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Suicide and other-cause mortality among heroin users in Taiwan: A prospective study

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HIGHLIGHTS

- Heroin users have a higher all-cause mortality rate and suicide rate.
- Females had higher standardized mortality ratio for suicide and total mortality.
- Younger age was related to a higher rate of overdose death.

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ABSTRACT

Aims: The present study investigates one-year incidence of mortality from suicide and other causes among heroin users in Taiwan.
Design: A prospective national register-based cohort study.
Setting: All heroin users who attended the methadone maintenance treatment (MMT) programs in all treatment centers in Taiwan.
Participants: The sample comprised 10,842 heroin users attending MMT. Between Jan 2006 and Dec 2007, cases were identified through the multiple-center register system and followed until Dec 2008 for date and cause of death on the Taiwan national mortality database.
Measurements: Standardized mortality ratios within one year of starting MMT were calculated as a ratio of actual versus expected numbers of deaths in the general population in Taiwan. Cox regression models were fitted to estimate the effects of gender, age, education and marital status as well as heroin related behaviors.
Findings: In total, 256 cases died, 67 through suicide. The mortality rate (per 100 person-years) in the first year of all-cause and suicide was 1.71 and 0.45 respectively, representing 7.5- and 18.4-fold age- and gender-standardized mortality ratio (SMR) compared to the general population. Besides, the mortality rate in the first year of overdoses, murder, HIV, somatic was 0.19, 0.02, 0.07, and 0.75 respectively, representing 68.4-, 27.7-, 76.8-, and 4.3-fold SMR increases to the general population. Older age and unemployment were independent risk factors for mortality. Females had higher standardized mortality ratio than males for suicide and all-cause mortality.
Conclusions: Results showed higher risk of suicide and other-cause mortality among heroin users in MMT than general population. Suicide is an important contributor to overall excess mortality among heroin users in MMT, and especially among women. Suicide prevention and physical health monitoring are important components of MMT programs.

1. Introduction

Heroin use is linked to premature death. An updated meta-analysis has reported the mortality rates estimated are between 0.38 and 7.76 per 100 person-years (PY), with a pooled mortality rate of 2.09 PY (Degenhardt et al., 2011). The rates are six to thirty times higher than in the general population (Darke, Degenhardt, & Mattick, 2007). The

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main causes of mortality are drug overdoses, trauma including suicide and homicide, and somatic causes including blood-borne infections (Clausen, Waal, Thoresen, & Gossop, 2009). Substance use is an independent indicator for suicide after controlling for depression, personality and life events (Cheng, Chen, Chen, & Jenkins, 2000), and the standardized mortality ratio (SMR) of suicide for heroin users is 14 times that expected of matched peers (Darke & Ross, 2002). In a national sample of drug abusers entering treatment services throughout England, it was found that more than a quarter of the patients reported suicidal thoughts before treatment (Gossop et al., 1998). It was also shown that 10.9% of heroin users attempted suicide within one month before attending the methadone maintenance treatment (MMT) (Chen et al., 2010).

Most studies of the problems and treatment responses of dependent opioid users have been conducted in Western countries (Degenhardt et al., 2011) and it is unclear whether such findings can be generalized to other sociocultural settings. In particular, only four studies of mortality among heroin dependent users have reported findings from Asia (Azim et al., 2008, 2009; Quan et al., 2007; Zhang et al., 2005). These found mortality rates that were higher than in most Western countries. However, the possible links between heroin dependence and mortality among Asian heroin users remain poorly understood since previous studies are limited by small sample size and selection bias. The present study investigates the incidence of suicide, overdoses, and all-cause mortality among more than 10,000 heroin users after attending the methadone maintenance treatment (MMT) in Taiwan.

2. Methods

Information including demographic factors and drug related behaviors was collected on all patients who attended MMT in any treatment center. This data was registered on a computerized MMT register system at the Centre for Disease Control, Department of Health, Taiwan (Taiwan CDC). The study sample comprised 10,842 cases identified through the multiple-center MMT register system between January 2006 and December 2007, and followed until December 2008 for date and cause of death on the Taiwan national mortality database. Both data was linked with anonymity for the researchers. The proposal is agreed by the ethical committee in Taoyuan Psychiatric Hospital. The proposal is agreed by the ethical committee in Taoyuan Psychiatric Hospital.

Using indirect standardization, annual age- and gender-specific mortality rates from Taiwanese national mortality statistics in 2007 were applied to the study sample to compute the expected numbers of deaths. Each person's first presentation within the study period was used in the calculation of risk over time. Since the register system started when MMT launched in Taiwan, it represented the first time ever on a methadone program for the heroin users. The standardized mortality ratio (SMR) within one year of starting MMT in the study sample was calculated as a ratio of actual deaths in heroin users versus the annual expected numbers of deaths derived from general population in Taiwan. Standardized mortality ratios were described as simple ratios rather than according to the convention of 100 = no difference, because of the large size of the effects. The Crude mortality rate (CMR) was a measure of the number of deaths against the person years of follow-up (PYFU) observed. PYFU is a summation of all participants' follow-up periods. CMR was expressed here as the number of deaths per 100 PY.

Information regarding the personal identification of all individuals (national identifier number, name, gender, location of residency and date of birth) recruited during the study period was checked against the databases of the national death register system. Within this system, all deaths from unnatural causes (suicide, overdoses and homicide) are decided on by a death verdict jointly assigned by a prosecutor and a coroner, whose main concern is the possibility of homicide. In a previous study in Taiwan, only 2 out of 117 suicides were judged to have been misclassified by coroners and prosecutors as accidental deaths (Cheng, 1995).

The risks of suicide, overdoses, death by somatic causes, and all-cause mortality (which included all unnatural deaths and deaths by natural causes) were calculated. Each person's first presentation within the study period was used in the calculation of risk over time.

All individuals traced until December 2008 by the national death register system for any length of time from their first presentation were entered into a survival analysis. The risks of suicide, of mortality excluding suicide and other-cause mortality during the follow-up period were calculated using survival curve. In the survival analysis, the time function was calculated as the number of months from the index episode of attending MMT to December 2008 (end of follow-up) for those who survived until then or until the date of death if this preceded the end of the follow-up interval. Cox regression models were fitted to estimate the effects of gender, age, education and marital status as well as heroin related behaviors (onset age, injection, comorbid substance) on survival. Hazard ratios with 95% confidence intervals were calculated. Analyses were carried out using the Statistical Package for the Social Sciences version 15.0 for Windows.

3. Results

A total of 10,842 cases of heroin users after seeking MMT were registered between Jan 2006 and Dec 2007. Follow-up information was available for all individuals until December 2008. The predominant route of heroin administration was by injection (91.3%, n = 9874). The use of amphetamines was also reported by 48.4% (n = 5229). The mean age of the sample was 36.8 years (range 16–78 years, SD = 8.4); 86.9% were males; 61.9% had fewer than nine years of education; over half were single and a quarter were married; 44.2% were unemployed.

In total, 256 (2.4%) of the sample died during the study period: 67 of these died through suicide (0.6%) and 28 (0.3%) due to overdoses. Among the causes of mortality, 112 (43.8%) of the deaths were due to somatic causes, 67 (26.2%) to suicide, 29 (11.3%) to overdoses, 10 (3.9%) to HIV, and 3 (1.2%) to murder. The incidence rate of all-cause mortality was 1.71 per 100 person-years (PY) and represented 7.5-fold age- and gender-standardized mortality ratio increases compared to

Table 1
Mortality rate per 100 person-years by age-group (N = 10,842).

Cause of death	Deaths				Crude mortality rate[a] (Person-years %)				SMR[b] (95% CI)
	<35	35–49	50+	Total	<35	35–49	50+	total	
Suicide	21	39	7	67	0.32	0.53	0.63	0.45	18.4 (13.2–24.8)
Overdoses	17	10	2	29	0.26	0.14	0.18	0.19	68.4 (41.1–106.8)
Murder	0	3	0	3	0.00	0.04	0.00	0.02	27.7 (5.6–80.9)
HIV	4	4	2	10	0.06	0.05	0.18	0.07	76.8 (28.0–167.2)
Somatic	23	65	24	112	0.35	0.88	2.15	0.75	4.3 (3.3–5.4)
All cause	81	137	38	256	1.24	1.86	3.40	1.71	7.5 (6.4–8.7)

[a] Follow-up year of cases were 6514.98, 7348.32 and 1117.29 years for ages <35, 35–49 and 50+, respectively.
[b] Standardized mortality ratios, standard population: overall Taiwan in 2007.

Table 2
Mortality rate of suicide, overdoses and all cause of death by gender: 1 year after admission date (N = 10,842).

Cause of death	Deaths (Crude mortality rate[a], person-years %)		SMR[b] (95% CI)	
	Male	Female	Male	Female
Suicide	59 (0.45)	8 (0.41)	13.5 (9.5–18.6)	27.0 (8.7–63.0)
Overdoses	26 (0.20)	3 (0.15)	42.5 (24.7–68.0)	157.4 (17.7–568.2)
Somatic	102 (0.78)	10 (0.51)	3.0 (2.3–3.8)	5.9 (1.6–15.1)
All cause	231 (1.77)	25 (1.28)	5.2 (4.4–6.1)	11.8 (6.1–20.6)

[a] Follow-up year of cases was 13029.25 and 1951.34 years for males and females, respectively.
[b] Standardized mortality ratio, standard population: overall Taiwan in 2007.

the general population in Taiwan. Heroin users in MMT had a higher incidence rate (0.75 per 100 person-years) of somatic-cause death than general population with the SMR of 4.3. Incidence of drug overdoses was 0.19 per 100 person-years, and suicide 0.45 per 100 person-years. These deaths showed 68.4- and 18.4-fold age- and gender-standardized increases, respectively (Table 1). There was also a higher HIV death rate with SMR of 76.8.

With regard to the effect of age on different types of mortality, older people (aged more than 50) had higher suicide, HIV, somatic causes and all-cause mortality rate, while young aged less than 35 was related to higher drug overdose death (Table 1). Men and women had similar rates of suicide and overdoses. All-cause mortality (crude mortality rate) was almost twice as high in men as in women. However, women had higher SMRs than men for suicide, overdose, and all-cause mortality compared to general population in Taiwan since female had lower expected death rates than men in the general population (Table 2). For the risk factors of mortality, the two independent factors were identified. These were older age and unemployment (Table 3).

4. Discussion

This prospective cohort study of Taiwanese MMT attendees showed that patients with a history of heroin use have a higher all-cause mortality rate, suicide rate and overdose mortality rate compared to the general population. More specifically, the study also found a differential effect of age on different types of mortality: older opioid dependent people had higher rates of death due to suicide, HIV, somatic causes, and all-cause mortality rate, while younger age was related to a higher rate of overdose death.

To our best knowledge, this is the first prospective study with a national cohort which has investigated the suicide and mortality of MMT participants in the Asian region. The present study also has the largest sample size compared to the four previous reports from Asia (Azim et al., 2008, 2009; Quan et al., 2007; Zhang et al., 2005). The incidence rate of all-cause mortality in the first year was 1.71 per 100 PY, representing 7.5 age- and gender-standardized increases. The finding is similar to that from a previous study in Taiwan. Chen et al. followed 1051 heroin users attending treatment of detoxification in one psychiatry center and found the annual mortality rate of patients was 1.94% (Chen, Kuo, & Tsai, 2001). Heroin users in Asia have been reported to have the highest mortality estimate (5.23 deaths per 100 PY), followed by Western Europe (2.22), North America (1.70), central Europe (1.55) and Australasia (1.08) (Degenhardt et al., 2011). The findings in the present study are more similar to those from North American studies and also findings from Europe but lower than that previously reported from Asia (Azim et al., 2008, 2009; Quan et al., 2007; Zhang et al., 2005).

The mortality rate reported in this study may also have been influenced by the sample selection process. Previous studies have shown that opioid users have a higher mortality risk when out of treatment than when in treatment (Brugal et al., 2005; Degenhardt et al., 2011). Engagement with MMT programs has been found to be associated

Table 3
Cox's Proportional Hazards Regression Models for the death from all cause with heroin use from Taiwan, 2007 (N = 10,842).

Variable	Proportion of deaths in category (%)	Un-adjusted hazard ratio		Adjusted hazard ratio	
		Estimate (95%CI)	P value	Estimate (95%CI)	P value
Gender					
Female	25/1421 (1.76)	1.00		1.00	
Male	231/9421 (2.45)	1.38 (0.91–2.09)	0.126	1.35 (0.84–2.17)	0.212
Age					
<35	81/4741 (1.71)	1.00		1.00	
35-54	137/5287 (2.59)	1.49 (1.14–1.97)	0.004	1.52 (1.11–2.07)	0.008
55+	38/814 (4.67)	2.74 (1.86–4.02)	<0.001	2.85 (1.83–4.43)	<0.001
Education					
<=9y	163/6379 (2.56)	1.00		1.00	
>9y	77/3922 (1.96)	0.77 (0.58–1)	0.054	0.87 (0.66–1.15)	0.335
Marital status					
Single	131/5525 (2.37)	1.00		1.00	
Married	55/2781 (1.98)	0.81 (0.59–1.12)	0.200	0.74 (0.53–1.04)	0.080
Divorced and widow	61/2277 (2.68)	1.13 (0.84–1.54)	0.417	1 (0.72–1.38)	0.997
Employment					
No	139/4784 (2.91)	1.00		1.00	
Yes	116/6036 (1.92)	0.67 (0.53–0.86)	0.002	0.64 (0.5–0.84)	0.001
Residence					
Urban	159/6990 (2.27)	1.00		1.00	
Rural	93/3823 (2.43)	1.10 (0.85–1.43)	0.453	0.86 (0.65–1.12)	0.263
Amphetamine					
No	151/5573 (2.71)	1.00		1.00	
Yes	105/5229 (2.01)	0.78 (0.6–1)	0.046	0.96 (0.72–1.27)	0.766
Injection					
No	20/943 (2.12)	1.00		1.00	
Yes	236/9868 (2.39)	1.1 (0.7–1.74)	0.68	0.89 (0.54–1.47)	0.655
Crime records (episodes)		0.98 (0.92–1.04)	0.471	0.97 (0.91–1.03)	0.344

with a lower mortality rate than for opioid-dependent persons not in treatment (Caplehorn & Drummer, 1999) or those who have left treatment (Bartu, Freeman, Gawthorne, Codde, & Holman, 2004; Buster, van Brussel, & van den Brink, 2002). This may be the reason why our result is lower than previous studies in Asia since the participants came from opioid users seeking maintenance treatment. Nonetheless, this population still has a much higher risk for premature death than the general population. Men have a higher crude mortality rate but a lower SMR than women. The finding is the same as that in European countries (Bargagli et al., 2006). The difference may be primarily due to the difference in general mortality between men and women (high mortality rate among adult men in general population) (Degenhardt et al., 2011).

The incidence rate of suicide mortality in the first year was 0.45 per 100 PY, representing an 18.4-fold age- and gender-standardized increase. As for overall mortality, men have a higher crude suicide rate but a lower SMR than women. Indeed, the SMR for suicide is nearly twice that for all-cause mortality. Suicide represents a substantial and important contribution to the overall excess mortality seen among heroin users in MMT. The present study found that women have a higher SMR than men for suicide. This finding differed from the results reported by a cohort study investigating fatal incidents of self-harm among those with previous self-harm history in Taiwan (Chen et al., 2011). Chen et al. reported that the suicide SMR was twice as high in men compared with women among a sample with a history of self-harm (Chen et al., 2011). It is suggested that female heroin users in MMT are at greater risk of suicide compared to non-using female peers than males are compared to their male peers (Darke & Ross, 2002). Whether the difference is merely due to the difference in general mortality between men and women or heroin use has unique risk for women needs further investigation. For example, heroin can affect the menstrual cycle (Schmittner, Schroeder, Epstein, & Preston, 2005) and menstrual cycle is associated with suicide (Dogra et al., 2007).

Few studies have explored the issue of age-specific mortality. We found a differential effect of age on different types of mortality. Older people had higher suicide, HIV, somatic causes and all-cause mortality rate, while younger age was related to higher overdose death. The results were similar to the findings from Norway (Clausen et al., 2009). In Clausen's study, they found younger opioid users were at greater risk of overdose while older users were at higher risk of both somatic and traumatic deaths. Another retrospective study from England and Wales also reported that older heroin users in MMT were more likely to die of pre-existing medical conditions, whereas deaths among younger users were associated with drug overdoses (Webb et al., 2003). Higher suicide and somatic related mortality in elder people is consistent with the findings in general population and in self-harm population (Chen et al., 2011). We found the effect of older age on all-cause mortality remained significant even after controlling for gender, education, marital status, injection, poly-substance use, and unemployment. Higher somatic mortality in older people may be due to that addiction is associated with an altered profile of common biomarkers of aging, such as chronic antigenic overload, immune stimulation, immune suppression and signs of accelerated aging (Reece, 2007). Increasing risk of death for older users by exacerbation of a pre-existing medical condition is also suggested (Webb et al., 2003). On the contrary, it has been reported that young heroin users have less knowledge of the risk factors for unintentional opioid overdose compared with older users (Neira-Leon et al., 2006), so younger people are more likely to die of overdose. We suggest that clinicians need to pay attention to the different risks for different age population such as overdose risk for young people but somatic problems or suicide risk for older users. Unemployment was also found to be an independent predictor of mortality effect and was also reported in another MMT cohort study in Spain (Brugal et al., 2005). Unemployment may be a marker of poor social integration or of the difficulty in obtaining access to and benefit from available health services (Brugal et al., 2005).

The study findings are subject to certain limitations. The study only looks at the mortality rate in heroin users over a one year period after seeking MMT. Whether the longer term effects are similar to this relatively short term finding needs further investigation. We do not have the exact treatment duration of MMT for participants and cannot estimate the effect of treatment on different mortality. We do not measure other important factors such as mental illness, HIV, or HCV, and cannot evaluate the effect of these factors on the observed mortality rate. Another limitation is that the cause of death could be incorrectly recorded.

5. Conclusion

The present study showed the greatly elevated risk of premature death among heroin users in Taiwan. The mortality rate is not higher than those from North American and Europe studies as previous Asia studies suggested. There was a high risk of premature death through suicide. Suicide should be recognized as an important contributor to the overall excess mortality among heroin users, and especially among female heroin users after seeking MMT. In addition to standard addiction-oriented interventions, treatment services should give attention to overdose prevention and to factors which are suggestive of suicide risk. In practice, it may be extremely difficult to draw a clear distinction between accidental and deliberate overdoses. However, drug dependent patients who report current suicidal ideation or a history of suicide attempts or self-harm may require special and immediate treatment response. Clinical services should be alert to this issue and should conduct a careful assessment where there are indications of suicidal risk (Gossop, 2003). There is also increasing awareness and concern about the physical health problems among drug users (Volkow & Li, 2005), and additional attention is needed for the monitoring and treatment of physical health problems since around 50% of the deaths in our study were caused by somatic problems.

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Contributors

Authors Vincent Chin-Hung Chen, Happy K.L. Tan designed the study and wrote the protocol. Author Sun-Yuan Chou, Kuen-Hong Wu, and Chia-Hsiang Chan conducted literature searches and provided summaries of previous research studies. Author Charles T.C. Lee conducted the statistical analysis. Author Vincent Chin-Hung Chen wrote the first draft of the manuscript. Author Charles T.C. Lee, Happy K.L. Tan and Michael Gossop modified the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare they have no conflicts of interest.

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