and advocacy activities focusing on the ICD-11 CDDR have been organized in China to facilitate better dissemination and implementation. The SMHC has organized and published a series of papers on the CDDR in the *Chinese Journal of Psychiatry*, the most reputable Chinese psychiatric journal. The series consists of two papers to introduce the CDDR themselves, the progress of their development, and updates on their implementation in China[4,5], and ten papers to introduce significant changes in the diagnosis of major disorders in the ICD-11 CDDR, including anxiety disorders, mood disorders, personality disorders, schizophrenia and other primary psychotic disorders, neurodevelopmental disorders, and disorders due to substance use.

Notably, the series also includes one paper discussing the research progress and controversy related to gaming disorder as a new mental disorder in the ICD-11[6]. Moreover, as knowledge and expertise on gaming disorder are currently lacking in China, the SMHC has led studies and developed a screening tool in Chinese, provided public health recommendations[7], contributed to the WHO collaborative project on the development of new international screening and diagnostic instruments for the disorder[8], and organized webinars to enhance the capacity for evaluating and treating the disorder, in collaboration with the WHO and other important partners.

Over more than 15 years of work, several factors have contributed to China's successful implementation of the CDDR. First, China's government plays a crucial role in setting and promoting international standards in national health care. Strong government endorsement for the ICD-11 provides an excellent climate for implementing and disseminating the CDDR. Second, identifying and empowering a local champion for implementing the CDDR in China is essential for providing leadership, overall coordination, resource mobilization, training, quality assurance, change management, and sustainability. Entrusted by the WHO, the SMHC has led implementation efforts and played a vital role in dealing with the immense challenges of implementing a new classification system. Third, public awareness campaigns and stakeholder engagement initiatives have raised knowledge of the benefits of ICD-11 CDDR implementation. Involving stakeholders such as the WHO, the National Health Commission, professional associations, leading research centers, health care professionals, and patient advocacy groups can help foster sustainable momentum and gain essential support for the implementation, contributing to its success.

In the future, we will continue promoting the utilization and dissemination of the ICD-11 CDDR in China, ultimately aiming to scale up mental health care in the country[9]. First, we will continue to deliver nation-wide training on the ICD-11 CDDR for mental health professionals, including psychiatrists, psychologists, general doctors, nurses, social workers, as well as health managers and policy makers. Second, an interactive network for adoption of the ICD-11 CDDR will be developed to advance research, training and clinical initiatives, thereby enhancing the quality of mental health care in the country. Third, further activities – such as developing new auxiliary diagnostic tools, screening tools, and teaching curricula based on the ICD-11 – will be undertaken to facilitate the local adaptation and application of the ICD-11 and the CDDR. Finally, China will continue strengthening international cooperation with international psychiatric experts and organizations to enhance mental health globally.

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How the ICD-11 and the CDDR address the public health dimensions of substance use

The use of psychoactive substances is highly prevalent and contributes substantially to risk behaviours, morbidity and mortality. The United Nations Office on Drugs and Crime World Drug Report[1] estimated that, in 2021, one in every 17 people aged 15-64 in the world had used an illicit drug in the year before. Users increased from 240 million in 2011 to 296 million in 2021, substantially more than accounted for by population growth.

Cannabis continued to be the most used illicit drug (219 million users, 4.3% of the global adult population); 36 million people had used amphetamines, 22 million cocaine, and 20 million methylenedioxymethamphetamine (MDMA or "ecstasy") or related drugs in the previous year. An estimated 60 million people engaged in non-medical opioid use, 31.5 million of whom used opiates (i.e., non-synthetic opioids; mainly heroin).

Globally, there is very limited implementation of efficient and effective prevention strategies for substance use[2], and there is a substantial treatment gap for disorders due to this use[3]. Global evidence has called attention to the need for a new and comprehensive conceptualization of substance use disorders that incorporates the full range of relevant conditions, from risky consumption to mental disorders linked to harmful drug use[4].

In response to these challenges, the World Health Organization (WHO) adopted a public health approach to the development of the classification of disorders due to substance use in the ICD-11. By public health approach, we refer to a broader perspective that integrates health and social aspects, aiming to benefit affected individuals and their community, and focusing on population well-being[5].

From a public health perspective, it is essential to identify persons who exhibit a hazardous use of substances that increases the risk of harmful psychological or medical consequences, but whose symptoms do not meet the diagnostic requirements for substance use disorders. These individuals can benefit from education, prevention, and community interventions. People with diagnosable disorders need harm reduction and treatment services of differing intensities and settings, depending on the nature of their condition and the substance involved. Those who suffer physical or psychological harm due to others' substance use should also be identified and may require services[6].

In line with this perspective, the range of psychoactive substances classified in the ICD-11 section on disorders due to substance use has been expanded, reflecting changes in the substances associated with public health impact in different parts of the world. An extended set of substance classes will help track patterns more accurately, in order to formulate appropriate clinical and social policy responses nationally and globally. For example, a new set of categories for disorders due to synthetic cannabinoids has been added. Synthetic cannabinoids are sprayed on natural herb mixtures to mimic the euphoric effect of cannabis, and can produce respiratory depression[7]. Their use is reported in high-income countries, but little information is available for low- and middle-income countries[1].

As described in the Clinical Descriptions and Diagnostic Requirements for ICD-11 Mental, Behavioural and Neurodevelopmental Disorders (CDDR)[8], four primary conditions are identified for each class of psychoactive substances, which are hierarchically and mutually exclusive from one another: a) *hazardous substance use*, which is conceptualized as a pattern of substance use that is sufficient in frequency or quantity to increase the risk of harmful physical or mental health consequences to the user or to others; since it involves incremental risk for harm that has not yet occurred, it is not considered a mental disorder (rather, it appears in the ICD-11 chapter on "Factors influencing health status or contact with health services", facilitating early attention and advice from health professionals); b) *episode of harmful substance use*, which refers to an episode that has already caused harm to a person's physical or mental health or has resulted in behaviour leading to harm to the health of others, but in the absence of a known pattern of substance use; c) *harmful pattern of substance use*, a sub-dependence diagnosis, characterized by a persistent and repetitive pattern of substance use that has directly caused harm to the person or to someone else through the person's behaviour; and d) *substance dependence*, when a disorder of substance use regulation has arisen from repeated or continuous use of a substance, typically accompanied by a strong internal drive to use it.

In the ICD-11, the substance dependence diagnosis has been simplified with respect to the ICD-10. It is based on the presence of at least two of three key features: a) impaired control over substance use, b) increasing priority given to substance use over other activities, and c) physiological features of tolerance or withdrawal. Physical and mental harm is very commonly seen in substance dependence, but is not a required feature.

The CDDR indicate that clinicians may assign other substance use diagnoses in addition to one of the four primary diagnoses, depending on the specific clinical situation, including substance intoxication, substance withdrawal, and a range of substance-induced mental disorders (delirium; psychotic, mood, anxiety, obsessive-compulsive, and impulse control disorders)[8]. Additional medical diagnoses can be assigned as appropriate to describe the consequences of substance use. Clinicians can also apply a range of specifiers offering more precision in diagnosis according to the severity, course, or other manifestations of the primary and additional diagnoses.

The classification of conditions related to substance use in the ICD-11 clearly corresponds to different types of intervention needs, consistent with the WHO services pyramid framework describing the optimal mix of services for mental health[9]. Hazardous use is an appropriate target for brief interventions as well as for public health programs and primary prevention. Harmful use can be responded to in generalist settings, such as primary care, using mild or more intensive interventions depending on whether the problem is a single episode or a harmful pattern of use, and on the substance involved. The most severe cases of substance dependence are appropriately treated in more intensive specialized settings, but they represent only a small portion of the overall disease burden related to substance use. Accordingly, the ICD-11 and the CDDR will help clinicians conceptualize and communicate the most appropriate forms of treatment for specific disorders, and support public health interventions for more common but less severe presentations.

Overall, the ICD-11 and the CDDR are valuable tools for helping to reduce the gap between those who need treatment and those who receive it. They will also support improvements in drug and health policies through better characterization of different groups of people affected by substance use, who experience different types of harm and have different needs. This includes improvements in the treatment system to provide more effective alternatives for severe alcohol and drug dependence.

Implementing the new diagnostic requirements can also support a better referral system that matches the needs of different users to the services provided. It can also support improved epidemiological studies and generate more valuable data for WHO member states by providing better categories that accurately re-

flect substance use outcomes. Finally, and importantly, the new classification supports implementing a public health model rather than focusing only on punishment and incarceration.

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Effects of cannabidiol on symptoms in people at clinical high risk for psychosis

There is an unmet treatment need for people at clinical high risk (CHR) for psychosis[1]. As only a minority of them go on to develop a psychotic disorder, interventions need to be particularly safe and well tolerated.

Cannabidiol (CBD), a non-intoxicating constituent of cannabis, has potential anxiolytic and antipsychotic properties[2] and a good safety profile. In two out of three clinical trials in patients with established psychosis, evidence of its antipsychotic efficacy has been reported[3-5]. However, there have not been trials of a period of treatment with CBD in CHR individuals. We assessed the clinical effects of a course of CBD treatment in people with a CHR state following a protocol approved by the National Research Ethics Service Committee London (Camberwell, St. Giles) (ISRCTN46322781).

The study was conducted on antipsychotic-naïve subjects attending early detection services in the UK who met one or more criteria for CHR state for psychosis: a) attenuated psychotic symptoms; b) brief limited intermittent psychosis (i.e., a psychotic episode lasting <1 week which remitted without treatment); c) recent functional decline and either schizotypal personality disorder or first-degree relative with psychosis. Key exclusion criteria were history of previous psychotic disorder or manic episode, neurological disorder, or current DSM-IV diagnosis of substance dependence.

Thirty-three subjects were recruited after they provided written informed consent. They were advised to refrain from using cannabis for 96 hours, alcohol for a minimum of 24 hours, nicotine for 6 hours, and any other recreational drugs for 2 weeks before entering the study, and to continue to refrain from using cannabis or other recreational drugs during the course of the study. Baseline assessments included the Comprehensive Assessment of At-Risk Mental States (CAARMS)[6]; the Spielberger State-Trait Anxiety Inventory, State Subscale (STAI-S)[7]; and the Positive and Negative Syndrome Scale (PANSS)[8].

Using a parallel group, double-blind, placebo-controlled design, participants were randomly allocated to either CBD (N=16) or placebo (N=17). They received either a CBD capsule or an identical-looking placebo capsule as a single daily oral dose, which they continued for 21 days. The dose of CBD (99.9% pure) was 600 mg/day, found to be effective and well-tolerated previously[4,9]. All clinical assessments were repeated after 7 and 21 days of treatment, except for the CAARMS, which was administered at baseline and at the end of treatment. Blood samples were collected before and after taking the study drug on days 1 and 21 to assay CBD plasma levels. The effects of treatment on symptoms were examined using analyses of variance with treatment (CBD vs. placebo) as the between-subject factor after controlling for baseline scores.

At baseline, the two treatment groups were comparable in demographic and clinical variables (see supplementary information). None of the participants received any psychotropic medication other than CBD or placebo during the course of the study. Two participants dropped out from the placebo arm. Following 21-day treatment (intention-to-treat, last observation carried forward analysis), CBD-treated participants had a lower total CAARMS score ($F_{1,30}$=7.168, p=0.012) than those receiving placebo, after controlling for baseline score. There were no significant differences between the treatment groups in the incidence of treatment-emergent side effects (see also supplementary information).

The CBD group also reported less distress associated with psychotic symptoms ($F_{1,30}$=4.66, p=0.039) and had a lower PANSS total score (p=0.042), after controlling for the respective baseline values. There was a greater reduction in the CAARMS negative symptoms (p=0.045), but not in the CAARMS positive symptoms (p=0.144), in CBD-treated patients. State anxiety levels following treatment were not different between the two groups (p=0.862).

When the analyses were restricted to participants with complete data for the respective measures, the CBD-treated group again had a lower total CAARMS score (p=0.033), with a trend for less distress associated with psychotic symptoms (p=0.072) and a lower total PANSS score (p=0.056). There were no group differences in the mean number of pills missed (p=0.85) or the proportion of patients who missed at least one pill (p=1.00). CBD levels were detectable in all except one out of 15 CBD participants with available data (see also supplementary information).