

Miscarriage Among Flight Attendants

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Background: Cosmic radiation and circadian disruption are potential reproductive hazards for flight attendants.

Methods: Flight attendants from 3 US airlines in 3 cities were interviewed for pregnancy histories and lifestyle, medical, and occupational covariates. We assessed cosmic radiation and circadian disruption from company records of 2 million individual flights. Using Cox regression models, we compared respondents (1) by levels of flight exposures and (2) to teachers from the same cities, to evaluate whether these exposures were associated with miscarriage.

Results: Of 2654 women interviewed (2273 flight attendants and 381 teachers), 958 pregnancies among 764 women met study criteria. A hypothetical pregnant flight attendant with median first-trimester exposures flew 130 hours in 53 flight segments, crossed 34 time zones, and flew 15 hours during her home-base sleep hours (10 pm–8 am), incurring 0.13 mGy absorbed dose (0.36 mSv effective dose) of cosmic radiation. About 2% of flight attendant pregnancies were likely exposed to a solar particle event, but doses varied widely. Analyses suggested that cosmic radiation exposure of 0.1 mGy or more may be associated with increased risk of miscarriage in weeks 9–13 (odds ratio = 1.7 [95% confidence interval = 0.95–3.2]). Risk of a first-trimester miscarriage with 15 hours or more of flying during home-base sleep hours was increased (1.5 [1.1–2.2]), as was risk with high physical job demands (2.5 [1.5–4.2]). Miscarriage risk was not increased among flight attendants compared with teachers.

Conclusions: Miscarriage was associated with flight attendant work during sleep hours and high physical job demands and may be associated with cosmic radiation exposure.

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The commercial aircraft cabin environment is the workplace of approximately 168,000 flight personnel in the United States, including pilots, copilots, and 93,100 flight attendants,¹ of whom 84% are female.² The International Agency for Research on Cancer (IARC) estimates 250,000 aircrew worldwide are monitored for radiation exposure³; US airline crew are not currently monitored. Reproductive problems among female flight attendants have been reported since the 1960s, including adverse pregnancy outcomes^{4–6} and menstrual irregularities.⁷ Workplace exposures of concern include cosmic ionizing radiation⁸ and circadian rhythm disruption.⁹ Galactic cosmic radiation generates secondary and tertiary radiation at aircraft altitudes,¹⁰ including neutrons and energetic photons (IARC-known human [group 1] carcinogens).³ Solar particle events (transient solar surface eruptions) are another source of cosmic radiation exposure. Flying across time zones or working during normal sleep hours can affect reproductive hormones with circadian regulation.¹¹ These exposures are different from those of other occupational groups exposed to terrestrial radiation or shift work.¹² We evaluated the risk of miscarriage among flight attendants and a comparison group of teachers and assessed whether cosmic radiation, circadian disruption, and other occupational exposures were associated with miscarriage.

METHODS

Questionnaire

The Institutional Review Board of the National Institute for Occupational Safety and Health approved the study; participants provided informed consent. Three US airlines with domiciles (or hubs) in 3 US cities¹³ provided work histories for female flight attendants employed during the study period (1 August 1992 to 31 July 1996). Teachers were selected as a comparison group because of minimal air travel and few reproductive hazards.¹⁴ Local school districts in the same regions provided work histories for teachers. Eligibility was

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determined as age 18–45 years during the study period; full-time employment as a flight attendant or teacher for at least 1 month during the study period; in a marital relationship anytime during the study period (to increase pregnancy likelihood); and not surgically sterilized before the study period. Women were further considered eligible for the analysis of miscarriage if they had reported 1 or more singleton pregnancies in the study period during which they were employed as a flight attendant or teacher. Medical and reproductive histories were obtained by computer-assisted telephone interviews conducted from 3 November 1999 through 13 April 2001, along with the following variables: occupational exposures during pregnancy (physical job demands, psychosocial stressors, and environmental tobacco smoke); age; use of tobacco, caffeine, alcohol, and recreational drugs; physical activity; paternal occupation; and whether a physician was consulted for a miscarriage. Miscarriage was defined as self-reported involuntary termination of a recognized pregnancy through the 20th gestational week; early miscarriage was considered 13 or fewer weeks. The estimated date of the last menstrual period (LMP) was considered the beginning date of the pregnancy and was calculated during the interview from self-reported gestational age and date at the end of the pregnancy.

Because of the potential for differential recall of pregnancy outcomes, medical records for confirmation of miscarriage were obtained if authorized by the study participant. Vital statistics data were obtained for reported births and fetal deaths. Birth certificates were also used to validate prior fetal losses within the study period if they were indicated on the certificate of a subsequent child and to calculate date of LMP when the mother's report was uncertain.

Exposure Assessment

Weekly exposures were estimated from the LMP through the date the pregnancy ended or was right-censored. Radiation and circadian disruption exposures were assessed from company records of work flights and uncompensated passenger flying and questionnaire report of commuter flying to and from the airline domicile city to work.^{13,15} Where records permitted, radiation and circadian disruption exposures during the 6 months prior to LMP were also estimated as an indicator of prepregnancy exposures. Teachers' air travel was estimated from the questionnaires.

For each single nonstop flight between 2 cities (flight segment), data were extracted from records, calculated, or imputed: date flight began, origin and destination cities, block time (airborne plus taxi times), and local departure and arrival times.¹³ We estimated cosmic radiation dose for more than 99.9% of 1,984,285 flight segments. The Federal Aviation Administration program CARI6P¹⁶ (screen version 17 September 2005) was used to estimate galactic cosmic radiation doses for each flight segment.^{13,15} Dynamic solar particle event dose-rate data from the National Aeronautics and Space Administration's Nowcast of Atmospheric Ionizing Radiation

for Aviation Safety model were applied to estimate solar particle event dose to add to galactic cosmic radiation dose for flight segments that possibly traveled through a solar particle event¹⁷; solar particle event dose rates are not calculated by CARI6P.^{18,19} To measure chronic circadian disruption, we used 2 metrics calculated from airline records: cumulative time zones crossed (without regard to travel direction) and Standard Sleep Interval travel, a separate measure of sleep disturbance (time spent flying during the time encompassing 10 pm to 8 am at the flight attendant's domicile).^{9,15} Both of these metrics are related to a biomarker of chronic circadian disruption in flight attendants, the day-to-day variance in flight attendant overnight melatonin excretion.⁹

Additional occupational exposures from the questionnaire included workplace exposures to environmental tobacco smoke and psychosocial stressors. High physical job demands was defined as (1) being on your feet (standing and walking) more than 8 hours/day or (2) 2 or more of the following: lifting or carrying objects that weigh at least 15 pounds more than 10 times a day, bending at the waist more than 25 times/day, and pushing or pulling heavy objects requiring at least 15 pounds of force or effort 20 or more times/day.

Statistical Methods

All analyses were performed using SAS software (version 9.3; SAS Institute Inc., Cary, NC). The rate of miscarriage by gestational week was estimated using lifetable methods.²⁰ We used Cox proportional hazards regression models modified for discrete time data to evaluate the risk of miscarriage in flight attendants compared with teachers, adjusting for potential confounders. Additional modeling limited to flight attendants evaluated cosmic ionizing radiation, time zones crossed, and Standard Sleep Interval travel in conjunction with occupational exposure to cigarette smoke and high physical job demands, adjusting for potential confounders. Models were fit using the PHREG procedure with the TIES = DISCRETE option. Discrete Cox model results are reported as odds ratios (ORs), which can be interpreted as relative risks.²¹ Robust sandwich variance estimates accounted for nonindependent pregnancy outcomes.²² Gestational age (weeks since LMP) was the underlying time variable. Because the risk of miscarriage can vary by gestational week, we evaluated the risk of early miscarriage (ie, in the first trimester, defined as through gestational week 13) but could not evaluate the risk of a late miscarriage (gestational weeks 14–20) or stillbirths due to the small numbers of events (187 early miscarriages vs. only 18 late miscarriages and 5 stillbirths). Because the week the pregnancy became known was not available, we excluded losses occurring in weeks 1–3 and followed pregnancies left-truncated at week 4 until the date the pregnancy ended. All pregnancies were right-censored at 13 weeks.

Cumulative absorbed dose, time zones crossed, and hours of Standard Sleep Interval travel were considered time dependent and evaluated from LMP through the cutoff week

(ie, the week of miscarriage within risk sets). Although other exposure approaches and cutpoints were considered, these exposures were dichotomized at the median cumulative exposure using static cutpoints based on all pregnancies ending in miscarriage in weeks 4–13. The use of dichotomous variables for exposure was intended to reduce the effects of collinearity and limited sample size in combined exposure models. Cigarette smoke and high physical job demands were treated as fixed exposures.

Because radiation dose and time zones crossed were highly correlated (Pearson correlation = 0.89) but less correlated with Standard Sleep Interval travel (Pearson correlations = 0.67 and 0.66, respectively), we evaluated the flying exposures one at a time and in combined models that considered 2 exposures simultaneously using 4 categories (low in both exposures, low in one but high in the other, and high in both exposures).

We evaluated confounding by demographic characteristics (race, Hispanic ethnicity, education, and income), physical variables (maternal age at LMP and body mass index), reproductive history (parity), lifestyle characteristics (cigarette smoking, alcohol consumption, home stress, use of very hot baths/hot tub/sauna, and high vigorous physical activity), medical history (thyroid condition, benign tumors of the reproductive organs, pelvic inflammatory disease, sexually transmitted infections, cervical procedures, fibroid procedures, infections, fever, injury, and x-rays to the torso), and workplace psychosocial stressors. First, associations of covariates with miscarriage and exposures were evaluated using log-binomial regression, *t* tests, chi-square tests, and nonparametric tests, as appropriate. Potential confounders that were associated with both the outcome and the exposure at a 20% significance level were identified and included in multivariate modeling. In models, confounding was evaluated by comparing crude and adjusted model estimates using a 15% change-in-estimate rule. The span of maternal age at the LMP among study pregnancies was less than 15 years; departures from linearity were not observed when higher order terms were included in the model.

A requirement of the study was that participants reported working as a flight attendant or school teacher during the pregnancy; however, for some flight attendant pregnancies, company flight records did not indicate any flying (working flights or uncompensated passenger flights) during the pregnancy (*n* = 79 pregnancies). Flight attendants have some control over which flights they choose to fly, which typically increases with seniority at commercial airlines. Because a flight attendant who elected to not fly during the pregnancy might be different from flight attendants who did fly during the pregnancy, we separated nonflyers from the low-exposed comparison group when we modeled the flying exposures.

We evaluated the proportional odds assumption for the occupational exposures by including a time-dependent interaction term in the model and performing a likelihood ratio

test for interaction. We report separate estimates for gestational weeks 4–8 and 9–13; we do not report estimates for the combined period 4–13 weeks when the proportional odds assumption was not met. Note that models of the 4- to 8-week time period include losses that occur in weeks 9–13 but censor them at week 8.

Sensitivity analyses included omitting miscarriages for which the pregnancy was not reported to a doctor and the miscarriage was not diagnosed or treated by a doctor or in a hospital (*n* = 5); omitting women diagnosed with certain immune disorders (arthritis, Crohn's disease, fibromyalgia, and eosinophilia-myalgia syndrome; *n* = 5); changing the starting week of pregnancy analysis to weeks 5, 6, or 7; analyzing with a log-binomial model (reanalyzing with time-varying covariates treated as fixed average values, ignoring proportional hazards assumptions); modeling exposures with time-dependent median cutpoints (rather than fixed median cutpoints); excluding nonflying flight attendants from models rather than categorizing them in a different group than the flight attendants with low exposures; and modeling solar particle events as time-dependent dichotomous exposures.

RESULTS

Study Population

Of 2595 eligible flight attendants among 5096 successfully contacted, 2273 (88%) agreed to be interviewed; after exclusions, 673 flight attendants had 1 or more eligible pregnancies for a total of 840 study pregnancies analyzed. Of 466 eligible teachers among 1582 successfully contacted, 381 (82%) agreed to be interviewed; 91 teachers had 1 or more eligible pregnancies for a total of 118 study pregnancies analyzed (eTable 1; <http://links.lww.com/EDE/A862>).

The miscarriage rate among study pregnancies by gestational week is shown in the Figure. We obtained 43% of flight attendants' birth and medical records and 30% of teachers' for the study of miscarriages or stillbirths. Of those, we confirmed the outcome for 82% of flight attendants and 100% of teachers. Of the 14 flight attendant miscarriages not confirmed, 13 were not reported on the birth or medical record and 1 birth certificate included an additional outcome (induced abortion) that could not be distinguished from the reported miscarriage.

Flight attendants were more likely to be white and of higher family income than teachers, who were more likely to be college graduates than flight attendants. Flight attendants were more likely to have had cervical procedures before or during pregnancy (11% vs. 4%). The 2 groups were similar in gravidity, parity, and number of previous miscarriages at the time of each pregnancy (Table 1). At work, flight attendants were more likely than teachers to be exposed to tobacco smoke (18% vs. 3%), incur high physical job demands (80% vs. 21%), and score higher on several workplace psychosocial stressors.

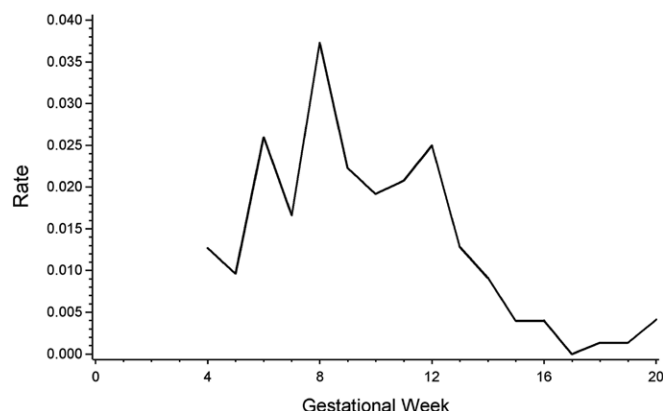


FIGURE. Miscarriage rate among study pregnancies by gestational week from the last menstrual period.

A hypothetical pregnant flight attendant with median first-trimester exposures flew 130 block hours in 53 flight segments, crossed 34 time zones, and flew 15 hours in the Standard Sleep Interval (Table 2). From these flights, she incurred an absorbed radiation dose of 0.13 mGy (effective dose = 0.36 mSv [proton radiation weighting factor (w_R) = 5]). In the same 3-month period, a teacher or nonflying flight attendant would receive an average of 0.14 mSv effective dose due to external irradiation from natural background: 0.083 mSv from space and 0.053 mSv from terrestrial radiation,²³ compared with the flying flight attendant who received an average of 0.49 mSv, including both occupational exposure and exposure to background radiation while not flying. Based on records from 6 months before pregnancy, flight attendants incurred estimated median annual estimates of 700 block hours in 280 flight segments, crossed 184 time zones, and flew 76 hours in the Standard Sleep Interval. They incurred a median absorbed dose of 0.68 mGy (effective dose = 1.8 mSv, range = 0–5.8 mSv). Cumulative total absorbed dose from galactic cosmic radiation was highly correlated with cumulative absorbed dose from particle-specific components (electromagnetic showers, muons, neutrons, pions, and protons) and with cumulative effective dose (results not shown). Only 2 solar particle events of potential dose significance occurred during the study period (30 October to 4 November 1992 and 20–22 February 1994). About 2% of flight attendant pregnancies were likely exposed to a solar particle event during the pregnancy, but solar particle event doses varied widely. The 2 highest estimated solar particle event doses were 0.29 and 0.44 mGy (0.81 and 1.2 mSv) from single flights flown by flight attendants when they were not pregnant.

Occupational Exposures and Miscarriage

Flight attendants were not more likely than teachers to experience a miscarriage (OR = 0.85 [95% confidence interval (CI) = 0.53–1.4], adjusted for first-trimester maternal age, parity, home stress, physical activity, and alcohol). Although adjustment for parity had little impact on the point estimates of our models (results not shown), it was included as a means

to address the presence or absence of young children in a household, which could in turn affect several of our exposures, including stress and lifting.

Occupational exposures among flight attendants were first considered one at a time (Table 3). Model 8 provided evidence of an association between higher levels of absorbed radiation dose (≥ 0.1 mGy) and miscarriage in weeks 9–13 (OR = 1.7 [95% CI = 0.95–3.2]). Higher Standard Sleep Interval travel (≥ 15 hours) was associated with miscarriage during the first trimester (model 15 = 1.5 [1.1–2.2]). Associations were not observed for higher numbers of time zones crossed and miscarriage. When exposure metrics were evaluated 2 at a time (models 16–24), we observed increased odds of miscarriage for Standard Sleep Interval travel ≥ 15 hours (models 21 and 24). The models also show a modest cosmic radiation–miscarriage association (models 18 and 21). Flight attendants who did not fly during the pregnancy had higher odds of miscarriage compared with actively flying flight attendants with low occupational exposures.

High physical job demands were a risk factor for miscarriage (OR = 2.5 [95% CI = 1.5–4.2]). We performed additional modeling adjusted for age and parity with the components of the composite metric: standing/walking, bending at the waist, lifting, and pushing/pulling, as defined in eTable 2 (<http://links.lww.com/EDE/A862>). Among these job-demand components, standing and walking for more than 8 hours/day (1.8 [1.2–2.8]) and bending at the waist more than 25 times/day (2.0 [1.1–3.5]) were risk factors for miscarriage.

In Table 4, we combine occupational exposures absorbed dose, Standard Sleep Interval travel, and physical demands together in the same set of models, adjusted for age and parity. Associations of individual exposures and other covariates with miscarriage were generally consistent with those in Table 3. The 5 high- and low-exposure categories were modeled with 4 degrees of freedom, which is equivalent to inclusion of a product term in these models. Inclusion or exclusion of a product term for radiation and Standard Sleep Interval travel did not meaningfully change the analysis results. Exposure to smoking by coworkers or passengers during the pregnancy was a risk factor for miscarriage in single-exposure analyses (OR = 1.8 [95% CI = 1.2–2.6]). When added to Table 4 combined occupational exposure models, there was reduced evidence of its association with miscarriage (eg, OR = 1.4 [95% CI = 0.78–2.4] in weeks 9–13; data not shown). Additional sensitivity analyses (results not shown) did not meaningfully change the analysis results.

DISCUSSION

In this study, we found associations between miscarriage in flight attendants and occupational exposure to circadian disruption and physical job demands. We also found evidence of an association between cosmic ionizing radiation during pregnancy and miscarriage among flight attendants, although the association was modest and may have been affected by multicollinearity with circadian disruption

TABLE 1. Study Demographic Variables and Other Covariates for the Miscarriage Analysis

Characteristic	Flight Attendants	Teachers
Study women; no.^a	673	91
Demographic variables		
Age at interview (years); median (range)	38 (26–49)	37 (29–49)
Nonwhite race; no. (%)	47 (7)	15 (16)
Hispanic ethnicity; no. (%)	48 (7)	3 (3)
Body mass index at interview (kg/m ²); median (range)	21 (17–38)	23 (17–45)
Education; no. (%)		
No college ^b	89 (13)	0 (0)
Some college	292 (43)	1 (1)
College graduate or higher	292 (43)	90 (99)
Annual family income; no. (%)		
Unknown	13	0
<\$50,000	92 (14)	21 (23)
\$50,000–\$74,999	166 (25)	26 (29)
\$75,000 or higher	402 (61)	44 (48)
Study pregnancies; no.^c	840	118
Time from end of pregnancy to interview (years); median (range)	5.5 (3.0–8.1)	5.6 (3.4–8.0)
Reproductive factors during pregnancy		
Age at last menstrual period (years); median (range)	32 (20–43)	31 (24–42)
Gravidity (no. previous pregnancies); no. (%)		
Unknown	30	0
0	298 (37)	49 (42)
1	272 (34)	28 (24)
2+	240 (30)	41 (35)
Parity (no. previous live births); no. (%)		
Unknown	16	0
No prior pregnancies	298	49
0	199 (38)	20 (29)
1	243 (46)	39 (57)
2+	84 (16)	10 (14)
No. previous miscarriages; no. (%)		
Unknown	23	0
No prior pregnancies	298	49
0	312 (60)	37 (54)
1	160 (31)	25 (36)
2+	47 (9)	7 (10)
Years since last pregnancy; median (range)	1.8 (0–19)	1.9 (0.3–14)
Occupational factors during pregnancy		
Job tenure at last menstrual period (years); median (range) ^d	6.3 (0.1–23)	NA
Exposed to coworkers', customers', or clients' smoke in pregnancy	152 (18)	4 (3)
Low job control at work in pregnancy ^e	216 (26)	18 (15)
Low supervisor support in pregnancy ^f	651 (79)	61 (53)
Somewhat hard or very hard physical effort at work in pregnancy	441 (53)	19 (16)
High physical job demands in pregnancy ^g	665 (80)	24 (21)
Lifting/carrying at least 15 pounds more than 10 times/day at work in pregnancy	433 (52)	12 (10)
Being on feet more than 8 hours/day at work in pregnancy	474 (57)	16 (14)
Bending at the waist more than 25 times/day at work in pregnancy	675 (82)	44 (38)
Pushing/pulling at least 15 pounds 20 or more times/day at work in pregnancy	521 (63)	8 (7)
Husband's occupation; no. (%)		
Reproductive hazard exposure possible ^h	159 (20)	19 (17)
Reproductive hazard exposure not likely	485 (61)	91 (83)
Flight crew	148 (19)	0 (0)

(Continued)

TABLE 1. (Continued)

Characteristic	Flight Attendants	Teachers
Lifestyle factors during pregnancy		
Smoked during first trimester	31 (4)	3 (3)
Lived with a smoker during pregnancy	47 (6)	10 (8)
Smoked or lived with a smoker during pregnancy	71 (9)	11 (9)
Caffeine use in first trimester ^d		
None	320 (39)	54 (46)
Low	330 (40)	41 (35)
High	179 (22)	23 (19)
Alcohol use in first trimester	208 (25)	26 (22)
Home stress in pregnancy ^j	230 (28)	34 (29)
Any children at home under age 4 years in pregnancy	278 (34)	36 (31)
Any use of very hot baths or hot tubs/sauna in pregnancy	199 (24)	38 (32)
High use (>4/month) of very hot baths or hot tubs/sauna in pregnancy	69 (8)	14 (12)
High vigorous physical activity (>120 minutes/week) in pregnancy	271 (33)	32 (27)
Medical factors during pregnancy		
Bladder, kidney, urinary tract infection in first trimester	20 (2)	1 (1)
Illness with fever in first trimester	13 (2)	1 (1)
Injury in first trimester ^k	8 (1)	0 (0)
Selected injury in first trimester ^l	7 (1)	0 (0)
X-rays or radiotherapy during first trimester or in 3 months before pregnancy	17 (2)	2 (2)
Thyroid condition prior to pregnancy or during first trimester	16 (2)	2 (2)
Benign tumor of the reproductive organs before or during pregnancy	52 (6)	7 (6)
Pelvic inflammatory disease before or during pregnancy	23 (3)	0 (0)
Chlamydia before or during pregnancy	36 (4)	5 (4)
Herpes, human papillomavirus, gonorrhea before or during pregnancy	46 (6)	7 (6)
Cervical procedures before or during pregnancy	89 (11)	5 (4)
Fibroid procedures before or during pregnancy	15 (2)	1 (1)

^aDue to missing values, sample size varies (660–673 for flight attendants; 90–91 for teachers).

^bPercentages may not sum to 100 due to rounding.

^cSummary statistics assume independence among the study pregnancies and are not adjusted for other variables. Due to missing values, sample size varies (792–840 for flight attendant pregnancies; 110–118 for teacher pregnancies).

^dJob tenure at last menstrual period is based on company-provided hire dates for flight attendant pregnancies and not available for teacher pregnancies.

^eLow job control defined as “your job allowed you to make a lot of decisions on your own”: never, seldom, or sometimes.

^fLow supervisor support defined as “management was concerned about the welfare of employees”: never, seldom, or sometimes.

^gHigh physical job demands defined as (1) being on your feet (including standing and walking) more than 8 hours/day or (2) 2 or more of the following: lifting or carrying objects that weigh at least 15 pounds more than 10 times a day, bending at the waist more than 25 times/day, and pushing or pulling heavy objects requiring at least 15 pounds of force or effort 20 or more times/day.

^hJob title, business, and main duties data for husbands during the pregnancy were categorized by expert judgment and consultation with National Institute for Occupational Safety and Health industrial hygienists, based on understanding of reproductive hazards in a variety of workplaces.

ⁱCaffeine use defined as any consumption of caffeinated coffee, tea, or soft drinks during the relevant time period. High caffeine use defined as daily caffeine consumption exceeding 85 mg computed from the usual number of drinks/day of caffeinated coffee (~85 mg/drink), tea (~40 mg/drink), and soft drinks (~36 mg/drink) during the relevant time period.

^jHome stress during pregnancy defined as 2 or more of the following: (1) responsibilities at home were shared with others never, seldom, or sometimes, (2) exposed to hostility or conflict at home sometimes, often, or all the time, and (3) having a close friend or family member with whom I could talk about my true feelings when I needed to never, seldom, or sometimes; or 1 or more of the following: (1) responsibilities at home were shared with others never or seldom, (2) exposed to hostility or conflict at home sometimes, often, or all the time, or (3) having a close friend or family member with whom I could talk about my true feelings when I needed to never or seldom.

^kIncludes all injuries reported for the question “during this pregnancy, did you have any serious injury or an accident with injury that required a visit to a doctor?”

^lLimited to self-reported falls, auto accidents, or shock reported for the question “during this pregnancy, did you have any serious injury or an accident with injury that required a visit to a doctor?”

NA indicates not available.

metrics. We initially evaluated other approaches to exposure metrics, including continuous and quartile cutpoint metrics for radiation and circadian disruption. Many of these earlier models exhibited strong signs of collinearity and diminished evidence of association between the metrics and miscarriage. The analyses we present with “high–low” exposure metrics, especially Standard Sleep Interval travel, were the least influenced by multicollinearity between radiation and circadian

disruption metrics and best able to describe the effects of separate metrics.

Evidence from atomic bomb survivor studies suggested a 50 mGy threshold for adverse reproductive outcomes in humans²⁵; however, lower x-ray exposures have been associated with miscarriage in nurses (1 or more hours a day self-reported exposure)²⁶ and veterinarians (more than 5 self-reported films/week).²⁷ Flight attendants’ prepregnancy

TABLE 2. Occupational Radiation and Circadian Disruption Exposures Among 840 Flight Attendant Study Pregnancies and 118 Teacher Study Pregnancies^a

Metric	Cumulative Exposure ^a				
	First Trimester ^b		Cumulative Weeks 1–20 ^c		Prior 6 Months ^d
	Flight Attendants	Teachers	Flight Attendants	Teachers	Flight Attendants
	Median (Max)	Median (Max)	Median (Max)	Median (Max)	Median (Max)
Flight characteristics					
No. flight segments	53 (140)	0 (4.1)	68.0 (210)	0 (4.7)	140 (390)
Block time (hours)	130 (310)	0 (5.9)	180 (430)	0 (6.4)	350 (700)
No. time zones crossed	34 (190)	0 (4.1)	41 (250)	0 (6.00)	92 (400)
Standard Sleep Interval travel (hours) ^e	15 (220)	0 (0)	19 (270)	0 (0)	38 (320)
Travel through solar particle event (%)	1.8	NA	2.0	NA	2.6
Absorbed dose (mGy)					
Electromagnetic showers	0.073 (0.27)	0 (0.0037)	0.095 (0.36)	0 (0.0039)	0.19 (0.56)
Muon	0.014 (0.046)	0 (0.00068)	0.019 (0.060)	0 (0.00072)	0.036 (0.093)
Neutron	0.029 (0.12)	0 (0.0014)	0.037 (0.16)	0 (0.0015)	0.073 (0.24)
Pion	0.0011 (0.0039)	0 (0.000056)	0.0015 (0.0052)	0 (0.000060)	0.0029 (0.0082)
Proton	0.015 (0.064)	0 (0.00077)	0.020 (0.084)	0 (0.00081)	0.039 (0.12)
Total	0.13 (0.51)	0 (0.0067)	0.17 (0.68)	0 (0.0071)	0.34 (1.0)
Total including solar particle events	0.13 (0.51)	NA	0.17 (0.68)	NA	0.34 (1.0)
Effective dose (mSv)					
Proton $w_R = 2$	0.31 (1.30)	0 (0.015)	0.39 (1.7)	0 (0.016)	0.77 (2.4)
Proton $w_R = 5$	0.36 (1.5)	0 (0.018)	0.46 (2.0)	0 (0.019)	0.90 (2.9)
Total including solar particle events, proton $w_R = 5$	0.36 (1.5)	NA	0.46 (2.0)	NA	0.91 (2.9)

^aResults reported to 2 significant figures. Minimum exposures were zero for all metrics. All statistics assume independence among the study pregnancies and are not adjusted for other variables. Although all study models used absorbed dose, we also present effective dose, a radiation protection metric. Median (maximum), except where indicated.

^bExposures during the first trimester were assessed for 840 flight attendant and 118 teacher pregnancies. Exposures were summed from week 1 through the earlier of week 13 and the week the pregnancy ended. For flight attendant pregnancies, Standard Sleep Interval travel was set to missing for 37 flight attendant pregnancies because they had only uncompensated passenger travel during the first trimester, and Standard Sleep Interval travel could not be estimated for these flights. For teacher pregnancies, metrics involving solar particle events could not be assessed and were set to missing; all exposure metrics are zero for 88 teacher pregnancies because they reported no air travel during the pregnancy; and for the remaining 30 teacher pregnancies, Standard Sleep Interval travel could not be assessed and was set to missing.

^cExposures during the first 20 weeks of pregnancy were assessed for 814 flight attendant pregnancies and 116 teacher pregnancies. Exposures were summed from week 1 through the earlier of week 20 and the week the pregnancy ended. Exposures are missing for 26 flight attendant and 2 teacher study pregnancies that contained time after the first-trimester outside of the window for which flight exposures were assessed.

^dCumulative exposures during the 6 months prior to the pregnancy were not available for any teacher pregnancies and not available for 82 flight attendants pregnancies because airline records were not provided for this time period.

^eEstimated time spent flying during the Standard Sleep Interval defined from 10:00 pm to 8:00 am at the flight attendant's domicile (home base).

NA indicates not available; w_R , radiation weighting factor.

exposure rates were also low compared with the 50 mGy threshold, but generally higher than during their first trimester; half had estimated annual doses between 0.7 and 2.0 mGy (effective dose = 1.8–5.8 mSv) prior to pregnancy. These studies suggest that the most highly exposed flight attendants, nurses, and veterinarians may be at increased risk for reproductive and other health effects.

The International Commission on Radiological Protection^{28,29} recommends effective dose limits of 20 mSv/year averaged over 5 years (100 mSv in 5 years) for radiation workers and 1 mSv/year for the public. The International Commission on Radiological Protection considers flight crew occupationally exposed to cosmic radiation. European Union Member States require airlines to educate workers about their radiation risks, assess exposure when dose is likely to exceed

1 mSv/year, and adjust work schedules so that no individual worker exceeds 6 mSv/year.³⁰ There are no official dose limits for US flight crew, although the National Council on Radiation Protection and Measurements reported that flight crew incur the largest average annual effective dose of all US radiation-exposed workers (3.07 mSv, 2006).²³ By comparison, the average annual dose for US Department of Energy workers was 0.59 mSv in 2006.²³ In our study, the highest solar particle event doses came from single flight segments (rather than from several flight segments flown during a solar particle event). If a pregnant flight attendant flew one of these segments during a solar particle event, she could easily approach or surpass the International Commission on Radiological Protection 1-mSv prenatal guideline¹⁸ or the National Council on Radiation Protection and Measurements 0.5-mSv recommended monthly

TABLE 3. Association of Occupational Exposures Among Flight Attendants with Early Miscarriage (Gestational Weeks 4–13) According to Time Period During Pregnancy^a

Variable ^b	Weeks 4–8				Weeks 9–13				Weeks 4–13			
	No. Pregnancies	No. Miscarriages	OR (95% CI)		No. Pregnancies	No. Miscarriages	OR (95% CI)		No. Pregnancies	No. Miscarriages	OR (95% CI)	
Any work flights ^c				Model 1				Model 2			Model 3	
Yes ^d	722	63	1.0		659	64	1.0		722	127	1.0	
No	75	15	2.2 (1.3–3.7)		60	5	0.78 (0.33–1.9)		75	20	1.5 (0.97–2.5)	
Coworkers or passengers smoked in pregnancy												
No ^d	651	55	1.0		596	51	1.0		651	106	1.0	
Yes	146	23	1.7 (1.0–2.9)		123	18	1.8 (1.0–3.0)		146	41	1.8 (1.2–2.6)	
Any work flights ^e				Model 4				Model 5			Model 6	
Yes ^d	722	63	1.0		659	64	1.0		722	127	1.0	
No	75	15	2.4 (1.4–4.1)		60	5	0.90 (0.37–2.2)		75	20	1.7 (1.1–2.8)	
Physical job demands in pregnancy ^e												
Low ^d	157	8	1.0		149	6	1.0		157	14	1.0	
High	640	70	2.2 (1.1–4.4)		570	63	2.8 (1.3–6.4)		640	133	2.5 (1.5–4.2)	
Cumulative absorbed dose (mGy) ^f				Model 7				Model 8			Model 9	
No work flights ^c	75	15	2.3 (1.3–4.1)		60	5	1.3 (0.46–3.6)		75	20		
<0.1	191	36	1.0		155	12	1.0		191	48	NR	
0.1+	531	27	0.95 (0.55–1.6)		504	52	1.7 (0.95–3.2)		531	79		
Cumulative time zones crossed				Model 10				Model 11			Model 12	
No work flights ^c	75	15	2.3 (1.3–4.1)		60	5	0.92 (0.35–2.4)		75	20	1.7 (1.0–2.9)	
<30 ^d	281	38	1.0		243	23	1.0		281	61	1.0	
30+	441	25	0.90 (0.54–1.5)		416	41	1.2 (0.70–2.0)		441	66	1.1 (0.75–1.6)	
Cumulative Standard Sleep Interval travel (hours)				Model 13				Model 14			Model 15	
No work flights ^c	75	15	2.5 (1.4–4.5)		60	5	1.2 (0.45–3.0)		75	20	2.0 (1.2–3.4)	
<15 ^d	342	39	1.0		303	24	1.0		342	63	1.0	
15+	380	24	1.2 (0.70–2.0)		356	40	1.8 (1.1–3.0)		380	64	1.5 (1.1–2.2)	
Absorbed dose and time zones crossed				Model 16				Model 17			Model 18	
No work flights ^c	75	15	2.3 (1.2–4.2)		60	5	1.2 (0.42–3.4)		75	20	1.9 (1.1–3.3)	
Low–low (<0.1 mGy and <30 zones) ^d	165	33	1.0		132	11	1.0		165	44	1.0	
Low–high (<0.1 mGy and ≥30 zones)	26	3	0.91 (0.36–2.3)		23	1	0.55 (0.07–4.2)		26	4	0.84 (0.36–2.0)	
High–low (≥0.1 mGy and <30 zones)	116	5	1.1 (0.41–2.9)		111	12	1.7 (0.79–3.9)		116	17	1.4 (0.79–2.5)	
High–high (≥0.1 mGy and ≥30 zones)	415	22	0.90 (0.51–1.6)		393	40	1.6 (0.83–3.1)		415	62	1.3 (0.84–1.9)	
Absorbed dose and Standard Sleep Interval travel				Model 19				Model 20			Model 21	
No work flights ^c	75	15	2.6 (1.4–4.8)		60	5	1.5 (0.51–4.4)		75	20	2.2 (1.2–3.9)	
Low–low (<0.1 mGy and <15 hours) ^d	164	28	1.0		136	9	1.0		164	37	1.0	
Low–high (<0.1 mGy and ≥15 hours)	27	8	1.8 (0.86–3.9)		19	3	2.5 (0.65–9.4)		27	11	2.0 (1.0–3.9)	
High–low (≥0.1 mGy and <15 hours)	178	11	1.1 (0.55–2.4)		167	15	1.6 (0.71–3.5)		178	26	1.3 (0.78–2.2)	
High–high (≥0.1 mGy and ≥15 hours)	353	16	1.0 (0.52–1.9)		337	37	2.3 (1.2–4.7)		353	53	1.6 (1.1–2.5)	

(Continued)

TABLE 3. (Continued)

Variable ^b	Weeks 4–8				Weeks 9–13				Weeks 4–13			
	No. Pregnancies		No. Miscarriages		No. Pregnancies		No. Miscarriages		No. Pregnancies		No. Miscarriages	
Time zones crossed and Standard Sleep Interval travel												
No work flights ^c	75		15		60		5		75		20	
Low–low (<30 zones and <15 hours) ^d	221		30		191		17		221		47	
Low–high (<30 zones and ≥15 hours)	60		8		52		6		60		14	
High–low (≥30 zones and <15 hours)	121		9		112		7		121		16	
High–high (≥30 zones and ≥15 hours)	320		16		304		34		320		50	
			Model 22				Model 23				Model 24	
			OR (95% CI)				OR (95% CI)				OR (95% CI)	
			2.6 (1.4–4.8)				1.0 (0.38–2.8)				1.9 (1.1–3.4)	
			1.0				1.0				1.0	
			2.0 (0.97–4.3)				1.6 (0.61–4.1)				1.8 (1.0–3.4)	
			1.1 (0.55–2.3)				0.68 (0.28–1.7)				0.91 (0.52–1.6)	
			0.96 (0.51–1.8)				1.6 (0.88–2.9)				1.4 (0.91–2.2)	

NR indicates not reported as the likelihood ratio test of proportional odds was statistically significant ($P = 0.037$).

^aModels of pregnancies in weeks 4–13 included 797 flight attendant study pregnancies (11 miscarriages in gestational weeks 1–3 and 32 pregnancies with 1 or more missing covariates were excluded).

^bAll models additionally adjusted for age at the last menstrual period and parity.

^cSome employed flight attendants did not incur work flights during the first trimester.

^dReference category.

^eHigh physical job demands defined as (1) being on your feet (including standing and walking) more than 8 hours/day or (2) 2 or more of the following: lifting or carrying objects that weigh at least 15 pounds more than 10 times a day, bending at the waist more than 25 times/day, and pushing or pulling heavy objects requiring at least 15 pounds of force or effort 20 or more times/day.

^fCumulative occupational exposure metrics were evaluated from the estimated date of last menstrual period through the cutoff week; cutpoints reflect the median exposure among cases.

limit during pregnancy.³¹ Resources are being developed to provide real-time and predictive information on solar particle events to flight crew and the public.^{32–34}

We found an increased risk of miscarriage in flight attendants who flew 15+ hours during their home-base sleep hours. This is a new finding; however, it is consistent with reports of adverse reproductive outcomes associated with night or rotating shift work.^{35,36} Time zones crossed and radiation metrics were highly correlated, but we attempted to separate the etiologic contributions of circadian disruption and radiation by including our other circadian metric, Standard Sleep Interval travel, in a 2-exposure model with simplified exposure levels. Both time zones crossed and Standard Sleep Interval travel are related to a circadian biomarker, the day-to-day variance in overnight melatonin excretion.⁹ Standard Sleep Interval travel may be the better circadian metric for flight crew studies, but it considers only flight time and not commuter or other personal time, and it, therefore, probably underestimates disrupted sleep.

Future research of this occupational group should consider employed nonflying flight attendants as a separate exposure group. Records-based identification of these workers was critical to our analysis, because their risk of miscarriage was found to be considerably higher than for flight attendants with low exposures. These participants maintained flight attendant employed status without flying by trading flights with other flight attendants, using state- or company-based benefits, performing another airline job while keeping flight attendant credentials, or having a doctor's order not to fly. They were more likely than those who did fly to have had 2 or more previous pregnancies, and the data suggested that they were more likely to have 2 or more previous miscarriages (10% vs. 5%). Thus, they may have avoided flying during pregnancy due to their previous miscarriages, which may also have been caused by earlier occupational exposures.

High physical job demands—specifically, prolonged standing/walking or bending at the waist—were also associated with increased miscarriage, congruent with prior studies.³⁷ The negative findings for occupational lifting contrast with results from a large Danish cohort, possibly due to our use of a relatively low-exposure threshold and dichotomous classification.³⁸

Although occupational environmental tobacco smoke exposure was a risk factor in single-exposure analyses (OR = 1.8 [95% CI = 1.2–2.6]), we did not adjust for it when evaluating the association of miscarriage with radiation and circadian rhythm disruption (Table 4). Environmental tobacco smoke was a likely proxy exposure for Standard Sleep Interval travel prior to the airlines' comprehensive smoking ban on long international overnight routes. Further, active smoking during the pregnancy was rare (4%) and did not meet criteria for confounding in our study because the rates of miscarriage among active smokers (26%) were comparable to those among nonsmokers (21%) (likelihood ratio $P = 0.55$). Environmental

TABLE 4. Association of Age, Parity, Physical Job Demands, Absorbed Dose, and Standard Sleep Interval Time (Analyzed Simultaneously) with Early Miscarriage (Gestational Weeks 4–13) According to Time Period^a

Variable ^b	Weeks 4–8			Weeks 9–13			Weeks 4–13		
	No.	Pregnancies	Miscarriages	OR (95% CI)	No.	Pregnancies	No.	Pregnancies	OR (95% CI)
				Model 1					Model 2
Age at last menstrual period (1 year)	797	78	1.1 (1.1–1.2)	719	69	1.0 (0.96–1.1)	797	147	1.1 (1.0–1.1)
Parity									
Nulliparous ^c	478	45	1.0	433	47	1.0	478	92	1.0
Parous	319	33	0.91 (0.56–1.5)	286	22	0.70 (0.43–1.2)	319	55	0.81 (0.57–1.2)
Physical job demands in pregnancy ^d									
Low ^e	157	8	1.0	149	6	1.0	157	14	1.0
High	640	70	2.2 (1.1–4.5)	570	63	2.8 (1.2–6.4)	640	133	2.5 (1.5–4.1)
Absorbed dose and Standard Sleep Interval travel ^e									
No work flights ^f	75	15	2.6 (1.4–4.9)	60	5	1.6 (0.54–4.6)	75	20	2.3 (1.3–4.0)
Low–low (<0.1 mGy and <15 hours) ^e	164	28	1.0	136	9	1.0	164	37	1.0
Low–high (<0.1 mGy and ≥15 hours)	27	8	1.8 (0.86–3.9)	19	3	2.4 (0.64–9.3)	27	11	2.0 (1.0–3.9)
High–low (≥0.1 mGy and <15 hours)	178	11	1.2 (0.55–2.4)	167	15	1.5 (0.69–3.4)	178	26	1.3 (0.76–2.1)
High–high (≥0.1 mGy and ≥15 hours)	353	16	0.97 (0.50–1.9)	337	37	2.3 (1.1–4.6)	353	53	1.6 (1.0–2.5)

^aModels of pregnancies in weeks 4–13 included 797 flight attendant study pregnancies (11 miscarriages in gestational weeks 1–3 and 32 pregnancies with 1 or more missing covariates were excluded).^bAll variables were included in each model; however, estimates for age and parity are not necessarily interpretable as total effects.²⁴^cReference category.^dHigh physical job demands defined as (1) being on your feet (including standing and walking) more than 8 hours/day or (2) 2 or more of the following: lifting or carrying objects that weigh at least 15 pounds more than 10 times a day, bending at the waist more than 25 times/day, and pushing or pulling heavy objects requiring at least 15 pounds of force or effort 20 or more times/day.^eCumulative occupational exposure metrics were evaluated from the estimated date of last menstrual period through the cutoff week; cutpoints reflect the median exposure among cases.^fSome employed flight attendants did not incur work flights during the first trimester.

tobacco smoke exposure has generally been associated with later adverse reproductive outcomes rather than with miscarriage.³⁹

This study's limitations include potential differential recall bias from self-report of outcome and gestational age information, although this information was verified/validated where possible; estimation rather than direct measurement of exposures; and possible multicollinearity of radiation and circadian disruption metrics. Occupational exposures estimated from the questionnaire were not trimester specific; physical job demands and other exposures may change throughout pregnancy. Finally, there is no ideal comparison group for flight attendants. Based on the differences we identified and other potential differences between these 2 occupational groups, our finding of no difference in flight attendants' risk of miscarriage compared with teachers would benefit from further examination.

The strengths of this study include the first assessment of flight attendant radiation and circadian disruption exposures from individual flight segments that allowed us to contrast correlated exposures in analyses and the first direct estimation of solar particle event doses in flight attendants. Pregnant flight attendants share circadian disruption and ergonomic concerns with pregnant workers on the ground who may also be on their feet, bend from the waist, or work the night shift. Ergonomic guidelines being developed for pregnant workers⁴⁰ should be adapted for pregnant flight crew, and guidelines need to be developed for pregnant shift workers on the ground and in the air. Unlike pregnant women on the ground, however, pregnant flight crew are occupationally exposed to cosmic radiation. Communication of the potential risk from exposure to cosmic radiation would allow them to make informed decisions about flying during pregnancy.

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