Mortality of Hospitalized Drug Users in the Czech Republic

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SUMMARY: Drug users are generally thought to experience higher mortality rates than those found among the general population. This study analyzes mortality rates among different subgroups of drug users in the Czech Republic. For this project, a retrospective cohort mortality study was conducted. A cohort of 12,207 persons aged 15 to 49 who had been hospitalized for drug related behavioral disorders was followed from 1997 to 2002. The study findings indicate that direct standardized mortality for the cohort of drug users was 16.78 per 1000 person-years (PY); 22.38 for men and 11.18 per 1000 PY for women. After reaching a peak in 1998, mortality rates began to decrease and stabilized around 14 per 1,000 PY from 2000 to 2002. When compared to the rates found in the general population, drug user mortality is eight times higher than nonuser rates (SMR = 8.15; 8.13 for men and 8.22 for women). These mortality rates are highest among polyvalent drug and opiate users and lowest among stimulant users. The authors conclude that the overall mortality of opiate users in the Czech Republic is relatively low when compared with those reported in similar European and non-European studies. There were few overdoses found in the cohort, and in sharp contrast to other available studies, no AIDS related cases were observed.

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● 1 INTRODUCTION

Mortality rates are considered to be one of the very basic indicators of health status in any population. Among different population subgroups, varying mortality rates can be expected. From the perspective of the risk of death, drug users comprise subgroups with higher risks of dying than is found among the general population (see, e.g., European Monitoring Centre for Drugs and Drug Addiction [EMCDDA], 2002; Vlahov et al., 2004; Wahren, Brandt, Allebeck, 1997).

The EMCDDA has defined drug-related deaths and mortality among drug users as one of five key indicators of drug epidemiology, and as such it complements other indicators of the health impacts of drug abuse. Mortality is assessed through longitudinal (cohort) studies that follow a defined group of drug users over time.

When standardization methods are applied to these samples, longitudinal studies allow comparisons of the levels of mortality found among drug users with those in the general population of the same gender and age.

Since 1998, data on drug-related deaths (overdoses) have been available in the Czech Republic (Mravcik et al., 2004; Zabransky, Vorel, Balikova, Sejvl, 2004; Zabransky, Vorel, 2001). Nevertheless, no detailed analysis of the mortality of drug users has been previously carried out in the Czech Republic. The results of this retrospective cohort mortality study represent a first attempt to fill the gap by providing information on the health consequences of drug use in the Czech Republic.

● 1 / 1 Mortality rates according to the type of the cohort

Longitudinal studies may only be carried out in selected groups of drug users, and these might not be representative of the entire population. Given that only a portion of users are in contact with helping services while others form a hidden population, no generalized information is available on their age and gender structure, and other characteristics (EMCDDA, 2002). Since cohort studies require a unique identifier for each person so that their vital status can be assessed over a period of several years, drug users who are already in contact with treatment centers or patients in substitution treatment programs are usually seen as the most suitable for longitudinal mortality studies.

Among the different cohorts identified for study, varying mortality rates are found (Bargagli, Sperati, Davoli, Forastiere, Perucci, 2001). Recent studies show that the highest mortality rates are observed among injecting drug users (IDU). For example, compared to the general population, the risk of death among Polish IDUs is about 11 times higher among men and 20 times higher among women (Moskalewicz, Sieroslawski, 1996). In Italy, these rates are 17 and 33 times higher, respectively, among IDUs (Cicco-

lallo, Morandi, Paravin, Sorio, Buiatti, 2000). A recent Chinese study also revealed that a long history of injection use is one of the most significant risk factors associated with high mortality (Zhang et al., 2005). Vlahov et al. (2004) pointed out that new-onset intravenous drug users represent one of the groups of drug users with the highest risk of death as compared to other subgroups.

Looking at its contribution to the overall mortality rates for 15 to 34 year olds, it was shown that IDUs comprised 16% and 9% of all deaths among men and women, respectively (Perucci, Forastiere, Rapiti, Davoli, Abeni, 1992). Similarly, regular use of opiates contributed 9.4% to the overall mortality of an Australian population aged 15 to 39 years (Hulse, English, Milne, Holman, 1999).

Generally, cohorts of problem drug users (PDUs) entering treatment reflect higher mortality rates than are found in the general population (Bargagli et al., 2001). Relatively high mortality rates when compared to the general population were observed in cohorts of clients of methadone treatment centers (10 times higher) and specialized drug clinics (17 times higher) (Perucci et al., 1991; Hickman et al., 2003). The length of regular drug use plays an important role as well; based on data from low-threshold centers, it was estimated that about 27% of drug users with a long history of problematic consumption (heroin, cocaine, and/or amphetamines) die within 20 years after having started regular drug use (Termorshuizen, Krol, Prins, van Ameijden, 2005). Regarding specific drug types, polyvalent users who reported heavy drinking and benzodiazepine and amphetamine users were defined as among the most at-risk groups as well (Gossop, Stewart, Treacy, Marsden, 2002). On the other hand, a French mortality study based on a cohort of persons arrested for drug use reported lower levels of mortality compared to the cohorts of PDUs mentioned above (five to nine times higher mortality among the cohort than was found in the general population) (Lopez, Martineau, Palle, 2004).

The level of mortality is affected by external factors as well. Davoli and colleagues (1997) and Galli and Musicco (1994) have linked the increase in mortality rates among drug users to the spread of HIV/AIDS in Italy at the beginning of the 1990s. At the same time, HIV positive status was proven to significantly elevate the mortality rate among injecting drug users (Frischer, Goldberg, Rahman, Berney, 1997).

● 1 / 2 The role of treatment

The relevant research has demonstrated that the level of mortality among drug users is influenced by the availability and quality of the treatment and services provided for them and that mortality rates tend to decrease in locations where there are high quality services (Ghodse, Oyefeso, Kilpatrick, 1998; Bartu, Freeman, Gawthorne, Codde, Holman, 2004). Oyefeso and colleagues (1999) recommended that the

quality of the treatment services should be improved with regard to the youngest group of drug users (15 to 19 year olds) who represent one of the most at-risk groups. Brugal and colleagues (2005) concluded that the effectiveness of lowthreshold methadone treatment contributed to a significant decline in the mortality rates among Spanish heroin users during the 1990s. Opiate users who never entered any drug treatment program had four times higher mortality rates then opiate users in maintenance treatment, resulting in a mortality risk that was 48 times higher than that of the general Austrian population (Risser et al., 2001). The risk of overdose death among those who left treatment was almost four times higher compared to that for those still in treatment (Davoli et al., 1993). Similarly, the mortality of exusers of opiates was significantly lower than that found among persons who had continued their drug use (Sorensen, Jepsen, Haastrup, Juel, 2005).

● 2 THE PRESENT STUDY

● 2 / 1 Data sources
In regard to this retrospective cohort mortality study in the Czech Republic, the cohort of drug users was defined as a set of persons who had been hospitalized for behavioral disorders connected with drug use, i.e., persons hospitalized for diagnoses F11-F19 according to the WHO International Classification of Diseases coding (ICD-10 coding) between 1997 and 2002 and who were 15 to 49 years old at the time of hospitalization. Persons hospitalized for tobacco related disorders (F17 diagnosis) were excluded prior to the construction of the cohort as were individuals hospitalized for alcohol related disorders (F10 diagnosis). Separate subcohorts were created for opiate (F11 diagnosis), stimulant (F15 diagnosis), and polyvalent drug users (F19 diagnosis). These data were not collected for the sole purpose of this cohort study; the data are based on annual reporting to the Hospitalization Register, run by the Czech Institute of Health Information and Statistics.

● 2 / 2 Methodology
For this study, in cases where an individual had been hospitalized more than once, the first hospitalization date was the only one considered so that every cohort member appeared only once during the given time period. Data from the hospitalization register were then linked with the general mortality register of the Czech Republic; the database linkage was made possible through a unique identification number assigned to each person in both data sets. Prior to the linkage, the identification number was ciphered by means of coding software to protect personal data. The software used for ciphering was approved by the Czech Office for Personal Data Protection.

For each cohort member, their life status was checked through the general mortality register, a search that re-sulted in the total number of deaths that had occurred within the cohort throughout the study period (1997–2002). Person-years of follow-up were calculated for each cohort member on the basis of the date of entry into the cohort (i.e., the date of hospitalization) and the date of death; those who survived were followed until December 31, 2002.

The mortality rate for drug users was calculated as a fraction of the number of recorded deaths and the total sum of person-years of follow-up. The overall mortality rates were observed separately for males and females. Specific mortality rates were calculated for opiate, stimulant, and polyvalent drug users.

Standardization methods were then used to compare the mortality rates among drug users with those found in the general population of the same age. The population of the Czech Republic in 2000 between 15 and 49 years old was treated as the standard. Both the direct and indirect standardizations were performed because they represent different views on mortality:

● The directly standardized mortality rate identifies mortality among drug users assuming they have the same age structure as the standard population.
● The standardized mortality ratio (SMR) is the result of indirect standardization and gives us the risk of mortality among drug users when compared to the general population.

Trends in the development of mortality over the respective time period are based on the number of deaths reported for every year and the sum of person-years of the cohort members followed in a given year, i.e., every cohort member contributed to the sum of the person-years with one year or less in case he/she was hospitalized or died in the given year.

● 2 / 3 Description of the cohort
From 1997 to 2002, a total of 12,207 persons between 15 and 49 years of age were hospitalized for behavioral disorders related to drug use (diagnoses F11–F19 according to ICD-10 coding). Of these, 2,406 were opiate users, 3,039 were stimulant users, and 3,323 were polyvalent users. Users of other drugs (372 cannabis users, 648 sedative and tranquilizer users, 27 cocaine users, 234 hallucinogen users, and 358 users of volatile substances) were not followed separately, although they still contribute to the total sum of person-years of the cohort. The mean age of the persons at the time of their recruitment into the cohort (i.e., at the time of hospitalization) was 24.1 years; the highest proportion of those hospitalized were between 20 and 24 years old. For a detailed description of the cohort see *Table 1* and *Figure 1*.

When linking the cohort of drug users with the general mortality register, 320 deaths were observed by the end of 2002; of the deceased, 252 were males and 68 were females. Altogether 114 deaths occurred among opiate users, 48 among stimulant users, and 103 among polyvalent users.

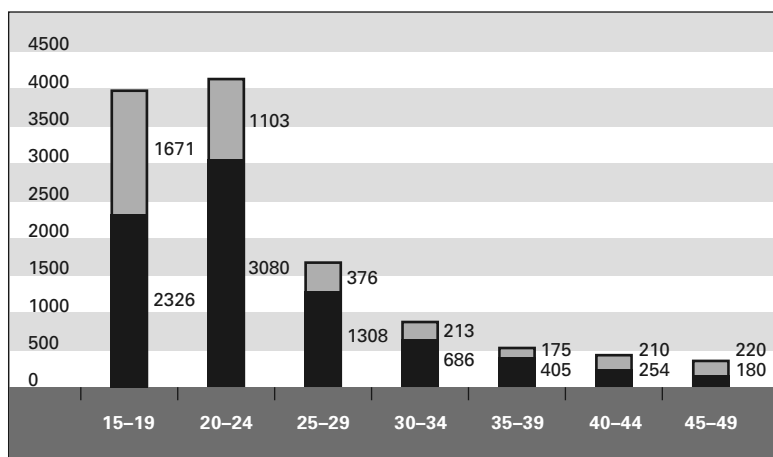|	Number of subjects in the cohort	Opiate users (F11)	Stimulant users (F15)	Polyvalent users (F19)	Mean age at enrollment into the cohort
Males	8,239	2,933	1,923	2,327	24.12
Females	3,968	1,273	1,116	996	23.99
Total	12,207	2,406	3,039	3,323	24.08

Table 1
Characteristics of the cohort

Figure 1
Age when recruited into the cohort
☐ females
■ males

Those who had died accounted for 2.62% of all subjects enrolled in the cohort. The mean age at death was 29.8 years, higher among women (33.0 years) compared to men (29.0 years) *(Table 2)*. The age structure of the deceased is reported in *Figure 2*.

	Number of deaths	% of deaths	Opiate users	Stimulant users	Polyvalent users	Mean age at death
Males	252	3.06	91	37	83	28.96
Females	68	1.71	23	11	20	32.99
Total	320	2.62	114	48	103	29.82

Table 2
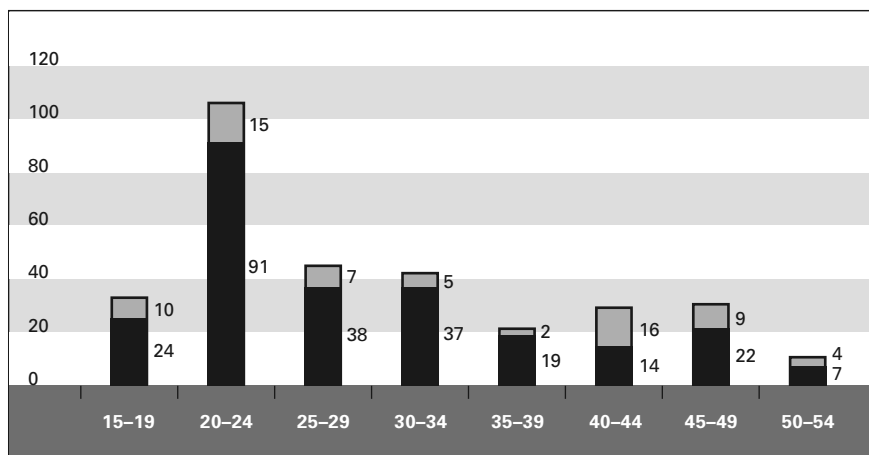Characteristics of the cohort – observed deaths

Figure 2
Age at time of death
☐ females
■ males

For each reported death, the cause of death is available in the form of a code based on the WHO International Classification of Diseases. Among these, 244 cases (76.3%) were attributable to injuries and poisoning, including 70 cases of overdoses (21.9% of the total number of deaths); 36 overdoses were reported among opiate users, eight among stimulant users, and 12 among polyvalent users.

Altogether 7.5% of these deaths were reported to be due to circulatory diseases, 4.7% were due to digestive diseases, and over 3% were due to neoplasm and respiratory diseases. Remarkably, no deaths due to AIDS were reported in this cohort through the end of 2002. Causes of death by subgroups of users are given in *Table 3*.

Table 3

Causes of death by sub-groups of users (abs. numbers)

	Opiate users	Stimulant users	Polyvalent users	All users
Neoplasm (dg. C00–C97)	8	0	1	11
Endocrine, nutritional and metabolic diseases (dg. E00–E90)	0	0	0	1
Mental and behavioral disorders (dg. F00-F99)	0	0	3	3
Diseases of the nervous system (dg. G00–G99)	1	2	2	6
Diseases of the circulatory system (dg. I00–I99)	9	3	6	24
Diseases of the respiratory system (dg. J00–J99)	3	1	4	10
Diseases of the digestive system (dg. K00–K93)	4	1	7	15
Diseases of the genitourinary system (dg. N00–N99)	1	0	0	3
Injury, poisoning and certain other consequences of external causes (dg. S00–T98)	87	41	79	244
Of them, overdoses	36	8	12	70
Total number of deaths	114	48	103	320
Unknown causes (dg. R00-R99)	1	0	1	3

● 3 RESULTS OF THE STUDY

● 3 / 1 Nonstandardized mortality rates

The gross mortality rate in the cohort for the entire follow-up period was 8.39 per thousand person-years (PY); 9.96 per 1000 PY for males and 5.31 per 1000 PY for females. The mortality rate increases with the age of the hospitalized drug users; the lowest mortality rate was observed in the 15 to 19 year age group (2.60 per 1000 PY) while the highest was observed in the 45 to 49 year age group (29.36 per 1000 PY). This trend observed among the cohort members corresponds with the overall trend of mortality rate increasing with age in the general population.

Among drug users, the highest mortality rates were observed for polyvalent drug users (10.29 per 1000 PY). Mortality rates for users of opiate-type drugs reached 8.56 per 1000 PY, and for stimulant users the figures were 4.92 per 1000 PY. The nonstandardized mortality rates are higher among men for all of the observed subgroups of drug users *(Table 4)*.

	Person-years (PY) of follow-up				Non-standardized mortality rates			
	Opiate users	Stimulant users	Polyvalent users	All users	Opiate users	Stimulant users	Polyvalent users	All users
Males	9,209.9	6,081.5	6,873.9	25,313.7	9.88	6.08	12.07	9.96*
Females	4,114.0	3,666.8	3,138.3	12,817.4	5.59	3.00	6.37	5.31*
Total	13,323.9	9,748.4	10,012.2	38,131.2	8.56	4.92	10.29	8.39

Table 4

Person-years of follow-up and non-standardized mortality rates (per 1000 PY of follow-up)

Note: *gender differences are statistically significant at alpha level 0.05*

The nonstandardized mortality rates presented above are strongly influenced by the age group of the deceased drug users; to eliminate the effect of the age structure, directly standardized mortality rates were calculated.

● **3 / 1** Directly standardized mortality ratio

As mentioned above, the age structure of the general population of the Czech Republic in 2000 was used as the standard for the direct standardization method.

The gross mortality rate of the Czech population of the same age group reached 2.13 per 1000 population (2.97 for men and 1.27 per 1000 population for women).

The direct standardized mortality rate for the cohort of drug users hospitalized in between 1997 and 2002 reached 16.78 per 1000 PY: 22.38 for men and 11.18 per 1000 PY for women. The highest level of mortality was found among opiate users (23.05 per 1000 PY), followed by polyvalent drug users (20.36 per 1000 PY for both genders). The mortality rates for specific subgroups of drug users by gender are summarized in *Table 5*; both gender differences and differences among subgroups of users were found to be statistically significant.

A slightly decreasing mortality rate trend was observed over time. After reaching a peak in 1998 when mortality was 27.21 per 1000 PY (for both genders together), mortality rates fell to 16.60 per 1000 PY in 1999 and the slope of the decrease stabilized at about 14 per 1000 PY. However, a relatively low mortality rate in 1997 could have been affected by the low number of cases of death observed within the first year of the follow-up of the cohort; that is, it does not necessarily mean that there was an increase in the mortality rate between 1997 and 1998.

	Opiate users	Stimulant users	Polyvalent users	All users
Males	28.02	6.93	30.18	22.38*
Females	16.92	8.37	9.65	11.18*
Total	23.05*	7.51*	20.36*	16.78

Table 5
Directly standardized mortality rates by subgroups of drug users
*** Note:** gender differences are statistically significant at alpha level 0.05;
differences among sub-groups of users are statistically significant
at alpha level 0.05*

Significant differences were recorded when focusing on the mortality of the subgroups of drug users. The mortality of polyvalent users peaked in 1998 with 53.75 per 1000 PY and fell rapidly in 1999. Since 1999 the mortality of polyvalent users has displayed a slightly increasing trend. Compared to polyvalent drug users, the mortality of opiate users peaked in 1999 and since then has remained on a higher level than the mortality of polyvalent drug users *(Figure 3)*.

Since 2001, a rising mortality of opiate users can be observed. The trends are visible in the changes in reported cases of death over time *(Table 6)*; the increase in the number of deaths of opiate users occurred in 1999 when 25 cases were reported compared to eight in 1998, while the increase in the cases of death of polyvalent drug users occurred in 1998 (16 cases) and fell to 11 in 1999. The mortality of stimulant users remained relatively low throughout this time.
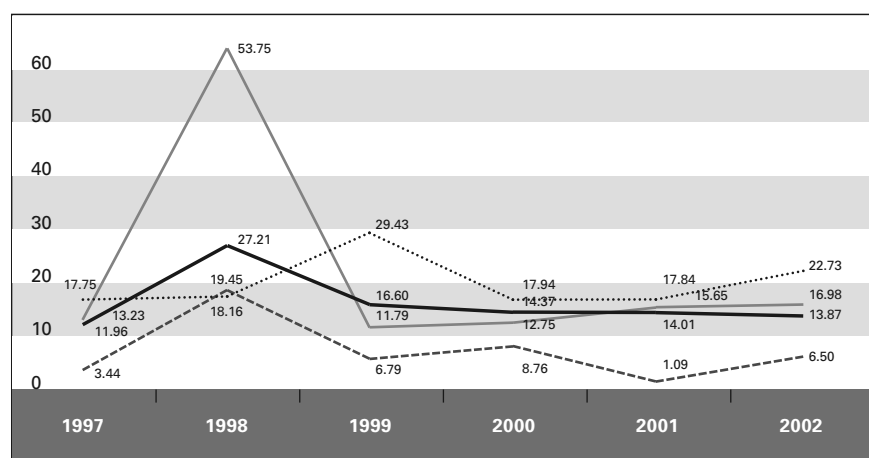

Figure 3
The development of mortality over time (both sexes, per 1,000 PY)
.... opiates
- - - - - - - - - - stimulants
———————— polyvalent
━━━━━━━━ all drugs

	Opiate users	Stimulant users	Polyvalent users	All users
1997	7	2	2	13
1998	8	4	16	36
1999	25	8	11	51
2000	25	11	20	66
2001	23	6	27	72
2002	26	17	27	82

Table 6
Cases of death by year and selected groups of drug users (both sexes)

● 3 / 1 Standartized mortality rates (SMR)

The standardized mortality ratio (SMR) expresses the risk of death among drug users in relation to the mortality found in the general population. The population of the Czech Republic in 2000 was again used as the standard. The formula for calculation of the SMR corresponds to the number of observed deaths of drug users in the given period of time divided by the number of expected deaths, which is based on the mortality of the general population and the number of person-years of follow-up of the cohort members.

The SMR for the followed cohort of drug users in between 1997 and 2002 reached 8.15; in other words, the mortality of drug users is 8.15 times higher than the mortality rate of the general population of the same age group. In this study, the SMR does not significantly differ by gender; the SMR for men was 8.13 while that for women reached 8.22. The 95% confidence interval for the SMR is reported in *Table 7*.

Opiate users have a risk of dying that is almost nine times higher than that shown for a comparable group from the general population (SMR = 8.96). The risk of death among stimulant users is six times higher and that for polyvalent drug users is almost nine times higher *(Figure 4)*. In the case of opiate users, the SMR for women is slightly higher than that for men (11.30 and 8.52, respectively). This trend can be observed among stimulant users as well: the SMR for women reached 7.84 compared to 5.87 for men. In the case of polyvalent drug users, the SMR reached a higher level for men (8.81) compared to women (7.88).

	Opiate users	95% CI	Stimulant users	95% CI	Polyvalent users	95% CI	All users	95% CI
Males	8.52	6.86–10.46	5.87	4.13– 8.09	8.81	7.02–10.92	8.13	7.16– 9.20
Females	11.30	7.16–16.95	7.84	3.92–14.02	7.88	4.82–12.17	8.22	6.39–10.43
Total	8.96*	7.39–10.76	6.22*	4.59– 8.25	8.61*	7.03–10.45	8.15	7.28– 9.09

Table 7
Standardized mortality ratios (SMR) and 95% confidence intervals (CI)
*** Note:** *differences among subgroups of users are statistically significant at alpha level 0.05*
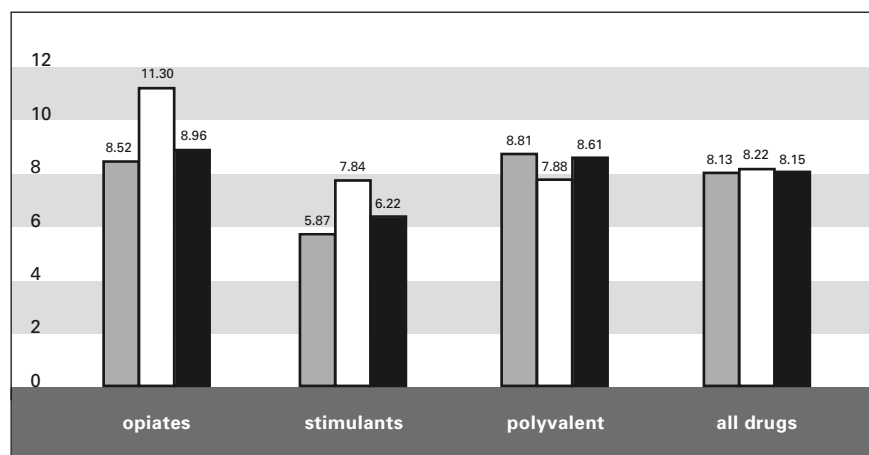

Figure 4
SMR by gender and subgroups of users
■ males
□ females
■ total

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● 3 DISCUSSION

The results of any mortality study are greatly influenced by the sample that is designated as the cohort. In this study conducted in the Czech Republic, persons hospitalized for behavioral disorders related to drug use (i.e., diagnoses F11–F19 according to the ICD-10 coding) comprised the cohort. We know that cohorts based on other data sets result in different mortality rates as has been demonstrated in cohort studies in other countries (e.g., Bargagli et al., 2006).

However, several factors that were not mentioned before play an important role in the mortality studies, such as the period of enrollment of subjects into the original cohort and the length of the follow-up period (EMCDDA, 2002). The means for ascertaining the life status of individual cohort members in the follow-up period can also influence the validity of the study. In this Czech cohort, individuals were considered to be alive at the end of the follow-up if they did not appear on the records of the mortality register over the study period. At the same time, cohort members were regarded as drug users for the entire follow-up period with no specific knowledge of their current drug use status over this time period, as this fact could no longer be provided for the individuals once they had been hospitalized for behavioral disorders.

Additional factors influence the level of mortality among drug users, including the type of drug being used, the length of time of drug use, and the frequency of use or route of administration. Specific data were not available for the purposes of this study, and thus the impact of these factors on mortality levels could not be assessed.

It seems clear that further research in the area of the mortality of drug users is needed in the Czech Republic. Several available data sets that could be studied over time in a longitudinal study include persons hospitalized with a secondary diagnosis related to drug-induced behavioral disorders reported through the Hospitalization Register, or methadone substitution treatment clients reported through the Register of Substitution. The comparison of these different cohort types could provide much more information regarding the impact of cohort type on the mortality results. The impact of other factors such as the route of administration of drugs, length of drug use and length of regular drug use, or the age at first drug use could be monitored through a prospective cohort study if more detailed information on drug users was to be reported into the Hospitalization Register or Substitution Register.

● 4 CONCLUSION

The mortality rate among Czech drug users is considerably higher than that found in the general population. During the observed period of 1997 to 2002, the mortality among drug users was eight times higher for both male and female drug users than it was for the general population. Gender differences were observed to be statistically significant for nonstandardized and directly standardized mortality rates. Significant differences were also observed when comparing mortality levels by subgroups of drug users; the highest mortality levels were found among opiate users (standardized mortality rate of 23.05 per 1000 PY of follow-up and SMR of 8.96) and polyvalent users (mortality rate of 20.36 per 1000 PY and SMR of 8.61). Within the followed cohort of hospitalized drug users, the lowest mortality level was observed among stimulant users (7.51 per 1000 PY and SMR of 6.22).

Over time, the mortality of drug users appears to have stabilized, with a slightly decreasing trend. Among specific subgroups of users, fluctuations result from changes in the relatively small number of cases of deaths reported; these fluctuations are especially visible among female drug users. This is also the reason why the mortality rate trends were not constructed separately for males and females.

In the Czech Republic, no AIDS related deaths among drug users have been reported so far, and the study suggested that overdoses accounted for about 20% of deaths among the followed cohort of persons who had been hospitalized for drug related disorders. More than 50% of all deaths observed among the cohort were attributable to injuries and other external causes that were not directly attributable to drug taking.

As suggested earlier, the results of this Czech cohort mortality study reveal lower rates than those found in retrospective cohort mortality studies carried out in other European countries. Results of these other studies show that the level of mortality of opiate users in European countries ranges from an SMR of nine in Amsterdam, Netherlands to 24 in Barcelona, Spain for male users and from 11 in Dublin, Ireland to 64 in Barcelona, respectively, for female users (EMCDDA, 2002). Similar results were found in Australia where the mortality of illicit opiate users was 13 times higher than that found in a comparable sample in the general population. That study also found that altogether 9.4% of total mortality in Australian population for those between 15 and 39 years old was attributable to regular use of opiates (Hulse et al., 1999). The higher mortality rates observed in several European countries to a certain extent can be explained by different time frames for the follow-up of the cohorts; most of these other studies were conducted in the late 1980s and early 1990s when an increasing number of AIDS-related deaths was reported as the leading cause of death among drug users (e.g. Bargagli et al., 2006; Galli, Musicco, 1994).

Detailed analyses of causes of death among drug users in Canada have also shown a close relationship of overdoses and the HIV status of drug users; there the mortality of drug users was closely associated with HIV status (adjusted hazards ratio of 2.67) and injecting drug (cocaine) use (AHR 2.23) (Tyndall et al., 2001).

Similar findings were observed in an American study on the causes of death among intravenous drug users; half of the patients hospitalized in public hospitals who had a history of drug use had died of AIDS related causes (Klatt, Mills, Noguchi, 1990). However, cohort mortality studies from the U.S. and Canada give only a limited comparability of the level of mortality among drug users with European studies, most specifically because of the different characteristics of those cohorts that are being reviewed.

REFERENCES

● Bargagli, A. M., Hickman, M., Davoli, M., Perucci, C. A., Schifano, P., Buster, M., Brugal, T., Vicente, J. (2006). Drug-related mortality and its impact on adult mortality in eight European countries. *European Journal of Public Health*, 16, 198–202.

● Bargagli, A. M., Sperati, A., Davoli, M., Forastiere, F., Perucci, C. A. (2001). Mortality among problem drug users in Rome: An 18-year follow-up study, 1980–97. *Addiction*, 96, 1455–1463.

● Bartu, A., Freeman, N. C., Gawthorne, G. S., Codde, J. P., Holman, C. D. (2004). Mortality in a cohort of opiate and amphetamine users in Perth, Western Australia. *Addiction*, 99, 53–60.

● Brugal, T., Domingo-Salvany, A., Puig, R., Barrio, G., Garcia de Olalla, P., de la Fuente, L. (2005). Evaluating the impact of methadone maintenance programs on mortality due to overdose and AIDS in a cohort of heroin users in Spain. *Addiction*, 100, 981–989.

● Ciccolallo, L., Morandi, G., Paravin, R., Sorio, C., Buiatti, E. (2000). Mortality risk in intravenous drug users in Emilia Romagna Region and its socio-demographic determinants. Results of a longitudinal study. *Epidemiologia e Prevenzione*, 24, 75–80.

● Davoli, M., Perucci, C. A., Rapiti, E., Bargagli, A. M., D´Ippoliti, D., Forastiere, F., Abeni, D. (1997). A persistent rise in mortality among injection drug users in Rome, 1980 to 1992. *American Journal of Public Health*, 87, 851–853.

● Davoli, M., Perucci, C. A., Forastiere, F., Doyle, P., Rapiti, E., Zaccarelli, M., Abeni, D. D. (1993). Risk factors for overdose mortality: A case-control study within a cohort of intravenous drug users. *International Journal of Epidemiology*, 22, 273–277.

● European Monitoring Centre for Drugs and Drug Addiction (2002). *Mortality of drug users in the EU: Co-ordination of implementation of new cohort studies, follow-up and analysis of existing cohorts and development of new methods and outputs*. EMCDDA Scientific Report. Lisbon: EMCDDA.

● 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.

● Galli, M., Musicco, M. (1994). Mortality of intravenous drug users living in Milan, Italy: Role of HIV-1 infection. COMCAT Study Group. *AIDS*, 8, 1457–1463.

● Ghodse, H., Oyefeso, A., Kilpatrick, B. (1988). Mortality of drug addicts in the United Kingdom 1967–1993. *International Journal of Epidemiology*, 27, 473–478.

● Gossop, M., Stewart, D., Treacy, S., Marsden, J. (2002). A prospective study of mortality among drug misusers during a 4-year period after seeking treatment. *Addiction*, 97, 39–47.

● Hickman, M., Carnwath, Z., Madden, P., Farrell, M., Rooney, C., Ashcroft, R. (2003). Drug-related mortality and fatal overdose risk: Pilot cohort study of heroin users recruited from specialist drug treatment sites in London. *Journal of Urban Health*, 80, 274–287.

● Hulse, G. K., English, D. R., Milne, E., Holman C. D. (1999). The quantification of mortality resulting from the regular use of illicit opiates. *Addiction*, 94, 221–229.

● Klatt, E. C., Mills, N. Z., Noguchi, T. T. (1990). Causes of death in hospitalized intravenous drug abusers. *Journal of Forensic Science*, 35, 1143–1148.

● Lopez, D., Martineau, H., Palle, C. (2004). Mortality of individuals arrested for heroin, cocaine or crack use. *Tendances*, 36, OFTD.

● Moskalewicz, J., Sieroslawski, J. (1996). Mortality of narcotic addicts using injections. *Przeglad Epidemiologiczny*, 50, 323–332.

● Mravcik, V., Korcisova, B., Lejckova, P., Miovska, L., Skrdlantova, E., Petros, O. (2004). *Annual report: The Czech Republic—2003 drug situation*. Prague: Office of the Government of the CR.

● Oyefeso, A., Ghodse, H., Clancy, C., Corkery, J., Goldfinch, R. (1999). Drug abuse-related mortality: A study of teenage addicts over a 20-year period. *Social Psychiatry and Psychiatric Epidemiology*, 34, 437–441.

● Perucci, C. A, Forastiere, F., Rapiti, E., Davoli, M., Abeni, D. D. (1992). The impact of intravenous drug use on mortality of young adults in Rome, Italy. *British Journal of Addiction*, 87, 1637–1641.

● Perucci, C. A., Davoli, M., Rapiti, E., Abeni, D. D., Forastiere, F. (1991). Mortality of intravenous drug users in Rome: A cohort study. *American Journal of Public Health*, 81, 1307–1310.

● Risser, D., Honigschnabl, S., Stichenwirth, M., Pfudl, S., Sebald, D., Kaff, A., Bauer, G. (2001). Mortality of opiate users in Vienna, Austria. *Drug and Alcohol Dependence*, 64, 251–256.

● Sorensen, H. J., Jepsen, P. W., Haastrup, S., Juel, K. (2005). Drug-use pattern, comorbid psychosis and mortality in people with a history of opioid addiction. *Acta Psychiatrica Scandinavica*, 111, 244–249.

● Termorshuizen, F., Krol, A., Prins, M., van Ameijden, E. J. (2005). Long-term outcome of chronic drug use: The Amsterdam cohort study among drug users. *American Journal of Epidemiology*, 161, 271–279.

● Tyndall, M. W, Craib, K. J., Currie, S., Li, K., O´Shaughnessy, M. V., Schechter, M. T. (2001). Impact of HIV infection on mortality in a cohort of injection drug users. *Journal of Acquired Immune Deficiency Syndrome*, 28, 351–357.

● Vlahov, D., Wang, C., Galai, N., Bareta, J., Mehta, S. H., Strathdee, S. A., Nelson, K. E. (2004). Mortality risk among new onset injection drug users. *Addiction*, 99, 946–954.

● Wahren, C. A., Brandt, L., Allebeck, P. (1997). Has mortality in drug addicts increased? A comparison between two hospitalized cohorts in Stockholm. *International Journal of Epidemiology*, 26, 1219–1226.

● Zabransky, T., Vorel, F. (2001). *Odhad poctu zemrelych v primem dusledku zneuzivani omamnych a psychotropnich latek a v souvislosti s nim – pilotni faze (odhad pro rok 1998)*. (Estimate of the number of deaths directly caused by drug use and in connection with drug use – a pilot study [Estimate for 1998]). *Adiktologie*, 2, 8–27.

● Zabransky, T., Vorel, F., Balikova, M., Sejvl, J. (2004). *Smrtelna predavkovani nelegalnimi drogami a tekavymi latkami v CR. Strucny souhrn a manual pro monitorovani*. (Fatal overdoses caused by illicit drugs and volatile substances in the Czech Republic. Summary and manual for monitoring). Praha: Urad vlady CR.

● Zhang, L., Ruan, Y. H., Jiang, Z. Q., Yang, Z. N., Liu, S. Z., Zhou, F., He, Y. X., Yin, L., Qin, G. M., Shao, Y. M. (2005). A 1-year prospective cohort study on mortality of injecting drug users. *Zhonghua Liu Xing Bing Xue Za Zhi*, 26, 190–193.