Addiction

Most deaths in patients on methadone are not drug related

Non drug-related morbidities are the most common cause of death as methadone-treated opioid dependent patients age, a study from Scotland has found.

The study authors used information from the Community Health Index and data on methadone prescriptions held within the Scottish National Prescribing Information System for 36,606 patients who had received one or more methadone prescriptions between 2009 and 2015.

During 193,813 person-years of follow-up there were 3,262 deaths in the cohort, of which 1,323 were drug related but the majority 1,939 (59%) were not drug related.

Of the drug-related deaths, 546 were methadone specific; 320 heroin specific; both heroin and methadone were implicated in 309 deaths, and buprenorphine in 27 deaths. There were 121 drug-related deaths in which neither heroin/morphine, methadone nor buprenorphine were implicated.

There were five main causes of non drug-related deaths, each of which was responsible for at least 10% of these deaths, and which together accounted for 75% (1,457):

- Neoplasms 377 (21%) of which 113 were malignant neoplasms of the bronchus or lung
- Accidents, intentional self-harm, assault 279 (14%)
- Diseases of the circulatory system 286 (15%)
- Digestive system conditions 303 (16%)
- Non-malignant respiratory system diseases 212 (11%)

Approximately half the deaths (54%) in those aged 35-44 years were not drug related (717 of 1,318). This proportion rose to 65% in the 45-54 year age group (589/907) and 89% (372/417) for those aged 55 years and older. In this older age group neoplasms alone accounted for 48% of non drug-related deaths.

Circulatory disease featured in 11% of methadone-specific drug-related deaths but only 5.7% of drug-related deaths in which heroin was implicated (36/629).

Respiratory disease was a factor in 14% of methadone-specific drug-related deaths and for 7.6% of drug-related deaths in which heroin was implicated (48/629).

Digestive system disease was mentioned for 8% of methadone-specific deaths but for only 1.4% of drug-related deaths in which heroin was implicated (9/629; $P < 0.00001$ for all ages).

The implications for clinical practice suggested by these findings include improving interventions to reduce comorbidity for those on methadone treatment for example through treatment of hepatitis C, support for smoking cessation and reducing alcohol consumption, and careful review of methadone dose for those patients with circulatory, respiratory and digestive comorbidity.

The study authors state:
'Our results do not undermine the strong evidence-base that, while clients receive opioid substitution therapy, their risk of dying is substantially reduced. But our findings do have actionable implications for clinical practice, namely: the major comorbidities of ageing methadone-clients need to be mitigated; or better managed.

'Treatment of clients' HCV-related liver disease by directly acting antivirals and smoking cessation treatment can mitigate leading cancers as well as circulatory, digestive and respiratory comorbidities.'

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Gao L, Robertson JR, Bird SM. Non drug-related and opioid-specific causes of 3262 deaths in Scotland's methadone-prescription clients, 2009-2015. *Drug Alcohol Depend* 2019;1972:262-70

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