

## Supplemental Online Content

McKetta S, Hoatson T, Hughes LD, et al. Disparities in mortality by sexual orientation in a large, prospective cohort of female nurses. *JAMA*. Published online April 25, 2024.  
doi:10.1001/jama.2024.4459

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### eReferences

This supplemental material has been provided by the authors to give readers additional information about their work.

## **eAppendix 1.** Recruitment strategy for the Nurses' Health Study 2

To recruit the study sample, investigators contacted state nursing boards in states with large populations and in states whose nursing boards were able to provide information on the nurses' sex as well as date of birth, age, or a surrogate for age (i.e., sequential license number). Investigators applied for and received magnetic listings from 14 states; most charged a fee for this service. NHS2 programmers processed the tapes and made further exclusions based on sex and age. The following states were included in the initial mailing: California, Connecticut, Indiana, Iowa, Kentucky, Massachusetts, Michigan, Missouri, New York, North Carolina, Ohio, Pennsylvania, South Carolina, and Texas; since initial recruitment, all 50 states are now represented. The strategy was to do a single mailing that invited women to enroll and then enroll only participants who would complete a single questionnaire after one request, thus identifying those who would be most likely to continue participation during the follow-up period. Return of the questionnaire was presumed to be informed consent. Participants are surveyed every two years using mailed or online questionnaires. Attrition is low with a >90% follow-up rate over 30+ years. The recruitment process and subsequent surveys received institutional review board (IRB) approval from both the Harvard T.H. Chan School of Public Health and Brigham and Women's Hospital. The investigators continue to work with these IRBs to assure compliance with new Health Insurance Portability and Accountability Act (HIPAA) regulations.

## eAppendix 2. Missingness

In the eligible sample of 116,149 participants, 90,833 (78%) had sexual orientation measures in 1995. Of the 22% missing this information, the modal source of missingness was item non-response (N=14,478), followed by not returning the 1995 questionnaire (N=10,224), followed by endorsing “prefer not to answer” (N=490) or “none of these” (N=124). In Supplemental Table 5, we show models examining all-cause mortality disparities across sexual orientation subgroups and different patterns of missingness.

For those with item non-response or non-informative sexual orientation (i.e., “prefer not to answer” or “none of these”), we used multiple imputation to predict missing values. We show these here in the Supplement, rather than in the main text, as there are no established best practices for predicting sexual orientation and we hesitate, therefore, to infer that results using imputed sexual orientation are more or less robust or accurate than those presented using complete case analysis. Nevertheless, we followed a protocol similar to that suggested by Elliott, et al. (2020) that used sociodemographic variables to predict missing values for sexual orientation among these respondents.

To impute missing sexual orientation data, we used multiple imputation with chained equations using the “Amelia” package in R (2016), which uses expectation maximization with bootstrapping. To predict sexual orientation, we used all study variables previously discussed in the “Methods” section (including race/ethnicity, smoking status, birth cohort), as well as sociodemographic variables (employment status, marital status, and state of residence) and subsequent measures of sexual orientation (assessed in 2009 and 2017) when they were available. We imputed 10 data sets and combined them using Rubin’s Rules. Models using imputed 1995 sexual orientation are shown in eTable 6, below.

**eTable 1.** Unadjusted model-based estimates of acceleration factors (AF), for time to mortality from baseline by reported sexual orientation among participants in the Nurses' Health Study 2

	Heterosexual (89,821, 98.9%)	LGB (1,012, 1.1%)	Lesbian (694, 0.8%)	Bisexual (318, 0.3%)
AF (95% CI), unadjusted	<i>1.00 (Reference)</i>	0.71 (0.62–0.81)	0.77 (0.65–0.92)	0.61 (0.49–0.76)

Abbreviation: LGB, lesbian, gay, and bisexual.

**eTable 2.** Model-based estimates of acceleration factors (AF), for time to mortality from baseline by reported sexual orientation among participants in the Nurses’ Health Study 2, with interaction by race and ethnicity

	Heterosexual (83,689, 98.9%)	LGB (944, 1.1%)	Lesbian (657, 0.8%)	Bisexual (287, 0.3%)
AF (95% CI), adjusted for birth cohort; <u>Non- Hispanic White participants only</u>	<i>1.00 (Reference)</i>	0.77 (0.67–0.89)	0.83 (0.70–0.99)	0.67 (0.53–0.85)
	Heterosexual (5,440, 98.9%)	LGB (62, 1.1%)	Lesbian (28, 0.5%)	Bisexual (34, 0.6%)
AF (95% CI), adjusted for birth cohort; <u>racial and ethnic minority participants only</u>	<i>1.00 (Reference)</i>	0.48 (0.31–0.75)	0.54 (0.28–1.02)	0.43 (0.24–0.78)

Abbreviation: LGB, lesbian, gay, and bisexual.

Table note: birth cohort categorized as 1945–49, 1950–54, 1955–59, 1960–64

Participants with “Other/unknown” or “Missing” race and ethnicity removed

p-value for interaction between LGB identity and minoritized racial or ethnic identity = 0.046

p-value for interaction between lesbian identity and minoritized racial or ethnic identity = 0.21

p-value for interaction between bisexual identity and minoritized racial or ethnic identity = 0.18

Due to small cells, further exploration of variation by specific racial or ethnic strata was not possible

**eTable 3.** Model-based estimates of acceleration factors (AF), for time to mortality from baseline by reported sexual orientation among participants in the Nurses' Health Study 2, modeled using alternative distributions for mortality outcomes

Distribution	Akaike Information Criterion	Statistic	Heterosexual (89,821, 98.9%)	Lesbian (694, 0.8%)	Bisexual (318, 0.3%)
Log-logistic (shown in main text)	60359	AF (95% CI), adjusted for birth cohort	<i>1.00 (Reference)</i>	0.80 (0.68–0.95)	0.63 (0.51–0.78)
Weibull	60360	AF (95% CI), adjusted for birth cohort	<i>1.00 (Reference)</i>	0.81 (0.68–0.95)	0.63 (0.52–0.78)
Generalized gamma	60362	AF (95% CI), adjusted for birth cohort	<i>1.00 (Reference)</i>	0.80 (0.68–0.95)	0.63 (0.51–0.78)
Log-normal	60479	AF (95% CI), adjusted for birth cohort	<i>1.00 (Reference)</i>	0.79 (0.64–0.97)	0.56 (0.43–0.73)
Exponential	61363	Hazard ratio (95% CI), adjusted for birth cohort	<i>1.00 (Reference)</i>	1.44 (1.08–1.90)	2.14 (1.51–3.03)

Table note: birth cohort categorized as 1945–49, 1950–54, 1955–59, 1960–64

**eTable 4.** Model-based risk for survival by reported sexual orientation among participants in the Nurses' Health Study 2, modeled using Cox Proportional Hazards models

	Heterosexual (89,821, 98.9%)	LGB (1012, 1.1%)	Lesbian (694, 0.8%)	Bisexual (318, 0.3%)
Hazard ratio (95% CI), unadjusted	<i>1.00 (Reference)</i>	1.76 (1.41–2.19)	1.54 (1.16–2.04)	2.25 (1.59–3.18)
Hazard ratio (95% CI), adjusted for birth cohort	<i>1.00 (Reference)</i>	1.66 (1.33–2.06)	1.44 (1.09–1.91)	2.16 (1.52–3.05)

Abbreviation: LGB, lesbian, gay, and bisexual.

Table note: birth cohort categorized as 1945–49, 1950–54, 1955–59, 1960–64

**eTable 5.** Model-based estimates of acceleration factors (AF), for time to mortality from baseline by reported sexual orientation among participants in the Nurses' Health Study 2, using only NDI-confirmed deaths with linked data through 2019

	Heterosexual (89,821, 98.9%)	LGB (1012, 1.1%)	Lesbian (694, 0.8%)	Bisexual (318, 0.3%)
Number of deaths	4,014 (4.5%)	73 (7.2%)	42 (6.1%)	31 (9.7%)
AF (95% CI), unadjusted	<i>1.00 (Reference)</i>	0.77 (0.68–0.87)	0.85 (0.72–1.00)	0.65 (0.53–0.79)
AF (95% CI), adjusted for birth cohort	<i>1.00 (Reference)</i>	0.79 (0.70–0.90)	0.87 (0.74–1.03)	0.66 (0.55–0.80)

Abbreviation: LGB, lesbian, gay, and bisexual.

Table note: birth cohort categorized as 1945–49, 1950–54, 1955–59, 1960–64



**eTable 6.** Model-based estimates of acceleration factors (AF), for time to mortality from baseline by reported sexual orientation among participants in the Nurses’ Health Study 2, including those who were missing measures of sexual orientation

	Heterosexual (89,821, 77.3%)	Lesbian (694, 0.6%)	Bisexual (318, 0.3%)	Missing due to item non- response (14,478, 12.5%)	Missing due to missing survey (10,224, 8.8%)	Missing due to endorsing “none of these” (124, 0.1%)	Missing due to endorsing “prefer not to answer” (490, 0.4%)
AF (95% CI), unadjusted	<i>1.00 (Reference)</i>	0.77 (0.64–0.91)	0.60 (0.48–0.75)	0.89 (0.85–0.93)	0.75 (0.72–0.79)	0.79 (0.51–1.22)	0.83 (0.66–1.03)
AF (95% CI), adjusted for birth cohort	<i>1.00 (Reference)</i>	0.80 (0.67–0.95)	0.62 (0.49–0.77)	0.87 (0.83–0.91)	0.72 (0.68–0.76)	0.89 (0.58–1.38)	0.88 (0.70–1.10)

Table notes: birth cohort categorized as 1945–49, 1950–54, 1955–59, 1960–64; there were 800 deaths among missing due to non-response, 732 deaths among those missing due to non-returned survey, 30 deaths among those who endorsed “prefer not to answer” and 8 deaths among missing due to endorsing “none of these”

**eTable 7.** Model-based estimates of acceleration factors (AF), for time to mortality from baseline by reported sexual orientation among participants in the Nurses' Health Study 2 with missing sexual orientation values imputed

	Heterosexual	LGB	Lesbian	Bisexual
AF (95% CI), unadjusted	<i>1.00 (Reference)</i>	0.79 (0.70–0.89)	0.82 (0.70–0.97)	0.74 (0.61–0.91)
AF (95% CI), adjusted for birth cohort	<i>1.00 (Reference)</i>	0.81 (0.72–0.91)	0.85 (0.72–0.99)	0.75 (0.61–0.91)

Abbreviation: LGB, lesbian, gay, and bisexual.

Table note: birth cohort categorized as 1945–49, 1950–54, 1955–59, 1960–64

Stratum values and percentages not shown because they varied by imputed data set

**eTable 8.** Cause-specific mortality among participants in Nurses' Health Study 2, by reported sexual orientation

Cause of death	Heterosexual	LGB
Cancer	1,363 (32.9%)	18 (22.2%)
Respiratory disease	78 (1.9%)	5 (6.2%)
Suicide	90 (2.2%)	4 (4.9%)
Cardiovascular disease	234 (5.6%)	3 (3.7%)
Diabetes	38 (0.9%)	2 (2.5%)
Neurological disease	119 (2.9%)	2 (2.5%)
Injury	19 (0.5%)	0 (0.0%)
All other causes	547 (13.2%)	9 (11.1%)
Missing	1,658 (40.0%)	38 (46.9%)

Abbreviation: LGB, lesbian, gay, and bisexual.

Table note: Cause of death data were coded manually by Nurses' Health Study 2 staff using follow-up information from participants' families (rather than NDI linkages) and therefore a large proportion are missing because they still await confirmation at the time of this publication

## eReferences

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