Socioeconomic status and the 25x25 risk factors as determinants of premature mortality: a multicohort study of 1.7 million men and women

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In 2011, WHO put in place the 25x25 initiative, a plan to cut mortality due to non-communicable diseases by 25% by 2025 with actions on 7 major risk factors (25x25 risk factors):
- harmful use of alcohol
- insufficient physical activity
- current tobacco use
- raised blood pressure
- intake of salt
- diabetes
- obesity

Background

- Socioeconomic circumstances influence all these factors but are never included as targets in global health strategies.
- However, they are modifiable by policies at the local, national, and international level as are risk factors targeted by existing global health strategies.

Objective: To compare the contribution of socioeconomic status to mortality and years-of-life-lost with that of the 25x25 conventional risk factors.
Data

- 48 independent prospective cohort studies (including Gazel) from Europe, the USA, and Australia with information on:
  - Socioeconomic status (occupational position)
  - 25x25 risk factors (high alcohol intake, physical inactivity, current smoking, hypertension, diabetes and obesity)
  - Mortality

1,751,479 participants (54% women)
Data

- Socioeconomic status (last known occupational position in 3 categories)
- Smoking (current/ never/former)
- Alcohol consumption: abstainers (0 units per week) / moderate (1–21 units per week for men, 1–14 per week for women) / or heavy (>21 units per week for men, >14 per week for women) drinkers.
- Physical inactivity: differently for each cohort
- Body-mass index (BMI): normal (18·5–<25 kg/m²), overweight (25–<30 kg/m²), or obese (≥30 kg/m²).
- Hypertension: SBP≥140 mm Hg or DBP ≥ 90 mm Hg or current intake of anti-hypertensive medication or self-reported hypertension
- Diabetes fasting glucose ≥ 7 mmol/L or 2 h post-load glucose ≥ 11·1 mmol/L or glycated haemoglobin A1c ≥ 6·5% or self-reported diabetes
- Data for salt intake only available from a few cohort studies so it was omitted from our analysis
Statistical analysis

- Analyses first performed separately in each study; estimates subsequently combined in a meta-analytical framework
- HR and 95% CIs generated using flexible parametric survival models on the cumulative hazards scale
- Separate models fitted for men and women and included marital status and race or ethnicity (minimally adjusted models)
- Models then mutually adjusted for all risk factors simultaneously (mutually adjusted)
- Population attributable fraction (PAF) calculated based on the HR and the proportion of participants exposed
- Years of life lost calculated as difference of the areas under the survival curves (from age 40 years to 85 years) comparing population exposed to a given risk factor with the reference population with no exposure
Results

- Over 26.6 million person-years at risk (mean follow-up 13.3 years), 310,277 participants died.
- In men, 43,765 (15.2% of total) with low occupational position died and 17,160 (11.5%) with high occupational position died.
- In women, 11,835 (9.4% of total) with low occupational position died and 8,292 (6.8%) with high occupational position died.
- Participants with low occupational position had higher mortality risk than did those with high occupational position, HR 1.42, 95% CI 1.38–1.45 for men HR 1.34, 1.28–1.39 for women.
### Results – HR SES and 25x25 risk factors

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Deaths</th>
<th>Participants</th>
<th>Time at risk (years)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low SES (reference high SES)</td>
<td></td>
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</tr>
<tr>
<td>Men</td>
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<td>619402</td>
<td>9835775</td>
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<tr>
<td>Women</td>
<td>48791</td>
<td>592157</td>
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<td>1.34 (1.28-1.39)</td>
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<tr>
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<td>325540</td>
<td>3749493</td>
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<td>Physical inactivity</td>
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<td>Men</td>
<td>39794</td>
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<td>398992</td>
<td>4941600</td>
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<td>High alcohol intake (reference moderate alcohol intake)</td>
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<tr>
<td>Men</td>
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<td>235245</td>
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<td>Women</td>
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<td>363666</td>
<td>4649162</td>
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<td>Hypertension</td>
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<td>Men</td>
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<td>273190</td>
<td>3184326</td>
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<td>Women</td>
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<td>391681</td>
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<td>Obesity (reference normal BMI)</td>
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<tr>
<td>Men</td>
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<td>636779</td>
<td>17632210</td>
<td>1.04 (0.98-1.11)</td>
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<td>Women</td>
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<td>815005</td>
<td>22310188</td>
<td>1.17 (1.10-1.24)</td>
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</table>

Association of low SES with mortality comparable to that of the other major risk factors
Results – HRs, mutually adjusted models

<table>
<thead>
<tr>
<th>Risk factor and outcomes</th>
<th>Minimally adjusted HR (95% CI)</th>
<th>Mutually adjusted HR (95% CI)</th>
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<tr>
<td>Low SES (reference high SES)</td>
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<tr>
<td>All-cause</td>
<td>1.46 (1.39-1.53)</td>
<td>1.26 (1.21-1.32)</td>
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<tr>
<td>CVD</td>
<td>1.52 (1.37-1.67)</td>
<td>1.29 (1.16-1.43)</td>
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<tr>
<td>Cancer</td>
<td>1.43 (1.34-1.52)</td>
<td>1.26 (1.19-1.34)</td>
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<tr>
<td>Other</td>
<td>1.45 (1.35-1.56)</td>
<td>1.25 (1.17-1.33)</td>
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<tr>
<td>Current smoking (reference never smoking)</td>
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<tr>
<td>All-cause</td>
<td>2.27 (2.14-2.39)</td>
<td>2.21 (2.10-2.33)</td>
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<tr>
<td>CVD</td>
<td>2.19 (1.98-2.42)</td>
<td>2.21 (2.00-2.44)</td>
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<tr>
<td>Cancer</td>
<td>2.64 (2.40-2.91)</td>
<td>2.52 (2.32-2.74)</td>
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<td>Other</td>
<td>2.05 (1.91-2.20)</td>
<td>1.99 (1.85-2.14)</td>
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<td>Diabetes</td>
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<td></td>
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<tr>
<td>All-cause</td>
<td>1.87 (1.72-2.03)</td>
<td>1.73 (1.60-1.88)</td>
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<td>CVD</td>
<td>2.18 (1.86-2.55)</td>
<td>1.92 (1.64-2.27)</td>
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<tr>
<td>Cancer</td>
<td>1.21 (1.06-1.38)</td>
<td>1.18 (1.04-1.34)</td>
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<tr>
<td>Other</td>
<td>2.21 (2.01-2.42)</td>
<td>2.08 (1.91-2.26)</td>
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<td>Physical inactivity</td>
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<tr>
<td>All-cause</td>
<td>1.43 (1.34-1.53)</td>
<td>1.28 (1.19-1.37)</td>
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<tr>
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<tr>
<td>Cancer</td>
<td>1.25 (1.15-1.36)</td>
<td>1.14 (1.06-1.23)</td>
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<tr>
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<td>1.50 (1.37-1.64)</td>
<td>1.34 (1.22-1.47)</td>
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<td>1.36 (1.23-1.51)</td>
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<td>1.19 (1.08-1.32)</td>
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<tr>
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<td>1.18 (1.09-1.27)</td>
<td>1.05 (0.97-1.14)</td>
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<tr>
<td>CVD</td>
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<td>1.22 (1.06-1.40)</td>
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<tr>
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<td>1.01 (0.92-1.10)</td>
<td>1.02 (0.94-1.11)</td>
</tr>
<tr>
<td>Other</td>
<td>1.17 (1.08-1.25)</td>
<td>1.01 (0.92-1.10)</td>
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</table>

Association between low socioeconomic status and mortality consistent across causes of death and remained significant in mutually adjusted models.
<table>
<thead>
<tr>
<th>Men</th>
<th>Deaths</th>
<th>Mean follow-up (years)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COLAUS</td>
<td>55</td>
<td>6.16</td>
<td>2.08 (0.98-4.38)</td>
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<td>NHIS 2009</td>
<td>86</td>
<td>3.32</td>
<td>1.23 (0.72-2.11)</td>
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<td>NHIS 2008</td>
<td>111</td>
<td>4.18</td>
<td>1.26 (0.78-2.00)</td>
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<td>MIDUS</td>
<td>133</td>
<td>11.61</td>
<td>1.21 (0.81-1.81)</td>
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<td>EPISODE</td>
<td>144</td>
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<td>1.64 (0.94-2.86)</td>
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<td>NHIS 2007</td>
<td>148</td>
<td>5.13</td>
<td>1.30 (0.85-1.99)</td>
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<td>INCDS</td>
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<td>1.74 (1.15-2.64)</td>
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<td>1.82 (1.29-2.58)</td>
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<td>190</td>
<td>3.86</td>
<td>1.21 (0.85-1.73)</td>
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<td>234</td>
<td>5.73</td>
<td>1.17 (0.85-1.60)</td>
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<td>7.00</td>
<td>1.09 (0.80-1.48)</td>
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<td>291</td>
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<td>WLSG</td>
<td>360</td>
<td>12.72</td>
<td>1.31 (1.04-1.65)</td>
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<td>10.05</td>
<td>1.90 (1.47-2.47)</td>
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<td>NHANES 2003</td>
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<td>7.39</td>
<td>1.19 (0.94-1.49)</td>
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<td>463</td>
<td>11.01</td>
<td>1.89 (1.49-2.39)</td>
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<td>NHANES 1999</td>
<td>479</td>
<td>10.51</td>
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<td>1.32 (1.05-1.64)</td>
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<td>11.94</td>
<td>1.47 (1.19-1.81)</td>
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<td>WHITEHALL</td>
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<td>8.15</td>
<td>1.53 (1.32-1.77)</td>
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<td>1.48 (1.27-1.72)</td>
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<td>15.45</td>
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<td>17.28</td>
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<td>Nunnemakers County</td>
<td>167</td>
<td>25.90</td>
<td>1.36 (1.23-1.54)</td>
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</tbody>
</table>

**Figure 1:** Mortality for low versus high occupational position in men in 46 cohort studies.
- HRs are adjusted for age, marital status, and race or ethnicity.
- Pooled HR is represented with a grey diamond.
### Results - Population Attributable Fraction

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Prevalence (%)</th>
<th>PAF (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low SES (intermediate/low)</td>
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<td></td>
</tr>
<tr>
<td>Men</td>
<td>25.1/42.4</td>
<td>18.94 (17.63 to 20.24)</td>
</tr>
<tr>
<td>Women</td>
<td>45.8/28.1</td>
<td>15.33 (12.76 to 17.90)</td>
</tr>
<tr>
<td>Current smoking (former/current)</td>
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</tr>
<tr>
<td>Men</td>
<td>32.8/27.1</td>
<td>29.04 (26.90 to 31.18)</td>
</tr>
<tr>
<td>Women</td>
<td>20.9/21.0</td>
<td>21.04 (19.02 to 23.07)</td>
</tr>
<tr>
<td>Diabetes</td>
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</tr>
<tr>
<td>Men</td>
<td>9.4</td>
<td>5.93 (4.85 to 7.00)</td>
</tr>
<tr>
<td>Women</td>
<td>8.7</td>
<td>6.88 (5.76 to 8.00)</td>
</tr>
<tr>
<td>Physical inactivity</td>
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<tr>
<td>Men</td>
<td>39.5</td>
<td>26.16 (23.01 to 29.31)</td>
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<tr>
<td>Women</td>
<td>46.2</td>
<td>23.41 (20.42 to 26.39)</td>
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<td>High alcohol intake</td>
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<tr>
<td>Men</td>
<td>10.0</td>
<td>4.34 (3.26 to 5.42)</td>
</tr>
<tr>
<td>Women</td>
<td>4.8</td>
<td>3.27 (2.34 to 4.20)</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Men</td>
<td>38.0</td>
<td>9.76 (7.92 to 11.60)</td>
</tr>
<tr>
<td>Women</td>
<td>31.4</td>
<td>8.21 (6.22 to 10.20)</td>
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<td>Obesity (overweight/obese)</td>
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<tr>
<td>Men</td>
<td>43.9/19.4</td>
<td>-5.57 (-8.84 to -2.31)</td>
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<tr>
<td>Women</td>
<td>28.9/22.0</td>
<td>3.55 (1.35 to 5.74)</td>
</tr>
</tbody>
</table>

PAF of low SES comparable to that of the other major risk factors.
Results: Years of Life Lost

Partial life expectancy at 40 years reduced by more than 2 years because of low SES. All other $25 \times 25$ factors were associated with decreased life expectancy, apart from BMI.
Interpretation

- **Comparable** health impact of low socioeconomic status to that of major risk factors → socioeconomic circumstances, in addition to the 25x25 factors, should be treated as a target for local and global health strategies, health risk surveillance, interventions and policy

- Limitations:
  - Use of single indicator of SES
  - Difficult to disentangle interconnected pathways
  - PAF assume causal relationships
  - Broad categorizations of risk factors and SES
  - Heterogeneity across cohorts
Conclusions

- Existing global strategies and actions defined in the 25 × 25 health plan and the Global Burden of Diseases surveillance programme potentially exclude a major determinant of health from the agenda.

- Similar to the risk factors targeted by existing global health strategies, socioeconomic circumstances are modifiable by policies at the local, national, and international levels:
  - promotion of early childhood development
  - poverty reduction
  - improvements to access to high-quality education
  - enacting of compulsory schooling laws
  - creation of safe home, school, and work environments (some examples)
Thank you for your attention