Appendix 3 Criteria for assessment of risk of bias

| Domain | Lower risk of bias | Higher risk of bias | Unclear risk of bias |
|---------------------------------------|--|--|--------------------------|
| Differential loss to follow- up | Subjects lost to follow- up did not significantly differ from the rest of the sample. | There were significant differences in characteristics likely to increase risk of bias between the baseline data reported for the whole sample and the baseline data of subjects lost to follow-up. | No information available |
| Measurement error - exposure | Available data suggest that the tool used to measure loneliness and/or social isolation was comparatively valid and reliable. | Loneliness and/or social isolation were assessed using a tool that was of limited validity and/or reliability. | No information available |
| Measurement error - outcome | Measure based on information from medical records, registers and/or death certificates. | Reliance on self- report of diagnosis. | No information available |
| Detection bias | Assessors were blinded to exposure. | Assessors were not blinded to exposure. | No information available |
| Confounding | Studies controlled for CVD risk factors correlated with loneliness/social isolation, i.e. gender (in mixed samples), age, socio-economic status. Note that measures relating to health (e.g. diabetes, health-behaviours) are not included in this list because of them potentially being on the causal pathway. | Studies did not control for age, gender and socio-economic status. | No information available |