

APPRAISALS IN META-JOURNAL HOUR 10
By: Nurul Iman Hafizah, BH Chew and Aazifah Ilham



The paper:

Rotating Night Shift Work and Healthy Aging After 24 Years of Follow-up in the Nurses' Health Study, doi: [10.1001/jamanetworkopen.2022.10450](https://doi.org/10.1001/jamanetworkopen.2022.10450)

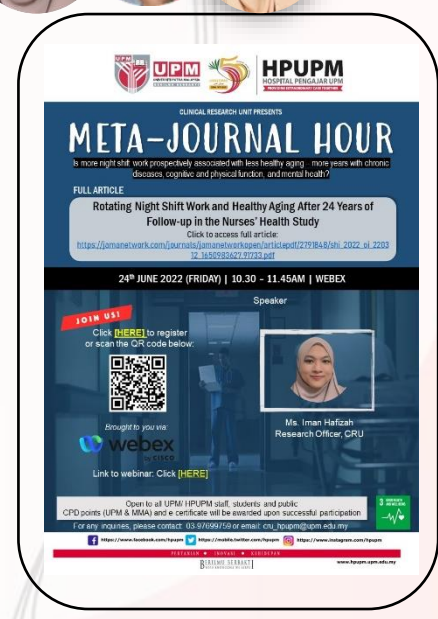
Why was this study conducted?

Health care workers are commonly engaged in night shift work due to the nature of the job. Previous literatures have suggested that working at night may cause disruption of circadian rhythm, sleep disturbances and other behavioural changes that may lead to increased risk of chronic diseases, mental disorders, cognitive impairment and even mortality¹⁻⁷. Existing studies^{4, 7-10} on rotating night shift work have primarily focused on individual health outcomes, but its association with overall health is scarce.

In this prospective study, the longitudinal follow-up data from the [Nurses' Health Study](#) was used to examine the association of duration of rotating night shift work with healthy aging (as measured by a full spectrum of health outcomes) among women nurses.

How was it done?

The Nurses' Health Study is a prospective cohort study of 121 701 US registered nurses aged 30 to 55 years that was started in 1976. Women were asked to report their history of rotating night shift work in 1988 which was the baseline of the present cohort study. In the primary analysis of the study, data on the overall health status including chronic diseases, physical function, mental health and memory function was analysed at the end of follow-up in the year 2012. This involved 46 318 women (age range 46 – 68 years). Those who had any of 11 main chronic diseases at baseline (n=17 872), missing information on rotating night shift work (n=13 552) or missing data on healthy aging phenotype in 2012 (n=12 300) were excluded from analyses. In addition, secondary analyses were conducted among 19 415 women who completed a cognitive function test when they reached 70 years of age in 2000. However, after excluding women with similar exclusion criteria in primary analysis, 14 273 women were included in the secondary analysis.



Watch the video recording on:

Click [\[HERE\]](#) and don't forget to subscribe to our channel!

Assessment of Healthy Aging

Healthy aging was defined as survival to at least 70 years of age and no major chronic diseases and no impairment in cognitive function, physical function, or mental health. Table below outlines detailed description of healthy aging assessments in the study:

Dimensions	Primary analysis: Healthy aging in 2012	Secondary analysis: Healthy aging in 1995 – 2000
Assessment of chronic diseases	Clinical diagnoses of 11 major chronic diseases ^a were queried on biennial questionnaire since 1988 which were then confirmed by professional staff through medical record or pathology report review, telephone interview or supplementary questionnaire.	
Assessment of cognitive function	Assessed through the Structured Telephone Interview for Dementia Assessment using 7 questions. No impairment in memory was defined as at most 1 memory concern.	Telephone Interview of Cognitive Status (TICS) was administered. Score of <31 out of 4 was considered cognitively impaired.
Assessment of physical function	Assessed by 10 questions ^b in the SF-36. Impairment of physical function was defined as any of the following: <ul style="list-style-type: none"> Limited at least a little on moderate activities or, Limited a lot on more difficult physical tasks 	
Assessment of mental health	Assessed using Geriatric Depression Scale-15 (GDS-15). Score range was 0 – 15, with lower scores indicating better mental health.	Evaluated by 5 questions ^c in the SF-36. A score between 1 (worst) and 6 (best) was assigned to each question. Good mental health as defined as a score >84.
Healthy aging	Defined as survival to at least 70 years of age and 4 health domains (no major chronic diseases and no impairment in cognitive function, physical function or mental health). Those who did not meet any of these criteria were defined as usual agers.	

Adapted from Table 1: Definition and dimensions of healthy aging (Shi, 2022)

^aMajor chronic diseases covers most common conditions that would significantly deteriorate human health, including cancer (except for nonmelanoma skin cancers), diabetes, myocardial infarction, coronary artery bypass graft surgery or percutaneous transluminal coronary angioplasty (as a surrogate for coronary artery disease), congestive heart failure, stroke, kidney failure, chronic obstructive pulmonary disease, Parkinson disease, multiple sclerosis, and amyotrophic lateral sclerosis.

^bThe 10 questions inquired about physical limitations in performing the following activities: moderate activities (eg, moving a table, pushing a vacuum cleaner, bowling, or playing golf); bathing and dressing yourself; walking 1 block; walking several blocks; walking more than 1 mile; vigorous activities (eg, running, lifting heavy objects, or strenuous sports); bending, kneeling, or stooping; climbing 1 flight of stairs; climbing several flights of stairs; and lifting or carrying groceries. Each question had 3 response choices: "Yes, limited a lot," "Yes, limited a little," or "No, not limited at all."

^cThe 5 questions were as follows: Have you been a very nervous person? Have you felt so down in the dumps nothing could cheer you up? Have you felt calm and peaceful? Have you felt downhearted and blue? And Have you been a happy person? There were 6 possible responses to each question ranging from none of the time to all of the time.

Assessment of Rotating Night Shift Work

In 1988, women were asked to report their total number of years of rotating night shift work (defined as at least 3 nights per month in addition to day and evening shifts) with 8 prespecified categories: Never, 1 to 2 years, 3 to 5 years, 6 to 9 years, 10 to 14 years, 15 to 19 years, 20 to 29 years and 30 years or more. Then, the duration of rotating night shift work was further categorized into 4 categories: Never, 1 to 5 years, 6 to 9 years and 10 years or more.

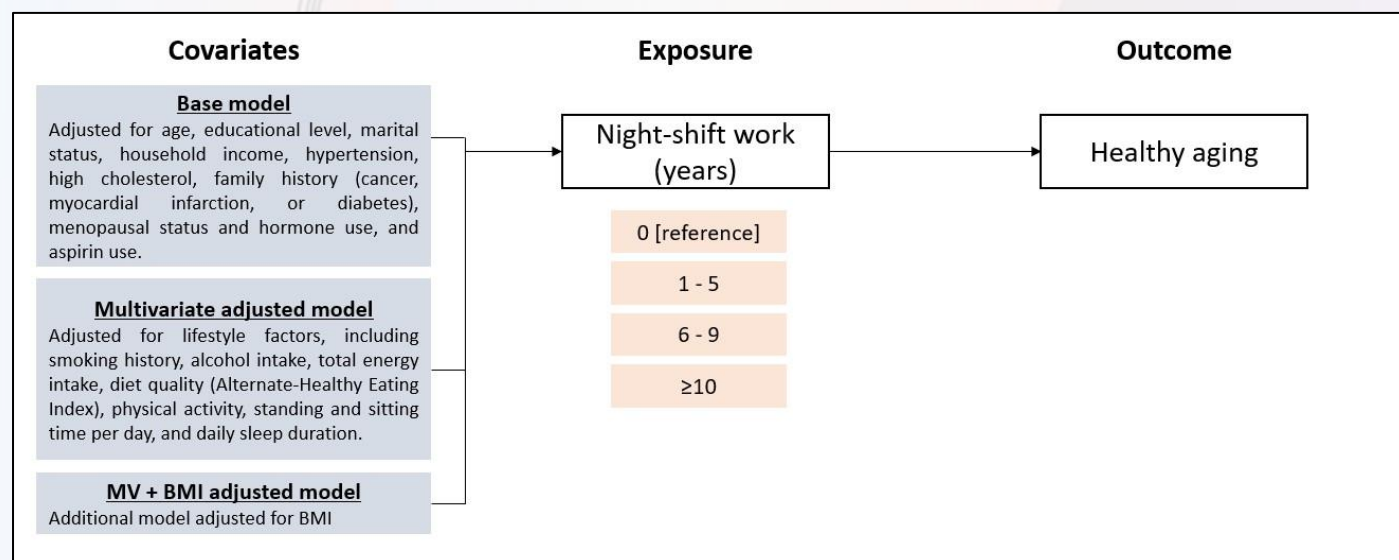
Assessment of Covariates

Information on a broad range of covariates was obtained:

Covariates	
Demographic characteristics	Marital status, race, educational level and household income
Lifestyle factors	Dietary data (total energy intake, alcohol and coffee consumption) Sleep behaviour (total hours of sleep and frequency of snoring) Physical activity (based on weekly Metabolic Equivalent of Task hours)
Family history	Cancer, myocardial infarction and diabetes
Clinical diagnoses	Hypertension and high cholesterol
Use of supplemental vitamins and aspirin	
Menopausal status and postmenopausal hormone use	

Statistical Analysis

Logistic regression models were used to estimate odds ratios (ORs) and 95% CIs for healthy aging across rotating night shift work categories (none, 1 – 5 years, 6 – 9 years and 10 years). An odd ratio smaller than 1 indicates decreased odds of healthy aging.



Data analyses were performed with SAS software, version 9.4 (SAS Institute Inc). A 2-sided $P < 0.05$ was considered statistically significant.

What was the finding?

Baseline characteristics of participants

Out of 46318 women nurses included in the primary analyses, 17786 (38.4%) remained free of the 11 chronic diseases, 7150 (15.4%) had no impairment of physical function, 19654 (42.4%) had good mental health, and 23 169 (50.0%) reported no impairment of memory function. A total of 3695 participants (8.0%) met all criteria of healthy aging; the rest were usual agers. The mean (SD) age of study participants at baseline was 55.4 (6.1) years. A total of 45 300 participants (97.8%) were White, 562 (1.2%) were Black, 98 (0.2%) were American Indian, 347 (0.8%) were Asian, and 11 (0.02%) were Hawaiian. Majority of the participants, $n = 27\ 480$ (59.3%) reported having ever engaged in

rotating night shift work, and 5384 (11.6%) reported at least 10 years of rotating night shift work. Compared with women with no history of rotating night shift work, those with more years of rotating night shifts were slightly older (mean [SD] age, 56.7 [6.0] years vs 55.1 [6.1] years), had less education (master's or doctorate degree, 341 [7.1%] vs 1880 [10.8%]), slept somewhat less (6.8 [1.1] hours per day vs 7.0 [1.0] hours per day), were more likely to be current smokers (1347 [25.0%] vs 3241 [17.2%] for those with no shift work) or regular snorers (538 [11.5%] vs 1451 [8.7%] for those with no shift work), had higher mean (SD) BMIs (26.4 [5.2] vs 25.1 [4.5] kg/m²), had less median (IQR) sitting time (2.2 [1.1 - 4.4] hours per day vs 4.4 [1.1-4.4] hours per day), and were more likely to have hypertension (983 [18.3%] vs 2940 [15.6%]). [Table 2](#) shows full age-adjusted baseline characteristics in 1988.

Primary analysis: Duration of rotating night shift work and healthy aging in 2012

[Table 3](#) summarizes the ORs of healthy aging in 2012 associated with rotating night shift work. Compared with women without rotating night shift work, the adjusted ORs for healthy aging were the lowest among those with 10 years or more of rotating night shift work, 0.79 (95% CI, 0.69-0.91) ($P = 0.001$ for trend). Longer years of rotating night shift work were consistently inversely associated with 4 individual dimensions of healthy aging in the multivariate-adjusted model. The multivariate-adjusted ORs comparing women with 10 years or more of rotating night shift work vs women without rotating night shift work were 0.83 (95% CI, 0.77-0.89) for being free of major chronic diseases ($P < 0.001$ for trend), 0.87 (95% CI, 0.78-0.96) for having good physical function ($P = 0.006$ for trend), 0.87 (95% CI, 0.81-0.93) for having good mental health ($P < 0.001$ for trend), and 0.91 (95% CI, 0.85-0.97) for having good memory function ($P < 0.001$ for trend).

Secondary analysis: Duration of rotating night shift work and healthy aging in 1995 – 2000

Of the 14 273 participants included in the analysis of short-term healthy aging, 8515 women (59.7%) had none of the 11 chronic diseases, 3454 (24.2%) had no impairment of physical function, 5317 (37.3%) had good mental health, and 11 056 (77.5%) reported no impairment of cognitive function. A total of 1386 participants (9.7%) met all criteria of healthy aging in 1995 to 2000; the rest were usual agers.

The associations of rotating night shift work with healthy aging in 1995 to 2000 were consistent with the primary analysis ([Table 4](#)). Compared with women without rotating night shift work, the adjusted ORs for healthy aging were the lowest among those with more than 5 years of rotating night shift work: 0.72 (95% CI, 0.56-0.92) for 6-9 years of shift work, and 0.73 (95% CI, 0.60-0.89) for 10 years or more of shift work ($P < 0.001$ for trend). Rotating night shift work was also inversely associated with 4 dimensions of healthy aging. The adjusted ORs comparing women with 10 years or more of rotating night shift work vs women without rotating night shift work were 0.84 (95% CI, 0.75-0.93) for being free of major chronic diseases ($P < .001$ for trend), 0.81 (95% CI, 0.71-0.92) for having good physical function ($P < 0.001$ for trend), 0.92 (95% CI, 0.82-1.03) for having good mental health ($P = 0.03$ for trend), and 0.89 (95% CI, 0.78-1.00) for having good memory function ($P = 0.02$ for trend). Additional adjustment for BMI did not change these associations.

How much can we take out from this research/paper?

This study is another important report from the Nurses' Health Study. For this study, it is important because it looked into an important research question of the relationship between certain amount of rotating night shift work in nurses and health at 70-year-old. The exposure was clearly defined and the outcomes were also defined and objectively measured. Many potential confounding factors were included in the analysis where the causal effect of the exposure on the outcomes was adjusted for. Additionally, sensitivity analyses were conducted, even with mediation analyses and propensity scoring in reducing differences between the comparing groups showed the results are essentially the same at both the short- and long-term timepoints. The age-adjusted sociodemographic characteristics were also compared to those included in the study and reported to be similar ([eTable 1](#)).

If the self-report of health status was accepted, proportion of those excluded, limitations of possible changes in the exposure over the period of follow-up are inherent to any long cohort study would need to be carefully considered in interpretation and application of the findings. These appear acceptable with supports from scientific plausibility on the relationship of the exposure-outcome, different analytical approaches where potential influences of factors were accounted for as much as possible.

The results were indeed very interesting! They show that the risk of not having healthy ageing was at least 20-60% higher in those on rotating night shift work for more than 10 years in the past prior to retirement. The higher risks were also observed among those at lower duration of 6-9 years but those clocked in ≤ 5 years were generally had the similar risk to those who reported never on rotating night shift duty. One interesting result was the practice of ≥ 7.5 MET-h/wk buffered the added risk of ≥ 10 years of rotating night shift work on unhealthy ageing ([eTable 5](#)).

The statistical analysis is very well done. On top of primary analysis using multivariable logistic regression to control the confounder the researchers did sensitivity analysis using propensity score as covariate and stratified analysis. Sensitivity

analysis determine the robustness and certainty of result on the effect of independent variables on dependent variable under a given set of assumptions with a different mathematical modelling.

For the past 10 years, publications using propensity score in medical research have been increasing dramatically. The robustness of propensity score has been investigated and the comparison between the robustness with logistic regression as adjustment of covariate has been established. The robustness of the finding of logistic regression and propensity score depend on the number of events per independent variable (IV). If the number of events per IV ≥ 8 , logistic regression is more robust and if < 8 , propensity score is better¹⁰.

In this study, the analysis using logistic regression showed consistent result even after adjustment with propensity score as covariates. Interestingly, the ORs were observed to be drastically lower among those who had more than 10 years of night shift work (eTable 3). Propensity scores are a good alternative to control for imbalances when there are seven or fewer events per IV. For example, observational studies with seven or fewer events per IV could benefit from propensity score to optimize the covariate similarity in exposed and unexposed groups.

Lastly, there is the external validity that require both subjective and scientific reconciliation. However, we believe this consideration would not affect the results and more likely change the effect sizes according to the local background risk of healthy aging, gender, intensity of night shift work over the same service duration, and socio-political environment differences. Scientifically, the explanation of the effect of disrupted circadian rhythm on health is the same on human bodies disregard of ethnicity and gender.

References

1. Kervezee L, Kosmadopoulos A, Boivin DB. Metabolic and cardiovascular consequences of shift work: the role of circadian disruption and sleep disturbances. *Eur J Neurosci*. 2020;51(1):396-412. doi:[10.1111/ejn.14216](https://doi.org/10.1111/ejn.14216)
2. Gao Y, Gan T, Jiang L, et al. Association between shift work and risk of type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of observational studies. *Chronobiol Int*. 2020;37(1):29-46. doi:[10.1080/07420528.2019.1683570](https://doi.org/10.1080/07420528.2019.1683570)
3. Rajaratnam SM, Howard ME, Grunstein RR. Sleep loss and circadian disruption in shift work: health burden and management. *Med J Aust*. 2013;199(8):S11-S15. doi:[10.5694/mja13.10561](https://doi.org/10.5694/mja13.10561)
4. Torquati L, Mielke GI, Brown WJ, Burton NW, Kolbe-Alexander TL. Shift work and poor mental health: a meta-analysis of longitudinal studies. *Am J Public Health*. 2019;109(11):e13-e20. doi:[10.2105/AJPH.2019.305278](https://doi.org/10.2105/AJPH.2019.305278)
5. Jørgensen JT, Karlsen S, Stayner L, Hansen J, Andersen ZJ. Shift work and overall and cause-specific mortality in the Danish nurse cohort. *Scand J Work Environ Health*. 2017;43(2):117-126. doi:[10.5271/sjweh.3612](https://doi.org/10.5271/sjweh.3612)
6. Marquié JC, Tucker P, Folkard S, Gentil C, Ansiau D. Chronic effects of shift work on cognition: findings from the VISAT longitudinal study. *Occup Environ Med*. 2015;72(4):258-264. doi:[10.1136/oemed-2013-101993](https://doi.org/10.1136/oemed-2013-101993)
7. Akerstedt T, Kecklund G, Johansson SE. Shift work and mortality. *Chronobiol Int*. 2004;21(6):1055-1061. doi:[10.1081/CBI-200038520](https://doi.org/10.1081/CBI-200038520)
8. Vetter C, Devore EE, Wegrzyn LR, et al. Association between rotating night shift work and risk of coronary heart disease among women. *JAMA*. 2016;315(16):1726-1734. doi:[10.1001/jama.2016.4454](https://doi.org/10.1001/jama.2016.4454)
9. Soledad Cepeda, Ray Boston, John T. Farrar, Brian L. Strom, Comparison of Logistic Regression versus Propensity Score When the Number of Events Is Low and There Are Multiple Confounders, *American Journal of Epidemiology*, Volume 158, Issue 3, 1 August 2003, Pages 280–287, <https://doi.org/10.1093/aje/kwg115>