Appendices and Prisma checklist

The effect of exposure to long working hours on stroke: A systematic review and meta-analysis from the WHO/ILO Joint Estimates of the Work-Related Burden of Disease and Injury

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Table of appendices

Appendix 1. Description of missing data requested and received

Study ID	Description of missing data	Person(s) from whom missing data were requested	Date of request(s)	Data received	**Response**
Conway 2017	Differentiate Ischemic Heart Disease from stroke (and if possible subtype)	Dr Conway	22/09/2018	23/10/2018	Not possible to differentiate
Jeong 2013	Asked to change reference group and provide details on models	Dr Jeong	22/09/2018	05/11/2018	Done (possible for short term)
Kim 2013	Asked to change reference, days/week, and details on models	Dr Kim	22/09/2018	03/12/2019	Done (except impossible to have information on hours worked per weeks)
Landsbergis 2013	Differentiate Ischemic Heart Disease from stroke (and if possible subtype)	Dr Landsbergis	22/09/2018	12/10/2018	Not individual data
Lin 2018	Differentiate Ischemic Heart Disease from stroke (and if possible subtype)	Dr Lin	22/09/2018	23/09/2018	Not possible individual data (ecological)
Mortensen 2018	Differentiate Ischemic Heart Disease from stroke (and if possible subtype)	Dr Mortensen	22/09/2018	24/10/2018	Focus only on informal work with data partly similar other study
O'Reilly 2013	Differentiate Ischemic Heart Disease from stroke (and if possible subtype)	Dr O'Reilly	22/09/2018	23/10/2018	Included in another study, cannot perform analyses during the project
Shin 2017	Differentiate Ischemic Heart Disease from stroke (and if possible subtype)	Dr Shin	22/09/2018		-
Tarumi 2003	Differentiate Ischemic Heart Disease from stroke (and if possible subtype)	Dr Tarumi	22/09/2018		-
Uchiyama 2005	Differentiate Ischemic Heart Disease from stroke (and if possible subtype)	Dr Uchiyama	22/09/2018		-
Kivimäki 2015	Obtain 40-48 and 49-54 hours/work with disaggregated related data (and if possible stroke subtype)	Dr Kivimäki	13/07/2018	12/072019	40-48 and 49-54 hours/work obtained
Choi 2008	Detail of number working hours and model details	Dr Choi	24/09/2018		-
Hannerz 2018	Asked for disaggregated data	Dr Hannerz	27/02/2019	14/03/2019	Done (except age)
Fadel 2019	Asked for Constances data and disaggregated data, additional models	Pr Zins and Goldberg	14/12/2018	14/01/2019	Done
Hayashi 2019	Asked to change reference and days/week, disaggregated	Dr Iso	3/06/2019		-

Appendix 2. Excluded studies and reasons for their exclusion

Study	**Reasons**
O'Reilly 2013	Duplicate (data separated in Kivimaki 2015)
Jang 2015	Duplicate (same data than Jeong)
Mortensen 2018	Duplicate (Whithall II available in Kivimaki 2015, and not hours at work only)
Won 2014	Design inappropriate (only compensated data)
Chung 2013	Design inappropriate (only compensated data)
Arnao 2016	No relevant exposure (not long working hours)
Boscher 2017	No relevant exposure (not long working hours)
Guan 2017	No relevant exposure (not long working hours)
Huang 2015	No relevant exposure (not long working hours)
Padyab 2014	No relevant exposure (not long working hours)
Poorabdian 2013	No relevant exposure (not long working hours)
Prajjwal 2017	No relevant exposure (not long working hours)
Szerencsi 2014	No relevant exposure (not long working hours)
Tam 2017	No relevant exposure (not long working hours)
Andersson 2007	Wrong outcomes (not stroke or mixed with other data)
Antropova 2009	Wrong outcomes (not stroke or mixed with other data)
Artazcoz 2007	Wrong outcomes (not stroke or mixed with other data)
Artazcoz 2009	Wrong outcomes (not stroke or mixed with other data)
Becher 2018	Wrong outcomes (not stroke or mixed with other data)
Cappuccio 2017	Wrong outcomes (not stroke or mixed with other data)
Caruso 2014	Wrong outcomes (not stroke or mixed with other data)
Choi 2008	Wrong outcomes (not stroke or mixed with other data)
Conway 2017	Wrong outcomes (not stroke or mixed with other data)
Ferrario 2012	Wrong outcomes (not stroke or mixed with other data)
Krause 2009	Wrong outcomes (not stroke or mixed with other data)
Landsbergis 2013	Wrong outcomes (not stroke or mixed with other data)

Lin 2018	Wrong outcomes (not stroke or mixed with other data)
Shin 2017	Wrong outcomes (not stroke or mixed with other data)
Tarumi 2003	Wrong outcomes (not stroke or mixed with other data)
Uchiyama 2005	Wrong outcomes (not stroke or mixed with other data)

Appendix 3. Search strategies and results

Database	Search String	Record Count: 01/01/2005-04/18/2018 (Unless Noted)
MEDLINE via OVID	1. exp "personnel staffing and scheduling"/ 2. "personnel staffing and scheduling".ti,ab,kw. 3. shift work schedule.ti,ab,kw. 4. work schedule tolerance.ti,ab,kw. 5. workload.kw. 6. workday shifts.ti,ab,kw. 7. overwork*.ti,ab,kw. 8. overtime.ti,ab,kw. 9. workweek*.ti,ab,kw. 10. (work* adj3 hour*).ti,ab,kw. 11. (work* adj3 schedul*).ti,ab,kw. 12. work* ad3 roster.ti,ab,kw. 13. (work* adj3 organi#ation).ti,ab,kw. 14. (work* adj3 time*).ti,ab,kw. 15. (work* adj3 overload*).ti,ab,kw. 16. (work* adj3 extend*).ti,ab,kw. 17. (work* adj3 compress*).ti,ab,kw. 18. (work* adj3 week*).ti,ab,kw. 19. (work* adj3 day?).ti,ab,kw. 20. (job? adj3 hour*).ti,ab,kw. 21. (job? adj3 schedul*).ti,ab,kw. 22. (job? adj3 roster).ti,ab,kw. 23. (job? adj3 organi#ation).ti,ab,kw. 24. (job? adj3 time*).ti,ab,kw. 25. (job? adj3 overload*).ti,ab,kw. 26. (job? adj3 extend*).ti,ab,kw.	443

	27. (job? adj3 compress*).ti,ab,kw. 28. (job? adj3 week*).ti,ab,kw. 29. (job? adj3 day?).ti,ab,kw. 30. (shift? adj3 hour*).ti,ab,kw. 31. (shift? adj3 schedul*).ti,ab,kw. 32. (shift? adj3 roster).ti,ab,kw. 33. (shift? adj3 organi#ation).ti,ab,kw. 34. (shift? adj3 time*).ti,ab,kw. 35. (shift? adj3 overload*).ti,ab,kw. 36. (shift? adj3 extend*).ti,ab,kw. 37. (shift? adj3 compress*).ti,ab,kw. 38. (shift? adj3 week*).ti,ab,kw. 39. (shift? adj3 day?).ti,ab,kw. 40. (work* and (life* or live*) and (balances* or imbalances* or unbalances* or interference*)).ti,ab,kw. 41. (work* and famil* and conflict*).ti,ab,kw. 42. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 43. exp Brain Ischemia/ 44. exp Intracranial Hemorrhages/ 45. exp Stroke/ 46. exp 'Intracranial embolism/ and thrombosis'/ 47. exp Brain infarction/ 48. Intracranial h?emorrhage.ti,ab,kw. 49. intracerebral h?emorrhage.ti,ab,kw. 50. Subarachnoid h?emorrhage.ti,ab,kw. 51. Cerebral infarction.ti,ab,kw. 52. Anterior Choroidal Artery Infarction.ti,ab,kw. 53. Posterior Chorodial Artery Infarction.ti,ab,kw. 54. Infarction, anterior cerebral artery/ 55. Infarction, posterior cerebral artery/	

	56. Carotid artery diseases/ 57. Carotid artery thrombosis/ 58. Carotid artery, internal, dissection/ 59. Subcortical Infarction.ti,ab,kw. 60. (Stroke$ or apoplex$).ti,ab,kw. 61. Cerebrovascular accident.ti,ab,kw. 62. Cerebrovascular disorder.ti,ab,kw. 63. Intracranial vascular disease.ti,ab,kw. 64. Intracranial vascular disorder.ti,ab,kw. 65. Stroke, Lacunar/ 66. intracranial arterial diseases/ 67. Cerebral arterial diseases/ 68. Basal ganglia cerebrovascular disease/ 69. Cerebrovascular occlusion.ti,ab,kw. 70. Cerebrovascular insufficienc$.ti,ab,kw. 71. Vertebral artery dissection/ 72. ((brain or cerebr$ or cerebell$ or vertebrobasil$ or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or middle cerebr$ or mca$ or anterior circulation) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$)).tw. 73. (isch?emi$ adj6 (stroke$ or apoplex$ or cerebral vasc$ or cerebrovasc$ or cva or attack$)).tw. 74. 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 75. exp Clinical Trial/ 76. trial$.tw. 77. experiment$.tw. 78. (intervention adj3 (study or studies or analys$)).tw. 79. Epidemiologic Studies/ 80. Observational Study/ 81. ((observational or epidemiologic$) adj (study or studies or analys$)).tw. 82. exp Cohort Studies/ 83. cohort$.tw.	

	84. (panel$ adj3 (study or studies or analys$ or data)).tw. 85. (follow up adj (study or studies or analys$)).tw. 86. (repeat$ adj measure$).tw. 87. longitudinal$.tw. 88. retrospective$.tw. 89. exp Case-control Studies/ 90. (case$ adj3 control$).tw. 91. (exposure$ adj4 (study or studies or analys$)).tw. 92. 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 93. 42 and 74 and 92	
PUBMED	(“Personnel staffing and scheduling” OR “shift work schedule” OR “work life balance” OR “work schedule tolerance” OR workload OR “Workday Shifts” OR overwork* OR overtime OR workweek* OR ((work* OR job* OR shift*) AND (hour* OR schedul* OR roster OR organization OR organisation OR time* OR overload* OR extend* OR compresse* OR week* OR day OR days)) OR (work* AND (life* OR live*) AND (balances* OR imbalances* OR unbalances* OR interference*)) OR (work* AND famil* AND conflict*)) AND (“Brain Ischemia” OR "brain infarction" OR "brain stem infarctions" OR "lateral medullary syndrome" OR "dementia, multi-infarct" OR "infarction, anterior cerebral artery" OR "infarction, middle cerebral artery" OR "infarction, posterior cerebral artery" OR "cerebral infarction" OR "hypoxia-ischemia, brain" OR "ischemic attack, transient" OR "vertebrobasilar insufficiency" OR "subclavian steal syndrome" OR “Intracranial Hemorrhages" OR "Stroke" OR "Intracranial embolism and thrombosis" OR "Brain infarction" OR "Intracranial hemorrhage" OR "Intracranial haemorrhage" OR "intracerebral haemorrhage" OR “cranial hematoma” OR “subdural hematoma” OR “epidural hematoma” OR "Subarachnoid hemorrhage" OR "Subarachnoid haemorrhage" OR "Cerebral infarction" OR "Anterior Choroidal Artery Infarction" OR "Posterior Chorodial Artery Infarction" OR "Infarction, anterior cerebral artery" OR "Infarction, posterior cerebral artery" OR "Carotid artery diseases" OR "Carotid artery thrombosis" OR "Carotid artery, internal, dissection" OR "Subcortical Infarction" OR Stroke OR strokes OR apoplex* OR "Cerebrovascular accident" OR "Cerebrovascular disorder" OR "Intracranial vascular disease" OR "Intracranial vascular disorder" OR "Stroke, Lacunar" OR "intracranial arterial diseases" OR "Cerebral arterial diseases" OR "Basal ganglia cerebrovascular disease" OR "Cerebrovascular occlusion" OR "Cerebrovascular insufficiency" OR "Cerebrovascular insufficiencies" OR "Vertebral artery dissection" OR ((brain OR cerebr* OR cerebell* OR vertebrobasil* OR hemispher* OR intracran* OR intracerebral OR infratentorial OR supratentorial OR "middle cerebral" OR "middle cerebellum" OR MCA* OR "anterior circulation") AND (ischemi* or infarct* or thrombo* or emboli* or occlus* or hypoxi*)) OR (ischemi* AND (stroke OR strokes OR apoplex* OR cerebrovasc* OR CVA OR attack*))) AND ("Clinical Trial" OR trial* OR experiment* OR "controlled trial" OR “intervention study” OR “intervention analysis” OR “intervention studies” OR "Epidemiologic Studies" OR "Observational Study" OR “observational studies” OR “observational analysis” OR "Cohort Studies" OR "prospective studies" OR "retrospective studies" OR “follow up study” OR “follow up studies” OR longitudinal* OR retrospective* OR "Case-control Studies")	6,391
EMBASE	(“Personnel staffing and scheduling” OR “shift work schedule” OR “work life balance” OR “work schedule tolerance” OR workload OR “Workday Shifts” OR overwork* OR overtime OR workweek* OR ((work* OR job* OR shift*) NEAR/3 (hour*	

	OR schedul* OR roster OR organization OR organisation OR time* OR overload* OR extend* OR compresse* OR week* OR day OR days)) OR (work* AND (life* OR live*) AND (balances* OR imbalances* OR unbalances* OR interference*)) OR (work* AND famil* AND conflict*)) AND (“Brain Ischemia” OR "brain infarction" OR "brain stem infarctions" OR "lateral medullary syndrome" OR "dementia, multi-infarct" OR "infarction, anterior cerebral artery" OR "infarction, middle cerebral artery" OR "infarction, posterior cerebral artery" OR "cerebral infarction" OR "hypoxia-ischemia, brain" OR "ischemic attack, transient" OR "vertebrobasilar insufficiency" OR "subclavian steal syndrome" OR “Intracranial Hemorrhages" OR "Stroke" OR "Intracranial embolism and thrombosis" OR "Brain infarction" OR "Intracranial hemorrhage" OR "Intracranial haemorrhage" OR "intracerebral haemorrhage" OR (hematoma NEAR/2 (subdural OR epidural OR cranial)) OR "Subarachnoid hemorrhage" OR "Subarachnoid haemorrhage" OR "Cerebral infarction" OR "Anterior Choroidal Artery Infarction" OR "Posterior Chorodial Artery Infarction" OR "Infarction, anterior cerebral artery" OR "Infarction, posterior cerebral artery" OR "Carotid artery diseases" OR "Carotid artery thrombosis" OR "Carotid artery, internal, dissection" OR "Subcortical Infarction" OR Stroke OR strokes OR apoplex* OR "Cerebrovascular accident" OR "Cerebrovascular disorder" OR "Intracranial vascular disease" OR "Intracranial vascular disorder" OR "Stroke, Lacunar" OR "intracranial arterial diseases" OR "Cerebral arterial diseases" OR "Basal ganglia cerebrovascular disease" OR "Cerebrovascular occlusion" OR "Cerebrovascular insufficiency" OR "Cerebrovascular insufficiencies" OR "Vertebral artery dissection" OR ((brain OR cerebr* OR cerebell* OR vertebrobasil* OR hemispher* OR intracran* OR intracerebral OR infratentorial OR supratentorial OR "middle cerebral" OR "middle cerebellum" OR MCA* OR "anterior circulation") NEAR/5 (ischemi* or infarct* or thrombo* or emboli* or occlus* or hypoxi*)) OR (ischemi* NEAR/6 (stroke OR strokes OR apoplex* OR cerebrovasc* OR CVA OR attack*))) AND ("Clinical Trial" OR trial* OR experiment* OR "controlled trial" OR (intervention NEAR/3 (study or studies or analys*)) OR "Epidemiologic Studies" OR "Observational Study" OR ((observational OR epidemiologic*) NEAR/1 (study or studies or analys*))OR "Cohort Studies" OR "prospective studies" OR "retrospective studies" OR cohort* OR (panel* NEAR/3 (study OR studies OR analys* OR data)) OR ("follow up" NEAR/1 (study OR studies OR analys$)) OR (repeat* NEAR/1 measure*) OR longitudinal* OR retrospective* OR "Case-control Studies" OR (case* NEAR/3 control*) OR (exposure* NEAR/4 (study or studies or analys*)))	
Scopus	(“Personnel staffing and scheduling” OR “shift work schedule” OR “work life balance” OR “work schedule tolerance” OR workload OR “Workday Shifts” OR overwork* OR overtime OR workweek* OR ((work* OR job* OR shift*) W/1 (hour* OR schedul* OR roster OR organization OR organisation OR time* OR overload* OR extend* OR compresse* OR week* OR day OR days)) OR (work* AND (life* OR live*) AND (balances* OR imbalances* OR unbalances* OR interference*)) OR (work* AND famil* AND conflict*)) AND (“Brain Ischemia” OR "brain infarction" OR "brain stem infarctions" OR "lateral medullary syndrome" OR "dementia, multi-infarct" OR "infarction, anterior cerebral artery" OR "infarction, middle cerebral artery" OR "infarction, posterior cerebral artery" OR "cerebral infarction" OR "hypoxia-ischemia, brain" OR "ischemic attack, transient" OR "vertebrobasilar insufficiency" OR "subclavian steal syndrome" OR “Intracranial Hemorrhages" OR "Stroke" OR "Intracranial embolism and thrombosis" OR "Brain infarction" OR "Intracranial hemorrhage" OR "Intracranial haemorrhage" OR "intracerebral haemorrhage" OR (hematoma W/2 (subdural OR epidural OR cranial)) OR "Subarachnoid hemorrhage" OR "Subarachnoid haemorrhage" OR "Cerebral infarction" OR "Anterior Choroidal Artery Infarction" OR "Posterior Chorodial Artery Infarction" OR "Infarction, anterior cerebral artery" OR "Infarction, posterior cerebral artery" OR "Carotid artery diseases" OR "Carotid artery thrombosis" OR "Carotid artery, internal, dissection" OR "Subcortical Infarction" OR Stroke OR strokes OR apoplex* OR "Cerebrovascular accident" OR "Cerebrovascular disorder" OR "Intracranial vascular disease" OR "Intracranial vascular disorder" OR "Stroke, Lacunar" OR "intracranial arterial diseases" OR "Cerebral arterial diseases" OR "Basal ganglia	6,212

	cerebrovascular disease" OR "Cerebrovascular occlusion" OR "Cerebrovascular insufficiency" OR "Cerebrovascular insufficiencies" OR "Vertebral artery dissection" OR ((brain OR cerebr* OR cerebell* OR vertebrobasil* OR hemispher* OR intracran* OR intracerebral OR infratentorial OR supratentorial OR "middle cerebral" OR "middle cerebellum" OR MCA* OR "anterior circulation") W/1 (ischemi* or infarct* or thrombo* or emboli* or occlus* or hypoxi*)) OR (ischemi* W/1 (stroke OR strokes OR apoplex* OR cerebrovasc* OR CVA OR attack*))) AND ("Clinical Trial" OR trial* OR experiment* OR "controlled trial" OR (intervention W/1 (study or studies or analys*)) OR "Epidemiologic Studies" OR "Observational Study" OR ((observational OR epidemiologic*) W/1 (study or studies or analys*))OR "Cohort Studies" OR "prospective studies" OR "retrospective studies" OR cohort* OR (panel* W/1 (study OR studies OR analys* OR data)) OR ("follow up" W/1 (study OR studies OR analys$)) OR (repeat* W/1 measure*) OR longitudinal* OR retrospective* OR "Case-control Studies" OR (case* W/1 control*) OR (exposure* W/1 (study or studies or analys*)))OR "Intracranial vascular disease" OR "Intracranial vascular disorder" OR "Stroke, Lacunar" OR "intracranial arterial diseases" OR "Cerebral arterial diseases" OR "Basal ganglia cerebrovascular disease" OR "Cerebrovascular occlusion" OR "Cerebrovascular insufficiency" OR "Cerebrovascular insufficiencies" OR "Vertebral artery dissection" OR ((brain OR cerebr* OR cerebell* OR vertebrobasil* OR hemispher* OR intracran* OR intracerebral OR infratentorial OR supratentorial OR "middle cerebral" OR "middle cerebellum" OR MCA* OR "anterior circulation") W/5 (ischemi* or infarct* or thrombo* or emboli* or occlus* or hypoxi*)) OR (ischemi* W/6 (stroke OR strokes OR apoplex* OR cerebrovasc* OR CVA OR attack*))) AND ("Clinical Trial" OR trial* OR experiment* OR "controlled trial" OR (intervention W/3 (study or studies or analys*)) OR "Epidemiologic Studies" OR "Observational Study" OR ((observational OR epidemiologic*) W/1 (study or studies or analys*))OR "Cohort Studies" OR "prospective studies" OR "retrospective studies" OR cohort* OR (panel* W/3 (study OR studies OR analys* OR data)) OR ("follow up" W/1 (study OR studies OR analys$)) OR (repeat* W/1 measure*) OR longitudinal* OR retrospective* OR "Case-control Studies" OR (case* W/3 control*) OR (exposure* W/4 (study or studies or analys*)))	
Web of Science	(“Personnel staffing and scheduling” OR “shift work schedule” OR “work life balance” OR “work schedule tolerance” OR workload OR “Workday Shifts” OR overwork* OR overtime OR workweek* OR ((work* OR job* OR shift*) NEAR/3 (hour* OR schedul* OR roster OR organization OR organisation OR time* OR overload* OR extend* OR compresse* OR week* OR day OR days)) OR (work* AND (life* OR live*) AND (balances* OR imbalances* OR unbalances* OR interference*)) OR (work* AND famil* AND conflict*)) AND (“Brain Ischemia” OR "brain infarction" OR "brain stem infarctions" OR "lateral medullary syndrome" OR "dementia, multi-infarct" OR "infarction, anterior cerebral artery" OR "infarction, middle cerebral artery" OR "infarction, posterior cerebral artery" OR "cerebral infarction" OR "hypoxia-ischemia, brain" OR "ischemic attack, transient" OR "vertebrobasilar insufficiency" OR "subclavian steal syndrome" OR “Intracranial Hemorrhages" OR "Stroke" OR "Intracranial embolism and thrombosis" OR "Brain infarction" OR "Intracranial hemorrhage" OR "Intracranial haemorrhage" OR "intracerebral haemorrhage" OR (hematoma NEAR/2 (subdural OR epidural OR cranial)) OR "Subarachnoid hemorrhage" OR "Subarachnoid haemorrhage" OR "Cerebral infarction" OR "Anterior Choroidal Artery Infarction" OR "Posterior Chorodial Artery Infarction" OR "Infarction, anterior cerebral artery" OR "Infarction, posterior cerebral artery" OR "Carotid artery diseases" OR "Carotid artery thrombosis" OR "Carotid artery, internal, dissection" OR "Subcortical Infarction" OR Stroke OR strokes OR apoplex* OR "Cerebrovascular accident" OR "Cerebrovascular disorder" OR "Intracranial vascular disease" OR "Intracranial vascular disorder" OR "Stroke, Lacunar" OR "intracranial arterial diseases" OR "Cerebral arterial diseases" OR "Basal ganglia cerebrovascular disease" OR "Cerebrovascular occlusion" OR	657

	"Cerebrovascular insufficiency" OR "Cerebrovascular insufficiencies" OR "Vertebral artery dissection" OR ((brain OR cerebr* OR cerebell* OR vertebrobasil* OR hemispher* OR intracran* OR intracerebral OR infratentorial OR supratentorial OR "middle cerebral" OR "middle cerebellum" OR MCA* OR "anterior circulation") NEAR/5 (ischemi* or infarct* or thrombo* or emboli* or occlus* or hypoxi*)) OR (ischemi* NEAR/6 (stroke OR strokes OR apoplex* OR cerebrovasc* OR CVA OR attack*))) AND ("Clinical Trial" OR trial* OR experiment* OR "controlled trial" OR (intervention NEAR/3 (study or studies or analys*)) OR "Epidemiologic Studies" OR "Observational Study" OR ((observational OR epidemiologic*) NEAR/1 (study or studies or analys*))OR "Cohort Studies" OR "prospective studies" OR "retrospective studies" OR cohort* OR (panel* NEAR/3 (study OR studies OR analys* OR data)) OR ("follow up" NEAR/1 (study OR studies OR analys$)) OR (repeat* NEAR/1 measure*) OR longitudinal* OR retrospective* OR "Case-control Studies" OR (case* NEAR/3 control*) OR (exposure* NEAR/4 (study or studies or analys*)))	
CISDOC	1 stroke work time 2 stroke work hour 3 stroke work duration 4 stroke work schedule 5 stroke work organize 6 stroke work overload 7 stroke work extend 8 stroke work week 9 stroke work day 10 stroke job time 11 stroke job hour 12 stroke job duration 13 stroke job schedule 14 stroke job organize 15 stroke job overload 16 stroke job extend 17 stroke job week 18 stroke job day 19 stroke shift time 20 stroke shift hour 21 stroke shift duration 22 stroke shift schedule 23 stroke shift organize 24 stroke shift overload 25 stroke shift extend 26 stroke shift week 27 stroke shift day	12
PsycINFO	(“Personnel staffing and scheduling” OR “shift work schedule” OR “work life balance” OR “work schedule tolerance” OR	138

	workload OR “Workday Shifts” OR overwork* OR overtime OR workweek* OR ((work* OR job* OR shift*) N3 (hour* OR schedul* OR roster OR organization OR organisation OR time* OR overload* OR extend* OR compresse* OR week* OR day OR days)) OR (work* AND (life* OR live*) AND (balances* OR imbalances* OR unbalances* OR interference*)) OR (work* AND famil* AND conflict*)) AND (“Brain Ischemia” OR "brain infarction" OR "brain stem infarctions" OR "lateral medullary syndrome" OR "dementia, multi-infarct" OR "infarction, anterior cerebral artery" OR "infarction, middle cerebral artery" OR "infarction, posterior cerebral artery" OR "cerebral infarction" OR "hypoxia-ischemia, brain" OR "ischemic attack, transient" OR "vertebrobasilar insufficiency" OR "subclavian steal syndrome" OR “Intracranial Hemorrhages" OR "Stroke" OR "Intracranial embolism and thrombosis" OR "Brain infarction" OR "Intracranial hemorrhage" OR "Intracranial haemorrhage" OR "intracerebral haemorrhage" OR (hematoma N2 (subdural OR epidural OR cranial)) OR "Subarachnoid hemorrhage" OR "Subarachnoid haemorrhage" OR "Cerebral infarction" OR "Anterior Choroidal Artery Infarction" OR "Posterior Chorodial Artery Infarction" OR "Infarction, anterior cerebral artery" OR "Infarction, posterior cerebral artery" OR "Carotid artery diseases" OR "Carotid artery thrombosis" OR "Carotid artery, internal, dissection" OR "Subcortical Infarction" OR Stroke OR strokes OR apoplex* OR "Cerebrovascular accident" OR "Cerebrovascular disorder" OR "Intracranial vascular disease" OR "Intracranial vascular disorder" OR "Stroke, Lacunar" OR "intracranial arterial diseases" OR "Cerebral arterial diseases" OR "Basal ganglia cerebrovascular disease" OR "Cerebrovascular occlusion" OR "Cerebrovascular insufficiency" OR "Cerebrovascular insufficiencies" OR "Vertebral artery dissection" OR ((brain OR cerebr* OR cerebell* OR vertebrobasil* OR hemispher* OR intracran* OR intracerebral OR infratentorial OR supratentorial OR "middle cerebral" OR "middle cerebellum" OR MCA* OR "anterior circulation") N5 (ischemi* or infarct* or thrombo* or emboli* or occlus* or hypoxi*)) OR (ischemi* N6 (stroke OR strokes OR apoplex* OR cerebrovasc* OR CVA OR attack*))) AND ("Clinical Trial" OR trial* OR experiment* OR "controlled trial" OR (intervention N3 (study or studies or analys*)) OR "Epidemiologic Studies" OR "Observational Study" OR ((observational OR epidemiologic*) N1 (study or studies or analys*))OR "Cohort Studies" OR "prospective studies" OR "retrospective studies" OR cohort* OR (panel* N3 (study OR studies OR analys* OR data)) OR ("follow up" N1 (study OR studies OR analys$)) OR (repeat* N1 measure*) OR longitudinal* OR retrospective* OR "Case-control Studies" OR (case* N3 control*) OR (exposure* N4 (study or studies or analys*)))	

Appendix 4. Details of risk of Bias for each study including on acquired stroke

Study ID	Domains	*Judgement*	Comment
Fadel 2019	**Study group**	*Low*	Inclusion criterion was age (among person affiliated) and proportion is high. Large sample and representativeness of French population (self-owner/ farmers excluded), allowed us to be confident on low risk of bias (https://www.constances.fr/index_EN.php).
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes since the cohort is not focused on that question and the association is not widely known (in addition SR and examination is performed at different steps). Each participant had a medical interview completed by a physician, including history of stroke (all subtypes together) and age of occurrence, diabetes, history of high blood pressure, dyslipidemia (hypercholesterolemia or hypertriglyceridemia), family history of cardiovascular events, and body mass index. The main outcome was having a stroke reported by a physician. Authors were contacted to confirmed (short-report published, many valuable information not mentioned in the paper for this reason but the previous submitted version).
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job. Moreover, survey is performed for another purpose. See the questionnaires and design https://www.constances.fr/questionnaires.php
	Outcome assessment	*Probably Low*	Physician interview, and the authors gave information why this stroke diagnosis is acknowledged to be valid (discussion)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), with and without other confounder. Logistic models were used for the association between LWH and stroke, adjusted by available cardiovascular risk factors. Additional models were stratified by occupation, age, and sex. For sensitivity analyses, models were ran using a 5-year lag from exposure to occurrence of stroke
	Incomplete Outcome Data	*Probably Low*	No incomplete data, sensitivity analyses performed (Web material provides additional analyses)
	Selective outcome reporting	*Probably Low*	No selective report suspected Authors were contacted to confirmed (short-report published, many valuable information not mentioned in the paper for this reason but the previous submitted version).
	Conflict of interests	*Low*	No conflict of interest detected. The authors are paid by their institutions. The CONSTANCES cohort study was supported and funded by the Caisse nationale d'assurance maladie; it is an "Infrastructure nationale en Biologie et Santé" and benefits from Agence National de la Recherche (ANR-11- INBS-0002) grant funding
	Other Bias	*Probably Low*	References were different, and no possibility to differentiate ischemic/ hemorrhagic stroke. NB authors that have done the bias assessment were not included in the Fadel paper.
Hannerz 2018	**Study group**	*Probably Low*	National database of representative of population, but response rate to interview was some years >70% though decreased.
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes since the cohort is not focused on that question and the association is not widely known (in addition SR and examination is performed at different steps.
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job The interviews cover various aspects of labour-market participation, including working hours and work schedules. The usual weekly working hours in the LFs are calculated by adding the hours usually worked in secondary jobs to the ones usually worked in a primary job. In total, 357,085 people participated in LFs at least once during 1999–2013 activity), medical history (diabetes, coronary heart disease, respiratory problems, family medical history), health perception, and psychosocial scales for depression and anxiety'
	Outcome assessment	*Low*	The endpoint of the present study was clinically registered hospital treatment or death (n<10%), The endpoint of the present study was clinically registered hospital treatment or death, with a stroke as the principal diagnosis/cause of death. In keeping with Kivimäki et al. [1], the following ICD- 10 codes were included in the case definition: I60 subarachnoid haemorrhage; I61 intracerebral haemorrhage; I63 cerebral infarction; I64 stroke, not specified as haemorrhage or infarction. In keeping with Fransson et al, this set of diagnoses will be called 'overall stroke'. It should, however, be noted that the set does not include traumatic strokes (which are found in the ICD-category s06 'intracranial inju- ries'), nor does it include the ICD-10 code I62 'other non-traumatic intracranial haemorrhage'
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant. The analysis was adjusted for sex, age (10-year classes), calendar time (2000–2004, 2005–2009, 2010–2014), time passed since start of follow-up (0–4 years, 5–9 years, ≥10 years) and socio-economic status (SES; low, medium, high, unknown). Age, calendar time and time passed since start of follow-up were treated as dynamic (time-varying) variables according to the classes above. Sensitivity analysis 1: Controlling for possible reverse causation Sensitivity analysis 2: Only stable exposure to working hours Secondary analysis: Distinguishing between types of stroke
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different and only 676 emigration/death, and 15 exits from national registry (0.45%)

	Selective outcome reporting	*Probably Low*	Protocol published is similar https://figshare.com/articles/The_association_between_long_working_hours_and_stroke_in_the_general_workforce_of_Denmark_a_study_protocol/4684951/1
	Conflict of interests	*Low*	Funding sources were limited to governmental agencies (The study was mainly funded by the institutions of the authors and partially supported by a grant from The Danish Working Environment Research Fund).
	Other Bias	*Probably Low*	No other source of bias was identified. However no information on duration, and the national context of regulation in Denmark; "2015 Eurofound EWCS survey results in Denmark: 91% of people are satisfied with working conditions in their job". The result is possibly related to mediation on good even long working hours. https://www.eurofound.europa.eu/country/denmark
Hayashi 2019	**Study group**	*High*	Japan public health center-based prospective (JPHC) study cohort (I and II) is an extremely high quality cohort, but1/ women are excluded and it is mentioned "average working hours for women (4.00 h/day) were approximately half the average for men (8.11 h/day) and it was much less for women than expected; papers from same cohort usually included Suita/Osaka, as recommended in the paper described the attrition in 2001 *(Tsugane S, Sobue T. Baseline survey of JPHC study--design and participation rate. Japan Public Health Center-based Prospective Study on Cancer and Cardiovascular Diseases. J Epidemiol. 2001 Oct;11(6 Suppl):S24-9. PubMed PMID:11763136*). For these reasons, the group rather quote as high risk of bias related to internal validity (even though we might be wrong)
	Blinding	*Probably Low*	Outcome is based on administrative data and though blinding was not reported it is unlikely knowledge of exposure might affect the outcome. Furthermore, outcome assessors were blind to lifestyle.
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Low*	The endpoint of the present study was clinically registered hospital treatment or death after review medical data (Stroke was confirmed in accordance with the National Survey of Stroke criteria. For each type of stroke, a definite diagnosis was established based on examination of computed tomography scans, magnetic resonance images, or autopsy)
	Confounding	*Probably Low*	Yes multiple models to include age and occupations (only men included),other risk factors, as well as Lag/ competitive models, though long working hours in hours/days (period of week is lacking) The first model was adjusted for baseline age (years). The second model was also adjusted for body mass index (BMI) (kg/m2), history of hypertension yes, no), history of diabetes mellitus (yes, no), history of hyperlipidemia (yes, no), smoking status (never, former, current), alcohol intake (never, former, <300 g [alcohol]/ week, ≥300 g/week), walking or standing time (<1 h/day, 1 to <3 h/day, ≥3 h/day), and sleep duration (hours). The third model was further adjusted for occupation (salaried employee, agriculture/forestry/fishery worker, self-employed, professional worker, multiple occupational worker, unclassified occupational worker, homemaker, and unemployed). For the sensitivity analysis accounting for the competing risk of death, the Fine and Gray model was used to estimate sub-hazard ratios of acute myocardial infarction and total stroke. Furthermore, we conducted the analysis by excluding acute myocardial infarction and stroke events that took place in the first 3 years of follow up to examine the reverse causation, as in a previous meta-analysis
	Incomplete Outcome Data	*Probably Low*	Missing data were clearly reported, and were low, correctly considered.
	Selective outcome reporting	*Probably Low*	No data on interaction between age, occupation and stroke but not significant overall, even don't have the protocol
	Conflict of interests	*Low*	No conflict of interest detected. This study was supported by the National Cancer Center Research and Development Fund (23-A-31 [toku] and 26-A-2; since 2011) and a Grant-in-Aid for Cancer Research from the Ministry of Health, Labour and Welfare of Japan (1989–2010).
	Other Bias	*Probably Low*	References different (reference include 44h/w after approximation), no duration of exposure with only under estimation of the effect
Jeong 2013	**Study group**	*Probably High*	Case control study but a nationwide, multicenter, and matched case-control study
	Blinding	*Probably Low*	Interviewers were blind to the study hypothesis, though not stated explicitly
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Low*	Optimal diagnostic procedure The target patients for registration were patients with a diagnosis of cerebral infarction, intracerebral hemorrhage, subarachnoid hemorrhage, (based on the ICD 10th ed.; I63, I61, I60,) between the ages of 20 and 65 who visited the emergency rooms of participating university hospitals. The survey was completed in the emergency room or in the ward by trained interviewers (nurses or emergency medical technicians) after acute treatment, and all non-fatal cases were registered

	Confounding	*Probably Low*	Age/ gender = case control. Other included. Only question is the occupation, but access to white and blue collar. A multivariate logistic regression analysis was conducted with CVDs as the dependent variable and short-term and long-term working hours as the independent variable. In the case of short-term working hours, the group working 40.1−50 hours was used as a reference, and in the case of long-term working hours, the group working 40.1−48 hours was used as a reference. Level of education, hypertension, diabetes, exercise, BMI, smoking and level of alcohol intake were used as covariates. Variables used for matching (age, gender and type of occupation) were not included in the multivariate logistic regression model
	Incomplete Outcome Data	*Probably Low*	No difference between missing and non-missing with reasons (Therefore, 410 cases were regarded as appropriate candidates for this study; however, an additional 62 cases were excluded due to missing information about working hours. Finally, 348 cases remained as the case group (99 cases of acute myocardial infarction, 57 cases of subarachnoid hemorrhage, 69 cases of intracerebral hemorrhage, and 123 cases of cerebral infarction).
	Selective outcome reporting	*Probably Low*	No selective report suspected: all relevant analyses/variables included (supplemental info provided by authors)
	Conflict of interests	*Low*	Funding sources from governmental agencies. This study was supported by grants from the Occupational Safety and Health Research Institute, Korean Occupational Safety and Health Agency (2010-OSHRI-1103), as a part of the Occupational Cardiovascular Disease Surveillance System. The authors declare that they have no conflicts of interest
	Other Bias	*Probably Low*	No duration but well design study
Kim 2013	**Study group**	*Probably High*	Case control study but a nationwide, multicenter, and matched case-control study The ABBA study was a prospective, nationwide, multicenter, and matched case-control study for the investigation of the effect of taking phenylpropanolamine (PPA) on the risk of HS in the Republic of Korea
	Blinding	*Low*	Interviewers were blind to the study hypothesis (as mentioned)
	Exposure assessment	*Probably Low*	Demographic, clinical, and work condition information was gathered during face-to-face interviews administered by trained nurses, and the best effort was made to avoid information bias. ABBA study participants were instructed to provide their information based on the regular job situation which they had been in for the longest period of time Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job. Moreover, survey is performed for another purpose (PPA, see above)
	Outcome assessment	*Low*	Optimal diagnostic procedure: hemorrhagic stroke, including both intracerebral haemorrhage (ICH) and sub-arachnoid haemorrhage (SAH), was confirmed by imaging studies including computed tomography or magnetic resonance imaging scans, or by xanthochromia on lumbar puncture
	Confounding	*Probably Low*	Age/ gender = case control. Other included. Only question is the occupation, but white and blue collar. Multivariable models were constructed using conditional logistic regression analyses with those variables whose univariate P-value<0·10 or with clinical importance, including years of education, family history of stroke, hypertension, diabetes, current habitual smoking, current habitual alcohol consumption, and PPA use. Each working condition index was entered into multivariable models independently. Stratified analyses were performed, according to the sub-type of HS, and identical models were applied as from composite HS analysis For each HS case, one hospital and one community controls were matched by gender and age (±5-year).
	Incomplete Outcome Data	*Probably Low*	No difference between missing and non-missing with reason The numbers of missing in cases: controls for each variable were as follows: years of education, 6 : 8; family history of stroke, 3 : 6; body mass index, 21 : 15; current habitual smoking, 2 : 17; current alcohol consumption, 5 : 19; occupation, 2 : 6; regular working time, 6 : 11; and duration of strenuous work, 4 : 25. In regression analysis, missing values were treated as additional categories for categorical variables and imputed by the mean values from the control group for continuous variables
	Selective outcome reporting	*Probably Low*	No selective report suspected though not mentioned.
	Conflict of interests	*Low*	Funding sources from governmental agencies. The ABBA study was primarily supported by the Korean Food and Drug Administration. This *post hoc* analysis was supported by research grants from the Korean Health 21 R&D Project, Ministry of Health and Welfare, Republic of Korea (A102065, A110490). The analyses and interpretations of the data and the final content of the article were produced independent of the financial sponsors
	Other Bias	*Probably Low*	References are different, only hemorrhagic stroke, no duration of exposure with only under estimation of the effect .
Kivimaki 2015 - ACL 1986	**Study group**	*Probably High*	Probabilistic sampling methods were employed and 30% of sampled households and 32% of sampled individuals were not interviewed. Furthermore, an oversampling of blacks and persons aged 60 years and older might represent a bias
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure

			(mail, phone, social network), including secondary job.
	Outcome assessment	*Probably Low*	Stroke was self-assessed but taking into account the importance/ severity without differential (stroke), and the lack of knowledge of association studied, no under and over diagnosis suspected (as found to have a fair validity of exposure)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Funding sources from governmental agencies. This study was supported by Grants P01AG05561 and R01AG09978-01 from the National Institute on Aging, National Institutes of Health, Bethesda, MD, and by a Health Investigator Award from the Robert Wood Johnson Foundation, Princeton, NJ.'
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect
Kivimaki 2015 - Alameda 1973	**Study group**	*Low*	Probabilistic sampling methods were employed, with a participation rate around 84%. In 1965, the Human Population Laboratory conducted a sample survey of the noninstitutionalized adult residents of Alameda County, using mail-back questionnaires that were placed in sampled households by interviewers.'
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Probably Low*	Stroke was self-assessed but taking into account the importance/ severity without differential (stroke), and the lack of knowledge of association studied, no under and over diagnosis suspected (as found to have a fair validity of exposure)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably High*	Though missing data for outcome reported and loss to follow-up seemed no different, the proportion of loss of follow-up at 40%
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Probably Low*	Funding sources were not reported and found in the retrieved study publications, but bias related to funding sources is unlikely (public founding)
	Other Bias	*Probably Low*	No other source of bias was identified.
Kivimaki 2015 - COPSOQ I 1997	**Study group**	*Probably High*	Low participation rate with the potential of introducing bias (e.g. people working long hours could be less available for answering the survey). The development of the questionnaire was based on a survey of a representative sample of 1858 Danish employees aged 20-59 years. The response rate was 62%; 49% were women
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Study conducted by NIOH researchers, with no perceived conflict of interests, and funded by the Service Center of the Danish Work Environment Council.
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - COPSOQ II 2004	**Study group**	*Probably High*	Low participation rate that might have the potential of introducing bias (e.g. people working long hours could be less available for answering the survey). The total sample included 8,000 adult respondents randomly selected from the Danish Centralized Civil Register (in Danish CPR). On their change of address form, Danish citizens have the possibility of indicating whether they would like to have survey exemption , hence, when the sample was drawn, approximately 10% of the population had survey exemption – in particular the age group 20–29 years. Survey exemption and a lower response rate in the youngest age group have led to some underrepresentation of the age group 20–29 in our sample.'; 'We received a total of 4,732 valid responses corresponding to a response rate of 60.4% – 1,215 respondents indicated that they were not in the work force or that they were self-employed, leaving us with final sample of 3,517 wage earners'
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.

	Outcome assessment	*Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Study conducted by NIOH researchers, with no perceived conflict of interests, and funded by the Service Center of the Danish Work Environment Council.
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - DWECS 2000	**Study group**	*Low*	Random representative sample, with 90% of participation rate. Statistic sample of the Danish population drawn from the Central Population Register; 'participation rate was 90% among eligible individuals'. It covers the full labour market, including both employees and the self-employed. The study contains information on more than 10,000 adults in Denmark, the majority of whom have been followed since 1990.'
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Funding sources from governmental agencies. DWECS is conducted by the National Institute for Occupational Health, NIOH (Arbejdsmiljøinstituttet, AMI).
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - FPS 2000	**Study group**	*Probably High*	Low participation rate (67 to 70%) with the potential of introducing bias (e.g. people working long hours could be less available for answering the survey). The eligible population of the original cohort included all employees who had been working for a minimum of six months in the target organizations, which included ten towns and six hospital districts, between 1991 and 2005 (n = 151,901)'; 'The first questionnaire survey, conducted in 1997-1998 in a sub-cohort, yielded responses from 16,952 employees (response rate 70%). In the second survey, the study population was expanded and data were obtained from 48,598 employees working in 3,771 work units (response rate 67%). The third survey, conducted in 2004 for those still employed by the organisations and in 2005 for respondents to the 1997-2002 surveys that had left the organisations by 2004, yielded responses from 56,506 participants (response rate 68%). The fourth survey, conducted in 2006 in a sub-cohort (employees working in the 10 towns), yielded responses from 34,393 respondents (response rate 69%). The fifth survey, conducted in 2008 among all approximately permanent and fixed-term employees in the service of the organisations at that time and in 2009 among employees who had left the organisations after responding to the surveys in 1997-2005, yielded responses from 69,475 participants (response rate 69%)'.
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job. It is mentioned "Computer-stored employer records covered all periods of full-time employment, including date of beginning and, when appropriate, termination of work contract as well as Statistics Finland's five-digit occupational codes"
	Outcome assessment	*Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Study conducted by academic researchers, with no perceived conflict of interests.
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - HeSSup 1998	**Study group**	*Probably High*	Low participation rate with the potential of introducing bias (e.g. people working long hours could be less available for answering the survey). The Time 1 postal survey in 1998 yielded, with a response rate of 40.0%, 25 901 participants.

	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Funding source was limited to government. 'J.V. and M.K. were supported by the Academy of Finland
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - IPAW 1996	**Study group**	*Probably High*	Low participation rate (76%) with the potential of introducing bias (e.g. people working long hours could be less available for answering the survey), Table 1 from Nielsen 2002
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	At the National Institute of Occupational Health (NIOH) in Copenhagen, Denmark, a large psychosocial intervention study was conducted in 1996: The Intervention Project on Absence and Well-being (IPAW)
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - MIDUS 1995	**Study group**	*Probably Low*	National probabilistic sample. Analysis were adjusted for the profile of respondents. For this paper, of the 3343 respondents in the 2011 MIDUS-RS, we first selected 2476 respondents who were married to or cohabiting with a partner. Next, following prior research (Grzywacz and Marks 2000), we included those under the age of 62 only (n=1825). Then we selected those who were working for pay (n = 1434). Lastly, we restricted the sample to those who answered the SAQ, which resulted in the final sample of N=980. Using Heckman's (1979) method, we evaluated possible bias from selecting respondents with a completed SAQ. Those included in our analytical sample were more likely to be older and have higher levels of education, and were less likely to be Hispanic. We then estimated the probability of being selected into the analytical sample (λ) and included it in our regression models. We found that λ had no significant effects in our models nor did it alter any patterns of findings discussed below, which suggests that our results were not biased by our sample restriction but without to be sure.
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job. It is mentioned :" Respondent's weekly work hours was measured as the number of hours of paid work at the respondent's main job and any other jobs in a typical week"
	Outcome assessment	*Probably Low*	Stroke was self-assessed but taking into account the importance/ severity without differential (stroke), and the lack of knowledge of association studied, no under and over diagnosis suspected (as found to have a fair validity of exposure)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably High*	Though missing data for outcome reported and loss to follow-up seemed no different, the proportion of loss of follow-up at 32%
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	No conflict of interest detected "supported by MacArthur Foundation Research Network on Successful Midlife Development"
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .

Kivimaki 2015 - NHANES 1982	**Study group**	*Low*	Probabilistic sampling methods were employed, with a participation rate 93%. NHANES I is a prospective cohort study of a national sample of the civilian noninstitutionalized population of the United States. The baseline survey, which included a standardized medical examination and questionnaires that covered various topics, took place from 1971 through 1974 and was augmented by an additional national sample in 1974-75. The original NHANES I sample included 20,729 persons 25 to 74 years of age. Data collection for a follow-up, used as the baseline for the present study because it included the first measurement of working hours, was conducted from 1982 to 1984. The follow-up study population included the 14,407 participants who were 25 to 74 years of age when they were examined at baseline in 1971-75. Follow-up data for the present study were derived from data collections in 1986 and 1992. Individuals who were working at baseline and who provided information on working hours and who participated in the follow-up wave were included in the present metaanalysis (n=4875).
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Probably Low*	Stroke was self-assessed but taking into account the importance/ severity without differential (stroke, defined using ICD9), and the lack of knowledge of association studied, no under and over diagnosis suspected (as found to have a fair validity of exposure).
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different and minor low of follow-up (4%)
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	The NHANES I Epidemiologic Follow up Study has been developed and funded by these agencies: National Institute on Aging; National Center for Health Statistics; National Cancer Institute; National Heart, Lung, and Blood Institute; National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases; National Institute of Mental Health; National Institute of Alcohol Abuse and Alcoholism; National Institute of Allergy and Infectious Diseases; and National Institute of Neurological and Communicative Disorders and Stroke. The field work was conducted by Westat, Inc., under contract No.23380-2049.
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - PUMA 1999	**Study group**	*Probably Low*	At baseline, 1914 of 2391 eligible employees participated in the survey (response rate 80.1%), but with a potential of introducing bias (e.g. people working long hours could be less available for answering the survey)
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes.
	Exposure assessment	*Probably Low*	Working hours were probably self-reported, which has been proved to provide precise estimates.
	Outcome assessment	*Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant.
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Not applicable*	Authors from the NIOH, Denmark. Funding sources from governmental agencies. The PUMA study has been funded by grants from The Work Environment Fund (Arbejdsmiljøfondet), The Danish Work Environment Service (Arbejdstilsynet), The Work Environment Council (Arbejdsmiljøra˚dets Servicecenter via Arbejdsministeriets sundhedsfremmepulje), and The Health Insurance Foundation (Sygekassernes Helsefond).
	Other Bias	*Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - Whitehall II 1991	**Study group**	*Probably High*	Low participation rate of civil servants (73%) with the potential of introducing bias (e.g. people working long hours could be less available for answering the survey). The Whitehall II study sample recruitment (phase 1) took place between late 1985 and early 1988 among all office staff, aged 35 to 55 years, from 20 London-based Civil Service departments.21 The response rate was 73% (6895 men and 3413 women)
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes.
	Exposure assessment	*Probably Low*	Working hours were self-reported, which has been proved to provide precise estimates.
	Outcome assessment	*Low*	Administrative records were used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant.

	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Funding sources: Medical Research Council (MRC, UK) British Heart Foundation (BHF, UK) National Heart, Lung and Blood Institute (NHLBI, US) National Institute on Aging (NIA, US) Economic and Social Research Council (ESRC, UK) Horizon 2020 (EU) European Research Council (ERC, EU)
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - WLSG 1992	**Study group**	*Probably Low*	Inclusion criterion was year of graduation, WLS sample was originally comprised of over 10,000 men and women who graduated from Wisconsin high schools in 1957.' 'The WLS has enjoyed excellent response rates. In 1993, 8,493 completed the telephone interview (94% completion rate among living respondents who could be located). The alcohol behaviors section of the interview was randomly subsampled at just under 80%, and participants who completed this section constituted the baseline sample of 6,489
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Probably Low*	Stroke was self-assessed but taking into account the importance/ severity without differential (stroke), and the lack of knowledge of association studied, no under and over diagnosis suspected (as found to have a fair validity of exposure)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	No conflict of interest detected. Since 1991, the WLS has been supported principally by the National Institutes for Health, National Institute on Aging, with additional support from the Vilas Estate Trust, the National Science Foundation, the Spencer Foundation, and the Grad'
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect (cf. above)
Kivimaki 2015 - WLSS 1993	**Study group**	*Probably Low*	Inclusion criterion was year of graduation he Wisconsin Longitudinal Study is a prospective cohort study of a random sample of 10317 participants (5326women, 4991 men) who were born between 1937 and 1940 and who graduated from Wisconsin high schools in 1957. The present study used data from the 1992–1993 data collection as the baseline, and 2003-2005 as the follow-up. The WLS sample is broadly representative of white, non-Hispanic American men and women who have completed at least a high school education
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Probably Low*	Stroke was self-assessed but taking into account the importance/ severity without differential (stroke), and the lack of knowledge of association studied, no under and over diagnosis suspected (as found to have a fair validity of exposure)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably High*	Though missing data for outcome reported and loss to follow-up seemed no different, the proportion of loss of follow-up at 26%
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	No conflict of interest detected Since 1991, the WLS has been supported principally by the National Institutes for Health, National Institute on Aging, with additional support from the Vilas Estate Trust, the National Science Foundation, the Spencer Foundation, and the Grad'
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - WOLF N 1996	**Study group**	*Probably Low*	Of all the invited employees, a total of 10 413 subjects both responded to the questionnaire and took part in the clinical examination, corresponding to a participation rate of 82%. Wolf S correspond to Stockholm county
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study

	Conflict of interests	*Low*	The collaborative part of this research was supported by the European Science Foundation Scientific Program "Social Variations in Health Expectancy in Europe." The study was supported by a grant from the Swedish Work Environment Fund (grant no 92–0919).'
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect
Kivimaki 2015 - WOLF S 1992	**Study group**	*Probably Low*	Of all the invited employees, a total of 10 413 subjects both responded to the questionnaire and took part in the clinical examination, corresponding to a participation rate of 82%. Wolf N correspond to Norrland,in Jämtland and Västernorrland counties
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
Kivimaki 2015 - WOLF N 1996	**Study group**	*Probably Low*	Of all the invited employees, a total of 10 413 subjects both responded to the questionnaire and took part in the clinical examination, corresponding to a participation rate of 82%. Wolf S correspond to Stockholm county
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)

Appendix 5. Details of risk of Bias for each study including on dying from stroke

Study ID	Domains	*Judgement*	Comment
Hannerz 2018	**Study group**	*Probably Low*	National database of representative of population, but response rate to interview was some years >70% though decreased.
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes since the cohort is not focused on that question and the association is not widely known (in addition SR and examination is performed at different steps.
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job The interviews cover various aspects of labour market participation, including working hours and work schedules. The usual weekly working hours in the LFs are calculated by adding the hours usually worked in secondary jobs to the ones usually worked in a primary job. In total, 357,085 people participated in LFs at least once during 1999–2013 activity), medical history (diabetes, coronary heart disease, respiratory problems, family medical history), health perception, and psychosocial scales for depression and anxiety'
	Outcome assessment	*Low*	The endpoint of the present study was clinically registered hospital treatment or death (n<10%), The endpoint of the present study was clinically registered hospital treatment or death, with a stroke as the principal diagnosis/cause of death. In keeping with Kivimäki et al. [1], the following ICD- 10 codes were included in the case definition: I60 subarachnoid haemorrhage; I61 intracerebral haemorrhage; I63 cerebral infarction; I64 stroke, not specified as haemorrhage or infarction. In keeping with Fransson et al, this set of diagnoses will be called 'overall stroke'. It should, however, be noted that the set does not include traumatic strokes (which are found in the ICD-category s06 'intracranial injuries'), nor does it include the ICD-10 code I62 'other non-traumatic intracranial haemorrhage'
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant. The analysis was adjusted for sex, age (10-year classes), calendar time (2000–2004, 2005–2009, 2010–2014), time passed since start of follow-up (0–4 years, 5–9 years, ≥10 years) and socio-economic status (SES; low, medium, high, unknown). Age, calendar time and time passed since start of follow-up were treated as dynamic (time-varying) variables according to the classes above. Sensitivity analysis 1: Controlling for possible reverse causation Sensitivity analysis 2: Only stable exposure to working hours Secondary analysis: Distinguishing between types of stroke
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different and only 676 emigration/death, and 15 exit from national registry (0.45%)
	Selective outcome reporting	*Probably Low*	Protocol published is similar https://figshare.com/articles/The_association_between_long_working_hours_and_stroke_in_the_general_workforce_of_Denmark_a_study_protocol/4684951/1
	Conflict of interests	*Low*	Funding sources were limited to governmental agencies (The study was mainly funded by the institutions of the authors and partially supported by a grant from The Danish Working Environment Research Fund).
	Other Bias	*Probably Low*	No other source of bias was identified. However no information on duration, and the national context of regulation in Denmark; "2015 Eurofound EWCS survey results in Denmark: 91% of people are satisfied with working conditions in their job". The result is possibly related to mediation by good conditions even with long working hours. https://www.eurofound.europa.eu/country/denmark
Hayashi 2019	**Study group**	*High*	Japan public health center-based prospective (JPHC) study cohort (I and II) is an extremely high quality cohort, but1/ women are excluded and it is mentioned "average working hours for women (4.00 h/day) were approximately half the average for men (8.11 h/day) ; papers from same cohort included Suita/Osaka and the paper described the attrition in 2001 mentioned a lower participation in Suita/Ozaka but a follow-up at this point *(Tsugane S, Sobue T. Baseline survey of JPHC study--design and participation rate. Japan Public Health Center-based Prospective Study on Cancer and Cardiovascular Diseases. J Epidemiol. 2001 Oct;11(6 Suppl):S24-9. PubMed PMID:11763136*). For these reasons, the group rather quote as high risk of bias related to internal validity (even though we might be wrong)
	Blinding	*Probably Low*	Outcome is based on administrative data and though blinding was not reported it is unlikely knowledge of exposure might affect the outcome. Furthermore, outcome assessors were blind to lifestyle.
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Low*	The endpoint of the present study was clinically registered hospital treatment or death after review medical data (Stroke was confirmed in accordance with the National Survey of Stroke criteria. For each type of stroke, a definite diagnosis was established based on examination of computed tomography scans, magnetic resonance images, or autopsy)

			Yes multiple models to include age and occupations (only men included),other risk factors, as well as Lag/ competitive models, though long working hours in hours/days (period of week is lacking) The first model was adjusted for baseline age (years). The second model was also adjusted for body mass index (BMI) (kg/m2), history of hypertension yes, no), history of diabetes mellitus (yes, no), history of hyperlipidemia (yes, no), smoking status (never, former, current), alcohol intake (never, former, <300 g [alcohol]/ week, ≥300 g/week), walking or standing time (<1 h/day, 1 to <3 h/day, ≥3 h/day), and sleep duration (hours). The third model was further adjusted for occupation (salaried employee, agriculture/forestry/fishery worker, self-employed, professional worker, multiple occupational worker, unclassified occupational worker, homemaker, and unemployed). For the sensitivity analysis accounting for the competing risk of death, the Fine and Gray model was used to estimate sub-hazard ratios of acute myocardial infarction and total stroke. Furthermore, we conducted the analysis by excluding acute myocardial infarction and stroke events that took place in the first 3 years of follow up to examine the reverse causation, as in a previous meta-analysis
	Confounding	*Probably Low*	
	Incomplete Outcome Data	*Probably Low*	Missing data clearly reported, but we don't have the protocol.
	Selective outcome reporting	*Probably Low*	No data on interaction between age, occupation and stroke but not significant overall
	Conflict of interests	*Low*	No conflict of interest detected. This study was supported by the National Cancer Center Research and Development Fund (23-A-31 [toku] and 26-A-2; since 2011) and a Grant-in-Aid for Cancer Research from the Ministry of Health, Labour and Welfare of Japan (1989–2010).
	Other Bias	*Probably Low*	References different (reference include 44h/w after approximation), no duration of exposure with only under estimation of the effect .
Kivimaki 2015 - COPSOQ I 1997	**Study group**	*Probably High*	Low participation rate with the potential of introducing bias (e.g. people working long hours could be less available for answering the survey). The development of the questionnaire was based on a survey of a representative sample of 1858 Danish employees aged 20-59 years. The response rate was 62%; 49% were women
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Probably Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Study conducted by NIOH researchers, with no perceived conflict of interests, and funded by the Service Center of the Danish Work Environment Council.
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - COPSOQ II 2004	**Study group**	*Probably High*	Low participation rate that might have the potential of introducing bias (e.g. people working long hours could be less available for answering the survey). The total sample included 8,000 adult respondents randomly selected from the Danish Centralized Civil Register (in Danish CPR). On their change of address form, Danish citizens have the possibility of indicating whether they would like to have survey exemption, hence, when the sample was drawn, approximately 10% of the population had survey exemption – in particular the age group 20–29 years. Survey exemption and a lower response rate in the youngest age group have led to some underrepresentation of the age group 20–29 in our sample.'; 'We received a total of 4,732 valid responses corresponding to a response rate of 60.4% – 1,215 respondents indicated that they were not in the work force or that they were self-employed, leaving us with final sample of 3,517 wage earners'
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Probably Low*	Administrative records were used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different

	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Study conducted by NIOH researchers, with no perceived conflict of interests, and funded by the Service Center of the Danish Work Environment Council.
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - DWECS 2000	**Study group**	*Low*	Random representative sample, with 90% of participation rate. Statistic sample of the Danish population drawn from the Central Population Register; 'participation rate was 90% among eligible individuals'. It covers the full labour market, including both employees and the self-employed. The study contains information on more than 10,000 adults in Denmark, the majority of whom have been followed since 1990.'
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Probably Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Funding sources from governmental agencies. DWECS is conducted by the National Institute for Occupational Health, NIOH (Arbejdsmiljøinstituttet, AMI).
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - FPS 2000	**Study group**	*Probably High*	Low participation rate (67 to 70%) with the potential of introducing bias (e.g. people working long hours could be less available for answering the survey). The eligible population of the original cohort included all employees who had been working for a minimum of six months in the target organizations, which included ten towns and six hospital districts, between 1991 and 2005 (n = 151,901)'; 'The first questionnaire survey, conducted in 1997-1998 in a sub-cohort, yielded responses from 16,952 employees (response rate 70%). In the second survey, the study population was expanded and data were obtained from 48,598 employees working in 3,771 work units (response rate 67%). The third survey, conducted in 2004 for those still employed by the organisations and in 2005 for respondents to the 1997-2002 surveys that had left the organisations by 2004, yielded responses from 56,506 participants (response rate 68%). The fourth survey, conducted in 2006 in a sub-cohort (employees working in the 10 towns), yielded responses from 34,393 respondents (response rate 69%). The fifth survey, conducted in 2008 among all approximately permanent and fixed-term employees in the service of the organisations at that time and in 2009 among employees who had left the organisations after responding to the surveys in 1997-2005, yielded responses from 69,475 participants (response rate 69%)'.
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job. It is mentioned "Computer-stored employer records covered all periods of full-time employment, including date of beginning and, when appropriate, termination of work contract as well as Statistics Finland's five-digit occupational codes"
	Outcome assessment	*Probably Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Study conducted by academic researchers, with no perceived conflict of interests.
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - HeSSup 1998	**Study group**	*Probably High*	Low participation rate with the potential of introducing bias (e.g. people working long hours could be less available for answering the survey). The Time 1 postal survey in 1998 yielded, with a response rate of 40.0%, 25 901 participants.
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Probably Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)

	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Funding source was limited to government. 'J.V. and M.K. were supported by the Academy of Finland
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - IPAW 1996	**Study group**	*Probably High*	Low participation rate (76%) with the potential of introducing bias (e.g. people working long hours could be less available for answering the survey), Table 1 from Nielsen 2002
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Probably Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	At the National Institute of Occupational Health (NIOH) in Copenhagen, Denmark, a large psychosocial intervention study was conducted in 1996: The Intervention Project on Absence and Well-being (IPAW)
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 **O'Reilly 2013**	**Study group**	*Low*	Data from Census studies, no attrition The Northern Ireland Mortality Study (NIMS) is a prospective record-linkage study, 2001Census returns for the whole enumerated population, to which subsequent registered deaths to 2009 have been linked in 8.7 years of follow-up. Of the 808 301 non-institutionalized enumerated men and women aged 20–59/64 years at the Census with full information on hours worked, 576 587 were economically active and 231 714 inactive (defined as people without a job at the time of the Census who had not actively sought work in the preceding 4 weeks and/or were not available to start work in the next 2 weeks). This latter group comprised 36.6% unable to work because of permanent sickness, 33.5% homemakers, 6.2% students, 7.3% retired and 16.4% others (mostly long-term unemployed and those who had never worked). T he final cohort for analysis comprised 414 949 people (270 011 men and 144 938 women) who were employed for at least 35 h/ week: 69.3% of this group worked 35–40 h, 13.9% worked 41–48 h, 7.3% 49–54 h and 9.4% 555 h/week
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes, data coming from a prospective record-linkage study (see above)
	Exposure assessment	*Probably Low*	Working hours were probably self-reported, which has been proved to provide precise estimates. The UK Census in 2001 asked 'How many hours a week do you usually work in your main job?', with expected responses stating, to the nearest whole hour, the average number of hours per week defines the usual working week for the majority of the population; the second represents more than worked in the 4 weeks prior to census. The first category usual but less than the limit recommended by the Working Time Directive; and >55 h was chosen as the upper category that has been cited most frequently in previous studies to define long working hours
	Outcome assessment	*Probably Low*	Death recorded using cerebrovascular disease (I60-I69) were reported using the following broad ICD10 classifications: cardiovascular disease (I60-I69)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant. Logistic regression quantified the risks associated with those working the longest hours (>55h per week) when compared with those working fewer hours. Models adjusted for other possible confounders including baseline health status were used to examine for health selection effects. Tests for interaction were used to determine if the health effects associated with long working hours differed by age, health status or occupational social class (marital status, number of dependent children, caregiving duties were also considered, though not included here).
	Incomplete Outcome Data	*Probably Low*	No incomplete data, sensitivity analyses performed
	Selective outcome reporting	*Probably Low*	No selective report suspected
	Conflict of interests	*Probably Low*	No conflict of interest detected. The NIMS is funded by the Health and Social Care Research and Development Division of the Public Health Agency (HSC R&D Division) and NISRA. The NILS-RSU is funded by the ESRC and the Northern Ireland Government

	Other Bias	*Probably Low*	Duration not included. Events before exposure not excluded (though stroke patients usually are unable to work for long working hours)
Kivimaki 2015 - PUMA 1999	**Study group**	*Probably Low*	At baseline, 1914 of 2391 eligible employees participated in the survey (response rate 80.1%), but with a potential of introducing bias (e.g. people working long hours could be less available for answering the survey)
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes.
	Exposure assessment	*Probably Low*	Working hours were probably self-reported, which has been proved to provide precise estimates.
	Outcome assessment	*Probably Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant.
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Not applicable*	Authors from the NIOH, Denmark. Funding sources from governamental agencies. The PUMA study has been funded by grants from The Work Environment Fund (Arbejdsmiljøfondet), The Danish Work Environment Service (Arbejdstilsynet), The Work Environment Council (Arbejdsmiljøra˚dets Servicecenter via Arbejdsministeriets sundhedsfremmepulje), and The Health Insurance Foundation (Sygekassernes Helsefond).
	Other Bias	*Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - Whitehall II 1991	**Study group**	*Probably High*	Low participation rate of civil servants (73%) with the potential of introducing bias (e.g. people working long hours could be less available for answering the survey). The Whitehall II study sample recruitment (phase 1) took place between late 1985 and early 1988 among all office staff, aged 35 to 55 years, from 20 London-based Civil Service departments.21 The response rate was 73% (6895 men and 3413 women)
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes.
	Exposure assessment	*Probably Low*	Working hours were self-reported, which has been proved to provide precise estimates.
	Outcome assessment	*Low*	Administrative records were used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant.
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	Funding sources: Medical Research Council (MRC, UK) British Heart Foundation (BHF, UK) National Heart, Lung and Blood Institute (NHLBI, US) National Institute on Aging (NIA, US) Economic and Social Research Council (ESRC, UK) Horizon 2020 (EU) European Research Council (ERC, EU)
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .
Kivimaki 2015 - WOLF N 1996	**Study group**	*Probably Low*	Of all the invited employees, a total of 10 413 subjects both responded to the questionnaire and took part in the clinical examination, corresponding to a participation rate of 82%. Wolf S correspond to Stockholm county
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)
	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	The collaborative part of this research was supported by the European Science Foundation Scientific Program "Social Variations in Health Expectancy in Europe." The study was supported by a grant from the Swedish Work Environment Fund (grant no 92–0919).'
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect
Kivimaki 2015 - WOLF S 1992	**Study group**	*Probably Low*	Of all the invited employees, a total of 10 413 subjects both responded to the questionnaire and took part in the clinical examination, corresponding to a participation rate of 82%. Wolf N correspond to Norrland,in Jämtland and Västernorrland counties
	Blinding	*Probably Low*	Absence of blinding judged as not significantly impacting outcomes (multipurpose)

	Exposure assessment	*Probably Low*	Working hours were self-reported, and might more representative of the total work exposure (mail, phone, social network), including secondary job.
	Outcome assessment	*Low*	Administrative record have been used Incident stroke in the IPD-Work studies was defined with hospital and mortality records (I60, I61, I63, I64 in ICD-10; 430, 431, 433, 434, 436 in ICD-9)
	Confounding	*Probably Low*	Analysis were adjusted to most important confounders (age, sex, SES), but other confounders may also be relevant
	Incomplete Outcome Data	*Probably Low*	No missing data for outcome reported and loss to follow-up not important/ no different
	Selective outcome reporting	*Not applicable*	Unpublished study
	Conflict of interests	*Low*	No conflict of interest detected Since 1991, the WLS has been supported principally by the National Institutes for Health, National Institute on Aging, with additional support from the Vilas Estate Trust, the National Science Foundation, the Spencer Foundation, and the Grad'
	Other Bias	*Probably Low*	No duration of exposure with only under estimation of the effect .

Appendix 6. Exploratory subgroup analyses to determine statistical heterogeneity of studies with "pure" fatal or non-fatal stroke events and studies with non-fatal and/or fatal stroke events ("mixed")

Fig. A6.1 Exploratory subgroup analysis, Acquired stroke (non-fatal stroke vs. mixed non-fatal/fatal stroke), worked 41-48 hours/week compared with worked 35-40 hours/week, cohort studies

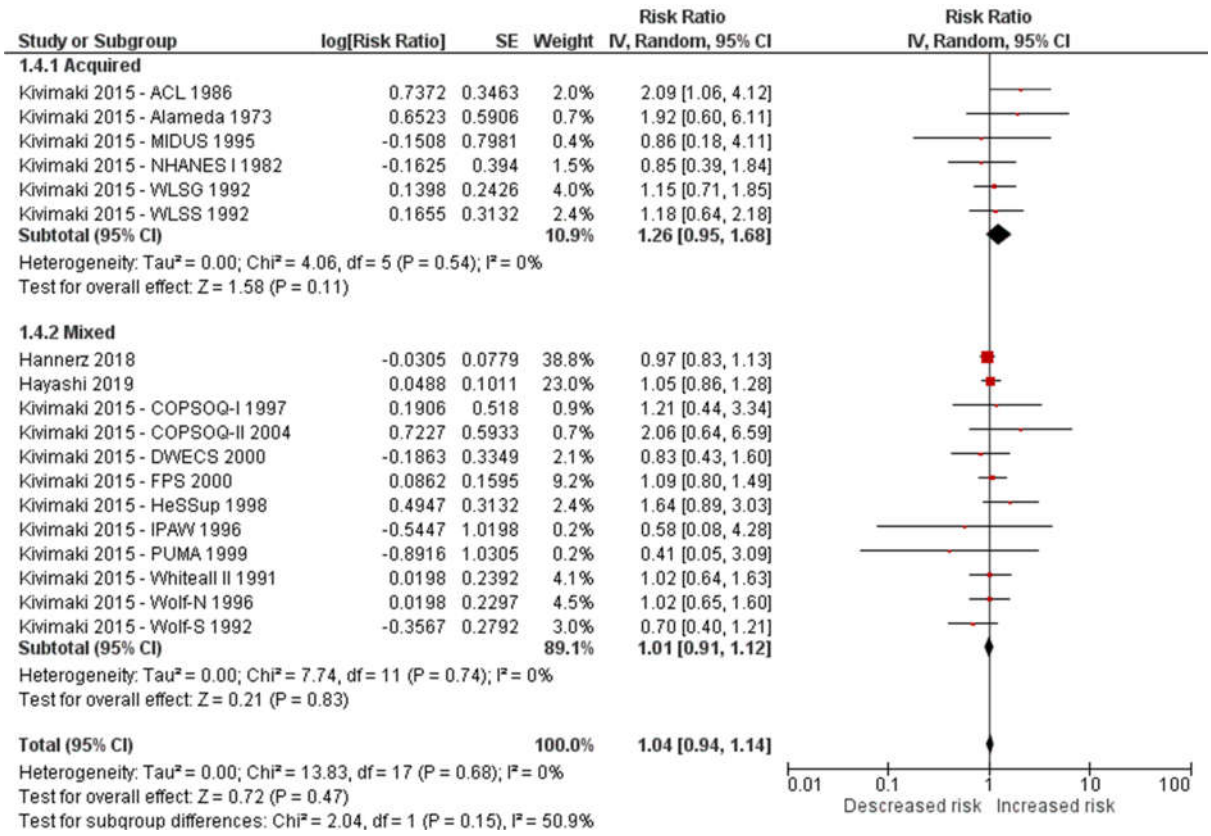


Fig. A6.2 Exploratory subgroup analysis, Acquired stroke (non-fatal stroke vs. mixed non-fatal/fatal stroke), worked 49-54 hours/week compared with worked 35-40 hours/week, cohort studies

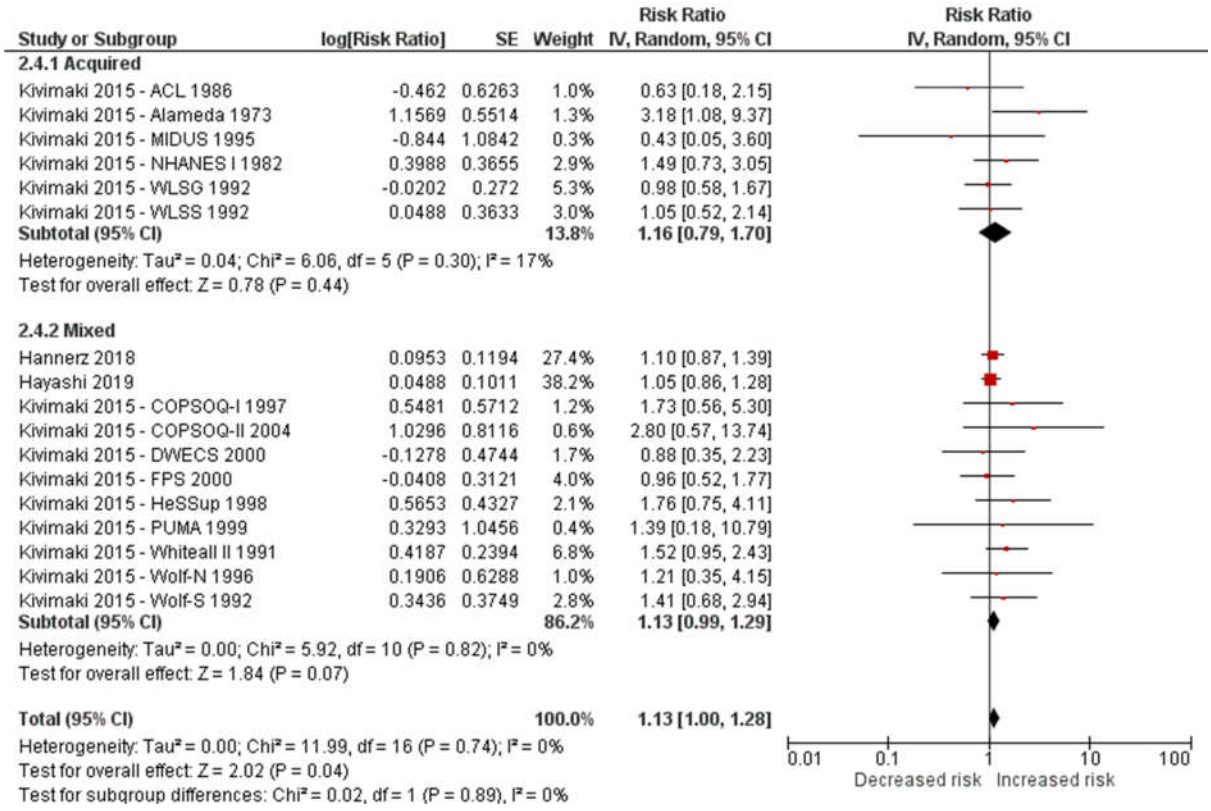


Fig. A6.3 Exploratory subgroup analysis, Acquired stroke (non-fatal stroke vs. mixed non-fatal/fatal stroke), worked ⩾55 hours/week compared with worked 35-40 hours/week, cohort studies

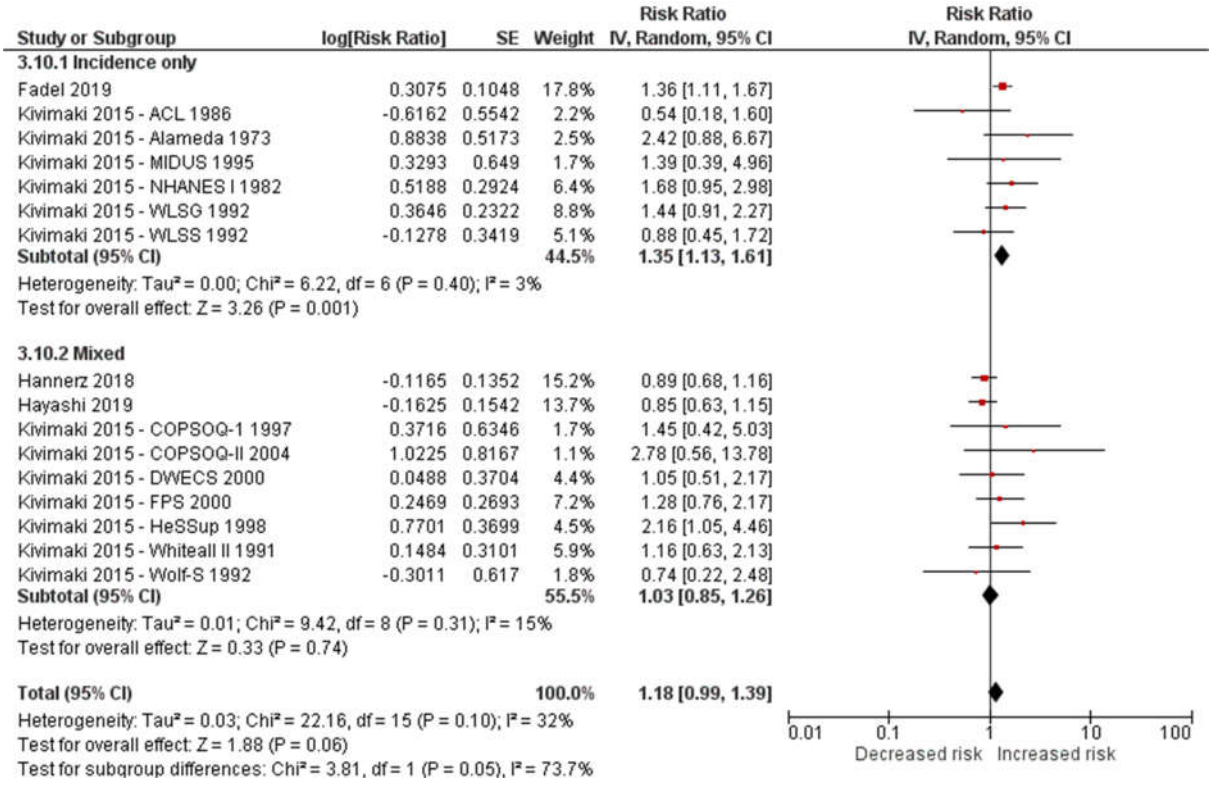
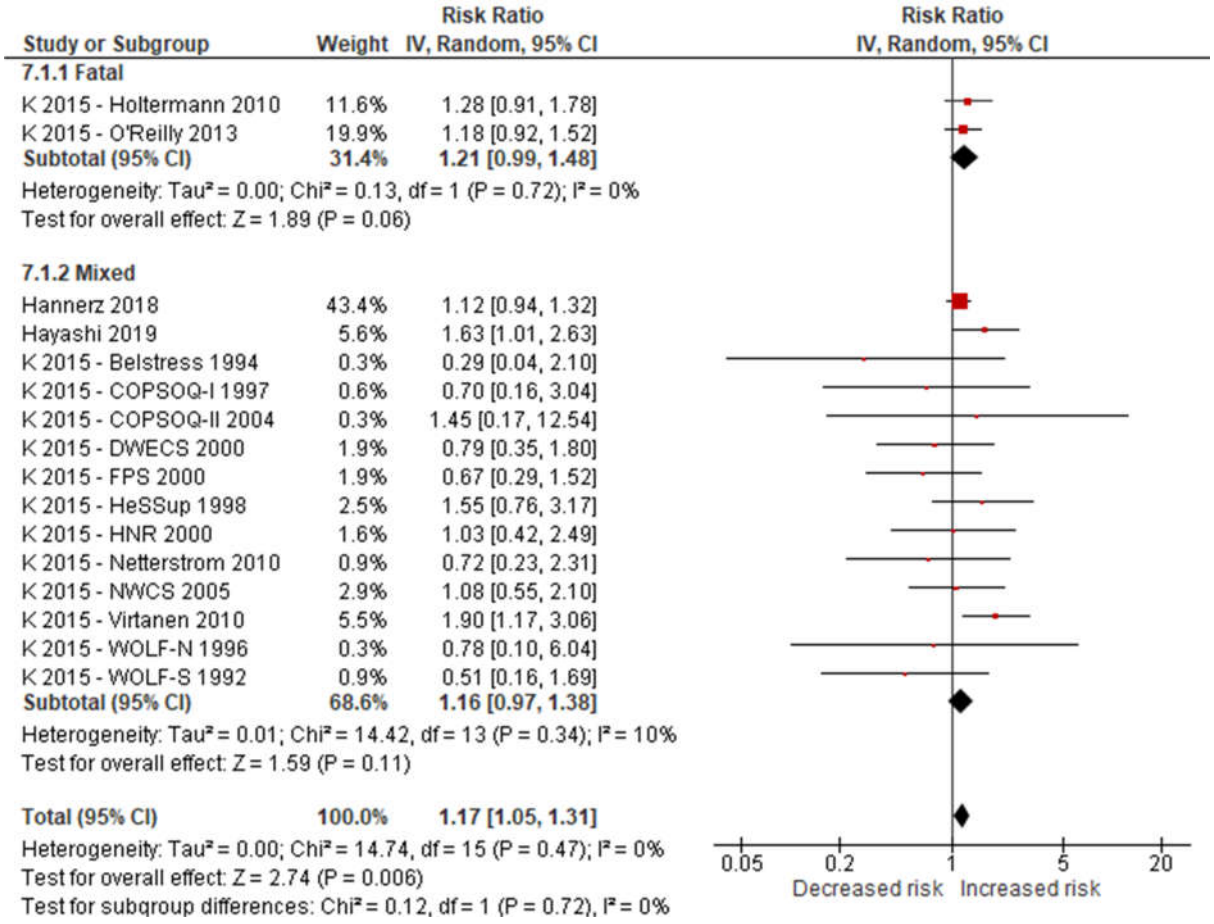


Fig. A6.4 Exploratory subgroup analysis, Died from stroke (fatal stroke vs. mixed non-fatal/fatal stroke), worked ⩾55 hours/week compared with worked 35-40 hours/week, cohort studies



Appendix 7. Additional subgroup analyses

A7.1. Has stroke (stroke prevalence*)*

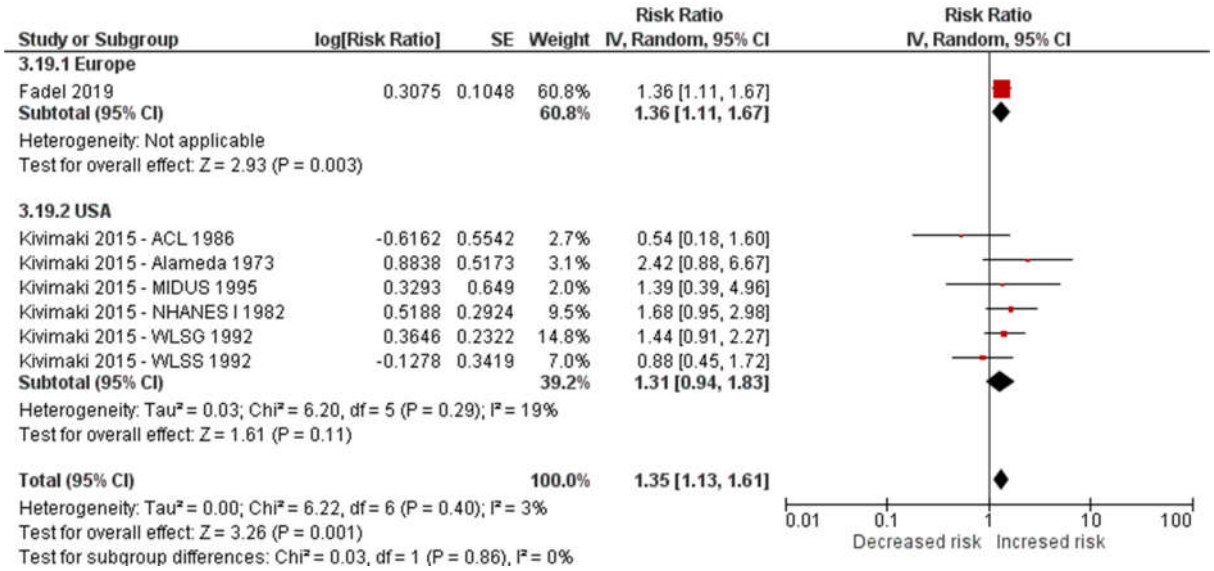
The systematic review identified no evidence on this outcome.

A7.2. Acquired stroke (stroke incidence)

A7.2.1. By WHO region

We did not find an obvious difference between the three WHO regions under study (Fig. A7.1).

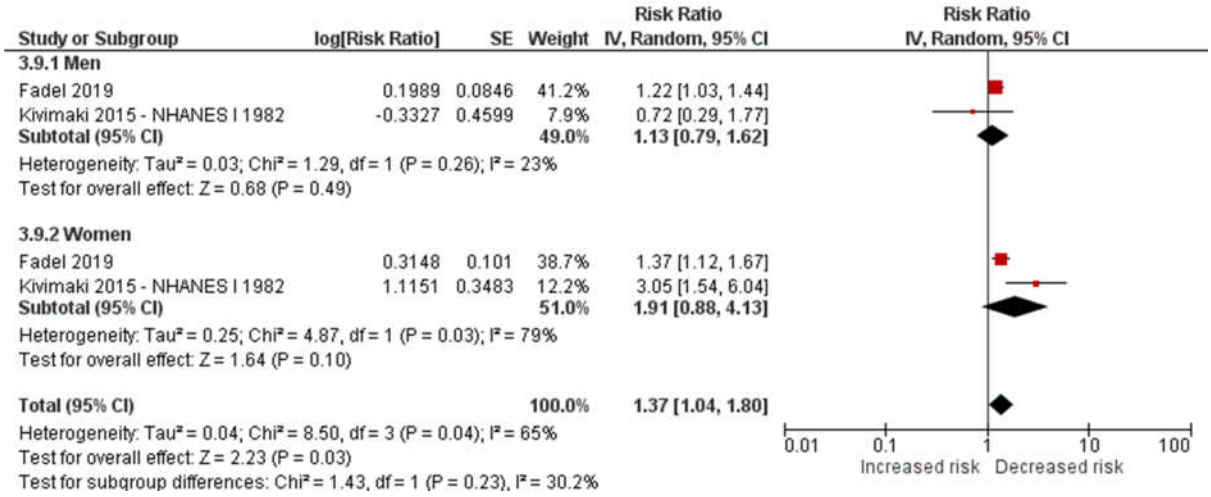
Fig. A7.1 Subgroup analysis by WHO region, Acquired stroke, worked ⩾55 hours/week compared with worked 35-40 hours/week, cohort studies



A7.2.2. By sex

There was no evidence for any difference in effect estimates by sex, though women seemed to have higher risk (Fig. A7.2)

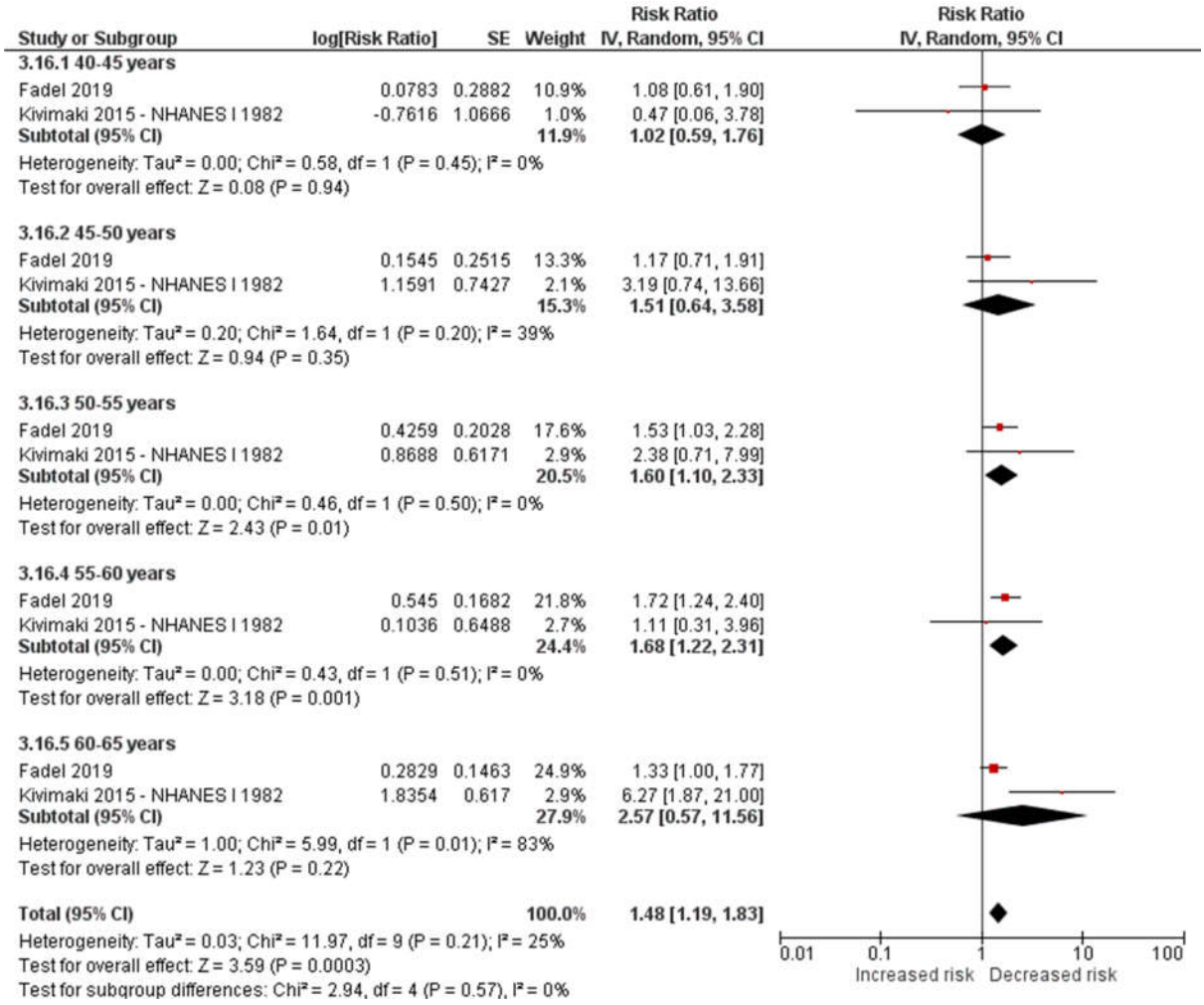
Fig. A7.2 Subgroup analysis by sex, Acquired stroke worked ⩾55 hours/week compared with worked 35-40 hours/week, cohort studies



A7.2.3. By age

For the age group available in the two studies, no differences were observed (though RR increased with age).

Fig. A7.3 Subgroup analysis by age group, Acquired stroke, worked ⩾55 hours/week compared with worked 35-40 hours/week, cohort studies



A7.2.4. By SES

In the Fadel study (Fadel et al. 2019), no difference between SES has been observed though intermediate SES seemed higher (Table 6).

A7.2.5. By industrial sector

In the Fadel study (Fadel et al. 2019), private and public activity sectors can be divided: a stronger association was found in the private sector 1.47 (1.10 -1.96) than public sectors (including Social security) 1.15 (0.82-1.62) (test for subgroup differences p = 0.28).

A7.2.6. By occupation

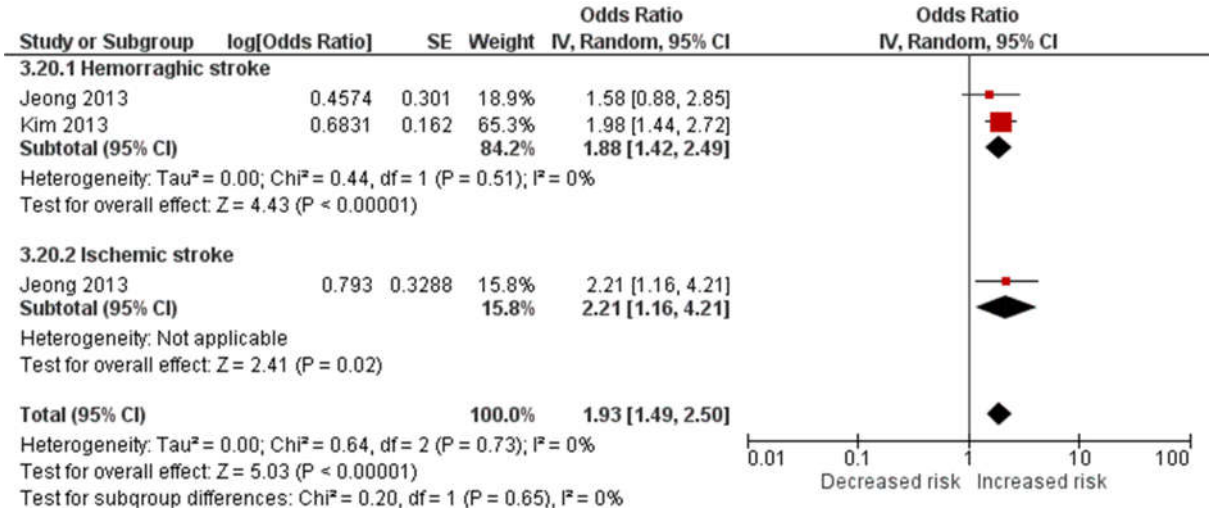
In the Fadel study (Fadel et al. 2019), the increase of risk seemed stronger in occupations with hard work (Table 6), but no significant subgroup differences were found (p=0.11).

A7.2.7. By type of stroke

Only one cohort study allowed stratification on stroke type (Hannerz et al. 2018): excess of risk existed for haemorrhagic stroke (not significant for ⩾55h/ week, RR 1.33 [0.82 - 2.15), but not for ischemic stroke (0.86 [0.61 - 1.22), with no significant subgroup difference (p=0.15).

Combining the two case-control studies with data on haemorrhagic/ ischemic stroke, we found no major differences (Fig. A7.4)

Fig. A7.4 Subgroup analysis by type of stroke, Acquired stroke, worked ⩾55 hours/week compared with worked 35-40 hours/week (*Haemorrhagic vs. ischemic stroke), case-control studies*

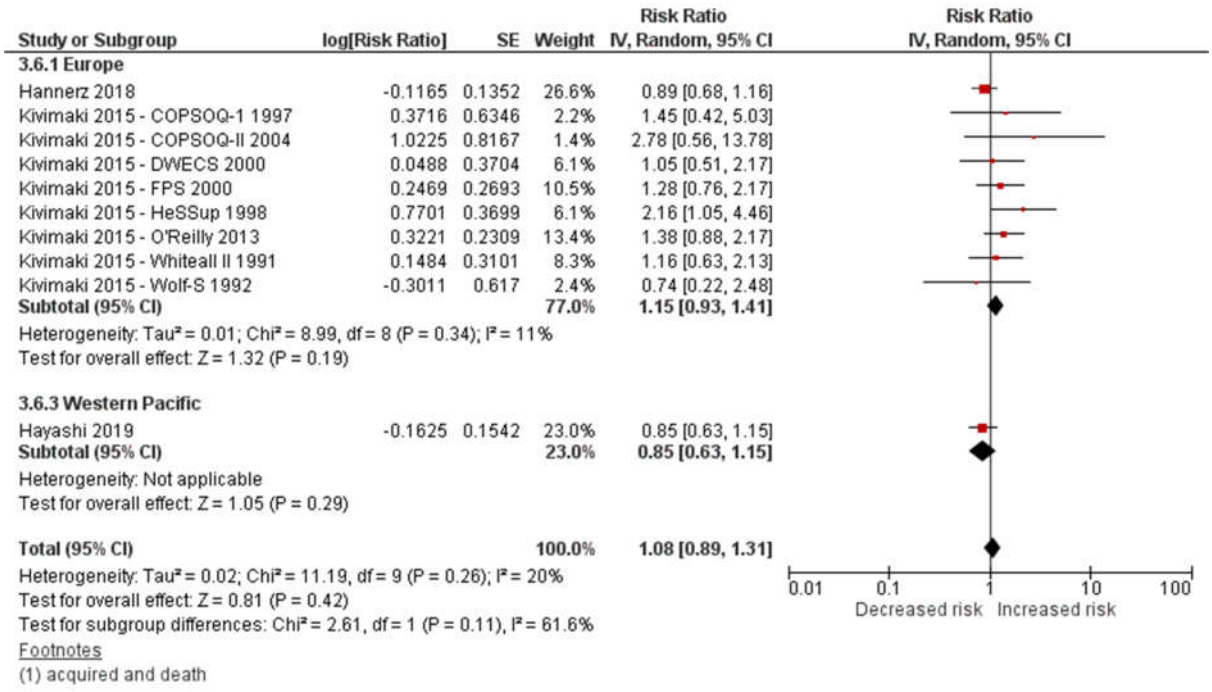


A7.3. Died from stroke (mortality from stroke)

A7.3.1 By WHO region

There was no evidence for any statistically significant difference in effect estimates by WHO region (test for subgroup differences P = 0.11) (Fig. A7.5).

Fig. A7.5 Subgroup analysis by WHO region, Died from stroke, worked ⩾55 hours/week compared with worked 35-40 hours/week, cohort studies



A7.3.2 By sex

Only one study provided effect estimates for men only, and we could therefore not assess differences in effect estimates by sex.

A7.3.3. By age group

Stratified analysis by age was available by one pooled estimate only. The Kivimaki 2015 systematic review and meta-analysis of individual-participant data from 20 unpublished studies including non-fatal or "mixed" (non-fatal or fatal) stroke events of an unclear number of participants reported an elevated risk with lower CI below 1effect modification by age on the risk of stroke of working ⩾55 hours/week, compared with working 35-40 hours/week (< 50 years: RR 1.19, 95% CI 0.91 to 1.57; ⩾ 50 years: RR 1.06, 95% CI 0.90 to 1.24; p = 0.50; 20 studies, number of participants not reported, I^2 not reported).

A7.3.4. By industrial sector

No studies provided effect estimates disaggregated by industrial sector, and we could therefore not assess differences in effect estimates by industrial sector.

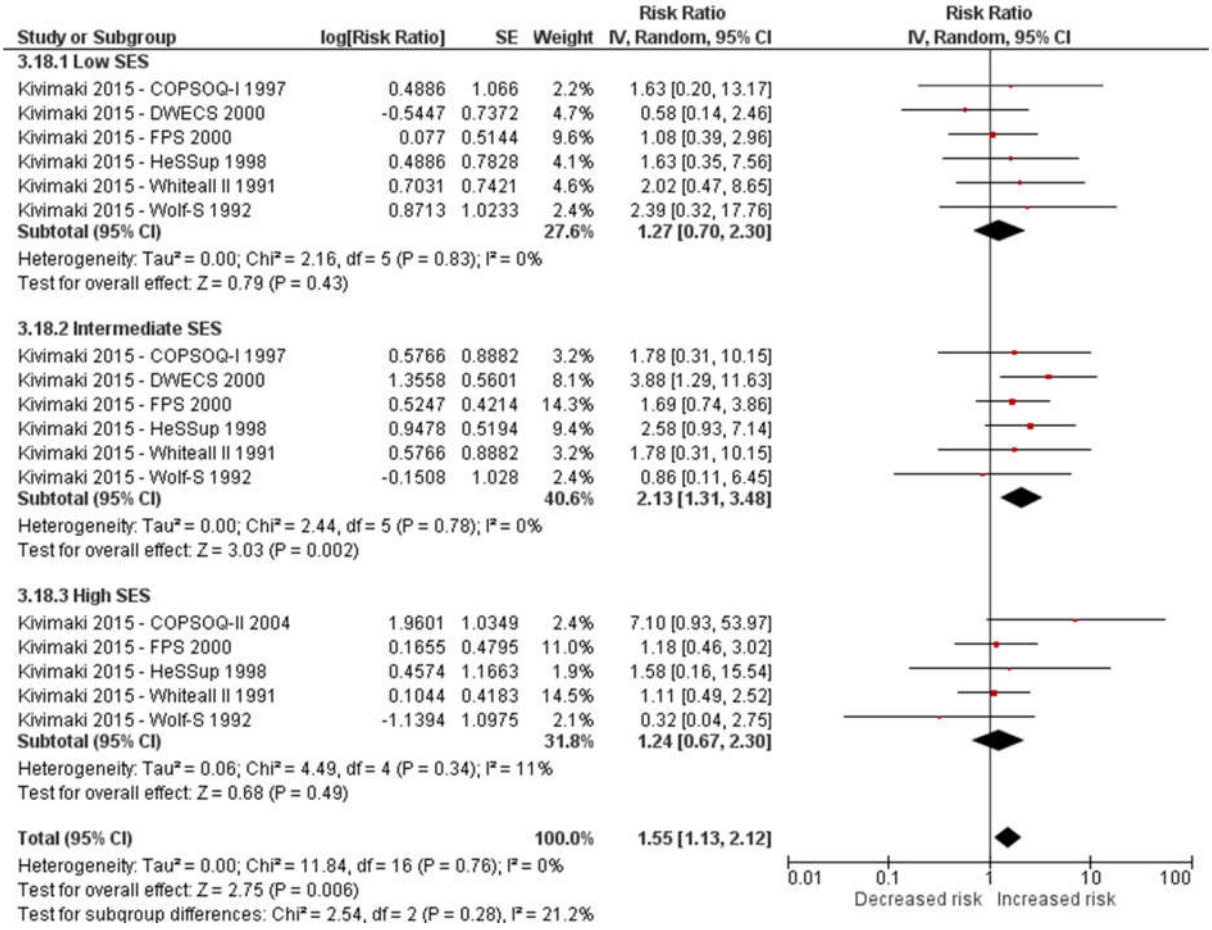
A7.3.5. By occupation

No studies provided effect estimates disaggregated by occupation, and we could therefore not assess differences in effect estimates by occupation.

A7.3.6. By SES

Again, subgroup analysis according to SES revealed a somewhat stronger effect in the intermediate SES group (Fig. A7.6)

Fig. A7.6 Subgroup analysis by SES, died from stroke, working ⩾ 55 hours/week compared with working. 35-40 hours/week, cohort studies

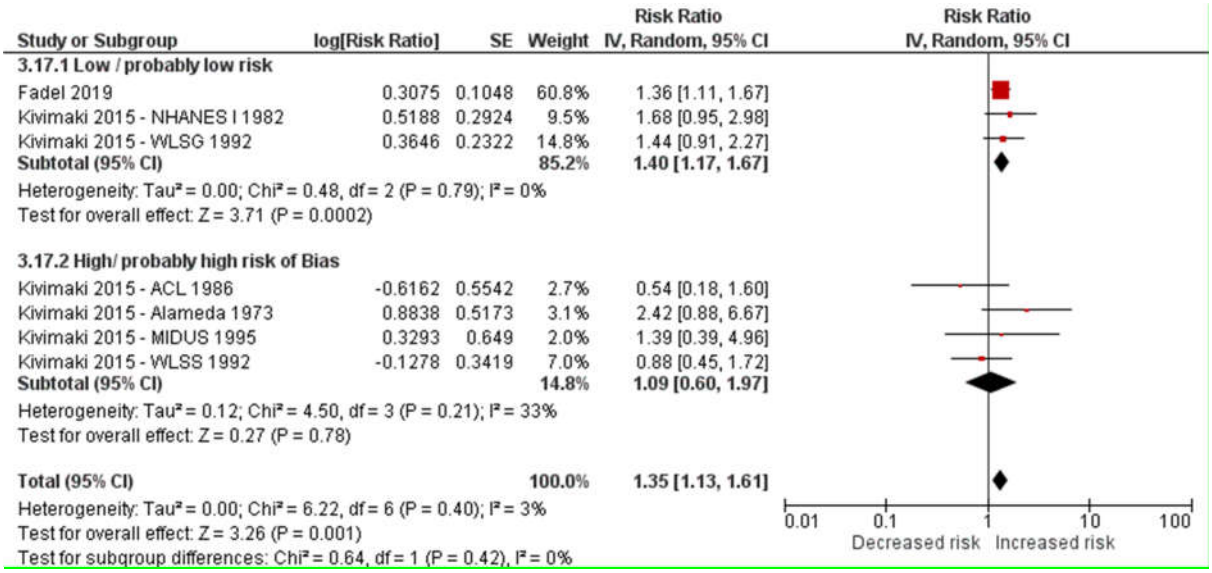


Appendix 8 Sensitivity analyses

A8.1.1. Studies judged to be of "low" or "probably low" risk of bias

There were no significant differences between studies with "low"/"probably low" risk of bias in all RoB domains and studies with at least one rating of "high" or "probably high" in any RoB domain" (Fig. A8.1).

Fig. A8.1. Sensitivity analysis, studies with low" / "probably low" risk of bias vs. "high" / "probably high" risk of bias), Acquired stroke, worked ⩾55 hours/week compared with worked 35-40 hours/week, cohort studies



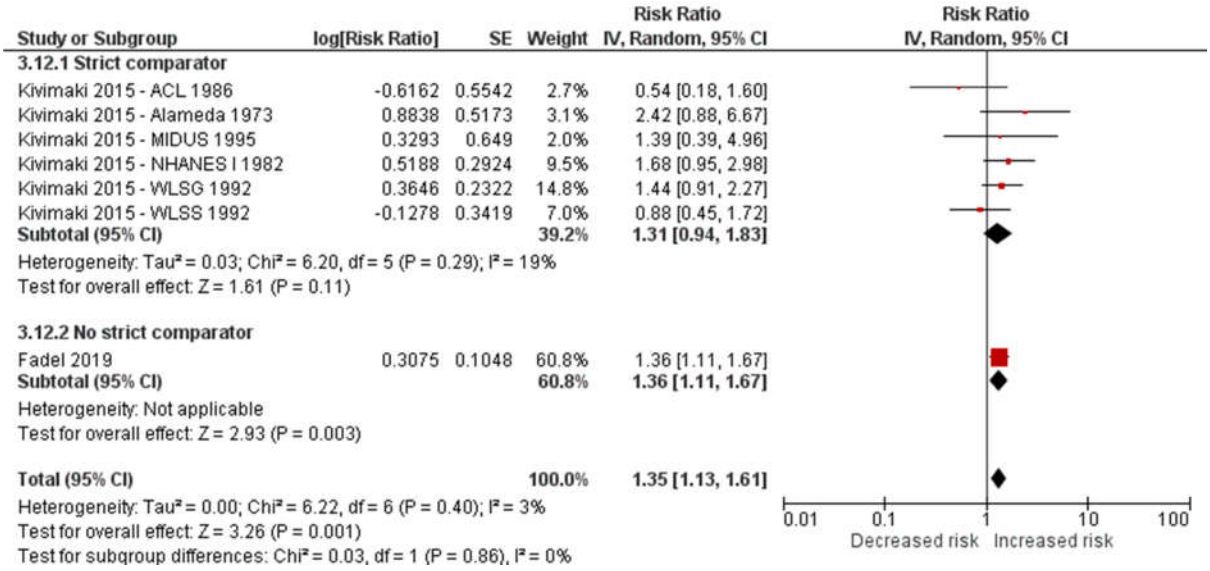
A8.1.2. Other statistical models

Based on Fadel 2019 (Fadel et al. 2019) data, it was possible to compare Relative risk (Generalized Linear Model), Hazard Ratio (Cox Model) and Odds Ratio (Logistic Model), and no difference (p=0.87) was observed: RR: 1.36 [1.10 - 1.67], HR : 1.27 [1.11 - 1.47] and OR : 1.30 [1.13 - 1.48].

A8.1.3. Exclusion of approximate comparator

Excluding studies with approximate comparators i.e. Fadel 2019 study (Fadel et al. 2019) from the main analysis yields similar results (though statistically non-significant in the sensitivity analysis): RR 1.35, 95% CI 1.13 to 1.61 (with Fadel 2019) and RR 1.31, 95% CI 0.94 to 1.83 (without Fadel 2019).

Fig. A8.2 Sensitivity analysis, studies with strict vs. approximate comparators, Acquired stroke, worked ⩾ 55 hours/week compared with worked 35-40 hours/week, cohort studies

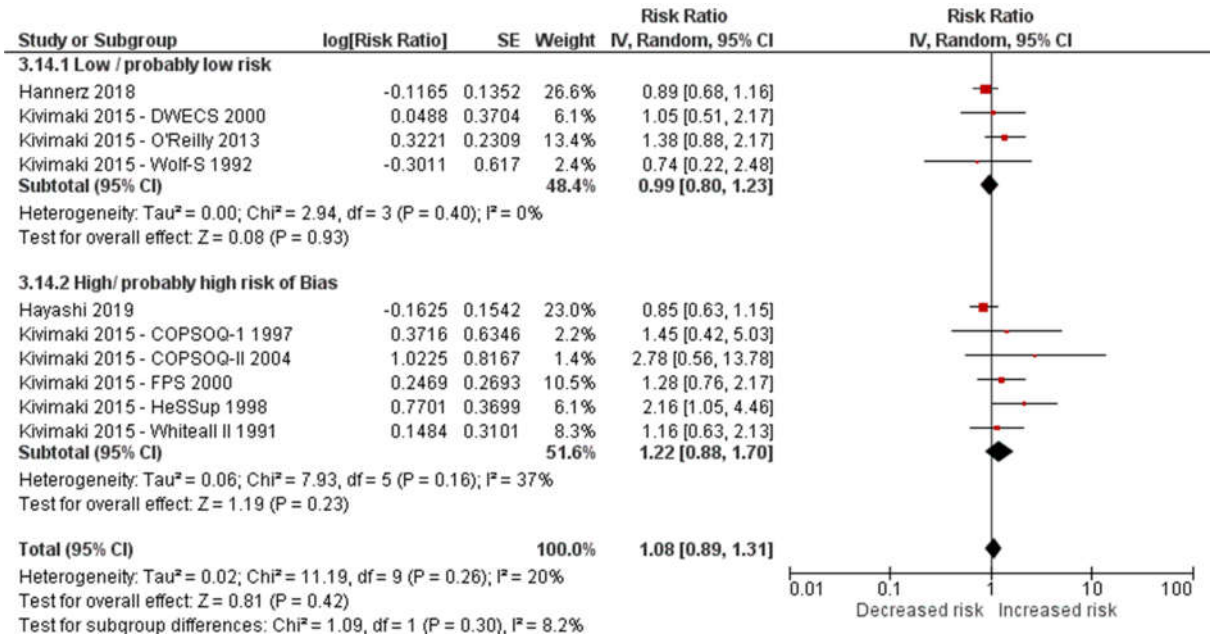


A8.2. Died from stroke (mortality from stroke)

A8.2.1. Studies judged to be of "low" or "probably low" risk of bias

There was no evidence for any difference between studies with "low"/"probably low" RoB ratings across all RoB domains and studies with any "high"/"probably high" RoB rating in at least one RoB domain (test for subgroup differences = 0.16) (Fig. A8.3).

Fig. A8.3. Sensitivity analysis, studies with low " / "probably low " risk of bias vs. "high " / "probably high " risk of bias), Died from stroke, worked ⩾55 hours/week compared with worked 35-40 hours/week, cohort studies



All studies defined stroke using or approximated ICD-10.

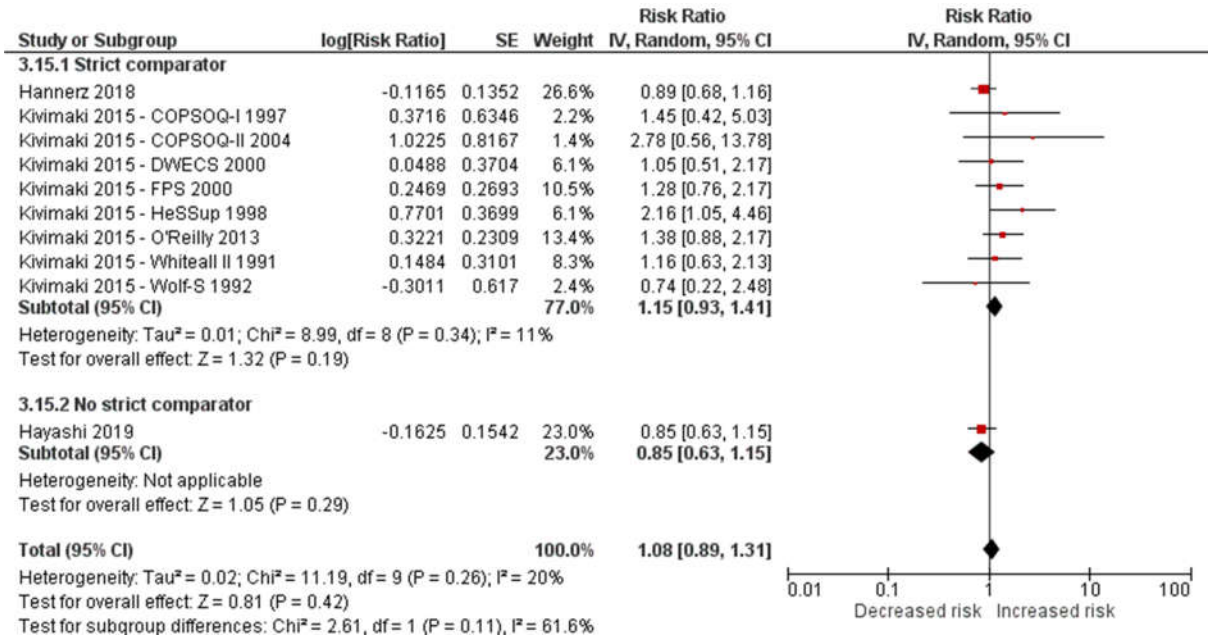
A8.2.2. Other statistical models

No data were able to be extracted for model comparison, though Kivimaki et al published on pooled data (Kivimaki et al. 2015c) (Kivimaki et al. 2015a). Kivimaki 2015 (Kivimaki et al. 2015a) (Kivimaki et al. 2015c) had also repeated the estimates for RR (fatal/ non-fatal stroke, age/sex/socioeconomic adjusted) RR: 1.33 [1.11 - 1.61], HR : 1.32 [0.99 - 1.76] and OR : 1.32 [0.99 - 1.78].

A8.2.3. Exclusion of approximate comparator

Exclusion of the Hayashi 2019 study from the main analysis (for fatal stroke) yields similar results (though statistically non-significant in the sensitivity analysis): RR 1.08, 95% CI 0.89 to 1.31(Hayashi et al. 2019) and RR 1.15, 95% CI 0.93 to 1.41 (without Hayashi 2019). (Fig. A8.4)

Fig. A8.4 Sensitivity analysis, studies with strict vs. approximate comparators, Died from stroke, worked ⩾ 55 hours/week compared with worked 35-40 hours/week, cohort studies



Appendix 9. Supplementary information on strength of evidence: Bradford Hill criteria

In the protocol, we had declared that we would estimate the strength of evidence using mechanistic and experimental data. Taking into account that the systematic review did not include studies of in vitro, animal, and mechanistic data, we present a discussion on judgement of causal association based on revised Bradford Hill criteria.

Temporal sequence: All cohort studies met this criterion as exposure was defined at a time when the study population was either free from outcomes, or when participants with prevalent outcome (stroke) were excluded from the study. Moreover, to reduce bias due to reverse causation, outcome events occurring during the first three years of follow-up were excluded from analysis in the majority of cohort studies (Kivimaki et al. 2015a). In Fadel (Fadel et al. 2019) there was a 5-year lag.

Strength of association: Overall, the cohort studies revealed a weak strength of associations, with no risk estimate approaching or exceeding the level of 2.0.

Consistency of associations: Five of the seven cohort studies on acquired stroke with a combined weight of 90% accounted for an acceptable consistency of findings with a low heterogeneity (I^2 3%) (Fig. 7). Among studies analysing risk of dying from stroke, seven of the 10 studies with a combined weight of 49.0% accounted for a much weaker consistency; heterogeneity was higher (I^2 20%) and tests for overall effect were significant (Fig. 9). In the recent Hannerz study (Hannerz et al. 2018), which found no effect of weekly extended work on overall stroke, two differences may explain the results. Firstly, working conditions in Denmark are among the best in Europe with 91% of workers satisfied of their work (https://www.eurofound.europa.eu/country/denmark), and it is likely that working even for a long time with good working conditions is generally less harmful (although the association with hemorrhagic strokes persisted in their study). Secondly, the duration of exposure and temporal sequence with the outcome, is not known. It is, thus, possible that given the overall working conditions in Denmark, people who have a long-term job do so for a short period of time. Similarly, a Japanese study, based on 91 cases, had a non-significant hazard ratio [1.20 (0.89-1.62)] for working exposures of 9 to 11 hours per day (compared to 7 to 9 hours per day). Differences between acquired and died from stroke might be explained by the low proportion of mortality studies and the difficulty in having enough information on cause of death (especially on the topic of long working hours).

Dose-response relationship: For acquired stroke studies, as previously stated, Kivimaki (Kivimaki et al. 2015a) showed that increasing the number of hours worked per week, increased the risk. Fadel 2019 (Fadel et al. 2019) studied years of exposure and showed a significant gradient with a threshold at 10 years.

Confounding: Although the link between long working hours and stroke may be influenced, or even mediated, by several behavioural and other work-related factors, and although residual confounding cannot be excluded, all results of the cohort studies entering our meta-analyses were adjusted for the

important confounding effects of age, sex and socioeconomic status. Therefore, this criterion was met at least to a substantial extent.

Biological plausibility: To our knowledge no cohort study exploring the effect of long working hours on stroke has included chemical, physical or biological indicators of pathways that can mediate the observed association, documenting evidence on its biological plausibility. Indeed, various studies have shown direct effects of certain working conditions on stroke and indirect effects by modifying associated behaviors as well as increasing cardiac electric instability and hypercoagulability among patients with a lengthy experience with long working hours. Shifts, night work and job strain have been particularly linked with bad working conditions that could be responsible for these poor health outcomes (Wong et al. 2019). With more time spent at work, exposure to different types of toxic substances or conditions is accumulating. Evidence on elevated stroke risks of toxic substances or conditions at work has been demonstrated for noise, shift work, physical activity (Theorell et al. 2016), and chronic psychosocial stress at work, as measured by 'job strain' (Kivimaki and Steptoe 2018) or effort-reward imbalance (Dragano et al. 2017). There is now growing evidence on chronic activation of stress-physiological pathways among working people exposed to job strain or effort-reward imbalance at work, thus affecting stroke development (Kivimaki and Steptoe 2018). Although the cohort studies on long working hours did not include data on these additional health-adverse exposures, it is likely that many occupations subjected to long working hours experience one or several of these conditions. Therefore, there is limited support for the notion of biological plausibility of the reported association, mainly due to adverse long-term effects of chronic activation of stress-physiological pathways. Finally, the consistency with systematic review on effect on long working hours and stroke where possible pathways are partly the same, gives another element for plausibility (and consistency).

Taken together, several of the Bradford Hill criteria of causality were met by the cohort studies included in this meta-analysis, either with a high degree or a limited degree of plausibility for stroke.

Appendix 10. Overview of the extracted data of the papers

Study ID	Outcome	Exposure	Risks	WHO Region (country)	Sex	Age (years)	Socio-Economic status/Education	Type
Fadel 2019	Acquired stroke	⩾ 10h/day more 50 days/year vs less	RR: 1.36 [1.10 - 1.67] HR : 1.27 [1.11 - 1.47] OR : 1.30 [1.13 - 1.48]	Europe (France)	Men : 1.22 [1.04 - 1.45] Women : 1.37 [1.10 - 1.67]	< 50 : 1.09 [0.81 - 1.49] ⩾ 50 : 1.28 [1.11 - 1.49]	High : 1.14 [0.81 - 1.58] Intermediate : 1.71 [1.19 - 2.49] Low : 1.68 [0.95 - 2.97	
Hannerz 2018	Acquired stroke (mixed with mortality)	⩾ 55h/week Vs 35-40h/week (also 41-18h /week) (also 49-54/week)	RR : 0.89 [0.69 - 1.16] 0.97 [0.83 - 1.13] 1.10 [0.86 - 1.39]	Europe (Denmark)				Hemorrhagic : 1.33 [0.82 - 2.15]* Ischemic : 0.86 [0.61 - 1.22] Hemorrhagic :1.10 [0.81 - 1.50] Ischemic :1.01 [0.83 - 1.23] Hemorrhagic :1.58 [1.01 - 2.46] Ischemic :0.85 [0.60 - 1.22]
Hayashi 2019	Acquired stroke	⩾ 11h/day	HR : 0.85 [0.62 - 1.15]	Asia (Japan)				Hemorrhagic :

Study ID	Outcome	Exposure	Risks	WHO Region (country)	Sex	Age (years)	Socio-Economic status/Education	Type
	(mixed with mortality)	vs 7 to <9h/day (also 9 to 11< h/day)	(only age adjusted 0.88 [0.67 - 1.17) (fully adjusted) 0.83 [0.60 - 1.13) 1.05 [0.86 - 1.28] (only age adjusted 1.04 [0.87 - 1.25) (fully adjusted) 1.06 [0.87 - 1.29)					0.64 [0.37 - 1.09]* Ischemic : 0.95 [0.64 - 1.41] Hemorrhagic : 1.15 [0.86 - 1.54] Ischemic : 0.97 [0.74 -1.27]
Jeong 2013	Acquired stroke	⩾ 55h/week vs < 40h/week (40-50h/week) (50 -55 h/weeks)	OR: 1.91 [1.19 - 3.06] (unadjusted : 2.02 [1.35 - 3.04) OR: 0.54 [0.30 - 0.97] (unadjusted : 0.43 [0.25 - 0.97] 0.27 [0.10 - 0.78] (unadjusted :	Asia (Republic of Korea)	Men (OR): 1.53 [0.89 - 2.63] Women : 3.40 [1.11 - 10.40] Men: 0.40 0.23-0.69 Women : 0.93 0.32-2.76 Men : 0.36 0.15-0.84 Women : 0.50 0.10-2.60	< 45 : 1.35 [0.55 - 3.31] 45-55 : 3.39 [1.53 - 7.52] ⩾ 55 : 1.29 [0.52 - 3.17] < 45 : 0.42 0.17-1.02 45-55:0.79 0.35-1.77 >55:0.28 0.11-0.70 < 45 : 0.22 0.06-0.87 45-55:0.92 0.31-2.75	High (more than high school graduation) : 2.89 [1.16 - 7.20] Low (lower): 1.71 [0.97 - 3.02] High:0.52 0.22-1.20 Low :0.49 0.27-0.88 High:0.68 0.18-2.59 Low :0.33 0.13-0.82	Hemorrhagic : 1.58 [0.87 - 2.85] Ischemic : 2.21 [1.16 - 4.21] Hemorrhagic :0.53 0.20-1.40 Ischemic :0.27 0.10-0.78 Hemorrhagic :0.41 0.21-0.82 Ischemic :0.54 0.30-0.97

Study ID	Outcome	Exposure	Risks	WHO Region (country)	Sex	Age (years)	Socio-Economic status/Education	Type
			0.30 [0.12 - 0.86]			>55: 0.08 0.01-0.71		
Kim 2013	Acquired stroke	⩾ 13h/day vs 5-8h/day (Only Hemorrhagic stroke) 9-12 h/day	OR: 1.98 [1.45 - 2.72] (unadjusted : 1.89 [1.38 - 2.58) Fully adjusted : 2.21 [1.54 - 3.17] 1.43 [1.16 - 1.76] unadjusted: 1.39 [1.13 - 1.71] Fully adjusted :1.56 [1.23 - 1.97]	Asia (Republic of Korea)				Hemorrhagic : 1.98 [1.45 - 2.72] Hemorrhagic: 1.43 [1.16 - 1.76]
Kivimaki 2015 (includes 14 records)	Acquired stroke (mixed with mortality)	⩾ 55h/week vs 36-40h/week (also 41-18h /week) (also 49-	RR : 1.33 [1.11 - 1.61] (RR 1.10 [0.94 - 1.28] (RR 1.27 [1.03 -	USA: 1.31 [0.94 - 1.83] Europe: 1.34 [1.05-1.71]	Men : 1.29 [1.04 - 1.60] Women : 1.63 [1.10 - 2.43]	< 50 : 1.14 [0.78 - 1.67] ⩾ 50 : 1.43 [1.11 - 1.84]	High : 1.29 [0.93 - 1.80] Intermediate : 1.79 [1.21 - 2.65] Low : 1.59 [1.15 - 2.19]	

Study ID	Outcome	Exposure	Risks	WHO Region (country)	Sex	Age (years)	Socio-Economic status/Education	Type
		54/week)	1.56] HR : 1.32 [0.99 - 1.76] OR : 1.32 [0.99 - 1.78]					

PRISMA checklist

Section/topic	#	Checklist item	Reported on page # (original manuscript)
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	3
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	5-7
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	8-14
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	15
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	14
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	17-20
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	15-16
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	90-97
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	17
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	20-21
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	17-21
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	21-22
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	22-23

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	22-23
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4-25
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	23
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	28-29, fig 2, app 2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	30-40
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	43-51
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	30-42,App 4 and 5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	51-59
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	61-66
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	59-71, App 7/8
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	66 -69
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	70-72-
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	72-74
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	74