Supplementary Material

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Hospital Frailty Risk Score (HFRS)

The HFRS it is a well-validated score derived from routinely collected hospital administration data. It is a weighted sum of <u>109 three-character</u> ICD-10 diagnostic codes present in a patient's records over the preceding two years. In the validation study, the HFRS ranged from zero to 99 (mean (SD) 9.0 (8.7)) The HFRS is categorized into low risk (<5), intermediate risk (5-15) and high risk (>15).

Diagnostic codes used to calculate the HFRS include infection, cerebrovascular disease, frailty syndromes (such as falls, cognitive impairment and fractures). Rather than including the full list of 109 codes here or in the manuscript, we kindly refer the editors to the list available open access at:

Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study - The Lancet

Table 1: ICD-10 codes for prevalent dementia (for exclusion)

| Prevalent de | mentia (for exclusion) | | | |
|--------------|---|--|--|--|
| F00.0 | Dementia in Alzheimer's disease with early onset | | | |
| F00.1 | Dementia in Alzheimer's disease with late onset | | | |
| F00.2 | Dementia in Alzheimer's disease, atypical or mixed type | | | |
| F00.9 | Dementia in Alzheimer's disease, unspecified | | | |
| G30.0 | Alzheimer's disease with early onset | | | |
| G30.1 | Alzheimer's disease with late onset | | | |
| G30.8 | Other Alzheimer's disease | | | |
| G30.9 | Alzheimer's disease, unspecified | | | |
| F01.0 | Vascular dementia of acute onset | | | |
| F01.1 | Multi-infarct dementia | | | |
| F01.2 | Subcortical vascular dementia | | | |
| F01.3 | Mixed cortical and subcortical vascular dementia | | | |
| F01.8 | Other vascular dementia | | | |

| F01.9 | Vascular dementia, unspecified | | | |
|-------|---|--|--|--|
| I67.3 | Binswanger disease | | | |
| F02.0 | Dementia in Pick disease | | | |
| F02.1 | Dementia in Creutzfeldt-Jakob disease | | | |
| F02.2 | Dementia in Huntington disease | | | |
| F02.3 | Dementia in Parkinson's disease | | | |
| F02.4 | Dementia in HIV | | | |
| F02.8 | Dementia in other specified disease classified elsewhere | | | |
| F10.6 | Mental and behavioural disorders due to use of alcohol, amnesic syndrome | | | |
| F10.7 | Mental and behavioural disorders due to use of alcohol, residual and late-onset psychotic | | | |
| | disorder (alcoholic dementia NOS etc) | | | |
| A81.0 | Creutzfeldt-Jakob disease | | | |
| F03 | Unspecified dementia | | | |
| F05.1 | Delirium superimposed on dementia | | | |
| G31.0 | Circumscribed brain atrophy | | | |
| G31.1 | Senile degeneration of the brain, not elsewhere classified | | | |
| G31.8 | Other specified degenerative diseases of the nervous system | | | |

Table 2: ICD-10 codes for delirium

| Delirium | |
|----------|---|
| F05.0 | Delirium not superimposed on dementia, so described |
| F05.8 | Other delirium |
| F05.9 | Delirium, unspecified |
| R41.0 | Disorientation, unspecified 'Confusion NOS' |

Table 3: Forty ICD-10 codes most commonly recorded as primary diagnoses for the total eligible sample(N = 626, 467)

| Rank | ICD-10 code | Count | Proportion | Diagnosis | |
|------|-------------|-------|------------|---|--|
| 1 | H26.9 | 53909 | 8.61 | Cataracts | |
| 2 | M17.1 | 13547 | 2.16 | Osteoarthritis of the knee | |
| 3 | J18.9 | 9524 | 1.52 | Pneumonia | |
| 4 | N39.0 | 9521 | 1.52 | Urinary tract infection | |
| 5 | R07.4 | 8010 | 1.28 | Chest pain | |
| 6 | I48 | 7377 | 1.18 | Atrial fibrillation and flutter | |
| 7 | K92.2 | 7280 | 1.16 | Gastrointestinal haemorrhage | |
| 8 | M16.1 | 7279 | 1.16 | Osteoarthritis of the hip | |
| 9 | Z50.9 | 7096 | 1.13 | Rehabilitation | |
| 10 | Z09.0 | 6874 | 1.1 | Follow-up after surgery | |
| 11 | C44.3 | 6728 | 1.07 | Skin cancer of the face | |
| 12 | R55 | 6571 | 1.05 | Syncope and collapse | |
| 13 | Z08.0 | 6121 | 0.98 | Follow-up after surgery for cancer | |
| 14 | Z12.1 | 5889 | 0.94 | Screening for cancer of gastrointestinal tract | |
| 15 | I21.4 | 5717 | 0.91 | Acute subendocardial myocardial infarction | |
| 16 | I25.11 | 5280 | 0.84 | Atherosclerotic heart disease | |
| 17 | 150.0 | 5224 | 0.83 | Congestive heart failure | |
| 18 | C61 | 5194 | 0.83 | Prostate cancer | |
| 19 | R19.5 | 5160 | 0.82 | Other faecal abnormalities | |
| 20 | J44.0 | 5021 | 0.8 | COPD with acute lower respiratory tract infection | |
| 21 | K40.90 | 4983 | 0.8 | Inguinal hernia without obstruction or gangrene | |
| 22 | N40 | 4919 | 0.79 | Hyperplasia of prostate | |
| 23 | G56.0 | 4693 | 0.75 | Carpal tunnel syndrome | |
| 24 | K57.30 | 4565 | 0.73 | Diverticular disease without abscess or perforation | |
| 25 | K21.9 | 4087 | 0.65 | Gastro-oesophageal disease with oesophagitis | |
| 26 | I20.0 | 4033 | 0.64 | Unstable angina | |
| 27 | A09.9 | 3947 | 0.63 | Gastroenteritis/colitis | |

| 28 | L03.11 | 3893 | 0.62 | Cellulitis of other part of limb | |
|----|--------|------|------|---|--|
| 29 | E11.39 | 3879 | 0.62 | Type 2 Diabetes Mellitus | |
| 30 | G45.9 | 3870 | 0.62 | Transient Ischaemic Attack | |
| 31 | K63.58 | 3827 | 0.61 | Polyp of the colon | |
| 32 | I20.9 | 3556 | 0.57 | Angina | |
| 33 | D50.9 | 3546 | 0.57 | Iron deficiency anaemia | |
| 34 | R10.4 | 3492 | 0.56 | Abdominal pain | |
| 35 | K59.0 | 3378 | 0.54 | Constipation | |
| 36 | I63.9 | 3368 | 0.54 | Cerebral infarction | |
| 37 | R19.4 | 3346 | 0.53 | Change in bowel habit | |
| 38 | S72.03 | 3250 | 0.52 | Fractured neck of femur | |
| 39 | J22 | 3162 | 0.5 | Acute lower respiratory tract infection | |
| 40 | R31 | 3033 | 0.4 | Haematuria | |

Table 4: ICD-10 codes for incident dementia

| New (Incident | New (Incident) Dementia – outcome data | | | | |
|---------------|---|--|--|--|--|
| F00.1 | Dementia in Alzheimer's disease with late onset | | | | |
| F00.2 | Dementia in Alzheimer's disease, atypical or mixed type | | | | |
| F00.9 | Dementia in Alzheimer's disease, unspecified | | | | |
| G30.1 | Alzheimer's disease with late onset | | | | |
| G30.8 | Other Alzheimer's disease | | | | |
| G30.9 | Alzheimer's disease, unspecified | | | | |
| F01.0 | Vascular dementia of acute onset | | | | |
| F01.1 | Multi-infarct dementia | | | | |
| F01.2 | Subcortical vascular dementia | | | | |
| F01.3 | Mixed cortical and subcortical vascular dementia | | | | |
| F01.8 | Other vascular dementia | | | | |
| F01.9 | Vascular dementia, unspecified | | | | |
| I67.3 | Binswanger disease | | | | |
| F02.0 | Dementia in Pick disease | | | | |
| F02.3 | Dementia in Parkinson's disease | | | | |
| F03 | Unspecified dementia | | | | |
| F05.1 | Delirium superimposed on dementia | | | | |
| G31.0 | Circumscribed brain atrophy | | | | |
| G31.1 | Senile degeneration of the brain, not elsewhere classified | | | | |
| G31.8 | Other specified degenerative diseases of the nervous system | | | | |

| Orthogram | G4 - 4° - 4° - | Germale | | Delirium ej | pisodes in landn | nark period |
|-----------|------------------------------|---------|-----------|-------------|------------------|-------------|
| Outcome | Statistic | Sample | 0 | 1 | 2 | 3+ |
| Death | Number at | Total | 38,940 | 24,736 | 7,166 | 4,315 |
| | risk | Men | 17,909 | 11,487 | 3,074 | 1,832 |
| | | Women | 21,031 | 13,249 | 4,092 | 2,483 |
| | Number of | Total | 12,561 | 9,789 | 3,712 | 2,602 |
| | events | Men | 5,801 | 4,590 | 1,634 | 1,142 |
| | | Women | 6,760 | 5,199 | 2,078 | 1,460 |
| | Person-years | Total | 105,364.2 | 63,763.6 | 16,697.6 | 9,273.7 |
| | of follow-up | Men | 48,276.7 | 29,504.1 | 7,025.0 | 3,786.3 |
| | | Women | 57,087.5 | 34,259.5 | 9,672.6 | 5,487.4 |
| | Incidence | Total | 11.9 | 15.4 | 22.2 | 28.1 |
| | rate per 100 person-years | Men | 12.0 | 15.6 | 23.3 | 30.2 |
| | | Women | 11.8 | 15.2 | 21.5 | 26.6 |
| Dementia | Number at | Total | 37,859 | 22,814 | 6,070 | 3,252 |
| | risk | Men | 17,492 | 10,719 | 2,625 | 1,402 |
| | | Women | 20,367 | 12,095 | 3,445 | 1,850 |
| | Number of | Total | 2,858 | 4,239 | 1,610 | 1,003 |
| | events | Men | 1,199 | 1,928 | 690 | 444 |
| | | Women | 1,659 | 2,311 | 920 | 559 |
| | Person-years | Total | 100,727.8 | 55,901.8 | 13,136.2 | 6,392.0 |
| | of follow-up | Men | 46,553.6 | 26,444.4 | 5,678.7 | 2,694.1 |
| | | Women | 54,174.3 | 29,457.4 | 7,457.5 | 3,697.8 |
| | Incidence | Total | 2.8 | 7.6 | 12.3 | 15.7 |
| | rate per 100 person-years | Men | 2.6 | 7.3 | 12.2 | 16.5 |
| | | Women | 3.1 | 7.8 | 12.3 | 15.1 |

Supplementary Analysis – Associations using a 24-month landmark period

 Table 5: Delirium episodes and the occurrence of death and dementia using a 24-month landmark period

Note: Person-years of follow-up was calculated as observation time subsequent to the landmark period.

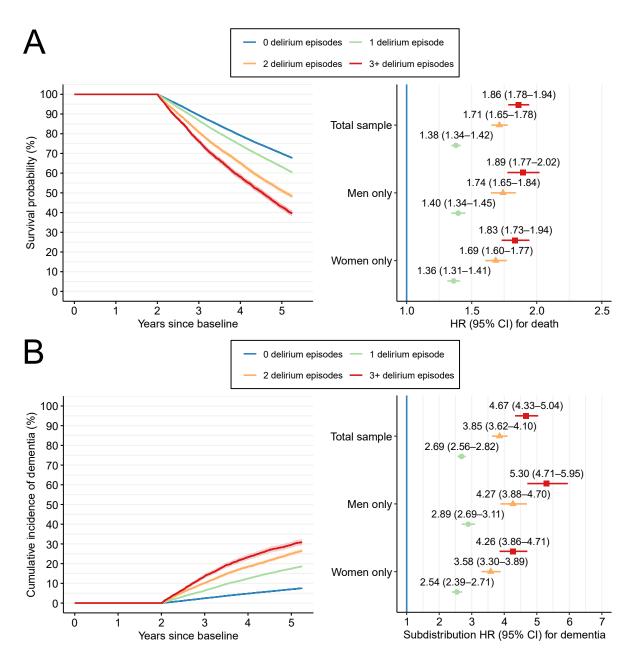


Figure 1A and B. Association of delirium episodes recorded within a 24-month landmark period with (A) death and (B) dementia. Associations presented in forest plots were adjusted for age and gender at baseline, as well as number of hospital episodes recorded within the landmark period.

| Outcome | Statistic | Sample | No delirium group | Delirium group |
|----------|------------------------|--------|-------------------|----------------|
| Death | Number at risk | Total | 571,256 | 55,211 |
| | | Men | 260,091 | 26,339 |
| | | Women | 311,165 | 28,872 |
| | Number of events | Total | 100,757 | 35,377 |
| | | Men | 47,731 | 17,403 |
| | | Women | 53,026 | 17,974 |
| | Person-years of | Total | 2,731,698.5 | 171,404.3 |
| | follow-up | Men | 1,237,326.0 | 77,862.0 |
| | | Women | 1,494,372.5 | 93,542.3 |
| | Incidence rate per 100 | Total | 3.7 | 20.6 |
| | person-years | Men | 3.9 | 22.4 |
| | | Women | 3.5 | 19.2 |
| Dementia | Number at risk | Total | 571,256 | 55,211 |
| | | Men | 260,091 | 26,339 |
| | | Women | 311,165 | 28,872 |
| | Number of events | Total | 33,505 | 13,966 |
| | | Men | 13,390 | 6,219 |
| | | Women | 20,115 | 7,747 |
| | Person-years of | Total | 2,683,183.2 | 151,842.2 |
| | follow-up | Men | 1,220,331.5 | 70,195.7 |
| | | Women | 1,462,851.7 | 81,646.5 |
| | Incidence rate per 100 | Total | 1.2 | 9.2 |
| | person-years | Men | 1.1 | 8.9 |
| | | Women | 1.4 | 9.5 |

Table 6: Delirium and the occurrence of death and dementia in the total eligible cohort (N = 626, 467)

Supplementary Analysis – Associations in the total eligible cohort (N = 626,467)

6

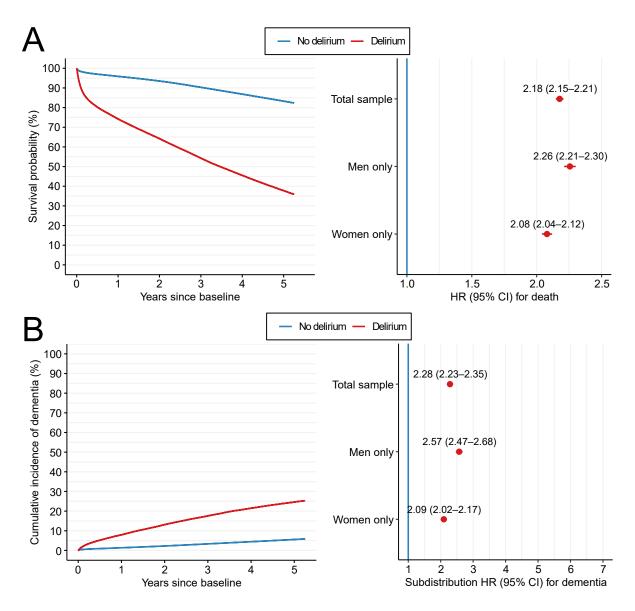
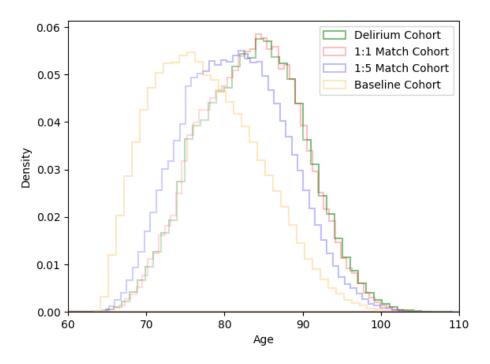


Figure 2A and 2B. Association of baseline delirium group with (A) death and (B) dementia. Associations presented in forest plots were adjusted for age, gender, Hospital Frailty Risk Score, primary diagnosis ICD-10 category, episode length of stay, and ICU length of stay.

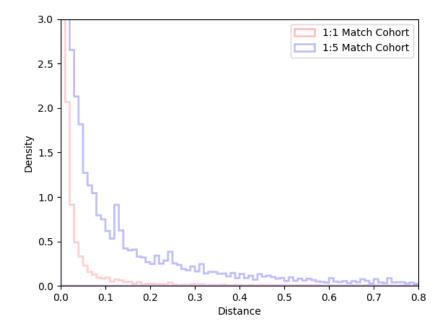
Figure 3A and 3B: Density plots of 1:1 and 1:5 matching for delirium and no delirium groups for A) age and B) overall matching distance.

A:



Note: baseline cohort = total eligible sample (N = 626, 467)

B:



STROBE Statement Checklist

| | Item No | Recommendation | Manuscript Page/s |
|---------------------------|------------|---|-------------------|
| Title and abstract | | : | |
| | 1 | (<i>a</i>) Indicate the study's design with a commonly used term in the title or the abstract | 1, 2 |
| | | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | 2 |
| Introduction | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 3 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 3 |
| Methods | | | |
| Study design | 4 | Present key elements of study design early in the paper | 3, 4 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 3-5 |
| Participants | 6 | (a) Cohort study Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow- up | 4, 5 |
| | | (b) Cohort study For matched studies, give matching criteria and number of exposed and unexposed | 4 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 4,5 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). | 4,5 |

| | Item No | Recommendation | Manuscript Page/s | | |
|------------------------|------------|---|-------------------|--|--|
| | | Describe comparability of assessment methods if there is more than one group | | | |
| Bias | 9 | Describe any efforts to address potential sources of bias | 5, 6 | | |
| Study size | 10 | Explain how the study size was arrived at | 4, 5 | | |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 5 | | |
| | | (<i>a</i>) Describe all statistical methods, including those used to control for confounding | 5, 6 | | |
| | | (<i>b</i>) Describe any methods 5, 6 used to examine subgroups and interactions | | | |
| Statistical methods | 12 | (c) Explain how missing data were addressed | NA | | |
| | | data were addressed(d) Cohort study Ifapplicable, explain how lossto follow-up was addressed | | | |
| | | (e) Describe any sensitivity analyses | 5, 6 | | |
| Results | | | | | |
| Participants | | (<i>a</i>) Report numbers of individuals at each stage of study eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 4, 5 | | |
| | | (b) Give reasons for non- participation at each stage | NA | | |
| | | (c) Consider use of a flow diagram | 5 | | |
| Descriptive data | 14* | (<i>a</i>)Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 7, 8 | | |
| | | (b) Indicate number of participants with missing | NA | | |

| | Item No | Recommendation | Manuscript Page/s | | | |
|-------------------|------------------------------------|---|-------------------|--|--|--|
| | data for each variable of interest | | | | | |
| | | (c) Cohort study Summarise follow-up time (eg average and total amount) | 9 | | | |
| Outcome data | 15* | <i>Cohort study</i> Report numbers of outcome events or summary measures over time | 9 | | | |
| Main results | 16 | (<i>a</i>) Report the numbers of individuals at each stage of the study eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 4-9 | | | |
| | | (<i>b</i>) Give reasons for non- participation at each stage | | | | |
| | | (c) Consider use of a flow diagram | 5 | | | |
| Other analyses | 17 | Report other analyses done eg analyses of subgroups and interactions, and sensitivity analyses | 10,11 | | | |
| Discussion | | | | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 11 | | | |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 14 | | | |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 15 | | | |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 14 | | | |
| Other information | | 1 | | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original | 17 | | | |

| Item No | Recommendation | Manuscript Page/s |
|------------|---|-------------------|
| | study on which the present article is based | |