

## **SUPPLEMENTAL MATERIAL**

**Supplementary Table S1:** Rates and rate ratios of fatal- and non-fatal cardiovascular disease for pre-diabetes subgroups, using the WHO/IEC criteria or the ADA criteria.

|                            | <b>Definition</b>                                | <b>Rate per 1000-PY</b> | <b>RR</b>        | <b>RR<sub>adj1</sub></b> | <b>RR<sub>adj2</sub></b> |
|----------------------------|--|-------------------------|------------------|--------------------------|--------------------------|
| <b>WHO/IEC</b>             |  |                         |                  |                          |                          |
| <u>Overall</u>             |  |                         |                  |                          |                          |
| Normal glycaemia           | FPG < 6.1 mmol/L and HbA <sub>1c</sub> < 6.0%    | 9.6 (8.8;10.5)          | ref              | ref                      | ref                      |
| Pre-diabetes               | FPG 6.1-6.9 mmol/L or HbA <sub>1c</sub> 6.0-6.4% | 15.1 (12.3;18.6)        | 1.58 (1.26;1.98) | 1.49 (1.19;1.88)         | 1.09 (0.86;1.37)         |
| <u>By HbA<sub>1c</sub></u> |  |                         |                  |                          |                          |
| Normal glycaemia           | HbA <sub>1c</sub> < 6.0%                         | 9.6 (8.8;10.5)          | ref              | ref                      | ref                      |
| Pre-diabetes               | HbA <sub>1c</sub> 6.0-6.4%                       | 19.8 (14.9;26.4)        | 2.06 (1.53;2.77) | 1.54 (1.14;2.08)         | 1.02 (0.75;1.39)         |
| <u>By FPG</u>              |  |                         |                  |                          |                          |
| Normal glycaemia           | FPG < 6.1 mmol/L                                 | 9.9 (9.1;10.8)          | ref              | ref                      | ref                      |
| Pre-diabetes               | FPG 6.1-6.9 mmol/L                               | 12.6 (9.6;16.6)         | 1.27 (0.95;1.69) | 1.13 (0.85;1.51)         | 0.92 (0.69; 1.23)        |
| <u>By 2hPG</u>             |  |                         |                  |                          |                          |
| Normal glycaemia           | 2hPG < 7.8 mmol/L                                | 8.8 (8.0;9.8)           | ref              | ref                      | ref                      |
| Pre-diabetes               | 2hPG 7.8-11.0 mmol/L                             | 12.1 (9.8;15.1)         | 1.37 (1.08;1.75) | 1.08 (0.84;1.37)         | 0.88 (0.69; 1.13)        |
| <b>ADA</b>                 |  |                         |                  |                          |                          |
| <u>Overall</u>             |  |                         |                  |                          |                          |
| Normal glycaemia           | FPG < 5.6 mmol/L and HbA <sub>1c</sub> < 5.7%    | 8.9 (8.0; 9.9)          | ref              | ref                      | ref                      |
| Pre-diabetes               | FPG 5.6-6.9 mmol/L or HbA <sub>1c</sub> 5.7-6.4% | 12.5 (11.1;14.2)        | 1.41 (1.20;1.67) | 1.35 (1.14;1.59)         | 1.07 (0.90;1.26)         |
| <u>By HbA<sub>1c</sub></u> |  |                         |                  |                          |                          |
| Normal glycaemia           | HbA <sub>1c</sub> < 5.7%                         | 8.8 (8.0;9.7)           | ref              | ref                      | ref                      |

|              |                            |                  |                  |                  |                  |
|--------------|----------------------------|------------------|------------------|------------------|------------------|
| Pre-diabetes | HbA <sub>1c</sub> 5.7-6.4% | 17.8 (15.1;21.0) | 2.03 (1.67;2.45) | 1.56 (1.29;1.90) | 1.12 (0.92;1.37) |
|              | HbA <sub>1c</sub> 5.7-5.9% | 16.7 (13.7;20.5) | 1.91 (1.53;2.38) | 1.49 (1.19;1.87) | 1.15 (0.91;1.44) |
|              | HbA <sub>1c</sub> 6.0-6.4% | 19.8 (14.9;26.4) | 2.26 (1.67;3.05) | 1.66 (1.22;2.25) | 1.00 (0.72;1.36) |

By FPG

|                  |                    |                 |                  |                  |                  |
|------------------|--------------------|-----------------|------------------|------------------|------------------|
| Normal glycaemia | FPG < 5.6 mmol/L   | 9.9 (9.0;10.9)  | ref              | ref              | ref              |
| Pre-diabetes     | FPG 5.6-6.9 mmol/L | 10.8 (9.3;12.6) | 1.09 (0.91;1.31) | 0.98 (0.81;1.18) | 0.89 (0.74;1.08) |
|                  | FPG 5.6-6.0 mmol/L | 10.1 (8.4;12.2) | 1.02 (0.82;1.26) | 0.93 (0.75;1.15) | 0.89 (0.72;1.10) |
|                  | FPG 6.1-6.9 mmol/L | 12.6 (9.6;16.6) | 1.27 (0.95;1.70) | 1.11 (0.83;1.49) | 0.90 (0.68;1.21) |

By 2hPG

|                  |                      |                 |                  |                  |                  |
|------------------|----------------------|-----------------|------------------|------------------|------------------|
| Normal glycaemia | 2hPG < 7.8 mmol/L    | 8.8 (8.0;9.8)   | ref              | ref              | ref              |
| Pre-diabetes     | 2hPG 7.8-11.0 mmol/L | 12.1 (9.8;15.1) | 1.37 (1.08;1.75) | 1.08 (0.84;1.37) | 0.88 (0.69;1.13) |

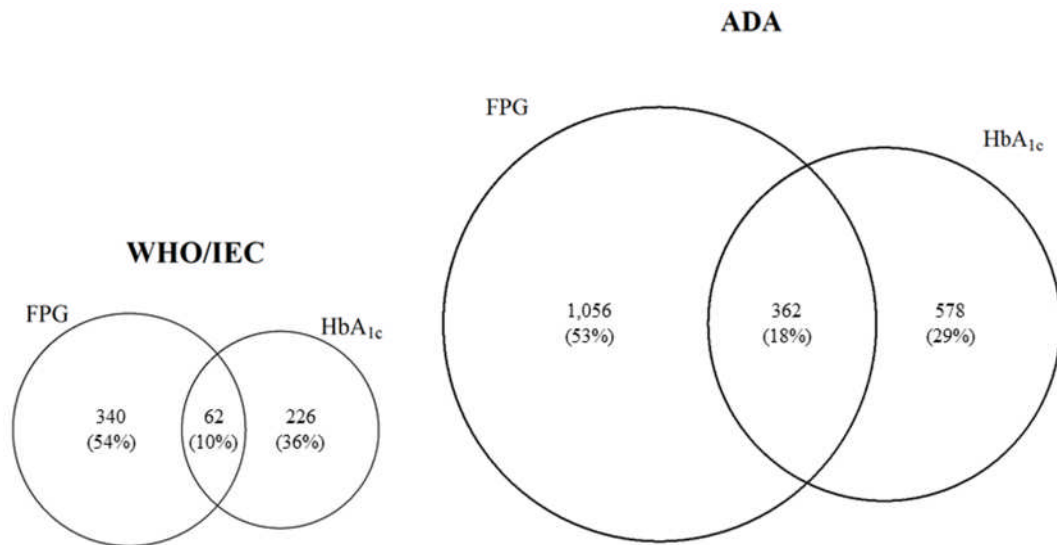
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IEC: International Expert Committee; FPG: fasting plasma glucose; 2hPG: 2-hour plasma glucose; RR: crude rate ratio; RR<sub>adj1</sub>: rate ratio adjusted for age, sex and ethnicity; RR<sub>adj2</sub>: rate ratio adjusted for age, sex, ethnicity, smoking, total cholesterol, HDL-cholesterol, systolic blood pressure, and use of antihypertensive treatment.

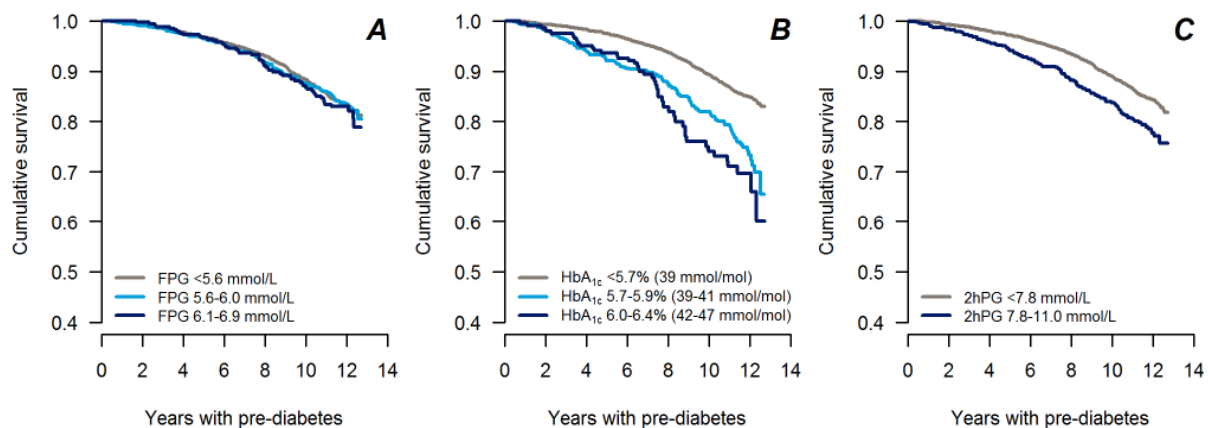
**Supplementary Table S2** Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for 10-year incidence of an event (cardiovascular disease or mortality) for pre-diabetes subgroups, using the WHO/IEC criteria or the ADA criteria.

|                            | <b>Definition</b>                                 | <b>Sensitivity</b> | <b>Specificity</b> | <b>PPV</b>       | <b>NPV</b>       |
|----------------------------|---|--------------------|--------------------|------------------|------------------|
| <u>Overall</u>             |   |                    |                    |                  |                  |
| WHO/IEC:                   | FPG 6.1-6.9 mmol/L or HbA <sub>1c</sub> 6.0-6.4 % | 0.17 (0.14;0.20)   | 0.89 (0.88;0.90)   | 0.17 (0.14;0.20) | 0.89 (0.88;0.89) |
| ADA                        | FPG 5.6-6.9 mmol/L or HbA <sub>1c</sub> 5.7-6.4 % | 0.45 (0.41;0.49)   | 0.64 (0.63;0.66)   | 0.15 (0.13;0.16) | 0.89 (0.88;0.90) |
| <u>By FPG</u>              |   |                    |                    |                  |                  |
| WHO:                       | FPG 6.1-6.9 mmol/L                                | 0.10 (0.07;0.12)   | 0.93 (0.92;0.94)   | 0.15 (0.12;0.19) | 0.88 (0.87;0.89) |
| ADA:                       | FPG 5.6-6.9 mmol/L                                | 0.29 (0.26;0.33)   | 0.74 (0.73;0.75)   | 0.13 (0.12;0.15) | 0.88 (0.87;0.89) |
| <u>By HbA<sub>1c</sub></u> |   |                    |                    |                  |                  |
| IEC:                       | HbA <sub>1c</sub> 6.0-6.4 %                       | 0.10 (0.07;0.12)   | 0.95 (0.95;0.96)   | 0.22 (0.17;0.27) | 0.89 (0.88;0.89) |
| ADA:                       | HbA <sub>1c</sub> 5.7-6.4 %                       | 0.27 (0.23;0.30)   | 0.84 (0.83;0.85)   | 0.18 (0.16;0.21) | 0.89 (0.88;0.90) |
| <u>By 2hPG</u>             |   |                    |                    |                  |                  |
| ADA & WHO                  | 2hPG 7.8-11.0 mmol/L                              | 0.20 (0.16;0.23)   | 0.86 (0.85;0.87)   | 0.15 (0.12;0.18) | 0.90 (0.89;0.91) |

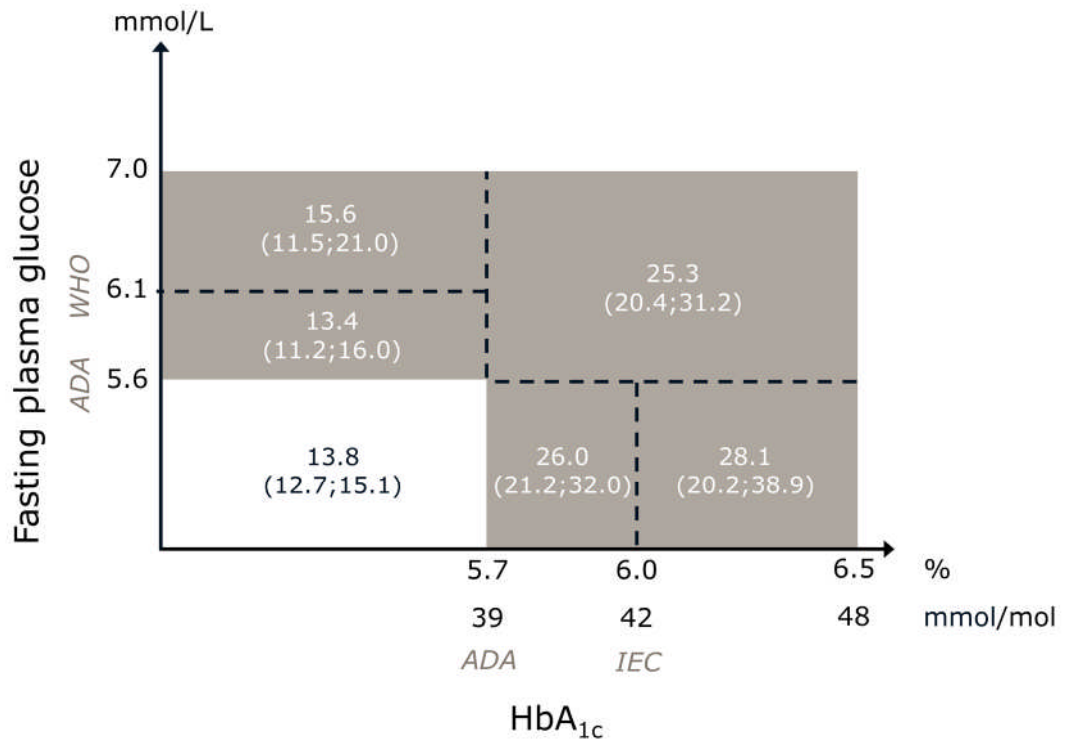
IEC: International Expert Committee; FPG: fasting plasma glucose; 2hPG: 2-hour plasma glucose



**Supplementary Figure S1** Venn diagrams for pre-diabetes by FPG and HbA<sub>1c</sub> defined by WHO/IEC and ADA. Circle sizes reflect the number of people with pre-diabetes for each criterion. Percentages show the relative distribution of pre-diabetes individuals within a criterion. ADA: American Diabetes Association; FPG: fasting plasma glucose; IEC: International Expert Committee; WHO: World Health Organization.



**Supplementary Figure S2:** Kaplan-Meier survival curves for an event (cardiovascular disease or mortality) for individuals with pre-diabetes (light blue and dark blue) versus normal glycaemia (grey), using fasting plasma glucose (A), HbA<sub>1c</sub> (B) or 2-hour glucose (C). Only the 4,730 participants with complete data on FPG, 2hPG and HbA<sub>1c</sub> are included. FPG: Fasting plasma glucose; 2hPG: 2-hour plasma glucose.



**Supplementary Figure S3** Incidence rates (95% CI) per 1000-PY by subgroups of pre-diabetes by the ADA criteria or WHO/IEC criteria for fasting plasma glucose and HbA<sub>1c</sub>. IEC: international expert committee; FPG: Fasting plasma glucose.