Association of metabolic syndrome with incident dementia: role of number and age at measurement of components in a 28-year follow-up of the Whitehall II cohort study

Marcos D. Machado-Fragua
Aurore Fayosse
Manasa-Shanta Yerramalla
Thomas van Sloten
Adam Tabak
Mika Kivimaki
Séverine Sabia
Archana Singh-Manoux

Supplementary data

Table S1. Sample characteristics at <60, 60 to <70, and ≥70 years overall and according to dementia status at the end of follow-up (31st March 2019).

Table S2. Role of the number of metabolic components at <60, 60 to <70, and ≥70 years on the association between metabolic syndrome and incidence of dementia.

Table S3. Association between metabolic syndrome components at <60, 60 to <70, and ≥70 years and incidence of dementia using inverse probability weighting to account for missing data.

Table S4. Association between the number of MetS components at <60, 60 to <70, and ≥70 years and incidence of dementia using inverse probability weighting to account for missing data.

Table S5. Alternate cutoff points to define metabolic risk at <60, 60 to <70, and ≥70 years and incidence of dementia using inverse probability weighting to account for missing data.

Figure S1. Flow chart of sample selection.

Figure S2. Association of number of metabolic syndrome components at age <60 (A), 60 to <70 (B), and ≥70 years (C) with dementia using restricted cubic splines.

Figure S3. Multistate models for the role of “high metabolic risk” at age <60 years in transition to cardiovascular disease (stroke, coronary heart disease or heart failure) and dementia using inverse probability weighting to account for missing data.
Table S1. Sample characteristics at <60, 60 to <70, and ≥70 years overall and according to dementia status at the end of follow-up (31st March 2019).

|                      | Total population | Dementia                   |     |
|----------------------|------------------|----------------------------|-----|
|                      |                  | No                     | Yes | p-value<sup>†</sup> |
| **At age <60 years** |                  |                        |     |                    |
| Age, M(SD)           | 55.1 (2.9)       | 55.0 (2.9)              | 55.0 (2.9) | 0.58 |
| Sex, women           | 2219 (30.5)      | 2074 (30.2)             | 145 (36.9) | 0.005 |
| Education, low       | 3249 (44.7)      | 3029 (44.1)             | 220 (56.0) | <0.001 |
| Ethnicity, non-white | 719 (9.9)        | 656 (9.6)               | 63 (16.0)  | <0.001 |
| Smoking, current smokers | 846 (11.6) | 796 (11.6)            | 50 (12.7)  | 0.76  |
| Alcohol consumption, moderate drinkers | 3881 (53.4) | 3704 (53.9)          | 177 (45.0) | <0.001 |
| Fruits and vegetables consumption, ≥twice/day | 2235 (30.8) | 2157 (31.4)         | 78 (19.9)  | <0.001 |
| Physical activity (moderate - vigorous), h/week, M(SD) | 3.3 (3.6) | 3.3 (3.5)             | 3.3 (3.5)  | 0.15  |
| Use of lipid-lowering drugs | 280 (3.9) | 270 (3.9)              | 10 (2.5)   | 0.17  |
| Use of antihypertensive drugs | 953 (13.1) | 883 (12.9)            | 70 (17.8)  | 0.01  |
| Use of glucose-lowering drugs, | 118 (1.6) | 106 (1.5)             | 12 (3.1)   | 0.02  |
| Metabolic syndrome components |      |                        |     |                    |
| Elevated WC          | 1286 (17.7)      | 1215 (17.7)             | 71 (18.1)  | 0.85  |
| Elevated triglycerides | 2163 (29.8) | 2040 (29.7)            | 123 (31.3) | 0.50  |
| Low HDL-C            | 1311 (18.1)      | 1224 (17.8)             | 87 (22.1)  | 0.03  |
| Elevated blood pressure | 3193 (44.0) | 2984 (43.4)         | 209 (53.2) | <0.001 |
| Elevated fasting glucose | 1662 (22.9) | 1562 (22.7)         | 100 (25.5) | 0.21  |
| **At age 60 to <70 years** |      |                        |     |                    |
| Age, M(SD)           | 65.0 (1.5)       | 65.0 (1.5)              | 65.0 (1.5) | 0.50  |
| Sex, women           | 1949 (29.3)      | 1796 (28.8)             | 153 (36.7) | 0.001 |
| Education, low       | 2916 (43.8)      | 2679 (42.9)             | 237 (56.8) | <0.001 |
| Ethnicity, non-white | 559 (8.4)        | 501 (8.0)               | 58 (13.9)  | <0.001 |
| Smoking, current smokers | 433 (6.5) | 402 (6.4)              | 31 (7.4)   | 0.20  |
| Alcohol consumption, moderate drinkers | 3589 (53.9) | 3387 (54.3)         | 202 (48.4) | <0.001 |
| Fruits and vegetables consumption, ≥twice/day | 2733 (41.0) | 2592 (41.5)         | 141 (33.8) | <0.001 |
| Physical activity (moderate - vigorous), h/week, M(SD) | 4.0 (3.6) | 4.0 (3.6)             | 4.0 (3.6)  | 0.74  |
| Use of lipid-lowering drugs | 1611 (24.2) | 1541 (24.7)          | 70 (16.8)  | <0.001 |
| Use of antihypertensive drugs | 2085 (31.3) | 1956 (31.3)            | 129 (30.9) | 0.87  |
| Use of glucose-lowering drugs, | 307 (4.6) | 280 (4.5)             | 27 (6.5)   | 0.06  |
| Metabolic syndrome components |      |                        |     |                    |
| Elevated WC          | 1900 (28.5)      | 1801 (28.9)             | 99 (23.7)  | 0.03  |
| Elevated triglycerides | 2608 (39.2) | 2460 (39.4)            | 148 (35.5) | 0.11  |
| Low HDL-C            | 2109 (31.7)      | 1987 (31.8)             | 122 (29.3) | 0.28  |
| Elevated blood pressure | 3876 (58.2) | 3631 (58.2)         | 245 (58.8) | 0.81  |
| Elevated fasting glucose | 1715 (25.8) | 1596 (25.6)         | 119 (28.5) | 0.18  |
| **At age ≥70 years** |      |                        |     |                    |
| Age, M(SD)           | 73.9 (1.9)       | 73.9 (1.9)              | 73.9 (1.9) | 0.09  |
| Sex, women           | 1060 (29.4)      | 969 (29.0)              | 91 (34.5)  | 0.05  |
| Education, low       | 1766 (49.0)      | 1611 (48.2)             | 155 (58.7) | 0.002 |
| Ethnicity, non-white | 348 (9.7)        | 309 (9.2)               | 39 (14.8)  | 0.003 |
| Smoking, current smokers | 108 (3.0) | 103 (3.1)              | 5 (1.9)    | 0.53  |
| Alcohol moderate, moderate drinkers | 1984 (55.0) | 1855 (55.5)         | 129 (48.9) | <0.001 |
| Fruits and vegetables consumption, ≥twice/day | 1450 (40.2) | 1370 (41.0)         | 80 (30.3)  | 0.002 |
| Physical activity (moderate - vigorous), h/week, M(SD) | 3.5 (3.3) | 3.5 (3.3)             | 3.5 (3.3)  | 0.20  |
| Use of lipid-lowering drugs | 1667 (46.2) | 1545 (46.2)          | 122 (46.2) | 0.99  |
| Use of antihypertensive drugs | 1798 (49.8) | 1651 (49.4)            | 147 (55.7) | 0.04  |
| Use of glucose-lowering drugs, | 258 (7.2) | 228 (6.8)             | 30 (11.4)  | 0.01  |
| Metabolic syndrome components |      |                        |     |                    |
| Elevated WC          | 1281 (35.5)      | 1194 (35.7)             | 87 (33.0)  | 0.37  |
| Condition                        | Count (Mean) | Count (Mean) | Count (Mean) | p-value |
|---------------------------------|--------------|--------------|--------------|---------|
| Elevated triglycerides          | 1923 (53.3)  | 1781 (53.3)  | 142 (53.8)   | 0.87    |
| Low HDL-C                       | 1810 (50.2)  | 1679 (50.2)  | 131 (49.6)   | 0.85    |
| Elevated blood pressure         | 2602 (72.1)  | 2407 (72.0)  | 195 (73.9)   | 0.51    |
| Elevated fasting glucose        | 977 (27.1)   | 885 (26.5)   | 92 (34.9)    | 0.003   |

M: mean; SD: standard deviation; WC: waist circumference; HDL-C: high density lipoprotein-cholesterol; Data are n (%), unless otherwise specified
* Mean (SD) age at assessment=55.1 (2.9) years; † Mean (SD) age at assessment=65.0 (1.5) years; ‡ Mean (SD) age at assessment=73.9 (1.9) years
§ p-value for difference in \( \chi^2 \) test (categorical data) or student’s t test (continuous data).
Table S2. Role of the number of metabolic components at <60, 60 to <70, and ≥70 years on the association between metabolic syndrome and incidence of dementia.

| Number of MetS components | N Dementia cases/Total | Rate of dementia/1000 person-years | HR (95% CI) |
|---------------------------|------------------------|-----------------------------------|-------------|
|                           |                        | Model 1§                          | Model 2‖    |
|                           |                        |                                    |             |
| At age <60 years*, Median (IQR) follow-up 20.8 (15.5, 26.2) years | | | |
| 0                         | 97/2325                | 2.08                              | 1 (Ref.)    | 1 (Ref.) |
| 1                         | 123/2145               | 2.85                              | 1.29 (0.99, 1.68) | 1.25 (0.96, 1.63) |
| 2                         | 92/1493                | 3.21                              | 1.57 (1.17, 2.09) | 1.48 (1.11, 1.98) |
| MetS (3-5)                | 81/1302                | 3.34                              | 1.58 (1.17, 2.13) | 1.50 (1.11, 2.02) |
| At age 60 years to <70 years†, Median (IQR) follow-up 10.4 (6.4, 15.6) years | | | |
| 0                         | 75/1409                | 4.65                              | 1 (Ref.)    | 1 (Ref.) |
| 1                         | 127/1753               | 6.20                              | 1.30 (0.98, 1.73) | 1.28 (0.96, 1.71) |
| 2                         | 100/1387               | 6.31                              | 1.42 (1.05, 1.92) | 1.38 (1.02, 1.86) |
| MetS (3-5)                | 115/2111               | 5.65                              | 1.49 (1.11, 2.01) | 1.40 (1.04, 1.89) |
| At age ≥70 years‡, Median (IQR) follow-up 4.2 (3.1, 7.1) years | | | |
| 0                         | 23/442                 | 8.90                              | 1 (Ref.)    | 1 (Ref.) |
| 1                         | 57/729                 | 13.26                             | 1.49 (0.92, 2.42) | 1.44 (0.88, 2.34) |
| 2                         | 48/650                 | 12.81                             | 1.50 (0.91, 2.47) | 1.45 (0.88, 2.39) |
| MetS (3-5)                | 136/1787               | 13.49                             | 1.54 (0.99, 2.40) | 1.47 (0.94, 2.30) |

MetS: Metabolic syndrome
* Mean (SD) age at assessment=55.1 (2.9) years
† Mean (SD) age at assessment=65.0 (1.5) years
‡ Mean (SD) age at assessment=73.9 (1.9) years
§ Model 1: analyses adjusted for sex, education, ethnicity, and birth cohort (5-year groups)
‖ Model 2: Model 1 plus adjustment for health-related behaviors (smoking, alcohol consumption, consumption of fruits and vegetables, and physical activity)
Table S3. Association between metabolic syndrome components at <60, 60 to <70, and ≥70 years and incidence of dementia using inverse probability weighting to account for missing data.

|                      | Elevated WC | Elevated triglycerides | Low HDL-C | Elevated blood pressure | Elevated fasting glucose |
|----------------------|-------------|------------------------|-----------|-------------------------|--------------------------|
|                      | No          | Yes                    | No        | Yes                     | No                       | Yes                     |
| **At age <60 years**, Median (IQR) follow-up 20.8 (15.5, 26.2) years |             |                        |           |                         |                          |                         |
| Dementia cases/total, No | 322/5979    | 71/1286                | 270/5102  | 123/2163                | 306/5954                 | 87/1311                 |
| Rate/1000 person-years | 2.78        | 3.21                   | 2.79      | 2.98                    | 2.69                     | 3.58                    |
| Cox regression, HR (95% CI) |            |                        |           |                         |                          |                         |
| Model 1§             | 1 (Ref.)    | 1.42 (1.09, 1.84)      | 1 (Ref.)  | 1.06 (0.85, 1.32)       | 1 (Ref.)                 | 1.32 (1.04, 1.67)       |
| Model 2¶             | 1 (Ref.)    | 1.36 (1.05, 1.77)      | 1 (Ref.)  | 1.00 (0.81, 1.25)       | 1 (Ref.)                 | 1.29 (1.01, 1.64)       |
| **At age 60 years to <70 years**, Median (IQR) follow-up 10.4 (6.4, 15.6) years |             |                        |           |                         |                          |                         |
| Dementia cases/total, No | 318/4760    | 99/1900                | 269/4052  | 148/2608                | 295/4551                 | 122/2109                |
| Rate/1000 person-years | 5.88        | 5.54                   | 5.83      | 5.71                    | 5.65                     | 6.14                    |
| Cox regression, HR (95% CI) |            |                        |           |                         |                          |                         |
| Model 1§             | 1 (Ref.)    | 1.06 (0.84, 1.36)      | 1 (Ref.)  | 1.17 (0.96, 1.44)       | 1 (Ref.)                 | 1.31 (1.06, 1.63)       |
| Model 2¶             | 1 (Ref.)    | 1.01 (0.79, 1.29)      | 1 (Ref.)  | 1.14 (0.92, 1.40)       | 1 (Ref.)                 | 1.26 (1.01, 1.56)       |
| **At age ≥70 years**, Median (IQR) follow-up 4.2 (3.1, 7.1) years |             |                        |           |                         |                          |                         |
| Dementia cases/total, No | 177/2327    | 87/1281                | 122/1685  | 142/1923                | 133/1798                 | 131/1810                |
| Rate/1000 person-years | 15.30       | 13.72                  | 14.03     | 15.37                   | 14.17                    | 15.32                   |
| Cox regression, HR (95% CI) |            |                        |           |                         |                          |                         |
| Model 1§             | 1 (Ref.)    | 0.94 (0.71, 1.24)      | 1 (Ref.)  | 1.11 (0.86, 1.43)       | 1 (Ref.)                 | 1.11 (0.86, 1.43)       |
| Model 2¶             | 1 (Ref.)    | 0.91 (0.69, 1.20)      | 1 (Ref.)  | 1.08 (0.84, 1.40)       | 1 (Ref.)                 | 1.09 (0.84, 1.40)       |

IQR: interquartile range; WC: waist circumference; HDL-C: high density lipoprotein-cholesterol.

* Mean (SD) age at assessment=55.1 (2.9) years
† Mean (SD) age at assessment=65.0 (1.5) years
‡ Mean (SD) age at assessment=73.9 (1.9) years
§ Model 1: analyses adjusted for sex, education, ethnicity, and birth cohort (5-year groups)
¶ Model 2: Model 1 plus adjustment for health-related behaviors (smoking, alcohol consumption, consumption of fruits and vegetables, and physical activity)
Table S4. Association between the number of MetS components at <60, 60 to <70, and ≥70 years and incidence of dementia using inverse probability weighting to account for missing data.

| Number of components | N Dementia cases/Total | Rate of dementia/1000 person-years | HR (95% CI) Model 1§ | HR (95% CI) Model 2|| |
|----------------------|------------------------|----------------------------------|----------------------|----------------------|----------------------|
| At age <60 years*, Median (IQR) follow-up 20.8 (15.5, 26.2) years | | | | | |
| 0                    | 97/2325                | 2.21                             | 1 (Ref.)             | 1 (Ref.)             | 1.14 (1.06, 1.23)    |
| 1                    | 123/2145               | 2.93                             | 1.26 (0.96, 1.65)    | 1.21 (0.93, 1.59)    |
| 2                    | 92/1493                | 3.27                             | 1.52 (1.14, 2.03)    | 1.44 (1.08, 1.92)    |
| 3                    | 47/823                 | 3.00                             | 1.31 (0.93, 1.86)    | 1.24 (0.87, 1.76)    |
| 4                    | 28/380                 | 4.21                             | 1.91 (1.26, 2.90)    | 1.84 (1.21, 2.79)    |
| 5                    | 6/99                   | 3.67                             | 1.89 (0.79, 4.50)    | 1.72 (0.70, 4.24)    |
| At age 60 to <70 years†, Median (IQR) follow-up 10.4 (6.4, 15.6) years | | | | | |
| 0                    | 75/1409                | 4.66                             | 1 (Ref.)             | 1 (Ref.)             | 1.09 (1.02, 1.17)    |
| 1                    | 127/1753               | 6.31                             | 1.32 (0.98, 1.78)    | 1.30 (0.97, 1.76)    |
| 2                    | 100/1387               | 6.20                             | 1.38 (1.01, 1.89)    | 1.34 (0.98, 1.83)    |
| 3                    | 68/1089                | 6.32                             | 1.50 (1.07, 2.11)    | 1.43 (1.02, 2.01)    |
| 4                    | 33/696                 | 5.05                             | 1.40 (0.91, 2.14)    | 1.29 (0.84, 1.98)    |
| 5                    | 14/326                 | 5.38                             | 1.68 (0.94, 3.01)    | 1.56 (0.87, 2.80)    |
| At age ≥70 years‡, Median (IQR) follow-up 4.2 (3.1, 7.1) years | | | | | |
| 0                    | 23/442                 | 10.25                            | 1 (Ref.)             | 1 (Ref.)             | 1.05 (0.97, 1.15)    |
| 1                    | 57/729                 | 15.27                            | 1.49 (0.90, 2.46)    | 1.43 (0.86, 2.36)    |
| 2                    | 48/650                 | 14.12                            | 1.42 (0.86, 2.37)    | 1.37 (0.82, 2.29)    |
| 3                    | 68/844                 | 16.10                            | 1.56 (0.96, 2.54)    | 1.49 (0.91, 2.43)    |
| 4                    | 50/683                 | 16.44                            | 1.63 (0.96, 2.76)    | 1.56 (0.93, 2.64)    |
| 5                    | 18/260                 | 13.59                            | 1.33 (0.71, 2.50)    | 1.21 (0.64, 2.29)    |

IQR: interquartile range; * Mean (SD) age at assessment=55.1 (2.9) years
† Mean (SD) age at assessment=65.0 (1.5) years
‡ Mean (SD) age at assessment=73.9 (1.9) years
§ Model 1: analyses adjusted for sex, education, ethnicity, and birth cohort (5-year groups)
|| Model 2: Model 1 plus adjustment for health-related behaviors (smoking, alcohol consumption, consumption of fruits and vegetables, and physical activity)
Table S5. Alternate cut-off points to define metabolic risk at <60, 60 to <70, and ≥70 years and incidence of dementia using inverse probability weighting to account for missing data.

| Metabolic risk | Dementia cases/total, No | Rate of dementia/1000 person-years | HR (95% CI) |
|---------------|-------------------------|------------------------------------|-------------|
|               |                         |                                    | Model 1§    | Model 2¶ |
| High defined as presence of ≥1 MetS components | | | | |
| At age <60 years* | | | | |
| No risk | 97/2325 | 2.21 | 1 (Ref.) | 1 (Ref.) |
| High risk | 296/4940 | 3.15 | 1.40 (1.11, 1.76) | 1.33 (1.06, 1.68) |
| At age 60 to <70 years† | | | | |
| No risk | 75/1409 | 4.66 | 1 (Ref.) | 1 (Ref.) |
| High risk | 342/5251 | 6.09 | 1.39 (1.07, 1.81) | 1.34 (1.04, 1.75) |
| At age ≥70 years‡ | | | | |
| No risk | 23/442 | 10.25 | 1 (Ref.) | 1 (Ref.) |
| High risk | 241/3166 | 15.35 | 1.51 (0.97, 2.35) | 1.44 (0.92, 2.25) |
| High metabolic risk defined as presence of ≥2 MetS components | | | | |
| At age <60 years* | | | | |
| No risk | 220/4470 | 2.56 | 1 (Ref.) | 1 (Ref.) |
| High risk | 173/2795 | 3.32 | 1.34 (1.10, 1.64) | 1.29 (1.06, 1.58) |
| At age 60 to <70 years† | | | | |
| No risk | 202/3162 | 5.59 | 1 (Ref.) | 1 (Ref.) |
| High risk | 215/3498 | 5.97 | 1.21 (0.99, 1.48) | 1.17 (0.96, 1.43) |
| At age ≥70 years‡ | | | | |
| No risk | 80/1171 | 13.40 | 1 (Ref.) | 1 (Ref.) |
| High risk | 184/2437 | 15.37 | 1.16 (0.88, 1.53) | 1.14 (0.86, 1.49) |
| High metabolic risk defined as presence of ≥3 MetS components (current clinical MetS definition) | | | | |
| At age <60 years* | | | | |
| No risk (non-MetS) | 312/5963 | 2.73 | 1 (Ref.) | 1 (Ref.) |
| High risk (MetS) | 81/1302 | 3.39 | 1.23 (0.96, 1.58) | 1.20 (0.94, 1.53) |
| At age 60 to <70 years† | | | | |
| No risk (non-MetS) | 302/4549 | 5.78 | 1 (Ref.) | 1 (Ref.) |
| High risk (MetS) | 115/2111 | 5.80 | 1.19 (0.96, 1.49) | 1.14 (0.91, 1.42) |
| At age ≥70 years‡ | | | | |
| No risk (non-MetS) | 128/1821 | 13.66 | 1 (Ref.) | 1 (Ref.) |
| High risk (MetS) | 136/1787 | 15.83 | 1.15 (0.89, 1.48) | 1.13 (0.87, 1.45) |

MetS: Metabolic syndrome.

* Mean (SD) age at assessment=55.1 (2.9) years; median (IQR) follow-up 20.8 (15.5, 26.2) years
† Mean (SD) age at assessment=65.0 (1.5) years; median (IQR) follow-up 10.4 (6.4, 15.6) years
‡ Mean (SD) age at assessment=73.9 (1.9) years; median (IQR) follow-up 4.2 (3.1, 7.1) years
§ Model 1: analyses adjusted for sex, education, ethnicity, and birth cohort (5-year groups)
¶ Model 2: Model 1 plus adjustment for health-related behaviors (smoking, alcohol consumption, consumption of fruits and vegetables, and physical activity)
Figure S1. Flow chart of sample selection.

**ANALYSIS POPULATION**

**ANALYSIS of METABOLIC SYNDROME AT <60 years (40-59.9) N=7265**

Exclusions:
- No linkage to electronic health records, N=10
- Died before age 40, N=159
- Prevalent dementia cases, N=0
- No participation between age 40-59.9, N=1698
- Missing data on metabolic syndrome, N=1275
- Missing data on covariates, N=1

Analysis population:
- 39% from 1991-93 wave
- 27% from 1997-99 wave
- 29% from 2002-04 wave
- 5% from 2007-09 wave

**ANALYSIS of METABOLIC SYNDROME AT 60 to <70 years (60-69.9) N=6660**

Exclusions:
- No linkage to electronic health records, N=10
- Died before age 60, N=586
- Prevalent dementia cases, N=5
- No participation between age 60-69.9, N=2005
- Missing data on metabolic syndrome, N=961
- Missing data on covariates, N=1

Analysis population:
- 1% from 1991-93 wave
- 20% from 1997-99 wave
- 21% from 2002-04 wave
- 23% from 2007-09 wave
- 23% from 2012-13 wave
- 12% from 2015-16 wave

**ANALYSIS of METABOLIC SYNDROME AT ≥70 years (70-84) N=3608**

Exclusions:
- No linkage to electronic health records, N=10
- Died before age 70, N=1487
- Prevalent dementia cases, N=34
- No participation between age 70-84, N=4563
- Missing data on metabolic syndrome, N=906
- Missing data on covariates, N=0

Analysis population:
- 4% from 2002-04 wave
- 29% from 2007-09 wave
- 24% from 2012-13 wave
- 43% from 2015-16 wave

**End of follow-up for dementia ascertainment:** March 31st 2019
Figure S2. Association of number of metabolic syndrome components at age <60 (A), 60 to <70 (B), and ≥70 years (C) with dementia using restricted cubic splines.

Number of metabolic syndrome components were modeled by restricted cubic splines with three age-specific knots in a Cox regression model adjusted for sex, education, ethnicity, and health-related behaviors (smoking, alcohol consumption, consumption of fruits and vegetables, and physical activity). Hazard ratios were calculated with no metabolic syndrome components as the reference.
Figure S3. Multistate models to examine the role of “high metabolic risk” at age <60 years in transition to cardiovascular disease (stroke, coronary heart disease or heart failure) and dementia using inverse probability weighting to account for missing data.

1) “High metabolic risk” at age <60 years defined as presence of ≥1 MetS components

2) “High metabolic risk” at age <60 years defined as presence of ≥2 MetS components

3) “High metabolic risk” at age <60 years defined as presence of ≥3 MetS components (current clinical MetS definition)

Role of “high metabolic risk” (defined as presence of ≥1, ≥2, or ≥3 MetS components) at age <60 years in the risk of transition from: A) “high metabolic risk” and CVD, B) CVD to dementia, and c) “high metabolic risk” to dementia in those free of CVD over the follow-up.

Analyses with age as timescale and adjusted for sex, education, ethnicity, and health-related behaviors at age <60 (smoking, alcohol consumption, consumption of fruits and vegetables, and physical activity)