ALICE RAP Position Paper

Toxicology-based risk assessment should be the driver and monitor of drug policy reform

INTRODUCTION

It is increasingly recognised that illegal drug policies are in need of reform - they bring considerable collateral damage through criminalization and violence due to vying for market dominance, they impair health, result in large prison populations and weaken governance around the world.[1] UNGASS 2016 provides a unique opportunity for opening the door to policy shifts, paving the way for reform of the global drug control regime to permit responsible legal regulation, as is happening with cannabis. There is no one simple pathway for effective reform; it will require experimentation and trial and error[2] and will also require a standard benchmark to address health outcomes across all drugs, legal and illegal. In the field of toxicology, risk assessment for human consumption of a wide range of products is based on margins of exposure (MOE) analysis.[3, 4] We propose MOE as the standard tool to drive reform and monitor drug policy worldwide.

WHAT IS MOE?

MOE measures the ratio of a benchmark or toxic dose (commonly the lowest dose which is 95% certain to cause no more than a 10% incidence of a negative health outcome in animals or humans) to human exposure.[4] An MOE of 1 means that the chemical is being consumed at the toxic dose, while an MOE of 100 means that the chemical is being consumed at one hundredth of the toxic dose; the higher the MOE, the lower the risk to human health. Benchmark doses can be estimated from human data such as clinical trials or epidemiological dose-response information, but such information is unavailable for most illegal drugs. For this reason, the currently available estimations rely on toxicity data from animal experiments. Exposure is commonly measured by survey data, or by population-based consumption data.

WHAT MOE Threshold?

Toxicology-based risk assessment uses different MOE thresholds as guidelines, depending on whether the benchmark dose is derived from animal or human studies.[4] Differing MOEs are often set for differing health outcomes, and whether or not products are voluntarily consumed. An MOE for individual daily drug use of less than 1 is considered high risk, an MOE of less than 10 as risk. This does not imply that an MOE greater than 10 is safe – only that there is lower risk. All public drug policies should aim to ensure that the MOE for individual daily use does not fall below 10, and that all policies should be driven and monitored by this value.

MOE for European drug users

MOEs have been estimated for individual daily drug use by Europeans, see above Figure.[5] The benchmark dose was obtained from animal experiments, and exposure amongst daily users from surveys. Special attention should be given for policies that manage the use of nicotine, cocaine, heroin and alcohol. The reason that alcohol is at the bottom with a MOE of 1.3 is due to the high exposure to alcohol amongst European drinkers (an average of 34 grams, over three drinks a day.

The research leading to these results or outcomes has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013), under Grant Agreement nº 266813 - Addictions and Lifestyle in Contemporary Europe – Reframing Addictions Project (ALICE RAP – www.alicerap.eu).

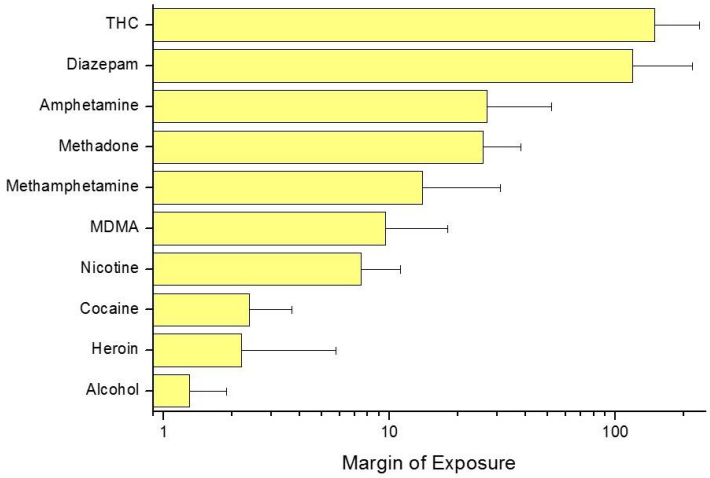

Figure | Margin of exposure for daily drug use estimated using probabilistic analysis. Source[5]

How to improve the MOE

MOE is driven by the ratio of the benchmark dose to exposure. So, MOEs can be improved by reducing the toxicity or potency of the drug, or by reducing individual exposure. Exposure can be changed by limiting economic and physical availability through setting minimum prices per mg or gram of the drug sold, increasing prices per mg or gram sold, and restricting hours or days of purchase.[6,7] Wherever high potency drug forms are available, independent of their legality, there will always be individuals who run into problems with heavy drug use. Evidence suggests that accessible advice and treatment for heavy users can reduce exposure (see[6,7]).

CONCLUSION

Drug-related harm goes beyond health and impacts many facets of societal well-being, as well as being driven by social attitudes and stigma. For health harms at least, a rational approach based on margins of exposure could be adopted. Acceptable levels of margin of exposure need to be determined. One option is that society acts on all drugs with a MOE of less than 100, concentrating on those drugs the lower the MOE, with policies for all drugs ensuring that the MOE for individual daily use never falls below 10.

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