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Jessica Joyous Van Meter Date

Delayed Mortality Related to the Bhopal Gas Disaster, 1984-1994

By

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Master of Public Health

Global Epidemiology

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Committee Chair

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An abstract of

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University

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2016

Abstract

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By Jessica Joyous Van Meter

Background: Much has been written about the Bhopal, India gas release disaster. However, detailed information on mortality by different exposure areas, age groups, gender, and period of time have not been analyzed.

Methods: A cohort was formed by the Indian Council of Medical Research (ICMR), made up of a random sample of areas considered severely, moderately, and mildly affected (n= 25457, 33613, 18267, 15707 included in the cohort, respectively). The cohort follow-up began on Dec. 4, 1984, the day after the disaster, and continued through 1993. We calculated standardized rate ratios by area and calendar time, and used a negative binomial regression model to estimate the mortality rate ratios by age, gender, area, and calendar period, with the population at risk used as an offset. The change in mortality rates over time was also analyzed

Results: The severely affected population had the highest mortality rate (2.44 times that of the control group, CI = 2.07, 2.89), and the moderately had a lower mortality rate (1.3 times that of the control group, CI=1.11, 1.53), across all years, genders, and ages. In analyses by time period within areas, significant excess mortality was seen only in severely and moderately affected areas in December 1984 vs 1991-93 (RR=35.16 and RR 5.99 respectively) and in in 1985-86 vs 1991-93 (RR=1.68 and RR=1.25 respectively). The excess mortality was also concentrated in the youngest groups, ages 0-9. We found an estimated 516 deaths attributable to the gas disaster Dec 4, 1984 -1986 in the sampled cohort, which would represent approximately 727 excess deaths overall. However, the exact number of deaths on the day of the disaster (Dec. 3) are not known, but are likely to greatly exceed our estimated number.

Conclusion: These findings support the hypothesis that the gas disaster was largely an acute event, with the majority of the mortality occurring within days of the event. However, there was continued increased mortality into 1985-86, particularly among those 0-9 years old and in the severely affected area. We could not estimate total excess deaths due to the lack of data for the day of the disaster.

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Background

Bhopal is a city in Madhya Pradesh, India (1). In 1984, the population of the city was approximately 700,000-800,000 people and the city was split into 56 administrative wards (1, 2). Bhopal is centrally located and connected by rail lines to all the major cities of India. This connectivity, combined with a large supply of water in the form of two natural lakes, made it an attractive site for industry (2).

Union Carbide built a factory in Bhopal in 1969 to mix and repackage pesticides produced in the United States for the Indian market. The factory and pesticides were intended to respond to food shortages of the 1960s, to help India better feed its rapidly growing population (2). In 1977, the Union Carbide India Limited factory began producing the pesticide Sevin on the premises, using alphanaphthol and methyl isocyanate (MIC) produced in the United States. In 1980, the factory started producing the MIC itself, drawing on technical advice and factory plans provided by the United States Union Carbide. The MIC was formed through the reaction of monomethylamine (MMA) and phosgene. The MIC was produced and then stored on site in three large tanks on the grounds until it was needed (1).

There were warnings and small leaks at the factory, but safety features (such as a refrigeration system and vent gas scrubbers) were still cut by late 1984 (1, 3, 4). Just after midnight on December 2/3, 1984, what is widely regarded as the worst chemical disaster ever took place. One tank containing an estimated 27-40 tons of MIC was contaminated with water, and the resulting reaction released its contents in gaseous form over the surrounding city for 1-2 hours (1-22). Inversion and low wind speed lessened the dispersion of this gas cloud. There were no air monitoring capabilities in place to measure the concentration of MIC over Bhopal, but the Central Water and Air Pollution board estimated it to be about 27 ppm, or about 1400

times the U.S. Occupational Safety and Health Administration's workplace standard (5, 6). Though much of the focus has been on MIC, over 20 chemical compounds were found in the storage tank remnants and the tissues of those exposed, most notably hydrogen cyanide (7). Little was known about the effects and treatment for MIC, and the other chemicals present were not yet known to area physicians, so doctors were left to treat based on symptoms alone (1, 7, 8). Autopsies revealed that "severe necrotizing lesions in the lining of the upper respiratory tract and bronchioles, alveoli, and lung capillaries" were the primary findings among those who died (8).

Immediately after the disaster, the Indian Council of Medical Research (ICMR) began studying the disaster (1, 9). Thirty-six wards in Bhopal were officially designated as "gas affected," which covered approximately 559,835 residents (10). However, the actual exposure levels varied based on distance from the disaster, atmospheric conditions, whether the person ran or stayed inside, and even what kind of housing the person lived within (8). There has been "no consensus" on how many people died initially, how many lived with chronic health problems resulting from the MIC gas, or how many died later due to lingering effects of the MIC (11). The 1989 compensation settlement listed 5295 dead, 4902 permanently disabled, and 42 severely injured. After a hunger strike by 5 female survivors, India's Minister of Chemicals and Fertilizers increased the official figures to 22917 deaths, 508432 permanently disabled, and 33871 severely injured based on research from the ICMR (12). The ICMR also estimates that about 75 percent of the deaths occurred in the first 72 hours (8).

Though more information is now publically available than in 1984, there is still a much that remains unknown when it comes to MIC. It is known that it is lighter than water, highly hygroscopic, and heavier than air (thus resistant to quick dispersion in the atmosphere) (2). Animal experiments have established alveolar membrane and tracheal epithelial cells are particularly vulnerable to the effects of MIC (8). Computational studies have shown both a possible mechanism for MIC disruption of normal methylation in cells, which could result in an increased cancer risk, and MIC down regulating key immune proteins which are active against

tuberculosis, thus increasing the risk of TB in the affected population (13, 14). Experiments in mammalian cell lines have shown DNA damage resulting from MIC exposure (10). Much remains unknown regarding exactly how MIC affects the human body, if there is a "safe" level of exposure, or how to treat those who are exposed to high levels of MIC (1).

Studies have linked many health issues to the Union Carbide factory's MIC contamination of Bhopal, besides the obvious mortality. The early effects seemed to center on the eyes, respiratory tract, and skin (5). In addition, reduced T cell and phagocytic activity pointed to immune down-regulation (8). There was also an increase in perinatal and neonatal among women pregnant at the time of the disaster, and an increase in under 5 mortality in children exposed or born to exposed parents (8, 15).

As time has passed, many chronic health issues are continuing to be seen among the exposed. Eye and respiratory issues are still seen, including "pulmonary fibrosis, bronchial asthma, chronic obstructive pulmonary disease (COPD), emphysema, recurrent chest infections, keratopathy and corneal opacities" (1, 8, 9, 16). Survivors have also been shown to have higher rates of neurological symptoms and psychologic issues than the unexposed (8, 9). Women who were either directly exposed or whose mothers were exposed have been described as experiencing "menstrual chaos" where they experience frequent periods, early menopause, and infertility (8). There was reported stunting in males before puberty and reduced head circumference in females following puberty (15). A study 24 years later showed significant increases in circulating inflammatory biomarkers (17). Another study of children who were prenatally exposed showed that they too had a hyper-immune response (18). A hospital-bases study has shown increasing rates of cancer among the exposed and their offspring with increasing time since the disaster, and increased rates of gallbladder cancer compared to a control population (7, 9, 19). Despite these studies showing increased morbidity, it remains controversial whether there were any deaths attributable to the accident aside from those at the time of accident in December 1984. This is a question we will address here, as well as estimating the overall number of deaths attributable to

the disaster, estimating age specific mortality from the disaster, and evaluating the mortality effects in different areas around the plant.

Methods

Data Source:

The data analyzed within this paper was collected by the Indian Council of Medical Research (ICMR) over the years 1984-1993 (1). The data collection methods have been detailed elsewhere by the ICMR (1). Briefly, the 56 wards in Bhopal were divided into 36 wards and 20 control wards based on the presence or absence of symptoms. They then separated the affected areas into mildly, moderately, and severely affected (estimated total populations of 416869, 71917, and 32476 respectively) based on reported deaths rates from December 3-6, 1984, as collected from municipal records and burial records. To conduct a cohort follow-up, localities within the areas were chosen at random; four from the presumed severely affected area (75.6% of the total population within the area designated as severely affected), six from the moderately (45.3% of the total population of the moderately affected area, three from the mild (4.17% of the total population of the mildly affected area), and three from the unexposed (4.76% of the total population of the control area) to reach the approximately 20,000 subjects per area that they aimed to include. In January through March, 1985, houses were numbered if needed, a door-to-door survey was conducted, and each participating family was given identifying materials for future reference. Initially data was collected from the cohort fortnightly, April 1985 through December 1986. The data was then collected once every six months, through the end of 1993. The data was reported on a yearly basis, with the exception of 1984 which is data only for December 4 through 31 or the days remaining in 1984 following the disaster. No documented data on deaths during the day of the disaster itself (Dec. 3, 1984) are available, making an overall estimate of excess deaths impossible. Data was not collected in 1994 or 1995, and resumed 1996-2010 but with slightly different methods as it had been outsourced to two other agencies. We

restrict our analyses for the 1984 to 1993 period. The 1984-1993 data was then validated by ICMR, and was published in 2004 with the delay attributed to a long wait for government clearance (1, 3, 11, 20). The data was considered incomplete by many, despite the 10 year delay in publication, and there was very little analysis included (20). This paper seeks to address that lack.

Statistics:

While analyzing the data, some departures from the way ICMR presented the data became useful. Since the mildly affected area and the control area had very similar mortality rates (in fact, the mild area had a lower death rate than the control area for December 1984 and for 1985), these areas were combined to create a "combined control area" (Figures 1-4). This helped decrease the instability that resulted from the smaller population numbers for these two populations. In these Figures the rates and rate ratios were age-standardized using the total population in each age group in that year across all areasas weights .To compare the mortality rates for December 1984 with the yearly mortality rates that were available for 1985-1993, the rates in 1984 were multiplied by 12 for all ages and areas, for the severe and moderate areas. Due to the very low mortality rates in the combined control area, with some age strata having no deaths in December 1984, multiplying by 12 still produced instability in this group. Therefore for the combined control area we used mortality for 1985 for the data in 1984. .

Furthermore, a number of age categories in different areas had 0 deaths when considered yearly in the period 1985-1993. For this reason we combined the data for two years (1985-86, 1987-88, 1989-1990) or three years (1991-1993). The combining of three years at the end of the period was needed because the cohort was smaller in later years as people migrated and were lost to follow-up (Table 2).

Standardized rates per 1000 people (deaths/population *1000) for each area and gender, were computed in Microsoft Excel. Excess attributable mortality was then computed from this

(RR-1/RR), and multiplied by the number of deaths, and then extrapolated out to estimate the whole population of each area (not just the sampled group included in the cohort), to get the excess number of deaths attributable to the disaster in those years (1984 and 1985-1986) which showed statistically significant increased mortality rates.

Modeling:

All modeling was done using SAS 9.4 software. Data on aggregate rates is often modeled using the Poisson distribution (T). However, the Poisson model showed overdispersion, likely due to the lack of data on a number of variables affecting mortality (smoking, income, etc.). Hence, we instead used a negative binomial model which is more appropriate when the Poisson model is over-dispersed. . In this model, observations were death in each time period (1984, 1985-86, 1987-88, 1989-1990, 1991-1993), by age, gender, and area, with the population at risk used as an offset. Variables for age, gender, and area were included in the model.

In addition to looking at the overall model, we looked at the change in mortality rates over time, within specific age groupings and exposure areas, by using an ordinal variable for time period (1,2,3,4,5). Ages were grouped into 0-9, 10-29, 30-59, and 60+ years for these sub-analyses.

Results

The cohort at baseline is approximately equally divided between severely affected, moderately affected, and mildly affected plus control areas for each 4 year age span (Table 1). The population is a little over half male (52.6%). The cohort is also approximately equally divided between the three areas within each gender (Table 1). The overall mortality and study population by year and area of exposure are given in Table 2.

The mortality rates are shown in Figures 1-4. The rate for 1984 clearly dwarves the rates for all other years, as would be expected since MIC exposure is largely believed to be an acute

event. Likewise, the rate for the severely affected population is much higher than for any other population in 1984 and still considerably higher in 1985. It then becomes more similar to the other populations. The mortality rates for the mildly affected and the control populations are similar in both 1984 and 1985, with the mildly affected actually having less mortality than the control population. The rates are similar for men and women.

The model results from the negative binomial model rate are presented in Figure 5. Ages 5-9, 10-19, and 20-29 years old all have significantly lower mortality rates than the reference age group (ages 0-4 years old). Ages 30-39 have a mortality rate that is not significantly different from that of the youngest group. The mortality rate then climbs for each successive age group, with the 70+ having a mortality rate approximately 14 times that of the youngest. The yearly mortality rate is highest for 1984 (6.69 times that of the reference years, 1991 through 1993). 1985-1986's mortality rate across all areas remains elevated (RR= 1.17) compared to the reference years (1991-93), but not is not statistically significant (CI 0.97-1.42), and the remaining years show no elevation in mortality vs. the referent. There is no significant difference in mortality rates between males and females. The severely affected population has the highest mortality rate (2.44 times that of the control group, CI = 2.07,2.89), and the moderately have a lower mortality rate (1.3 times that of the control group, CI=1.11, 1.53), across all years and ages, and for males and females combined

When we examined the mortality rate ratios over time, holding area and age group constant, as shown in Figures 6 through 20. There was a significant decrease over time within the severely affected group for all ages together (p-value<.0001 for all years, and p-value=.0012 as well as for years 1985-1993). There was a small decline in mortality within the moderate population over the study, but this was only significant when 1984 was included (p= 0.0002). The control population had no significant change in mortality rates over time when all ages were combined. Much of the significant decline in mortality over time appears to be in the 0-9 population, with p-values <.0001 with and without the inclusion of 1984, for all exposure groups.

Interestingly, this was also true for the control population, though at a much lower rate of decline (-.47 for the control area versus -0.65 for the moderately affected, and -1.36 for the severely affected), This indicates that childhood mortality was falling for all Bhopal residents in the period 1984-1993, but faster for those affected by the gas disaster; the severe and moderate areas started from a much higher mortality in 1984. When 1984 is excluded from the data, a stronger negative trend over time is still apparent in the severe area (-0.84), but both moderate and control areas have the similar negative trends (-0.055 and -0.58), suggesting that there was still elevated mortality in the younger age group in the severely affected area.

For those aged 10-29 and 30-59 years, there was not a significant change in mortality rates over time when 1984 was excluded, indicating that the only change in mortality seen was due to the gas disaster itself. The 60+ age group only had a significant decrease in mortality over time among the most severely exposed and only when 1984 was included. This population actually had a small increase in mortality rates over time among the control group (0.18 with a p-value of 0.0022).

The excess mortality attributable to the disaster within the severely affected area was calculated to be 98% (or 384 deaths in the total population of the area) in 1984 and 40% (or 172 deaths) in 1985-86. In the moderately affected area, the excess mortality was 44% (or 22 deaths) in 1984 and 19% (or 150 deaths) in 1985-86. This indicates that approximately 727 people died from the gas disaster between December 4, 1984 and December 31, 1985 who would not have otherwise died. Figure 19 shows this excess mortality along with the estimated mortality for December 3, the day of the gas release. The death toll for this date is highly disputed, so we used one of the lower estimates, 3000 deaths (4, 7). The real number may be higher (estimates range as high as 15000), but this at least gives an idea of the relative scale between the day of the accident, the rest of the month of December, and the two following years.

Table 1. Selected baseline characteristics of the cohort followed from December 1984 through 1993. Percentages are the proportion of the total population in question (i.e. 0-4 year olds) who were in that exposure category.

Cohort Characteristic	N (%)				
Age in years	Severely Affected	Moderately Affected	Mildly Affected	Control	Total
0-4	3422 (30.5%)	3899 (34.8%)	1900 (16.9%)	2015 (17.9%)	11236
5-9	3503 (27.2%)	4662 (36.2%)	2301 (17.8%)	2429 (18.8%)	12895
10-14	3195 (27.3%)	4470 (38.2%)	2236 (19.1%)	1812 (15.5%)	11713
15-19	2577 (25.9%)	3850 (38.7%)	2145 (21.6%)	1378 (13.8%)	9950
20-24	2673 (26.0%)	3683 (35.8%)	2275 (22.1%)	1662 (16.1%)	10293
25-29	2462 (28.4%)	2866 (33.1%)	1695 (19.6%)	1642 (18.9%)	8665
30-34	1812 (26.7%)	2242 (33.0%)	1350 (19.9%)	1389 (20.4%)	6793
35-39	1418 (26.2%)	1886 (34.9%)	1041 (19.2%)	1064 (19.7%)	5409
40-44	1193 (28.2%)	1513 (35.7%)	806 (19.0%)	721 (17.0%)	4233
45-49	854 (25.6%)	1322 (39.7%)	683 (20.5%)	475 (14.2%)	3334
50-54	822 (29.5%)	1064 (38.1%)	538 (19.3%)	366 (13.1%)	2790
55-59	368 (23.7%)	614 (39.5%)	379 (24.4%)	195 (12.5%)	1556
60-64	669 (31.0%)	784 (36.3%)	417 (19.3%)	287 (13.3%)	2157
65-69	174 (24.0%)	286 (39.4%)	171 (23.6%)	94 (13.0%)	725
70+	315 (24.3%)	472 (36.4%)	330 (25.5%)	178 (13.7%)	1295
Total	25457 (27.4%)	33613 (36.1%)	18267 (19.6%)	15707 (16.9%)	93044
Gender					
Male	13449 (27.5%)	17612 (35.9%)	9472 (19.3)	8462 (17.3%)	48995
Female	12008 (27.2%)	16019 (36.3%)	8800 (20.0%)	7254 (16.5%)	44081

Table 2. Total population in the study per years and per exposure area, with the number of deaths given in parentheses.

	Severe	Moderate	Control
Dec., 1984	25457 (308)	33613 (23)	33974 (8)
1985-86	24494 (333)	33192 (362)	33672 (238)
1987-88	19253 (131)	25768 (156)	26938 (137)
1989-90	16803 (133)	22772 (178)	23545 (152)
1991-93	12862 (148)	16518 (206)	18041 (195)

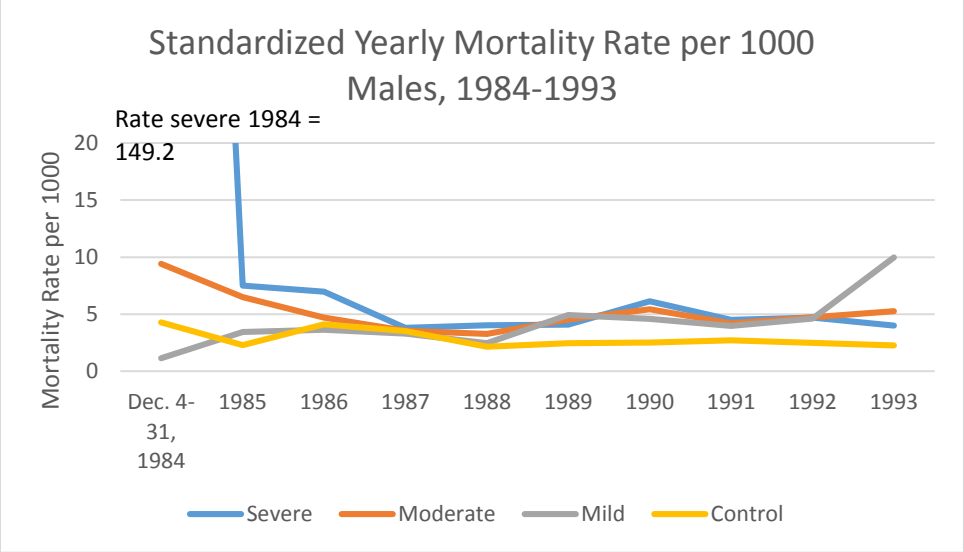

Figure 1. Mortality rates per 1000 males. Please note that the 1984 rates (for December only) are multiplied by 12 in order to give a yearly rate that can be compared to the other years. The y-axis is truncated to show detail; the mortality rates in the severely affected area for 1984 is 149.2 in the males.

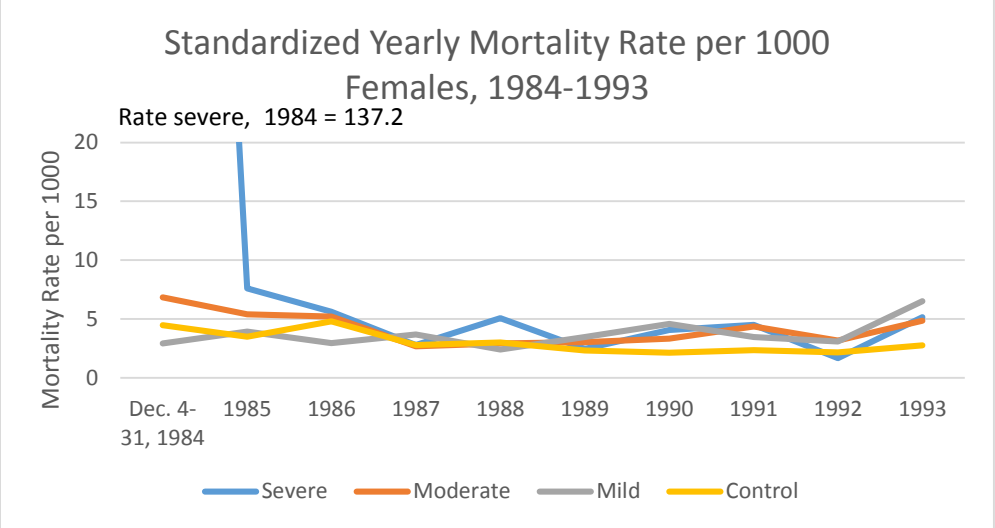

Figure 2. Mortality rates per 1000 females. Please note that the 1984 rates (for December only) are multiplied by 12 in order to give a yearly rate that can be compared to the other years. The y-axis is truncated to show detail; the mortality rates in the severely affected area for 1984 is 137.2 in the females.

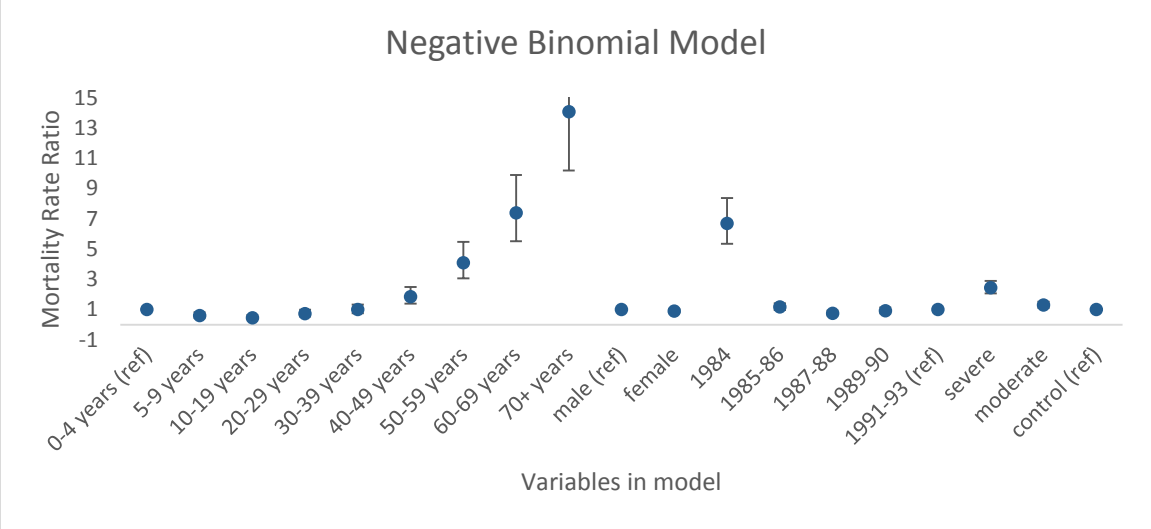

Figure 3. The mortality rate ratios from the Negative Binomial model which includes age, gender, and exposure area. The Y-axis is truncated to show detail. The upper limit of the confidence interval for age 70+ is 19.44.

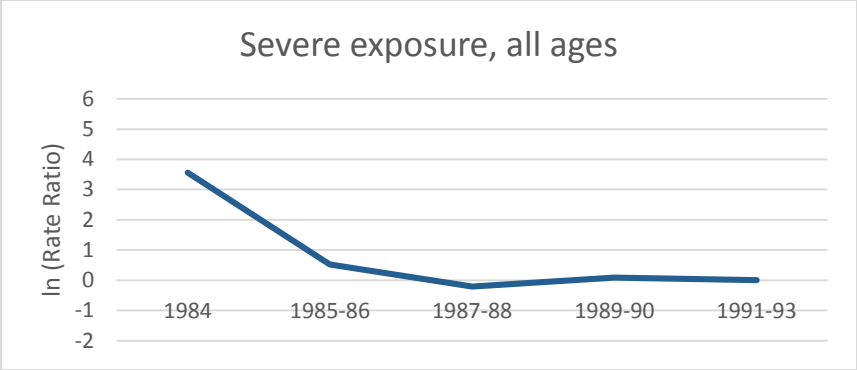

Figure 4. Mortality rate ratios over time when age is held constant, among those in the severe exposure area, based on model. The p-value for trend is <.0001 for all years, and is 0.0016 when 1984 is exluded from the model.

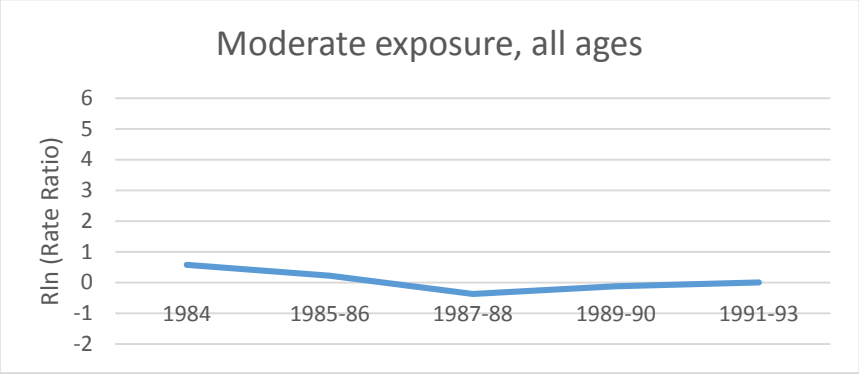

Figure 5. Mortality rate ratios over time when age is held constant, among those in the moderate exposure area, based on model. The p-value for negative trend is .0002 for all years, and is 0.173 when 1984 is exluded from the model.

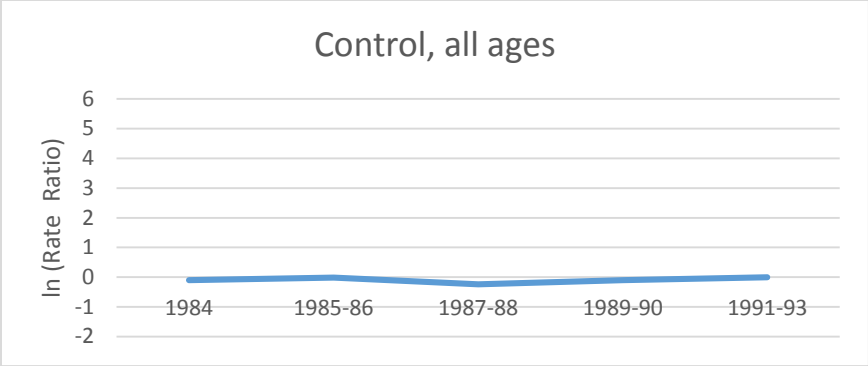

Figure 6. Mortality rate ratios over time when age is held constant, among those in the combined control area, based on model The p-values for trend were 0.77 with 1984 and 0.82 without 1985.

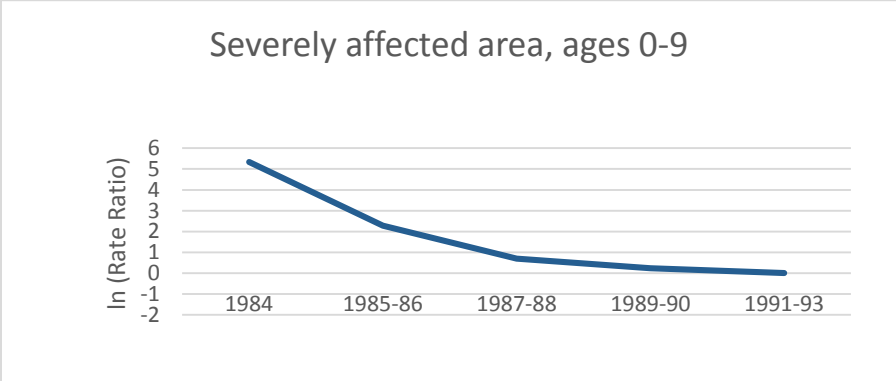

Figure 7. Mortality rate ratios over time among 0-9 year olds in the severe exposure area, based on model. The p-value for trend is <.0001 for the model, with and without 1984.

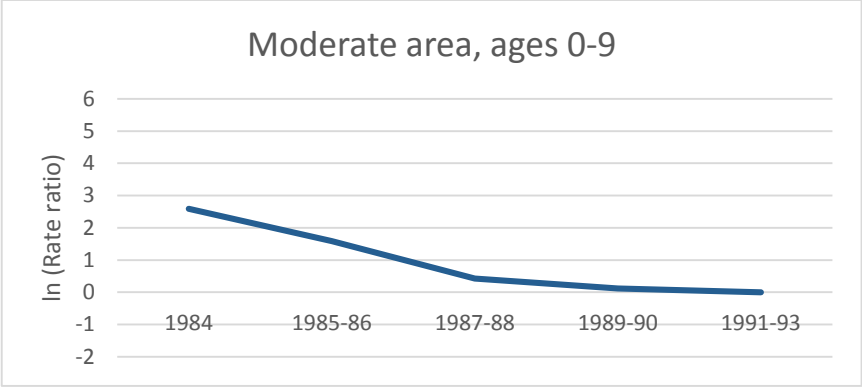

Figure 8. Mortality rate ratios over time among 0-9 year olds in the moderate exposure area, based on model. The p-value for trend is <.0001 for the model, with and without 1984.

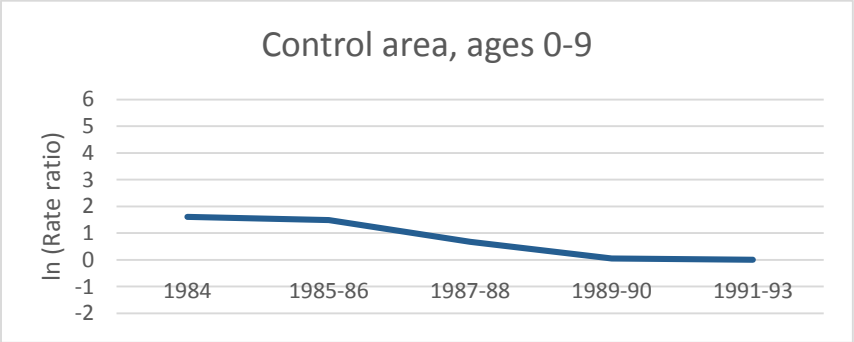

Figure 9. Mortality rate ratios over time among 0-9 year olds in the combined control exposure area, based on model. The p-value for trend is <.0001 for the model, with and without 1984.

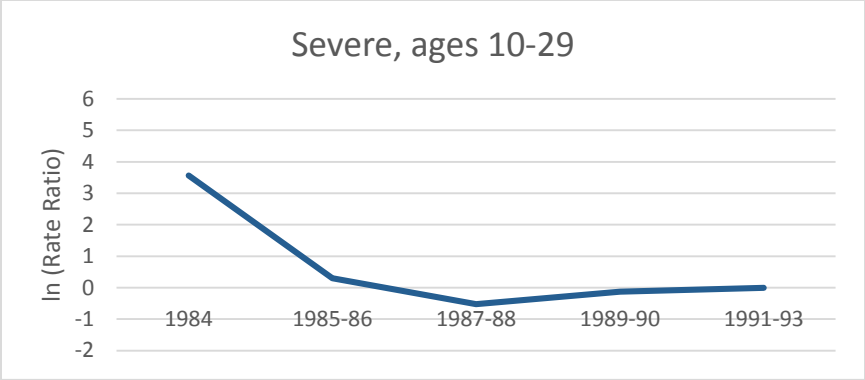

Figure 10. Mortality rate ratios over time among 10-29 year olds in the severely exposed area, based on model. The p-value for trend is <.0001 for the model, and .35 when 1984 is excluded from the model.

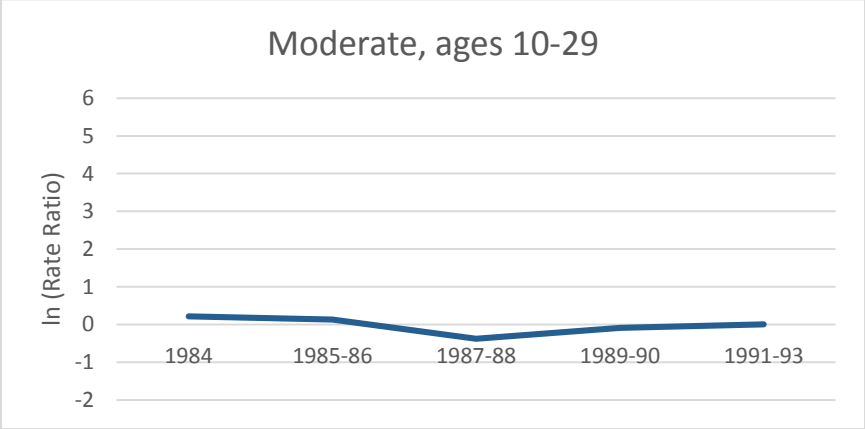

Figure 11. Mortality rate ratios over time among 10-29 year olds in the moderately exposed area, based on model. The p-value for trend is .53 for the model, and .72 when 1984 is excluded from the model.

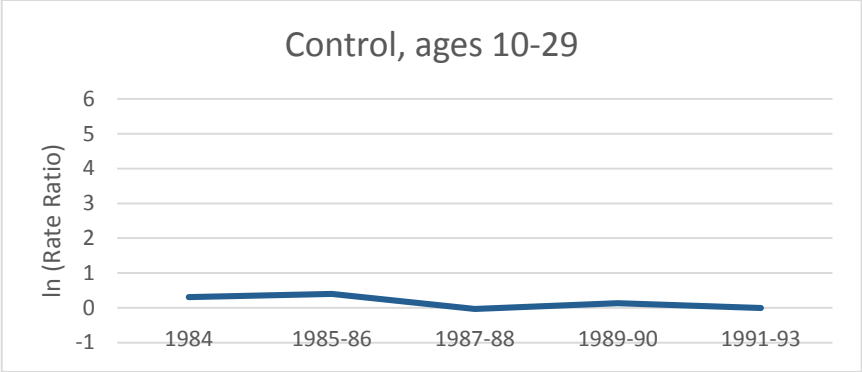

Figure 12. Mortality rate ratios over time among 10-29 year olds in the combined control area, based on model. The p-value for a negative trend is .11 for the model, and .13 when 1984 is excluded from the model.

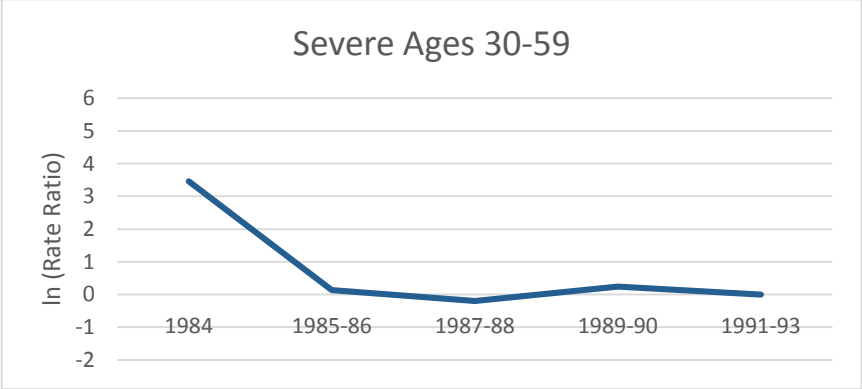

Figure 13. Mortality rate ratios over time among 30-59 year olds in the severely exposed area, based on the model. The p-value for trend is <.0001 for the model, and .91 when 1984 is excluded from the model.

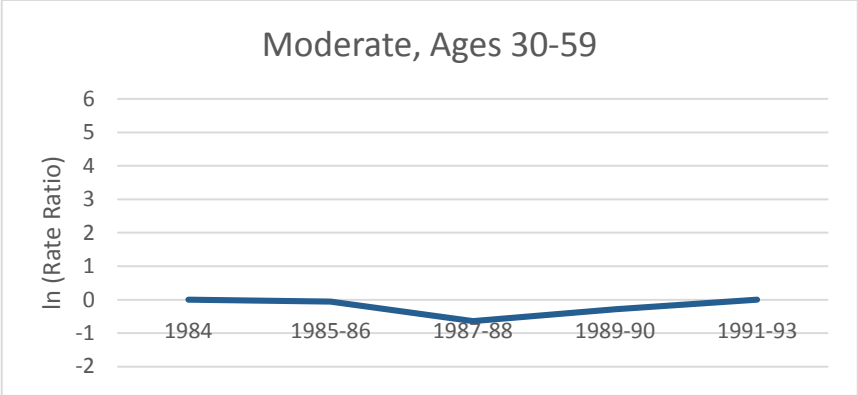

Figure 14. Mortality rate ratios over time among 30-59 year olds in the moderately exposed area, based on model. The p-value for trend is .94 for the model, and .52 when 1984 is excluded from the model.

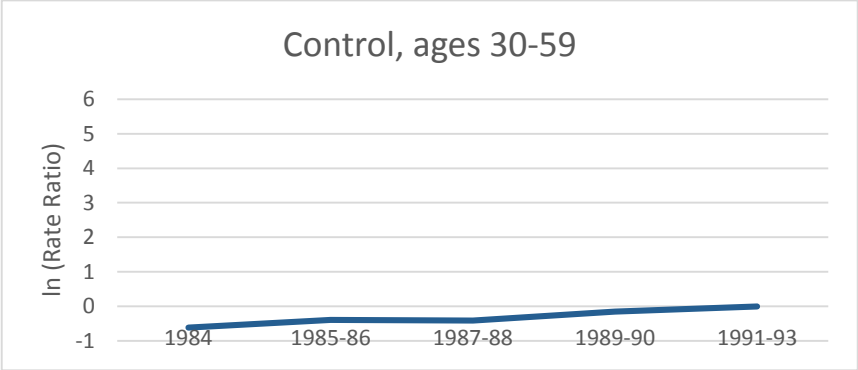

Figure 15. Mortality rate ratios over time among 30-59 year olds in the combined control area, based on model. In contrast to most other figures, here the rate of death in increasing over time. The p-value for trend is .02 for the model, and .07 when 1984 is excluded from the model.

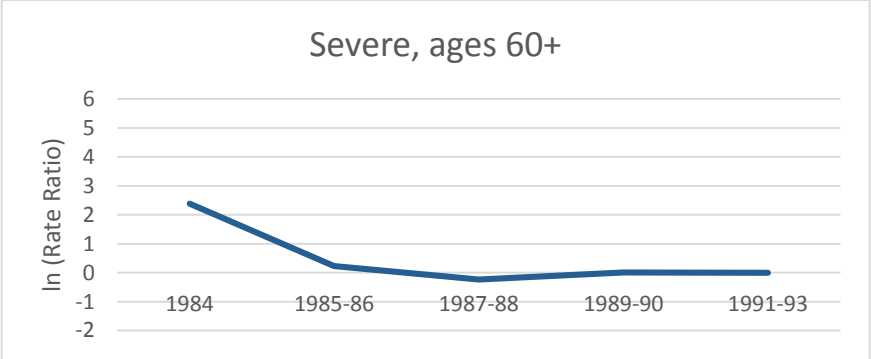

Figure 16. Mortality rate ratios over time among those over 60 years old in the severely exposed area, based on model. The p-value for trend is <.0001 for the model, and .53 when 1984 is excluded from the model.

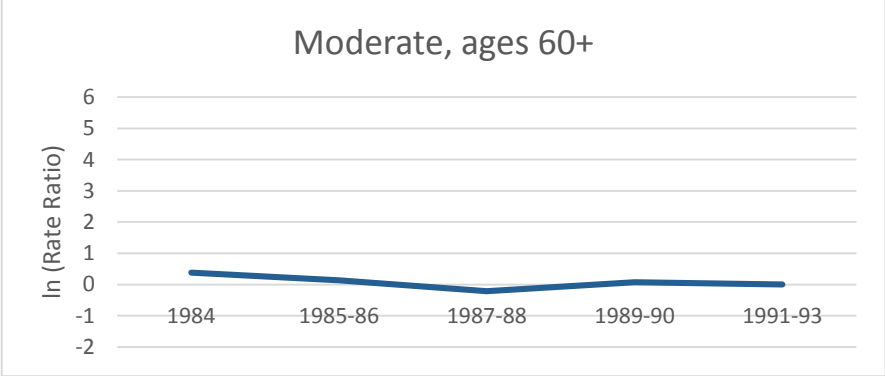

Figure 17. Mortality rate ratios over time among those over 60 years old in the moderately exposed area, based on model. The p-value for trend is .31 for the model, and .77 when 1984 is excluded from the model.

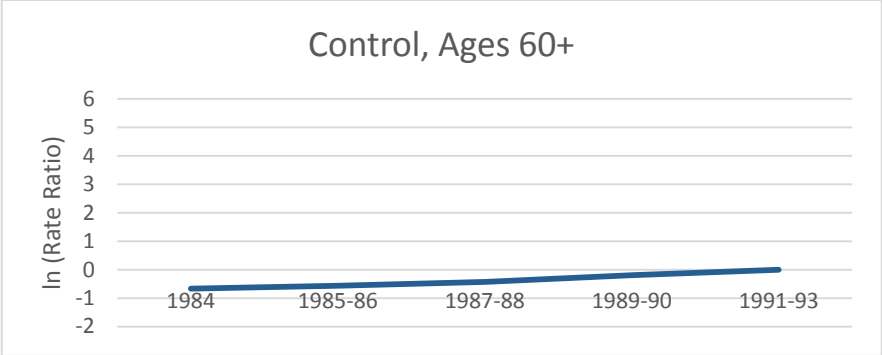

Figure 18. Mortality rate ratios over time among those over 60 years old in the combined control area, based on model The p-value for the *positive* trend is .002 for the model, and .0077 when 1984 is excluded from the model.

Discussion

From this data, it appears that the gas disaster was largely an acute occurrence and the bulk of the mortality occurred within December 1984. There was some remaining increased mortality seen after 1984, primarily in 1985, among the most severely exposed, and among those ages 0-9 years old. These findings are consistent with what others have found (5).

This study suffers from some notable limitations. The data on some possible confounders (such as housing type, smoking rates, socio-economic status, and reactions to the gas disaster itself) are either lacking in detail/quality or absent from the study (1, 5). Likewise, the loss to follow up due to migration out of the area is concerning (22). It is impossible to know about the mortality of those who were not followed. Also, the follow up within this study is relatively short. There is no indication, therefore, of whether later generations may be affected or whether there may be slower effects (such as increased rates of cancer) that can not be seen in the first ten years (13, 15, 22).

However, the study and this analysis does show the trends within the population, indicating that the lethal, non-immediate mortality was largely within the first years and mostly

among children. It also provides some understanding of the disaster which may prove helpful in the event of future industrial disasters, as well as highlighting clinical and epidemiological inadequacies that were brought to light by the Bhopal disaster (8).

The Bhopal Memorial Hospital and Research Center, a super-specialty hospital built to treat the gas victims, issued 270,000 smart cards to gas victims and their offspring by 2000 (11). They plan to study ailments within this group, and hopefully these and other studies may continue to illuminate the effects of the Bhopal Gas Disaster.

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