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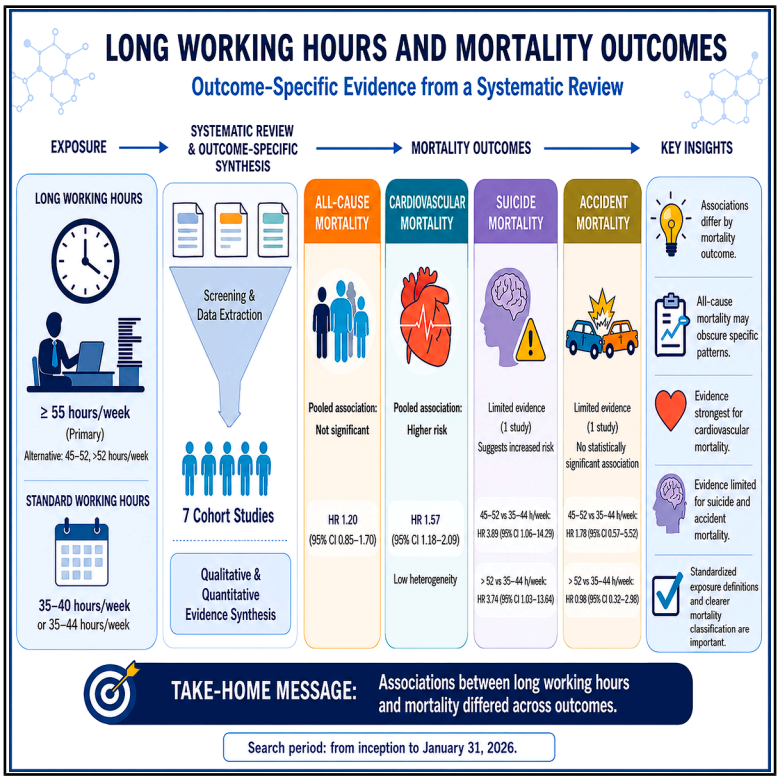
Long working hours and mortality outcomes: A systematic review with outcome-specific evidence synthesis

Graphical abstract



Highlights

- Long working hours showed different associations across mortality outcomes
- Working 55 or more hours per week was linked to higher cardiovascular mortality
- No significant pooled association was observed for all-cause mortality
- Evidence for suicide and accident mortality remains limited

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In brief

Health sciences; Medicine; Medical specialty; Internal medicine; Cardiovascular medicine; Patient social context; Working condition

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Meta-analysis/systematic review

Long working hours and mortality outcomes: A systematic review with outcome-specific evidence synthesis

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SUMMARY

Long working hours are a major occupational health concern, but whether their associations differ across mortality outcomes remains unclear. We searched six databases from inception to January 31, 2026 and conducted a systematic review with outcome-specific evidence synthesis of longitudinal studies. Seven original cohort studies were included. Long working hours, commonly defined as 55 or more hours per week, were associated with higher cardiovascular mortality, whereas the pooled association with all-cause mortality was not statistically significant. The only eligible prospective cohort study suggested increased suicide mortality at 45–52 and more than 52 h per week, while no significant association was observed for accident mortality. These findings indicate that mortality associations of long working hours are outcome specific and highlight the need for prospective studies with standardized exposure definitions and clearer classification of cause-specific mortality.

INTRODUCTION

Long working hours have become a major occupational health concern worldwide.[1–3] During the COVID-19 pandemic, teleworking and work intensification may have further increased exposure in some settings.[4–6] In the World Health Organization (WHO)/International Labor Organization (ILO) Joint Estimates, long working hours are commonly defined as working 55 h or more per week,[7–9] and this exposure was estimated to account for 745,194 deaths from ischemic heart disease and stroke globally in 2016.[10] In East Asia, the public-health relevance of excessive working time has long been reflected in the concepts of karoshi and karojisatsu,[11,12] which refer to overwork-related cardiovascular or cerebrovascular death and suicide due to overwork, respectively.[13–15] These observations suggest that the health consequences of excessive working time may extend beyond a single disease category and may involve multiple fatal outcomes.

A growing epidemiological literature has linked long working hours to adverse cardiovascular and mental health outcomes, including coronary heart disease,[16,17] stroke,[18,19] depressive symptoms,[20,21] anxiety symptoms,[21] and sleep disturbances.[22] Systematic reviews and meta-analyses have most consistently supported associations with cardiovascular outcomes, particularly ischemic heart disease and stroke,[7,8,10] while evidence has also accumulated for depressive symptoms and sleep disturbances.[20,23] Recent reviews suggest that long working hours are associated with a modest increase in cardiovascular risk.[7,24] A large European multicohort study further suggested elevated early cardiovascular death, but not overall mortality, among employees working long hours.[25] More recent cohort studies have extended the mortality literature by reporting higher all-cause mortality in China,[26] higher cardiovascular mortality in the United States,[27] and increased suicide mortality—whereas accident mortality was not statistically significant—in Korea.[28] Taken together, these findings suggest that the mortality consequences of long working hours may differ across fatal endpoints rather than follow a single uniform pattern.

Despite this growing literature, the mortality evidence remains fragmented and difficult to interpret as a whole. Most previous syntheses have been endpoint specific, focusing on specific cardiovascular endpoints or broader non-fatal health outcomes rather

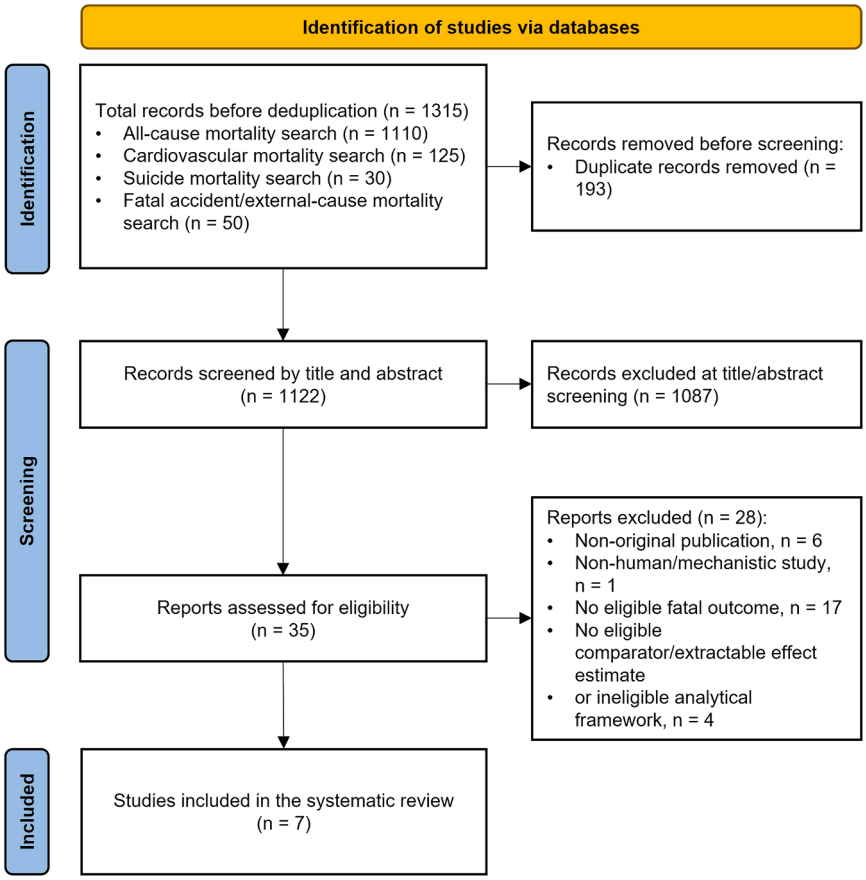

Figure 1. PRISMA flow diagram of study selection

than jointly evaluating multiple mortality endpoints within a single analytic framework. At the same time, the original cohort studies differ in exposure thresholds, occupational context, geographic setting, and reported effect measures, and they have examined different fatal outcomes, including all-cause mortality,[25,26,29,30] cardiovascular mortality,[25,27,29,31] suicide mortality,[28] and accident mortality.[28] Because all-cause mortality and cause-specific mortality are related but analytically distinct endpoints, combining them indiscriminately may obscure clinically relevant outcome-specific patterns.[32,33] An updated review that synthesizes these fatal outcomes separately is therefore needed to clarify where the evidence is most consistent and where important gaps remain.

Accordingly, we conducted a systematic review and outcome-specific evidence synthesis of longitudinal studies to evaluate the association between long working hours and four prespecified mortality outcomes: all-cause mortality, cardiovascular mortality, suicide mortality, and accident mortality. By examining these endpoints separately and prioritizing comparable effect measures, we aimed to clarify whether the mortality associations of long working hours differ across fatal outcomes and to provide a clearer summary of the available evidence.

RESULTS

Study selection

The database search yielded 1,315 records before deduplication, including 1,110 from the all-cause mortality search, 125 from the cardiovascular mortality search, 30 from the suicide mortality search, and 50 from the fatal accident/external-cause mortality search. After removal of 193 duplicates, 1,122 records were screened by title and abstract, of which 1,087 were excluded. Thirty-five full-text reports were assessed for eligibility, and 28 were excluded for the following reasons: non-original publication (n = 6), non-human/mechanistic study (n = 1), no eligible fatal outcome (n = 17), or no eligible comparator, extractable effect estimate, or eligible analytical framework (n = 4). Ultimately, seven original cohort studies[25–31] were included in the final systematic review (Figure 1).

Study characteristics and methodological quality

The seven included studies were conducted in China,[26] Northern Ireland in the UK,[29] Denmark,[30] Finland/Sweden/Denmark/the UK,[25] Italy,[31] the United States,[27] and Korea.[28] Sample sizes ranged from 4,051 to 11,903,540 participants. Most studies defined long working hours as ≥55 h/week compared with standard working hours of 35–40 or 35–44 h/week, although alternative cut-points were used in some cohorts. Four studies reported all-cause mortality,[25,26,29,30] four reported cardiovascular mortality,[25,27,29,31] and one study reported suicide mortality and accident mortality[28] (Table 1). According to the Newcastle-Ottawa scale (NOS), four studies were rated as high quality and three as moderate quality (Table 2). Detailed item-level assessments across the NOS domains are presented in Table S2.

Cardiovascular mortality

Four studies reported associations between long working hours and cardiovascular mortality.[25,27,29,31] However, only two studies[25,27] provided sufficiently comparable overall hazard ratios (HRs) for quantitative pooling. In the primary meta-analysis, long working hours were associated with a significantly higher risk of cardiovascular mortality, with a pooled HR of 1.57 (95% confidence interval [CI] 1.18–2.09). Between-study heterogeneity was negligible (I^2 = 0.0%, p = 0.7005) (Figure 2A). Among the studies retained for qualitative synthesis (Table 1), O'Reilly and Rosato[29] reported an elevated cardiovascular mortality risk among men in routine/semi-routine occupations (HR 1.49, 95% CI 1.10–2.00), whereas Alicandro et al.[31] found no statistically significant association in sex-specific cause-specific models (men: cause-specific HR (cHR) 0.95, 95% CI 0.89–1.02; women: cHR 1.19, 95% CI 0.95–1.49).

Table 1. Characteristics of studies included in the systematic review

Study	country/region	design/population	exposure contrast	mortality outcome(s)	main adjusted estimate
Huang et al., 2023	China	retrospective cohort; adults aged 18–65 years from the China Health and Nutrition Surveys (*N* = 10,269)	≥55 vs. 35–40 h/week	all-cause mortality	HR 1.49 (95% CI 1.02–2.18)
O'Reilly and Rosato, 2013	Northern Ireland, UK	census-based longitudinal cohort; employed adults aged 20–59/64 years (*N* = 414,949)	≥55 vs. 35–40 h/week	all-cause mortality; cardiovascular mortality	in men in routine/semi-routine occupations: all-cause mortality HR 1.31 (95% CI 1.11–1.55); cardiovascular mortality HR 1.49 (95% CI 1.10–2.00)
Hannerz and Soll-Johanning, 2018	Denmark	cohort study based on the Danish Labor Force Survey; employees aged 20–64 years (*N* = 159,933)	>48 vs. 32–40 h/week	all-cause mortality	RR 0.92 (95% CI 0.80–1.05)
Ervasti et al., 2021	Finland, Sweden, Denmark, and the UK	multicohort prospective study; working-age adults from the IPD-Work consortium (primary analysis *N* = 59,599)	≥55 vs. 35–40 h/week	all-cause mortality; cardiovascular mortality	overall mortality: HR 1.04 (95% CI 0.84–1.29); cardiovascular mortality: HR 1.68 (95% CI 1.08–2.61) in the primary analysis
Alicandro et al., 2020	Italy	census-based cohort; active workers aged 20–64 years (*N* = 11,903,540)	≥55 vs. 35–40 h/week	cardiovascular mortality	men: cHR 0.95 (95% CI 0.89–1.02); women: cHR 1.19 (95% CI 0.95–1.49)
Gu et al., 2025	United States	prospective cohort; employed adults in MIDUS without prior myocardial infarction or stroke at baseline (*N* = 4,051)	≥55 vs. 35–40 h/week	cardiovascular mortality	HR 1.50 (95% CI 1.03–2.17)
Lee et al., 2020	Korea	prospective cohort; employed workers from KNHANES linked to death records (*N* = 14,484)	45–52 vs. 35–44 h/week; >52 vs. 35–44 h/week	suicide mortality; accident mortality	suicide mortality: HR 3.89 (95% CI 1.06–14.29) for 45–52 h/week and HR 3.74 (95% CI 1.03–13.64) for >52 h/week; no significant association was observed for accident mortality

CI, confidence interval; cHR, cause-specific hazard ratio; HR, hazard ratio; KNHANES, Korean National Health and Nutrition Examination Survey; MIDUS, Midlife in the United States; RR, rate ratio.

All-cause mortality

Four studies evaluated all-cause mortality.[25,26,29,30] Two studies[25,26] with comparable overall HR were included in the secondary meta-analysis, which yielded a pooled HR of 1.20 (95% CI 0.85–1.70), indicating no statistically significant association between long working hours and all-cause mortality. Moderate between-study heterogeneity was observed (I^2 = 61.7%, p = 0.1061) (Figure 2B). At the individual-study level, Huang et al.[26] reported a significant positive association for ≥55 versus 35–40 h/week (HR 1.49, 95% CI 1.02–2.18), whereas Ervasti et al.[25] reported no clear association (HR 1.04, 95% CI 0.84–1.29). The remaining two studies were synthesized qualitatively because their estimates were not directly comparable with the pooled HR-based analysis (Table 1): Hannerz and Soll-Johanning[30] reported a null association for >48 versus 32–40 h/week (rate ratio (RR) 0.92, 95% CI 0.80–1.05), while O'Reilly and Rosato[29] observed an increased risk only in men in routine/semi-routine occupations (HR 1.31, 95% CI 1.11–1.55).

Suicide mortality and accident mortality

Only one eligible prospective cohort study[28] reported suicide mortality and accident mortality (Table 1). Compared with 35–44 h/week, working 45–52 h/week was associated with a higher risk of suicide mortality (HR 3.89, 95% CI 1.06–14.29), and a similarly increased risk was observed for >52 h/week (HR 3.74, 95% CI 1.03–13.64). In contrast, no statistically significant

Table 2. Methodological quality of the included original studies assessed using the Newcastle-Ottawa scale

Study	selection	comparability	outcome	total NOS score	quality category
Huang et al., 2023	★★★★	★★	★★☆	8/9	high
O'Reilly and Rosato, 2013	★★★★	★★	★★☆	8/9	high
Hannerz and Soll-Johanning, 2018	★★★☆	★☆	★★★	7/9	moderate
Ervasti et al., 2021	★★★★	★★	★★★	9/9	high
Alicandro et al., 2020	★★★☆	★☆	★★★	7/9	moderate
Gu et al., 2025	★★★★	★★	★★★	9/9	high
Lee et al., 2020	★★★☆	★☆	★★★	7/9	moderate

NOS, Newcastle–Ottawa Scale.

associations were observed for accident mortality at either 45–52 h/week (HR 1.78, 95% CI 0.57–5.52) or >52 h/week (HR 0.98, 95% CI 0.32–2.98). As detailed in Table 3, the accident mortality endpoint in this cohort included transport accidents and other accidental injuries based on registry-derived external-cause definitions, rather than workplace injuries alone.

DISCUSSION

In this systematic review and outcome-specific evidence synthesis of longitudinal studies, we found that the association between long working hours and mortality differed across fatal endpoints rather than following a uniform pattern. Long working hours were associated with a significantly higher risk of cardiovascular mortality in the primary quantitative synthesis, with negligible between-study heterogeneity, whereas the pooled association with all-cause mortality was not statistically significant and showed moderate heterogeneity. The only eligible prospective cohort study also suggested elevated risks of suicide mortality at both 45–52 and >52 h/week, while evidence for accident mortality remained limited and did not show a statistically significant association in that cohort. Taken together, these findings indicate that an undifferentiated focus on all-cause mortality may obscure clinically relevant outcome-specific associations. By synthesizing evidence separately across fatal endpoints, the present review clarifies that the current evidence base is most consistent for cardiovascular mortality, whereas evidence for suicide and accident mortality remains limited and requires further prospective investigation.

The most consistent evidence in the present review was observed for cardiovascular mortality. Notably, the pooled association for this outcome was based on two studies[25,27] that reported comparable overall HRs and showed a consistent direction of effect, with negligible between-study heterogeneity. This pattern provides more coherent evidence for an association between long working hours and cardiovascular mortality, although the broader qualitative evidence remained somewhat mixed because some cohorts reported subgroup-specific rather than overall estimates or used sex-specific cause-specific models.[29,31] The inclusion of the recent US prospective study by Gu et al.[27] updated and strengthened the evidence base for cardiovascular mortality beyond earlier reviews. The observed pattern is also biologically plausible, as long working hours may increase sustained psychosocial stress,[34,35] reduce recovery time,[36] impair sleep,[22,37] and promote adverse cardiometabolic responses,[38–41] all of which have been linked to cardiovascular risk and cardiovascular mortality.[42–44] These mechanisms may help explain why a clearer association was observed for cardiovascular mortality than for all-cause mortality in the present review.

By contrast, the pooled association with all-cause mortality was not statistically significant. This finding should not be interpreted as evidence of no effect; rather, it suggests that all-cause mortality may be too broad a composite endpoint to capture the more specific fatal consequences of long working hours. Unlike cardiovascular mortality, all-cause mortality is a broader composite endpoint that includes fatal outcomes with heterogeneous mechanisms and potentially different relationships to working-time exposure.[32,45] This may partly explain why a clearer association was observed for cardiovascular mortality than for all-cause mortality in the present review. This interpretation is also supported by the moderate heterogeneity observed in the pooled analysis and by the inconsistency of study-level findings,[46] with some cohorts reporting positive associations and others showing null results.[25,26,29,30] In this context, an exclusive focus on all-cause mortality may underestimate clinically relevant outcome-specific risks and obscure important differences across fatal endpoints. The present review therefore suggests that long working hours may be more meaningfully understood through cause-specific mortality patterns than through all-cause mortality alone.[10,25,26,29,30]

The heterogeneity across studies is itself informative and likely reflects genuine contextual differences rather than random variation alone. Several sources are likely relevant. First, the definition of long working hours was not fully uniform across studies, ranging from the WHO/ILO-relevant threshold of ≥55 h/week to >48 h/week or intermediate categories such as 45–52 h/week. Second, the included studies were conducted in markedly different settings, including East Asia,[26] Europe,[25,29–31] and the United States,[27] where labor regulation, occupational structure, social protection, and baseline mortality patterns may differ substantially. Third, occupational composition and reporting strategies also varied, with some studies providing overall population-level estimates[25–28,30] and others reporting subgroup-specific associations only,[29,31] such as estimates restricted to men in routine/semi-routine occupations or sex-specific cause-specific models. Finally, outcome definitions and ascertainment strategies were not entirely uniform across studies, particularly for less commonly reported endpoints. These differences likely contributed to the more heterogeneous pattern observed for

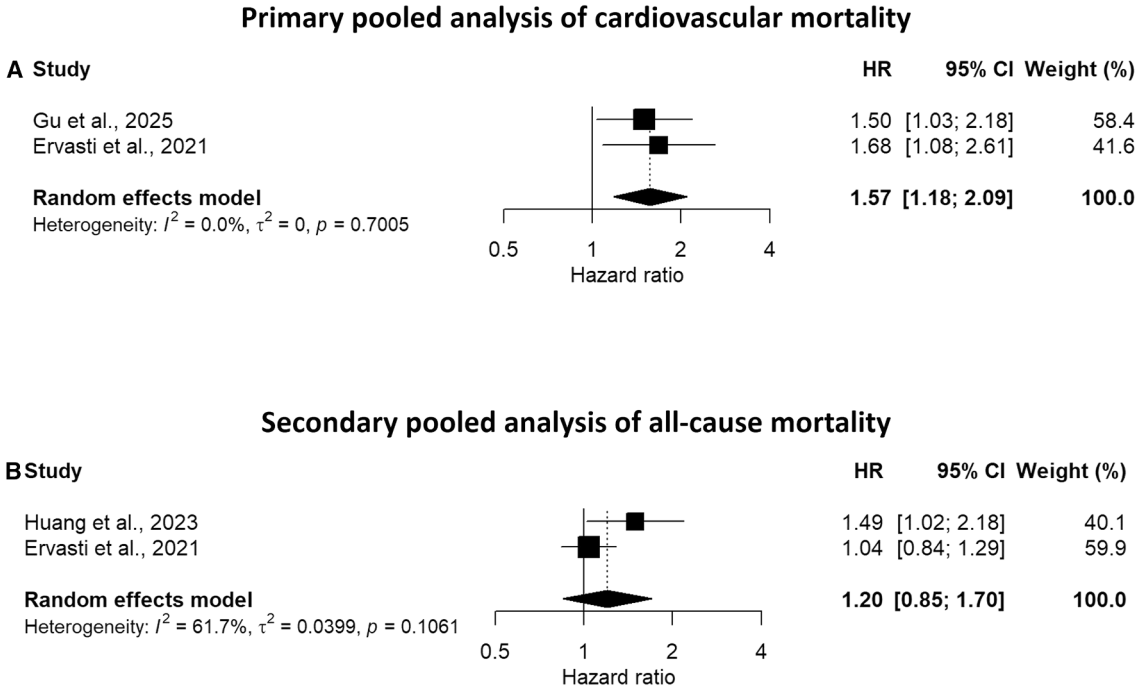

Figure 2. Pooled associations of long working hours with cardiovascular and all-cause mortality

(A) Presents the primary pooled analysis of cardiovascular mortality, and (B) presents the secondary pooled analysis of all-cause mortality. Forest plots show HR, 95% CI, and study weights under the random-effects model for mortality outcomes comparing long working hours with standard working hours. Squares represent study-specific estimates, with square size proportional to study weight, and diamonds represent pooled estimates. Detailed exposure contrasts and study characteristics are provided in Table 1. Abbreviation: HR, hazard ratio; CI, confidence interval.

all-cause mortality and to the broader qualitative variation across studies. By contrast, cardiovascular mortality appeared more consistent only after quantitative pooling was restricted to studies with comparable exposure contrasts, outcome definitions, and effect measures. Because each pooled outcome included only a very limited number of studies, formal subgroup analyses or meta-regression to evaluate sources of heterogeneity were not feasible; accordingly, these factors were explored descriptively rather than quantitatively.

The findings for suicide mortality and accident mortality also merit attention, although the current evidence remains limited. In the only eligible prospective cohort,[28] long working hours were associated with elevated risks of suicide mortality at both 45–52 and >52 h/week, suggesting that mental health-related fatal outcomes may represent an important but understudied consequence of prolonged working time. By contrast, no statistically significant association was observed for accident mortality in the same cohort. This apparent difference should be interpreted cautiously, however, because the available evidence for both outcomes was derived from a single study, the CIs were wide, and the accident-related endpoint reflected transport accidents and other accidental injuries rather than workplace injuries alone. Accordingly, the present review does not support definitive conclusions for either outcome, but it does indicate that

Table 3. Study-specific associations of long working hours with suicide mortality and accident mortality

Outcome	exposure comparison	adjusted HR (95% CI)	interpretation
Suicide mortality	45–52 vs. 35–44 h/week	3.89 (1.06–14.29)	significant positive association
Suicide mortality	>52 vs. 35–44 h/week	3.74 (1.03–13.64)	significant positive association
Accident mortality[a]	45–52 vs. 35–44 h/week	1.78 (0.57–5.52)	not statistically significant
Accident mortality	>52 vs. 35–44 h/week	0.98 (0.32–2.98)	not statistically significant

HR, hazard ratio; CI, confidence interval.

Data were derived from a prospective cohort study of employed workers in Korea using the Korean National Health and Nutrition Examination Survey linked to the national death registry. Working hours were categorized as 15–34, 35–44, 45–52, and >52 h/week, with 35–44 h/week as the reference group. The Cox model was adjusted for age, sex, household income, education, occupation, and depressive symptoms. No meta-analysis was performed for these two outcomes because only one eligible study was identified.

[a]Accident mortality in the eligible Korean cohort included transport accidents and other accidental injuries according to registry-based external-cause definitions, rather than workplace injuries alone.

suicide mortality may warrant closer attention in future longitudinal studies and that accident-related mortality should be assessed using more clearly defined and context-specific fatal injury categories.

The present review has several strengths that enhance both the interpretability and the contribution of the findings. A major strength is that it moved beyond undifferentiated summaries of mortality by synthesizing all-cause mortality and prespecified cause-specific mortality outcomes separately. This outcome-specific strategy allowed the review to identify a more coherent signal for cardiovascular mortality while also clarifying that the evidence base remains sparse for suicide mortality and accident mortality. The review also avoided inappropriate aggregation by not treating HR, RR, and odds ratio (OR) as interchangeable and by restricting quantitative pooling to studies with sufficiently comparable effect measures, exposure contrasts, and outcome definitions. In addition, potential overlap between cohorts was also assessed explicitly before outcome-specific synthesis. These design features improve the methodological coherence of the review.

Future research should prioritize standardized definitions of long working hours, clearer classification of cause-specific mortality, and the reporting of comparable outcome-specific effect estimates. More prospective studies are especially needed for suicide mortality and accident mortality, with better differentiation of workplace and non-workplace accidental deaths. Repeated exposure assessment and more detailed characterization of occupational and psychosocial factors would help improve comparability across studies and strengthen causal interpretation.

Current evidence suggests that the association between long working hours and mortality is outcome specific. The most consistent evidence was observed for cardiovascular mortality, whereas the pooled association with all-cause mortality was not statistically significant, and evidence for suicide mortality and accident mortality remains limited. Further prospective studies with standardized exposure and outcome definitions are needed.

Limitations of the study

This review has several limitations. First, the evidence base for each outcome remained limited, with only two studies available for quantitative pooling for cardiovascular mortality and all-cause mortality, and only a single cohort informing suicide mortality and accident mortality. Second, definitions of long working hours were not fully standardized across studies, which constrained comparability and prevented formal assessment of exposure-response relationships. Third, working hours were generally measured at baseline or over a limited period and were analyzed categorically, which may have introduced exposure misclassification and reduced sensitivity to longer-term working-time patterns. Fourth, residual confounding remains possible, particularly for psychosocial work characteristics, employment insecurity, and baseline mental health, despite the generally moderate-to-high methodological quality of the included studies. Fifth, some fatal endpoints were not defined uniformly across studies, which may have further contributed to between-study variation. Finally, restriction to English-language peer-reviewed publications may have introduced language bias, and publication bias could not be formally assessed because too few studies were available for each pooled analysis.[47]

RESOURCE AVAILABILITY

Lead contact

Further information and requests for resources should be directed to and will be fulfilled by the lead contact, Yeen Huang (huangyeen@gzucm.edu.cn).

Materials availability

This study did not generate new unique reagents, materials, or experimental models.

Data and code availability

- Data reported in this paper will be shared by the lead contact upon request.
- This paper does not report original code.
- Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request.

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AUTHOR CONTRIBUTIONS

Conceptualization, X.S., D.Z., Y.X., J.H., R.W., and Y.H.; methodology, R.W. and Y.H.; investigation, Y.X. and J.H.; formal analysis, R.W. and Y.H.; data curation, R.W. and Y.H.; writing – original draft, X.S. and D.Z.; writing – review and editing, R.W. and Y.H.; supervision, R.W. and Y.H.; funding acquisition, Y.H. and R.W. All authors critically reviewed the manuscript and approved the final version.

DECLARATION OF INTERESTS

The authors declare no competing interests.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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SUPPLEMENTAL INFORMATION

Supplemental information can be found online at https://doi.org/10.1016/j.isci.2026.116294.

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REFERENCES

1. Härmä, M., Kecklund, G., and Tucker, P. (2024). Working hours and health - key research topics in the past and future. Scand. J. Work. Environ. Health *50*, 233–243. https://doi.org/10.5271/sjweh.4157.
2. van der Hulst, M. (2003). Long workhours and health. Scand. J. Work. Environ. Health *29*, 171–188. https://doi.org/10.5271/sjweh.720.
3. Frank, J., Mustard, C., Smith, P., Siddiqi, A., Cheng, Y., Burdorf, A., and Rugulies, R. (2023). Work as a social determinant of health in high-income countries: past, present, and future. Lancet *402*, 1357–1367. https://doi.org/10.1016/S0140-6736(23)00871-1.
4. Peters, S.E., Dennerlein, J.T., Wagner, G.R., and Sorensen, G. (2022). Work and worker health in the post-pandemic world: a public health perspective. Lancet Public Health *7*, e188–e194. https://doi.org/10.1016/s2468-2667(21)00259-0.
5. Giusti, E.M., Veronesi, G., Gianfagna, F., Magnavita, N., Campana, F., Borchini, R., Iacoviello, L., and Ferrario, M.M. (2024). The independent and interactive effects of changes in overtime and night shifts during the COVID-19 pandemic on burnout among nurses: a longitudinal study. Scand. J. Work. Environ. Health *50*, 475–484. https://doi.org/10.5271/sjweh.4176.
6. Küppers, L., Göbel, J., Aretz, B., Rieger, M.A., and Weltermann, B. (2024). Associations between COVID-19 Pandemic-Related Overtime, Perceived Chronic Stress and Burnout Symptoms in German General Practitioners and Practice Personnel-A Prospective Study. Healthcare (Basel) *12*, 479. https://doi.org/10.3390/healthcare12040479.
7. Li, J., Pega, F., Ujita, Y., Brisson, C., Clays, E., Descatha, A., Ferrario, M.M., Godderis, L., Iavicoli, S., Landsbergis, P.A., et al. (2020). The effect of exposure to long working hours on ischaemic heart disease: A systematic review and meta-analysis from the WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury. Environ. Int. *142*, 105739. https://doi.org/10.1016/j.envint.2020.105739.
8. Descatha, A., Sembajwe, G., Pega, F., Ujita, Y., Baer, M., Boccuni, F., Di Tecco, C., Duret, C., Evanoff, B.A., Gagliardi, D., et al. (2020). 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. Environ. Int. *142*, 105746. https://doi.org/10.1016/j.envint.2020.105746.
9. Pachito, D.V., Pega, F., Bakusic, J., Boonen, E., Clays, E., Descatha, A., Delvaux, E., De Bacquer, D., Koskenvuo, K., Kröger, H., et al. (2021). The effect of exposure to long working hours on alcohol consumption, risky drinking and alcohol use disorder: A systematic review and meta-analysis from the WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury. Environ. Int. *146*, 106205. https://doi.org/10.1016/j.envint.2020.106205.
10. Pega, F., Náfrádi, B., Momen, N.C., Ujita, Y., Streicher, K.N., Prüss-Üstün, A.M., Descatha, A., Driscoll, T., Fischer, F.M., Godderis, L., et al. (2021). Global, regional, and national burdens of ischemic heart disease and stroke attributable to exposure to long working hours for 194 countries, 2000-2016: A systematic analysis from the WHO/ILO Joint Estimates of the Work-related Burden of Disease and Injury. Environ. Int. *154*, 106595. https://doi.org/10.1016/j.envint.2021.106595.
11. Hiyama, T., and Yoshihara, M. (2008). New occupational threats to Japanese physicians: karoshi (death due to overwork) and karojisatsu (suicide due to overwork). Occup. Environ. Med. *65*, 428.3–429. https://doi.org/10.1136/oem.2007.037473.
12. Kondo, N., and Oh, J. (2010). Suicide and karoshi (death from overwork) during the recent economic crises in Japan: the impacts, mechanisms and political responses. J. Epidemiol. Community Health *64*, 649–650. https://doi.org/10.1136/jech.2009.090787.
13. Yamauchi, T., Yoshikawa, T., Takamoto, M., Sasaki, T., Matsumoto, S., Kayashima, K., Takeshima, T., and Takahashi, M. (2017). Overwork-related disorders in Japan: recent trends and development of a national policy to promote preventive measures. Ind. Health *55*, 293–302. https://doi.org/10.2486/indhealth.2016-0198.
14. Takahashi, M. (2019). Sociomedical problems of overwork-related deaths and disorders in Japan. J. Occup. Health *61*, 269–277. https://doi.org/10.1002/1348-9585.12016.
15. Amagasa, T., Nakayama, T., and Takahashi, Y. (2005). Karojisatsu in Japan: characteristics of 22 cases of work-related suicide. J. Occup. Health *47*, 157–164. https://doi.org/10.1539/joh.47.157.
16. Kivimäki, M., Jokela, M., Nyberg, S.T., Singh-Manoux, A., Fransson, E.I., Alfredsson, L., Bjorner, J.B., Borritz, M., Burr, H., Casini, A., et al. (2015). Long working hours and risk of coronary heart disease and stroke: a systematic review and meta-analysis of published and unpublished data for 603,838 individuals. Lancet *386*, 1739–1746. https://doi.org/10.1016/S0140-6736(15)60295-1.
17. Trudel, X., Brisson, C., Talbot, D., Gilbert-Ouimet, M., and Milot, A. (2021). Long Working Hours and Risk of Recurrent Coronary Events. J. Am. Coll. Cardiol. *77*, 1616–1625. https://doi.org/10.1016/j.jacc.2021.02.012.
18. Fadel, M., Sembajwe, G., Li, J., Leclerc, A., Pico, F., Schnitzler, A., Roquelaure, Y., and Descatha, A. (2023). Association between prolonged exposure to long working hours and stroke subtypes in the CONSTANCES cohort. Occup. Environ. Med. *80*, 196–201. https://doi.org/10.1136/oemed-2022-108656.
19. Fadel, M., Sembajwe, G., Gagliardi, D., Pico, F., Li, J., Ozguler, A., Siegrist, J., Evanoff, B.A., Baer, M., Tsutsumi, A., et al. (2019). Association Between Reported Long Working Hours and History of Stroke in the CONSTANCES Cohort. Stroke *50*, 1879–1882. https://doi.org/10.1161/STROKEAHA.119.025454.
20. Virtanen, M., Jokela, M., Madsen, I.E., Magnusson Hanson, L.L., Lallukka, T., Nyberg, S.T., Alfredsson, L., Batty, G.D., Bjorner, J.B., Borritz, M., et al. (2018). Long working hours and depressive symptoms: systematic review and meta-analysis of published studies and unpublished individual participant data. Scand. J. Work. Environ. Health *44*, 239–250. https://doi.org/10.5271/sjweh.3712.
21. Virtanen, M., Ferrie, J.E., Singh-Manoux, A., Shipley, M.J., Stansfeld, S.A., Marmot, M.G., Ahola, K., Vahtera, J., and Kivimäki, M. (2011). Long working hours and symptoms of anxiety and depression: a 5-year follow-up of the Whitehall II study. Psychol. Med. *41*, 2485–2494. https://doi.org/10.1017/S0033291711000171.
22. Virtanen, M., Ferrie, J.E., Gimeno, D., Vahtera, J., Elovainio, M., Singh-Manoux, A., Marmot, M.G., and Kivimäki, M. (2009). Long working hours and sleep disturbances: the Whitehall II prospective cohort study. Sleep *32*, 737–745. https://doi.org/10.1093/sleep/32.6.737.
23. Allison, P., Tiesman, H.M., Wong, I.S., Bernzweig, D., James, L., James, S.M., Navarro, K.M., and Patterson, P.D. (2022). Working hours, sleep, and fatigue in the public safety sector: A scoping review of the research. Am. J. Ind. Med. *65*, 878–897. https://doi.org/10.1002/ajim.23407.
24. Virtanen, M., and Kivimäki, M. (2018). Long Working Hours and Risk of Cardiovascular Disease. Curr. Cardiol. Rep. *20*, 123. https://doi.org/10.1007/s11886-018-1049-9.
25. Ervasti, J., Pentti, J., Nyberg, S.T., Shipley, M.J., Leineweber, C., Sørensen, J.K., Alfredsson, L., Bjorner, J.B., Borritz, M., Burr, H., et al. (2021). Long working hours and risk of 50 health conditions and mortality outcomes: a multicohort study in four European countries. The Lancet

Regional Health - Europe *11*, 100212. https://doi.org/10.1016/j.lanepe.2021.100212.

26. Huang, Y., Xiang, Y., Zhou, W., Li, G., Zhao, C., Zhang, D., and Fang, S. (2023). Long working hours and all-cause mortality in China: A 26-year follow-up study. Scand. J. Work. Environ. Health *49*, 539–548. https://doi.org/10.5271/sjweh.4115.
27. Gu, Y., Matthews, T.A., and Li, J. (2025). Long working hours and cardiovascular disease mortality: Prospective evidence from the United States. Prev. Med. *191*, 108225. https://doi.org/10.1016/j.ypmed.2025.108225.
28. Lee, H.-E., Kim, I., Kim, H.-R., and Kawachi, I. (2020). Association of long working hours with accidents and suicide mortality in Korea. Scand. J. Work. Environ. Health *46*, 480–487. https://doi.org/10.5271/sjweh.3890.
29. O'Reilly, D., and Rosato, M. (2013). Worked to death? A census-based longitudinal study of the relationship between the numbers of hours spent working and mortality risk. Int. J. Epidemiol. *42*, 1820–1830. https://doi.org/10.1093/ije/dyt211.
30. Hannerz, H., and Soll-Johanning, H. (2018). Working hours and all-cause mortality in relation to the EU Working Time Directive: a Danish cohort study. Eur. J. Public Health *28*, 810–814. https://doi.org/10.1093/eurpub/cky027.
31. Alicandro, G., Bertuccio, P., Sebastiani, G., La Vecchia, C., and Frova, L. (2020). Long working hours and cardiovascular mortality: a census-based cohort study. Int. J. Public Health *65*, 257–266. https://doi.org/10.1007/s00038-020-01361-y.
32. Varadhan, R., Weiss, C.O., Segal, J.B., Wu, A.W., Scharfstein, D., and Boyd, C. (2010). Evaluating health outcomes in the presence of competing risks: a review of statistical methods and clinical applications. Med. Care *48*, S96–S105. https://doi.org/10.1097/MLR.0b013e3181d99107.
33. Ferreira-Gonzalez, I., Busse, J.W., Heels-Ansdell, D., Montori, V.M., Akl, E.A., Bryant, D.M., Alonso-Coello, P., Alonso, J., Worster, A., Upadhye, S., et al. (2007). Problems with use of composite end points in cardiovascular trials: systematic review of randomised controlled trials. BMJ *334*, 786. https://doi.org/10.1136/bmj.39136.682083.AE.
34. Lee, K., Suh, C., Kim, J.E., and Park, J.O. (2017). The impact of long working hours on psychosocial stress response among white-collar workers. Ind. Health *55*, 46–53. https://doi.org/10.2486/indhealth.2015-0173.
35. Baek, S.U., and Yoon, J.H. (2024). Effect of long working hours on psychological distress among young workers in different types of occupation. Prev. Med. *179*, 107829. https://doi.org/10.1016/j.ypmed.2023.107829.
36. van Amelsvoort, L.G.P.M., Kant, I.J., Bültmann, U., and Swaen, G.M.H. (2003). Need for recovery after work and the subsequent risk of cardiovascular disease in a working population. Occup. Environ. Med. *60 Suppl 1*, i83–i87. https://doi.org/10.1136/oem.60.suppl_1.i83.
37. Qiu, D., Li, Y., Li, R., He, J., Ouyang, F., Luo, D., and Xiao, S. (2022). Long working hours, work-related stressors and sleep disturbances among Chinese government employees: A large population-based follow-up study. Sleep Med. *96*, 79–86. https://doi.org/10.1016/j.sleep.2022.05.005.
38. Killick, R., Stranks, L., and Hoyos, C.M. (2022). Sleep Deficiency and Cardiometabolic Disease. Clin. Chest Med. *43*, 319–336. https://doi.org/10.1016/j.ccm.2022.02.011.
39. Trudel, X., Brisson, C., Gilbert-Ouimet, M., Vézina, M., Talbot, D., and Milot, A. (2020). Long Working Hours and the Prevalence of Masked and Sustained Hypertension. Hypertension *75*, 532–538. https://doi.org/10.1161/HYPERTENSIONAHA.119.12926.
40. Li, X., Li, J., Ren, X., Xia, T., Arah, O.A., and Chen, L. (2025). The associations of long working hours and unhealthy diet with cardiometabolic outcomes and mortality in US workers. Prev. Med. *195*, 108275. https://doi.org/10.1016/j.ypmed.2025.108275.
41. Baek, S.U., Won, J.U., Lee, Y.M., and Yoon, J.H. (2024). Association between long working hours and metabolic dysfunction-associated steatotic liver disease: a nationwide population-based study in Korea. Public Health *232*, 188–194. https://doi.org/10.1016/j.puhe.2024.04.034.
42. Kivimäki, M., and Kawachi, I. (2015). Work Stress as a Risk Factor for Cardiovascular Disease. Curr. Cardiol. Rep. *17*, 74. https://doi.org/10.1007/s11886-015-0630-8.
43. Vaccarino, V., and Bremner, J.D. (2024). Stress and cardiovascular disease: an update. Nat. Rev. Cardiol. *21*, 603–616. https://doi.org/10.1038/s41569-024-01024-y.
44. Descatha, A., Landsbergis, P., Li, J., Sembajwe, G., and Fadel, M. (2024). Long working hours and cardiovascular diseases, time for preventive action. Occup. Med. (Lond.) *74*, 567–568. https://doi.org/10.1093/occmed/kqae078.
45. Cordoba, G., Schwartz, L., Woloshin, S., Bae, H., and Gotzsche, P.C. (2010). Definition, reporting, and interpretation of composite outcomes in clinical trials: systematic review. BMJ *341*, c3920. https://doi.org/10.1136/bmj.c3920.
46. Higgins, J.P.T., Thompson, S.G., Deeks, J.J., and Altman, D.G. (2003). Measuring inconsistency in meta-analyses. BMJ *327*, 557–560. https://doi.org/10.1136/bmj.327.7414.557.
47. Cumpston, M., Li, T., Page, M.J., Chandler, J., Welch, V.A., Higgins, J.P., and Thomas, J. (2019). Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst. Rev. *10*, ED000142. https://doi.org/10.1002/14651858.ED000142.
48. Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E., et al. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ *372*, n71. https://doi.org/10.1136/bmj.n71.
49. Morgan, R.L., Whaley, P., Thayer, K.A., and Schünemann, H.J. (2018). Identifying the PECO: A framework for formulating good questions to explore the association of environmental and other exposures with health outcomes. Environ. Int. *121*, 1027–1031. https://doi.org/10.1016/j.envint.2018.07.015.
50. Farrah, K., Young, K., Tunis, M.C., and Zhao, L. (2019). Risk of bias tools in systematic reviews of health interventions: an analysis of PROSPERO-registered protocols. Syst. Rev. *8*, 280. https://doi.org/10.1186/s13643-019-1172-8.
51. Stang, A. (2010). Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur. J. Epidemiol. *25*, 603–605. https://doi.org/10.1007/s10654-010-9491-z.
52. Brockwell, S.E., and Gordon, I.R. (2001). A comparison of statistical methods for meta-analysis. Stat. Med. *20*, 825–840. https://doi.org/10.1002/sim.650.
53. Higgins, J.P.T., Thompson, S.G., and Spiegelhalter, D.J. (2009). A re-evaluation of random-effects meta-analysis. J R Stat Soc Ser A Stat Soc *172*, 137–159. https://doi.org/10.1111/j.1467-985X.2008.00552.x.

STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Deposited data		
Published studies included in this systematic review and meta-analysis	This paper and cited original studies	See Tables 1 and 3, Supplementary Tables, and References
PROSPERO protocol registration	University of York, PROSPERO	PROSPERO: CRD42024622703
PRISMA 2020 statement	Page et al., 2021	https://doi.org/10.1136/bmj.n71[48]
Newcastle–Ottawa Scale (NOS)	Wells et al.	https://ohri.ca/en/who-we-are/core-facilities-and-platforms/ottawa-methods-centre/newcastle-ottawa-scale
PubMed	National Library of Medicine	https://pubmed.ncbi.nlm.nih.gov/
Embase	Elsevier	https://www.elsevier.com/products/embase
Web of Science Core Collection	Clarivate	https://clarivate.com/
Scopus	Elsevier	https://www.elsevier.com/products/scopus
Cochrane Library	Cochrane/Wiley	https://www.cochranelibrary.com/
APA PsycInfo	American Psychological Association	https://www.apa.org/pubs/databases/psycinfo
Software and algorithms		
R version 4.2.2	R Foundation for Statistical Computing	https://www.r-project.org
meta package	CRAN	version 8.2.1
EndNote X9.1	Clarivate Analytics	https://endnote.com/

EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

Not applicable. This study is a systematic review and meta-analysis and does not involve human participants, animals, or *in vitro* experimental models.

METHOD DETAILS

Study design and reporting standard

This study was a systematic review and outcome-specific evidence synthesis of observational longitudinal studies examining the association between long working hours and mortality outcomes. Quantitative meta-analysis was performed only when at least two eligible studies reported sufficiently comparable time-to-event effect estimates for the same outcome. The review was designed, conducted, and reported in accordance with the PRISMA 2020 statement.[48]

PECO framework

The review question was defined according to the PECO framework for exposure-outcome questions[49]: Population (P): employed or economically active adults of working age from community-based, occupational, census-linked, or register-based cohorts. Exposure (E): long working hours assessed at the individual level, expressed primarily in hours per week; a threshold of $\geq$55 h/week was commonly used. Comparator (C): standard or reference working hours as defined by the original study, most commonly 35–40 or 35–44 h/week. Outcome (O): mortality outcomes, including all-cause mortality, cardiovascular mortality, suicide mortality, and accident mortality.

Target population represented by eligible studies

Because this study synthesized published evidence rather than recruiting participants directly, participant characteristics were defined according to each original study. In general, eligible cohorts included employed or economically active adults of working age, typically aged 18–65 years, or the country-specific working-age range used in the source study.

Literature search

A systematic literature search was conducted in PubMed, Embase, Web of Science Core Collection, Scopus, the Cochrane Library, and APA PsycInfo from database inception to January 31, 2026. The search strategy combined controlled vocabulary and free-text terms for two core concepts: long working hours and mortality outcomes. Outcome-related terms were expanded to capture all-cause mortality as well as prespecified cause-specific mortality outcomes, including cardiovascular, suicide, and accident-related mortality. The full electronic search strategies for all databases are provided in Table S1. The search was designed to capture studies examining long working hours in relation to mortality-related endpoints. In addition to general mortality terms, broader cardiovascular and accident-related terms were initially included during electronic searching to maximize sensitivity. However, only studies reporting prespecified mortality outcomes were eligible for the final review. To identify additional studies, we also manually screened the reference lists of relevant reviews and eligible original articles and conducted citation tracking through Web of Science.

Eligibility criteria

Studies were eligible if they met all of the following criteria: (1) Original longitudinal observational design, including prospective cohort studies, retrospective cohort studies, census-linked cohort studies, or register-based cohort studies; (2) Inclusion of working-age employed or economically active adults; (3) Assessment of individual-level working hours; (4) Reporting of at least one eligible fatal outcome; (5) Provision of an effect estimate with a 95% confidence interval, including hazard ratio (HR), risk ratio (RR), odds ratio (OR), cause-specific hazard ratio, or sufficient information to derive the estimate.

Studies were excluded if they were: (1) reviews, systematic reviews, or meta-analyses; (2) editorials, commentaries, letters without original data, conference abstracts, case reports, or case series; (3) cross-sectional studies without longitudinal mortality follow-up; (4) studies reporting only non-fatal outcomes; (5) studies without extractable or interpretable effect estimates for the eligible fatal outcomes. Because formal full-text screening and data extraction were conducted in English, eligibility was restricted to peer-reviewed articles published in English.[47]

Exposure and outcome definitions

The primary exposure was long working hours, measured in hours per week. Because exposure operationalization varied across studies, we accepted the original study definitions and extracted the exposure contrast most relevant to long working hours versus standard working hours. Particular attention was given to contrasts using the WHO/ILO-relevant threshold of $\geq$55 h/week,[9,10,25] although lower or alternative cut-points, such as 45–52 or >52 h/week, were also retained when they represented the prespecified long-hours category in the original cohort. Long working hours were treated as a categorical exposure, not as a continuous exposure, because the included studies predominantly reported grouped weekly working hours rather than per-unit exposure-response estimates.

Eligible outcomes were restricted to mortality outcomes, including all-cause mortality,[25,26,29,30] cardiovascular mortality,[25,27,29,31] suicide mortality,[28] and accident mortality.[28] Outcome ascertainment was accepted when based on linkage to death registries, national mortality databases, census-linked records, or other official mortality sources used in the original studies. For accident mortality, we extracted the most specific available definition from each source study and recorded whether the endpoint referred to workplace accidents, transport accidents, commuting accidents, or broader accidental external-cause deaths.

Study selection

After removal of duplicates, two reviewers (Y.X. and J.H.) independently screened titles and abstracts, followed by full-text assessment of potentially eligible reports. Disagreements were resolved by discussion. When consensus could not be reached, a third senior reviewer (R.W.) adjudicated the final decision. The study selection process is summarized in the PRISMA flow diagram (Figure 1).

Assessment of potentially overlapping cohorts

To avoid duplicate inclusion of the same underlying population, we assessed potential overlap across studies by comparing the country, cohort or database name, recruitment years, follow-up period, sample size, exposure definition, and outcome definition. When multiple reports appeared to arise from the same or overlapping cohort, we retained the report with the most relevant outcome definition, the most complete adjustment set, and/or the longest follow-up for a given outcome-specific synthesis. Each cohort contributed only one estimate per outcome-specific quantitative analysis. No overlapping cohorts were identified among the studies included in the final outcome-specific syntheses.

Data extraction

Two reviewers (Y.X. and J.H.) independently extracted data using a standardized extraction form. The following information was collected from each eligible study: first author, publication year, country or region, cohort or data source, study design, participant characteristics, sample size, follow-up duration, working-hour categories, outcome definition and ascertainment method, covariates included in the fully adjusted model, and the most fully adjusted effect estimate with its 95% CI.

Risk of bias assessment

Because all studies included in the final synthesis were observational longitudinal studies, methodological quality was assessed using the Newcastle–Ottawa Scale (NOS) for cohort studies[50,51] developed by Wells and colleagues. Two reviewers (Y.X. and J.H.) independently evaluated each study across the domains of selection, comparability, and outcome assessment. Disagreements were resolved by discussion and, where necessary, consultation with a third reviewer (R.W.). For the purpose of this review, NOS scores were categorized *a priori* as high quality (8–9 points), moderate quality (6–7 points), and low quality ($\leq$5 points). Risk-of-bias assessment was used to support interpretation of the evidence and descriptive comparison across studies.

Ethical considerations

No primary ethical review was required as analyses utilized deidentified, publicly available data from studies with original participant consent. Public stakeholders were not involved in study design or dissemination.

QUANTIFICATION AND STATISTICAL ANALYSIS

We synthesized the evidence separately for the prespecified outcomes of all-cause mortality, cardiovascular mortality, suicide mortality, and accident mortality. We did not generate an overall pooled effect across all-cause mortality and cause-specific mortality outcomes because these endpoints are conceptually overlapping and clinically heterogeneous. Quantitative synthesis was undertaken only when studies were considered sufficiently comparable in terms of outcome definition, exposure contrast, and effect measure.[47]

For each eligible study, we extracted the most fully adjusted effect estimate reported by the authors. Because HR, RR, and OR are not directly equivalent, these measures were not treated as interchangeable without justification. Quantitative meta-analysis was restricted to studies reporting comparable effect measures for the same outcome, with priority given to HR for mortality endpoints. OR and RR that could not be validly combined with HR-based estimates were retained in the qualitative synthesis. Ratio effect measures were analyzed on the log scale.

Random-effects meta-analysis was performed only when at least two studies reported sufficiently comparable estimates for the same outcome and comparable exposure contrasts. In practice, all-cause mortality and cardiovascular mortality were eligible for quantitative synthesis using HR. HR were log-transformed before pooling, and their standard errors were derived from the reported 95% CI. Pooled estimates were calculated using a random-effects model with the restricted maximum likelihood (REML) estimator.[52,53]

Suicide mortality and accident mortality were synthesized narratively because only one eligible prospective cohort study was identified for each outcome. Studies reporting subgroup-specific estimates only, or effect measures not comparable with those used in the outcome-specific meta-analysis, were also retained in the qualitative synthesis rather than pooled quantitatively.

Between-study heterogeneity was assessed using Cochran's Q test, the I^2 statistic, and the between-study variance (τ^2).[46] Given the expected clinical and methodological diversity across studies, including differences in country, occupational setting, exposure thresholds, and outcome ascertainment, a random-effects framework was chosen *a priori*. Potential sources of heterogeneity, including geographic region, definition of long working hours, occupational type, and study quality, were explored descriptively rather than through formal meta-regression because the number of studies available for each pooled outcome was limited.

Formal assessment of publication bias using funnel plots or Egger's regression test was not performed for the outcome-specific meta-analyses because each quantitative synthesis included fewer than 10 studies, making such tests unstable and difficult to interpret.[47]

All statistical analyses were performed using R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria) with the meta package (version 8.2.1). All tests were two-sided.