Fluctuations in heroin purity and the incidence of fatal heroin overdose in South Western Sydney, 1993-1995

Shane Darke, Wayne Hall,
Don Weatherburn & Bronwyn Lind

Technical Report No. 58

FLUCTUATIONS IN HEROIN PURITY AND THE INCIDENCE OF FATAL HEROIN OVERDOSE IN SOUTH WESTERN SYDNEY, 1993-1995

Shane Darke[1], Wayne Hall[1], Don Weatherburn[2] & Bronwyn Lind[2]

1 National Drug and Alcohol Research Centre
University of New South Wales, Australia

2 New South Wales Bureau of Crime Statistics and Research

ISBN **0 947229 94 9**

TABLE OF CONTENTS

LOCATION OF FIGURES AND TABLES

ACKNOWLEDGMENTS

The authors wish to thank the staff at Westmead Coroners Court, Glebe Coroners Court, Campbelltown Court, Moss Vale Court, Camden Court and the Division of Analytical Laboratories. In particular, we would like to thank Noel Drew, Allan Hodda, Carol Hopping and Joanne Ross for their assistance.

EXECUTIVE SUMMARY

In order to determine the role played by heroin purity in fatal heroin overdoses, time series analyses were conducted on the purity of street heroin seizures in south western Sydney and overdose fatalities in that region. A total of 322 heroin samples were analysed by fortnightly periods between February 1993 to January 1995. A total of 61 overdose deaths occurred in the region in the study period, and were allocated to the appropriate fortnights. Alcohol was detected in 33% of cases, as were benzodiazepines.

Cross correlation plots revealed a significant correlation of 0.57 at time lag zero between mean purity of heroin samples per fortnight and number of overdose fatalities, accounting for 32% of the variance in fatalities. Similarly, there was a significant correlation of 0.50 at time lag zero between the highest heroin purity per fortnight and number of overdose fatalities, accounting for 25% of the variance in fatalities. The correlation between range of heroin purity and number of deaths per fortnight was 0.40, accounting for 16% of the variance in fatalities. A simultaneous multiple regression on scores adjusted for first order correlation indicated both the mean level of heroin purity and the range of heroin purity were independent predictors of the number of deaths per fortnight.

Overall, the results indicate that the occurrence of overdose fatalities was moderately associated with both the average heroin purity and the range of heroin purity over the period 1993-1995

1.0 INTRODUCTION

Deaths attributed to overdose remain the largest contributor to excess mortality associated with heroin use[1,2]. Excess mortality rates have been estimated to be 13 times those expected among peers of the same age and gender[3], although excess mortality rates as high as 22 have been reported among this population[4]. In Australia, the incidence of fatal heroin overdose has increased from 10.7 per million in 1979 to 67.0 per million in 1995, representing a rise from 70 deaths in 1979 to 550 in 1995[5]. A sharp increase in opioid-related mortality has also been reported elsewhere[6,7].

The causes of heroin overdose, and the rise in overdose fatalities remain unclear[8]. The classical depiction of a fatal `overdose', as the result of a quantity or quality (purity) of heroin in excess of the person's current tolerance to the drug, is the most long-standing and widely accepted explanation for death due to heroin. A natural consequence of this view is that fluctuations in heroin purity are seen as a major cause of heroin-related deaths. Media reports regularly speak of "killer heroin" batches of unusual purity. Heroin users themselves believe that variations in purity are the major cause of non-fatal and fatal overdoses[9].

Others, however, dispute the primacy given to the role of heroin *per se*, and of heroin purity, in the aetiology of overdose[8,10-14]. These authors raise three major points. First, that morphine levels in fatal overdose cases have been skewed towards the lower end of the range, with large proportions of cases having morphine concentrations below toxic levels[11,13-15]. If highly pure heroin was the major or sole cause of death, one would expect to find relatively high blood levels of morphine at autopsy in persons whose tolerance had not diminished. In fact, morphine concentrations in fatalities overlap those detected in heroin users who died of causes other than overdose[13] or in living heroin users[16,17].

Second, the `typical' overdose victim is an older, dependent user, presumably

with a high tolerance for opioids[2,14,18,19]. Finally, the concomitant use of heroin with the central nervous system (CNS) depressants alcohol[14,19-21], and benzodiazepines[1,7,14] is associated with the majority of "heroin" overdoses, focusing attention on aetiological factors other than heroin purity. The presence of alcohol at autopsy has also been related to lower blood morphine concentrations[14,21].

Despite the generally accepted role given to purity fluctuations in causing heroin overdose, little work has been conducted directly relating purity to number of overdose deaths. The only study known to the authors in which this was attempted was reported by Ruttenber and Luke[19]. In regression analysis, heroin concentration accounted for 24% of the variance in heroin overdose fatalities that occurred in the District of Columbia between 1979 and 1982.

The current study builds on an earlier study conducted by Weatherburn and Lind[22], in which street heroin seizures in south western Sydney (SWS) were analysed for purity over a two year period. This region has, in recent years, become the major distribution point for heroin in Sydney. The average heroin purity of these samples was 59%. There was a great deal of variation in the purity of samples, with samples ranging from 13% to 80%.

The existence of a heroin purity time series over a two year period provided a basis for analysing the relationship between fluctuations in purity and fatal heroin overdoses in the same region. The current study specifically examined the relationship between variations in heroin purity and fatal overdoses in the SWS region for the two year period February 1993 to January 1995. It involved cross correlating time series data on these two variables over the same period.

2.0 METHOD

2.1 *Procedure*

2.1.1 Heroin samples

The methodology for obtaining heroin samples is described in full by Weatherburn and Lind[22]. Briefly, samples were collected over a two year period, from February 1993 to January 1995 in the Sydney suburb of Cabramatta, located in the South Western Sydney Area Health Service region. Cabramatta has in recent years become the major distribution point for heroin in the Sydney region. The samples were obtained as undercover purchases made by police officers from Cabramatta Patrol, or were recovered from people arrested for heroin possession by these officers.

A total of 322 heroin samples were obtained and analysed over the study period. For the purpose of time series analysis, the study period was divided into 52 fortnightly periods. The median number of samples obtained per fortnight was 6 (range 0-13). No sample was collected in fortnight 17. The mean of samples taken in fortnights 16 and 18 was taken as an estimate of purity for that period. Similarly, the highest purity value of samples from fortnights 16 and 18 were also used to estimate the highest purity for fortnight 17.

2.1.2 Heroin-related fatalities

The coronial files of all cases positive for blood morphine at autopsy and occurring in the South Western Sydney Area Health Service region between February 1993 and January 1995 were inspected. Each case was examined to ascertain whether it was a heroin-related fatality, or death due to other causes. Heroin-related fatalities were determined by circumstances of death, police investigations and autopsy pathology conclusions. Cases due to other causes were excluded from the study. The specific date of deaths was recorded, as were toxicological analyses, circumstances of death and demographic details. A total of 61 heroin-related fatalities were identified SWS over the study period. Each fatality was assigned to the appropriate fortnight of the study period.

2.2 *Measures*

In all fortnight periods, except for fortnight 17, more than one sample was obtained. Where more than one sample was obtained for a period, the highest and mean purities were recorded for the purposes of analysis. The highest heroin purity per fortnight was analysed, as the highest purity samples would be expected to relate to number of deaths if purity is a significant factor in these deaths. As the range of purity per fortnight may be a factor, range per fortnight was also recorded.

2.3 *Analyses*

In order to determine if a relationship existed between fluctuations in heroin purity and number of overdose fatalities, time series analyses were conducted. Cross correlation functions (CCF) were examined between heroin purity series and fatal overdose series over the study period. Specifically, CCFs were estimated between the following data series: mean heroin purity and fortnightly deaths, highest heroin purity and fortnightly deaths, and range of heroin purity and fortnightly deaths. CCFs provide contemporaneous Pearson correlations at time lag zero. Where series were autocorrelated, they were differenced in order to remove trends, and the transformed series were used to estimate cross correlations between heroin purity and overdose fatalities.

In order to determine independent predictors of the number of fortnightly heroin-related fatalities, simultaneous multiple regression were performed on differenced variables. Backwards elimination of variables was used to select the most appropriate model.

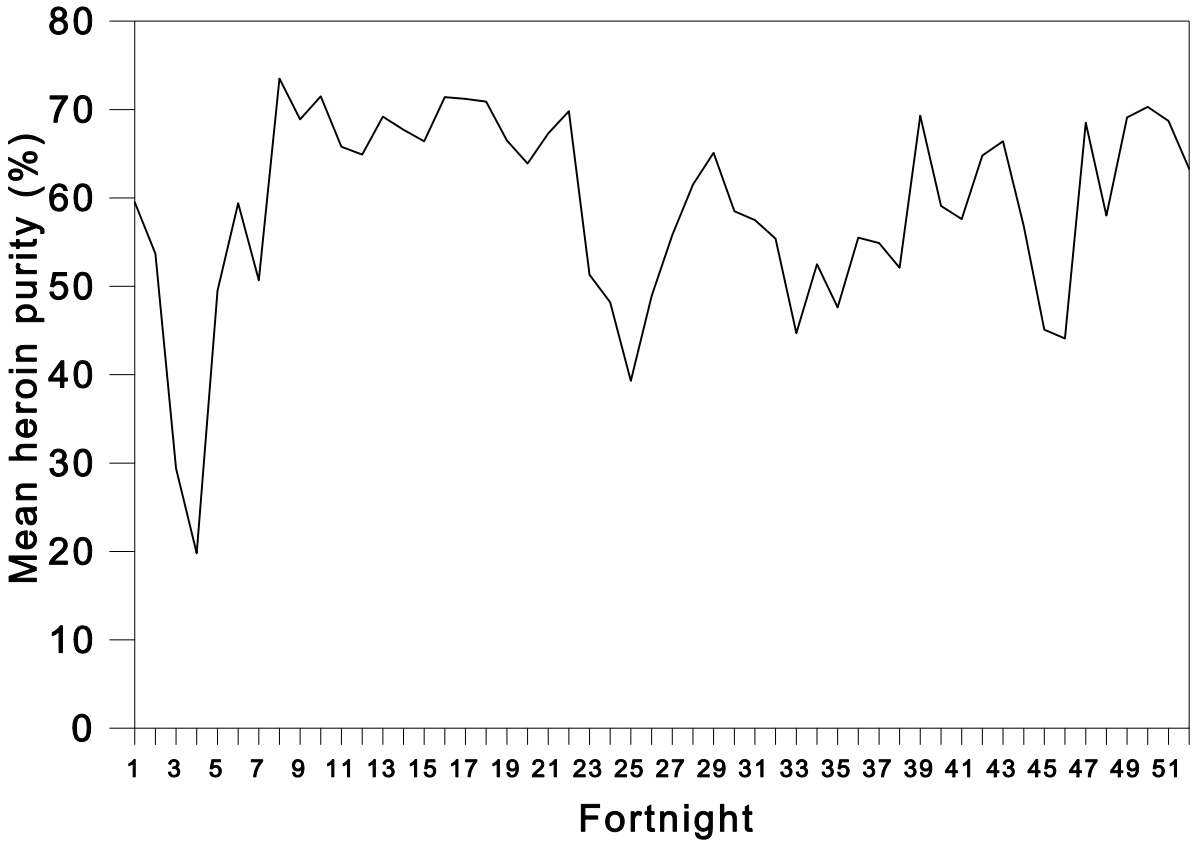
All analyses were conducted in the time series module of SYSTAT[23].

3.0 RESULTS

3.1 *Heroin purity*

As reported in Weatherburn and Lind[22], the mean heroin purity of samples collected over the study period was 58.7% (SD 14.8, range 13.2-79.8%). The mean purity of samples collected for each fortnight are shown in Figure 1. The highest mean purity for any fortnight period was 73.5% and the lowest was 19.8%. Highest heroin purity for fortnightly periods ranged from 22.7%-79.8%. The mean range of the purity of heroin samples per fortnight was 26.5%, with the range per fortnight varying from 5.9%-62.2.%.

Figure 1: Mean heroin-purity per fortnight, February 1993-January 1995



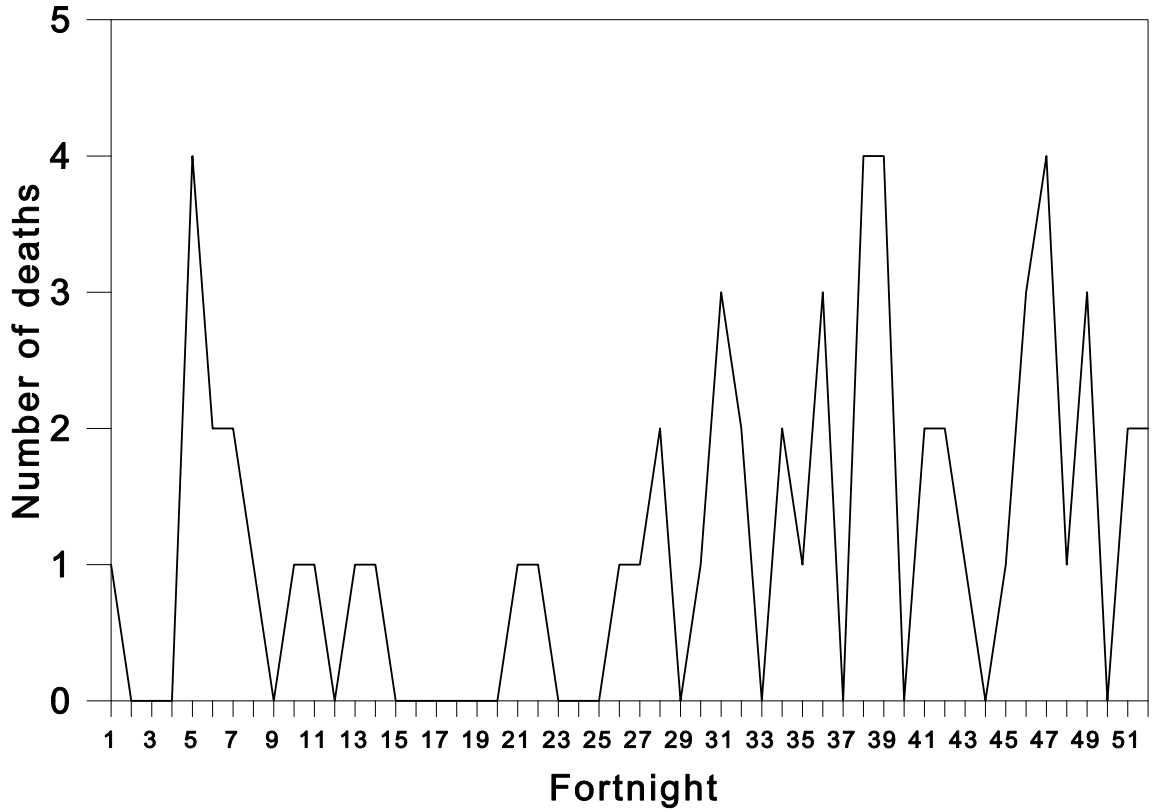
3.2 *Heroin-related fatalities*

The mean age of the 61 fatal overdose cases was 29.2 years (SD 6.8, range 16-50), with 87% male. The number of deaths in fortnightly periods ranged from

0 to 4. Nearly all subjects (60/61) were classified as long-term dependent heroin users, on the basis of police and witness statements contained in the coronial files. The number of overdose fatalities by fortnightly period is shown in Figure 2.

Figure 2

Number of deaths per fortnight, February 1993-January 1995



The median blood morphine levels at autopsy was 0.36 mg/L (range 0.06-4.5 mg/L). Alcohol was detected in 33% of cases (median BAC=0.17 g/100ml, range 0.02-0.33 g/100ml), as were benzodiazepines. Seven percent of subjects had both alcohol and benzodiazepines detected in their blood addition to morphine.

3.3 *Autocorrelations*

There was a significant autocorrelation of mean fortnightly heroin purity at time

lag 1 (r=0.61) (Appendix 1), indicating a significant relationship between purity concentrations in consecutive time periods. In order to remove trends from the series for the purposes of cross correlations, the series was differenced (Appendix 1). The resultant series had no significant autocorrelations. As there were no autocorrelations or partial autocorrelations in the transformed series, these data were employed for cross correlations with heroin fatalities.

A plot of highest fortnightly purity also showed a significant autocorrelation at time lag 1 (r=0.50) (Appendix 1). As with the mean purity series, the highest purity series was differenced to remove trend. After differencing, there were no significant autocorrelations (Appendix 1). An inspection of a plot of partial autocorrelations also revealed no significant correlations in the transformed data. As there were no significant autocorrelations or partial autocorrelations in the transformed series, these data were employed for calculating cross correlations with heroin fatalities.

There were no significant autocorrelations for the range of heroin purity. The correlation between the range of heroin purity in a period and that following it (time lag 1) was 0.07 (Appendix 1). An inspection of a plot of partial autocorrelations also revealed no significant correlations. As there were no significant autocorrelations, the series was left unchanged for calculating cross correlations.

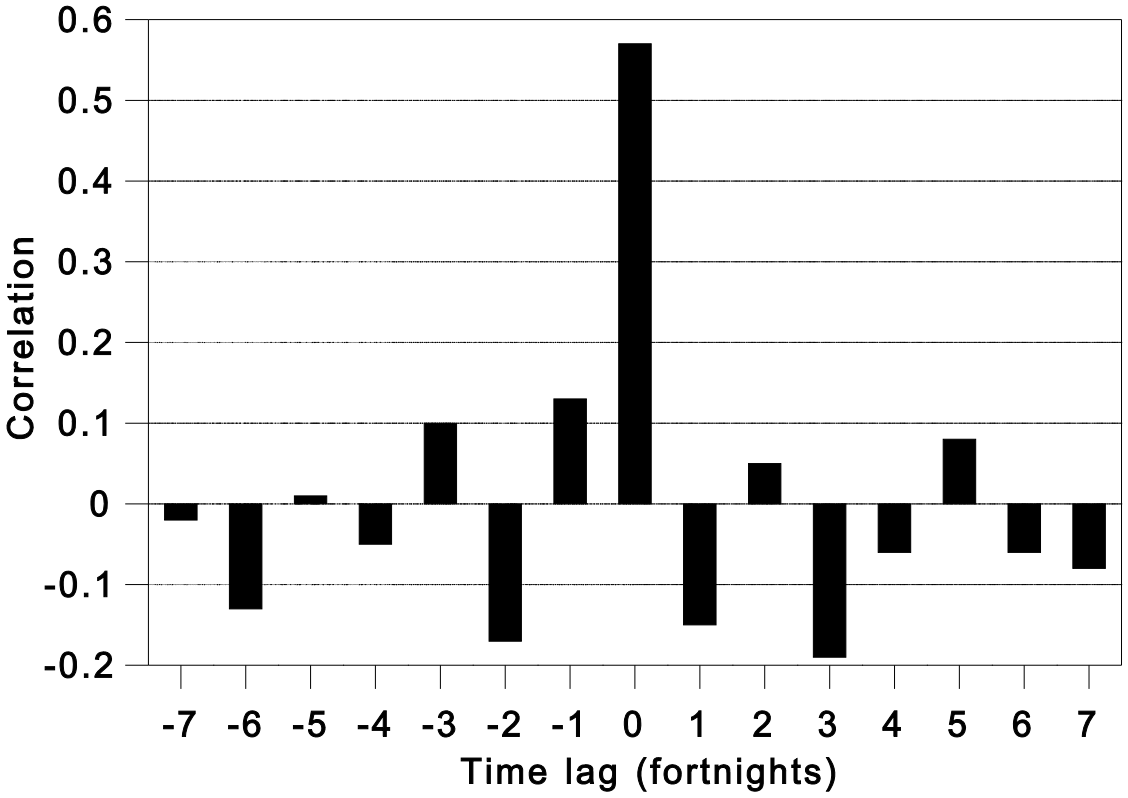
There were no significant autocorrelations for the fatal overdose series (Appendix 1). The correlation between number of deaths in a period and that following it (time lag 1) was 0.16. An inspection of a plot of partial autocorrelations also revealed no significant correlations. As there were no significant autocorrelations, the series was left unchanged for calculating cross correlations.

3.4 *Cross correlations*

3.4.1 Mean purity

Cross correlations were conducted between the transformed mean purity series and the overdose fatalities series (Figure 3). The cross correlation plot revealed a Pearson correlation of 0.57 at time lag zero, indicating that changes in mean heroin purity accounted for 32% of the variance in heroin fatalities in the same fortnightly period. There were no other significant correlations at any other time lag.

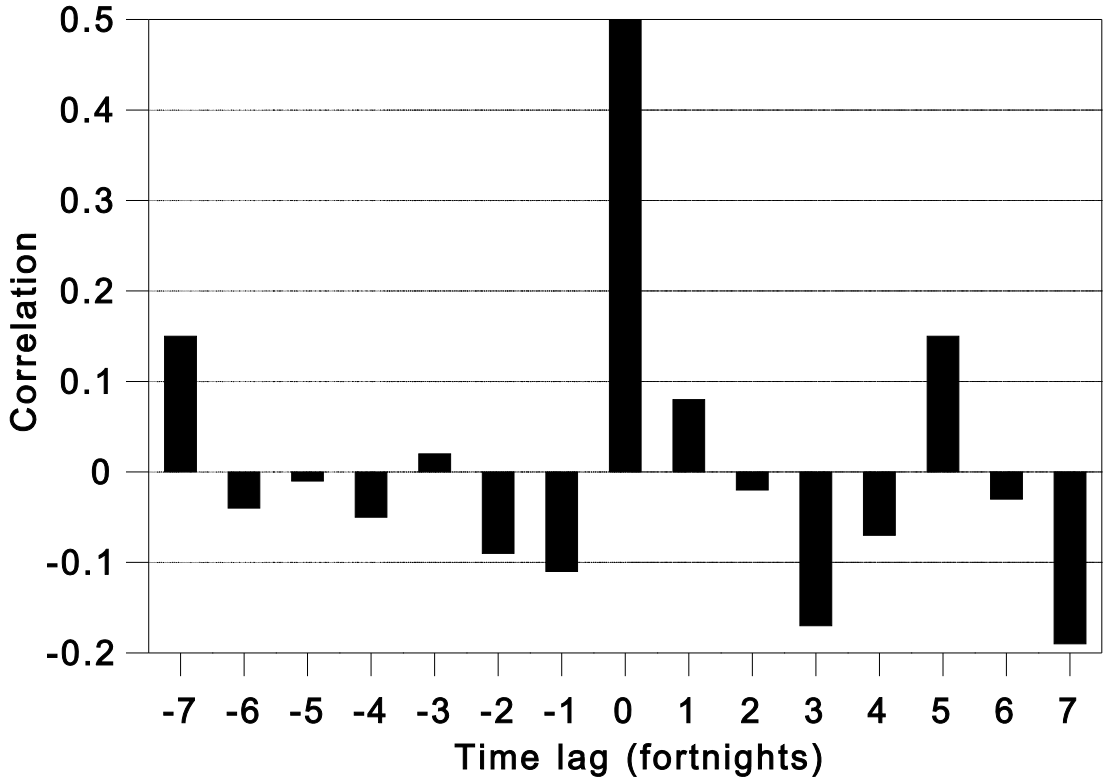
Figure 3: Cross correlation plot of mean heroin purity and fatalities



3.4.2 Highest purity

The cross correlation plot of the transformed highest purity series and fatal overdose cases is presented in Figure 4. There was a correlation at lag zero of 0.50, indicating that changes in heroin purity accounted for 25% of the variance in overdose fatalities in the contemporaneous period. There were no significant cross correlations at any other time lag.

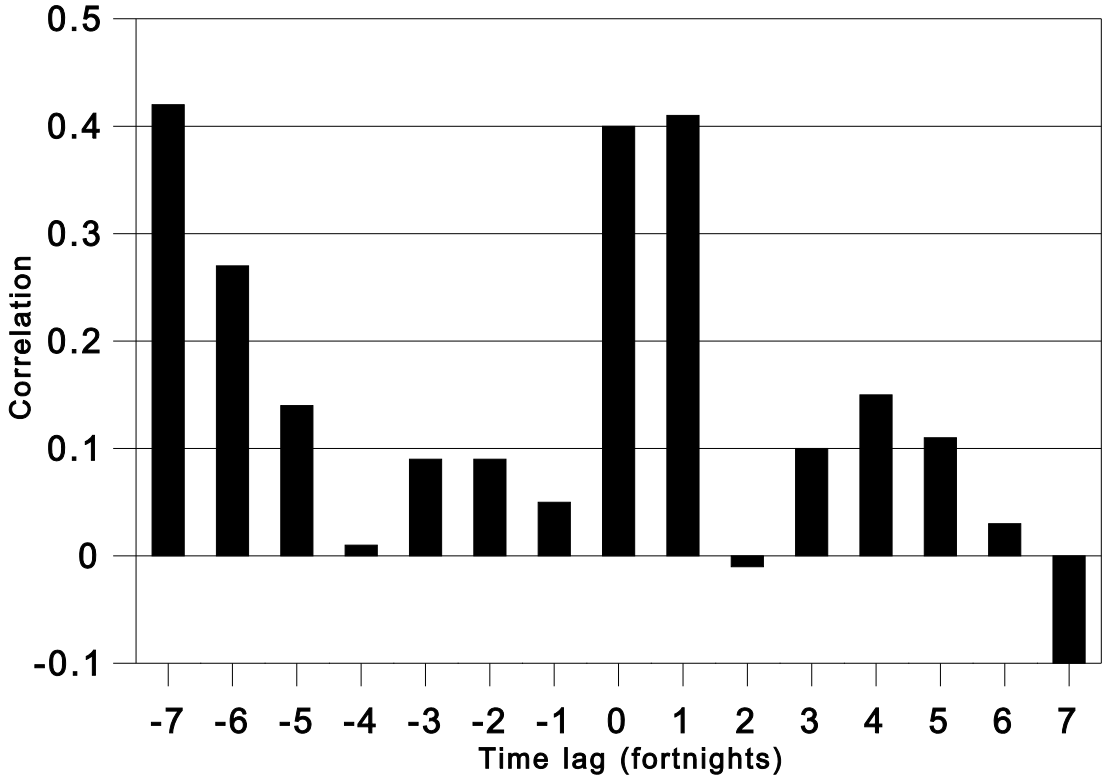
Figure 4: Cross correlation plot of highest heroin purity and fatalities



3.4.3 Range of purity

The cross correlation plot of the range of heroin purity per fortnight and fatal overdose cases is presented in Figure 5. There was a correlation at lag zero of 0.40, indicating that changes in the range of heroin purity accounted for 16% of the variance in overdose fatalities in the contemporaneous period. There were also significant cross correlations at time lag 1 (0.41) and time lag -7 (0.42).

Figure 5: Cross correlation plot of range of heroin purity and heroin-related fatalities



3.5 *Independent predictors of heroin-related fatalities*

As the range of heroin purity was also moderately correlated with the number of deaths at time lag 0, a simultaneous multiple regression was performed. The aim of this analysis was to determine whether both the mean level of heroin purity and the range of purity were independent predictors of the number of fatalities per fortnight. Both differenced mean heroin purity per fortnight and range of purity per fortnight were entered into the model. The model is displayed in Table 1.

Table 1: Simultaneous multiple regression predicting heroin-related fatalities per fortnight

Variable	Estimate	Standard Error	t value	P

Mean heroin purity	0.05	0.01	4.3	.001
Range of heroin purity	0.03	0.01	3.1	.01

R^2=0.40, F=15.7 (2,48), p<.001

As can be seen, both the mean heroin purity and the range of purity were independent predictors of number of fatalities per fortnight. The model was significant, and accounted for 40% of the variance.

4.0 DISCUSSION

The major finding from this study was the existence of a moderate correlation between heroin purity and contemporaneous overdose fatalities. Variations in mean and highest heroin purity accounted for 32% and 25% respectively of the variance in overdose fatalities occurring in the same period. These results are similar to those reported by Ruttenber and Luke[19], in which purity accounted for a quarter of the variance in overdose fatalities. Similarly, the range of the purity of samples accounted for 16% of the variance in fatalities that occurred in the same period, even though the purity of heroin samples ranged between 13% and 80%.

It is of particular note that both the mean heroin purity and the range of heroin purity were independent predictors of the number of fatalities per fortnight. Thus, in terms of the role played by purity in such fatalities, it is not only the variability of the heroin purity, but the mean level that the samples range around. A range of 50% around a mean of 20% (10%-30%)purity does not have the same implications as the same range around a mean of 60% (30%-90%). The current data provide the first indication that both factors may be of importance. Overall, however, the model containing both factors accounted for only 40% of the variance.

The current data are consistent with the arguments raised by authors cited above disputing the exclusive role of heroin attribute to variations in heroin purity in the aetiology of overdose. Variations in heroin purity would appear to play a role in the aetiology of heroin-related deaths, but that role is not the sole one.

It is impossible, of course, to determine how representative the seized samples were of all heroin samples in the region at the time of the study. Nonetheless, the current time series data are the most comprehensive yet collected, and this is only the second study of its kind ever conducted. It should also be emphasised that these were street level seizures, and not large scale seizures, in which purity may be unrelated to that sold at street level. There is certainly no reason to believe that they are unrepresentative of street level heroin, although given the relatively small numbers per period there may be some error associated with both mean purity and range of purity.

The high proportion of cases in which another CNS depressant was detected in toxicological analyses are consistent with previous studies[1,14,19]. It points to the aetiological role of factors other than purity in the aetiology of heroin-related deaths. In a third of cases alcohol was detected at autopsy, and a third had

benzodiazepines detected. In fact, the median BAC of case in which alcohol was detected was 0.17g/100ml, over three times the legal limit for driving in Australia. Both alcohol and benzodiazepines depress respiration, which is the proximal cause of death in heroin overdoses[24]. When these drugs are in conjunction with heroin, a normally tolerated dose of heroin may prove fatal. Morphine concentrations among cases in the current study ranged as low as 0.06mg/L, well below the toxic level for opioid naive individuals.

The demographic characteristics of fatal cases were consistent with earlier reports. The mean age of subjects was 29 years, with all but one fatality occurring in a person classified as heroin dependent. Such long-term older heroin users would be expected to have considerable tolerance to variations in opioid purity. The moderate correlation between the range of purity per fortnight and number of deaths also illustrates this point.

The current data have implications for the reduction of the morbidity and mortality associated with heroin overdose. Focussing interventions solely on purity *per se* is not only factually incorrect, but distracts heroin users from taking action to prevent overdose fatalities. Heroin users need to be made aware that purity is not the only, or most reality remediable, factor in heroin overdose. The role of other CNS depressants in "heroin" overdoses should be emphasised, and heroin users counselled against concurrent use of heroin with alcohol and benzodiazepines.

In summary, heroin purity was moderately correlated with overdose deaths. Heroin purity is an aetiological factor in heroin overdose, but not necessarily the most remediable factor in preventing heroin overdoses.

5.0 REFERENCES

1. O'DOHERTY, M. & FARRINGTON, A. (1997) Estimating local opioid addict mortality, *Addiction Research*, 4, 321-327.

2. OPPENHEIMER, E., TOBUTT, C., TAYLOR, C. & ANDREW, T. (1994) Death and survival in a cohort of heroin addicts from London clinics: a 22 year follow-up, *Addiction*, 89, 1299-1308.

3. ENGLISH, D.R., HOLMAN, C.D.J., MILNE, E., WINTER, M.G., HULSE, G.K., CODDE, J.P. et al (1995) *The Quantification of Drug Caused Morbidity and Mortality in Australia (1995 Edition)* (Canberra, Commonwealth Department of Human Services and Health).

4. FRISCHER, M., GOLDBERG, D., RAHMAN, M. & BERNEY, L. (1997) Mortality and survival among a cohort of drug injectors in Glasgow, 1982-1994, *Addiction*, 92, 419-427.

5. HALL, W. & DARKE, S. (1997) *Trends in opiate overdose deaths in Australia, 1997-1995*. National Drug and Alcohol Research Centre Monograph No. 49 (Sydney, National Drug and Alcohol Research Centre).

6. DE LA FUENTE, L., BARRIO, G., VICENTE, J., BRAVO, M.J. & SANTACREU, J. (1995) The impact of drug-related deaths on mortality among young adults, *American Journal of Public Health*, 85, 102-105.

7. SANCHEZ, J., RODRIGUEZ, B., DE AL FUENTE, L., BARRIO, G., VINCENTE, J., ROCA, J. et al. (1995) Opiates or cocaine: mortality from acute reactions in six major Spanish cities, *Journal of Epidemiology and Public Health*, 49, 54-60.

8. DARKE, S. & ZADOR, D. (1996) Fatal heroin overdose: A review, *Addiction*, 91, 1757-1764.

9. DARKE, S., ROSS, J. & HALL, W. (1996) Overdose among heroin users in Sydney, Australia I. Prevalence and correlates of non-fatal overdose, *Addiction*, 91, 405-411.

10. BRESCHER, E.M. (1972) The "heroin overdose" mystery and other hazards of addiction. In Brescher, E.M. *Licit and Illicit Drugs* (Boston, Little, Brown and Co)

11. FUGELSTAD, A. (1994) Heroin deaths in Stockholm, 1986-1991, *Paper presented to the Fifth International Conference on the Reduction of Drug Related Harm*, Toronto, 1994.

12. MANNING, F.J. & INGRAHAM, L.H. (1983) Drug "overdoses" among U.S. soldiers in Europe, 1978-1979. I. Demographics and toxicology, *International Journal of the Addictions*, 18, 89-98.

13. MONFORTE, J.R. (1977) Some observations concerning blood morphine concentrations in narcotic addicts, *Journal of Forensic Sciences*, 22, 718-724.

14. ZADOR, D., SUNJIC, S. & DARKE, S. (1996) Heroin-related deaths in New South Wales, 1992: Toxicological findings and circumstances, *Medical Journal of Australia*, 164, 204-207.

15. KINTZ, P., MANGIN, P., LUGNIER, A.A. & CHAUMONT, A.J. (1989) Toxicological data after heroin overdose, *Human Toxicology*, 8, 487-489.

16. ADERJAN, R., HOEMANN, S., SCHMITT, G. & SKOPP, G. (1995) Morphine and morphine glucuronides in serum of heroin consumers and in heroin-related deaths determined by HPLC with native fluorescence detection, *Journal of Analytical Toxicology*, 19, 163-168.

17. DARKE, S., SUNJIC, S., ZADOR, D. & PROLOV, T. (1997) A comparison

of blood toxicology of heroin-related deaths and current heroin users in Sydney, Australia, *Drug and Alcohol Dependence*, 47, 45-53.

18. COTTRELL, D., CHILDS-CLARKE, A. & GHODSE, A.H. (1985) British opiate addicts: an 11-year follow-up, *British Journal of Psychiatry*, 146, 448-450.

19. RUTTENBER, A.J. & LUKE, J.L. (1984) Heroin-related deaths: new epidemiologic insights, *Science*, 226, 14-20.

20. LEVINE, B., GREEN, D. & SMIALEK, J.E. (1995) The role of ethanol in heroin deaths, *Journal of Forensic Sciences*, 40, 808-810.

21. RUTTENBER A.J., KALTER H.O. & SANTINGA, P. (1990) The role of ethanol abuse in the etiology of heroin-related death, *Journal of Forensic Sciences*, 35, 891-900.

22. WEATHERBURN, D. & LIND, B. (1997) The impact of law enforcement activity on a heroin market, *Addiction*, 92, 557-569.

23. WILKINSON, L. (1990) *SYSTAT: The System for Statistics*, (Evanston IL., SYSTAT Inc).

24. PROUDFOOT, A.T. (1988) Diamorphine overdosage. In Scott, D.B. (ed) *Diamorphine. Its chemistry, pharmacology and clinical use* (New York, Woodhead-Faulkner).

APPENDIX 1: AUTOCORRELATION PLOTS

Figure A1: Autocorrelation plot of mean heroin purity

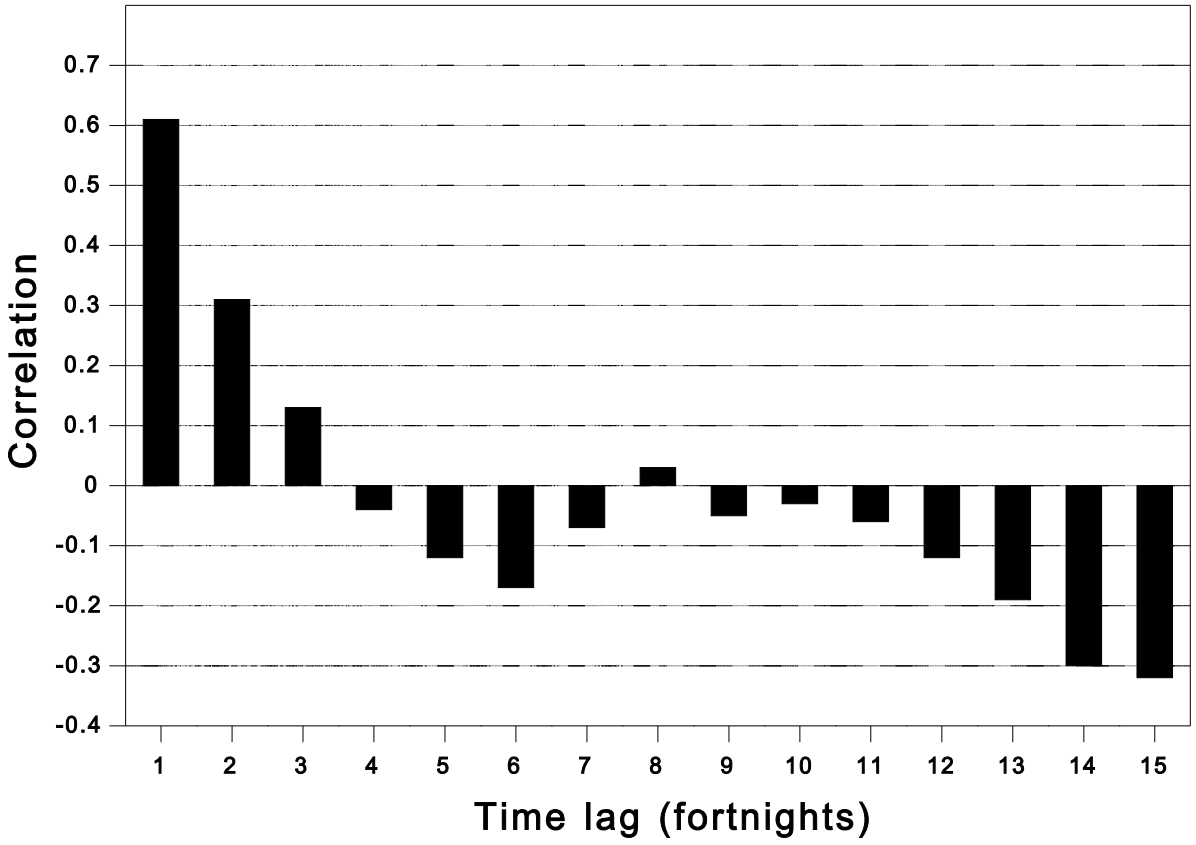


Figure A2: Autocorrelation plot of differenced mean heroin purity

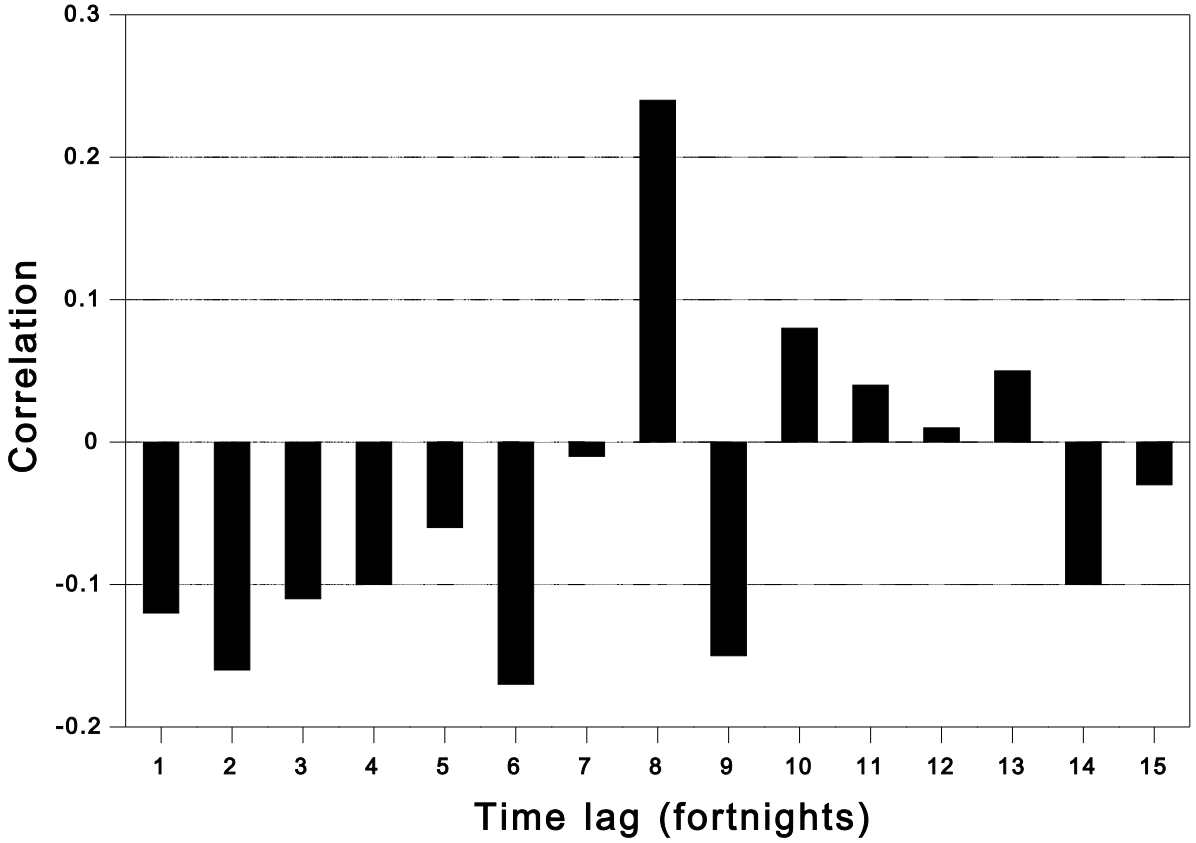


Figure A3: Autocorrelation plot of highest heroin purity

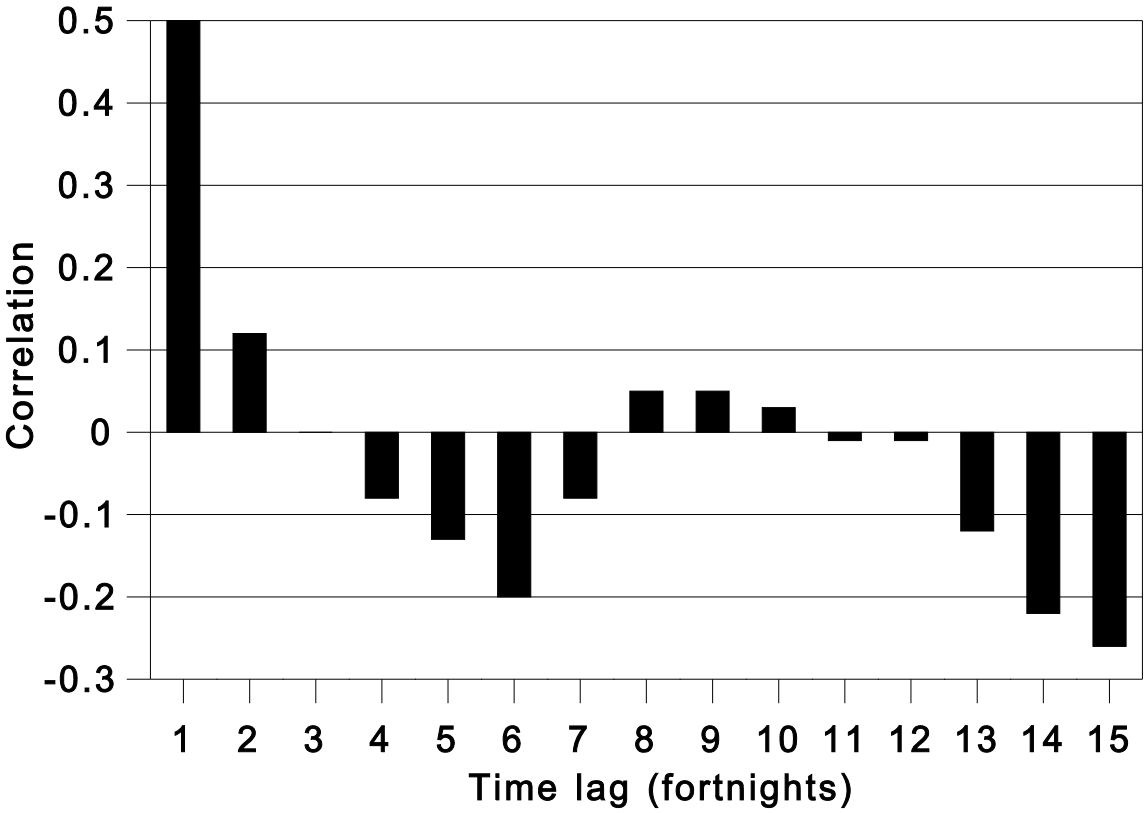


Figure A4: Autocorrelation plot of differenced highest heroin purity

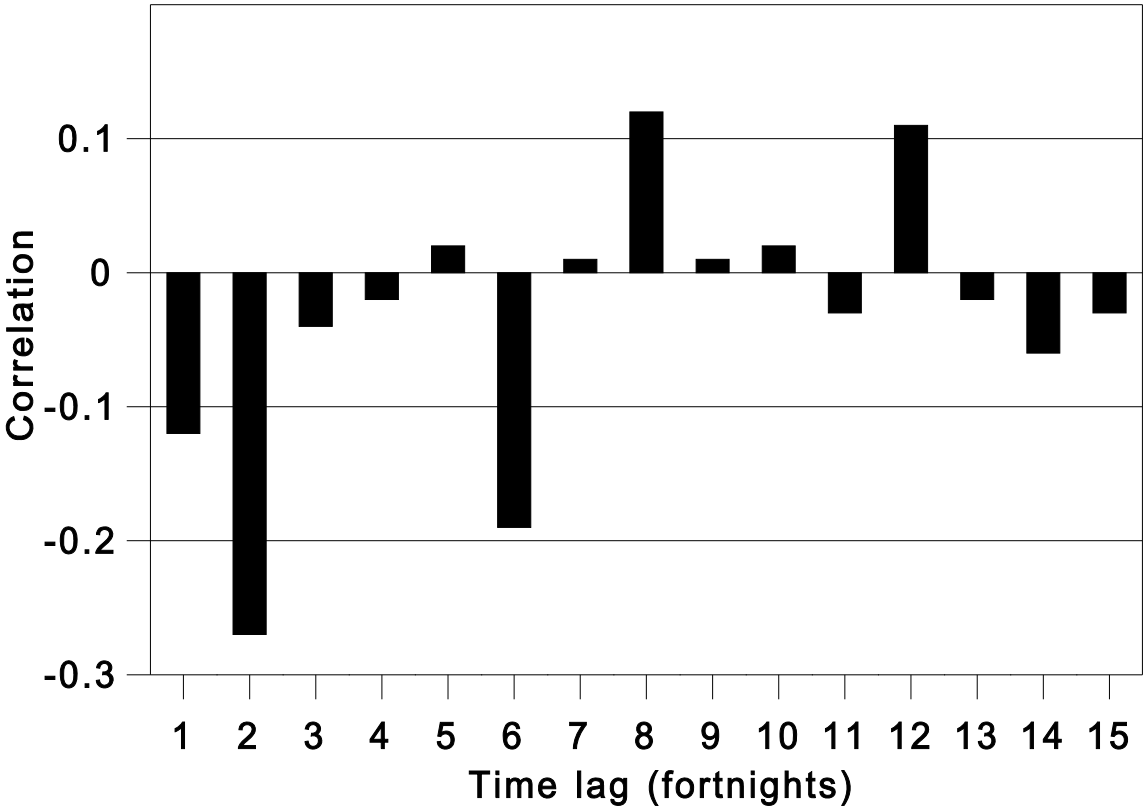


Figure A5: Autocorrelation plot of range of heroin purity

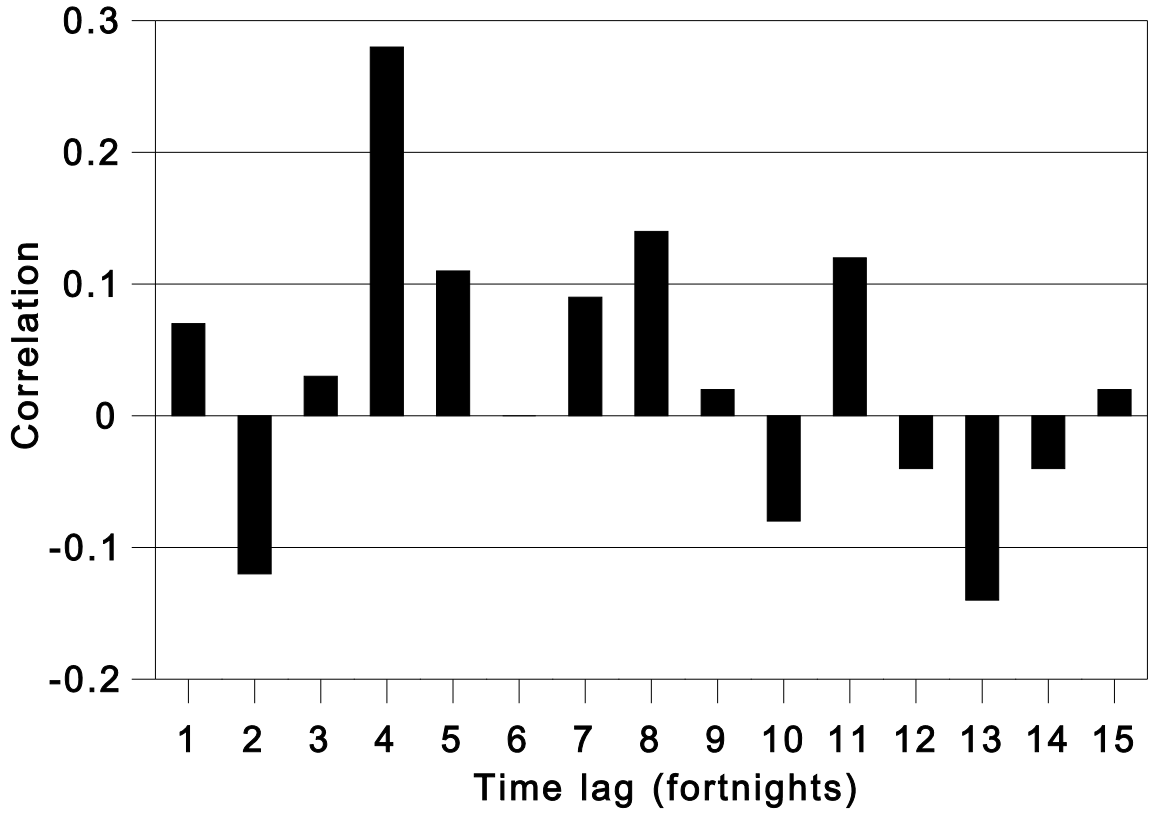


Figure A6: Autocorrelation plot of fatal overdose cases