Blood pressure in frail older adults: associations with cardiovascular outcomes and all-cause mortality

**Supplementary Material**

**Contents**

**Appendix 1:** Flow diagram to show population selection and exclusions

**Appendix 2:** Baseline median systolic blood pressure and hazard ratio of all-cause mortality, stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date and sex.

**Appendix 3:** Baseline median systolic blood pressure and hazard ratio of all-cause mortality, stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, sex, blood pressure decline and cardiovascular risk.

**Appendix 4:** Baseline median diastolic blood pressure and hazard ratio of all-cause mortality, stratified by eFI frailty status**.** Adjusted for index of multiple deprivation, age at index date, and sex.

**Appendix 5:** Baseline systolic blood pressure and hazard ratio of incident myocardial infarction or related procedure (competing risk model with death as competing risk), stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, and sex.

**Appendix 6:** Baseline systolic blood pressure and hazard ratio of incident myocardial infarction or related procedure (competing risk model with death as competing risk), stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, sex, blood pressure decline and cardiovascular risk.

**Appendix 7:** Baseline systolic blood pressure and hazard ratio of incident heart failure (competing risk model with death as competing risk), stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, and sex.

**Appendix 8:** Baseline systolic blood pressure and incident heart failure (competing risk model with death as competing risk), stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, sex, blood pressure decline and cardiovascular risk.

**Appendix 9:** Baseline systolic blood pressure and incident stroke (competing risk model with death as competing risk), stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, and sex.

**Appendix 10:** Baseline systolic blood pressure and incident stroke (competing risk model with death as competing risk), stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, sex, blood pressure decline and cardiovascular risk.

**Appendix 11:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality, stratified by eFI frailty status in 75 to 84 year olds by prevalent diagnosed hypertension status at baseline. Adjusted for index of multiple deprivation, age at index date, and sex.

**Appendix 12:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality in 75 to 84 year olds without prevalent heart failure at baseline, stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, and sex.

**Appendix 13:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality in 75 to 84 year olds without prevalent cancer at baseline, stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, and sex.

**Appendix 14:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality in 75 to 84 year olds by prevalent diabetes at baseline, stratified by eFI frailty. Adjusted for index of multiple deprivation, age at index date, and sex.

**Appendix 15:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality in 75 to 84 year olds with SBP decline prior to baseline versus no decline in 75 to 84 year olds, stratified by eFI frailty status. Adjusted for index of multiple deprivation and sex.

**Appendix 16:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality in 75 to 84 year olds excluding those who died within 6 months of index date (N=7092 excluded), stratified by eFI frailty status Adjusted for index of multiple deprivation, age at index date, and sex.

**Appendix 17:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality in 75 to 84 year olds by smoking status, stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, and sex.

**Appendix 18: Supplementary Methods Data Analysis**

**Appendix 19:** Hypertension coding adapted from QoF

**Appendix 20:** Heart failure coding adapted from QoF

**Appendix 21:** Diabetes coding adapted from QoF

**Appendix 22:** ICD10 codes for myocardial infarction

**Appendix 23:** ICD10 codes for stroke

**Appendix 1:** Flow diagram to show population selection and exclusions

(n=510, 503)

(n=640, 471)

Exclusion

  Age at end of follow-up <75

  Age of BP measurement >72

 (n=876,802)

(n=1,517,273)

Assessed for eligibility (n=1,942,484 )

Exclusion

  <3 blood pressure measurements in 3 year lead-in period prior to index date

 (n=129,968)

Exclusion

  Insufficient follow-up period

limitations: 14th November 2014

Not registered at practice

Died within 30 days of index

 (n=94,523)

Included in analysis

(n=415, 980)

Data cleaning

  Patient not registered at participating

practice within study dates or BP

measures outside study dates

(n=425,211)

**Appendix 2:** Baseline median systolic blood pressure and hazard ratio of all-cause mortality, stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date and sex.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** |
| **<120** | 1.50 | 1.42 | 1.58 | <0.001 | 1.65 | 1.57 | 1.74 | <0.001 | 1.60 | 1.44 | 1.78 | <0.001 |
| **120-129** | 1.11 | 1.07 | 1.16 | <0.001 | 1.16 | 1.12 | 1.21 | <0.001 | 1.16 | 1.06 | 1.27 | <0.001 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.95 | 0.93 | 0.98 | <0.001 | 0.88 | 0.86 | 0.91 | <0.001 | 0.94 | 0.87 | 1.01 | 0.11 |
| **150-159** | 0.94 | 0.92 | 0.97 | <0.001 | 0.88 | 0.85 | 0.91 | <0.001 | 0.84 | 0.77 | 0.92 | <0.001 |
| **160-169** | 0.99 | 0.96 | 1.02 | 0.67 | 0.90 | 0.87 | 0.94 | <0.001 | 0.86 | 0.78 | 0.95 | <0.001 |
| **170-179** | 1.09 | 1.05 | 1.13 | <0.001 | 0.97 | 0.92 | 1.02 | 0.22 | 0.88 | 0.76 | 1.01 | 0.07 |
| **≥180** | 1.26 | 1.20 | 1.33 | <0.001 | 1.12 | 1.05 | 1.20 | <0.001 | 1.04 | 0.87 | 1.25 | 0.64 |
|  | **Age ≥ 85 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** |
| **<120** | 1.41 | 1.30 | 1.52 | <0.001 | 1.49 | 1.39 | 1.60 | <0.001 | 1.22 | 1.06 | 1.41 | 0.01 |
| **120-129** | 1.20 | 1.13 | 1.28 | <0.001 | 1.23 | 1.16 | 1.31 | <0.001 | 1.14 | 1.02 | 1.29 | 0.03 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.85 | 0.81 | 0.89 | <0.001 | 0.85 | 0.81 | 0.90 | <0.001 | 0.77 | 0.69 | 0.86 | <0.001 |
| **150-159** | 0.76 | 0.72 | 0.80 | <0.001 | 0.73 | 0.69 | 0.77 | <0.001 | 0.68 | 0.61 | 0.77 | <0.001 |
| **160-169** | 0.75 | 0.71 | 0.79 | <0.001 | 0.75 | 0.70 | 0.79 | <0.001 | 0.63 | 0.55 | 0.73 | <0.001 |
| **170-179** | 0.75 | 0.70 | 0.80 | <0.001 | 0.77 | 0.71 | 0.83 | <0.001 | 0.65 | 0.54 | 0.79 | <0.001 |
| **>=180** | 0.83 | 0.77 | 0.89 | <0.001 | 0.84 | 0.77 | 0.91 | <0.001 | 0.62 | 0.49 | 0.78 | <0.001 |

**Appendix 3:** Baseline median systolic blood pressure and hazard ratio of all-cause mortality, stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, sex, blood pressure decline and cardiovascular risk.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** |
| **<120** | 1.50 | 1.42 | 1.58 | <0.001 | 1.65 | 1.57 | 1.74 | <0.001 | 1.60 | 1.44 | 1.78 | <0.001 |
| **120-129** | 1.11 | 1.07 | 1.16 | <0.001 | 1.16 | 1.12 | 1.21 | <0.001 | 1.16 | 1.06 | 1.27 | <0.001 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.95 | 0.93 | 0.98 | <0.001 | 0.88 | 0.86 | 0.91 | <0.001 | 0.94 | 0.87 | 1.01 | 0.11 |
| **150-159** | 0.94 | 0.92 | 0.97 | <0.001 | 0.88 | 0.85 | 0.91 | <0.001 | 0.84 | 0.77 | 0.92 | <0.001 |
| **160-169** | 0.99 | 0.96 | 1.02 | 0.67 | 0.90 | 0.87 | 0.94 | <0.001 | 0.86 | 0.78 | 0.95 | <0.001 |
| **170-179** | 1.09 | 1.05 | 1.13 | <0.001 | 0.97 | 0.92 | 1.02 | 0.22 | 0.88 | 0.76 | 1.01 | 0.07 |
| **≥180** | 1.26 | 1.20 | 1.33 | <0.001 | 1.12 | 1.05 | 1.20 | <0.001 | 1.04 | 0.87 | 1.25 | 0.64 |
|  | **Age ≥ 85 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** |
| **<120** | 1.41 | 1.30 | 1.52 | <0.001 | 1.49 | 1.39 | 1.60 | <0.001 | 1.22 | 1.06 | 1.41 | 0.01 |
| **120-129** | 1.20 | 1.13 | 1.28 | <0.001 | 1.23 | 1.16 | 1.31 | <0.001 | 1.14 | 1.02 | 1.29 | 0.03 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.85 | 0.81 | 0.89 | <0.001 | 0.85 | 0.81 | 0.90 | <0.001 | 0.77 | 0.69 | 0.86 | <0.001 |
| **150-159** | 0.76 | 0.72 | 0.80 | <0.001 | 0.73 | 0.69 | 0.77 | <0.001 | 0.68 | 0.61 | 0.77 | <0.001 |
| **160-169** | 0.75 | 0.71 | 0.79 | <0.001 | 0.75 | 0.70 | 0.79 | <0.001 | 0.63 | 0.55 | 0.73 | <0.001 |
| **170-179** | 0.75 | 0.70 | 0.80 | <0.001 | 0.77 | 0.71 | 0.83 | <0.001 | 0.65 | 0.54 | 0.79 | <0.001 |
| **>=180** | 0.83 | 0.77 | 0.89 | <0.001 | 0.84 | 0.77 | 0.91 | <0.001 | 0.62 | 0.49 | 0.78 | <0.001 |

**Appendix 4:** Baseline median diastolic blood pressure and hazard ratio of all-cause mortality, stratified by eFI frailty status**.** Adjusted for index of multiple deprivation, age at index date, and sex.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years** |
|  | **Non-frail** |  | **Mild frailty** |  | **Moderate to severe frailty** |
| **diastolic blood pressure (mmHg)** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** | **HR** |
| **<80** | 1.08 | 1.06 | 1.10 | <0.001 | 1.19 | 1.16 | 1.21 | <0.001 | 1.19 |
| **80-90 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 |
| **≥90** | 1.08 | 1.06 | 1.11 | <0.001 | 1.07 | 1.03 | 1.11 | <0.001 | 1.01 |
|  | **Age ≥ 85 years** |
|  | **Non-frail** |  | **Mild frailty** |  | **Moderate to severe frailty** |
| **diastolic blood pressure (mmHg)** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** | **HR** |
| **<80** | 1.15 | 1.12 | 1.19 | <0.001 | 1.18 | 1.14 | 1.22 | <0.001 | 1.20 |
| **80-90 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 |
| **≥90** | 1.02 | 0.98 | 1.07 | 0.35 | 0.99 | 0.94 | 1.05 | 0.84 | 0.91 |

**Appendix 5:** Baseline systolic blood pressure and hazard ratio of incident myocardial infarction or related procedure (competing risk model with death as competing risk), stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, and sex.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | 1.21 | 1.06 | 1.39 | 0.006 | 1.02 | 0.89 | 1.18 | 0.733 | 1.14 | 0.84 | 1.54 | 0.407 |
| **120-129** | 1.12 | 1.02 | 1.22 | 0.013 | 0.94 | 0.85 | 1.03 | 0.168 | 1.08 | 0.86 | 1.36 | 0.52 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 1.03 | 0.98 | 1.09 | 0.27 | 0.95 | 0.89 | 1.02 | 0.146 | 1.11 | 0.93 | 1.32 | 0.263 |
| **150-159** | 1.07 | 1.01 | 1.14 | 0.028 | 1.01 | 0.94 | 1.09 | 0.701 | 1.22 | 1.00 | 1.49 | 0.046 |
| **160-169** | 1.22 | 1.15 | 1.31 | <0.001 | 1.14 | 1.05 | 1.23 | 0.002 | 1.36 | 1.09 | 1.69 | 0.006 |
| **170-179** | 1.26 | 1.16 | 1.38 | <0.001 | 1.21 | 1.09 | 1.35 | <0.001 | 1.76 | 1.33 | 2.32 | <0.001 |
| **≥180** | 1.47 | 1.32 | 1.64 | <0.001 | 1.68 | 1.46 | 1.92 | <0.001 | 2.30 | 1.64 | 3.23 | <0.001 |
|  | **Age ≥ 85 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** |
| **<120** | 0.88 | 0.64 | 1.21 | 0.441 | 0.82 | 0.60 | 1.12 | 0.218 | 0.68 | 0.32 | 1.45 | 0.322 |
| **120-129** | 0.80 | 0.63 | 1.00 | 0.048 | 0.86 | 0.70 | 1.07 | 0.185 | 1.00 | 0.60 | 1.67 | 0.991 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.95 | 0.82 | 1.09 | 0.45 | 0.98 | 0.84 | 1.15 | 0.843 | 1.30 | 0.88 | 1.91 | 0.191 |
| **150-159** | 0.99 | 0.86 | 1.15 | 0.935 | 1.09 | 0.93 | 1.28 | 0.271 | 1.58 | 1.06 | 2.35 | 0.024 |
| **160-169** | 1.10 | 0.95 | 1.28 | 0.212 | 1.31 | 1.11 | 1.54 | 0.001 | 1.63 | 1.07 | 2.49 | 0.024 |
| **170-179** | 1.00 | 0.83 | 1.21 | 0.988 | 1.26 | 1.03 | 1.55 | 0.026 | 1.92 | 1.14 | 3.22 | 0.014 |
| **>=180** | 1.21 | 0.99 | 1.48 | 0.069 | 1.55 | 1.22 | 1.96 | <0.001 | 1.11 | 0.53 | 2.30 | 0.784 |

**Appendix 6:** Baseline systolic blood pressure and hazard ratio of incident myocardial infarction or related procedure (competing risk model with death as competing risk), stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, sex, blood pressure decline and cardiovascular risk.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** |
| **<120** | 1.21 | 1.06 | 1.39 | 0.005 | 1.03 | 0.89 | 1.18 | 0.707 | 1.09 | 0.79 | 1.50 | 0.585 |
| **120-129** | 1.12 | 1.03 | 1.22 | 0.011 | 0.94 | 0.85 | 1.03 | 0.171 | 1.09 | 0.86 | 1.37 | 0.497 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 1.03 | 0.97 | 1.09 | 0.276 | 0.95 | 0.89 | 1.02 | 0.13 | 1.11 | 0.93 | 1.34 | 0.255 |
| **150-159** | 1.07 | 1.01 | 1.14 | 0.029 | 1.01 | 0.94 | 1.09 | 0.751 | 1.24 | 1.01 | 1.52 | 0.036 |
| **160-169** | 1.22 | 1.14 | 1.31 | <0.001 | 1.13 | 1.05 | 1.23 | 0.002 | 1.37 | 1.10 | 1.72 | 0.006 |
| **170-179** | 1.26 | 1.16 | 1.38 | <0.001 | 1.21 | 1.08 | 1.35 | 0.001 | 1.86 | 1.41 | 2.47 | <0.001 |
| **≥180** | 1.47 | 1.32 | 1.64 | <0.001 | 1.67 | 1.46 | 1.91 | <0.001 | 2.25 | 1.58 | 3.20 | <0.001 |
|  | **Age ≥ 85 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** |
| **<120** | 0.89 | 0.65 | 1.22 | 0.465 | 0.83 | 0.61 | 1.13 | 0.233 | 0.76 | 0.35 | 1.62 | 0.473 |
| **120-129** | 0.80 | 0.63 | 1.00 | 0.049 | 0.87 | 0.70 | 1.07 | 0.189 | 1.13 | 0.67 | 1.90 | 0.646 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.95 | 0.82 | 1.09 | 0.461 | 0.98 | 0.84 | 1.15 | 0.847 | 1.27 | 0.84 | 1.92 | 0.261 |
| **150-159** | 1.00 | 0.86 | 1.15 | 0.968 | 1.10 | 0.94 | 1.29 | 0.256 | 1.68 | 1.11 | 2.55 | 0.015 |
| **160-169** | 1.10 | 0.95 | 1.28 | 0.206 | 1.32 | 1.12 | 1.55 | 0.001 | 1.77 | 1.14 | 2.75 | 0.011 |
| **170-179** | 1.00 | 0.83 | 1.20 | 0.983 | 1.26 | 1.03 | 1.55 | 0.027 | 2.08 | 1.21 | 3.56 | 0.008 |
| **>=180** | 1.21 | 0.99 | 1.48 | 0.069 | 1.56 | 1.23 | 1.97 | <0.001 | 1.31 | 0.62 | 2.74 | 0.479 |

**Appendix 7:** Baseline systolic blood pressure and hazard ratio of incident heart failure (competing risk model with death as competing risk), stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, and sex.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** |
| **<120** | 1.29 | 1.11 | 1.51 | 0.001 | 1.34 | 1.16 | 1.56 | <0.001 | 0.92 | 0.61 | 1.37 | 0.67 |
| **120-129** | 1.23 | 1.11 | 1.35 | <0.001 | 1.06 | 0.95 | 1.18 | 0.288 | 1.07 | 0.82 | 1.40 | 0.603 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 1.03 | 0.97 | 1.11 | 0.351 | 1.02 | 0.94 | 1.10 | 0.656 | 1.02 | 0.83 | 1.26 | 0.864 |
| **150-159** | 1.13 | 1.05 | 1.21 | 0.001 | 1.13 | 1.04 | 1.22 | 0.005 | 1.10 | 0.87 | 1.39 | 0.418 |
| **160-169** | 1.21 | 1.12 | 1.31 | <0.001 | 1.18 | 1.08 | 1.30 | <0.001 | 1.30 | 1.00 | 1.68 | 0.051 |
| **170-179** | 1.38 | 1.25 | 1.52 | <0.001 | 1.29 | 1.13 | 1.46 | <0.001 | 1.29 | 0.90 | 1.86 | 0.168 |
| **≥180** | 1.66 | 1.47 | 1.87 | <0.001 | 1.47 | 1.24 | 1.74 | <0.001 | 1.44 | 0.90 | 2.31 | 0.127 |
|  | **Age ≥ 85 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** | **HR** | **LCI** | **UCI** | **p value** |
| **<120** | 0.83 | 0.57 | 1.20 | 0.315 | 0.93 | 0.68 | 1.27 | 0.651 | 0.69 | 0.32 | 1.47 | 0.335 |
| **120-129** | 1.19 | 0.95 | 1.48 | 0.132 | 0.86 | 0.68 | 1.09 | 0.211 | 0.87 | 0.52 | 1.43 | 0.574 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 1.05 | 0.89 | 1.23 | 0.571 | 0.98 | 0.83 | 1.16 | 0.829 | 0.91 | 0.62 | 1.35 | 0.639 |
| **150-159** | 1.12 | 0.96 | 1.31 | 0.163 | 0.97 | 0.82 | 1.16 | 0.738 | 0.99 | 0.66 | 1.50 | 0.962 |
| **160-169** | 1.23 | 1.04 | 1.45 | 0.015 | 1.19 | 1.00 | 1.43 | 0.052 | 0.85 | 0.53 | 1.34 | 0.48 |
| **170-179** | 1.21 | 0.99 | 1.48 | 0.06 | 1.10 | 0.87 | 1.39 | 0.407 | 1.22 | 0.68 | 2.20 | 0.499 |
| **>=180** | 1.54 | 1.25 | 1.90 | <0.001 | 0.98 | 0.73 | 1.32 | 0.897 | 1.44 | 0.76 | 2.73 | 0.258 |

**Appendix 8:** Baseline systolic blood pressure and incident heart failure (competing risk model with death as competing risk), stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, sex, blood pressure decline and cardiovascular risk.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR mortality** | **LCI** | **UCI** | **p value** | **HR mortality** | **LCI** | **UCI** | **p value** | **HR mortality** | **LCI** | **UCI** | **p value** |
| **<120** | 1.30 | 1.11 | 1.51 | 0.001 | 1.35 | 1.16 | 1.57 | 1.164 | 0.88 | 0.58 | 1.36 | 0.573 |
| **120-129** | 1.23 | 1.12 | 1.36 | <0.001 | 1.06 | 0.95 | 1.18 | 0.954 | 1.08 | 0.82 | 1.42 | 0.606 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 1.03 | 0.96 | 1.11 | 0.353 | 1.02 | 0.94 | 1.10 | 0.940 | 1.00 | 0.81 | 1.24 | 0.99 |
| **150-159** | 1.13 | 1.05 | 1.21 | 0.001 | 1.12 | 1.03 | 1.22 | 1.034 | 1.07 | 0.84 | 1.36 | 0.588 |
| **160-169** | 1.21 | 1.12 | 1.31 | <0.001 | 1.18 | 1.08 | 1.30 | 1.077 | 1.32 | 1.02 | 1.72 | 0.038 |
| **170-179** | 1.38 | 1.25 | 1.52 | <0.001 | 1.29 | 1.13 | 1.46 | 1.135 | 1.23 | 0.84 | 1.78 | 0.289 |
| **≥180** | 1.66 | 1.47 | 1.87 | <0.001 | 1.47 | 1.24 | 1.75 | 1.242 | 1.47 | 0.91 | 2.35 | 0.112 |
|  | **Age ≥ 85 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR mortality** | **LCI** | **UCI** | **p value** | **HR mortality** | **LCI** | **UCI** | **p value** | **HR mortality** | **LCI** | **UCI** | **p value** |
| **<120** | 0.83 | 0.57 | 1.19 | 0.309 | 0.93 | 0.68 | 1.27 | 0.649 | 0.54 | 0.23 | 1.29 | 0.166 |
| **120-129** | 1.18 | 0.95 | 1.47 | 0.143 | 0.86 | 0.68 | 1.09 | 0.212 | 0.86 | 0.52 | 1.44 | 0.574 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 1.04 | 0.89 | 1.22 | 0.588 | 0.98 | 0.83 | 1.16 | 0.821 | 0.88 | 0.59 | 1.32 | 0.542 |
| **150-159** | 1.12 | 0.95 | 1.31 | 0.167 | 0.97 | 0.81 | 1.15 | 0.718 | 0.99 | 0.65 | 1.50 | 0.951 |
| **160-169** | 1.22 | 1.04 | 1.44 | 0.016 | 1.20 | 1.00 | 1.43 | 0.050 | 0.87 | 0.54 | 1.39 | 0.55 |
| **170-179** | 1.21 | 0.99 | 1.48 | 0.065 | 1.11 | 0.88 | 1.40 | 0.396 | 1.30 | 0.72 | 2.34 | 0.383 |
| **>=180** | 1.53 | 1.24 | 1.88 | <0.001 | 0.99 | 0.73 | 1.33 | 0.928 | 1.63 | 0.86 | 3.10 | 0.137 |

**Appendix 9:** Baseline systolic blood pressure and incident stroke (competing risk model with death as competing risk), stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, and sex.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | 0.91 | 0.75 | 1.12 | 0.38 | 0.91 | 0.73 | 1.12 | 0.367 | 0.74 | 0.46 | 1.19 | 0.217 |
| **120-129** | 1.01 | 0.90 | 1.14 | 0.849 | 1.00 | 0.87 | 1.15 | 0.986 | 0.81 | 0.58 | 1.14 | 0.223 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 1.10 | 1.02 | 1.19 | 0.014 | 1.14 | 1.03 | 1.25 | 0.009 | 0.88 | 0.68 | 1.13 | 0.309 |
| **150-159** | 1.16 | 1.07 | 1.25 | <0.001 | 1.10 | 0.99 | 1.22 | 0.068 | 1.00 | 0.76 | 1.32 | 1 |
| **160-169** | 1.28 | 1.18 | 1.40 | <0.001 | 1.20 | 1.07 | 1.34 | 0.002 | 1.02 | 0.74 | 1.42 | 0.893 |
| **170-179** | 1.47 | 1.32 | 1.63 | <0.001 | 1.45 | 1.25 | 1.68 | <0.001 | 0.76 | 0.45 | 1.28 | 0.306 |
| **≥180** | 1.79 | 1.57 | 2.04 | <0.001 | 1.97 | 1.64 | 2.37 | <0.001 | 1.34 | 0.76 | 2.36 | 0.315 |
|  | **Age ≥ 85 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | 0.93 | 0.62 | 1.38 | 0.703 | 0.72 | 0.48 | 1.09 | 0.122 | 1.11 | 0.55 | 2.23 | 0.78 |
| **120-129** | 1.05 | 0.81 | 1.37 | 0.708 | 0.97 | 0.74 | 1.27 | 0.833 | 0.87 | 0.49 | 1.55 | 0.638 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 1.12 | 0.94 | 1.34 | 0.213 | 0.96 | 0.79 | 1.17 | 0.697 | 0.98 | 0.62 | 1.54 | 0.915 |
| **150-159** | 1.24 | 1.04 | 1.48 | 0.019 | 1.17 | 0.95 | 1.43 | 0.131 | 1.10 | 0.69 | 1.77 | 0.677 |
| **160-169** | 1.14 | 0.94 | 1.38 | 0.18 | 1.11 | 0.89 | 1.38 | 0.345 | 0.81 | 0.47 | 1.40 | 0.45 |
| **170-179** | 1.42 | 1.14 | 1.76 | 0.001 | 1.53 | 1.19 | 1.97 | 0.001 | 1.35 | 0.73 | 2.52 | 0.342 |
| **>=180** | 1.48 | 1.17 | 1.88 | 0.001 | 1.50 | 1.11 | 2.02 | 0.009 | 0.99 | 0.42 | 2.33 | 0.988 |

**Appendix 10:** Baseline systolic blood pressure and incident stroke (competing risk model with death as competing risk), stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, sex, blood pressure decline and cardiovascular risk.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | 0.91 | 0.75 | 1.12 | 0.373 | 0.91 | 0.73 | 1.12 | 0.367 | 0.74 | 0.46 | 1.21 | 0.235 |
| **120-129** | 1.01 | 0.90 | 1.14 | 0.856 | 1.00 | 0.87 | 1.15 | 0.985 | 0.82 | 0.58 | 1.16 | 0.259 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 1.10 | 1.02 | 1.19 | 0.014 | 1.14 | 1.03 | 1.25 | 0.009 | 0.85 | 0.66 | 1.09 | 0.205 |
| **150-159** | 1.16 | 1.07 | 1.25 | 0 | 1.10 | 0.99 | 1.22 | 0.068 | 0.96 | 0.72 | 1.28 | 0.762 |
| **160-169** | 1.29 | 1.18 | 1.40 | 0 | 1.20 | 1.07 | 1.34 | 0.002 | 0.95 | 0.68 | 1.33 | 0.762 |
| **170-179** | 1.47 | 1.32 | 1.63 | 0 | 1.45 | 1.25 | 1.68 | 0 | 0.78 | 0.46 | 1.31 | 0.345 |
| **≥180** | 1.79 | 1.57 | 2.04 | 0 | 1.97 | 1.64 | 2.37 | 0 | 1.38 | 0.78 | 2.44 | 0.274 |
|  | **Age ≥ 85 years** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | 0.92 | 0.62 | 1.38 | 0.693 | 0.72 | 0.48 | 1.10 | 0.127 | 1.00 | 0.46 | 2.19 | 0.998 |
| **120-129** | 1.05 | 0.81 | 1.37 | 0.705 | 0.97 | 0.74 | 1.27 | 0.839 | 0.88 | 0.47 | 1.64 | 0.688 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 1.12 | 0.94 | 1.34 | 0.215 | 0.96 | 0.79 | 1.18 | 0.698 | 1.05 | 0.65 | 1.71 | 0.843 |
| **150-159** | 1.23 | 1.03 | 1.47 | 0.02 | 1.17 | 0.95 | 1.43 | 0.131 | 1.19 | 0.73 | 1.95 | 0.491 |
| **160-169** | 1.14 | 0.94 | 1.38 | 0.179 | 1.11 | 0.90 | 1.38 | 0.337 | 0.84 | 0.47 | 1.50 | 0.553 |
| **170-179** | 1.42 | 1.15 | 1.76 | 0.001 | 1.53 | 1.19 | 1.97 | 0.001 | 1.48 | 0.77 | 2.84 | 0.241 |
| **>=180** | 1.49 | 1.17 | 1.89 | 0.001 | 1.50 | 1.11 | 2.03 | 0.008 | 1.17 | 0.49 | 2.80 | 0.723 |

**Appendix 11:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality, stratified by eFI frailty status in 75 to 84 year olds by prevalent diagnosed hypertension status at baseline. Adjusted for index of multiple deprivation, age at index date, and sex.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years with hypertension** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR mortality** | **LCI** | **UCI** | **p value** | **HR mortality** | **LCI** | **UCI** | **p value** | **HR mortality** | **LCI** | **UCI** | **p value** |
| **<120** | 1.91 | 1.69 | 2.16 | <0.001 | 1.88 | 1.72 | 2.05 | <0.001 | 1.63 | 1.40 | 1.91 | <0.001 |
| **120-129** | 1.18 | 1.10 | 1.27 | <0.001 | 1.24 | 1.17 | 1.32 | <0.001 | 1.21 | 1.08 | 1.36 | 0.001 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.95 | 0.91 | 0.99 | 0.011 | 0.90 | 0.86 | 0.94 | <0.001 | 0.97 | 0.89 | 1.06 | 0.539 |
| **150-159** | 0.92 | 0.89 | 0.96 | <0.001 | 0.89 | 0.86 | 0.93 | <0.001 | 0.85 | 0.77 | 0.94 | 0.002 |
| **160-169** | 0.97 | 0.93 | 1.01 | 0.104 | 0.91 | 0.87 | 0.95 | <0.001 | 0.86 | 0.76 | 0.96 | 0.007 |
| **170-179** | 1.03 | 0.98 | 1.09 | 0.22 | 0.99 | 0.93 | 1.05 | 0.67 | 0.87 | 0.75 | 1.02 | 0.077 |
| **≥180** | 1.24 | 1.17 | 1.32 | <0.001 | 1.13 | 1.05 | 1.22 | 0.002 | 1.06 | 0.88 | 1.28 | 0.523 |
|  | **Age 75 to 84 years without hypertension** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | 1.45 | 1.36 | 1.54 | <0.001 | 1.49 | 1.40 | 1.59 | <0.001 | 1.53 | 1.32 | 1.77 | <0.001 |
| **120-129** | 1.09 | 1.04 | 1.14 | <0.001 | 1.08 | 1.03 | 1.14 | 0.004 | 1.09 | 0.95 | 1.26 | 0.232 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.94 | 0.91 | 0.97 | <0.001 | 0.89 | 0.85 | 0.93 | <0.001 | 0.87 | 0.76 | 1.00 | 0.055 |
| **150-159** | 0.95 | 0.91 | 0.99 | 0.013 | 0.92 | 0.87 | 0.97 | 0.004 | 0.88 | 0.72 | 1.07 | 0.19 |
| **160-169** | 1.01 | 0.96 | 1.06 | 0.745 | 1.01 | 0.93 | 1.09 | 0.853 | 0.98 | 0.76 | 1.25 | 0.852 |
| **170-179** | 1.19 | 1.10 | 1.28 | <0.001 | 1.03 | 0.90 | 1.18 | 0.634 | 1.04 | 0.65 | 1.67 | 0.867 |
| **>=180** | 1.22 | 1.09 | 1.36 | <0.001 | 1.43 | 1.16 | 1.76 | 0.001 | 0.90 | 0.43 | 1.90 | 0.781 |

**Appendix 12:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality in 75 to 84 year olds without prevalent heart failure at baseline, stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, and sex.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years without prevalent heart failure** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | 1.45 | 1.38 | 1.52 | <0.001 | 1.59 | 1.52 | 1.67 | <0.001 | 1.32 | 1.18 | 1.49 | <0.001 |
| **120-129** | 1.13 | 1.10 | 1.17 | <0.001 | 1.17 | 1.13 | 1.22 | <0.001 | 1.08 | 0.99 | 1.19 | 0.094 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.94 | 0.91 | 0.96 | <0.001 | 0.87 | 0.85 | 0.90 | <0.001 | 0.85 | 0.79 | 0.91 | <0.001 |
| **150-159** | 0.91 | 0.89 | 0.94 | <0.001 | 0.85 | 0.82 | 0.87 | <0.001 | 0.76 | 0.70 | 0.83 | <0.001 |
| **160-169** | 0.95 | 0.92 | 0.97 | <0.001 | 0.86 | 0.83 | 0.89 | <0.001 | 0.75 | 0.68 | 0.82 | <0.001 |
| **170-179** | 1.00 | 0.97 | 1.04 | 0.788 | 0.91 | 0.87 | 0.95 | <0.001 | 0.79 | 0.69 | 0.90 | 0.001 |
| **>=180** | 1.13 | 1.08 | 1.17 | <0.001 | 1.03 | 0.97 | 1.09 | 0.351 | 0.87 | 0.73 | 1.02 | 0.093 |

**Appendix 13:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality in 75 to 84 year olds without prevalent cancer at baseline, stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, and sex.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years excluding prevalent cancer** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | 1.49 | 1.40 | 1.58 | <0.001 | 1.67 | 1.58 | 1.76 | <0.001 | 1.67 | 1.49 | 1.88 | <0.001 |
| **120-129** | 1.10 | 1.05 | 1.15 | <0.001 | 1.17 | 1.12 | 1.22 | <0.001 | 1.18 | 1.07 | 1.31 | 0.001 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.96 | 0.93 | 0.98 | 0.003 | 0.88 | 0.85 | 0.91 | <0.001 | 0.93 | 0.86 | 1.01 | 0.09 |
| **150-159** | 0.95 | 0.92 | 0.98 | <0.001 | 0.87 | 0.84 | 0.90 | <0.001 | 0.84 | 0.76 | 0.93 | <0.001 |
| **160-169** | 0.99 | 0.96 | 1.03 | 0.669 | 0.89 | 0.85 | 0.93 | <0.001 | 0.84 | 0.75 | 0.94 | 0.002 |
| **170-179** | 1.09 | 1.05 | 1.14 | <0.001 | 0.98 | 0.93 | 1.04 | 0.517 | 0.86 | 0.73 | 1.00 | 0.053 |
| **≥180** | 1.30 | 1.23 | 1.37 | <0.001 | 1.13 | 1.05 | 1.22 | 0.001 | 0.96 | 0.79 | 1.17 | 0.689 |

**Appendix 14:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality in 75 to 84 year olds with and without prevalent diabetes at baseline, stratified by eFI frailty. Adjusted for index of multiple deprivation, age at index date, and sex.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years with diabetes** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | 1.77 | 1.44 | 2.18 | <0.001 | 1.63 | 1.44 | 1.85 | <0.001 | 1.52 | 1.26 | 1.83 | <0.001 |
| **120-129** | 1.15 | 1.01 | 1.30 | 0.038 | 1.24 | 1.14 | 1.35 | <0.001 | 1.19 | 1.03 | 1.37 | 0.021 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 1.03 | 0.94 | 1.12 | 0.542 | 0.90 | 0.84 | 0.96 | 0.002 | 0.94 | 0.84 | 1.07 | 0.351 |
| **150-159** | 1.05 | 0.95 | 1.15 | 0.343 | 0.88 | 0.82 | 0.95 | 0.001 | 0.88 | 0.75 | 1.03 | 0.11 |
| **160-169** | 1.06 | 0.95 | 1.19 | 0.262 | 0.89 | 0.81 | 0.97 | 0.01 | 0.80 | 0.66 | 0.98 | 0.031 |
| **170-179** | 1.15 | 0.99 | 1.33 | 0.067 | 0.94 | 0.82 | 1.07 | 0.353 | 1.03 | 0.78 | 1.36 | 0.828 |
| **≥180** | 1.31 | 1.07 | 1.60 | 0.008 | 1.10 | 0.91 | 1.33 | 0.309 | 0.99 | 0.69 | 1.44 | 0.975 |
|  | **Age 75 to 84 years without diabetes** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | 1.49 | 1.41 | 1.57 | <0.001 | 1.65 | 1.56 | 1.74 | <0.001 | 1.64 | 1.45 | 1.87 | <0.001 |
| **120-129** | 1.11 | 1.07 | 1.15 | <0.001 | 1.14 | 1.09 | 1.19 | <0.001 | 1.16 | 1.04 | 1.30 | 0.01 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.94 | 0.92 | 0.97 | <0.001 | 0.87 | 0.84 | 0.90 | <0.001 | 0.93 | 0.85 | 1.03 | 0.153 |
| **150-159** | 0.94 | 0.91 | 0.96 | <0.001 | 0.87 | 0.84 | 0.90 | <0.001 | 0.83 | 0.74 | 0.92 | <0.001 |
| **160-169** | 0.99 | 0.96 | 1.02 | 0.497 | 0.89 | 0.85 | 0.93 | <0.001 | 0.87 | 0.78 | 0.98 | 0.025 |
| **170-179** | 1.08 | 1.04 | 1.13 | <0.001 | 0.95 | 0.90 | 1.01 | 0.106 | 0.82 | 0.69 | 0.97 | 0.019 |
| **>=180** | 1.25 | 1.19 | 1.32 | <0.001 | 1.11 | 1.03 | 1.19 | 0.009 | 1.04 | 0.85 | 1.28 | 0.701 |

**Appendix 15:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality in 75 to 84 year olds with SBP decline prior to baseline versus no decline in 75 to 84 year olds, stratified by eFI frailty status. Adjusted for index of multiple deprivation and sex.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years never smokers** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | 1.50 | 1.36 | 1.65 | <0.001 | 1.78 | 1.62 | 1.95 | <0.001 | 1.42 | 1.15 | 1.75 | 0.001 |
| **120-129** | 1.10 | 1.03 | 1.17 | 0.005 | 1.22 | 1.13 | 1.31 | <0.001 | 1.33 | 1.13 | 1.57 | 0.001 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.95 | 0.91 | 0.99 | 0.017 | 0.86 | 0.82 | 0.91 | <0.001 | 0.89 | 0.77 | 1.01 | 0.080 |
| **150-159** | 0.92 | 0.88 | 0.96 | <0.001 | 0.86 | 0.81 | 0.91 | <0.001 | 0.78 | 0.67 | 0.92 | 0.002 |
| **160-169** | 0.96 | 0.91 | 1.01 | 0.105 | 0.88 | 0.83 | 0.94 | <0.001 | 0.91 | 0.77 | 1.07 | 0.241 |
| **170-179** | 1.06 | 1.00 | 1.13 | 0.056 | 0.88 | 0.81 | 0.96 | 0.005 | 0.86 | 0.68 | 1.09 | 0.218 |
| **≥180** | 1.14 | 1.06 | 1.24 | 0.001 | 1.08 | 0.97 | 1.21 | 0.166 | 1.16 | 0.89 | 1.52 | 0.280 |
|  | **Age 75 to 84 years ex-smokers** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | 1.47 | 1.35 | 1.59 | <0.001 | 1.58 | 1.47 | 1.69 | <0.001 | 1.67 | 1.46 | 1.91 | <0.001 |
| **120-129** | 1.10 | 1.03 | 1.16 | 0.002 | 1.12 | 1.06 | 1.18 | <0.001 | 1.09 | 0.97 | 1.23 | 0.162 |
| **130-139 (reference)** | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   | 1.00 | 1.00 | 1.00 |   |
| **140-149** | 0.97 | 0.93 | 1.01 | 0.138 | 0.88 | 0.85 | 0.92 | <0.001 | 0.96 | 0.87 | 1.06 | 0.388 |
| **150-159** | 0.96 | 0.92 | 1.01 | 0.091 | 0.87 | 0.83 | 0.91 | <0.001 | 0.85 | 0.75 | 0.96 | 0.008 |
| **160-169** | 1.02 | 0.97 | 1.07 | 0.453 | 0.89 | 0.84 | 0.94 | <0.001 | 0.79 | 0.68 | 0.92 | 0.002 |
| **170-179** | 1.07 | 1.00 | 1.15 | 0.050 | 0.99 | 0.91 | 1.07 | 0.753 | 0.83 | 0.67 | 1.02 | 0.076 |
| **>=180** | 1.30 | 1.19 | 1.42 | <0.001 | 1.10 | 0.98 | 1.24 | 0.089 | 0.93 | 0.71 | 1.23 | 0.628 |

**Appendix 16:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality in 75 to 84 year olds excluding those who died within 6 months of index date (N=7092 excluded) in 75 to 84 year olds, stratified by eFI frailty status Adjusted for index of multiple deprivation, age at index date, and sex.



**Appendix 17:** Sensitivity analysis of baseline median systolic blood pressure and hazard ratio of all-cause mortality in 75 to 84 year olds by smoking status, stratified by eFI frailty status. Adjusted for index of multiple deprivation, age at index date, and sex.

|  |  |
| --- | --- |
|  | **Age 75 to 84 years never smokers** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | **1.50** | **1.36** | **1.65** | **<0.001** | **1.78** | **1.62** | **1.95** | **<0.001** | **1.42** | **1.15** | **1.75** | **0.001** |
| **120-129** | **1.10** | **1.03** | **1.17** | **0.005** | **1.22** | **1.13** | **1.31** | **<0.001** | **1.33** | **1.13** | **1.57** | **0.001** |
| **130-139 (reference)** | **1.00** | **1.00** | **1.00** |  | **1.00** | **1.00** | **1.00** |  | **1.00** | **1.00** | **1.00** |  |
| **140-149** | **0.95** | **0.91** | **0.99** | **0.017** | **0.86** | **0.82** | **0.91** | **<0.001** | **0.89** | **0.77** | **1.01** | **0.080** |
| **150-159** | **0.92** | **0.88** | **0.96** | **<0.001** | **0.86** | **0.81** | **0.91** | **<0.001** | **0.78** | **0.67** | **0.92** | **0.002** |
| **160-169** | **0.96** | **0.91** | **1.01** | **0.105** | **0.88** | **0.83** | **0.94** | **<0.001** | **0.91** | **0.77** | **1.07** | **0.241** |
| **170-179** | **1.06** | **1.00** | **1.13** | **0.056** | **0.88** | **0.81** | **0.96** | **0.005** | **0.86** | **0.68** | **1.09** | **0.218** |
| **≥180** | **1.14** | **1.06** | **1.24** | **0.001** | **1.08** | **0.97** | **1.21** | **0.166** | **1.16** | **0.89** | **1.52** | **0.280** |
|  | **Age 75 to 84 years ex-smokers** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | **1.47** | **1.35** | **1.59** | **<0.001** | **1.58** | **1.47** | **1.69** | **<0.001** | **1.67** | **1.46** | **1.91** | **<0.001** |
| **120-129** | **1.10** | **1.03** | **1.16** | **0.002** | **1.12** | **1.06** | **1.18** | **<0.001** | **1.09** | **0.97** | **1.23** | **0.162** |
| **130-139 (reference)** | **1.00** | **1.00** | **1.00** |  | **1.00** | **1.00** | **1.00** |  | **1.00** | **1.00** | **1.00** |  |
| **140-149** | **0.97** | **0.93** | **1.01** | **0.138** | **0.88** | **0.85** | **0.92** | **<0.001** | **0.96** | **0.87** | **1.06** | **0.388** |
| **150-159** | **0.96** | **0.92** | **1.01** | **0.091** | **0.87** | **0.83** | **0.91** | **<0.001** | **0.85** | **0.75** | **0.96** | **0.008** |
| **160-169** | **1.02** | **0.97** | **1.07** | **0.453** | **0.89** | **0.84** | **0.94** | **<0.001** | **0.79** | **0.68** | **0.92** | **0.002** |
| **170-179** | **1.07** | **1.00** | **1.15** | **0.050** | **0.99** | **0.91** | **1.07** | **0.753** | **0.83** | **0.67** | **1.02** | **0.076** |
| **>=180** | **1.30** | **1.19** | **1.42** | **<0.001** | **1.10** | **0.98** | **1.24** | **0.089** | **0.93** | **0.71** | **1.23** | **0.628** |

|  |  |
| --- | --- |
|  | **Age 75 to 84 years current smokers** |
|  | **Non-frail** | **Mild frailty** | **Moderate to severe frailty** |
| **systolic blood pressure (mmHg)** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** | **HR**  | **LCI** | **UCI** | **p value** |
| **<120** | **1.46** | **1.28** | **1.67** | **<0.001** | **1.57** | **1.36** | **1.82** | **<0.001** | **2.08** | **1.50** | **2.87** | **<0.001** |
| **120-129** | **1.13** | **1.02** | **1.25** | **0.015** | **1.16** | **1.04** | **1.31** | **0.010** | **1.16** | **0.88** | **1.53** | **0.292** |
| **130-139 (reference)** | **1.00** | **1.00** | **1.00** |  | **1.00** | **1.00** | **1.00** |  | **1.00** | **1.00** | **1.00** |  |
| **140-149** | **0.94** | **0.87** | **1.01** | **0.072** | **0.95** | **0.87** | **1.04** | **0.244** | **1.08** | **0.85** | **1.36** | **0.548** |
| **150-159** | **1.02** | **0.95** | **1.10** | **0.621** | **0.98** | **0.89** | **1.08** | **0.645** | **1.04** | **0.79** | **1.36** | **0.789** |
| **160-169** | **1.09** | **1.00** | **1.18** | **0.042** | **0.96** | **0.86** | **1.07** | **0.454** | **1.11** | **0.81** | **1.52** | **0.513** |
| **170-179** | **1.24** | **1.12** | **1.37** | **<0.001** | **1.20** | **1.04** | **1.39** | **0.012** | **1.10** | **0.74** | **1.64** | **0.646** |
| **>=180** | **1.34** | **1.19** | **1.51** | **<0.001** | **1.33** | **1.10** | **1.61** | **0.004** | **1.03** | **0.54** | **1.97** | **0.929** |

**Appendix 18: Supplementary Methods Data Analysis**

Data source and linkage

Data from analysis was obtained from the Clinical Practice Research Datalink (CPRD). <https://www.cprd.com/> The data is anonymised at source and provided with linkages to additional datasets as required and funded for research. The data used for this analysis was linked to Hospital Episode Statistics (HES). At the point of data provision, this linkage was for approximately 75% of the practices in England, which were therefore the focus of this study.

Data cleaning

The data provided by CPRD is provided in separate files with unique anonymised patient identifiers enabling linkage of each participant with a medication, tests and medical file. CPRD performs quality checks at practice level to ensure that each practice is delivering the expected data. We also applied a two stage data quality procedure during data preparation for test results, e.g. blood pressure and cholesterol measurement. Initially, measurement recorded with an erroneous unit of measure (e.g. mmHg) were excluded. This was followed by the exclusion of measurements in the 0.5 and 95.5 percentiles, to exclude potential outliers and erroneous recordings, and ensure clinical sense is maintained.

**CPRD codes**

In order to increase the validity and reproducibility of our clinical coding, we have used coding from established sources where possible.

Mortality outcomes were ascertained from the Office for National Statistics death registry data, linked and provided anonymously by CPRD. Death dates were established from death certification dates from this data.

We used the rules from the Quality of Outcomes Framework (QoF)[1] for hypertension, diabetes and heart failure ascertainment. QoF rules have been generated to enable data extraction from different GP databases for monitoring and quality assurance of specific diseases, enabling extraction of “Read” codes. Read codes provide a hierarchical coding system for patient information including diagnoses. [2]

**Appendix 19:** Hypertension coding adapted from QoF

|  |  |  |
| --- | --- | --- |
| **medcode** | **readcode** | **readterm** |
| 204 | G2...00 | Hypertensive disease |
| 8732 | G2...11 | BP - hypertensive disease |
| 799 | G20..00 | Essential hypertension |
| 351 | G20..11 | High blood pressure |
| 15377 | G20<0.001 | Malignant essential hypertension |
| 1894 | G201.00 | Benign essential hypertension |
| 4372 | G202.00 | Systolic hypertension |
| 83473 | G203.00 | Diastolic hypertension |
| 10818 | G20z.00 | Essential hypertension NOS |
| 3712 | G20z.11 | Hypertension NOS |
| 7329 | G24..00 | Secondary hypertension |
| 31755 | G24<0.001 | Secondary malignant hypertension |
| 59383 | G240000 | Secondary malignant renovascular hypertension |
| 73293 | G240z00 | Secondary malignant hypertension NOS |
| 57288 | G241.00 | Secondary benign hypertension |
| 25371 | G241000 | Secondary benign renovascular hypertension |
| 51635 | G241z00 | Secondary benign hypertension NOS |
| 34744 | G244.00 | Hypertension secondary to endocrine disorders |
| 16059 | G24z.00 | Secondary hypertension NOS |
| 31387 | G24z000 | Secondary renovascular hypertension NOS |
| 42229 | G24zz00 | Secondary hypertension NOS |
| 18765 | G2y..00 | Other specified hypertensive disease |
| 7057 | G2z..00 | Hypertensive disease NOS |

**Appendix 20:** Heart failure coding adapted from QoF

|  |  |  |
| --- | --- | --- |
| **medcode** | **readcode** | **readterm** |
| 18853 | 662f.00 | New York Heart Association classification - class I |
| 13189 | 662g.00 | New York Heart Association classification - class II |
| 19066 | 662h.00 | New York Heart Association classification - class III |
| 51214 | 662i.00 | New York Heart Association classification - class IV |
| 22262 | G1yz100 | Rheumatic left ventricular failure |
| 2062 | G58..00 | Heart failure |
| 1223 | G58..11 | Cardiac failure |
| 398 | G58<0.001 | Congestive heart failure |
| 2906 | G580.11 | Congestive cardiac failure |
| 10079 | G580.12 | Right heart failure |
| 10154 | G580.13 | Right ventricular failure |
| 9524 | G580.14 | Biventricular failure |
| 23707 | G580000 | Acute congestive heart failure |
| 32671 | G580100 | Chronic congestive heart failure |
| 27884 | G580200 | Decompensated cardiac failure |
| 11424 | G580300 | Compensated cardiac failure |
| 94870 | G580400 | Congestive heart failure due to valvular disease |
| 884 | G581.00 | Left ventricular failure |
| 23481 | G581.11 | Asthma - cardiac |
| 43618 | G581.12 | Pulmonary oedema - acute |
| 5942 | G581.13 | Impaired left ventricular function |
| 5255 | G581000 | Acute left ventricular failure |
| 27964 | G582.00 | Acute heart failure |
| 101138 | G583.00 | Heart failure with normal ejection fraction |
| 101137 | G583.11 | HFNEF - heart failure with normal ejection fraction |
| 4024 | G58z.00 | Heart failure NOS |
| 12590 | G58z.11 | Weak heart |
| 17278 | G58z.12 | Cardiac failure NOS |

**Appendix 21:** Diabetes coding adapted from QoF

|  |  |  |
| --- | --- | --- |
| **medcode** | **readcode** | **readterm** |
| 1549 | C10E.00 | Type 1 diabetes mellitus |
| 12455 | C10E.11 | Type I diabetes mellitus |
| 51261 | C10E.12 | Insulin dependent diabetes mellitus |
| 47582 | C10E000 | Type 1 diabetes mellitus with renal complications |
| 102946 | C10E012 | Insulin-dependent diabetes mellitus with renal complications |
| 47649 | C10E100 | Type 1 diabetes mellitus with ophthalmic complications |
| 99311 | C10E111 | Type I diabetes mellitus with ophthalmic complications |
| 98071 | C10E112 | Insulin-dependent diabetes mellitus with ophthalmic comps |
| 42831 | C10E200 | Type 1 diabetes mellitus with neurological complications |
| 101735 | C10E212 | Insulin-dependent diabetes mellitus with neurological comps |
| 47650 | C10E300 | Type 1 diabetes mellitus with multiple complications |
| 91942 | C10E311 | Type I diabetes mellitus with multiple complications |
| 45276 | C10E312 | Insulin dependent diabetes mellitus with multiple complicat |
| 43921 | C10E400 | Unstable type 1 diabetes mellitus |
| 49949 | C10E411 | Unstable type I diabetes mellitus |
| 54600 | C10E412 | Unstable insulin dependent diabetes mellitus |
| 18683 | C10E500 | Type 1 diabetes mellitus with ulcer |
| 93878 | C10E511 | Type I diabetes mellitus with ulcer |
| 98704 | C10E512 | Insulin dependent diabetes mellitus with ulcer |
| 69993 | C10E600 | Type 1 diabetes mellitus with gangrene |
| 102112 | C10E611 | Type I diabetes mellitus with gangrene |
| 18387 | C10E700 | Type 1 diabetes mellitus with retinopathy |
| 95343 | C10E711 | Type I diabetes mellitus with retinopathy |
| 93875 | C10E712 | Insulin dependent diabetes mellitus with retinopathy |
| 35288 | C10E800 | Type 1 diabetes mellitus - poor control |
| 72702 | C10E812 | Insulin dependent diabetes mellitus - poor control |
| 40682 | C10E900 | Type 1 diabetes mellitus maturity onset |
| 96235 | C10E911 | Type I diabetes mellitus maturity onset |
| 97849 | C10E912 | Insulin dependent diabetes maturity onset |
| 69676 | C10EA00 | Type 1 diabetes mellitus without complication |
| 62613 | C10EA11 | Type I diabetes mellitus without complication |
| 99719 | C10EA12 | Insulin-dependent diabetes without complication |
| 68105 | C10EB00 | Type 1 diabetes mellitus with mononeuropathy |
| 46301 | C10EC00 | Type 1 diabetes mellitus with polyneuropathy |
| 91943 | C10EC11 | Type I diabetes mellitus with polyneuropathy |
| 101311 | C10EC12 | Insulin dependent diabetes mellitus with polyneuropathy |
| 10418 | C10ED00 | Type 1 diabetes mellitus with nephropathy |
| 102163 | C10ED12 | Insulin dependent diabetes mellitus with nephropathy |
| 39070 | C10EE00 | Type 1 diabetes mellitus with hypoglycaemic coma |
| 99716 | C10EE12 | Insulin dependent diabetes mellitus with hypoglycaemic coma |
| 49554 | C10EF00 | Type 1 diabetes mellitus with diabetic cataract |
| 100770 | C10EF12 | Insulin dependent diabetes mellitus with diabetic cataract |
| 93468 | C10EG00 | Type 1 diabetes mellitus with peripheral angiopathy |
| 18642 | C10EH00 | Type 1 diabetes mellitus with arthropathy |
| 54008 | C10EJ00 | Type 1 diabetes mellitus with neuropathic arthropathy |
| 30323 | C10EK00 | Type 1 diabetes mellitus with persistent proteinuria |
| 30294 | C10EL00 | Type 1 diabetes mellitus with persistent microalbuminuria |
| 102620 | C10EL11 | Type I diabetes mellitus with persistent microalbuminuria |
| 10692 | C10EM00 | Type 1 diabetes mellitus with ketoacidosis |
| 62209 | C10EM11 | Type I diabetes mellitus with ketoacidosis |
| 40837 | C10EN00 | Type 1 diabetes mellitus with ketoacidotic coma |
| 66145 | C10EN11 | Type I diabetes mellitus with ketoacidotic coma |
| 22871 | C10EP00 | Type 1 diabetes mellitus with exudative maculopathy |
| 97894 | C10EP11 | Type I diabetes mellitus with exudative maculopathy |
| 55239 | C10EQ00 | Type 1 diabetes mellitus with gastroparesis |
| 95636 | C10ER00 | Latent autoimmune diabetes mellitus in adult |
| 758 | C10F.00 | Type 2 diabetes mellitus |
| 22884 | C10F.11 | Type II diabetes mellitus |
| 18777 | C10F000 | Type 2 diabetes mellitus with renal complications |
| 57278 | C10F011 | Type II diabetes mellitus with renal complications |
| 47321 | C10F100 | Type 2 diabetes mellitus with ophthalmic complications |
| 100964 | C10F111 | Type II diabetes mellitus with ophthalmic complications |
| 34268 | C10F200 | Type 2 diabetes mellitus with neurological complications |
| 98616 | C10F211 | Type II diabetes mellitus with neurological complications |
| 65267 | C10F300 | Type 2 diabetes mellitus with multiple complications |
| 43227 | C10F311 | Type II diabetes mellitus with multiple complications |
| 49074 | C10F400 | Type 2 diabetes mellitus with ulcer |
| 91646 | C10F411 | Type II diabetes mellitus with ulcer |
| 12736 | C10F500 | Type 2 diabetes mellitus with gangrene |
| 18496 | C10F600 | Type 2 diabetes mellitus with retinopathy |
| 49655 | C10F611 | Type II diabetes mellitus with retinopathy |
| 25627 | C10F700 | Type 2 diabetes mellitus - poor control |
| 47315 | C10F711 | Type II diabetes mellitus - poor control |
| 47954 | C10F900 | Type 2 diabetes mellitus without complication |
| 53392 | C10F911 | Type II diabetes mellitus without complication |
| 62674 | C10FA00 | Type 2 diabetes mellitus with mononeuropathy |
| 95351 | C10FA11 | Type II diabetes mellitus with mononeuropathy |
| 18425 | C10FB00 | Type 2 diabetes mellitus with polyneuropathy |
| 50527 | C10FB11 | Type II diabetes mellitus with polyneuropathy |
| 12640 | C10FC00 | Type 2 diabetes mellitus with nephropathy |
| 102201 | C10FC11 | Type II diabetes mellitus with nephropathy |
| 46917 | C10FD00 | Type 2 diabetes mellitus with hypoglycaemic coma |
| 98723 | C10FD11 | Type II diabetes mellitus with hypoglycaemic coma |
| 44982 | C10FE00 | Type 2 diabetes mellitus with diabetic cataract |
| 93727 | C10FE11 | Type II diabetes mellitus with diabetic cataract |
| 37806 | C10FF00 | Type 2 diabetes mellitus with peripheral angiopathy |
| 59253 | C10FG00 | Type 2 diabetes mellitus with arthropathy |
| 103902 | C10FG11 | Type II diabetes mellitus with arthropathy |
| 35385 | C10FH00 | Type 2 diabetes mellitus with neuropathic arthropathy |
| 1407 | C10FJ00 | Insulin treated Type 2 diabetes mellitus |
| 64668 | C10FJ11 | Insulin treated Type II diabetes mellitus |
| 34450 | C10FK00 | Hyperosmolar non-ketotic state in type 2 diabetes mellitus |
| 26054 | C10FL00 | Type 2 diabetes mellitus with persistent proteinuria |
| 60796 | C10FL11 | Type II diabetes mellitus with persistent proteinuria |
| 18390 | C10FM00 | Type 2 diabetes mellitus with persistent microalbuminuria |
| 85991 | C10FM11 | Type II diabetes mellitus with persistent microalbuminuria |
| 32627 | C10FN00 | Type 2 diabetes mellitus with ketoacidosis |
| 51756 | C10FP00 | Type 2 diabetes mellitus with ketoacidotic coma |
| 25591 | C10FQ00 | Type 2 diabetes mellitus with exudative maculopathy |
| 63690 | C10FR00 | Type 2 diabetes mellitus with gastroparesis |
| 95539 | C10FS00 | Maternally inherited diabetes mellitus |

We used the International Classification of Diseases (ICD-10)[3] for cerebrovascular disease in order to increase the specificity and excluded Transient Ischaemic Attack. We also used ICD-10 codes for myocardial infarction, supplemented by OPCS Classification of Interventions and Procedures[4] for coronary angioplasty, coronary artery bypass graft and open angioplasty to incorporate significant coronary disease for which intervention had prevented myocardial infarction but in which there was significant disease.

**Appendix 22:** ICD10 codes for myocardial infarction

**ICD 10 Label code**

|  |  |
| --- | --- |
| I20.0 | Unstable angina |
| I21 | Acute myocardial infarction |
| I21.0 | Acute transmural myocardial infarction of anterior wall |
| I21.1 | Acute transmural myocardial infarction of inferior wall |
| I21.2 | Acute transmural myocardial infarction of other sites |
| I21.3 | Acute transmural myocardial infarction of unspecified site |
| I21.4 | Acute subendocardial myocardial infarction |
| I21.9 | Acute myocardial infarction, unspecified |
| I22 | Subsequent myocardial infarction |
| I22.0 | Subsequent myocardial infarction of anterior wall |
| I22.8 | Subsequent myocardial infarction of other sites |
| I22.9 | Subsequent myocardial infarction of unspecified site |

**Appendix 23 :** ICD10 codes for stroke

**ICD 10 Label code**

|  |  |
| --- | --- |
| I61 | Intracerebral haemorrhage |
| I61.0 | Intracerebral haemorrhage in hemisphere, subcortical |
| I61.1 | Intracerebral haemorrhage in hemisphere, cortical |
| I61.2 | Intracerebral haemorrhage in hemisphere, cortical |
| I61.3 | Intracerebral haemorrhage in brain stem |
| I61.4 | Intracerebral haemorrhage in cerebellum |
| I61.5 | Intracerebral haemorrhage, intraventricular |
| I61.6 | Intracerebral haemorrhage, intraventricular |
| I61.7 | Intracerebral haemorrhage, multiple localized |
| I61.8 | Other intracerebral haemorrhage |
| I61.9 | Intracerebral haemorrhage, unspecified |
| I63 | Cerebral infarction |
| I63.0 | Cerebral infarction due to thrombosis of precerebral arteries |
| I63.1 | Cerebral infarction due to embolism of precerebral arteries |
| I63.2 | Cerebral infarction due to unspecified occlusion or stenosis of precerebral arteries |
| I63.3 | Cerebral infarction due to thrombosis of cerebral arteries |
| I63.4 | Cerebral infarction due to embolism of cerebral arteries |
| I63.5 | Cerebral infarction due to unspecified occlusion or stenosis of cerebral arteries |
| I63.6 | Cerebral infarction due to cerebral venous thrombosis, nonpyogenic |
| I63.8 | Other cerebral infarction |
| I63.9 | Cerebral infarction, unspecified |
| 164 | Stroke, not specified as haemorrhage or infarction |
|  | Cerebrovascular accident NOS |

Blood pressure and cholesterol were established from the test files. As previously described, BP values at baseline was based on the median value over the preceeding 3 year period.

Methods for establishing Body Mass Index, smoking status and quintiles of Index of Multiple Deprivation have been previously described[5,6].

The electronic frailty Index (eFI) was used to ascertain baseline frailty category. The eFI is based on the Rockwood frailty index, and designed for implementation in electronic medical records. This cumulative model includes 36 specified symptoms, signs, diseases, disabilities, and abnormal laboratory values, collectively referred to as deficits by Clegg at al. [7]. Implementation rules, and medical and pharmacological codes were provided by personal communication by the author, Andrew Clegg [7]. The index is scored fit (0 to <0.12), mildly frail (0.12 to <0.24), moderately frail (0.24 to < 0.36), and severely frail (0.36 to 1).