

National List of Essential Medicines in India: A Story of Deprivation of Substance Use Disorder Treatment

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The essential medicines list (EML) is a list of drugs that contains selected medications that are effective and safe in treating the most important disorders of the health system. The World Health Organization (WHO) publishes the WHO Model List of Essential Medicines (WHO-EML), which forms the basis for various countries to draft their EML.¹ The WHO-EML comprises two lists: the core list and the complementary list. The core list consists of the drugs that are essential and require minimal additional health resources. The complementary list consists of drugs that require additional training or special types of equipment. As of now, at least 156 developed and developing nations, including India, have published their EML.² India published its latest National List of Essential Medicines (NLEM) in 2015,³ with another list of EML of psychotropic medications in accordance with the Mental Healthcare Act 2017, in 2019. The Indian NLEM 2015 contains 376 drugs, with 13

psychotherapeutic agents, compared to the WHO EML list of 414 drugs in 2015.³

Principles and Process of Forming the Indian NLEM

The principles of forming the NLEM state that any drugs that fulfill certain basic requirements are included in the NLEM, including that a drug must be essential and the disease concerned must be a public health concern.⁴ Once included, the drug should significantly contribute to a reduction of the burden of the disease concerned. The drug should have proven efficacy, cost-effectiveness, and safety, to be used with reasonable ease and an acceptable risk-benefit ratio.



Furthermore, drugs are also classified based on their essentiality and need for being stocked in a primary, secondary, or tertiary care facility. The drugs that are included are single medicines and not a fixed-dose combination unless the combination is rational and has a proven benefit (such as, the combination has proven to be advantageous over individual ingredients administered separately, in terms of increasing efficacy, reducing adverse events, and/or improving compliance). Finally, the drug should be licensed in India and be aligned with the disease's current treatment guidelines.

On the other hand, a drug would be deleted from the list if (a) it is banned in India, (b) there are reports of concerns of the safety profile, (c) a drug with better efficacy, safety profile, or cost-effectiveness is now available, (d) the disease for which the drug is used is no longer a public health concern in India, or (e) in case of antimicrobial drugs, the drug has been rendered ineffective due to resistance.

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HOW TO CITE THIS ARTICLE: Parmar A, Pal A, Sharma P. National List of Essential Medicines in India: A Story of Deprivation of Substance Use Disorder Treatment. *Indian J Psychol Med.* 2021;43(6):531–534.

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Submitted: 24 Aug. 2020
Accepted : 22 Oct. 2020
Published Online: 7 Dec. 2020



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ACCESS THIS ARTICLE ONLINE
Website: journals.sagepub.com/home/szj
DOI: 10.1177/0253717620972942

Implementation and Practical Impacts of the Inclusion of Drugs in the NLEM

The selection of essential medicines is the first step towards improving the overall quality of health care and promoting rational drug use. Listing of a drug in the NLEM warrants that the drug is always available in sufficient quantity, at affordable cost, and with assured quality. The selection of essential medicines is one of the core principles of framing the National Medicine Policy (NMP), which aims to ensure access, quality, and rational use of drugs. The WHO endorses the framing and implementation, by all the countries, of an NMP that provide a framework for resolving the problems in pharmaceuticals. Along with the NLEM, the Indian government also introduced the National Pharmaceutical Pricing Policy (NPPP) to increase the availability of essential medicines in 2011, which was subsequently amended in 2012.⁵ This policy includes 652 commonly used drugs. The NLEM and NPPP have been expected to result in a drop of 10% in essential drugs' prices. Also, some industry-led initiatives across the world are considered a result of the inclusion of drugs in the EML. Large pharmaceutical companies are criticized for not making efforts to promote the availability and affordability of essential medicines, which has led to a range of actions, including reduced drug pricing, donations, and technology transfer agreements. Thus, the NLEM might act as a major tool to make the drugs available and affordable to the public.⁴

The NLEM and Substance Use Disorders in India

It has been reinforced that EML will address most disorders that are of public health concern, but the drugs used in the management of substance use disorders (SUD) have been largely neglected. To put matters further into perspective, Target 3.5 of the "sustainable development goals" states that countries should "strengthen the prevention and treatment of substance abuse, including narcotic drug

abuse and harmful use of alcohol."⁶ But a closer look at our EML shows an almost negligible representation of medications used for the treatment of SUDs (except for naloxone under the heading of antidotes and other substances used in poisoning). We hereby discuss the three most common SUDs, namely tobacco, alcohol, and opioids use disorders, in the Indian context and the need to include in the NLEM the medicines used to treat these SUDs.

Medications for Tobacco Use Disorders

Among the SUDs, tobacco use is the most prevalent in India. As per the National Mental Health Survey (NMHS) 2016, tobacco use disorder is the most common psychiatric condition (with a prevalence of 20.9%).⁷ Similar findings are reported by the Global Adult Tobacco Survey (GATS) 2 in 2016, with a 28.6% prevalence of current use of tobacco.⁸ Tobacco use is associated with significant morbidity and mortality. In 2015, around 11.5% of global deaths were attributable to smoking. Out of this, about 52% took place in four countries (one being India). Smoking is amongst the five leading risk factors for disability-adjusted life year (DALYs).⁹ In India, tobacco use is associated with more than 1 million deaths every year (9.5% of all deaths). Cardiovascular diseases are the most common cause of tobacco-related mortality, as well as premature deaths.¹⁰ Thus, the use of tobacco is a significant public health concern.

Despite this, the NLEM, published and revised four times to date (1996, 2003, 2011, and 2015), has failed to include drugs used to treat tobacco use disorder. Nicotine replacement therapy (NRT), bupropion, and varenicline are well established and effective first-line medications for tobacco use disorder.¹¹ The National Tobacco Control Programme (now renamed as National Program for Tobacco Control and Drug Addiction Treatment) also talks about setting up and strengthening of cessation facilities, including providing pharmacotherapy at the district level, as a key activity. The NLEM 2015 process suggests that any medicine, as and when recommended under the national program, should be included in the NLEM.¹² Therefore, given

the evidence for NRT in the treatment of tobacco use disorder and the fact that it is present in the WHO-EML, the authors suggest the inclusion of NRT in the NLEM of India. NRT must be made available from the Primary Health Centers (PHC) level. In contrast, the other medications like bupropion and varenicline may be made available from secondary care centers where specialists are likely to be available under the District Mental Health Programme (DMHP).

Medications for Alcohol Use Disorders

Alcohol is also a major cause of morbidity and mortality, like tobacco.¹³ Alcohol is found to be one crucial barrier to sustainable development goals globally.¹⁴ The global strategy to reduce the harmful use of alcohol, 2010, by the WHO suggests that reducing alcohol use and associated health and social conditions is a major public health priority.¹⁵ As per the Global Status Report on Alcohol and Health 2018, the harmful use of alcohol resulted in three million deaths (5.3% of all deaths) worldwide and 132.6 million DALYs, that is, 5.1% of all DALYs for that year.¹⁶ The prevalence of alcohol use disorder in India as per the NMHS 2016 was 4.6%. The recent National Survey on Extent and Pattern of Substance Use 2019 reported 160 million alcohol users in India, with almost 57 million problem users requiring treatment/help. The Global Burden of Disease study suggested an increase in the per capita consumption of alcohol in India. Correspondingly, alcohol-attributable death rates are also increasing.¹⁴

The gold-standard drugs for the management of alcohol withdrawal are long-acting benzodiazepines like diazepam or chlordiazepoxide.¹⁷ But, the current EML has no provision for such drugs. The NLEM has drugs like lorazepam (listed under drugs to treat anxiety disorders), which can be used alternatively. In terms of safety, cost-effectiveness, and reliability in treating the potentially fatal alcohol withdrawal condition, a benzodiazepine (preferably a short-acting one that can be used in different age groups and in those with medical comorbidities) should be included in the list. Anti-craving drugs such as naltrexone and acamprosate

and deterrent drugs like disulfiram are effective drugs in treating alcohol use disorder.¹⁸ Despite the enormous burden related to alcohol use globally, the WHO has also failed to include these medications in the EML.¹⁹ There have been calls to include medications used for alcohol use disorder treatment into this list.²⁰ Thus, given the evidence for benzodiazepines in treating alcohol withdrawal, we suggest the inclusion of drugs like diazepam or lorazepam in the NLEM. We also pitch to include disulfiram, naltrexone, and acamprosate in the NLEM. These medications must be made available from the PHC level.

Medications for Opioid Use Disorders

Finally, opioid use disorders (OUD) are also important public health concerns globally and in the Indian context as they are important contributors to the global disease burden. The Global Burden of Disease study estimated 31.8 million DALYs and 1.3% of all DALYs were attributable to drug use disorders (major contributors being opioids).²¹ As per the National Survey on Extent and Pattern of Substance Use 2019 of India, there are 23 million opioid users in India, of which around 8 million are problem users (fulfilling the criteria for either dependence or harmful use). Almost 0.85 million people use drugs (primarily opioids) through the injecting route.

Methadone and buprenorphine are both effective and safe in treating OUD. Medication-assisted treatment using buprenorphine/methadone is the first-line treatment option supported by most international and national OUD treatment guidelines.²² Also, another important role of opioid substitution therapy (OST) comes in HIV/AIDS prevention among People Who Inject Drugs (PWID).²³ Scientific evidence accumulated over the last three decades suggests that OST has an important role in HIV/AIDS prevention, treatment, and care. In India, among all the high-risk groups, the highest prevalence of HIV is found amongst PWID.²⁴ The National AIDS Control Organisation (NACO)-supported centers are the major providers of OST in India. Thus, scientific evidence suggests a major role of OST as a public health tool in treating OUD and HIV/AIDS prevention, care, and treatment among PWID.

In OUD management, the most widely used drugs in India are buprenorphine and buprenorphine–naloxone combination (BNX). BNX has proven efficacy and safety over plain buprenorphine tablets in terms of the prevention of diversion. But, neither buprenorphine/BNX nor methadone is included in Indian EML. On the contrary, the WHO-EML contains both methadone and buprenorphine in its complimentary list. Interestingly, codeine, fentanyl, and morphine find a place in the core list of the WHO-EML as chronic pain medications. As BNX is available as office-based dispensing, there have been calls to include BNX in the core list of WHO-EML.²⁵ Also, studies from the west have reported its use for long-term maintenance therapy to be cost-effective even in primary care settings.²⁶ Thus, the inclusion of BNX in the NLEM might boost OST services in India.

It is interesting to note that naloxone, a medication to treat opioid overdose, made it into the NLEM. However, the most effective medications in preventing opioid overdose, that is, opioid agonists in the form of maintenance treatment, are missing from the list.^{27–28} In 2015, the central government notified the list of “essential narcotic drugs” for medical and scientific purposes under section 8 of the Narcotic Drugs and Psychotropic Substances Act 1985. The list includes methadone along with codeine, morphine, hydrocodone, oxycodone, and fentanyl. This amendment encourages the use of methadone rather than buprenorphine, which failed to make it to the list. This approach is deemed paradoxical because methadone is highly regulated, while buprenorphine can be prescribed on an outpatient basis internationally. There are recent suggestions to urgently form the Essential Psychotropic Drugs list and include buprenorphine in the essential NLEM.²⁹ Lastly, naltrexone, an opioid antagonist acknowledged to be reliably safe and effective in treating OUD, is also an unworthy omission from the list. Thus, given the evidence for BNX in the treatment of OUD (both for acute withdrawal management and long-term maintenance) and the fact that it is widely used at OST centers run by NACO for HIV prevention purpose (and in a way, its use is essential in these settings), it must also be included in the NLEM and made available from

secondary care centers where specialists are likely to be available under DMHP. After ensuring proper training of PHC staff, BNX may also be considered at the PHC level. This will help expand OST services in government settings and NGO and private sectors.²⁹

The Way Ahead

The list of essential medicines is dynamic. The NLEM 2015 was prepared using a complex process consisting of (a) constitution of core-committee members by the Ministry of Health and Family Welfare, (b) core-committee meeting to outline the process and inviting experts' nominations, (c) preparation of source document, (d) consultations across the country, and (e) final deliberations by the core committee. The revision considered and deliberated on every stakeholder and expert's opinions through wider consultations. Thus, experts from the field of addiction medicine and the professional bodies may get more actively involved in future consultations and pitch to include these drugs. Civil society organizations working in the area of substance use may also place their viewpoint before the core committee. Other deliberations, such as a session on the NLEM organized during the Annual Conference of Indian Pharmacological Society 2009, were also considered for making the NLEM 2011. Thus, a wider discussion about the essential medicines on the scientific forums may also help get involved in the process.

Conclusion

NLEM is a dynamic list that is ever-evolving, yet medications for SUD have been neglected in it.²⁰ On the other hand, the NLEM includes medications used to manage all other major causes of morbidities and mortalities, including antibiotics, medicines for cardiovascular illnesses, antineoplastic and immunosuppressant agents, and insulin, among many others. This becomes an important contemporary issue, considering the rising burden of SUD in India. The inclusion of medication in an essential drug list may have a game-changing impact (the most remarkable example being the inclusion of antiretroviral agents for HIV/AIDS treatment in 2002 and the recent inclusion of direct-acting antivirals for HCV).³⁰ Fortifying the NLEM will shed light on this epidemic of SUD in

India and strengthen treatment options in its management.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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