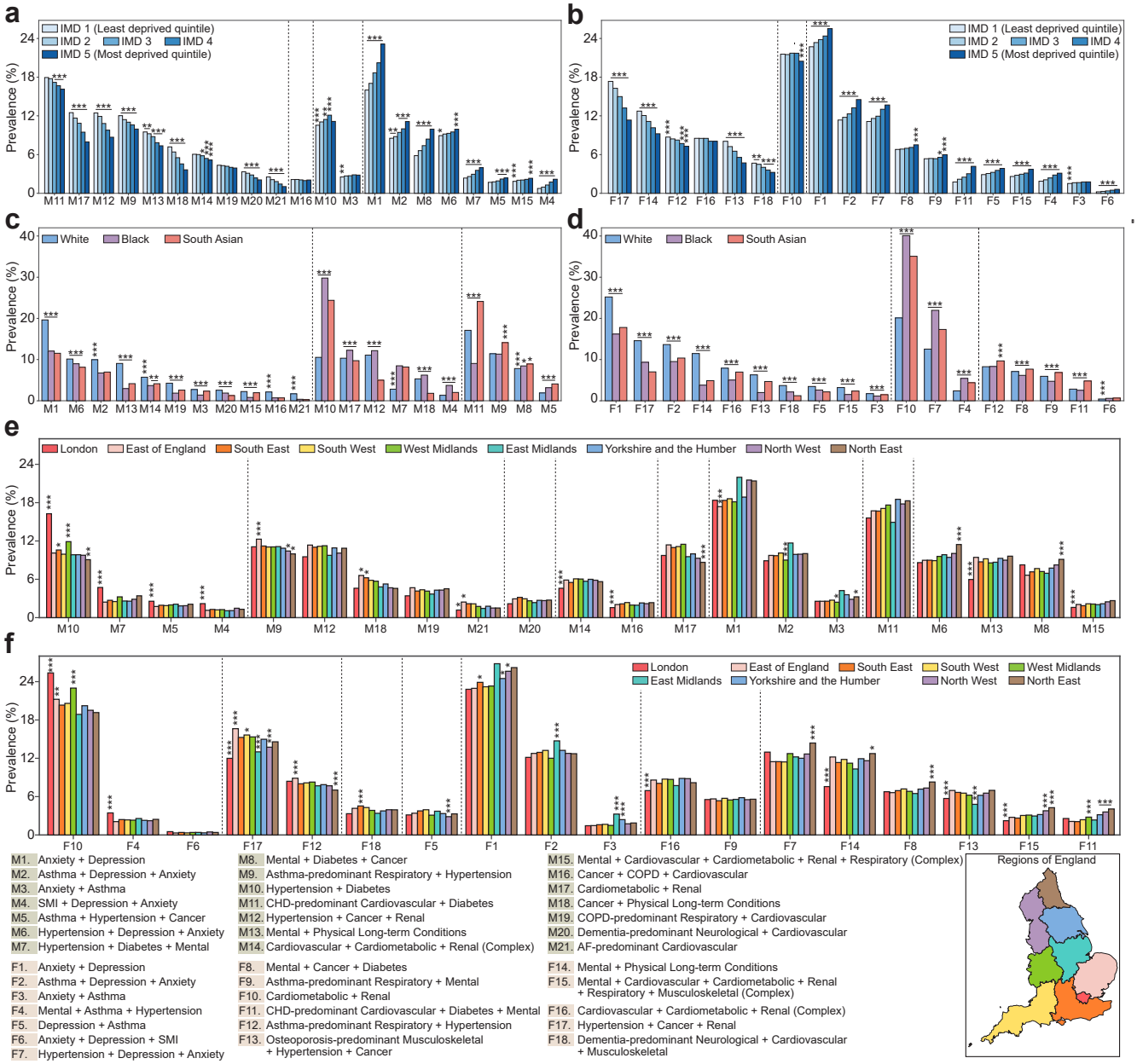


Figure S9: Association between multimorbidity and social factors. a, b, Prevalence of multimorbidity profiles across IMD quintiles, from least deprived (IMD 1) to most deprived (IMD 5), for males and females, respectively. For each profile, the prevalence across IMD quintiles is shown. Profiles (i.e., sets of five bars) are sorted according to the IMD quintile with the highest prevalence within each profile. If multiple profiles share the same leading IMD quintile, they are further ordered by descending prevalence within that quintile. Vertical dashed lines separate profiles by the leading IMD quintile. **c, d,** Prevalence of multimorbidity profiles across ethnic groups (White, Black, and South Asian), for males and females, respectively. For each profile, the prevalence across ethnic groups is shown. Profiles (i.e., sets of three bars) are sorted according to the ethnic group with the highest prevalence within each profile. If multiple profiles share the same leading ethnic group, they are further ordered by descending prevalence within that group. Vertical dashed lines separate profiles by the leading ethnic group. **e, f,** Prevalence of multimorbidity profiles across nine regions of England, for males and females, respectively. For each profile, the prevalence across regions is shown. Profiles (i.e., sets of nine bars) are sorted according to the region with the highest prevalence within each profile. If multiple profiles share the same leading region, they are further ordered by descending prevalence within that region. Vertical dashed lines separate profiles by the leading region. A map of the regions is provided for reference. In all panels, each bar represents the prevalence of a profile within a specific group. For each bar, statistical significance was assessed using pairwise two-sided Z-tests with Bonferroni correction, comparing it to the other groups within the same profile. The largest (i.e., least significant) p-value among the comparisons is shown. Asterisks indicate significance levels (*p-value < 0.05, **p-value < 0.01, ***p-value < 0.001). Error bars for 95% confidence intervals are not shown, as the large sample size yields very narrow intervals with minimal impact on interpretability. IMD: Index of Multiple Deprivation.

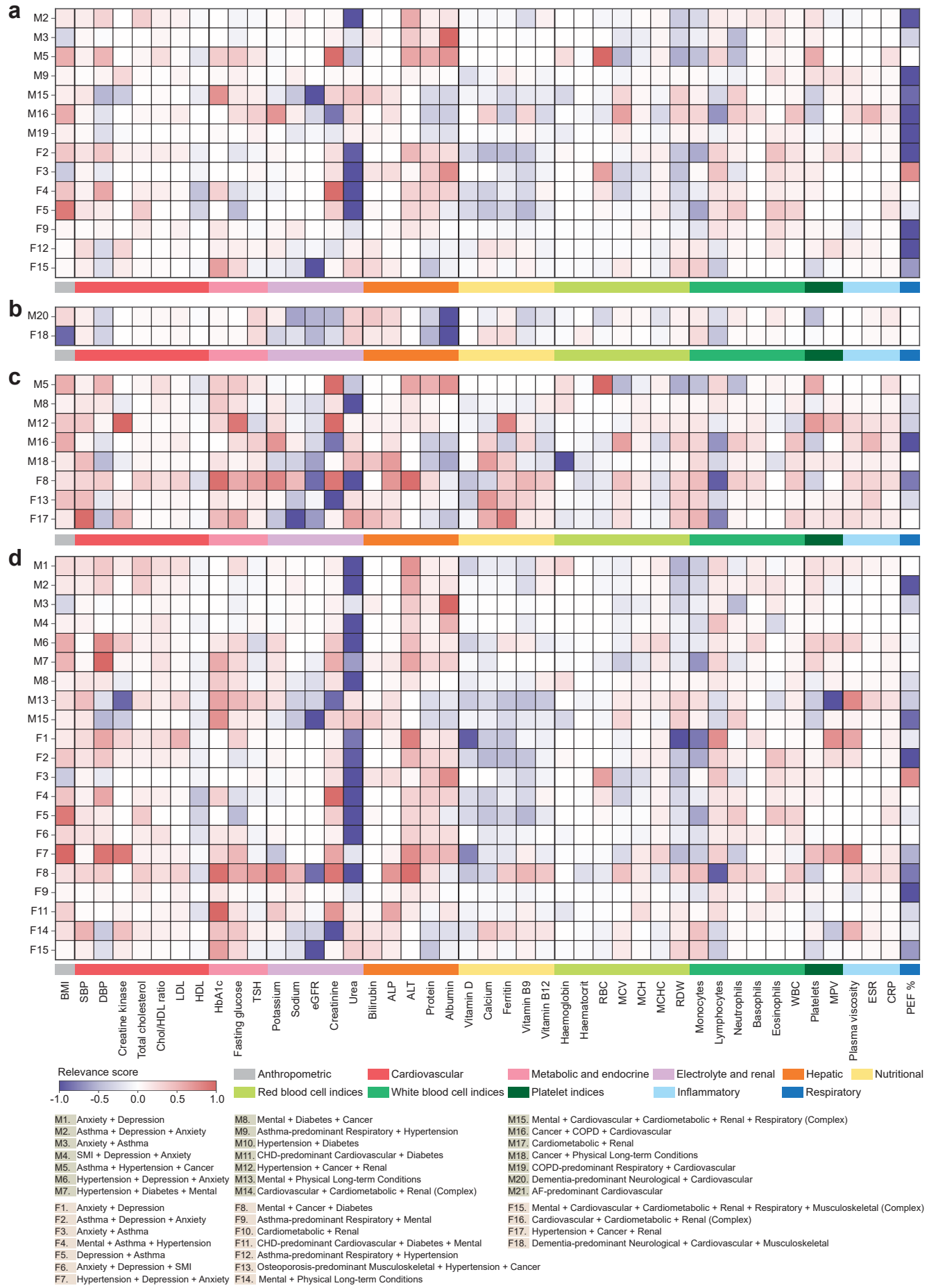


Figure S10: Relevance of clinical markers across specific groups of multimorbidity profiles (Part I). a, Respiratory-related profiles, **b** Neurological-related profiles, **c,** Cancer-related profiles, **d,** Mental health-related profiles. The heatmaps show the clinical relevance of each marker (columns) to each multimorbidity profile (rows), using identical methodology to Fig. 6. Profiles appear in multiple panels when spanning disease systems.

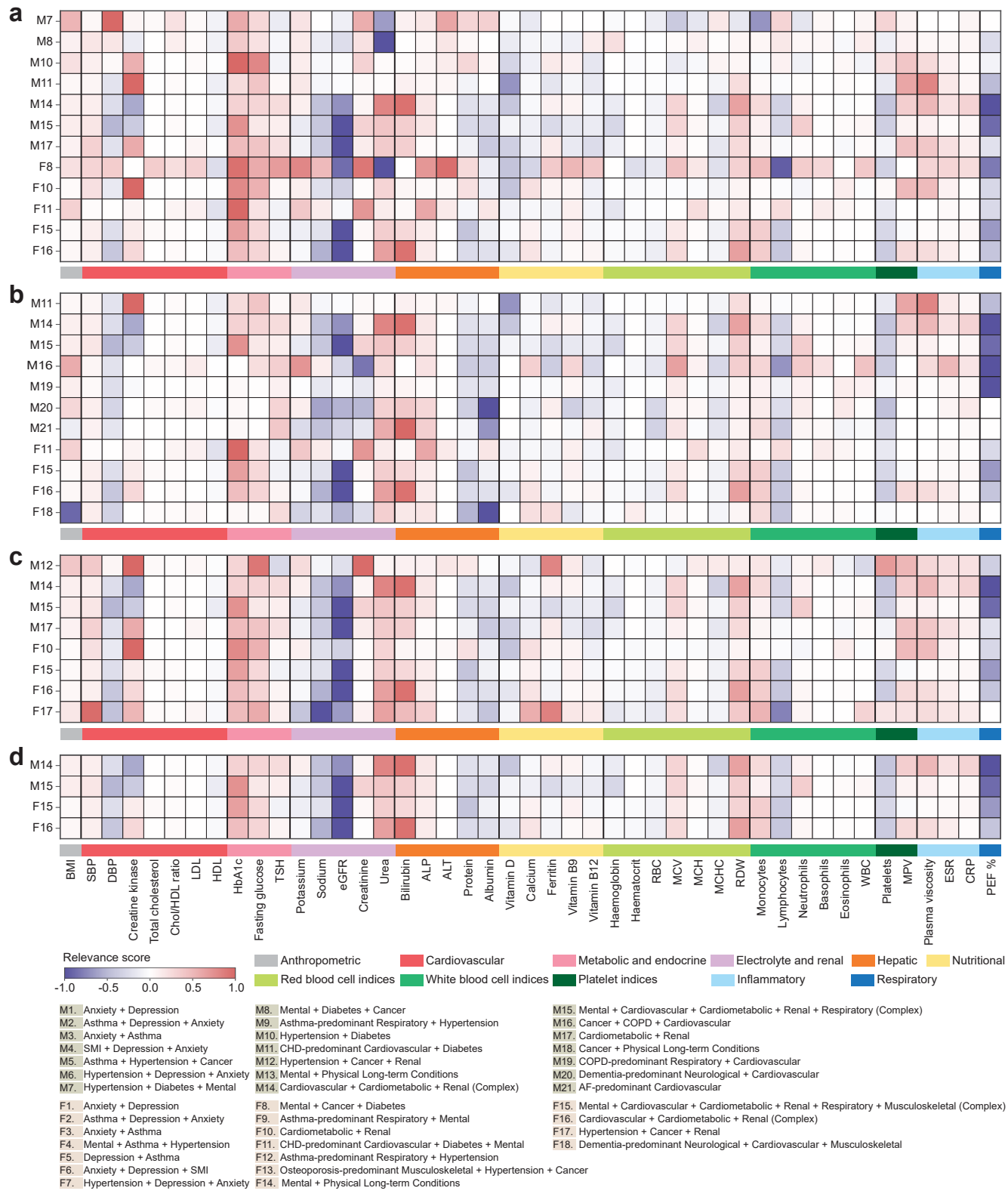


Figure S11: Relevance of clinical markers across specific groups of multimorbidity profiles (Part II). a, Cardiometabolic-related profiles, **b,** Cardiovascular-related profiles, **c** Renal-related profiles, **d,** Complex profiles. The heatmaps show the clinical relevance of each marker (columns) to each multimorbidity profile (rows), using identical methodology to Fig. 6. Profiles appear in multiple panels when spanning disease systems.

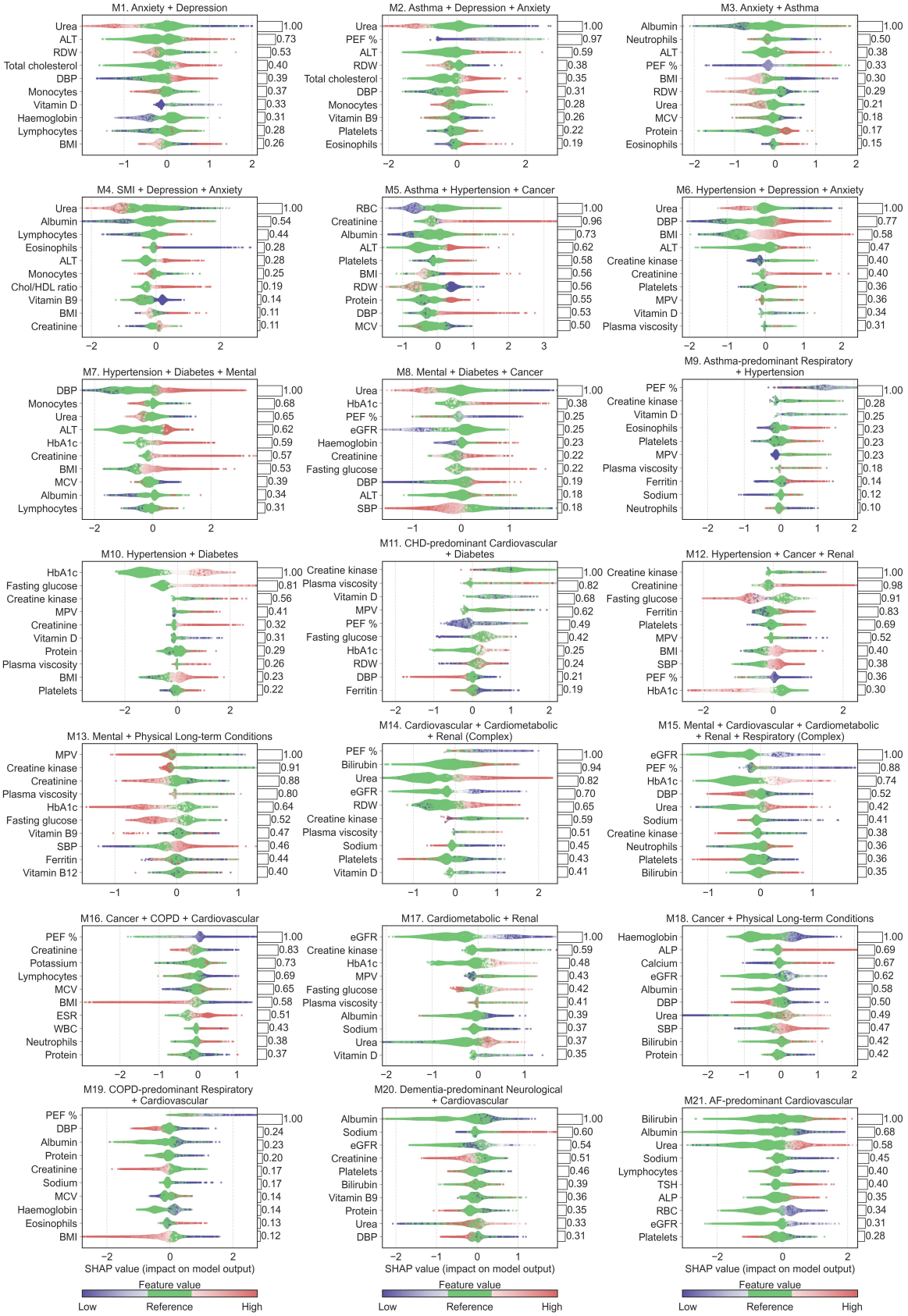


Figure S12: Beeswarm plots for each multimorbidity profile in males. In the beeswarm plot, each dot represents an individual, with its horizontal position (SHAP value) indicating the impact of a given marker on the model's prediction. Dots are coloured according to marker values relative to a reference range, with green indicating normal values. When multiple dots share the same x position, they accumulate vertically to reflect density. The bar plots on the right display the relevance scores of corresponding markers based on the positive SHAP contributions of abnormally high or low marker values, which correspond to the relevance scores in Fig. 6a. Top ten important markers for each profile are shown.

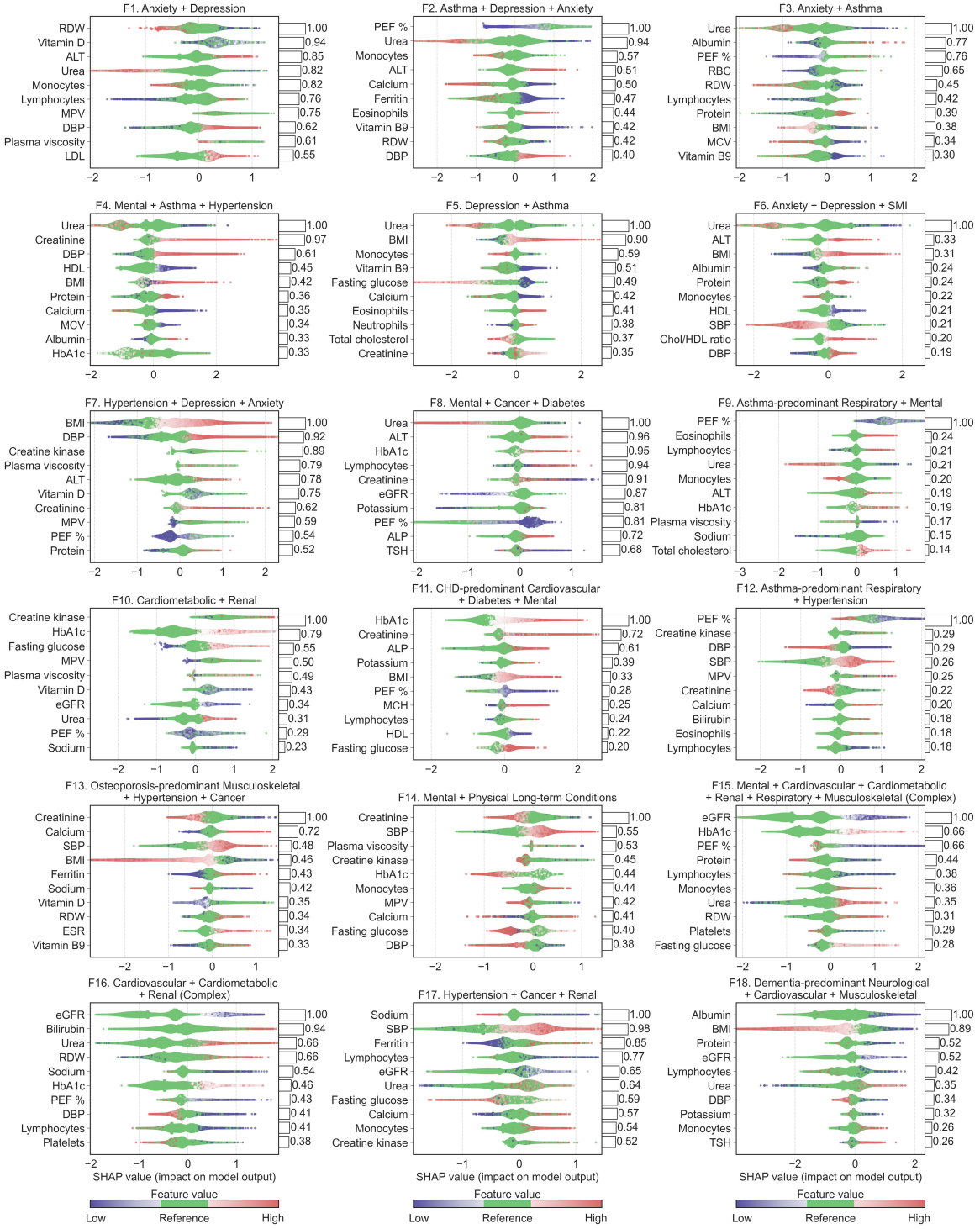


Figure S13: Beeswarm plots for each multimorbidity profile in females. In the beeswarm plot, each dot represents an individual, with its horizontal position (SHAP value) indicating the impact of a given marker on the model's prediction. Dots are coloured according to marker values relative to a reference range, with green indicating normal values. When multiple dots share the same x position, they accumulate vertically to reflect density. The bar plots on the right display the relevance scores of corresponding markers based on the positive SHAP contributions of abnormally high or low marker values, which correspond to the relevance scores in Fig. 6b. Top ten important markers for each profile are shown.

Supplementary Tables

Table S1: Characteristics of the study population by socioeconomic deprivation, ethnicity, and geographic regions.

	Socioeconomic deprivation, n (%)					
Sex	IMD 1 (least deprived)	IMD 2	IMD 3	IMD 4	IMD 5 (most deprived)	Unknown
Male	264,798 (18.56)	277,660 (19.46)	274,229 (19.22)	298,320 (20.91)	310,289 (21.75)	1,407 (0.10)
Female	353,772 (18.74)	368,195 (19.50)	364,930 (19.33)	393,674 (20.85)	405,635 (21.49)	1,743 (0.09)
	Ethnicity, n (%)					
Sex	White	Black	South Asian	Mixed	Other	Unknown
Male	1,048,953 (73.52)	39,141 (2.74)	53,293 (3.74)	12,008 (0.84)	24,563 (1.72)	248,745 (17.44)
Female	1,409,930 (74.68)	50,483 (2.67)	56,264 (2.98)	17,913 (0.95)	27,168 (1.44)	326,191 (17.28)
	Geographic regions, n (%)					
Sex	London	East of England	South East	South West	West Midlands	East Midlands
Male	217,744 (15.26)	58,483 (4.10)	243,261 (17.05)	203,710 (14.28)	244,212 (17.12)	33,069 (2.32)
Female	276,972 (14.67)	78,770 (4.17)	333,153 (17.65)	270,105 (14.31)	320,847 (16.99)	44,590 (2.36)
Sex	Yorkshire and the Humber	North West	North East	Unknown		
Male	62,332 (4.37)	281,880 (19.76)	62,305 (4.37)	19,707 (1.38)		
Female	81,878 (4.34)	372,362 (19.72)	82,780 (4.39)	26,492 (1.40)		

IMD, index of multiple deprivation.

Table S2: Units and reference ranges of clinical markers used in the study.

Clinical marker	Unit	Reference range[a]
ALP (Alkaline phosphatase)	U/L	30-130
ALT (Alanine aminotransferase)	U/L	0-50/0-35
Albumin	g/L	35-50
BMI (Body mass index)	kg/m^2	18.5-24.9
Basophils	$\times 10^9$/L	0-0.1
Bilirubin	umol/L	0-21
CRP (C-reactive protein)	mg/L	0-5
Calcium	mmol/L	2.2-2.6
Chol/HDL ratio (Total cholesterol:HDL cholesterol ratio)	ratio	0.0-4.0
Creatinine	umol/L	59-104/45-84
Creatine kinase	U/L	40-320/25-200
DBP (Diastolic blood pressure)	mmHg	60-80
ESR (Erythrocyte sedimentation rate)	mm/hr	0-14/0-20
Eosinophils	$\times 10^9$/L	0.1-0.4/0.0-0.5
eGFR (Estimated glomerular filtration rate)	$mL/min/1.73m^2$	$\geq$60
Fasting glucose	mmol/L	3.9-5.4
Ferritin	ug/L	30-340/30-310
HDL (High-density lipoprotein cholesterol)	mmol/L	$\geq$ 1.0/ $\geq$ 1.2
Haematocrit	ratio	0.40-0.54/0.37-0.47
Haemoglobin	g/L	130-180/115-165
HbA1c	ug/L	0-42
LDL (Low-density lipoprotein cholesterol)	mmol/L	0.0-3.0
Lymphocytes	$\times 10^9$/L	1.0-4.0
MCH (Mean corpuscular haemoglobin)	pg	27-32
MCHC (Mean corpuscular haemoglobin concentration)	g/L	315-345
MCV (Mean corpuscular volume)	fL	83-101
MPV (Mean platelet volume)	fL	7.2-11.7
Monocytes	$\times 10^9$/L	0.2-0.8
Neutrophils	$\times 10^9$/L	1.8-7.5
PEF % (Peak expiratory flow percentage)	%	80-120
Platelets	$\times 10^9$/L	140-400
Plasma viscosity	mPA·s	1.50-1.72
Potassium	mmol/L	3.5-5.3
Protein	g/L	60-80
RBC (Red blood cell count)	$\times 10^{12}$/L	4.5-6.5/3.5-5.8
RDW (Red cell distribution width)	%	11.8-14.5/12.2-16.1
SBP (Systolic blood pressure)	mmHg	90-120
Sodium	mmol/L	133-146
TSH (Thyroid stimulating hormone)	mU/L	0.4-4.0
Total Chol. (Total cholesterol)	mmol/L	0.0-5.0
Urea	mmol/L	2.5-7.8
Vitamin B9	ng/mL	3-20
Vitamin B12	pg/mL	180-1000
Vitamin D	nmol/L	$\geq$50
WBC (White blood cell count)	$\times 10^9$/L	3.6-11.0

[a] Reference ranges for clinical markers are provided as male/female if there is a sex difference; otherwise, a single range is reported.

Table S3: Population distribution, prevalence, mean number of conditions among multimorbidity profiles in males.

Profile	<18	18–24	25–34	35–44	45–54	55–64	65–74	75–84	≥85
M1	5,581 (0.39) 2.00 (0.07)	44,091 (3.09) 2.01 (0.10)	136,314 (9.74) 2.28 (0.47)	127,769 (9.78) 2.09 (0.29)	107,462 (9.05) 2.17 (0.37)	72,265 (7.05) 2.43 (0.59)			
M2	4,694 (0.33) 2.32 (0.47)	34,927 (2.45) 2.49 (0.50)	28,506 (2.04) 2.01 (0.08)	85,303 (6.53) 2.55 (0.65)	54,913 (4.62) 2.63 (0.71)				
M3	5,904 (0.41) 2.00 (0.00)	21,471 (1.50) 2.00 (0.00)	28,737 (2.05) 2.01 (0.15)						
M4	835 (0.06) 2.26 (0.51)	8,314 (0.58) 2.40 (0.60)	18,723 (1.34) 2.50 (0.66)						
M5	2,744 (0.19) 2.05 (0.24)	7,364 (0.52) 2.16 (0.45)	26,717 (1.91) 2.23 (0.55)						
M6				7,591 (0.58) 3.06 (0.24)	79,206 (6.67) 3.01 (0.97)	95,803 (9.34) 3.16 (1.06)			
M7				44,577 (3.41) 2.44 (0.84)					
M8				28,949 (2.22) 2.20 (0.58)	42,408 (3.57) 2.42 (0.89)	73,575 (7.18) 2.91 (1.35)			
M9				27,402 (2.10) 2.19 (0.46)	48,936 (4.12) 2.32 (0.64)	87,750 (8.56) 2.57 (0.89)	76,176 (9.47) 2.93 (1.05)		
M10					58,582 (4.93) 2.18 (0.49)	64,479 (6.29) 2.31 (0.50)	97,239 (12.08) 2.82 (0.91)		
M11					52,434 (4.41) 2.68 (1.00)	110,503 (10.78) 2.97 (1.15)	137,599 (17.10) 3.08 (1.06)	102,693 (19.74) 3.38 (1.13)	20,194 (9.52) 3.26 (1.21)
M12						65,339 (6.37) 2.45 (0.83)	117,636 (14.62) 2.50 (0.78)		
M13							100,473 (12.48) 3.13 (1.18)	48,466 (9.32) 3.59 (1.37)	12,882 (6.07) 3.99 (1.42)
M14							35,033 (4.35) 4.57 (1.51)	51,548 (9.91) 4.94 (1.57)	20,132 (9.49) 5.86 (1.34)
M15							16,411 (2.04) 6.61 (1.23)	15,543 (2.99) 7.04 (1.30)	6,610 (3.12) 7.03 (1.34)
M16							29,650 (3.68) 2.79 (1.01)		
M17								120,804 (23.23) 2.90 (1.07)	61,335 (28.92) 3.53 (1.24)
M18								63,259 (12.16) 3.14 (1.04)	26,449 (12.47) 3.10 (0.91)
M19								50,633 (9.73) 3.46 (1.42)	22,208 (10.47) 3.93 (1.52)
M20								27,083 (5.21) 3.48 (1.40)	17,109 (8.07) 3.28 (1.26)
M21									25,150 (11.86) 3.76 (1.28)

Each cell presents the population (prevalence, %), mean number of conditions per individual (SD) for the multimorbidity profile within the corresponding age band.

Table S4: Population distribution, prevalence, mean number of conditions among multimorbidity profiles in females.

Profile	<18	18–24	25–34	35–44	45–54	55–64	65–74	75–84	≥85
F1	13,898 (0.74) 2.01 (0.11)	96,994 (5.14) 2.02 (0.16)	190,841 (10.39) 2.03 (0.16)	230,597 (13.75) 2.12 (0.33)	192,927 (12.81) 2.15 (0.35)	144,093 (11.14) 2.38 (0.53)			
F2	10,154 (0.54) 2.33 (0.47)	32,940 (1.74) 3.00 (0.05)	99,301 (5.41) 2.61 (0.49)	140,380 (8.37) 2.55 (0.61)	81,829 (5.43) 2.76 (0.67)				
F3	7,643 (0.40) 2.00 (0.00)	29,764 (1.58) 2.00 (0.02)	28,737 (2.05) 2.01 (0.15)						
F4	2,866 (0.15) 2.10 (0.34)	13,304 (0.70) 2.30 (0.62)	42,915 (2.34) 2.33 (0.66)						
F5		33,473 (1.77) 2.00 (0.00)	49,762 (2.71) 2.00 (0.00)						
F6			7,717 (0.42) 3.27 (0.45)						
F7				58,681 (3.50) 2.56 (0.88)	111,893 (7.43) 2.99 (0.91)	162,979 (12.60) 3.17 (1.02)			
F8				31,395 (1.87) 2.17 (0.55)	50,357 (3.34) 2.25 (0.63)	55,919 (4.32) 2.39 (0.79)	50,684 (4.91) 2.73 (1.07)		
F9				12,377 (0.74) 2.13 (0.45)	48,465 (3.22) 2.41 (0.83)	72,127 (5.58) 2.74 (1.03)			
F10					77,874 (5.17) 2.26 (0.56)	111,683 (8.64) 2.32 (0.63)	99,840 (9.67) 2.98 (0.94)	206,791 (28.24) 2.95 (1.05)	74,026 (19.52) 3.41 (1.17)
F11					17,024 (1.13) 3.46 (1.51)	45,653 (3.53) 3.81 (1.66)			
F12						43,423 (3.36) 2.49 (0.65)	104,410 (10.11) 2.86 (1.00)	58,643 (8.01) 3.29 (1.28)	15,773 (4.16) 4.54 (1.69)
F13						31,417 (2.43) 2.61 (0.91)	50,240 (4.87) 2.72 (0.93)	61,264 (8.37) 2.99 (1.02)	21,188 (5.59) 2.85 (1.06)
F14							136,349 (13.21) 3.16 (0.98)	113,759 (15.54) 3.61 (1.33)	43,948 (11.59) 4.03 (1.40)
F15							29,669 (2.87) 6.14 (1.19)	26,363 (3.60) 7.05 (1.25)	19,132 (5.04) 7.02 (1.33)
F16							55,508 (5.38) 3.88 (1.46)	87,739 (11.98) 4.26 (1.57)	75,926 (20.02) 4.53 (1.48)
F17							181,436 (17.57) 2.47 (0.79)	63,586 (8.69) 3.06 (0.95)	69,518 (18.33) 3.08 (1.12)
F18								23,912 (3.27) 3.44 (1.35)	59,797 (15.76) 3.45 (1.19)

Each cell presents the population (prevalence, %), mean number of conditions per individual (SD) for the multimorbidity profile within the corresponding age band.

Table S5: Pairwise statistical comparisons of IMD quintiles within each multimorbidity profile.

Profile	**IMD pairwise comparisons** (p-value)									
Males	(1, 2)	(1, 3)	(1, 4)	(1, 5)	(2, 3)	(2, 4)	(2, 5)	(3, 4)	(3, 5)	(4, 5)
M1	6.22e-24	1.29e-146	0.00e+00	0.00e+00	2.82e-55	2.96e-209	0.00e+00	1.31e-48	0.00e+00	2.84e-166
M2	7.68e-03	2.66e-30	3.10e-78	5.05e-234	4.86e-16	3.46e-54	2.30e-193	1.47e-11	9.00e-98	1.94e-45
M3	2.03e-03	5.68e-05	1.06e-13	5.32e-11	1.00e+00	5.93e-04	1.72e-02	1.67e-02	2.39e-01	1.00e+00
M4	6.73e-16	1.33e-84	9.54e-244	0.00e+00	4.88e-30	5.79e-147	3.87e-302	1.28e-45	9.02e-147	4.57e-32
M5	4.40e-01	1.80e-08	5.52e-42	1.05e-70	4.89e-04	1.46e-31	2.10e-57	1.02e-13	7.48e-32	2.06e-04
M6	1.88e-02	7.13e-05	2.10e-12	1.91e-36	1.00e+00	2.26e-04	2.12e-21	5.24e-02	1.46e-15	2.56e-07
M7	1.92e-07	5.45e-40	2.45e-151	3.35e-258	2.28e-14	6.94e-97	1.81e-187	2.57e-37	7.12e-99	3.28e-16
M8	1.94e-31	2.29e-115	1.30e-302	0.00e+00	1.54e-28	6.59e-145	0.00e+00	6.78e-45	9.34e-260	8.82e-95
M9	2.76e-11	3.07e-30	9.87e-63	1.14e-138	2.45e-05	6.83e-22	7.95e-73	5.17e-06	3.48e-39	5.64e-16
M10	1.24e-08	8.07e-25	2.66e-74	7.54e-12	6.57e-05	4.11e-34	1.00e+00	9.62e-14	2.29e-03	6.20e-31
M11	8.47e-01	3.93e-12	2.04e-35	4.06e-73	2.09e-07	4.83e-27	3.53e-61	1.63e-06	2.69e-26	1.57e-07
M12	1.32e-08	6.04e-77	7.65e-223	0.00e+00	1.84e-36	1.14e-148	0.00e+00	2.43e-37	2.66e-165	6.39e-48
M13	4.11e-03	2.13e-19	1.18e-108	7.32e-188	6.59e-08	2.26e-78	1.13e-147	4.64e-37	2.75e-87	2.02e-11
M14	1.00e+00	2.90e-03	3.06e-24	6.35e-48	2.53e-02	7.48e-22	8.39e-45	1.64e-10	2.09e-27	1.43e-04
M15	3.67e-05	4.01e-07	1.96e-15	8.54e-35	1.00e+00	3.47e-03	3.09e-14	7.70e-02	3.54e-11	1.23e-04
M16	1.00e+00	1.00e+00	2.41e-04	6.61e-01	1.00e+00	4.70e-05	3.00e-01	3.58e-02	1.00e+00	1.25e-01
M17	2.42e-20	3.11e-77	1.40e-287	0.00e+00	6.60e-20	5.85e-159	0.00e+00	3.53e-66	0.00e+00	1.03e-95
M18	8.45e-30	2.49e-138	0.00e+00	0.00e+00	2.41e-42	1.87e-208	0.00e+00	4.96e-62	1.93e-260	2.28e-71
M19	1.00e+00	3.71e-02	1.17e-08	2.97e-15	6.58e-01	4.73e-06	9.23e-12	1.65e-02	1.73e-06	3.65e-01
M20	1.34e-05	1.64e-25	2.19e-104	1.00e-191	3.50e-08	2.52e-64	5.78e-136	3.49e-27	1.12e-77	5.49e-14
M21	8.15e-23	3.39e-70	1.04e-190	0.00e+00	2.17e-14	3.28e-84	2.12e-241	2.31e-29	1.68e-138	6.48e-43
Females	(1, 2)	(1, 3)	(1, 4)	(1, 5)	(2, 3)	(2, 4)	(2, 5)	(3, 4)	(3, 5)	(4, 5)
F1	6.86e-10	8.16e-28	4.29e-63	1.92e-177	2.91e-05	2.74e-24	6.67e-107	1.97e-07	1.47e-65	3.12e-31
F2	2.90e-07	6.36e-35	3.24e-135	0.00e+00	1.76e-11	3.49e-83	5.91e-279	1.85e-33	1.31e-177	1.75e-60
F3	4.87e-04	3.31e-05	7.65e-15	2.10e-16	1.00e+00	6.64e-04	1.09e-04	7.61e-03	1.63e-03	1.00e+00
F4	1.48e-10	1.16e-49	6.16e-162	1.25e-259	6.91e-16	1.84e-94	1.58e-173	1.30e-33	2.01e-85	3.80e-13
F5	2.30e-04	1.16e-16	8.18e-57	1.45e-115	1.18e-04	1.37e-31	1.15e-78	1.17e-12	4.79e-46	1.22e-11
F6	1.15e-06	1.29e-25	1.41e-70	4.79e-140	3.58e-07	3.01e-37	8.13e-94	1.33e-12	1.69e-51	4.92e-15
F7	2.70e-09	1.17e-26	1.88e-137	1.17e-246	3.37e-05	2.26e-78	1.31e-165	3.45e-44	3.53e-113	3.23e-17
F8	1.00e+00	2.58e-02	8.62e-07	1.21e-32	3.43e-01	7.97e-05	1.78e-28	2.12e-01	1.04e-18	5.04e-11
F9	1.00e+00	1.00e+00	3.57e-04	1.28e-31	1.00e+00	1.05e-02	9.88e-28	8.05e-04	5.52e-31	1.59e-14
F10	1.00e+00	1.00e+00	1.00e+00	5.98e-30	2.54e-01	2.89e-01	1.84e-27	1.00e+00	1.55e-39	1.68e-40
F11	2.93e-38	2.84e-106	7.52e-282	0.00e+00	1.00e-18	9.96e-119	0.00e+00	6.08e-44	0.00e+00	1.23e-163
F12	1.50e-04	1.99e-11	1.05e-54	3.69e-115	6.08e-02	2.88e-29	1.19e-76	6.93e-17	3.15e-55	4.16e-12
F13	4.26e-38	1.91e-137	0.00e+00	0.00e+00	7.61e-33	1.62e-195	0.00e+00	1.06e-67	3.10e-262	2.73e-66
F14	1.37e-17	7.76e-96	8.93e-267	0.00e+00	2.32e-33	5.17e-151	0.00e+00	3.88e-42	7.39e-167	5.16e-44
F15	4.70e-06	1.50e-18	2.13e-41	6.53e-163	4.82e-04	5.20e-17	4.52e-111	6.62e-05	4.88e-74	2.74e-44
F16	1.00e+00	1.00e+00	6.55e-11	7.00e-12	1.00e+00	1.03e-10	1.10e-11	8.29e-11	8.79e-12	1.00e+00
F17	5.13e-33	5.30e-161	0.00e+00	0.00e+00	8.40e-51	4.41e-309	0.00e+00	7.92e-108	0.00e+00	2.53e-141

The statistical significance was assessed using pairwise two-sided Z-tests with Bonferroni correction. IMD: Index of Multiple Deprivation.

Table S6: Pairwise statistical comparisons of ethnic groups within each multimorbidity profile.

Profile	**Ethnicity pairwise comparisons** (p-value)		
Males	(White, Black)	(White, South Asian)	(Black, South Asian)
M1	2.06e-302	0.00e+00	3.88e-02
M2	1.08e-97	1.07e-113	5.45e-01
M3	2.50e-58	1.43e-07	9.63e-25
M4	0.00e+00	1.28e-39	1.36e-55
M5	3.45e-71	1.37e-270	9.03e-13
M6	4.19e-13	5.18e-50	1.52e-05
M7	0.00e+00	0.00e+00	3.33e-01
M8	1.33e-05	4.84e-20	3.44e-02
M9	1.00e+00	6.40e-80	2.48e-35
M10	0.00e+00	0.00e+00	8.70e-75
M11	0.00e+00	0.00e+00	0.00e+00
M12	6.74e-11	0.00e+00	0.00e+00
M13	0.00e+00	0.00e+00	2.64e-21
M14	6.46e-65	3.09e-53	1.63e-03
M15	4.63e-80	4.01e-05	5.31e-46
M16	5.66e-85	5.90e-115	1.00e+00
M17	7.61e-34	2.67e-05	9.90e-34
M18	9.43e-15	4.11e-279	9.02e-272
M19	1.15e-120	1.98e-79	6.53e-13
M20	3.89e-17	1.27e-77	3.30e-13
M21	2.68e-91	1.03e-138	1.01e-01
Females	(White, Black)	(White, South Asian)	(Black, South Asian)
F1	0.00e+00	0.00e+00	1.34e-11
F2	4.37e-156	2.18e-109	1.02e-05
F3	1.14e-23	1.12e-05	4.21e-06
F4	0.00e+00	1.52e-193	4.29e-15
F5	4.75e-25	9.86e-63	4.40e-06
F6	1.77e-07	9.94e-16	4.43e-01
F7	0.00e+00	7.35e-243	6.01e-81
F8	2.33e-15	6.75e-07	1.26e-21
F9	4.41e-29	5.63e-19	8.25e-49
F10	0.00e+00	0.00e+00	1.40e-63
F11	4.59e-04	1.99e-164	1.17e-83
F12	1.00e+00	6.09e-32	3.02e-14
F13	0.00e+00	7.77e-54	1.41e-127
F14	0.00e+00	0.00e+00	4.40e-18
F15	2.90e-100	3.50e-29	3.26e-22
F16	3.95e-124	1.08e-15	7.98e-40
F17	6.45e-238	0.00e+00	1.65e-43
F18	3.56e-75	1.95e-208	9.54e-31

The statistical significance was assessed using pairwise two-sided Z-tests with Bonferroni correction.

Table S7: Maximum p-values from pairwise comparisons across regions within each multimorbidity profile.

Profile	**Maximum p-values from pairwise comparisons between regions** (p-value)								
Males	London	East of England	South East	South West	West Midlands	East Midlands	Yorkshire and the Humber	North West	North East
M1	1.00e+00	6.00e-04	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00
M2	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	0.00e+00	1.00e+00	1.00e+00	1.00e+00
M3	1.00e+00	1.00e+00	1.00e+00	7.90e-01	1.00e+00	0.00e+00	4.79e-02	1.66e-01	4.79e-02
M4	0.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	7.37e-02	1.00e+00
M5	0.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00
M6	1.87e-01	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	0.00e+00
M7	0.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.61e-01	1.00e+00
M8	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	0.00e+00
M9	1.00e+00	0.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	4.28e-02	3.09e-02
M10	0.00e+00	1.00e+00	2.42e-02	1.00e+00	0.00e+00	1.00e+00	1.00e+00	1.00e+00	3.60e-03
M11	5.86e-02	1.00e+00	1.00e+00	1.00e+00	1.00e+00	5.86e-02	1.00e+00	1.00e+00	1.00e+00
M12	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00
M13	0.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00
M14	0.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00
M15	0.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	2.88e-01	2.88e-01
M16	0.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00
M17	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	2.00e-04
M18	1.00e+00	4.06e-02	4.06e-02	1.00e+00	1.00e+00	1.00e+00	7.88e-02	1.00e+00	1.00e+00
M19	3.81e-01	1.00e+00	1.00e+00	1.00e+00	1.00e+00	3.81e-01	1.00e+00	1.00e+00	1.00e+00
M20	1.00e+00	1.00e+00	1.25e-01	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00
M21	2.70e-03	4.00e-03	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00
Females	London	East of England	South East	South West	West Midlands	East Midlands	Yorkshire and the Humber	North West	North East
F1	1.00e+00	1.00e+00	1.11e-02	1.00e+00	1.00e+00	6.79e-01	1.11e-02	2.44e-02	6.79e-01
F2	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	0.00e+00	1.00e+00	1.00e+00	1.00e+00
F3	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	0.00e+00	0.00e+00	4.29e-01	4.29e-01
F4	0.00e+00	5.78e-01	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00
F5	1.00e+00	1.00e+00	1.00e+00	7.01e-01	1.00e+00	1.00e+00	1.00e+00	0.00e+00	1.00e+00
F6	2.68e-01	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00
F7	3.03e-01	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	0.00e+00
F8	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	0.00e+00
F9	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00
F10	0.00e+00	3.50e-03	1.00e+00	8.62e-01	0.00e+00	1.00e+00	1.00e+00	6.89e-01	1.00e+00
F11	1.69e-01	1.00e+00	1.00e+00	1.00e+00	0.00e+00	1.00e+00	0.00e+00	0.00e+00	0.00e+00
F12	1.00e+00	8.00e-04	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	4.00e-04
F13	0.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	0.00e+00	1.00e+00	1.00e+00	1.00e+00
F14	0.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	0.00e+00	1.00e+00	4.89e-01	3.95e-02
F15	0.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	0.00e+00	0.00e+00
F16	0.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	3.77e-01	1.00e+00	1.00e+00	1.00e+00
F17	0.00e+00	0.00e+00	1.00e+00	4.39e-02	1.00e+00	8.00e-04	1.00e+00	8.00e-04	8.14e-01
F18	1.00e+00	1.00e+00	2.00e-04	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00	1.00e+00

For each region, statistical significance was assessed using pairwise two-sided Z-tests with Bonferroni correction, comparing the region to all others within the same profile. The maximum (i.e., least significant) p-value among these comparisons is reported.