III. Psychotropic substances

17. In the preamble to the 1971 Convention, it was recognized that the use of psychotropic substances for medical and scientific purposes was indispensable and that their availability for such purposes should not be unduly restricted. This remains the overarching principle of that Convention.

18. Conducting a comprehensive assessment of the availability of psychotropic substances depends on the availability of adequate, reliable and accurate consumption data. Unlike for narcotic drugs, submission of data on the consumption of psychotropic substances is not mandatory under the 1971 Convention. However, in its resolution 54/6, the Commission on Narcotic Drugs encouraged Member States to report data on the consumption of psychotropic substances for medical and scientific purposes to INC in a voluntary basis.

19. Considerable improvement in the voluntary submission of data on the consumption of psychotropic substances has been observed since the adoption of Commission on Narcotic Drugs resolution 54/6, rendering it feasible for INC to undertake the first analysis of the availability of internationally controlled psychotropic substances using reported consumption data as the basis. The amount of data submitted on the consumption of psychotropic substances, however, varies significantly across the regions of the world.

20. Psychotropic substances are essential for the treatment and management of a wide range of medical conditions, in particular mental and neurological health conditions, and the induction of anaesthesia in pre-operative procedures. Prescribing practices vary greatly and substances are used differently in different countries for the treatment of similar conditions, making the establishment of treatment protocols and the standardization of treatment measures highly complex.

21. Despite the important role that internationally controlled psychotropic substances play in the medical environment, assessing their global, regional and national availability remains a challenge as neither comprehensive data at the national level nor well-established ways of assessing the appropriate level of use of psychotropic substances to meet demand exist.

22. In the light of the above complexity, the scope of analysis for the present report is limited to four controlled substances listed in the 20th edition of the WHO Model List of Essential Medicines: diazepam, lorazepam, midazolam and phenobarbital.

23. First adopted in 1977, the concept of essential medicines was updated in 2012 and refers to those medicines that satisfy the priority health-care needs of the population. According to WHO, essential medicines are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. They are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford.

24. Comprising a core and a complementary list, the Model List of Essential Medicines is updated every two years and categorizes essential medicines for priority conditions. Depending on the particular use of the essential medicines, some of them may be listed under more than one category. Among the four aforementioned substances, diazepam and

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[For each psychotropic substance listed in Schedules I, II, III and IV of the 1971 Convention, the reporting authority should indicate (in grams or kilograms, as applicable) the substance consumed during the year in question, i.e., supplied to any person or enterprise for retail distribution, medical use or scientific research.


The core model list is defined as a list of minimum medicines needed for a basic health-care system. The complementary list contains essential medicines for the treatment of priority diseases for which specialized diagnostic or monitoring facilities and/or specialist training are needed.
midazolam are listed under three categories, and lorazepam and phenobarbital are listed under one. Focusing on the priority conditions, diazepam is used to treat anxiety disorders and all four substances (diazepam, lorazepam, midazolam and phenobarbital) are used to treat epilepsy.

25. In order to provide an approximate indication of some of the demand for diazepam, lorazepam, midazolam and phenobarbital, the main global trends in the prevalence of anxiety disorders and epilepsy were first examined in 2006 and 2016. Examinations of the trends and patterns in the consumption of diazepam, lorazepam, midazolam and phenobarbital were undertaken in both 2012 and 2016.

26. The analysis presented below points to three main findings since the publication of the supplement to the annual report of INCB for 2015:

(a) Despite an increasing number of people living with anxiety disorders and epilepsy around the globe, in the majority of countries for which data on the consumption of psychotropic substances were provided to INCB, the availability of some essential psychotropic substances for consumption in the treatment of those conditions has declined since 2012;

(b) While 80 per cent of people with epilepsy live in low- and middle-income countries, their level of consumption of some related psychotropic substances remains largely unknown. The limited data submitted to INCB, however, suggest that consumption of psychotropic substances is concentrated in high-income countries;

(c) The difference between the countries for which the highest and the lowest consumption rates were reported widened between 2012 and 2016, confirming the growing global consumption gap.

Global burden of disease and mental health disorders

27. While the global burden of disease caused by some non-communicable diseases (for instance, cancer, diabetes, and cardiovascular and lung diseases) is relatively well known, an increasing health burden caused by people with mental and neurological disorders (for example depression, anxiety disorders, bipolar disorder, schizophrenia and dementia) is also affecting many countries, at all stages of development. WHO estimates that non-communicable diseases kill 15 million people aged between 30 and 70 each year, causing 70 per cent of all deaths worldwide. Over 300 million people suffer from depression and about 50 million live with dementia.

WHO data also suggest that non-communicable diseases account for about 20 per cent of all years lived with disability; mental and neurological disorders such as major depression and anxiety disorders are among the leading causes of years lived with disability. Worse still, mental and neurological disorders can lead to or be a consequence of non-communicable diseases and frequently occur in the same person, thereby aggregating the risk of suicide for people living with those conditions.

Anxiety disorders

28. Slightly more than 270 million people were estimated to be living with anxiety disorders in 2016, making it the ninth leading cause of global years lived with disability. Compared with 2006, both the total number of people living with anxiety disorders and the years lived with disability caused by anxiety disorders increased in 2016. Years lived with disability caused by anxiety disorders seem to be evenly distributed across economies with varying levels of income: in 2016, anxiety disorders were one of the leading 10 causes of years lived with disability in many countries, from low- to high-income countries. The burden of anxiety disorders falls disproportionately on females: anxiety was one of the main conditions contributing to higher years lived with disability rates in women in 2016. According to WHO, women have a higher prevalence of anxiety disorder than men across all regions of the world. In particular, 7.7 per cent of the female population in the Americas were estimated to suffer from anxiety disorders in 2015, compared with 3.6 per cent of men in the same region.

11 Diazepam is listed under medicines for anxiety disorders, medicines for other common symptoms in palliative care, and anticonvulsants/antiepileptics. Midazolam is listed under pre-operative medication and sedation for short-term procedures, medicines for other common symptoms in palliative care, and anticonvulsants/antiepileptics.
12 Both lorazepam and phenobarbital are listed as anticonvulsants/antiepileptics.
13 As diazepam can also be used for the treatment of other conditions such as phobia, agitation, aggression and psychosis, in addition to anxiety disorders, the prevalence trend of anxiety disorders can only be indicative of part of the demand for the substance. A similar rationale also applies to lorazepam, midazolam and phenobarbital.
14 Diazepam, lorazepam, midazolam and phenobarbital are hereinafter referred to as essential antiepileptics under international control.
29. Given the increase in the prevalence of anxiety disorders and their associated health burden, an increasing demand for treatment and medication to treat anxiety disorders in countries with economies at all stages of development would be expected between 2006 and 2016, with bigger demand for those countries having a higher number of women.

**Diazepam: reported consumption**

30. In 2012, one year following the adoption of Commission on Narcotic Drugs resolution 54/6, competent national authorities of 48 countries reported data on the consumption of diazepam (see map 3). In comparison, competent national authorities from a total of 71 countries and territories reported data on the consumption of diazepam in 2016, an increase of 48 per cent over five years. Most of the data on the consumption of diazepam came from North America and Europe.

31. In 2012, 10 countries in Europe, Brazil and Chile had the highest rate of consumption of diazepam (out of the 48 countries worldwide for which data were reported), with above 3 S-DDD per 1,000 inhabitants per day. Consumption of between 1 and 3 S-DDD per 1,000 inhabitants per day was reported for parts of North America, South America and Europe, along with Algeria, China, Costa Rica and Georgia. Competent national authorities that submitted data on national consumption in 2012 of below 1 S-DDD per 1,000 inhabitants per day were mostly from countries in West Asia and Africa.

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*While competent national authorities submit their annual consumption data of psychotropic substances to INCB in kilograms, the consumption rates of different psychotropic substances are expressed in S-DDD per 1,000 inhabitants per day throughout the present report. Specifically, the consumption rate is calculated using the following formula: annual availability for reported consumption divided by 365 days; the result obtained is then divided by the population of the country, in thousands, during the year in question, and then by the defined daily dose (this is 10 mg for diazepam). The term S-DDD is used by INCB as a technical unit of measurement for the purpose of statistical analysis and is not a recommended prescription dose.*

*Assuming that anxiety disorders are treated only by diazepam, a consumption rate of 10 S-DDD per 1,000 inhabitants per day for diazepam suggests that, on average, 1 per cent of the population receives treatment for anxiety disorders daily.*
In 2016, the majority of the countries where the highest rate of consumption of diazepam was reported were again in Europe (Estonia, Finland, Lithuania, Montenegro and Serbia), together with Bolivia (Plurinational State of), Brazil, Chile, Israel and Uruguay, all of which had a consumption rate higher than 4 S-DDD per 1,000 inhabitants per day (see map 4). The competent national authorities of about 10 other countries in Europe, along with Argentina, Georgia, Guyana, New Zealand and the United States, reported consumption ranging between 2 and 4 S-DDD per 1,000 inhabitants per day. The consumption of diazepam in 2016 for the majority of countries in Africa and Asia that reported data was below 0.5 S-DDD per 1,000 inhabitants per day.
33. Among all the 40 countries and territories for which consumption data were submitted for both 2012 and 2016, 25 had a lower rate of consumption of diazepam in 2016 (see map 5).

34. While Global Burden of Disease data seem to suggest an increasing global demand for treatment and medication for people living with anxiety disorders between 2006 and 2016, the majority of countries for which data on the consumption of diazepam were submitted to INCB had a decline in their consumption level over the period 2012–2016. Such declines were more commonly found in those countries with a consumption rate of less than 1 S-DDD per 1,000 inhabitants per day.

35. The global trend depicted in map 5 should be interpreted with great care and a number of caveats need to be mentioned. Firstly, while the submission of data on the consumption of psychotropic substances has improved considerably over the past five years, the amount of data submitted remained very low overall, thereby rendering a comprehensive assessment of the global situation impossible. Secondly, as the term S-DDD assumes a certain average maintenance dose per day for a drug used for its main indication and in adult patients, the actual prescription dose might be different from that of the assumed average maintenance dose, depending on the condition of the patient (age, health condition, severity of the condition, etc.). Thirdly, as anxiety disorders can also be effectively treated with psychological interventions and/or with substances other than diazepam, including substances not under international control, a decrease in the consumption of diazepam over the past few years does not necessarily point to a lack of treatment and/or medication for people living with anxiety disorders. Lastly, an increase in the consumption rate of diazepam does not necessarily suggest that no shortage of the required treatment and medication exists, as people living with anxiety disorders might not have been given a proper diagnosis for their condition.

36. Bearing in mind the above caveats, map 5 illustrates considerable disparities in the consumption of diazepam across the globe between 2012 and 2016, given the significant differences between the highest and the lowest rate of consumption. In particular, the difference between the countries with the highest and the lowest consumption rate of diazepam widened, from 10.781 S-DDD per 1,000 inhabitants per day in 2012 to 15.992 per 1,000 inhabitants per day in 2016, suggesting a growing consumption gap of diazepam among countries for which data was provided to INCB.

Epilepsy

37. As defined by WHO, epilepsy is a chronic disorder of the brain that can affect people of all ages. According to the latest WHO estimates, about 50 million people worldwide currently live with epilepsy, making it one of the most common neurological diseases globally. At a given point in time, between 4 and 10 per 1,000 people of the general population are estimated to have active epilepsy, and epilepsy was ranked 26 in the leading causes of years lived with disability in 2016. The need for antiepileptics is much higher in low- and middle-income countries, given that 80 per cent of people with epilepsy live in low- and middle-income countries. For instance, epilepsy was one of the 10 leading causes of years lived with disability in Sao Tome and Principe and Senegal in 2016.

Reported consumption of essential antiepileptics under international control

38. In 2012, the competent national authorities of nearly 50 countries and territories submitted data on the consumption of at least one of the four essential antiepileptics under international control to INCB. In comparison, the authorities of a total of 74 countries and territories did so in 2016, with most data being submitted from countries in North America and Europe.

39. In 2012, Brazil, Canada and seven countries in Europe had a consumption rate of above 10 S-DDD per 1,000 inhabitants per day for the essential antiepileptics under international control to INCB. In comparison, the authorities of a total of 74 countries and territories did so in 2016, with most data being submitted from countries in North America and Europe.

40. In 2012, Brazil, Canada and seven countries in Europe had a consumption rate of above 10 S-DDD per 1,000 inhabitants per day for the essential antiepileptics under international control to INCB. In comparison, the authorities of a total of 74 countries and territories did so in 2016, with most data being submitted from countries in North America and Europe.

23 Global Burden of Disease is research first commissioned by the World Bank in 1990 and subsequently institutionalized at WHO. Findings in the present section are mostly extracted from “Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016”.

24 “Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries, 1990–2016” , figure 1.

25 “Epilepsy”.

26 “Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016”, figure 7.

27 Finland, Lithuania, Luxembourg, Montenegro, Netherlands, Switzerland and the former Yugoslav Republic of Macedonia.
41. In comparison, in 2016, the countries with the highest consumption rates, of more than 10 S-DDD per 1,000 inhabitants per day, were Canada and countries in Europe and South America (see map 7). A rate of consumption of between 5 and 10 S-DDD per 1,000 inhabitants per day was reported by the competent national authorities of New Zealand and some countries in the Americas and Europe. The majority of countries in Africa and Asia for which data were submitted on consumption of essential antiepileptics under international control in 2016 had a consumption rate of below 0.5 S-DDD per 1,000 inhabitants per day.
42. Of the 41 countries for which consumption data were submitted for both 2012 and 2016, 28 had a lower average rate of consumption of essential antiepileptics under international control in 2016 compared with 2012. The 13 countries with a higher rate of consumption of essential antiepileptics under international control in 2016 as compared with 2012 were in Africa, Europe and South America (see map 8).

43. Despite the fact that 80 per cent of people with epilepsy live in low- and middle-income countries, very little is known about the rate of consumption of essential antiepileptics under international control in those countries: data on consumption of those substances was provided from only 6 low-income countries (out of a total of 31) and 39 middle-income countries (out of a total of 109) in 2016 (see figure XI). By way of comparison, information was provided from 25 high-income countries (out of a total of 78) regarding the availability of those substances for consumption.

44. Keeping in mind the above-mentioned limitations, data provided to INCB revealed that, in 2016, over half (52 per cent) of some essential antiepileptics under international control were consumed in high-income countries and only 1 per cent was consumed in low-income countries.

45. As in the case of diazepam, the global trends shown in map 8 and figure XI should be interpreted with great care, and several caveats need to be mentioned. Firstly, the
amount of data on consumption of psychotropic substances remained rather low overall, and varied considerably among countries with different income levels during the designated period. In particular, the amount of data on the consumption of psychotropic substances submitted from countries in Africa and Asia is very low. Secondly, as the term S-DDD assumes a certain average maintenance dose per day for a drug used for its main indication in adults, the actual prescription dose might be different from that of the assumed average maintenance dose, depending on the condition of the patient (age, health condition, severity of the condition, etc.). Thirdly, as epilepsy can be treated with substances other than the four essential antiepileptics under international control, the decrease in the consumption rate shown in map 8 does not necessarily point to a lack of medication for people living with epilepsy. Lastly, a higher rate of consumption of the essential antiepileptics under international control does not necessarily suggest that there is no shortage of the required treatment and medication for epilepsy, as the four essential antiepileptic drugs are not solely used for the management of epilepsy. In particular, lorazepam and midazolam have much broader applications, and in some countries they are not considered as a first-line treatment for the management of epilepsy.

46. Bearing in mind the above, considerable disparities existed in the consumption of essential antiepileptics under international control across the globe between 2012 and 2016, given the significant differences between the highest and the lowest rate of consumption. In particular, the gap between the country with the highest and the lowest consumption rate of essential antiepileptics under international control widened, from 23.181 S-DDD per 1,000 inhabitants per day in 2012 to 33.961 per 1,000 inhabitants per day in 2016, suggesting a growing consumption gap of essential antiepileptics under international control.

Importance of quality data on the consumption of psychotropic substances

47. Given the multiple uses of psychotropic substances for a wide range of health conditions and the varying prescription practices in different countries, the analysis presented in the present section (based on the prevalence trends of two health conditions (anxiety disorders and epilepsy) and the consumption data reported to INCB since 2012) is, at best, a very preliminary assessment of the global availability of four essential psychotropic substances in a much-simplified context.

48. In fact, a comprehensive assessment of the availability of all psychotropic substances under international control, including those that are most commonly prescribed, is particularly challenging. For instance, changes in the consumption level of the four essential antiepileptics under international control (map 8) can be quite different from the changes in the consumption level of all benzodiazepines under international control (map 9) in some countries, suggesting that the assessment of the availability of these substances can be rather dependent on the scope of analysis.

49. Given such challenges, reliable data from competent national authorities are an essential starting point for the analysis of the availability of psychotropic substances. While data may be available in some countries with well-developed data-collection systems in place, other countries lack such systems. INCB stands ready to assist and guide Governments in improving their data-collection mechanisms, in particular with regard to data on the consumption of psychotropic substances. INCB encourages the competent national authorities of those countries that already have such data-collection systems in place to submit their data on the consumption of psychotropic substances in a regular, timely and consistent manner.

50. As stated above, there is currently no well-established way of assessing adequate levels of consumption of psychotropic substances under international control. However, assuming that the available data are sufficient and reliable, thresholds for high and low use of psychotropic substances could be considered. Such thresholds would present a new approach to measuring the availability of psychotropic substances for the treatment of mental health disorders and would provide a helpful guide for the analysis of adequate levels of consumption. Benchmarking the consumption of psychotropics would ultimately allow INCB and national Governments to monitor medical and scientific needs for psychotropic substances with a view to ensuring that needs for medical purposes are met. The Board therefore recommends that WHO and relevant international organizations work with INCB to those ends.