

## **SUPPLEMENTAL MATERIAL**

**Table S1. Cardiovascular Disease and Cancer Definitions in NHANES III.**

|                                     | <b>ICD-10</b>                       |
|-------------------------------------|-------------------------------------|
| <b>Cardiovascular disease (CVD)</b> | I00-I09, I11, I13, I20-I51, I60-I69 |
| <b>Heart disease</b>                | I00-I09, I11, I13, I20-I51          |
| <b>Stroke</b>                       | I60-I69                             |
| <b>Cancer</b>                       | C00-C97                             |

Variable definitions constructed using ICD-10 and self-reported data fields with choice-, disease- or procedure-specific codes between brackets are shown.

Abbreviations: ICD, International Classification of Diseases.

**Table S2. Sensitivity analysis in participants with completed data on all variables.**

|                            | LDL-C levels ( <i>n</i> = 9,962) |                  |                 |                  |                  |                         |
|----------------------------|----------------------------------|------------------|-----------------|------------------|------------------|-------------------------|
|                            | < 70 mg/dL                       | 70-99.9 mg/dL    | 100-129.9 mg/dL | 130-159.9 mg/dL  | 160-189.9 mg/dL  | ≥ 190 mg/dL             |
| <b>All-cause mortality</b> |                                  |                  |                 |                  |                  |                         |
| Model 1                    | <b>1.68 (1.13-2.50)</b>          | 1.00 (0.79-1.26) | 1 (ref)         | 0.90 (0.77-1.05) | 0.88 (0.72-1.08) | 1.17 (0.91-1.50)        |
| Model 2                    | <b>1.51 (1.03-2.21)</b>          | 0.98 (0.78-1.23) | 1 (ref)         | 0.90 (0.77-1.06) | 0.84 (0.69-1.02) | 1.13 (0.85-1.49)        |
| Model 3                    | <b>1.49 (1.02-2.17)</b>          | 0.99 (0.78-1.24) | 1 (ref)         | 0.90 (0.76-1.05) | 0.83 (0.68-1.01) | 1.14 (0.86-1.51)        |
| Model 4                    | <b>1.47 (1.02-2.11)</b>          | 0.99 (0.78-1.24) | 1 (ref)         | 0.88 (0.75-1.03) | 0.84 (0.69-1.03) | 1.16 (0.89-1.52)        |
| <b>CVD mortality</b>       |                                  |                  |                 |                  |                  |                         |
| Model 1                    | 1.55 (0.88-2.73)                 | 1.19 (0.76-1.87) | 1 (ref)         | 1.12 (0.72-1.73) | 1.25 (0.87-1.79) | <b>1.61 (1.06-2.44)</b> |
| Model 2                    | 1.36 (0.77-2.38)                 | 1.18 (0.75-1.86) | 1 (ref)         | 1.13 (0.71-1.79) | 1.18 (0.78-1.80) | 1.55 (1.00-2.42)        |
| Model 3                    | 1.31 (0.74-2.34)                 | 1.20 (0.78-1.85) | 1 (ref)         | 1.12 (0.71-1.76) | 1.18 (0.77-1.79) | <b>1.58 (1.01-2.46)</b> |

|                         |                          |                  |         |                  |                  |                         |
|-------------------------|--------------------------|------------------|---------|------------------|------------------|-------------------------|
| Model 4                 | 1.31 (0.74-2.31)         | 1.19 (0.77-1.82) | 1 (ref) | 1.09 (0.69-1.73) | 1.18 (0.76-1.82) | <b>1.60 (1.03-2.50)</b> |
| <b>CHD mortality</b>    |                          |                  |         |                  |                  |                         |
| Model 1                 | 0.94 (0.23-3.81)         | 1.20 (0.78-1.86) | 1 (ref) | 1.16 (0.75-1.80) | 1.28 (0.85-1.94) | <b>1.83 (1.09-3.06)</b> |
| Model 2                 | 0.78 (0.19-3.11)         | 1.20 (0.77-1.86) | 1 (ref) | 1.17 (0.73-1.87) | 1.21 (0.75-1.96) | 1.74 (0.98-3.07)        |
| Model 3                 | 0.75 (0.19-3.02)         | 1.21 (0.79-1.86) | 1 (ref) | 1.16 (0.73-1.85) | 1.21 (0.74-1.96) | <b>1.76 (1.00-3.11)</b> |
| Model 4                 | 0.73 (0.18-2.93)         | 1.19 (0.78-1.83) | 1 (ref) | 1.16 (0.73-1.84) | 1.22 (0.74-1.98) | <b>1.83 (1.04-3.19)</b> |
| <b>Stroke mortality</b> |                          |                  |         |                  |                  |                         |
| Model 1                 | 3.75 (0.99-14.27)        | 1.17 (0.33-4.17) | 1 (ref) | 0.97 (0.43-2.21) | 1.13 (0.50-2.55) | 0.84 (0.29-2.45)        |
| Model 2                 | <b>4.00 (1.05-15.16)</b> | 1.13 (0.32-4.03) | 1 (ref) | 0.95 (0.42-2.14) | 1.06 (0.46-2.43) | 0.82 (0.28-2.44)        |
| Model 3                 | <b>3.85 (1.00-14.78)</b> | 1.15 (0.33-4.01) | 1 (ref) | 0.93 (0.42-2.10) | 1.03 (0.44-2.42) | 0.83 (0.28-2.49)        |
| Model 4                 | <b>4.46 (1.16-17.17)</b> | 1.13 (0.33-3.86) | 1 (ref) | 0.87 (0.38-1.98) | 0.98 (0.40-2.37) | 0.79 (0.26-2.34)        |

Values are hazard ratio (95% confidence interval) and are weighted.

Model 1: adjusted for age, sex, and race/ethnicity.

Model 2: model 1+ education level, marital status, family income level, smoking status, alcohol intake, and physical activity.

Model 3: model 2+ C-reactive protein level.

Model 4: model 3+ BMI, hypertension, diabetes, respiratory diseases, liver diseases, chronic kidney disease, and cholesterol-lowering drugs.

**Table S3. Sensitivity analysis in participants not taking lipids lowering drugs in baseline.**

|                            | LDL-C levels ( <i>n</i> = 13,740) |                  |                 |                         |                         |                         |
|----------------------------|-----------------------------------|------------------|-----------------|-------------------------|-------------------------|-------------------------|
|                            | < 70 mg/dL                        | 70-99.9 mg/dL    | 100-129.9 mg/dL | 130-159.9 mg/dL         | 160-189.9 mg/dL         | ≥ 190 mg/dL             |
| <b>All-cause mortality</b> |                                   |                  |                 |                         |                         |                         |
| Model 1                    | <b>1.69 (1.25-2.28)</b>           | 1.04 (0.87-1.24) | 1 (ref)         | <b>0.89 (0.80-1.00)</b> | 0.88 (0.76-1.02)        | 1.03 (0.86-1.24)        |
| Model 2                    | <b>1.50 (1.13-2.00)</b>           | 1.01 (0.85-1.20) | 1 (ref)         | <b>0.90 (0.82-0.99)</b> | <b>0.86 (0.75-0.99)</b> | 1.02 (0.84-1.24)        |
| Model 3                    | <b>1.50 (1.12-2.00)</b>           | 1.01 (0.85-1.20) | 1 (ref)         | <b>0.89 (0.81-0.98)</b> | <b>0.86 (0.75-0.98)</b> | 1.03 (0.85-1.25)        |
| Model 4                    | <b>1.44 (1.08-1.92)</b>           | 1.02 (0.85-1.21) | 1 (ref)         | <b>0.90 (0.81-1.00)</b> | 0.88 (0.77-1.02)        | 1.04 (0.84-1.28)        |
| <b>CVD mortality</b>       |                                   |                  |                 |                         |                         |                         |
| Model 1                    | <b>1.80 (1.14-2.85)</b>           | 1.26 (0.84-1.90) | 1 (ref)         | 1.16 (0.84-1.59)        | 1.22 (0.92-1.62)        | 1.39 (0.99-1.96)        |
| Model 2                    | <b>1.60 (1.02-2.52)</b>           | 1.24 (0.83-1.86) | 1 (ref)         | 1.18 (0.86-1.61)        | 1.22 (0.93-1.61)        | 1.39 (1.00-1.93)        |
| Model 3                    | <b>1.59 (1.01-2.52)</b>           | 1.24 (0.83-1.86) | 1 (ref)         | 1.17 (0.85-1.59)        | 1.22 (0.92-1.61)        | <b>1.40 (1.01-1.95)</b> |
| Model 4                    | 1.54 (0.97-2.44)                  | 1.28 (0.85-1.93) | 1 (ref)         | 1.18 (0.86-1.63)        | 1.27 (0.96-1.68)        | <b>1.42 (1.01-2.00)</b> |

**CHD mortality**

|         |                  |                  |         |                  |                  |                         |
|---------|------------------|------------------|---------|------------------|------------------|-------------------------|
| Model 1 | 1.34 (0.71-2.53) | 1.31 (0.84-2.03) | 1 (ref) | 1.20 (0.86-1.69) | 1.23 (0.89-1.71) | <b>1.56 (1.02-2.38)</b> |
| Model 2 | 1.15 (0.62-2.15) | 1.28 (0.84-1.97) | 1 (ref) | 1.22 (0.88-1.71) | 1.24 (0.90-1.71) | <b>1.55 (1.02-2.35)</b> |
| Model 3 | 1.15 (0.62-2.13) | 1.28 (0.83-1.97) | 1 (ref) | 1.22 (0.87-1.70) | 1.24 (0.89-1.71) | <b>1.56 (1.03-2.37)</b> |
| Model 4 | 1.08 (0.58-2.04) | 1.32 (0.85-2.04) | 1 (ref) | 1.24 (0.87-1.75) | 1.30 (0.93-1.81) | <b>1.59 (1.03-2.44)</b> |

**Stroke mortality**

|         |                         |                  |         |                  |                  |                  |
|---------|-------------------------|------------------|---------|------------------|------------------|------------------|
| Model 1 | <b>3.48 (1.39-8.71)</b> | 1.12 (0.50-2.49) | 1 (ref) | 1.02 (0.59-1.74) | 1.19 (0.75-1.86) | 0.88 (0.47-1.66) |
| Model 2 | <b>3.31 (1.37-8.00)</b> | 1.10 (0.51-2.37) | 1 (ref) | 1.02 (0.61-1.72) | 1.14 (0.73-1.80) | 0.87 (0.46-1.62) |
| Model 3 | <b>3.34 (1.39-8.02)</b> | 1.10 (0.51-2.38) | 1 (ref) | 1.01 (0.60-1.68) | 1.13 (0.71-1.79) | 0.89 (0.48-1.64) |
| Model 4 | <b>3.63 (1.58-8.38)</b> | 1.16 (0.55-2.48) | 1 (ref) | 1.01 (0.59-1.72) | 1.14 (0.72-1.81) | 0.89 (0.46-1.72) |

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Values are hazard ratio (95% confidence interval) and are weighted.

Model 1: adjusted for age, sex, and race/ethnicity.

Model 2: model 1+ education level, marital status, family income level, smoking status, alcohol intake, and physical activity.

Model 3: model 2+ C-reactive protein level.

Model 4: model 3+ BMI, hypertension, diabetes, respiratory diseases, liver diseases, and chronic kidney disease.