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COVID-19 and addiction

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**Highlights:**

- Addiction and COVID-19 fuel each other to cause a global public health threat.
- Resumption of deaddiction service and relaxation of accessibility of prescription drugs are needed.
- Psychiatrists must be prepared for imminent hike in withdrawal symptoms and addictive behaviors.

**Abstract:**

Background and aims: 2019-coronavirus disease (COVID-19) is causing insurmountable psychosocial impact on the whole mankind. Marginalized community, particularly those with substance use disorders (SUD), are particularly vulnerable to contract the infection and also likely to suffer from greater psychosocial burden. This article analyses the intricate bi-directional relationship between COVID-19 and addiction.

Methods: Pubmed and Google Scholar are searched with the following key terms- “COVID-19”, “SARS-CoV2”, “Pandemic”, “Addiction”, “Opioid”, “Alcohol”, “Smoking”, “Addiction Psychiatry”, “Deaddiction”, “Substance use disorders”, “Behavioral addiction”. Few newspaper reports related to COVID-19 and addiction have also been added as per context.

Results: People with SUD are at greater risk of worse COVID-19 outcome. There is surge of addictive behaviors (both new and relapse) including behavioral addiction in this period. Withdrawal emergencies and death are also being increasingly reported. Addicted people are especially facing difficulties in accessing the healthcare services which are making them prone to procure drugs in illegal means.

Conclusion: COVID-19 and addiction are the two pandemics which are on the verge of collision causing major public health threat. While every effort must be taken to make the public aware of deleterious effects of SUD on COVID-19 prognosis, the resumption of deaddiction services and easier accessibility of prescription drugs are needs of the hour.

**Key words:** COVID-19; SARS-CoV2; Pandemic; Addiction; Smoking; Alcohol; Opioid; Behavioral addiction; Internet

**Introduction:**

*“.....Modern life, too, is often a mechanical oppression and liquor is the only mechanical relief. Let me know if my books make any money and I will come to Moscow and we will find somebody that drinks and drink my royalties up to end the mechanical oppression.”* – Earnest Hemingway in 1935.

These words from the famous American novelist sound germane to the current time probably more than ever in the history of human civilization. Substance Use Disorders (SUD), characterized by an array of mental, physical, and behavioral symptoms, a great public health concern, claim directly or indirectly the lives of millions of people every year. Alcohol consumption and illicit drug addiction cost around 1.5 % of the global burden of disease and it can be as high as 5% in some nations according to recent data [1]. The 2019-coronavirus disease (COVID-19), undoubtedly the greatest public health catastrophe of our times, has been making universal concern throughout the world over the past few months and is throwing up several challenges for us in numerous ways. The primary measures to contain the outbreak, like home confinement and sustained lockdown, are eventually leading to insurmountable economic burden at community level and are propelling the mass to face various unwelcome emotional reactions, psychological difficulties, behavioral changes including excessive substance abuse [2]. On the other hand, people suffering from SUD belong to the marginalized community and are invariably more prone to contract infection during the COVID-19 pandemic [3,4]. This review intends to highlight the bi-directional relationship between COVID-19 and addiction, and analyze how these two menaces interact with each other to impose a greater public health threat.

**Method of literature search:**

Pubmed and Google Scholar have been searched with the following key terms- “COVID-19”, “SARS-CoV2”, “Pandemic”, “Addiction”, “Opioid”, “Alcohol”, “Smoking”, “Addiction Psychiatry”, “Deaddiction”, “Substance use disorders”, “Behavioral addiction” (time limit- 1<sup>st</sup> November, 2019 to 27<sup>th</sup> May, 2020). Few leading news paper reports related to COVID-19 and addiction have also been added where deemed appropriate.

### **Substance abuse as the risk factor for acquiring SARS-CoV2:**

People with SUD are at heightened risk for pulmonary infections due to- 1) substance abuse related pre-existing cardio-pulmonary morbidities, 2) mucociliary dysfunction, 3) compromised immunity 4) altered health-seeking behavior and inadequate access to health care delivery, 5) failure of rehabilitation strategies due to social distancing, and 6) housing instability [5]. Individuals with pre-morbid respiratory and cardiac pathologies (i.e. chronic obstructive pulmonary disease, cardiovascular diseases) are established as high-risk population to acquire novel severe acute respiratory system corona virus (SARS-CoV2) and it leads to greater mortality [6,7]. As SUD is associated with plethora of cardio-respiratory and metabolic ailments, it's highly probable that they are also at the heightened risk for COVID-19 [8].

Smoking has been found to be an adverse prognostic indicator of COVID-19 [9-12]. Apart from traditional risks imposed by smoking on cardio-pulmonary health [13], the specific risk factor related to COVID-19 is increased expression of type-2 angiotensin converting enzyme (ACE2) among smokers [8,14]. Thus, the nicotineric pathway mediated overexpression of ACE-2, the putative receptor for SARS-CoV2 might be associated with increased virion entry [8,14-18]. It is yet to be unfurled whether smoking is actually an independent risk factor for COVID-19 and does not get confounded by age, sex, ethnicity and comorbidities [19]. Contradictory evidences of non-association (sometimes even negative association) of smoking and COVID-19 severity

among have also come up, albeit these studies are limited by small, heterogenous study population, underreporting of smoking status and statistical fallacies [20-23]. Future research must be directed to delineate more stringent association between smoking status (both current and past), associated comorbidities and COVID-19, possibility of transmission of SARS-CoV2 via secondhand smoking, hazards of e-cigarettes and vaping [24]. Based on some perplexing data revealing a negative association between smoking and COVID-19 and the fact that nicotine might possess a immunomodulatory effect to blunt the cytokine storm, there is a newly generated interest in using nicotine as a therapeutic against SARS-CoV2 [22,25-27]. Above all, the conflicting findings of the studies should be taken with utmost care so that wrong or aberrant messages at the present time of “infodemic” do not influence the public health measures to mitigate smoking [28].

A similar health-risk might be imposed by alcohol consumption, although there is lack of systematic data regarding alcohol consumption and COVID-19 risk. Dysfunctional immune system, vitamin deficiency, heightened risk of aspiration pneumonia, associated liver and cardiometabolic diseases, increased risk of thrombosis- all can act synergistically to cause worse health outcome [29]. Extra caution should be taken regarding the misinformation surrounding any protective effects of alcohol against COVID-19 [30].

Those who take opioid for therapy are at risk of fatal overdose. Opioid overdose can cause respiratory depression and hypoxemia which in turn lead to cardiopulmonary and neurological complications and worsen outcome of COVID-19 [31].

Methamphetamine, an increasingly abused drug can cause lung injury, pulmonary hypertension, and cardiomyopathy. Experts have advised to be vigilant regarding the possibility of increased risk for worse COVID-19 outcomes among methamphetamine abusers [32].



Behaviors associated with substance abuse provide recipe for community spread of the virus. SARS-CoV-2-laden particles drift through mephitic vaping and wafting smoke [33]. Repeated spitting habits are customary in tobacco-chewers [34]. High risk behavior such as sharing of cigarettes, alcohol and needles between peers increases the chance of outbreak [35]. A hugely criticized decision taken by the Government was to open the liquor shop to upgrade the fallen economy leading to huge crowd in front of liquor shop disrupting the social distancing as well [36].

### **Surge of substance addictive behavior during COVID-19:**

Acute and chronic stressors have well been attributed to the inception and protraction of many SUDs among general public. Serotonergic modulation of the dopaminergic pathways leads to reduced activation of the mesolimbic reward circuit of brain in people with depression; and addictive substances like alcohol and others produce prolific activation of the reward system bringing temporary pleasure to them. Furthermore, alcoholic beverages when used for prolonged duration result in neuronal adaptations in the stress and reward pathways and flares up the neuroendocrine responses and stress reactivity, which in turn aggravate alcohol-related cravings when a stressful situation arrives [37,38] (figure-1).

The unique situation created by the COVID-19 pandemic in terms of chronic social isolation, physical distancing, and sustained lockdown across many countries are resulting in various undesirable outcomes with respect to health and wellbeing [2]. A big chunk of the world population has been encountering newly developed concomitant psychosocial stressors such as prolonged home confinement, depression and panic due to unknown nature of the disease, fear of contracting infection, vulnerability, work from home, anxiety regarding flow of income, fear of losing jobs [39]. On top of that, abrupt unemployment are posing extreme difficulties for people

of low-income groups like small businessmen, migrant workers and daily earners to make both ends meet in this hard time and causing unparalleled distress among them due to sheer uncertainty of the future [40-42]. Distressed person may take refuge in addictive substances, whichever is cheap and readily available to allay their negative feelings. This can potentially trigger the development of SUD in high-risk groups and also a spike in incidence of SUD among general population as well [43-45].

Authorities of many a countries deemed alcohol and tobacco to be an “essential commodity” that too during the lockdown and even promoted its business through wide relaxation of the licensing rules. Reportedly a surge in the sale of alcohol has been observed within the lockdown period, again reinforcing the origin of SUD in population [46-49]. Klemperar et al have revealed that both tobacco and electronic cigarette addicts have responded to the newly developed stressors by increasing their number and frequency of use [50]. While Klemperar et al have found nearly a third perceive this period as an opportunity to quit [50], a Google trend analysis study has not shown any increase in internet search related to “smoking cessation” [51]. Expert has cautioned over possibility of increased frequency of smoking among current smokers and greater chance of relapse among ex-smokers [52]. Increased frequency of home drinking and cigarette smoking (secondhand smoke) increases the likelihood of direct negative impact on family members, especially children [47,53].

#### **Deleterious effects of the pandemic on the addicts- when aggression meets desperation:**

There is widespread concern that physical and social functioning as well as mental well-being of the substance users and addicts will be abysmally affected by the COVID-19 crisis [54]. Prolonged travel-ban across the world has limited the supply of recreational substances in the market, making a way for the shoot up of adulterated and toxic substitutes at cheaper price in the

streets. Moreover, many reports are there that substance trippers are obtaining their needs at an exorbitant price and sometimes by illegal ways [55,56]. This has nefarious implications like verboten and hostile activities in the addicts, stock-piling of required substances at residences, further financial strain and frailty, and unfortunately, rise in black marketing [44,46]. Both unavailability and abundance of substances bring about mood changes leading to irritability, aggression, misplaced priorities, generalized disrespect towards societal norms and inability to uphold the familial values among the addicts. Expenses of money chasing behind the substances which are presently being sold at much higher cost leave the family members wretched leading to familial disharmony and incidences of domestic violence [49,57,58]. When craving goes out of their control, many addicts are often propelled to self-destructive conduct. Combination of alcohol with other psychotropic and narcotic drugs can often prove lethal, and prompt medical attention is critical in these cases which can be difficult amidst the COVID-crisis. Furthermore, many of alcohol-dependent persons have reportedly found their sanctum in homemade alcoholic spirits, sanitizers (containing non-edible alcohol) and substances which have been proved being more parlous and often mortal [59-61] (figure-2).

One may envisage that it is the high time to curb addiction problem as hindered availability of resources, altered ambience and limited peer pressure are there as well as parties, carousing, frolics are nowadays out of scope because of strict governmental strategies implemented to check community transmission of COVID-19 [48,62]. Inaccessibility undoubtedly reduces the substance exposure but at the cost of more pronounced cravings and withdrawal effects. The hospitals in India are already dealing with substantially increased number of alcohol-withdrawal cases which at times are claiming lives and incontestably putting sheer burden on the already strained health care system [63-66].

**Behavioral addiction:**

Apart from the COVID-19 pandemic and surge in SUD, “infodemic” and internet addiction along with its different allies of behavioral addictions in different forms have surfaced in this unprecedented time of human history. COVID-19 pandemic and lockdown have given birth to a hidden current of behavioral addictions, which is sufficient enough to exert its powerful shock affecting predominantly adolescents and young adults. Lockdown, isolation, loss of job, financial burden, stress, depression, anxiety, phobia and lastly availability of plenty leisure time all together put forward a fertile field on which behavioral addictions starts growing relentlessly. Literature shows that usage of internet, particularly websites related to pornography and video gaming has been markedly increased in this period of lockdown [67]. Among behavioral addictions, internet addiction (use of social media particularly), internet sex, video games top the list [67,68]. Apart from its ill effects on mental health, increased screen time leads to decreased physical activity, altered eating habits and disrupted circadian rhythm which ultimately culminate into magnitude of cardiometabolic disorders, obesity, diabetes [2,69]. Due to financial burden and uncertain future problem gambling is looming large [70,71]. Eating disorders and compulsive buying are probably less prevalent in Indian scenario, yet increasingly being reported in Western countries [72,73]. COVID 19 pandemic and its psychosocial associates actually made one apparently invisible vicious cycle which starts with stress, depression, social isolation, anxiety, excess leisure time with cheap internet services leading to surge of behavioral addictions which in turn results in mood changes, irritability, anxiety and stress only to hold firmly the initiators and sequential ignition of this viscous cascade with lingering aftermath.

**Special mentions on marginalized population:**

Different cohorts of the community have different vulnerabilities to COVID-19 infection and related psychopathology. There already exists a high prevalence of SUD among the homeless populace, migrant workers, prisoners and other marginalized communities and they are at increased risk of contracting the virus and facilitating transmission amongst others [2,32,74]. Medical students and residents are particularly at vulnerable stage of their career due to psychological toll while caring for COVID-19 patients, impaired learning ecosystem and future uncertainty [75]. Health-care workers are particularly vulnerable to behavioral addiction which has been found to be related with acute stress reaction during COVID-19 pandemic [76].

#### **Opioid and injection drug users:**

Opioid crisis and its management is perhaps the most debated one among SUD in COVID-19 era. Opiate addicts are particularly facing challenge at this time due to greater marginalization, difficulty in accessing specific health-care, imposed restriction on drugs, closure of deaddiction centers, increased risk of life-threatening withdrawal and usage of illicit opiates [77]. While to mitigate these problems loosening of restriction regarding accessibility of prescription opioids, home-based self injection strategy and long-acting formulations of methadone and buprenorphine have been suggested, there is also fear of overdosage [31,78]. Moreover, opiate users may misinterpret COVID-19 symptoms as opioid withdrawal and treat it by self-administering opioids [79]. The calls for actions for special care towards opioid users from various clinical societies might sound a far-reaching ambition from Indian perspective due to lack of structured opioid substitution programs, provision for home-based administration of opioid substitutes, lack of tele-care and augmented social stigma [44,80].

#### **Difficulties faced by patients undergoing deaddiction therapy:**

Addiction is popularly known as a disease of isolation and the treatment protocols for substance users are aimed at returning to a drug-free life through family support, socialization, cognitive and behavioral therapy apart from medications. The whole thing is gradually achieved through various sessions and requires establishment of connections in between addicts and their therapists. Nevertheless, social distancing, which is of paramount importance to keep the community transmission at bay, is indubitably playing as a detrimental factor in relapse of SUD during these days [32]. Often persons with SUDs themselves are reluctant to consultation and become non-compliant to therapeutics. Since facilities to provide support and interventions are prorogued nowadays in the wake of COVID-19, having continuous motivation for deaddiction therapy has been greatly difficult [79]. It should be remembered that recovery from addiction is a long-lasting process and incidence of unchecked cross addiction can occur at any stage, more likely during the early days of recovery. Individuals may find a newly available substitute that triggers the dopamine reward center of brain in the same way and set out to bring the “feel-good” effects. Thus, even after successfully recovering from SUD, a person can start up a new addiction again that gives birth to a vicious cycle.

Stigma associated with SUD and COVID-19 act synergistically in the addict people rendering them marginalized, and aloof. Specious yet stubborn beliefs even among health care providers, that an addict lacks moral values, distance them from retrieving basic as well as special health care [81]. Many of those addicts who are currently undergoing rehabilitation programs are not getting uninterrupted supply of medicines, appointment for their treating therapists, swift therapies for withdrawal manifestations and social support due to complete lock-down of transport, premature discharge from hospitals, altered triage system in hospitals [32,79]. Most of the private clinics and detox centers have been being closed now for over months pending

pandemic's containment, and forced the disinclined patients to attend government hospitals only [44]. Hospitals being already overburdened to manage this health disaster, community of addicts is being pushed further afar even if they come with symptoms of COVID-19 and alike illnesses [79,82]. Albeit, extended tele-health facilities are somewhat to quell and palliate the misery, condition of developing and under-developed countries like India are afflicting [44].

### **Way forward and conclusion:**

Addictive behavior and COVID-19 form the dangerous duo which fuels each other's propagation. If a nation has to recover from this disastrous pandemic, the special need for the marginalized strata of the society must be addressed with the utmost care [83]. A strong support system must be built and Government, society, family and health care providers should play their due responsibilities. Government and legislative bodies must act towards upholding the social security of the substance addicts, maintaining the availability and accessibility of prescription drugs, uninterrupted deaddiction and harm-reduction services [79,81,84]. While due care must be taken to prevent and treat withdrawal symptoms, cessation of addictive behavior must be promoted at every opportunity [52,85,86]. These marginalized sections of the society must receive easy-to-understand proper advice regarding basic preventive measures against COVID-19. Behavioral addiction, although often overlooked, should be taken care of. Close monitoring of internet contents and its usage by children and other vulnerable groups is to be done by family members. Engagement in family-time, physical exercise, creative works are potential measures to mitigate the internet addiction [67]. Reinforcement of the tele-psychiatry communication may supplement the ongoing traditional psychiatric care [87]. Last but not the least, proper education will help people to concede health hazards of substance use, even if recreational and elixir of an addiction-free livelihood.

**Figure legends:**

1. Figure-1: Etiologies of substance use disorders
2. Figure-2: Bidirectional relationship between COVID-19 and addiction

**References:**

1. GBD 2016 Alcohol and Drug Use Collaborators. The global burden of disease attributable to alcohol and drug use in 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Psychiatry*. 2018;5:987-1012.
2. Dubey S, Biswas P, Ghosh R, Chatterjee S, Dubey MJ, Chatterjee S, et al. Psychosocial impact of COVID-19. *Diabetes Metab Syndr*. 2020; DOI: 10.1016/j.dsx.2020.05.035
3. Ornell F, Moura HF, Scherer JN, Pechansky F, Kessler F, von Diemen L. The COVID-19 Pandemic and its Impact on Substance Use: Implications for Prevention and Treatment. *Psychiatry Res*. 2020;289:113096.
4. Columb D, Hussain R, O'Gara C. Addiction Psychiatry and COVID-19 - Impact on patients and service provision. *Ir J Psychol Med*. 2020 May 21:1-15. doi: 10.1017/ipm.2020.47.
5. Schulte MT, Hser YI. Substance Use and Associated Health Conditions throughout the Lifespan. *Public Health Rev*. 2014;35(2). doi: 10.1007/BF03391702.
6. Alqahtani JS, Oyelade T, Aldhahir AM, Alghamdi SM, Almehmadi M, Alqahtani AS, et al. Prevalence, Severity and Mortality associated with COPD and Smoking in patients with COVID-19: A Rapid Systematic Review and Meta-Analysis. *PLoS One*. 2020;15:e0233147.
7. Aggarwal G, Cheruiyot I, Aggarwal S, Wong J, Lippi G, Lavie CJ, et al. Association of Cardiovascular Disease With Coronavirus Disease 2019 (COVID-19) Severity: A Meta-Analysis. *Curr Probl Cardiol*. 2020 Apr 28:100617.



8. Olds JL, Kabbani N. Is nicotine exposure linked to cardiopulmonary vulnerability to COVID-19 in the general population? *FEBS J.* 2020 Mar 18;10.1111/febs.15303.
9. Vardavas CI, Nikitara K. COVID-19 and smoking: A systematic review of the evidence. *Tob Induc Dis.* 2020;18:20.
10. Berlin I, Thomas D, Le Faou AL, Cornuz J. COVID-19 and smoking. *Nicotine Tob Res.* 2020 Apr 3:ntaa059.
11. Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Lian N, et al. The impact of COPD and smoking history on the severity of COVID-19: A systemic review and meta-analysis. *J Med Virol.* 2020 Apr 15. doi: 10.1002/jmv.25889.
12. Patanavanich R, Glantz SA. Smoking is Associated with COVID-19 Progression: A Meta-Analysis. *Nicotine Tob Res.* 2020 May 13:ntaa082.
13. Cattaruzza MS, Zagà V, Gallus S, D'Argenio P, Gorini G. Tobacco smoking and COVID-19 pandemic: old and new issues. A summary of the evidence from the scientific literature. *Acta Biomed.* 2020;91:106-12.
14. Leung JM, Yang CX, Tam A, Shaipanich T, Hackett TL, Singhera GK, et al. ACE-2 expression in the small airway epithelia of smokers and COPD patients: implications for COVID-19. *Eur Respir J.* 2020;55:2000688.
15. Brake SJ, Barnsley K, Lu W, McAlinden KD, Eapen MS, Sohal SS. Smoking Upregulates Angiotensin-Converting Enzyme-2 Receptor: A Potential Adhesion Site for Novel Coronavirus SARS-CoV-2 (Covid-19). *J Clin Med.* 2020;9:841.
16. Russo P, Bonassi S, Giacconi R, Malavolta M, Tomino C, Maggi F. COVID-19 and Smoking. Is Nicotine the Hidden Link? *Eur Respir J.* 2020 Apr 27:2001116.

17. Smith JC, Sausville EL, Girish V, Yuan ML, Vasudevan A, John KM, et al. Cigarette smoke exposure and inflammatory signaling increase the expression of the SARS-CoV-2 receptor ACE2 in the respiratory tract. *Dev Cell*. 2020 May 16. doi: 10.1016/j.devcel.2020.05.012.
18. Cai G, Bossé Y, Xiao F, Kheradmand F, Amos CI. Tobacco Smoking Increases the Lung Gene Expression of ACE2, the Receptor of SARS-CoV-2. *Am J Respir Crit Care Med*. 2020 Apr 24. doi: 10.1164/rccm.202003-0693LE.
19. Cai H. Sex difference and smoking predisposition in patients with COVID-19. *Lancet Respir Med*. 2020;8:e20.
20. Lippi G, Henry BM. Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19). *Eur J Intern Med*. 2020;75:107-8.
21. Rossato M, Russo L, Mazzocut S, Di Vincenzo A, Fioretto P, Vettor R. Current Smoking is Not Associated with COVID-19. *Eur Respir J*. 2020:2001290.
22. Farsalinos K, Barbouni A, Niaura R. Systematic review of the prevalence of current smoking among hospitalized COVID-19 patients in China: could nicotine be a therapeutic option? *Intern Emerg Med*. 2020 May 9:1–8. doi: 10.1007/s11739-020-02355-7.
23. Lo E, Lasnier B. Active smoking and severity of coronavirus disease 2019 (COVID-19): The use of significance testing leads to an erroneous conclusion. *Eur J Intern Med*. 2020 May 8:S0953-6205(20)30188-6.
24. Leung JM, Sin DD. Smoking, ACE-2, and COVID-19: Ongoing Controversies. *Eur Respir J*. 2020 May 19:2001759. doi: 10.1183/13993003.01759-2020.
25. Garufi G, Carbognin L, Orlandi A, Tortora G, Bria E. Smoking habit and hospitalization for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-related pneumonia: The

- unsolved paradox behind the evidence. *Eur J Intern Med.* 2020 Apr 23:S0953-6205(20)30163-1.
26. Polosa R, Caci G. COVID-19: counter-intuitive data on smoking prevalence and therapeutic implications for nicotine. *Intern Emerg Med.* 2020 May 19:1–4. doi: 10.1007/s11739-020-02361-9.
  27. Tindle HA, Newhouse PA, Freiberg MS. Beyond Smoking Cessation: Investigating Medicinal Nicotine to Prevent and Treat COVID-19. *Nicotine Tob Res.* 2020 May 8:ntaa077. doi: 10.1093/ntr/ntaa077.
  28. Leung JM, Yang CX, Sin DD. Reply to: "Current Smoking is Not Associated with COVID-19". *Eur Respir J.* 2020 May 4:2001340.
  29. Testino G. Are Patients With Alcohol Use Disorders at Increased Risk for Covid-19 Infection? *Alcohol Alcohol.* 2020 May 13:agaa037.
  30. USA Today. Fact check: To minimize coronavirus risk, use alcohol for sanitizing, not for drinking. 2020. Available from: <https://www.usatoday.com/story/news/factcheck/2020/03/20/fact-check-drinking-alcohol-wont-reduce-coronavirus-risk/2881704001/> (last accessed on 27<sup>th</sup> May, 2020)
  31. Becker WC, Fiellin DA. When Epidemics Collide: Coronavirus Disease 2019 (COVID-19) and the Opioid Crisis. *Ann Intern Med.* 2020 Apr 2:M20-1210. doi: 10.7326/M20-1210.
  32. Volkow ND. Collision of the COVID-19 and Addiction Epidemics. *Ann Intern Med.* 2020 Apr 2:M20-1212. doi: 10.7326/M20-1212.
  33. Shekhar S, Hannah-Shmouni F. Hookah smoking and COVID-19: call for action. *CMAJ.* 2020;192:E462.

34. Hindustan Times. Spitting in public, chewing tobacco could spread Covid-19, govt warns. 2020. Available from: <https://www.hindustantimes.com/india-news/spitting-in-public-chewing-tobacco-could-spread-covid-19-govt-warns/story-MA3z2ztbol7tyyD1TDkAWM.html> (last accessed on 27<sup>th</sup> May, 2020)
35. Mungmungpantipantip R, Wiwanitkit V. Sharing Alcoholic Drinks and a COVID-19 Outbreak. *Alcohol Alcohol*. 2020 May 13;agaa028.
36. The Hindu. Congress, BJP leaders criticise Tamil Nadu's decision to reopen TASMAL liquor outlets. 2020. Available from: <https://www.thehindu.com/news/national/tamil-nadu/congress-bjp-leaders-criticise-tamil-nadus-decision-to-reopen-tasmal-liquor-outlets/article31509088.ece> (last accessed on 27<sup>th</sup> May, 2020)
37. Höflich A, Michenthaler P, Kasper S, Lanzenberger R. Circuit Mechanisms of Reward, Anhedonia, and Depression. *Int J Neuropsychopharmacol*. 2019;22:105-18.
38. Clay JM, Parker MO. Alcohol use and misuse during the COVID-19 pandemic: a potential public health crisis? *Lancet Public Health*. 2020;5:e259.
39. Lima CKT, Carvalho PMM, Lima IAAS, Nunes JVAO, Saraiva JS, de Souza RI, et al. The emotional impact of Coronavirus 2019-nCoV (new Coronavirus disease). *Psychiatry Res*. 2020;287:112915.
40. Kawohl W, Nordt C. COVID-19, unemployment, and suicide. *Lancet Psychiatry*. 2020;7:389-90.
41. Mamun MA, Ullah I. COVID-19 suicides in Pakistan, dying off not COVID-19 fear but poverty? - The forthcoming economic challenges for a developing country. *Brain Behav Immun*. 2020 May 11:S0889-1591(20)30861-8.

42. Bhuiyan AKMI, Sakib N, Pakpour AH, Griffiths MD, Mamun MA. COVID-19-Related Suicides in Bangladesh Due to Lockdown and Economic Factors: Case Study Evidence from Media Reports. *Int J Ment Health Addict*. 2020 May 15;1-6. doi: 10.1007/s11469-020-00307-y.
43. Ornell F, Moura HF, Scherer JN, Pechansky F, Kessler F, von Diemen L. The COVID-19 Pandemic and its Impact on Substance Use: Implications for Prevention and Treatment. *Psychiatry Res*. 2020 May 13;289:113096.
44. Arya S, Gupta R. COVID-19 outbreak: Challenges for Addiction services in India. *Asian J Psychiatr*. 2020;51:102086.
45. Marsden J, Darke S, Hall W, Hickman M, Holmes J, Humphreys K, et al. Mitigating and learning from the impact of COVID-19 infection on addictive disorders. *Addiction*. 2020 Apr 6. doi: 10.1111/add.15080.
46. Rehm J, Kilian C, Ferreira-Borges C, Jernigan D, Monteiro M, Parry CDH, et al. Alcohol use in times of the COVID 19: Implications for monitoring and policy. *Drug Alcohol Rev*. 2020;39:301-4.
47. Reynolds J, Wilkinson C. Accessibility of 'essential' alcohol in the time of COVID-19: Casting light on the blind spots of licensing? *Drug Alcohol Rev*. 2020;39:305-8.
48. Hefler M, Gartner CE. The tobacco industry in the time of COVID-19: time to shut it down? *Tob Control*. 2020;29:245-6.
49. Finlay I, Gilmore I. Covid-19 and alcohol-a dangerous cocktail. *BMJ*. 2020 May 20;369:m1987. doi: 10.1136/bmj.m1987.

50. Klemperer EM, West JC, Peasley-Miklus C, Villanti AC. Change in tobacco and electronic cigarette use and motivation to quit in response to COVID-19. *Nicotine Tob Res.* 2020 Apr 28:ntaa072.
51. Heerfordt C, Heerfordt IM. Has there been an increased interest in smoking cessation during the first months of the COVID-19 pandemic? A Google Trends study. *Public Health.* 2020;183:6-7.
52. Patwardhan P. COVID-19: Risk of increase in smoking rates among England's 6 million smokers and relapse among England's 11 million ex-smokers. *BJGP Open.* 2020 Apr 7:bjgpopen20X101067.
53. Egbe CO, Ngobese SP. COVID-19 lockdown and the tobacco product ban in South Africa. *Tob Induc Dis.* 2020 May 6;18:39.
54. Da BL, Im GY, Schiano TD. COVID-19 Hangover: A Rising Tide of Alcohol Use Disorder and Alcohol-Associated Liver Disease. *Hepatology.* 2020 May 5. doi: 10.1002/hep.31307.
55. Hamilton I. Even in a pandemic, young people are still exploited by county lines drug gangs. *BMJ Opinion.* 2020. Available from: <https://blogs.bmj.com/bmj/2020/05/21/ian-hamilton-even-pandemic-young-people-still-exploited-county-lines-drug-gangs/>
56. Hamilton I. What will covid-19 mean for the illegal drug market and people dependent upon it? *BMJ Opinion.* 2020. Available from: <https://blogs.bmj.com/bmj/2020/03/31/ian-hamilton-covid-19-mean-illegal-drug-market-people-dependent/>
57. Choenni V, Hammink A, van de Mheen D. Association Between Substance Use and the Perpetration of Family Violence in Industrialized Countries: A Systematic Review. *Trauma Violence Abuse.* 2017;18:37-50.

58. Crane CA, Oberleitner LM, Devine S, Easton CJ. Substance Use Disorders and Intimate Partner Violence Perpetration among Male and Female Offenders. *Psychol Violence*. 2014;4:322-33.
59. News18. Alcoholics Turn to Sanitisers During Lockdown; Madhya Pradesh Officials Claim Ignorance. 2020. Available from: <https://www.news18.com/news/india/alcoholics-turn-to-sanitisers-during-lockdown-madhya-pradesh-officials-claim-ignorance-2603997.html> (last accessed on 16<sup>th</sup> May 2020).
60. The New Indian Express. Home brew: Sanitiser turns liquor for many in Karnataka amid lockdown. 2020. Available from: <https://www.newindianexpress.com/states/karnataka/2020/apr/18/home-brew-sanitiser-turns-liquor-for-many-in-karnataka-amid-lockdown-2131674.html> (last accessed on 16<sup>th</sup> May 2020).
61. Hindustan Times. Unable to get liquor, man drinks mixture of sanitizer and cough syrup, dies. 2020. Available from: <https://www.hindustantimes.com/india-news/unable-to-get-liquor-man-drinks-mixture-of-sanitizer-and-cough-syrup-dies/story-7Dm07kg6bRRWPKmAS7BWOM.html> (last accessed on 16<sup>th</sup> May 2020).
62. The Times of India. How to use lockdown as an oppportunity to overcome alcohol addiction. 2020. Available from: <https://timesofindia.indiatimes.com/life-style/health-fitness/health-news/how-to-use-lockdown-to-de-addict-yourself-and-ways-to-manage-withdrawal-symptoms/articleshow/75494592.cms> (last accessed on 16<sup>th</sup> May 2020).
63. News18. Amid Coronavirus Lockdown, States Across India Witness Surge in Suicide Cases Due to Alcohol Withdrawal Symptoms. 2020 Available from: <https://www.news18.com/news/india/amid-coronavirus-lockdown-states-across-india->

witness-surge-in-deaths-due-to-alcohol-withdrawal-symptoms-2561191.html (last accessed on 16<sup>th</sup> May 2020).

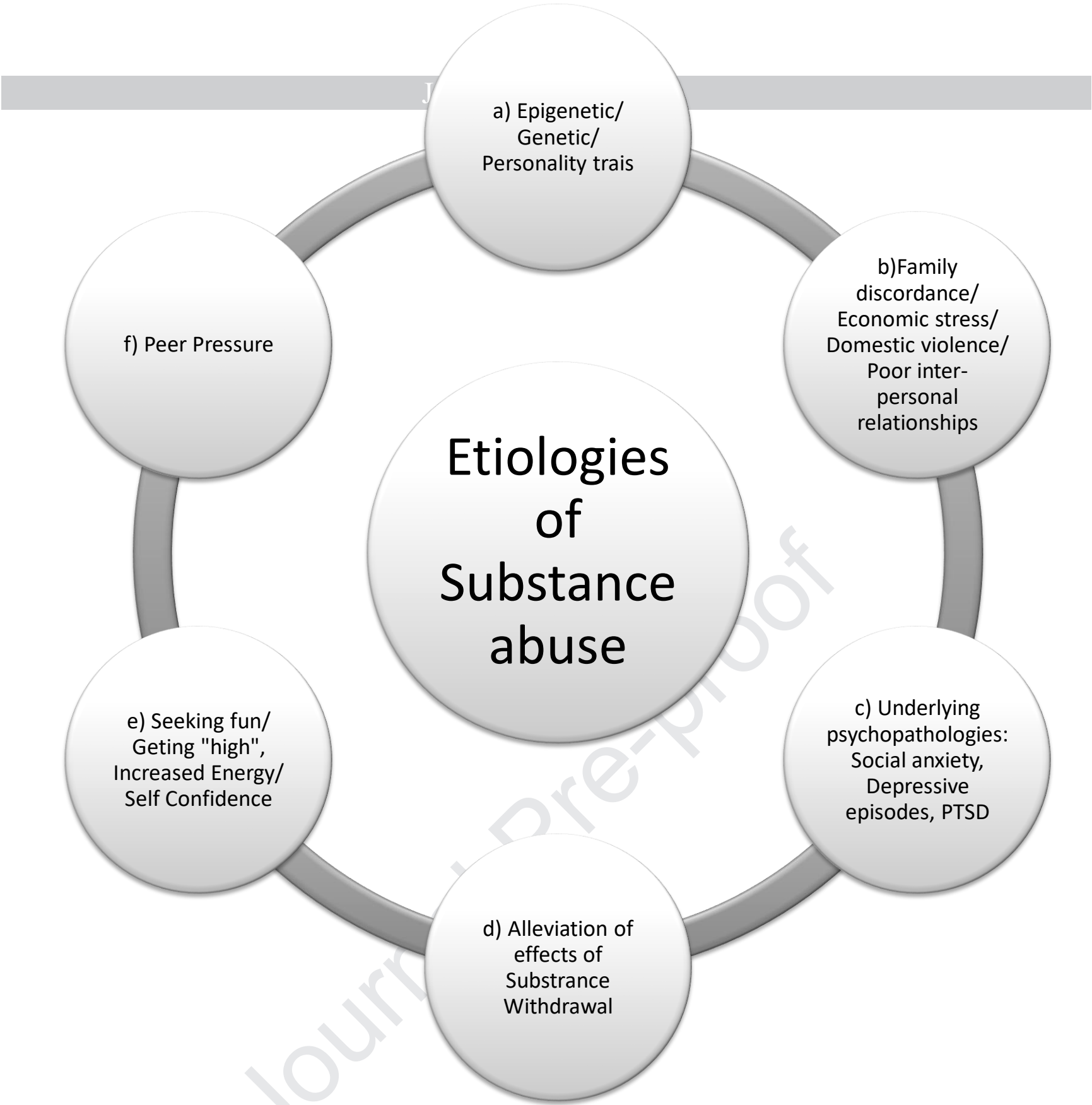
64. Narasimha VL, Shukla L, Mukherjee D, Menon J, Huddar S, Panda UK, et al. Complicated Alcohol Withdrawal-An Unintended Consequence of COVID-19 Lockdown. *Alcohol Alcohol*. 2020 May 13:agaa042.
65. Varma RP. Alcohol withdrawal management during the Covid-19 lockdown in Kerala. *Indian J Med Ethics*. 2020;V:105-6.
66. Rani S, Sahoo S, Parveen S, Mehra A, Subodh BN, Grover S. Alcohol-related self-harm due to COVID-19 pandemic: Might be an emerging crisis in the near future: A case report. *Indian J Psychiatry*. 2020;62:333-5.
67. Király O, Potenza MN, Stein DJ, King DL, Hodgins DC, Saunders JB, et al. Preventing problematic internet use during the COVID-19 pandemic: Consensus guidance. *Compr Psychiatry*. 2020;100:152180.
68. King DL, Delfabbro PH, Billieux J, Potenza MN. Problematic online gaming and the COVID-19 pandemic. *J Behav Addict*. 2020 Apr 29. doi: 10.1556/2006.2020.00016.
69. Ghosh R, Dubey MJ, Chatterjee S, Dubey S. Impact of COVID-19 on children: Special focus on psychosocial aspect. *Minerva Pediatr*. 2020; doi: 10.23736/S0026-4946.20.05887-9 (in press)
70. Håkansson A, Fernández-Aranda F, Menchón JM, Potenza MN, Jiménez-Murcia S. Gambling during the COVID-19 crisis - A cause for concern? *J Addict Med*. 2020 May 18. doi: 10.1097/ADM.0000000000000690.
71. Schalkwyk MC, Cheetham D, Reeves A, Petticrew M. Covid-19: we must take urgent action to avoid an increase in problem gambling and gambling related harms. *BMJ Opinion*. 2020.



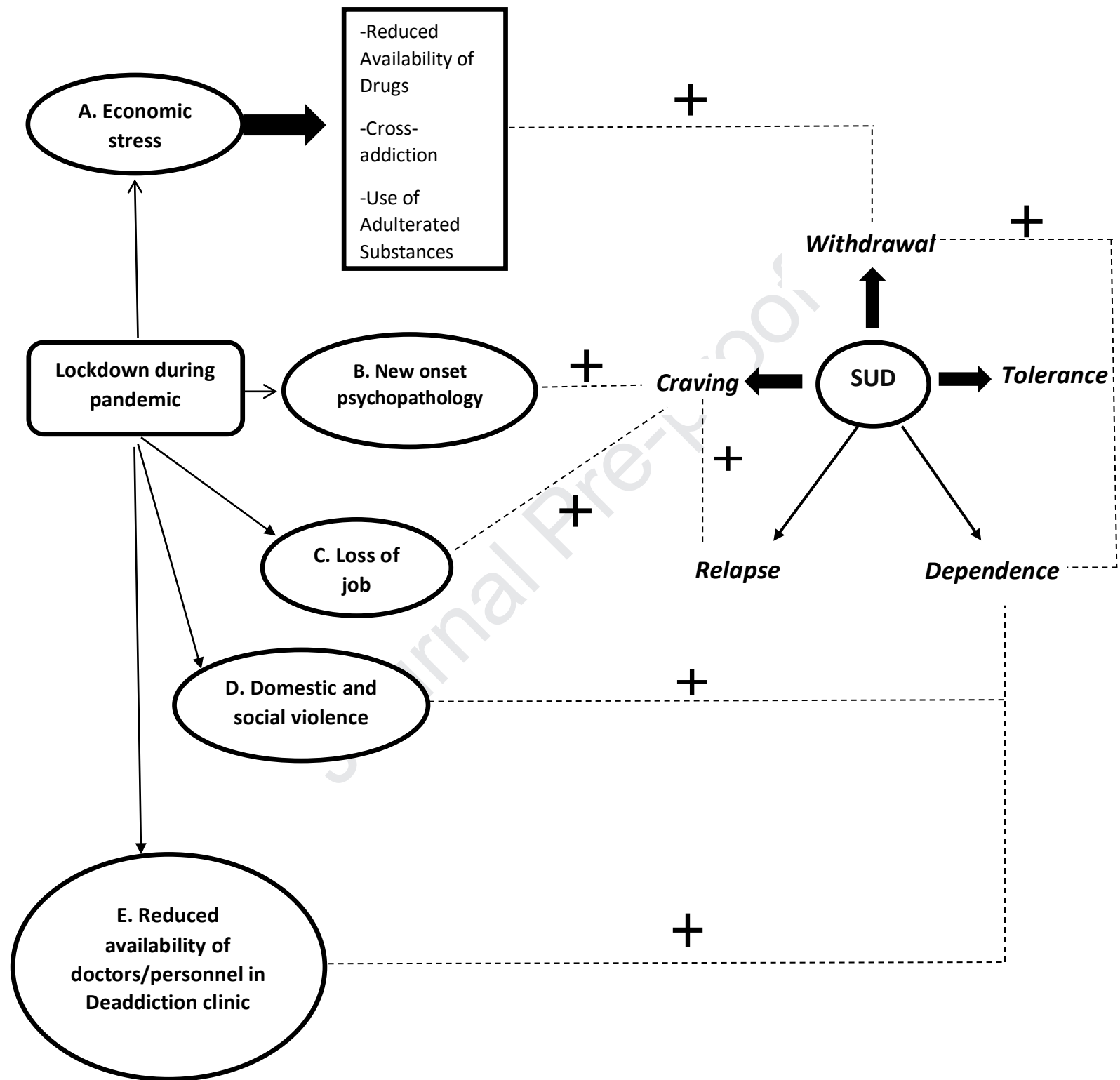
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72. Touyz S, Lacey H, Hay P. Eating disorders in the time of COVID-19. Version 2. *J Eat Disord.* 2020;8:19.
73. Watanabe M. Beyond Retail Therapy The Case Against Pandemic Shopping. 2020. Available from: <https://www.bitchmedia.org/article/compulsive-online-shopping-COVID-19> (last accessed on 16<sup>th</sup> May 2020).
74. Matsuzaki M, Vu QM, Gwadz M, Delaney JAC, Kuo I, Trejo MEP, et al. Perceived access and barriers to care among illicit drug users and hazardous drinkers: findings from the Seek, Test, Treat, and Retain data harmonization initiative (STTR). *BMC Public Health.* 2018;18:366.
75. Biswas P. India's medical students and residents grapple with uncertain futures in the face of covid-19. *BMJ Opinion.* Available from: <https://blogs.bmj.com/bmj/2020/05/22/payel-biswas-indias-medical-students-and-residents-grapple-with-uncertain-futures-in-the-face-of-covid-19/>
76. Li Y, Wang Y, Jiang J, Valdimarsdóttir UA, Fall K, Fang F, et al. Psychological distress among health professional students during the COVID-19 outbreak. *Psychol Med.* 2020 May 11:1-3. doi: 10.1017/S0033291720001555.
77. Sun Y, Bao Y, Kosten T, Strang J, Shi J, Lu L. Editorial: Challenges to Opioid Use Disorders During COVID-19. *Am J Addict.* 2020;29:174-5.
78. Vecchio S, Ramella R, Drago A, Carraro D, Littlewood R, Somaini L. COVID19 pandemic and people with opioid use disorder: innovation to reduce risk. *Psychiatry Res.* 2020;289:113047.

79. Dunlop A, Lokuge B, Masters D, Sequeira M, Saul P, Dunlop G, et al. Challenges in maintaining treatment services for people who use drugs during the COVID-19 pandemic. Version 2. *Harm Reduct J*. 2020;17:26.
80. Wherley S, Chatterjee S. India's growing problem of injecting drug misuse. *BMJ*. 2015;350:h397.
81. Jenkins WD, Bolinski R, Bresett J, Van Ham B, Fletcher S, Walters S, et al. COVID-19 During the Opioid Epidemic - Exacerbation of Stigma and Vulnerabilities. *J Rural Health*. 2020 Apr 11. doi: 10.1111/jrh.12442.
82. Jiang H, Su H, Zhang C, Liu X, Li R, Zhong N, et al. Challenges of methadone maintenance treatment during the COVID-19 epidemic in China: Policy and service recommendations. *Eur Neuropsychopharmacol*. 2020 Apr 13:S0924-977X(20)30093-6.
83. Hamilton I. Covid-19—are we rationing who we care about? *BMJ Opinion*. 2020. Available from: <https://blogs.bmj.com/bmj/2020/03/16/ian-hamilton-covid-19-are-we-rationing-who-we-care-about/>
84. Hamilton I. Loosening regulations on controlled drugs during the covid-19 pandemic. *BMJ Opinion*. 2020. Available from: <https://blogs.bmj.com/bmj/2020/04/30/ian-hamilton-loosening-regulations-on-controlled-drugs-during-the-covid-19-pandemic/>
85. Eisenberg SL, Eisenberg MJ. Smoking Cessation During the COVID-19 Epidemic. *Nicotine Tob Res*. 2020 May 4:ntaa075. doi: 10.1093/ntr/ntaa075.
86. Chick J. Alcohol and COVID-19. *Alcohol Alcohol*. 2020 May 13:agaa039. doi: 10.1093/alcalc/agaa039.
87. Yao H, Chen JH, Xu YF. Rethinking online mental health services in China during the COVID-19 epidemic. *Asian J Psychiatr*. 2020;50:102015.



Abbreviation: PTSD, post traumatic stress disorder



Abbreviation: SUD, substance abuse disorder

# Conflicts of Interest Statement

COVID-19 and Addiction- A tale of two diabolical nemeses

Manuscript title: \_\_\_\_\_

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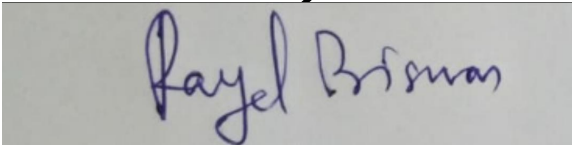

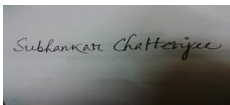
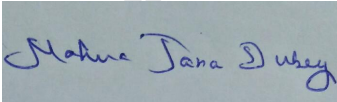

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