STRESSJEM

Shift and Night Work and All-Cause and Cause-Specific Mortality: Prospective Results From the STRESSJEM Study

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CONFIRMATORY moderate confidence

BOTTOM LINE

- Shift and/or night work is significantly associated with all-cause, cardiovascular, cancer, preventable mortality, and suicide among men — a 12% to 47% increase in hazard depending on outcome and exposure type
- Among women, shift work (especially without night work) is associated with all-cause, cancer, and preventable mortality, though many associations did not reach significance due to lower statistical power
- The associations were consistent across current, cumulative, and recency-weighted exposure metrics, strengthening confidence in the findings
- These results come from the largest study to date on this topic (1.5 million employees, 17-year mean follow-up)

1,511,456	884	1.39
PATIENTS	WEEKS	HR

Clinical Question

- Among French employees followed over 26 years, is occupational exposure to shift work and/or night work associated with increased all-cause and cause-specific mortality (cardiovascular, cancer, preventable, and suicide)?
- Does the association vary by gender, type of exposure (shift alone, night alone, combined), and temporal exposure measure (current, cumulative, recency-weighted)?

Major Points

- Shift without night work showed the strongest and most consistent associations with mortality among men: HR 1.39 (95% CI 1.32–1.46) for all-cause, HR 1.42 (1.26–1.61) for cardiovascular, HR 1.47 (1.35–1.61) for cancer, HR 1.39 (1.19–1.63) for suicide — all significant with $p < 0.001$
- Night without shift work was independently associated with all-cause mortality among men (HR 1.12, 95% CI 1.06–1.18, $p < 0.001$) and cardiovascular mortality (HR 1.17, 1.02–1.34, $p < 0.05$)
- Combined night and shift work was associated with all mortality outcomes among men, but contrary to expectations, was not more harmful than either exposure alone
- Among women, shift without night work increased all-cause mortality (HR 1.13, 1.03–1.25, $p < 0.01$), cancer mortality (HR 1.21, 1.05–1.41, $p < 0.05$), and breast cancer mortality (HR 1.48, 1.12–1.94, $p < 0.01$)
- Cerebrovascular disease mortality was elevated for both genders: HR 1.47 (1.11–1.94) for men with shift work and HR 2.37 (1.03–5.46) for women with night work
- When follow-up was extended beyond the last job, associations generally attenuated, suggesting some reversibility of exposure effects, though among women new associations emerged for night work and all-cause and preventable mortality, suggesting delayed effects

Study Design & Population

- Prospective cohort study using the STRESSJEM (STRESs au travail et pathologies cardiovasculaires: le projet JEM) project
- Three linked data sources: (1) DADS-INSEE panel — a 1/24th random sample of the French national working population with complete job histories 1976–2002; (2) SUMER survey — occupational exposure data used to construct the job-exposure matrix; (3) INSERM-CépiDc national mortality registry via the COSMOP linkage program

- Exposure assessed through a validated JEM constructed using CART segmentation on SUMER survey data (49,984 employees), assigning probability of shift and night work based on occupation, economic activity, and company size
- Three time-varying exposure measures: current (probability at any given day), cumulative (mean daily probability over entire follow-up), and recency-weighted cumulative (5-year weighted window favoring recent exposure)
- Binary exposure classification: dichotomized at JEM probability thresholds of 0.42 for shift work and 0.255 for night work
- Cox proportional hazards models with age as the time scale, adjusted for calendar time and biomechanical, physical, chemical, and biological occupational exposures
- Gender-stratified analyses throughout
- Sensitivity analyses: continuous JEM exposure, lowest exposure imputation for multiple jobholders, adjustment for occupation

- Initial cohort: 1,511,456 employees from the DADS-INSEE panel
- Analyzed: 1,496,332 (806,317 men, 704,789 women) after excluding 15,214 with completely missing job histories
- Mean age at cohort entry: 28 years (men), 27 years (women)
- Mean follow-up duration: 17 years
- 22,105 deaths during follow-up until end of last job (17,826 men, 4,279 women for all-cause mortality)
- 118,748 deaths when follow-up extended to end of study period (89,554 men, 29,194 women)
- Men were more likely than women to be exposed to shift and night work

Baseline Characteristics

Characteristic	Value
Enrolled	1,511,456
Analyzed	1,496,332
Female	47.1%
Men N	806317.0
Women N	704789.0
Mean Age Men At Entry	28
Mean Age Women At Entry	27
Mean Followup Years	17
Total Deaths End Last Job	22105.0
Total Deaths End Followup	118748.0

Relevant Guidelines

IARC (International Agency for Research on Cancer) (2020)

GROUP 2A — PROBABLY CARCINOGENIC

Night shift work classified as probably carcinogenic to humans (Group 2A), based on limited evidence for cancer in humans combined with sufficient evidence for cancer in experimental animals and strong mechanistic evidence

ILO / EU Directive 2003/88/EC (2003)

REGULATORY DIRECTIVE

Night workers should not work more than an average of 8 hours per 24-hour period; member states shall ensure that night workers are entitled to free health assessments before assignment and at regular intervals thereafter

GUIDELINE CONTEXT

- IARC (2020) classifies night shift work as Group 2A — probably carcinogenic to humans, based on limited evidence for cancer in humans, sufficient evidence in animals, and strong mechanistic evidence from circadian disruption
- EU Working Time Directive (2003/88/EC) limits night worker hours to an average of 8 per 24-hour period and mandates regular health assessments
- No specific guideline addresses shift work and all-cause or cardiovascular mortality prevention — this study adds to the evidence base that may inform future occupational health recommendations

Interventions

- **Exposed group:** Employees classified as exposed to shift work (probability ≥ 0.42) and/or night work (probability ≥ 0.255) by the JEM
- Shift work: defined as any shift system; night work: any working period between midnight and 5:00 AM more than 52 nights/year (ILO definition)
- Three exposure combinations studied: shift without night, night without shift, and combined night and shift
- **Reference group:** Employees with JEM probability below both thresholds — neither shift nor night work exposure
- Exposure was time-varying across the follow-up period, allowing for job changes

SHIFT AND/OR NIGHT WORK EXPOSURE

JEM-assessed probability of exposure dichotomized at 0.42 (shift) and 0.255 (night)

NEITHER SHIFT NOR NIGHT WORK

Reference group: below JEM exposure threshold

Outcomes

- **All-cause mortality** (primary): 22,105 deaths until end of last job; 118,748 deaths until end of follow-up
- **Cardiovascular mortality** (ICD-10 I00–I99): 3,092 deaths (men) and 486 deaths (women) — ischemic heart disease and cerebrovascular disease analyzed separately
- **Cancer mortality** (ICD-10 C00–C99): 5,733 deaths (men) and 1,907 deaths (women) — respiratory/intrathoracic malignancies and breast cancer analyzed separately
- **Suicide**: 1,638 deaths (men) and 366 deaths (women)
- **Preventable mortality** (OECD/Eurostat definition): 11,924 deaths (men) and 1,974 deaths (women) — includes smoking-related, alcohol-related, and external causes of death
- Key findings among men (current exposure, shift without night work): all-cause HR 1.39 (1.32–1.46), cardiovascular HR 1.42 (1.26–1.61), cancer HR 1.47 (1.35–1.61), suicide HR 1.39 (1.19–1.63), preventable HR 1.39 (1.31–1.48) — all $p < 0.001$, meaning 39–47% increased hazard of death across all studied outcomes
- Among women, notable findings include breast cancer mortality HR 1.48 (1.12–1.94, $p < 0.01$) and cerebrovascular mortality HR 2.37 (1.03–5.46, $p < 0.05$) with night work

PRIMARY ENDPOINT

All-cause mortality (men, shift without night work, current exposure)

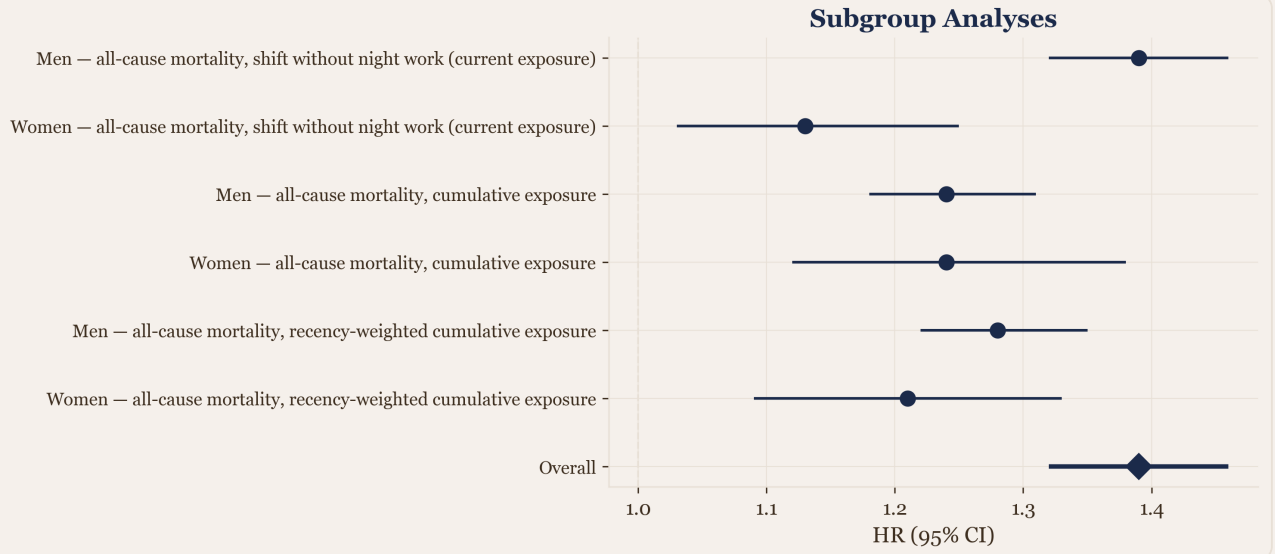
Metric	Value
Outcome type	time-to-event
HR	**1.39** (95% CI 1.32–1.46)
P-value	**<0.001**

Secondary Outcomes

Outcome	Shift and/or night work exposure	Neither shift nor night work	Effect	95% CI	P-value
All-cause mortality — men, night without shift work (current)	NR%	NR%	HR 1.12	1.06–1.18	<0.001
All-cause mortality — men, night and shift work (current)	NR%	NR%	HR 1.24	1.18–1.30	<0.001
All-cause mortality — women, shift without night work (current)	NR%	NR%	HR 1.13	1.03–1.25	<0.01
Cardiovascular mortality — men, shift without night work (current)	NR%	NR%	HR 1.42	1.26–1.61	<0.001
Cardiovascular mortality — men, night and shift work (current)	NR%	NR%	HR 1.29	1.14–1.46	<0.001
Cancer mortality — men, shift without night work (current)	NR%	NR%	HR 1.47	1.35–1.61	<0.001
Cancer mortality — women, shift without night work (current)	NR%	NR%	HR 1.21	1.05–1.41	<0.05
Suicide — men, shift without night work (current)	NR%	NR%	HR 1.39	1.19–1.63	<0.001
Preventable mortality — men, shift without night work (current)	NR%	NR%	HR 1.39	1.31–1.48	<0.001
Breast cancer mortality — women, shift without night work (current)	NR%	NR%	HR 1.48	1.12–1.94	<0.01
Cerebrovascular disease mortality — women, night without shift work (current)	NR%	NR%	HR 2.37	1.03–5.46	<0.05

Visualizations

Subgroup Analysis



Critical Appraisal

LIMITATIONS & CRITICISMS

- **Exposure misclassification:** The JEM assigns group-level exposure probabilities, not individual exposure. This introduces non-differential misclassification and imprecision, known to bias effect estimates toward the null. The JEM for night work had lower validity among women specifically
- **Residual confounding:** Models adjusted for other occupational exposures but not for individual lifestyle factors (smoking, alcohol, BMI, diet, physical activity) or direct socioeconomic status. Shift workers tend to have lower SES and higher smoking prevalence, and the strong association with smoking-related mortality (HR 1.52 in men) raises concern about uncontrolled behavioral confounding
- **Healthy worker effect:** Selection effects to enter and remain in shift/night work (self-selection of healthier workers with greater tolerance) likely underestimate the true association. This is partially mitigated by the cumulative exposure analyses
- **Exposure definition limitations:** No data on permanent vs. rotating shifts, direction of rotation, number of consecutive nights, or start/end times of shifts. Night work was defined broadly (≥52 nights/year) without dose gradation
- **Limited observation window:** Job history data covered only 1976–2002, preventing assessment of lifetime exposure. Mid-censoring was used for rare periods of missing data rather than imputation
- **Underpowered for women:** Many exposure-outcome associations among women had wide confidence intervals crossing the null, particularly for night work and combined exposure categories with small numbers of deaths
- **No causal inference:** As an observational cohort, causal conclusions cannot be drawn despite the large sample size and long follow-up. The time-varying Cox models address temporality but cannot establish causation
- **Historical cohort:** Data are from 1976–2002; working conditions, shift patterns, and occupational health protections have evolved since then, potentially limiting applicability to current workforces

FUNDING & CONFLICTS

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Discussion Questions

METHODOLOGY

1. How does the use of a job-exposure matrix (JEM) to assess shift and night work exposure affect the validity of the findings compared to individual-level exposure assessment?

JEM assigns group-level probabilities of exposure based on job title, introducing non-differential misclassification that typically biases results toward the null. This is a fundamental methodological trade-off in large cohort studies.

Suggested Answer

JEMs assess exposure at the group level (job title), not the individual level, leading to within-group misclassification and reduced exposure variance. This non-differential misclassification is well-documented to bias effect estimates toward the null, meaning the true associations may be stronger than reported. However, JEMs eliminate recall bias and self-report bias, and are the only feasible method for cohorts of this size without prospective individual exposure measurement.

STATISTICS

2. The three exposure metrics (current, cumulative, recency-weighted cumulative) produced similar AIC values and effect estimates. What are the implications for understanding dose-response and latency?

Different temporal exposure metrics should theoretically capture different aspects of the exposure-disease pathway (acute vs. cumulative effects), and their convergence is notable.

Suggested Answer

The similar AIC values suggest that none of the three temporal models fits the data substantially better than the others, which may reflect limited contrast between metrics when exposure is relatively stable over time in occupational cohorts. The convergence of results across metrics provides robustness but limits our ability to distinguish acute from cumulative dose-response relationships. The finding that mortality associations weakened when follow-up extended beyond the last job suggests some reversibility, which would favor current over cumulative exposure models.

CLINICAL APPLICABILITY

3. Given the associations between shift work and smoking-related mortality and external causes of death, how should we interpret whether shift work is a direct risk factor or a marker for behavioral mediators?

The strong associations with smoking-related causes and external causes (accidents/injuries) suggest that behavioral pathways (smoking, fatigue-related accidents) may mediate the shift work-mortality association, which has different prevention implications than direct biological mechanisms.

Suggested Answer

The associations with smoking-related mortality (HR 1.52 in men) and external causes (HR 1.15 in men) suggest that behavioral pathways are important mediators. Shift workers have higher smoking prevalence, altered eating patterns, and increased accident risk due to fatigue and circadian disruption. These behavioral mediators are modifiable targets for prevention. However, the concurrent associations with cardiovascular and breast cancer mortality suggest direct biological mechanisms (circadian disruption, hormonal changes) also contribute. Prevention should address both pathways: workplace health programs targeting smoking and lifestyle, plus schedule optimization to minimize circadian disruption.

EXTERNAL VALIDITY

4. The study found substantially weaker associations among women, with many non-significant results. Does this reflect a true gender difference in susceptibility or a methodological limitation?

Women had fewer deaths, lower exposure prevalence, and the JEM for night work had lower validity among women — all of which reduce statistical power and may mask true effects.

Suggested Answer

The weaker findings among women are most likely due to methodological limitations rather than true gender differences in susceptibility. Women had far fewer deaths (4,279 vs. 17,826 for all-cause), lower exposure prevalence (they were less likely to be exposed to shift and night work), and the JEM for night work had lower validity among women specifically. These factors collectively reduce statistical power. The authors note the study was 'underpowered to detect all exposure-outcome associations, especially among women.' Notably, where power was adequate (breast cancer, cerebrovascular disease), significant associations emerged among women, supporting the view that power — not biology — explains the gender discrepancy.

ETHICS OR CONTROVERSY

5. The study adjusted for occupational exposures (biomechanical, physical, chemical, biological) but not for lifestyle factors like smoking, alcohol, diet, or socioeconomic status directly. How does this residual confounding affect interpretation?

Occupational cohort studies using administrative data often lack individual-level lifestyle and socioeconomic confounders, raising questions about the attributability of observed associations to shift/night work versus correlated social determinants.

Suggested Answer

The absence of individual-level adjustment for smoking, alcohol use, BMI, diet, and direct socioeconomic status is a significant limitation. Shift workers tend to have lower socioeconomic status, higher smoking rates, and less healthy dietary patterns. The occupational exposures (physical, chemical, biological) serve as partial proxies for job type and social position, but residual confounding by lifestyle factors likely inflates the effect estimates. The strong associations with smoking-related mortality specifically support this concern. While the authors note that JEM-based assessment tends to underestimate true effects, residual confounding works in the opposite direction, and disentangling these biases is not possible with the available data.

Overall Assessment

CONFIRMATORY moderate confidence

Large prospective cohort (1.5 million) with 17-year follow-up confirms associations between shift/night work and multiple mortality outcomes, strengthening existing evidence from smaller studies and meta-analyses, but the observational design and JEM-based exposure assessment preclude causal conclusions.

Further Reading

Psychosocial Work Factors of the Job Strain Model and All-Cause Mortality: The STRESSJEM Prospective Cohort Study

Companion STRESSJEM paper examining job strain and mortality using the same cohort and methods, providing context for occupational exposure-mortality associations

PMID: 33079757 · DOI: 10.1097/PSY.0000000000000878

Night-shift work, breast cancer incidence, and all-cause mortality: an updated meta-analysis of prospective cohort studies

Contemporary meta-analysis (31 studies, 9.3 million participants) quantifying night-shift work associations with breast cancer and cardiovascular mortality

PMID: 34775538 · DOI: 10.1007/s11325-021-02523-9

Night work and mortality: prospective study among Finnish employees over the time span 1984 to 2008

Key prior prospective study showing 2.25-fold higher mortality risk among female night workers, with individual-level exposure data for comparison

PMID: 22621357 · DOI: 10.3109/07420528.2012.675262

Psychosocial factors at work from the job strain model and preventable mortality in France: The STRESSJEM prospective study

STRESSJEM study of job strain and preventable mortality, sharing identical methodology and cohort definition for cross-reference

PMID: 32603796 · DOI: 10.1016/j.ypmed.2020.106178

- Niedhammer I et al. Psychosocial Work Factors of the Job Strain Model and All-Cause Mortality: The STRESSJEM Prospective Cohort Study. Psychosom Med. 2021;83(1):62-70. PMID: 33079757. Companion STRESSJEM paper using identical methods to examine job strain and mortality
- Wei F et al. Night-shift work, breast cancer incidence, and all-cause mortality: an updated meta-analysis of prospective cohort studies. Sleep Breath. 2022;26(4):1509-1526. PMID: 34775538. Meta-analysis of 31 studies confirming night shift associations with breast cancer and cardiovascular mortality
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