Mortality among the Residents of the Three Mile Island Accident Area: 1979–1992

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The largest U.S. population exposed to low-level radioactivity released by an accident at a nuclear power plant is composed of residents near the Three Mile Island (TMI) Plant on 28 March 1979. This paper (a collaboration of The University of Pittsburgh and the Pennsylvania Department of Health) reports on the mortality experience of the 32,135 members in this cohort for 1979–1992. We analyzed standardized mortality ratios (SMRs) using a local comparison population and performed relative risk regression modeling to assess overall mortality and specific cancer risks by confounding factors and radiation-related exposure variables. Total mortality was significantly elevated for both men and women (SMRs = 109 and 118, respectively). All heart disease accounted for 43.3% of total deaths and demonstrated elevated SMRs for heart disease of 113 and 130 for men and women, respectively; however, when controlling for confounders and natural background radiation, these elevations in heart disease were no longer evident. Overall cancer mortality was similar in this cohort as compared to the local population (male SMR = 100; female SMR = 101). In the relative risk modeling, there was a significant effect for all lymphatic and hematopoietic tissue in males in relation to natural background exposure ($p = 0.04$). However, no trend was noted. We found a significant linear trend for female breast cancer risk in relation to increasing levels of TMI-related likely γ-exposure ($p = 0.02$). Although such a relationship has been noted in other investigations, emissions from the TMI incident were significantly lower than in other documented studies. Therefore, it is unlikely that this observed increase is related to radiation exposure on the day of the accident. The mortality surveillance of this cohort does not provide consistent evidence that radioactivity released during the TMI accident has a significant impact on the mortality experience of this cohort to date. However, continued follow-up of these individuals will provide a more comprehensive description of the morbidity and mortality experience of the cohort. *Key words*: dose–response relationship, epidemiology, ionizing radiation, mortality, neoplasms, nuclear reactors. *Environ Health Perspect* 108:545–552 (2000). [Online 28 April 2000]

http://ehpnet1.niehs.nih.gov/docs/2000/108p545-552talbott/abstract.html

An incident at the Three Mile Island (TMI) nuclear power plant on 28 March 1979 produced a relatively small environmental release of radioactivity that consisted primarily of xenon and iodine radioisotopes. Scientists computed individual maximum and likely γ- and β-radiation doses based on residential location and the amount of time each person spent in the 5-mile area during the 10 days after the accident (*1*). Gur et al. (*1*) determined that the average likely and maximum whole-body γ-doses for individuals in this area were 9 mrem (0.09 mSv) and 25 mrem (0.25 mSv), respectively. The radiation from the TMI nuclear accident was considered minimal as compared to the approximately 300 mrem (3 mSv) annual effective dose received by an individual in the United States from natural background (*2*).

Although it has been postulated that radiation from a nuclear accident and natural background radiation exposures act on the biologic system in the same way (*3,4*) and that the health effects produced by these types of radioactivity are indistinguishable, available human data are insufficient to confirm this hypothesis (*5*). In addition, the long-term consequences from low-dose radiation are clearly of recent concern to the public. Consequently, soon after the TMI incident, public health researchers began to monitor whether this brief low-dose radiation exposure exerted any effects on the health of those people living near the nuclear facility.

Past research efforts included a survey conducted by the Pennsylvania Department of Health (PDoH; Harrisburg, PA) on the > 35,000 people living near the TMI facility (*1,6,7*). The survey included a characterization of the radiation exposure to local inhabitants and a careful follow-up of the local inhabitants' mortality and cancer morbidity status over time (*1,6,7*). This population provides a unique opportunity to study the long-term health effects associated with low levels of radiation. Given this opportunity, it is important to assess whether the absence of increased physical health effects can be observed in this low-level radiation-exposed population to confirm the estimates of several scientific reports that such health consequences were unlikely (*8*).

Within 2 months of the accident, the PDoH developed and implemented a TMI Population Registry to track possible health effects to the local population (*9*). This registry was a special population census conducted within a 5-mile radius of the TMI facility to ascertain the number and characteristics of the local residents, including sociodemographic information, medical history, cigarette smoking status, and previous radiation exposure history. It was estimated that 93–94% of the targeted population was interviewed, with < 4% of the canvassed households either refusing to respond or unobtainable for other reasons. The registry included 35,946 individuals living within the 5-mile radius of the TMI nuclear reactor (*9*).

An initial mortality follow-up study by the PDoH examined mortality from 1979 to 1985 (*6*). Age-adjusted standardized mortality ratios (SMRs) were calculated to determine if the number of observed deaths among the TMI cohort was greater than what would be expected in the TMI population. Regression modeling demonstrated that neither estimated maximum nor likely whole-body γ-doses were associated with all-cause, noncancer, or total cancer mortality when controlling for the confounding factors. The authors cautioned that the 6-year follow-up period was short when evaluating most cancers.

In 1985, a separate study was initiated by Columbia University; the study sought to ascertain cancer cases that occurred before and after the TMI accident (*10,11*). The study cohort included individuals who resided within a 10-mile radius of the TMI nuclear facility and encompassed nearly 160,000 persons. The study area was divided into 69 study tracts and cancer cases within each tract were ascertained for the 1975–1985 period. Estimates of emissions delivered to these

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We thank N. Wald for guidance in the preparation of this manuscript. We also thank K. Ramaswamy and J. Bratz for their early contributions and continuing support of this project.

This research was supported by a grant from the Three Mile Island Public Health Fund.

Received 30 September 1999; accepted 28 December 1999.

tracts were derived from mathematical dispersion models; the model of accident emissions was validated by readings from off-site dosimeters. Pre- and postaccident trends in cancer rates for the 10-year time period were examined. Cancer rates were adjusted for population density, income, and education. Analyses were limited because personal risk factor information (i.e., smoking and education) was not collected. For accident emissions, the researchers failed to find definite effects of exposure on the cancer types and population subgroups studied. No association was seen for leukemia in adults or for childhood cancers as a group. However, non-Hodgkin lymphoma showed elevated risks relative to both accident and routine emissions; the odds ratios assuming a 5-year latency were 2.0 [95% confidence interval (CI), 1.2–3.5] and 2.13 (CI, 1.29–3.51), respectively. The odds ratio for lung cancer and accident emissions was 1.75 (CI, 1.47–2.08); the odds ratio for lung cancer and routine emissions was 1.55 (CI, 1.18–2.03). Background γ-radiation also showed a slight trend in risk for lung cancer, with an odds ratio of 1.1 (CI, 0.9–1.4) (*11*).

To further assess the effects of the accident, the University of Pittsburgh (Pittsburgh, PA), in collaboration with the PDoH, is continuing a mortality follow-up through the year 1999. We report here on the general and cause-specific mortality experience of this population (termed the UPitt/PDoH TMI cohort) during the 1979–1992 period.

Methods

A total of 35,946 residents were initially enrolled in the TMI census. Data collected included individual information on education, occupation, smoking status, residential history, medical history, previous radiation exposure (treatment or occupational), and daily travel in and out of the area during the 10 days after the accident (*9*).

The final UPitt/PDoH TMI cohort consisted of 32,135 individuals after excluding people based on six criteria: *a*) individuals with unknown γ-and β-exposure levels, *b*) those living beyond the 5-mile radius, *c*) those born after 28 March 1979, *d*) those with unknown residential history, *e*) those who established residency after 28 March 1979, and *f*) those who were duplicated in the TMI census.

Gur et al. (*1*) computed individual estimated average likely and maximum whole-body γ-doses from the TMI accident radio-activity releases based on residential location and the amount of time each person spent in the 5-mile area during the 10 days after the accident.

The present study assigned natural environmental background exposure estimates (not including TMI radioactivity releases) based on a direct measurement recorded with a scintillation detector and associated instrumentation from a 1976 airborne radon survey (*12*). These data were applied to the portion of the Hatch et al. (*10*) 69 study tracts, which covers the 5-mile radius of the UPitt/PDoH TMI cohort. The natural background exposure estimates within each zip code were then averaged and assigned a quartile of exposure.

SMRs. We examined the total and cause-specific mortality experiences of the UPitt/PDoH TMI cohort for the period of 28 March 1979 through 31 December 1992. We jointly classified the person-years at risk contributed by each cohort member by sex, race, age, and time periods using the modified life table technique of the Occupational Cohort Mortality Analysis Program (OCMAP-PLUS), created at the University of Pittsburgh (*13*).

We computed expected counts of deaths by multiplying average annual race-, sex-, age-, and time-specific mortality rates by the person-years at risk in the corresponding race-, sex-, age-, and time-specific intervals in the cohort. We computed the expected counts of death using three counties surrounding the TMI study area [defined as an aggregate of Dauphin, Lancaster, and York counties (the Pennsylvania three-county comparison)] and the state of Pennsylvania as standard comparison populations. We obtained the mortality rates from the Mortality and Population Data System (*14*), which is maintained at the University of Pittsburgh.

Excess and deficit mortalities were expressed as SMRs. We identified statistically significant deviations of the SMR below and above 100, indicating deficit and excess mortality risks, respectively, using Poisson probabilities. No formal probability adjustments were made for the multiple statistical comparisons performed. Because of the small numbers of nonwhite cohort members, we based these analyses on white cohort members only.

Relative risk (RR) regression. We used RR regression to investigate the dependence of the internal cohort rates for six outcomes of interest, including all malignant neoplasms; cancer of the bronchus, trachea, and lung (BTL); cancer of the breast (females only); cancer of the lymphatic and hematopoietic tissue excluding chronic lymphocytic leukemia and Hodgkin disease (LHT); cancer of the central nervous system (CNS); and all heart disease. We chose the four cancer sites because of their radiosensitive nature (*15*). We excluded chronic lymphocytic leukemia and Hodgkin disease from further analysis in the all lymphatic and hematopoietic tissue cancer grouping because they rarely have been linked to radiation exposure (*16*). We analyzed these outcomes on combinations of the three exposure-related covariates and the potential confounding factors. Natural background radiation was considered a predictor variable as well as a confounding variable in the maximum and likely γ-models.

We performed the RR modeling separately for each of the six time-to-event outcomes. For each outcome, we constructed risk sets from the cohort data file, with age as the primary time dimension. A risk set consisted of a case (cause-specific outcome) and all other cohort members who were alive and at risk at the age that the case died. To adjust for birth cohort effects, we restricted the risk sets to include only individuals born within 1 month of the corresponding case. We constructed the risk sets using the RISK-SET module of the OCMAP-PLUS software (*13*).

Multiplicative RR models of the form $\lambda(t) = \lambda_0(t) \exp[\mathbf{x}(t)\beta]$ were fit to the internal cohort rates. Mathematical details of the models are given elsewhere (*17–19*). In this model, $\lambda_0(t)$ is the hazard of an event at age t for an individual with baseline levels of all covariates; $\mathbf{x}(t)$ is a vector of covariates (exposures and/or confounders), and β is the corresponding parameter vector estimated by partial likelihood. We used the conditional logistic regression program in STATA (*20*) to estimate β from the explicitly constructed risk sets.

The potential confounders considered included smoking (never or ever), education at the time of the accident (< 12 or ≥ 12 years), work in a radiation field (ever, never, or unknown), and external background radiation (low, low medium, or high). The radiation-related exposure variables included estimated maximum and likely γ-exposure during the 10 days after the accident (0–7, 8–20, 21–34, or ≥ 35 mrem and 0–2, 3–7, 8–15, or ≥ 16 mrem, respectively) and external background exposure (low, low medium, and high medium). We used the lowest category of each risk factor as a baseline for the estimated RR; that category always had an RR value of 1.00. Individual RR estimates were statistically significant if their CIs did not include 1.00. All models were based on white cohort members who were ≥ 18 years of age on the day of the accident.

Potential confounders were screened by identifying variables that were individually significant before adding to a model as an adjustment factor. We assessed the statistical significance of each main effect with a likelihood ratio statistic. All tests were done at the 0.05 significance level and no adjustment was made for multiple comparisons. For the quantitative exposure variables that exhibited a monotonic increasing or decreasing pattern in the parameter estimates, we conducted a test for linear trend (based on equally spaced scores).

Results

Age, race, sex, education levels, occupation, and smoking history. Table 1 shows a demographic summary of the UPitt/PDoH TMI cohort. The mean age at the time of census registration was 32.9 years. Approximately 97% of the cohort was white; 2.8% was of other races. A total of 5,150 (46.1%) males and 5,858 (50.0%) females ≥ 18 years of age graduated from high school. An additional 1,384 (12.4%) males and 850 (7.3%) females attained an advanced degree. Approx-imately 34% of those in the cohort ≥ 18 years of age were current or past smokers. A total of 768 (6.7%) men and 350 (3.0%) women reported working in radiation-related jobs (nuclear plant, other nuclear-related industry, or medical profession).

Estimated radiation levels on the day of the accident. Figure 1 shows the maximum and likely γ-radiation levels for the UPitt/PDoH TMI cohort during the 10 days after the accident (*4*). Approximately 15% (5,032 individuals) were exposed to > 40 mrem (0.4 mSv) maximum γ-radiation (the equivalent of approximately three chest X rays). The average likely γ-dose was 10.4 mrem (0.10 mSv), with 3,539 individuals (11.1%) exposed to > 20 mrem (0.20 mSv). Less than 2.1% received the highest levels of estimated maximum or likely γ-radiation.

Figure 2 presents the mean likely 10-day cumulative whole-body γ-dose in millirems within a 5-mile radius of the TMI area by civil division. The highest exposures were reported in Lower Swatara, Royalton, and Goldsboro.

Natural background radiation exposure before the TMI accident. Figure 3 presents crude estimates of natural background radiation exposure for the TMI area. The quartiles of exposure for the UPitt/PDoH TMI cohort lie largely in the first three categories: low (5.7–7.2 μR/hr), low medium (7.3–7.9 μR/hr), and high medium (8.0–8.7 μR/hr). The highest quartile (8.8–10.5 μR/hr) is largely outside of the 5-mile radius, and the high–medium exposure area lies mainly in the northwest and southeast quadrants, which are not close in proximity to the TMI plant. The majority of the individuals in the UPitt/PDoH cohort resided in the lowest background exposure areas.

General mortality patterns. We examined the general mortality experience of the UPitt/PDoH TMI cohort to assess relationships between mortality and exposure to radiation from the TMI accident. Table 2 shows observed deaths and SMRs for males and females during the 1979–1992 study period. There was a total of 1,934 male deaths, which resulted in slightly elevated overall mortality when compared to the general population of the three-county aggregate (SMR = 109, $p < 0.05$). Deaths due to heart disease were also significant (SMR = 116, $p < 0.05$). A total of 1,925 female deaths yielded a statistically significant excess in overall mortality (SMR = 118, $p < 0.05$). Females also exhibited an excess in all heart disease (SMR = 130, $p < 0.05$). Nonmalignant respiratory disease was also significantly higher in females (SMR = 124, $p < 0.05$). Total and cause-specific mortality rates were also compared to the state of Pennsylvania as a whole and to a new state comparison that excluded Philadelphia County (data not shown). Similar results were found.

Mortality patterns by exposure variables. Tables 3–5 show sex-specific SMRs for the radiation exposure variables for those ≥ 18 years of age. The lowest exposure group in the maximum and likely γ-categories (< 8 and < 3 mrem, or < 0.08 and < 0.03 mSv, respectively) exhibited significant excesses in overall mortality for males and females [SMRs = 122.2 and 122.4; SMRs = 142.3 and 142.7 ($p < 0.01$)]. In women, individuals in the highest maximum and likely γ-exposure groups also showed an increased SMR [≥ 35 and ≥ 16 mrem (0.35 and ≥ 0.16 mSv); SMR = 123.2 and 122.9, respectively ($p < 0.01$)].

Although significantly elevated ($p < 0.05$), SMRs for all heart disease did not increase by natural background radiation level in males. Women in the low–medium and high–medium natural background

Table 1. Demographic summary of the PDoH TMI cohort.

	1979 cohort[a]	1992 cohort[a]
Persons (*n*)	32,135	28,456
Households (*n*)	11,832	10,320
Mean age (years)	32.9	41.5
Median age (years)	29.0	39.0
White (%)	97.2	97.2
Smokers (%)	33.8	28.0

[a]After exclusionary criteria were applied.

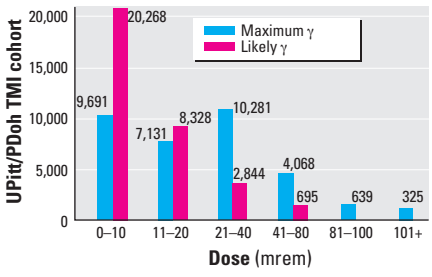

Figure 1. Distribution of estimated maximum and likely γ-dose.

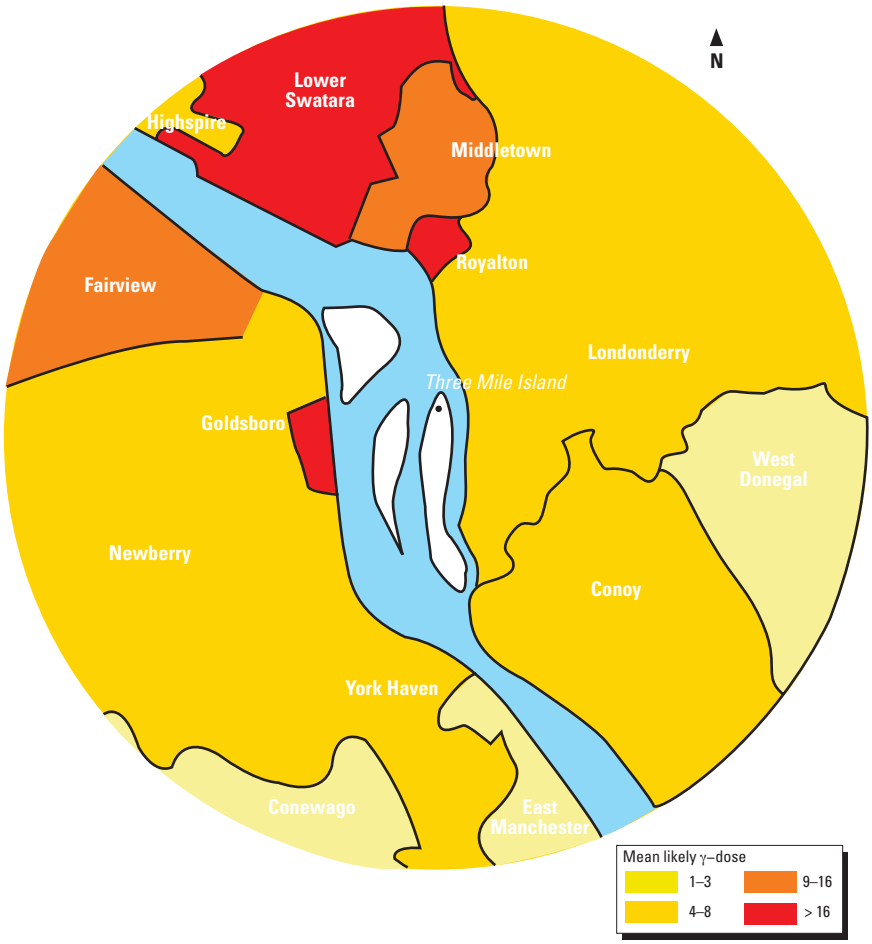

Figure 2. Mean likely whole-body γ-dose (millirem) within a 5-mile radius of TMI, by civil division.

exposure categories displayed significantly elevated SMRs for all heart disease ($p < 0.01$). No relationship was noted between increasing maximum and likely γ-exposure and increasing SMRs for both males and females.

Males in the high–medium natural background area showed increases in SMRs for BTL cancers (SMR = 146.9, $p < 0.05$); the lowest maximum and likely γ-levels also showed increases in SMRs for BTL cancers [SMRs = 148.1 and 141.0 ($p < 0.05$)]. No significant relationship was observed in all malignancies, LHT cancers, and CNS cancers for men or women.

RR regression. Tables 6 and 7 show the results from the RR regression modeling for males and females. The RRs and associated CIs are shown for each cause of interest, along with a global p-value and a trend p-value where appropriate. Univariate models for smoking and education were fit but are not shown. If the confounder was a significant predictor of risk, multivariate models were fit adjusting for the confounder. Additionally, all maximum and likely γ-models were adjusted for level of background radiation exposure.

As shown in Table 6, even though background exposure was not a significant predictor of male cancer risk, the RRs for the low–medium and high–medium groups were elevated (RRs = 1.00, 1.14, and 1.14, respectively). Neither maximum γ-exposure nor likely γ-exposures were significant predictors of cancer risk with RRs < 1. Because smoking was a significant individual predictor of cancer mortality, the models adjusting for smoking were also fit for the three exposure-related risk factors. No significant predictors were noted after adjusting for smoking, although the individual RRs for external background exposure (with adjustment for smoking) were still elevated (RRs = 1.00, 1.14, and 1.14).

Although not shown, both smoking and education were univariate significant predictors of risk ($p < 0.001$ and $p = 0.03$, respectively) for male BTL cancer. The individual RRs for natural background level of exposure exhibited an increasing trend (RRs = 1.00, 1.03, and 1.55; $p = 0.06$). This trend in the estimates for background exposure was further attenuated after controlling for smoking and education ($p = 0.14$). After adjustment for smoking, education, and background radiation level, neither maximum nor likely γ-radiation levels were significant predictors of male BTL cancer.

The RR models for all cancer of LHT in males show that only natural background exposure was a significant predictor of risk ($p = 0.04$), with no apparent trend with increasing levels of exposure. Some levels of maximum γ-exposure were elevated but not statistically significant after adjustment for background radiation exposure.

The RR models for cancer of the CNS in males (Table 6) were fit using the exact logistic regression module in LogXact (*21*) (because of the small number of cases, $n = 6$). None of the variables was a statistically significant predictor of risk, although some levels of maximum γ-and likely γ-exposure were elevated. The CIs on the individual estimates are extremely wide because of data sparseness.

The RRs for maximum γ-exposures were suggestive of a protective effect for heart disease in males. Because both smoking and education were significant predictors of heart disease ($p < 0.001$), models for the exposure variables were fit controlling for both factors. After adjustment for these confounders as

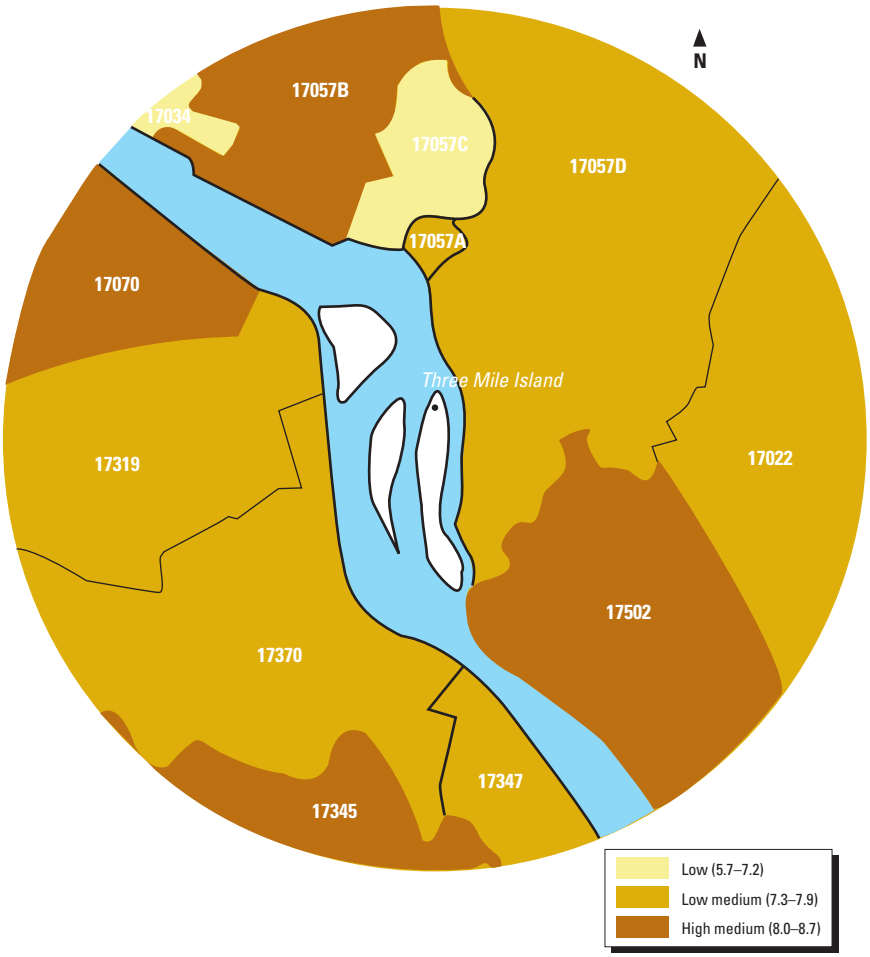

Figure 3. Background radiation estimates by civil division/zip code (millirad per hour). 17057A, Royalton; 17057B, Lower Swatara; 17057C, Middletown; 17057D, Londonderry.

Table 2. Observed (Obs) and SMR_c (SMR based on corresponding county rates) for specific causes of death, PDoH TMI cohort, 1979–1992 for Pennsylvania three-county comparison, white males and females.

	Total mortality			
	White males (n = 15,539)[a]		White females (n = 15,707)[b]	
Cause of death	Obs	SMR_c	Obs	SMR_c
All causes of death	1,934	109*	1,925	118*
All malignant neoplasm	423	100	384	101
Respiratory system cancer	151	106	58	103
Central nervous system cancer	–	–	–	–
Breast cancer	2	311	78	102
Thyroid cancer	–	–	–	–
Leukemia	19	115	17	108
All other lymphopoietic cancer	18	100	24	125
Nonmalignant respiratory disease	156	110	126	124*
All heart disease	817	116*	853	130*
All external causes	156	109	61	109

[a]200,092.9 person-years. [b]202,608.3 person-years. *$p < 0.05$.

Table 3. Observed (Obs) and SMRs for selected causes of death,[a] UPitt/PDoH TMI cohort, white males,[b] 1979–1992.

	All causes			All heart causes			All malignancies			BTL cancer			All lymphatic and hematopoetic			CNS cancers		
Risk factor	Obs	SMR	CI	Obs	SMR	CI	Obs	SMR	CI	Obs	SMR	CI	Obs	SMR	CI	Obs	SMR	CI
Background radiation																		
Low	660	108.2*	100.1–116.8	279	115.5*	102.4–129.9	137	92.6	77.7–109.5	48	100.6	74.2–133.4	10	69.7	33.4–128.3	2	59.3	7.2–214.2
Low medium	860	107.2*	100.1–114.6	358	112.4*	101.0–124.7	188	101.4	87.4–117.0	56	96.6	72.9–125.4	27	148.6	97.9–216.2	3	68.6	14.2–200.4
High medium	405	108.1*	97.8–119.1	177	122.1*	104.7–141.4	96	106.3	86.1–129.9	43	146.9*	106.3–197.9	6	66.7	24.5–145.2	1	43.4	1.1–241.7
Maximum gamma																		
< 8 mrem	558	122.2*	112.3–132.8	252	135.1*	118.9–152.9	116	116.4	96.2–139.6	44	148.1*	107.6–198.8	10	104.2	50.0–191.6	2	92.6	11.2–334.5
8–19 mrem	538	108.0	99.1–117.5	221	114.5*	99.9–130.7	114	91.9	75.8–110.4	37	90.2	63.5–124.3	8	65.5	28.3–129.0	2	64.9	7.8–234.4
20–34 mrem	406	95.3	86.2–105.0	168	100.0	85.4–116.3	98	96.5	78.3–117.6	35	108.0	75.2–150.2	13	130.7	69.6–223.5	2	84.7	10.2–306.0
≥ 35 mrem	432	105.0	95.4–115.4	176	110.5	94.7–128.0	95	95.5	77.3–116.8	31	96.2	65.4–136.6	12	121.7	62.9–212.6	0	–	–
Likely gamma																		
< 3 mrem	533	122.4**	112.2–133.2	233	131.9**	115.5–149.9	103	109.7	89.6–133.1	39	141.0*	100.3–192.8	9	98.4	45.0–186.7	2	98.8	12.0–356.9
3–7 mrem	432	104.0	94.4–114.2	182	112.5	96.8–130.1	102	100.6	82.1–122.2	31	93.8	63.7–133.1	10	100.2	48.0–184.2	1	39.9	1.0–222.4
8–15 mrem	501	99.2	90.7–108.3	205	103.5	89.8–118.7	119	96.1	79.6–115.0	42	104.0	74.9–140.6	15	124.0	69.4–204.5	3	101.4	20.9–296.2
≥ 16 mrem	468	107.4	97.9–117.6	197	115.7*	100.1–133.0	10	93.7	76.1–114.0	35	102.2	71.2–142.1	9	86.5	39.6–164.3	0	–	–

[a]Adjusted by age. [b]As compared to the Pennsylvania three-county comparison. *$p < 0.05$. **$p < 0.01$.

Table 4. Observed (Obs) and SMRs for selected causes of death,[a] UPitt/PDoH TMI cohort, white females,[b] 1979–1992.

	All causes			All heart causes			All malignancies			BTL cancer			All lymphatic and hematopoetic			CNS cancers		
Risk factor	Obs	SMR	CI	Obs	SMR	CI	Obs	SMR	CI	Obs	SMR	CI	Obs	SMR	CI	Obs	SMR	CI
Background radiation																		
Low	654	101.6	94.0–109.7	288	111.6	99.1–125.3	135	90.0	75.5–106.6	21	93.4	57.8–142.7	13	81.0	43.1–138.5	2	62.0	7.5–224.0
Low medium	908	128.6**	120.4–137.3	415	143.7**	130.2–158.2	172	111.1	80.3–128.3	22	100.3	62.8–151.8	23	140.2	88.9–210.3	7	198.2	79.7–408.4
High medium	358	130.8**	117.6–145.0	148	144.7**	122.3–170.0	74	102.2	95.1–129.0	12	106.9	55.2–186.8	11	146.4	73.1–261.9	3	166.2	34.3–485.6
Maximum gamma																		
< 8 mrem	682	142.3**	131.8–153.4	355	171.7**	154.3–190.5	99	107.0	86.9–130.2	14	114.6	62.7–192.3	15	149.9	83.9–247.2	2	106.4	12.9–384.4
8–19 mrem	425	102.7	93.2–113.0	163	103.7	88.4–120.9	102	96.0	78.3–116.5	17	103.1	60.1–165.1	13	116.7	62.1–199.5	5	195.3	63.4–455.8
20–34 mrem	399	101.9	92.1–112.4	167	107.6	91.9–125.2	91	98.2	79.1–120.6	9	65.0	29.7–123.4	13	131.9	70.2–225.5	2	95.4	11.5–344.6
≥ 35 mrem	419	123.2**	111.7–135.6	168	128.7**	110.0–149.7	92	106.8	86.1–131.0	16	121.3	69.3–197.0	7	77.7	31.2–160.0	3	146.7	30.3–428.7
Likely gamma																		
< 3 mrem	676	142.7**	132.2–153.9	358	174.6**	157.0–193.6	86	95.9	76.7–118.4	12	102.9	53.2–179.8	12	122.0	63.1–213.2	2	108.5	13.1–392.0
3–7 mrem	306	102.0	90.9–114.1	105	94.7	77.4–114.6	88	109.2	87.6–134.6	19	149.7	90.1–233.7	12	143.9	74.4–251.5	4	199.4	54.3–510.6
8–15 mrem	496	101.7	93.0–111.1	209	108.2	94.1–124.0	110	94.9	78.0–114.3	10	57.3	27.5–105.4	14	113.7	62.2–190.8	3	115.8	23.9–338.4
≥ 16 mrem	447	122.9**	111.8–134.8	181	128.7**	110.6–148.9	100	109.4	89.0–133.1	15	107.6	60.2–177.5	10	104.8	50.2–192.7	3	140.1	28.9–409.4

[a]Adjusted by age. [b]As compared to the Pennsylvania three-county comparison. **$p > 0.01$.

well as for natural background radiation, maximum γ-radiation remained significant ($p = 0.04$), but there was no apparent trend.

As shown in Table 7, the results for all malignant neoplasms for females show no statistically significant predictors after control for smoking. The results for BTL cancer for females show both the smoking (results not shown) and likely γ-exposure were significant predictors. Likely gamma exposure remained statistically significant after controlling for smoking and background radiation ($p = 0.03$).

For the models for all LHT in females, only education was a statistically significant predictor of risk (results not shown). Natural background exposure was borderline statistically significant ($p = 0.09$).

There were also data sparseness problems with the modeling of CNS cancer in females (Table 7). No individual variables were significant predictors of risk.

There were no potential confounders or exposure variables that were statistically significant for female breast cancer. However, there were elevated RRs for both maximum γ-exposure and likely γ-exposure that exhibited increasing trends with level of exposure (RRs = 1.00, 1.20, and 1.40; RRs = 1.76, 1.76, and 2.42, maximum and likely, respectively). Only the trend for likely γ-exposure was statistically significant.

For heart disease in females (Table 7), all risk factors were individually statistically significant. Risk estimates for background exposure were elevated with a statistically significant trend apparent (estimated risk ratios were 1.00, 1.23, and 1.30, respectively; trend $p = 0.007$). After controlling for smoking and education, this association was attenuated and no longer significant. Maximum γ- and likely γ-exposures both exhibited a significant negative association with all heart disease when environmental background was included as a confounder. These relationships remained significantly negative after additional control for education and smoking ($p = 0.005$; $p < 0.001$, respectively).

Discussion

The current study presents the most extensive follow-up of the mortality experience of the 32,135 individuals living within a 5-mile radius of the TMI reactor facility at the time of the accident. In 1992, the lost-to-follow-up of this cohort was negligible ($n = 121$). The overall mortality experience from all causes for the UPitt/PDoH TMI cohort was significantly higher than the mortality experience of the surrounding three-county area.

Table 5. SMRs for breast cancer,[a] PDoH TMI cohort, white females,[b] 1979–1992.

	Breast cancer		
Risk factor	Obs	SMR	CI
Background radiation			
Low	33	113.1	77.8–158.8
Low medium	31	98.5	66.9–139.9
High medium	14	92.5	50.6–155.0
Maximum gamma			
< 8 mrem	16	88.2	50.4–143.2
8–19 mrem	22	101.3	63.5–153.3
20–34 mrem	19	103.0	62.0–160.8
≥ 35 mrem	21	119.4	73.9–182.6
Likely gamma			
< 3 mrem	11	63.2	31.6–113.2
3–7 mrem	18	107.2	63.5–169.3
8–15 mrem	24	103.9	66.6–154.7
≥ 16 mrem	25	134.2	86.9–198.1

Obs, observed.
[a]Adjusted by age. [b]As compared to the Pennsylvania three-county comparison.

However, the largest contributor to overall mortality was all heart disease, accounting for 1,670 of the 3,859 total deaths (43.3%). There was no elevation in mortality due to all malignant neoplasm for males or females in the UPitt/PDoH TMI cohort (SMR = 100 and 101, respectively). The SMR for heart disease was significantly elevated for both males and females. SMRs were not adjusted for any of the confounding factors.

An earlier PDoH mortality study (*6*) also reported an increase for all heart disease deaths. No control was made for confounding factors in that investigation. Only 20% of the UPitt/PDoH TMI cohort who were ≥ 18 years of age at the time of the accident had some education beyond high school, as compared to 34% in the three-county

Table 6. Summary of RR regression modeling, white males, 18+ years of age, 1979–1992.[a]

Cause of death	Background, RR (CI)			Maximum γ (mrem),[b] RR (CI)				Likely γ (mrem),[b] RR (CI)			
	Low	Low medium	High medium	< 8	8–19	20–34	≥ 35	3	3–7	8–15	≥ 16
All malignant neoplasm	1.00	1.14 (0.90–1.45) G $p = 0.49$	1.14 (0.86–1.51)	1.00	0.76 (0.56–1.03)	0.89 (0.63–1.24) G $p = 0.22$	0.78 (0.57–1.05)	1.00	0.85 (0.63–1.14)	0.88 (0.64–1.22) G $p = 0.50$	0.79 (0.58–1.08)
All malignant neoplasm[c]	1.00	1.14 (0.89–1.44) G $p = 0.52$	1.14 (0.86–1.51)	1.00	0.80 (0.58–1.08)	0.93 (0.66–1.31) G $p = 0.34$	0.80 (0.59–1.09)	1.00	0.87 (0.64–1.18)	0.92 (0.66–1.2) G $p = 0.56$	0.81 (0.59–1.10)
BTL cancer	1.00	1.03 (0.69–1.55) G $p = 0.10$; T $p = 0.06$	1.55 (1.00–2.41)	1.00	0.63 (0.38–1.04)	0.73 (0.42–1.27) G $p = 0.15$	0.59 (0.36–0.97)	1.00	0.68 (0.41–1.14)	0.76 (0.45–1.30) G $p = 0.24$	0.67 (0.41–1.09)
BTL cancer[d]	1.00	1.01 (0.66–1.53) G $p = 0.22$; T $p = 0.14$	1.42 (0.90–2.21)	1.00	0.72 (0.43–1.21)	0.84 (0.48–1.48) G $p = 0.44$	0.68 (0.41–1.14)	1.00	0.72 (0.43–1.21)	0.80 (0.46–1.39) G $p = 0.53$	0.72 (0.44–1.18)
LHT cancer	1.00	2.41 (0.99–5.84) G $p = 0.04$	0.83 (0.24–2.89)	1.00	1.55 (0.47–5.17)	3.40 (1.06–10.92) G $p = 0.12$	2.71 (0.88–8.30)	1.00	0.91 (0.28–2.87)	2.18 (0.75–6.29) G $p = 0.88$	1.30 (0.42–4.12)
CNS cancer[e]	1.00	0.99 (0.11–12.22) G $p = 0.9999$	0.99 (0.01–22.65)	1.00	1.15 (0.07–17.82)	1.46 (0.06–32.66) G $p = 0.999$; T $p = 0.999$	–	1.00	0.71 (0.01–16.03)	1.67 (0.12–28.97) G $p = 0.85$	–
All heart disease	1.00	0.97 (0.82–1.16) G $p = 0.47$	1.10 (0.90–1.35)	1.00	0.93 (0.74–1.17)	0.69 (0.53–0.90) G $p = 0.01$	0.78 (0.62–0.99)	1.00	0.96 (0.77–1.20)	0.82 (0.64–1.05) G $p = 0.47$	0.87 (0.69–1.09)
All heart disease[d]	1.00	0.91 (0.76–1.08) G $p = 0.30$	1.05 (0.85–1.30)	1.00	1.05 (0.83–1.33)	0.77 (0.59–1.01) G $p = 0.04$	0.84 (0.66–1.07)	1.00	1.07 (0.85–1.35)	0.91 (0.71–1.17) G $p = 0.50$	0.92 (0.73–1.17)

Abbreviations: G, global; T, trend. [a]Risk sets were adjusted to include only individuals born within 1 month of the corresponding case. [b]Models for maximum and likely γ were adjusted for background. [c]Model adjusted by smoking status. [d]Model adjusted by smoking status and educational level. [e]Exact models used due to small numbers of observed deaths.

Table 7. Summary of RR regression modeling, white females, 18+ years of age, 1979–1992.[a]

Cause of death	Background, RR (CI)			Maximum γ (mrem),[b] RR (CI)				Likely γ (mrem),[b] RR (CI)			
	Low	Low medium	High medium	< 8	8–19	20–34	≥ 35	3	3–7	8–15	≥ 16
All malignant neoplasm	1.00	1.26 (0.99–1.60) G $p = 0.16$	1.15 (0.86–1.55)	1.00	0.84 (0.60–1.16)	0.93 (0.65–1.32) G $p = 0.54$	1.05 (0.76–1.44)	1.00	1.14 (0.82–1.58) G $p = 0.55$	1.08 (0.76–1.52)	1.25 (0.90–1.73)
All malignant neoplasm[c]	1.00	1.29 (1.01–1.64) G $p = 0.11$	1.16 (0.86–1.56)	1.00	0.84 (0.60–1.16)	0.94 (0.66–1.34) G $p = 0.53$	1.05 (0.76–1.44)	1.00	1.14 (0.82–1.60) G $p = 0.53$	1.10 (0.78–1.56)	1.27 (0.92–1.76)
BTL cancer	1.00	1.24 (0.66–2.31) G $p = 0.71$; T $p = 0.43$	1.31 (0.63–2.72)	1.00	0.78 (0.34–1.80)	0.46 (0.17–1.17) G $p = 0.25$	1.00 (0.45–2.20)	1.00	1.45 (0.66–3.16) G $p = 0.03$	0.44 (0.17–1.13)	1.00 (0.46–2.62)
BTL cancer[c]	1.00	1.24 (0.66–2.33) G $p = 0.78$	1.18 (0.56–2.52)	1.00	0.81 (0.35–1.88)	0.49 (0.18–1.31) G $p = 0.44$	0.92 (0.40–2.10)	1.00	1.73 (0.77–3.92) G $p = 0.03$	0.52 (0.20–1.34)	1.09 (0.46–2.62)
LHT cancer[d]	1.00	2.15 (0.99–4.92) G $p = 0.09$	2.04 (0.76–5.36)	1.00	1.00 (0.40–2.45)	1.52 (0.58–3.99) G $p = 0.31$	0.56 (0.20–1.57)	1.00	1.20 (0.49–2.96) G $p = 0.88$	1.32 (0.50–3.52)	0.91 (0.35–2.39)
CNS cancer[e]	1.00	4.24 (0.76–48.87) G $p = 0.10$	1.23 (0.08–18.12)	1.00	1.82 (0.23–22.53)	1.48 (0.08–25.75) G $p = 0.84$	2.24 (0.24–28.01)	1.00	3.62 (0.34–186.92) G $p = 0.55$; T $p = 0.02$	3.64 (0.25–213.62	3.75 (0.29–204.09)
Breast cancer	1.00	0.74 (0.44–1.25) G $p = 0.53$	0.83 (0.43–1.60)	1.00	1.02 (0.47–2.20)	1.20 (0.53–2.71) G $p = 0.77$; T $p = 0.30$	1.40 (0.67–2.93)	1.00	1.76 (0.76–4.08) G $p = 0.17$; T $p = 0.02$	1.76 (0.73–4.22)	2.42 (1.07–5.46)
All heart disease	1.00	1.23 (1.04–1.46) G $p = 0.02$; T $p = 0.007$	1.30 (1.05–1.61)	1.00	0.59 (0.46–0.75)	0.55 (0.42–0.71) G $p < 0.001$	0.69 (0.55–0.86)	1.00	0.49 (0.38–0.63) G $p < 0.001$	0.59 (0.46–0.75)	0.66 (0.53–0.82)
All heart disease[f]	1.00	1.07 (0.89–1.28) G $p = 0.24$; T $p = 0.10$	1.21 (0.97–1.50)	1.00	0.67 (0.52–0.86)	0.64 (0.49–0.84) G $p = 0.005$	0.75 (0.60–0.95)	1.00	0.54 (0.42–0.70) G $p < 0.001$	0.68 (0.53–0.87)	0.72 (0.58–0.90)

Abbreviations: G, global; T, trend. [a]Risk sets were adjusted to include only individuals born within 1 month of the corresponding case. [b]Models for maximum and likely γ were adjusted for background. [c]Model adjusted by smoking status. [d]Model adjusted by education status. [e]Exact models used due to small numbers of observed deaths. [f]Model adjusted by smoking status and educational level.

comparison group (*22*). There are known increases in cardiovascular disease risk factors (such as smoking, obesity, alcohol, etc.) by education level that may account for some of this increase. When controlling for confounders and radiation factors in the current RR regression analysis for all heart disease, the elevations in risk were no longer apparent.

We selected the four specific cancer sites (cancers of the BTL, lymph and hematopoetic tissue, CNS, and breast) for further examination because of previously documented increases in mortality in other studies of low-level radiation exposure (*15*). Cancer of the thyroid was also initially chosen because of its radiosensitive nature (*23–26*). However, there were no deaths from thyroid cancer in this cohort.

There was a significant overall effect for natural background radiation exposure in the low–medium category (RR = 2.41) for cancers of the LHT in males. However, there is no dose–response relationship of LHT and increased background levels. Hence, this relationship is probably due to other confounders or risk factors not accounted for in this analysis.

We observed a borderline significant increasing trend in risk with increasing natural background radiation for lung cancer in males, which is similar to the findings of Hatch et al. (*10*). After adjusting for smoking status and education level in our study, this trend was further attenuated (p = 0.14). Higher mean levels of indoor radon exposure have been documented in the TMI geographic area (*27*). It has been suggested that indoor radon concentrations, a known risk factor for lung cancer (*15,16*), may be correlated with natural background radiation (*28*). Thus, it is conceivable that the observed increase in risk may be associated with indoor radon exposure.

A significant overall relationship between likely γ-exposure and BTL cancer was observed in females even after controlling for background radiation exposure, education, and smoking status. However, there was not a consistent dose–response trend in this relationship.

Although there was no overall significant effect of likely γ-exposure to the risk of breast cancer in women, an intriguing finding of this study was a significant linear trend in the RR regression for day-of-the-accident likely γ-exposure and breast cancer mortality (p = 0.02) and a nonsignificant trend for maximum γ-exposure (p = 0.30). There is a well-established relationship of ionizing radiation and breast cancer risk that has been demonstrated in numerous studies, (*15,16,29–32*). However, all of these studies reflect considerably higher absorbed doses than those in the present study. The precise levels of risk associated with low doses and low-dose rates remain uncertain (*15,16,29*). In addition, the current study did not gather information on parity, age at menarche, radiation therapy, and family history of breast cancer, which are all well known breast cancer risk factors. Additional follow-up studies such as a nested case–control design may be warranted if the present trend of an increase in breast cancer risk with accident emissions continues over time.

Additional radioactivity exposure from the TMI accident included a β-radiation dose of the released noble gases to the skin and the internal dose from the inhaled and digested radionuclides. β-Radiation is less penetrative than γ-radiation and has a shorter range in air (30 inches for xenon-133). Considering shelter, clothing, and other shielding factors, the health impact from β-radiation was substantially reduced to an unknown extent (*33*). The internal dose was estimated to constitute no more than 0.4–9.4% of the total whole-body dose (*34*). Regardless of the uncertainties of estimating, we did not observe any significant health impacts on the population in TMI in the present study. There was one thyroid cancer death among the cohort during this 13-year period. However, the overall SMR was not > 1.0 (*35*). Cancer morbidity patterns may be quite different from mortality patterns. Thus, a continuous surveillance of cancer mortality and morbidity rates, including thyroid cancer, is currently being conducted among this UPitt/PDoH TMI cohort.

In conclusion, the mortality surveillance of this cohort to date does not provide consistent evidence that low-dose radiation releases during the TMI accident had any measurable impact on the mortality experience. Most notably, the increased risk of mortality for heart disease in males and in females, observed overall, was no longer apparent after controlling for confounders and natural external background radiation. However, because the latency period for most cancers is 15 years or more, continued follow-up will provide a more comprehensive description of the mortality experience of the people residing in the TMI area at the time of the accident (*15*). In addition, the PDoH cancer registry will be an invaluable resource in assessing whether the cancer incidence experience of this cohort mirrors the mortality risks seen in the surrounding three-county area.

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