

# Causes and Rates of Death among Methadone Maintenance Patients Before and After the Onset of the HIV/AIDS Epidemic

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## Abstract

Causes of death and the mortality rates of active methadone patients and those who had left treatment were compared. Prior to the HIV epidemic, death rates among discharged methadone patients were more than twice that of patients who continued with their methadone treatment. However, the death rate from heroin-related causes in the post-treatment period was 51 times the rate among active patients. Alcohol-related conditions were the leading causes of death in patients more than 30 years old on methadone. During the post-treatment period, alcohol-related deaths were second to those of heroin-related causes. Alcohol-related deaths were particularly pronounced among black patients. Death rates among active male and female patients were identical, but the death rate for discharged female patients was greater than for discharged males.

With the onset of the HIV epidemic in the 1980s, AIDS-related causes became the major cause of death in treatment. However, other causes of death, such as alcohol and other medical conditions, identified prior to the AIDS epidemic, persisted. AIDS-related deaths peaked in the mid-1990s and have recently subsided. However, within the past two years, deaths related to HCV have increased to 9% of all patient deaths in a major methadone program. With the emergence of HCV, deaths from this cause are expected to eclipse AIDS-related deaths within the next decade.

**Key Words:** Methadone maintenance, mortality rate, causes of death, HIV/AIDS

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OUTCOMES OF TWO COHORTS of methadone maintenance (MM) patients, during and post-treatment, were described in detail in a seminal, NIDA-sponsored study by Dole and Joseph (1). The first cohort consisted of all patients admitted to MM treatment in New York City between 1966–1967 (n = 647), and the second, a stratified, random sample of 897 patients drawn from the roughly 17,000 admissions to MM treatment in New York City 1972. Outcomes were examined over a 10-year period, 1966–1976, and the findings showed superior patient functioning during maintenance treatment compared to the period after treatment. Twenty-five months after leaving treatment, 66% of patients who left in good standing relapsed to opiate and/or other drug abuse.

Among patients discharged for cause, 98% relapsed to opiates and/or other drug abuse.

It was noted that alcoholism was the major medical problem during treatment and after discharge, affecting about 30% of all patients; and that complications of alcoholism were the leading causes of death among patients more than 30 years old. For patients under age 30, by contrast, the leading cause of death was violence. It was typically associated with relapse and exposure to the risks of illicit-drug-related activities.

In 1981, secondary analysis of these data focused on causes of death and death rates. The mortality data for the during and after treatment intervals were examined separately. The ten-year study period ending in 1976 is one which can safely be said to have preceded the HIV/AIDS epidemic, which began in earnest in 1981. The results were recorded in an internal report for the New York State Division of Substance Abuse Services (now, the Office of Alcoholism and Substance Abuse Services, OASAS) by Joseph et al. (2), but not published.

The present article is intended to rectify this omission by presenting the findings of the 1981

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report. In addition, we discuss selected results on mortality and MM treatment covering the HIV/AIDS era to the present, relying on data from Richman (3, 4) and Petry et al. (5). The intent is to explore changes in mortality, associated with HIV/AIDS among MM patients, during these two time periods.

## Methods

### **Mortality During Treatment and After Discharge from Methadone Maintenance, Prior to the AIDS Epidemic: Findings from the Joseph, Appel, and Schmeidler (1981) Report**

The objectives of the 1981 study were: (a) to compare during treatment and after discharge mortality rates for the 1544 patients in the two admission cohorts comprising the study; (b) to present the distribution of all categories of death for active and discharged patients; (c) to compare death rates among active and discharged patients to death rates in the general population; and (d) to describe selected characteristics of the patients who died.

All deaths which occurred during treatment were accounted for. However, it was not possible to account for all post-treatment deaths. Analytically, patient histories were classified into cycles of admission and discharge, and patients included in the project had as many as three such cycles during the study period. A number of patients known to have life-threatening conditions at discharge, such as active tuberculosis, cancer, alcoholism, and drug addiction, could not be located despite extensive record searches and contacts with family, friends, and acquaintances.

Since opiate addiction can mask symptoms of serious illness, it is likely that some patients at high risk of death did not seek treatment. Having “disappeared” from the streets, and not identified in institutional records, some of these former patients may have become part of the pool of “unidentifiable” deceased in the records of Bureaus of Vital Statistics in New York City and elsewhere.

As a result, the number of post-treatment deaths observed here must be considered a conservative estimate. As evidence for this, project staff were able to obtain information on four deaths from institutional records outside New York City, after extensive tracking by phone and letter. The possibility clearly exists that other former patients died outside New York City after discharge.

Causes of death were classified as follows: (a) drug-related, (b) violence, (c) accident, (d)

medical, and (e) unknown. The causation category “drug-related” was subdivided into opiate-only, opiate with alcohol, opiate with non-opiate drugs, non-opiate-only, and alcohol-only. Cause-of-death information was developed from reasons indicated on official death certificates, from autopsy reports, and from other relevant sources, including medical and clinical data from patients’ programs. Descriptions of causes of death such as “alcohol only” is for ease of communication — actual causes could be cirrhosis and alcoholic hepatitis, among others, which may be traceable to chronic alcoholism.

Finally, mortality rates were constructed by tabulating the number of deaths of a given type in relation to the amount of time that the individuals involved were in a given status, i.e., in treatment or out of treatment. Thus, mortality rates are specified as rates per 1,000 person-years for each status.

## Results

Among the 1,544 patients studied, there were 176 deaths from all causes during the 10-year study period of 1966-1976. Deaths were verified through hospital and treatment program records, social security records, records of the Bureaus of Vital Statistics in New York City and other localities, prison records, newspaper accounts, records of the New York City Medical Examiner’s Office, and family records.

The results, presented in Table 1, show the numbers of deaths and death rates during treatment and after discharge, for the various causes of death, including the five subclasses of “drug-related.” Overall, there were 93 deaths during treatment and 83 deaths after leaving treatment. Converted to rates reflecting differences in time spent in treatment compared to out of treatment, the post-treatment death rate of 35.2 (per thousand person-years) was more than double the rate of 15.2 during treatment.

An even greater divergence was observed for the results pertaining to drug-related deaths. There were 37 during-treatment and 56 after leaving treatment. The findings for opiate-related deaths were especially striking: there were only 2 such deaths during treatment and 36 after treatment. One of the two deaths during treatment was of a patient under treatment for only three days; the second death was of a noncompliant patient who reported to the clinic only intermittently. Neither patient was pharmacologically stable. These values convert to death rates of 15.3 post-treatment and 0.3 during-treatment. The

post-treatment death rate where the cause was opiate-related was thus 51 times as large as the during-treatment rate.

The data on deaths classified as alcohol-related are also shown in Table 1. Many more of the during-treatment cohort died of alcohol-related causes than did the post-treatment group, although the adjusted rate in the latter group was slightly higher (7.2/1000 person-years vs. 5.1/1000 person-years). A similar pattern of higher during-treatment death rates compared to post-treatment death rates was found for the deaths related to medical causes, 4.2, versus 2.6 respectively.

Another way of characterizing the data is to compare the several categories of causation during treatment and after treatment in terms of relative contribution to the overall death rate. For during-treatment deaths, for example, 39.5% of the overall rate is accounted for by drug-related causes, mainly alcohol; 30.5% by medical causes; and 30.5% by the remaining categories combined (i.e., violence, accidents, and "unknown"). For post-treatment deaths, however, over two thirds of the (higher) overall death rate, 67.4%, is attributable to drug-related causes; 7.1%, to medical causes; and 25.5%, to the several other causes. In other words, drugs of all kinds play a substantially more important role in post-treatment mortality than they do for during-treatment mortality.

Mortality data were obtained from the NYC Department of Health for the population living in the following areas: Central Harlem, East Harlem, Morrisania, Mott-Haven, Bedford-Stuyvesant, Brownsville, Fort Greene, Williamsburg-Greenhaven, and Jamaica-East. Death rates for these nine areas were combined for the years 1974, 1975, and 1976, and averaged. Separate rates were computed for the age groups 18–24, 25–44, and 45–64. Death rates for the same age ranges were computed for the follow-up study subjects, one set for the during-treatment period and another for the post-treatment period.

The results are presented in Table 2. The death rates of patients are higher than those for the general population. The biggest difference in rates was found for the 25–44 age group. The rate for the general population involved the number of deaths per 1000 population per year; the rate for patients, on the other hand, involved the number of deaths relative to the cumulative years of all patients in treatment (or after treatment) adjusted to a base of 1000 patient years.

Selected features of patient addiction histories are presented in Tables 3 and 4. Table 3 shows that, compared to patients who were alive at follow-up, patients who died started using heroin somewhat later, had addiction histories that were 2–4 years longer, and first entered treatment when 4–6 years older. However, the average age

**TABLE 1**  
*Numbers of Deaths and Death Rates by Treatment Status and Cause of Death*

Cause of Death	n	During-Maintenance		Post-Maintenance	
		Rate per 1000 Person-Years	n	Rate per 1000 Person-Years	n
Drug-Related	37	6.0	56	24.0	
Total Opiates	2	0.3	36	15.3	
Opiates only	2	0.3	19	8.1	
With Alcohol	0	0	15	6.4	
With nonopiates	0	0	2	0.9	
Alcohol	31	5.1	17	7.2	
Nonopiates	4	0.7	3	1.3	
Violence	15	2.5	14	6.0	
Accident	5	0.8	1	0.4	
Unknown	8	1.3	6	2.6	
Medical	28	4.6	6	2.6	
Total	93	15.2	83	35.2	

**TABLE 2**  
*Patient Deaths and Rates for Various Age Groups by Treatment Status  
 and Compared to Selected New York City Death Rates in 1974, 1975 and 1976*

Age Group	n	During-Maintenance Rate per 1000 Person-Years	n	Post-Maintenance Rate per 1000 Person-Years	Average Selected N.Y.C. Rates*
18–24	6	8.3	4	10.8	1.6**
25–44	74	15.7	68	38.6	3.3
45–64	13	18.9	11	58.4	11.6

\* Death rates among the general population were obtained from the New York City Department of Health for the following areas: Central Harlem, East Harlem, Morrisania, Mott Haven, Bedford-Stuyvesant, Brownsville, Fort Green, Williamsburg-Greenhaven, and Jamaica-East. Rates for the years 1974, 1975, and 1976 were combined and averaged.

\*\* The average selected N.Y.C. rates depend on number of deaths per year per 1000 population in an area using 1970 census data. While similar to the rates developed for patients (rates per 1000 person-years at risk) the two rates are not completely comparable.

**TABLE 3**  
*Addiction History and Treatment Characteristics for Various Categories of Follow-up Subjects*

Patient Category	Characteristics				
	Years (Mean ± SD) Age of First Heroin Use	Years (Duration ± SD) of Addiction	Years (Mean ± SD) Age When First Entered Methadone Treatment	Months (Duration ± SD) of Methadone Treatment	Months (Duration ± SD) of Post-Maintenance Observation
Died in Treatment n = 93	20.1 ± 5	14 ± 7	34 ± 8	41 ± 33	6 ± 15
Died After Treatment n = 83	19.5 ± 5	14 ± 6	34 ± 7	24 ± 23	26 ± 24
Continuously Active n = 511	18.7 ± 4	12 ± 7	30 ± 8	76 ± 35	—
Discontinuously Active n = 262	18.7 ± 5	11 ± 7	29 ± 7	49 ± 32	22 ± 20
Discharged n = 594	18.9 ± 4	10 ± 7	28 ± 7	27 ± 29	33 ± 23

**TABLE 4**  
*Numbers of Deaths and Death Rates by Treatment Status, Sex and Ethnicity*

	n	During-Maintenance Rate per 1000 Person-Years	n	Post-Maintenance Rate per 1000 Person-Years
Sex				
Male	77	15.0	65	33.0
Female	16	15.0	18	45.0
Ethnicity				
Black	48	19.0	52	47.0
White	27	12.0	18	26.0
Hispanic	18	15.0	13	25.0
Total*	93	15.2	83	35.2

\*Total is for sex or ethnicity

at death among patients who died was essentially the same for those who died during and after treatment, 38.5 and 38.1 years of age respectively.

Table 4 shows the sex and ethnic backgrounds of patients who died during treatment and after discharge. Consistent with the roughly 3-to-1 ratio of males to females in MM treatment, more males than females died during treatment and after discharge. However, male and female death rates were identical during treatment. After discharge, the female death rate was higher than the male death rate.

The death rate for blacks was slightly higher than the rates for whites and Hispanics. In the post-treatment group, however, whites and Hispanics had nearly the same rate, while the rate for blacks was nearly double that of the latter groups. As shown in Table 5, alcohol-related conditions were a major cause of death among blacks, both during and especially after treatment. Sixty-one percent (61%) of the alcohol-related deaths occurred among blacks in the during-treatment group. In the post-treatment period, 91% of these deaths occurred among blacks. It is important to note that for combined during- and post-treatment groups, 71% of the patients had a known moderate-to-severe recorded alcohol problem before admission (6).

As shown in Table 6, the death rate during the month after admission is more than double the overall during-treatment death rate. Similarly, the death rate in the first month after discharge is more than double the overall post-treatment death rate.

### Discussion

These findings on mortality among patients during, roughly, the first decade of experience with MMT in New York City are encouraging and

disturbing at the same time. The retrospective analysis of an observational study without controls, produced remarkably similar results to those in the study by Gronbladh et al. in which randomized and waiting list controls were included (7).

The results are disturbing on a number of counts, not the least of which is the high rate of mortality associated with alcoholism, especially among black patients. In 1997, the New York State Office of Alcoholism and Substance Abuse Services was able to offer alcoholism treatment for methadone maintenance patients within the state's own treatment facilities, after educating the staff about methadone maintenance.

### Mortality among Methadone Maintenance Patients After Onset of the HIV/AIDS Epidemic

The question arises as to how mortality has changed among MM patients, active as well as discharged, since the onset of the HIV/AIDS epidemic in the early 1980s. One of the most dramatic and well-documented changes has been the overall increase in mortality among active methadone patients brought about by AIDS (3). In the report just cited, mortality data were developed and compiled for all clinics of the Beth Israel Medical Center's (BIMC) Methadone Maintenance Treatment Program (MMTP) in New York City, beginning in 1977, with findings through 1986, and preliminary 1987 results.

The mortality rate used was the percentage of patients in treatment during a given year who died in that year. Numbers of patients treated annually between 1981 and 1986 varied from a low of 8,347 in 1983 to a high of 9,011 in 1986. The mortality rate remained stable at 1% between 1977 and 1980, and was also 1% for 1981, the first year of the AIDS epidemic. In each year

**TABLE 5**  
*Numbers of Alcohol Deaths and Alcohol Death Rates by Treatment Status and Ethnicity*

Ethnicity	n	During-Maintenance*		Post-Maintenance*	
		Rate per 1000 Person-Years	n	Rate per 1000 Person-Years	n
Black	19	7.6	29	26.0	
White	5	2.2	1	1.5	
Hispanic	7	5.7	2	3.8	
Total	31	5.1	32	13.6	

\*Seventy-one percent of patients who died from alcohol related diseases had records of drinking problems before admission to methadone maintenance treatment.

Alcohol history prior to entering treatment of the remaining 29% could not be located.

**TABLE 6**  
*Number of Deaths and Death Rates by Time in Treatment and by Time After Treatment*

Interval — (Months)		Number of Deaths	Years at Risk	Death Rate
During Treatment				
0.1	1	7	171.4	40.8
1.1	3	4	320.3	12.5
3.1	6	6	430.0	14.0
6.1	9	10	383.0	26.0
9.1	12	4	348.0	11.0
12.1	12	11	1133.0	9.7
24.1	24	8	916.0	8.7
36.1	48	12	650.0	18.5
48.1	60	7	445.3	15.7
60.1		24	1332.0	18.0
Total		93	6130.0	15.2
After Treatment				
0.1	1	9	100.0	90.0
1.1	3	6	184.0	33.0
3.1	6	7	250.0	28.0
6.1	9	10	224.0	45.0
9.1	12	4	204.0	20.0
12.1	24	23	620.0	37.0
24.1	36	5	365.0	14.0
36.1	48	7	195.0	36.0
48.1	60	5	99.0	51.0
60.1		7	114.0	61.0
Total		83	2355.0	35.2

thereafter, the mortality rate increased, reaching 2.5% in 1985 and in 1986; from available results at the time of the report, the rate was projected to increase further to 3.3% for 1987. The impact of AIDS on patient mortality was demonstrated by data on AIDS-related deaths relative to all deaths in 1982 and in 1986. The AIDS-related mortality rate was 4.3% in 1982 and 39.5% in 1986, with the total number of deaths having more than doubled from 122 in 1982 to 236 in 1986.

Interestingly, as Richman's findings demonstrate (3), the absolute numbers of patients dying from other causes, e.g., chronic liver disease related to alcohol, violence, acute infectious diseases, were similar in 1982 and 1986, though the rate of drug-related deaths nearly doubled from 5.4% in 1982 (6 of 112) to 10.2% in 1986 (24 of 236). In short, while some of the causes of mortality prior to AIDS continued to be prevalent, the increased mortality among MM patients in 1986 compared to 1982 was caused largely by AIDS. Joseph and Springer (8), using a wider variety of data sources for the period of mid-1985 through mid-1987, reached a similar conclusion.

Another extensive study of mortality among MM patients was undertaken by Petry et al. (5). It covered deaths occurring in another New York

City MMTP, this one administered by the Albert Einstein College of Medicine (AECOM). It covered the years from 1975 through 1986, thus also capturing the early years of the AIDS epidemic. Causes of death were classified as AIDS, trauma (accident, violence, non-drug-induced suicide), drug overdose, alcohol-related, and medical. The data show large increases in the number of deaths in 1986 compared to 1981 — over 70 compared to about 20, with the bulk of the increase attributable to AIDS and medical causes, and a small increase in alcohol-related deaths. Interestingly, a closer examination of Richman's 1987 mortality data (3) for eight categories of medical conditions, e.g., endocarditis, heart disease, malignancy, cerebral hemorrhage, renal disease, non-alcohol liver disease, etc., showed increases for six of the eight categories, consistent with the findings by Petry et al. for medical causes (5). Trauma and drug overdose causes, on the other hand, showed a slight decline.

The mortality assessment project undertaken by Richman and colleagues for the BIMC MMTP has continued through the present. Some preliminary findings indicate that the AIDS-related mortality rate among MM patients increased each year from 1987 and peaked in 1995 — the rate in

that year was over 65%. The rate has declined significantly in the past four years to about 29%. However, in the second year of the HIV/AIDS epidemic, 1982, the rate was 4.3%. So even very recently, AIDS-related mortality among active MM patients in the BIMC system was nearly seven times its rate very early in the epidemic.

Causes of death and AIDS-related mortality among discharged MM patients appear to be less well-documented. A recent meta-analysis of studies on the risk of death in and out of methadone maintenance treatment (9) found that heroin addicts were about one-fourth as likely to die while receiving methadone maintenance as they were when not in MM treatment. The specific impact of MM seemed to reside in its ability to reduce the risk of heroin overdose or suicide. Apparently unaware of the Richman report (4), the authors also speculate that the relative risk of death during maintenance has probably increased considerably because of AIDS-related mortality.

The analysis did not address the issue of mortality among former MM patients as distinguished from treatment-naïve heroin addicts, which was partially addressed in a Swedish study by Gronbladh et al. (9). The latter study covered both voluntary discharges from MM in good standing and discharges for cause. The yearly death rate for the patients discharged in good standing, 1.65, was very comparable to the rate for active patients, 1.4, though in terms of causes, none of the active MM patients died of heroin overdose, while 50% of voluntary discharges (3/6) and 61.5% of involuntary discharges (16/26) died for this reason. No deaths related to AIDS were reported in the Gronbladh study.

Another focus of the BIMC death-monitoring project has been to identify nonalcoholic liver disease as a cause of death among MM patients. Some deaths in this category have been due to hepatitis B, but clearly, the rate for nonalcoholic liver disease overall has been increasing due largely to hepatitis C. With the identification of the virus and the recent availability of an antibody test for it (10), the BIMC death monitoring project has started reporting hepatitis C deaths separately. In 1999, hepatitis C was the cause of 9% of all patient deaths; along with unspecified liver disease, nonalcoholic liver disease represented 11% of total deaths. The number of hepatitis C deaths in 1998 was the same as in 1999, though total deaths were fewer. Thus, the pattern of mortality among active MM patients is shifting again: HIV/AIDS has declined (due partly to antiretroviral therapy) and hepatitis C has increased. In view of the long incubation period for hepatitis C

sequelae, mortality associated with them may soon eclipse mortality from AIDS.

This article was intended mainly to present findings on mortality for methadone maintenance patients both during and after treatment, findings from the Dole-Joseph follow-up study (1) which covered the 10-year period 1966–1976. Secondly, we wished to present selected findings on the same issues since the onset of the HIV/AIDS epidemic in 1981, to begin addressing how the numbers and kinds of deaths among patients had changed and in what respects they were continuous with the pre-AIDS era.

The mortality findings from the Dole-Joseph study are unequivocal in showing a higher overall mortality rate after discharge compared to during treatment, and an extremely high opiate-related rate after as compared to during treatment, a 51-fold difference. This difference helps confirm the efficacy of methadone maintenance treatment in reducing the opiate-related death rate. However, we had very little data on possible differences between patients who died during treatment compared to those who died after treatment aside from their receipt of MMT. We did find there was no difference in average age for patients who died during and those who died after treatment. Since narcotics use can mask symptoms of serious illness, which by the time of admission may be at advanced stages, the opportunity to receive medical care following admission may be to no avail for vulnerable patients. This would help explain the higher death rate related to medical causes during treatment compared to after treatment. Other findings of note concerned the powerful role of alcohol-related causes of death both during and after treatment, and the disproportionate vulnerability of black patients in this respect. The majority of alcoholic patients were clinically compliant and died during treatment; the smaller percentage of alcoholic patients who presented behavior problems were discharged and died after treatment. Also of interest is that male and female death rates were identical during treatment while the female death rate after treatment was higher than the rate for males, contrary to what is found in the general population in the same age range.

The findings of Richman (3, 4) and Petry et al. (5) were reviewed to begin examining how the AIDS epidemic affected the numbers and kinds of mortality among active and discharged MM patients. Even though these two sources covered the earliest period of the epidemic, from 1981 to 1986, it became clear that AIDS had become the dominant cause of death after 1983 (preliminary

unpublished data). The findings of Petry et al. (5) showed that medical causes of death increased, and to a lesser extent, alcohol-related causes. Richman's results indicate that the number of deaths due to causes identified prior to the AIDS period remained relatively stable after the onset of the AIDS epidemic in 1983. In addition, she reported a large increase in drug-related causes.

The meta-analysis of mortality studies among active and discharged patients and untreated addict controls by Caplehorn et al. (9) makes clear that this area needs more systematic investigation. Samples of decedents have been small, categories of causes of death, variable, and ways of computing mortality rates among patients and among general population comparison samples, also variable. The differential survival of active MM patients compared to discharged patients and untreated heroin addicts is a consistent finding from the limited data available. Systematic, objective data on mortality among MM patients is essential for supporting expansion of treatment capacity to enhance treatment outcomes, and also to curtail HIV/AIDS transmission among injection drug users. Emblematic of the dynamic nature of causes of mortality among MM patients are the very preliminary data on deaths from hepatitis C (10). Along with the decline in AIDS-related deaths, they suggest that a major shift in the pattern of MM patient mortality is underway.

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