Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.
Table 1. List of 42 Conditions Used to Define Multimorbidity and Their Prevalence in the Analytic Sample

| Condition                                                                 | N  | (%)  |
|---------------------------------------------------------------------------|----|------|
| hypertension                                                              | 74,932 | (36.2) |
| painful condition                                                          | 44,420 | (21.5) |
| cancer (any)                                                               | 22,143 | (10.7) |
| asthma                                                                    | 22,095 | (10.7) |
| treated dyspepsia                                                          | 20,932 | (10.1) |
| coronary heart disease                                                     | 15,691 | (7.6)  |
| thyroid disorders                                                          | 14,784 | (7.1)  |
| diabetes                                                                  | 14,382 | (7.0)  |
| depression                                                                 | 9,707  | (4.7)  |
| psoriasis or eczema                                                        | 6,614  | (3.2)  |
| prostate disorders                                                         | 6,456  | (3.1)  |
| rheumatoid arthritis, other inflammatory polyarthropathies & systemic connective tissue disorders | 5,667 | (2.7) |
| stroke and TIA                                                             | 5,573  | (2.7)  |
| osteoporosis                                                               | 5,502  | (2.7)  |
| chronic obstructive pulmonary disease                                      | 5,037  | (2.4)  |
| migraine                                                                   | 4,926  | (2.4)  |
| irritable bowel syndrome                                                   | 4,576  | (2.2)  |
| glaucoma                                                                   | 3,646  | (1.8)  |
| diverticular disease of intestine                                          | 3,512  | (1.7)  |
| anxiety & other neurotic, stress related & somatoform disorders             | 3,454  | (1.7)  |
| atrial fibrillation                                                        | 2,591  | (1.3)  |
| inflammatory bowel disease                                                | 1,841  | (0.9)  |
| epilepsy                                                                   | 1,524  | (0.7)  |
| chronic sinusitis                                                          | 1,314  | (0.6)  |
| endometriosis                                                              | 1,162  | (0.6)  |
| pernicious anaemia                                                         | 772    | (0.4)  |
| Meniere’s disease                                                          | 752    | (0.4)  |
| bronchiectasis                                                             | 745    | (0.4)  |
| chronic fatigue syndrome                                                  | 706    | (0.3)  |
| peripheral vascular disease                                                | 655    | (0.3)  |
| schizophrenia (and related non-organic psychosis) or bipolar disorder      | 633    | (0.3)  |
| Parkinson’s disease                                                        | 623    | (0.3)  |
| chronic kidney disease                                                     | 607    | (0.3)  |
| multiple sclerosis                                                         | 577    | (0.3)  |
| viral hepatitis                                                             | 485    | (0.2)  |
| chronic liver disease                                                      | 441    | (0.2)  |
| heart failure                                                              | 432    | (0.2)  |
| alcohol problems                                                           | 245    | (0.1)  |
| treated constipation                                                       | 228    | (0.1)  |
| polycystic ovary                                                           | 61     | (0.03) |
| anorexia or bulimia                                                        | 56     | (0.03) |
| other psychoactive substance misuse                                        | 19     | (0.01) |

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## eTable 2. ICD Codes Used to Ascertain Dementia

| ICD-9                              | ICD-10                                |
|------------------------------------|---------------------------------------|
| 331.0, 290.4, 331.1, 290.2, 290.3, 291.2, 294.1, 331.2, 331.5 | F00, F00.0, F00.1, F00.2, F00.9, G30, G30.0, G30.1, G30.8, G30.9, F01, F01.0, F01.1, F01.2, F01.3, F01.8, F01.9, I67.3, F02.0, G31.0, A81.0, F02, F02.1, F02.2, F02.3, F02.4, F02.8, F03, F05.1, F10.6, G31.1, G31.8 |

Abbreviations: ICD, International Classification of Disease
**eTable 3. Eight-Class Cluster Solution of Disease Using Latent Class Analysis of Men and Women, Including Sex as a Condition**

| Cluster | % of training sample (n = 74,874) | Male probability | Lead condition | Subsidiary condition 1 | Subsidiary condition 2 |
|---------|-----------------------------------|-------------------|----------------|------------------------|-----------------------|
| 1       | 13.1                              | 0.0               | Pain (54.2%)   | Dyspepsia (30.0%)       | Hypertension (23.6%)  |
| 2       | 15.3                              | 100               | Hypertension (87.8%) | Diabetes (37.7%)       | CHD (36.1%)           |
| 3       | 8.8                               | 100               | Pain (46.1%)   | Hypertension (36.7%)   | Dyspepsia (30.8%)     |
| 4       | 8.1                               | 7.0               | Hypertension (94.2%) | Diabetes (24.6%)       | Dyspepsia (20.9%)     |
| 5       | 19.8                              | 40.5              | Cancer (100%)  | Hypertension (60.8%)   | Pain (26.7%)          |
| 6       | 9.3                               | 45.5              | Asthma (100%)  | Hypertension (49.6%)   | Pain (28.4%)          |
| 7       | 18.9                              | 9.5               | Thyroid (100%) | Hypertension (49.1%)   | Pain (28.1%)          |
| 8       | 6.9                               | 48.8              | Hypertension (100%) | Pain (100%)           | Dyspepsia (8.2%)      |

* In 5 out of 8 clusters there is a predominant sex, i.e. probability of men contributing to cluster is either <10% or 100%.
**eTable 4. Baseline Characteristics of Participants by Incident Dementia**

| Characteristics, N (%)                        | No incident dementia (N = 200,778) | Incident dementia (N = 6,182) | Total sample (N = 206,960) |
|----------------------------------------------|------------------------------------|-------------------------------|---------------------------|
| Age in years, mean (SD)                      | 64.1 (2.8)                         | 65.7 (2.7)                    | 64.1 (2.8)                |
| Men                                          | 94,754 (47.2)                      | 3,224 (52.2)                  | 97,978 (47.3)            |
| Non-white ethnicity                          | 5,583 (2.8)                        | 206 (3.3)                     | 5,789 (2.8)              |
| Education                                    |                                    |                               |                           |
| College, university or professional qualification | 84,784 (42.2)                      | 2,082 (33.7)                  | 86,866 (41.9)            |
| Secondary school or vocational qualification  | 61,892 (30.8)                      | 1,787 (28.9)                  | 63,679 (30.8)            |
| No qualification                             | 54,102 (27.0)                      | 2,313 (37.4)                  | 56,415 (27.3)            |
| Socioeconomic status in tertiles             |                                    |                               |                           |
| 1 (least deprived)                           | 43,681 (21.8)                      | 1,177 (19.0)                  | 44,858 (21.7)            |
| 2                                            | 123,189 (61.4)                     | 3,587 (58.0)                  | 126,776 (61.3)           |
| 3 (most deprived)                            | 33,908 (16.9)                      | 1,418 (22.9)                  | 35,326 (17.0)            |
| APOE-ε4 carrier                              | 54,902 (27.3)                      | 3,345 (54.1)                  | 58,247 (28.1)            |
| Multimorbidity                               | 85,658 (42.7)                      | 3,543 (57.3)                  | 89,201 (43.1)            |
| Follow-up in years, mean (SD)                | 11.9 (2.1)                         | 9.2 (2.8)                     | 11.8 (2.2)               |

Abbreviations: APOE, Apolipoprotein E, N, Number of participants, SD, Standard Deviation.
**eTable 5.** Cox Proportional Hazards Models for the Association Between Number of Multimorbid Conditions and Incident Dementia

|                     | 0-1        | 2          | 3          | 4          | 5          | 6          |
|---------------------|------------|------------|------------|------------|------------|------------|
| **Dementia cases**  | 2,639      | 1,661      | 982        | 533        | 233        | 134        |
| **Sample**          | 117,759    | 48,883     | 24,644     | 10,030     | 3,687      | 1,957      |
| **Hazard Ratio**    | 1 (Reference) | 1.41      | 1.61        | 2.19      | 2.59    | 3.15      |
| (95% CI)            | (1.32-1.50) | (1.49-1.73) | (1.99-2.40) | (2.26-2.96) | (2.65-3.75) |
| **Incidence Rate (95% CI)** | 1.87       | 2.88       | 3.43       | 4.69       | 5.65       | 6.37       |
|                     | (1.80-1.94) | (2.75-3.03) | (3.23-3.66) | (4.30-5.10) | (4.97-6.42) | (5.38-7.54) |

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**eTable 6. Cox Proportional Hazards Models of the Interaction of Multimorbidity and Sociodemographic Characteristics With Incident Dementia**

| Age (p-value for interaction = 0.10) | No Multimorbidity | Multimorbidity |
|-------------------------------------|-------------------|----------------|
| <65 years                           |                   |                |
| 940                                | 70,488            | 1,073          |
| 1 (reference)                      | 1.10 (1.03-1.17)  | 1.77 (1.62-1.93)|
| 1,073                              | 45,436            | 43,765         |
| 1.61 (1.52-1.72)                   | 2.00 (1.88-2.12)  |
| ≥65 years                           |                   |                |
| 1,699                              | 47,271            | 2,470          |
| 1 (reference)                      | 3.03 (2.89-3.18)  | 1.61 (1.52-1.72)|
| 2,470                              | 43,765            | 2.00 (1.88-2.12)|
| 4.93 (4.74-5.13)                   |                    |

| Sex (p-value for interaction = 0.36) |                   |                |
| Men                                 |                   |                |
| 1,408                               | 55,956            | 1,816          |
| 1 (reference)                      | 2.12 (2.01-2.23)  | 1.59 (1.49-1.71)|
| 1,816                              | 42,022            | 3.79 (3.62-3.97)|
| Women                               |                   |                |
| 1,231                               | 61,803            | 1,727          |
| 1 (reference)                      | 1.64 (1.55-1.74)  | 1.67 (1.55-1.80)|
| 1,727                              | 47,179            | 2.00 (1.88-2.12)|
| 3.09 (2.94-3.24)                   |                    |

| Ethnicity (p-value for interaction = 0.46) |                   |                |
| White                                |                   |                |
| 2,569                                | 114,860           | 3,407          |
| 1 (reference)                      | 1.86 (1.79-1.94)  | 1.62 (1.54-1.71)|
| 3,407                              | 86,311            | 3.39 (3.28-3.51)|
| Non-white                           |                   |                |
| 70                                  | 2,899             | 136            |
| 1 (reference)                      | 2.05 (1.62-2.59)  | 1.81 (1.36-2.42)|
| 136                                | 2,890             | 2.00 (1.88-2.12)|
| 4.13 (2.94-4.89)                   |                    |

| Education (p-value for interaction = 0.94) |                   |                |
| College or higher                   |                   |                |
| 977                                 | 52,629            | 1,105          |
| 1 (reference)                      | 1.54 (1.45-1.64)  | 1.64 (1.51-1.79)|
| 1,105                              | 34,237            | 2.75 (2.59-2.91)|
| Secondary school or vocational      |                   |                |
| 796                                 | 36,834            | 991            |
| 1 (reference)                      | 1.80 (1.68-1.93)  | 1.61 (1.46-1.77)|
| 991                                | 26,845            | 2.00 (1.88-2.12)|
| 4.93 (4.22-4.81)                   |                    |
| No qualification                    |                   |                |
| 866                                 | 28,296            | 1,447          |
| 1 (reference)                      | 2.56 (2.40-2.74)  | 1.63 (1.50-1.78)|
| 1,447                              | 28,119            | 2.00 (1.88-2.12)|
| 4.47 (4.25-4.71)                   |                    |

| Socioeconomic status in tertiles (p-value for interaction = 0.24) |                   |                |
| 1 (least deprived)              |                   |                |
| 581                                | 27,304            | 596            |
| 1 (reference)                    | 1.76 (1.62-1.90)  | 1.49 (1.33-1.67)|
| 596                               | 17,554            | 2.87 (2.64-3.10)|
| 2                                 | 1,554             | 2,033          |
| 1 (reference)                    | 1.77 (1.69-1.86)  | 1.66 (1.55-1.77)|
| 2,033                            | 53,738            | 3.24 (3.10-3.39)|
| 3 (most deprived)                |                   |                |
| 504                                | 17,417            | 914            |
| 1 (reference)                    | 2.44 (2.24-2.67)  | 1.68 (1.51-1.88)|
| 914                               | 17,909            | 2.00 (1.88-2.12)|
| 4.51 (4.22-4.81)                 |                    |

* Abbreviations: CI, Confidence Interval.
* All models adjusted for age, ethnicity, education, socioeconomic status and APOE-ε4. Specific covariates are dropped from the model where that covariate is the effect modifier of interest.
* Incidence rate per 1,000 person-years

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eTable 7. Probabilities and Observed vs Expected Ratios for 41 Conditions Within 7 Clusters in Women

| Condition                        | Hypertension, diabetes & CHD | Pain, dyspepsia & depression | Cancer | Thyroid disorders | Pain, osteoporosis & dyspepsia | Asthma & COPD | Pain & hypertension |
|----------------------------------|-------------------------------|-----------------------------|--------|------------------|-------------------------------|---------------|---------------------|
|                                  | Expected P | O/E | P | O/E | P | O/E | P | O/E | P | O/E | P | O/E | P | O/E |
| hypertension                    | 0.545         | 1.000 | 1.83 | 0.263         | 0.48 | 0.434 | 0.80 | 0.504         | 0.93 | 0.124 | 0.23 | 0.313 | 0.58 | 1.000 | 1.83 |
| depression                       | 0.109         | 0.091 | 0.83 | 0.231         | 2.12 | 0.071 | 0.65 | 0.071         | 0.65 | 0.120 | 1.10 | 0.088 | 0.81 | 0.028 | 0.25 |
| painful condition                | 0.408         | 0.184 | 0.45 | 0.625         | 1.53 | 0.309 | 0.76 | 0.302         | 0.74 | 0.455 | 1.11 | 0.351 | 0.86 | 1.000 | 2.45 |
| asthma                           | 0.216         | 0.181 | 0.84 | 0.102         | 0.47 | 0.094 | 0.43 | 0.092         | 0.42 | 0.073 | 0.34 | 1.000 | 4.63 | 0.059 | 0.27 |
| coronary heart disease           | 0.087         | 0.154 | 1.77 | 0.043         | 0.49 | 0.042 | 0.48 | 0.076         | 0.88 | 0.138 | 1.59 | 0.059 | 0.68 | 0.038 | 0.44 |
| treated dyspepsia                | 0.203         | 0.185 | 0.91 | 0.374         | 1.84 | 0.123 | 0.60 | 0.134         | 0.66 | 0.241 | 1.19 | 0.172 | 0.85 | 0.094 | 0.46 |
| diabetes                         | 0.103         | 0.230 | 2.24 | 0.020         | 0.19 | 0.053 | 0.51 | 0.088         | 0.86 | 0.117 | 1.14 | 0.050 | 0.48 | 0.054 | 0.52 |
| thyroid disorders                | 0.207         | 0.078 | 0.38 | 0.117         | 0.57 | 0.119 | 0.58 | 1.000         | 4.83 | 0.086 | 0.42 | 0.135 | 0.65 | 0.000 | 0.00 |
| rheumatoid arthritis             | 0.067         | 0.072 | 1.08 | 0.035         | 0.52 | 0.034 | 0.51 | 0.064         | 0.96 | 0.188 | 2.80 | 0.055 | 0.82 | 0.015 | 0.23 |
| COPD                             | 0.044         | 0.039 | 0.89 | 0.030         | 0.68 | 0.021 | 0.48 | 0.022         | 0.49 | 0.078 | 1.77 | 0.121 | 2.75 | 0.004 | 0.10 |
| anxiety                          | 0.039         | 0.030 | 0.77 | 0.107         | 2.73 | 0.022 | 0.57 | 0.022         | 0.57 | 0.033 | 0.84 | 0.018 | 0.47 | 0.005 | 0.12 |
| irritable bowel syndrome         | 0.062         | 0.037 | 0.59 | 0.191         | 3.08 | 0.031 | 0.49 | 0.025         | 0.41 | 0.039 | 0.62 | 0.049 | 0.79 | 0.012 | 0.20 |
| alcohol problems                 | 0.001         | 0.001 | 0.76 | 0.004         | 3.91 | 0.001 | 0.72 | 0.000         | 0.00 | 0.002 | 1.68 | 0.001 | 0.90 | 0.000 | 0.00 |
| drug misuse                      | 0             | 0.000 | 0.00 | 0.001         | 0.00 | 0.000 | 0.00 | 0.000         | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 |
| treated constipation             | 0.003         | 0.002 | 0.58 | 0.007         | 2.45 | 0.001 | 0.32 | 0.003         | 1.11 | 0.004 | 1.40 | 0.002 | 0.63 | 0.000 | 0.00 |
| stroke and TIA                   | 0.042         | 0.082 | 1.94 | 0.016         | 0.37 | 0.023 | 0.55 | 0.029         | 0.70 | 0.074 | 1.76 | 0.015 | 0.36 | 0.016 | 0.39 |
| chronic kidney disease           | 0.005         | 0.012 | 2.40 | 0.003         | 0.69 | 0.004 | 0.71 | 0.003         | 0.52 | 0.004 | 0.79 | 0.002 | 0.45 | 0.002 | 0.46 |
| diverticular disease             | 0.044         | 0.041 | 0.93 | 0.091         | 2.08 | 0.023 | 0.53 | 0.021         | 0.47 | 0.042 | 0.95 | 0.040 | 0.92 | 0.025 | 0.56 |
| atrial fibrillation              | 0.015         | 0.023 | 1.51 | 0.007         | 0.48 | 0.009 | 0.63 | 0.017         | 1.14 | 0.031 | 2.08 | 0.009 | 0.61 | 0.004 | 0.29 |
| peripheral vascular disease      | 0.005         | 0.007 | 1.30 | 0.005         | 0.97 | 0.003 | 0.54 | 0.002         | 0.42 | 0.016 | 1.31 | 0.002 | 1.28 | 0.001 | 0.03 |
| heart failure                    | 0.003         | 0.004 | 1.21 | 0.001         | 0.27 | 0.002 | 0.79 | 0.003         | 0.87 | 0.008 | 1.57 | 0.003 | 0.84 | 0.001 | 0.46 |
| glaucoma                         | 0.029         | 0.032 | 1.11 | 0.026         | 0.88 | 0.024 | 0.83 | 0.021         | 0.74 | 0.055 | 1.91 | 0.023 | 0.81 | 0.012 | 0.42 |
| epilepsy                         | 0.012         | 0.010 | 0.84 | 0.008         | 0.64 | 0.010 | 0.86 | 0.011         | 0.92 | 0.039 | 1.29 | 0.009 | 0.72 | 0.000 | 0.03 |
| schizophrenia                    | 0.006         | 0.005 | 0.87 | 0.005         | 0.86 | 0.002 | 0.27 | 0.010         | 1.64 | 0.012 | 2.00 | 0.004 | 0.62 | 0.000 | 0.00 |
| psoriasis or eczema              | 0.056         | 0.042 | 0.75 | 0.089         | 1.58 | 0.027 | 0.47 | 0.029         | 0.52 | 0.092 | 1.64 | 0.087 | 1.55 | 0.015 | 0.26 |

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| Disorder                      | O/E 1  | O/E 2  | O/E 3  | O/E 4  | O/E 5  | O/E 6  | O/E 7  | O/E 8  | O/E 9  | O/E 10 | O/E 11 | O/E 12 | O/E 13 |
|-------------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| inflammatory bowel disease    | 0.016  | 0.015  | 0.96   | 0.010  | 0.60   | 0.012  | 0.76   | 0.006  | 0.39   | 0.051  | 3.19   | 0.014  | 0.89   | 0.007  | 0.42   |
| migraine                      | 0.061  | 0.036  | 0.59   | 0.163  | 2.66   | 0.044  | 0.72   | 0.031  | 0.51   | 0.068  | 1.11   | 0.037  | 0.60   | 0.012  | 0.19   |
| chronic sinusitis             | 0.013  | 0.007  | 0.56   | 0.031  | 2.35   | 0.009  | 0.68   | 0.006  | 0.46   | 0.012  | 0.94   | 0.020  | 1.53   | 0.002  | 0.13   |
| anorexia or bulimia           | 0.001  | 0.001  | 0.76   | 0.001  | 1.39   | 0.001  | 0.81   | 0.000  | 0.21   | 0.003  | 2.50   | 0.001  | 1.40   | 0.000  | 0.00   |
| bronchiectasis                | 0.009  | 0.008  | 0.84   | 0.006  | 0.67   | 0.005  | 0.58   | 0.004  | 0.40   | 0.019  | 2.12   | 0.023  | 2.56   | 0.000  | 0.04   |
| Parkinson's disease           | 0.004  | 0.003  | 0.75   | 0.001  | 0.28   | 0.003  | 0.66   | 0.001  | 0.34   | 0.014  | 3.57   | 0.004  | 0.91   | 0.000  | 0.00   |
| multiple sclerosis            | 0.006  | 0.006  | 1.04   | 0.005  | 0.79   | 0.005  | 0.79   | 0.003  | 0.51   | 0.016  | 2.70   | 0.004  | 0.71   | 0.002  | 0.27   |
| viral hepatitis               | 0.004  | 0.002  | 0.54   | 0.009  | 2.31   | 0.003  | 0.70   | 0.004  | 0.94   | 0.003  | 0.65   | 0.002  | 0.60   | 0.001  | 0.20   |
| chronic liver disease         | 0.005  | 0.003  | 0.65   | 0.006  | 1.10   | 0.003  | 0.67   | 0.004  | 0.72   | 0.012  | 2.48   | 0.002  | 0.35   | 0.002  | 0.42   |
| osteoporosis                  | 0.081  | 0.058  | 0.71   | 0.054  | 0.66   | 0.080  | 0.99   | 0.053  | 0.65   | 0.251  | 3.09   | 0.075  | 0.93   | 0.021  | 0.26   |
| chronic fatigue syndrome      | 0.001  | 0.006  | 6.09   | 0.026  | 26.02  | 0.005  | 4.80   | 0.006  | 6.36   | 0.005  | 5.47   | 0.010  | 9.56   | 0.000  | 0.41   |
| endometriosis                 | 0.02   | 0.016  | 0.82   | 0.041  | 2.03   | 0.013  | 0.65   | 0.012  | 0.58   | 0.024  | 1.18   | 0.014  | 0.68   | 0.006  | 0.32   |
| Meniere’s disease             | 0.008  | 0.007  | 0.88   | 0.012  | 1.48   | 0.005  | 0.61   | 0.005  | 0.61   | 0.015  | 1.90   | 0.003  | 0.33   | 0.007  | 0.84   |
| pernicious anaemia            | 0.011  | 0.008  | 0.69   | 0.005  | 0.50   | 0.002  | 0.21   | 0.026  | 2.34   | 0.027  | 2.50   | 0.005  | 0.50   | 0.003  | 0.30   |
| polycystic ovary              | 0.001  | 0.001  | 0.63   | 0.002  | 2.13   | 0.001  | 0.95   | 0.002  | 1.90   | 0.001  | 0.56   | 0.001  | 0.78   | 0.001  | 1.01   |
| cancer                        | 0.202  | 0.086  | 0.42   | 0.057  | 0.28   | 1.000  | 4.95   | 0.089  | 0.44   | 0.065  | 0.32   | 0.121  | 0.60   | 0.000  | 0.00   |

Abbreviations: O/E, Observed/Expected, P, Probability, CHD, Coronary Heart Disease, COPD, Chronic Obstructive Pulmonary Disease, TIA, Transient Ischemic Attack
Orange cells flag O/E > 1; of these the 3 highest probability conditions > 0.10 are marked as blue.

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**eTable 8. Probabilities and Observed vs Expected Ratios for 40 Conditions Within 6 Clusters in Men**

| Condition                      | Hypertension, pain & dyspepsia | Pain, dyspepsia & prostate disorders | CHD, hypertension & stroke | Asthma, COPD & psoriasis | Diabetes & hypertension | Cancer |
|--------------------------------|--------------------------------|-------------------------------------|---------------------------|--------------------------|-------------------------|--------|
|                                | Expected                       | P                                  | O/E                       | P                        | O/E                     | P      | O/E |
| hypertension                   | 0.657                          | 1.000                              | 1.522                     | 0.008                    | 0.12                    | 0.737  | 1.122 | 0.511 | 0.778 | 0.845 | 1.286 | 0.614 | 0.935 |
| depression                     | 0.07                           | 0.071                              | 1.014                     | 0.142                    | 2.029                   | 0.055  | 0.786 | 0.055 | 0.786 | 0.033 | 0.471 | 0.041 | 0.586 |
| painful condition              | 0.351                          | 0.431                              | 1.228                     | 0.542                    | 1.544                   | 0.260  | 0.741 | 0.264 | 0.752 | 0.215 | 0.613 | 0.257 | 0.732 |
| asthma                         | 0.176                          | 0.015                              | 0.085                     | 0.065                    | 0.369                   | 0.074  | 0.420 | 1.000 | 5.682 | 0.069 | 0.392 | 0.000 | 0.000 |
| coronary heart disease         | 0.226                          | 0.000                              | 0.000                     | 0.083                    | 0.367                   | 1.000  | 4.425 | 0.115 | 0.509 | 0.164 | 0.726 | 0.154 | 0.681 |
| treated dyspepsia              | 0.185                          | 0.194                              | 1.049                     | 0.336                    | 1.816                   | 0.155  | 0.838 | 0.151 | 0.816 | 0.082 | 0.443 | 0.139 | 0.751 |
| diabetes                       | 0.197                          | 0.040                              | 0.203                     | 0.051                    | 0.259                   | 0.174  | 0.883 | 0.079 | 0.401 | 1.000 | 0.076 | 0.060 | 0.305 |
| thyroid disorders              | 0.047                          | 0.049                              | 1.043                     | 0.075                    | 1.596                   | 0.044  | 0.936 | 0.031 | 0.660 | 0.043 | 0.915 | 0.033 | 0.702 |
| rheumatoid arthritis           | 0.033                          | 0.037                              | 1.121                     | 0.055                    | 1.667                   | 0.028  | 0.848 | 0.032 | 0.970 | 0.014 | 0.424 | 0.026 | 0.788 |
| COPD                           | 0.057                          | 0.040                              | 0.702                     | 0.070                    | 1.228                   | 0.054  | 0.947 | 0.129 | 2.263 | 0.023 | 0.404 | 0.033 | 0.579 |
| anxiety                        | 0.027                          | 0.029                              | 1.074                     | 0.061                    | 2.259                   | 0.016  | 0.593 | 0.017 | 0.630 | 0.008 | 0.296 | 0.017 | 0.630 |
| irritable bowel syndrome       | 0.022                          | 0.024                              | 1.091                     | 0.057                    | 2.591                   | 0.009  | 0.409 | 0.017 | 0.773 | 0.004 | 0.182 | 0.012 | 0.545 |
| alcohol problems               | 0.004                          | 0.004                              | 1.000                     | 0.008                    | 2.000                   | 0.002  | 0.500 | 0.003 | 0.750 | 0.000 | 0.000 | 0.003 | 0.750 |
| drug misuse                    | 0.000                          | 0.000                              | 0.000                     | 0.001                    | 0.000                   | 0.000  | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| treated constipation           | 0.001                          | 0.001                              | 1.000                     | 0.002                    | 2.000                   | 0.001  | 1.000 | 0.001 | 1.000 | 0.001 | 1.000 | 0.002 | 2.000 |
| stroke and TIA                 | 0.07                           | 0.088                              | 1.257                     | 0.072                    | 1.029                   | 0.091  | 1.300 | 0.036 | 0.514 | 0.056 | 0.800 | 0.051 | 0.729 |
| chronic kidney disease         | 0.007                          | 0.010                              | 1.429                     | 0.004                    | 0.571                   | 0.010  | 1.429 | 0.003 | 0.429 | 0.007 | 1.000 | 0.008 | 1.143 |
| diverticular disease           | 0.023                          | 0.026                              | 1.130                     | 0.042                    | 1.826                   | 0.014  | 0.609 | 0.020 | 0.870 | 0.013 | 0.565 | 0.018 | 0.783 |
| atrial fibrillation            | 0.034                          | 0.042                              | 1.235                     | 0.054                    | 1.588                   | 0.028  | 0.824 | 0.018 | 0.529 | 0.018 | 0.529 | 0.028 | 0.824 |
| peripheral vascular disease    | 0.007                          | 0.007                              | 1.000                     | 0.010                    | 1.429                   | 0.011  | 1.571 | 0.004 | 0.571 | 0.007 | 1.000 | 0.004 | 0.571 |
| heart failure                  | 0.006                          | 0.006                              | 1.000                     | 0.007                    | 1.167                   | 0.008  | 1.333 | 0.004 | 0.667 | 0.004 | 0.667 | 0.002 | 0.333 |
| prostate disorders             | 0.117                          | 0.135                              | 1.154                     | 0.242                    | 2.068                   | 0.073  | 0.624 | 0.081 | 0.692 | 0.048 | 0.410 | 0.070 | 0.598 |
| glaucoma                       | 0.035                          | 0.040                              | 1.143                     | 0.056                    | 1.600                   | 0.024  | 0.686 | 0.025 | 0.714 | 0.025 | 0.714 | 0.030 | 0.857 |
| epilepsy                       | 0.014                          | 0.014                              | 1.000                     | 0.028                    | 2.000                   | 0.011  | 0.786 | 0.007 | 0.500 | 0.006 | 0.429 | 0.012 | 0.857 |
| schizophrenia                  | 0.006                          | 0.006                              | 1.000                     | 0.017                    | 2.833                   | 0.003  | 0.500 | 0.004 | 0.667 | 0.004 | 0.667 | 0.002 | 0.333 |
| Condition                      | O/E 1 | O/E 2 | O/E 3 | O/E 4 | O/E 5 | O/E 6 | O/E 7 | O/E 8 | O/E 9 | O/E 10 |
|-------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|
| psoriasis or eczema           | 0.063 | 0.060 | 0.952 | 0.113 | 1.794 | 0.040 | 0.635 | 0.088 | 1.397 | 0.027  |
| inflammatory bowel disease    | 0.016 | 0.014 | 0.875 | 0.030 | 1.875 | 0.011 | 0.688 | 0.015 | 0.938 | 0.010  |
| migraine                      | 0.022 | 0.025 | 1.136 | 0.058 | 2.636 | 0.008 | 0.364 | 0.015 | 0.682 | 0.002  |
| chronic sinusitis             | 0.011 | 0.013 | 1.182 | 0.024 | 2.182 | 0.003 | 0.273 | 0.010 | 0.909 | 0.003  |
| anorexia or bulimia           | 0.005 | 0.003 | 0.600 | 0.007 | 1.400 | 0.002 | 0.400 | 0.013 | 2.600 | 0.001  |
| bronchiectasis                | 0.006 | 0.006 | 1.000 | 0.014 | 2.333 | 0.005 | 0.833 | 0.003 | 0.500 | 0.002  |
| Parkinson's disease           | 0.003 | 0.003 | 1.000 | 0.006 | 2.000 | 0.001 | 0.333 | 0.001 | 0.333 | 0.002  |
| multiple sclerosis            | 0.004 | 0.003 | 0.750 | 0.011 | 2.750 | 0.002 | 0.500 | 0.002 | 0.500 | 0.001  |
| viral hepatitis               | 0.004 | 0.003 | 0.750 | 0.007 | 1.750 | 0.002 | 0.500 | 0.001 | 0.250 | 0.005  |
| chronic liver disease         | 0.004 | 0.003 | 0.750 | 0.007 | 1.750 | 0.002 | 0.500 | 0.001 | 0.250 | 0.004  |
| osteoporosis                  | 0.011 | 0.008 | 0.727 | 0.025 | 2.273 | 0.008 | 0.727 | 0.013 | 1.182 | 0.002  |
| chronic fatigue syndrome      | 0.003 | 0.003 | 1.000 | 0.009 | 3.000 | 0.002 | 0.667 | 0.002 | 0.667 | 0.002  |
| Meniere’s disease             | 0.006 | 0.007 | 1.167 | 0.013 | 2.167 | 0.002 | 0.333 | 0.003 | 0.500 | 0.002  |
| pernicious anaemia            | 0.005 | 0.004 | 0.800 | 0.010 | 2.000 | 0.003 | 0.600 | 0.003 | 0.600 | 0.006  |
| cancer                        | 0.157 | 0.000 | 0.000 | 0.056 | 0.357 | 0.000 | 0.000 | 0.146 | 0.930 | 0.070  |

Abbreviations: O/E, Observed/Expected, P, Probability, COPD, Chronic Obstructive Pulmonary Disease, TIA, Transient Ischemic Attack
Orange cells flag O/E > 1; of these the 3 highest probability conditions > 0.05 are marked as blue.
**eTable 9. Sex-Stratified Cox Proportional Hazards Models for the Association Between Disease Clusters and Incident Dementia in the Test Sample**

| Disease clusters* | Dementia cases | Sample | % Participants in cluster | Hazard Ratio (95% CI)b | Incident Rate (95% CI)c |
|-------------------|----------------|--------|--------------------------|------------------------|------------------------|
| **Female**        |                |        |                          |                        |                        |
| No multimorbidity | 1,231          | 61,803 | 1 (reference)            | 1.64 (1.55-1.74)       |                        |
| Hypertension (100%), pain (50%), dyspepsia (22%) | 81 | 2,156 | 22.9% | 1.56 (1.25-1.96) | 3.11 (2.50-3.87) |
| Cancer (100%)     | 48             | 1,599  | 17.0% | 1.42 (1.06-1.90) | 2.99 (1.95-3.44) |
| Asthma (100%), COPD (11%), psoriasis (10%) | 49 | 1,457 | 15.5% | 1.60 (1.20-2.13) | 2.80 (2.12-3.70) |
| Pain (61%), dyspepsia (35%), osteoporosis (16%) | 47 | 1,416 | 15.0% | 1.58 (1.18-2.12) | 2.78 (2.09-3.70) |
| Thyroid disorders (100%) | 28 | 1,062 | 11.3% | 1.16 (0.80-1.69) | 2.21 (1.52-3.20) |
| Hypertension (89%), diabetes (47%), CHD (24%) | 53 | 1,040 | 11.0% | 2.10 (1.59-2.77) | 4.41 (3.37-5.78) |
| Depression (100%), pain (41%), anxiety (14%) | 26 | 704  | 7.5% | 1.92 (1.30-2.83) | 3.07 (2.09-4.51) |
| **Male**          |                |        |                          |                        |                        |
| No multimorbidity | 1,408          | 55,956 | 1 (reference)            | 2.12 (2.01-2.23)       |                        |
| Hypertension (100%), CHD (28%), dyspepsia (19%) | 96 | 2,269 | 26.9% | 1.54 (1.26-1.90) | 3.69 (3.02-4.51) |
| Pain (100%), hypertension (69%) | 67 | 2,097 | 24.9% | 1.14 (0.89-1.45) | 2.76 (2.18-3.51) |
| Diabetes (100%), hypertension (84%), CHD (28%) | 88 | 1,401 | 16.6% | 2.28 (1.83-2.83) | 5.79 (4.70-7.13) |
| Asthma (100%), psoriasis (12%), COPD (11%) | 45 | 1,265 | 15.0% | 1.34 (1.00-1.80) | 3.07 (2.29-4.11) |
| Dyspepsia (32%), cancer (26%), CHD (25%) | 42 | 954  | 11.3% | 1.55 (1.14-2.11) | 3.92 (2.90-5.30) |
| Depression (100%), dyspepsia (21%), anxiety (14%) | 16 | 447  | 5.3% | 1.63 (1.00-2.67) | 3.23 (1.98-5.28) |

Abbreviations: CI, Confidence Interval.
* Each cluster was characterised by the three health conditions with the highest probabilities above 5% of contributing to that cluster, excluding conditions where their observed prevalence was equal to or less than that of the total population of men and women: expected prevalence.
b All models adjusted for age, ethnicity, education, socioeconomic status and APOE-ε4
c Incidence rate per 1,000 person-years
eFigure. SABIC Values for Disease Cluster Solutions

A. Women

B. Men