

# The challenging issue of polydrug consumption: new trends of a deep-seated public health threat

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To the Editor,

Substance abuse is a deeply entrenched and multifaceted issue causing hundreds of fatal and non-fatal intoxications all over the World. Over the last decades, continuous changes in the number and types of substances have been observed in the illicit market, posing constantly new challenges to governments and drug enforcement agencies. Indeed, the recent COVID-19 pandemic and ensuing global restrictions have accelerated the dynamic evolution of drugs consumption patterns (1). The psychological distress caused by the restrictive measures have exacerbated latent psychiatric conditions, driving fragile people to drug abuse and diversion of prescription drugs. Moreover, the drug market became more complex as a response to the limits imposed by the pandemic, preferring the e-commerce via specialized websites and the already used dark web. The patterns of consumption have evolved as well, resulting in the rise of cannabis and the non-medical use of pharmaceutical drugs, while stimulants drugs commonly associated to recreational settings slightly decreased in popularity (2). According to recent data, about 6000 overdose deaths involving illicit drugs occurred in the European Union alone in 2020, representing an estimated mortality rate of 17.4 deaths per million for the adult population (3). Notably, drug related deaths mostly occurred due to polydrug toxicity, which typically involves combinations of illicit opioids, other illicit drugs and benzodiazepines consumed for recreational purposes, causing or contributing to the fatality (3). The term “polydrug use” refers to the

use, of a wide spectrum of substance, either concurrently or subsequently (2). The measure of polydrug consumption is difficult to conduct in the routine practices due to the lack of specific model for the common ground description. The reasons behind multiple drug consumption are several, such as the achievement of synergistic effects or conversely, to balance the negative effects of certain psychotropic substances, or even the unavailability of the preferred drugs. Furthermore, the intake of multiple drugs may occur unintentionally as a consequence of drug adulteration with other psychotropic drugs. Although the polydrug use is relatively rare, the phenomenon is certainly underestimated. In fact, only seven countries were able to provide precise data in the European Union, while the others have not assessed its incidence (3). To date, few studies have been conducted on the possible pharmacological interactions between different drugs, although some findings showed that drugs combination may increase the risk of fatal outcomes. Recently, Rock et al. (4) observed that cannabis related deaths associated with polydrug consumption accounted for 96% of cases, whereas the blood concentrations of  $\Delta^9$ -THC were much lower than those in non-fatal intoxications. Against such a backdrop, toxicological analysis plays a crucial role in identifying the real cause of intoxications and the implementation of up-to-date good practices is essential in toxicology laboratories (5). In that concern, effective toxicological screening and confirmatory analytical methods should be focused on the research of different drug classes, thus enabling the detection and quantification of multiple drugs in

a single analytical protocol, also considering the unconventional matrices (6). Most importantly, pharmacological studies should be conducted to elucidate the possible harmful effects of polydrug consumption.

**Conflict of Interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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