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## **COVID-19 and substance abuse: A systematic review and meta-analysis: Has the pandemic affected cannabis- and hard drugs use?**

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# Master Thesis

## COVID-19 and substance abuse: A systematic review and meta-analysis

*Has the pandemic affected cannabis- and hard drugs use?*



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## ABSTRACT

### Background

Stress, isolation and unemployment caused by the worldwide COVID-19 lockdowns and quarantines are believed to greatly impact mental health and substance use habits. Our aim was to investigate the relation of COVID-19 with cannabis, cocaine, amphetamine, fentanyl, heroin and methamphetamine use.

### Method

Systematic review and meta-analyses. Databases were searched until April 2<sup>nd</sup> 2021

### Results

For cannabis use, two analyses were performed based on the type of data. An increase in the number of cannabis users was found during COVID-19 ( $k = 8$ ,  $N = 4814$ ,  $Z = 2.12$ ,  $p = 0.034$ ). No difference was found in the amount of cannabis used at the two different time points ( $k = 5$ ,  $N = 1165$ ,  $p = 0.110$ ). There were no significant changes found in hard drug use during the COVID-19 pandemic relative to before its restrictions; cocaine ( $k = 10$ ,  $N = 1193293$ ,  $p = 0.121$ ), amphetamine ( $k = 3$ ,  $N = 387973$ ,  $p = 0.982$ ), fentanyl ( $k = 3$ ,  $N = 1189864$ ,  $p = 0.065$ ), heroin ( $k = 4$ ,  $N = 1138243$ ,  $p = 0.438$ ) and methamphetamine ( $k = 5$ ,  $N = 387973$ ,  $p = 0.134$ ).

### Conclusion

There is evidence that COVID-19 is associated with a small increase in the number of cannabis users. We found no evidence for an increase in the amount of cannabis used or the number of hard drug users before and during COVID-19. Consequently, in the clinical field of psychology, it might be better to invest more (of the limited) resources in alleviating mental health problems such as depression, anxiety, feelings of isolation and stress as opposed to problems with substance (ab)use, which showed to be less reactive than initially imagined.

## **INTRODUCTION**

The COVID-19 (Coronavirus disease 2019) pandemic has undoubtedly influenced all of our lives one way or another. With such an influential event taking place, it is important to be aware of the possible consequences. Stress, isolation and unemployment caused by the worldwide lockdowns and quarantines are stated to greatly impact mental health and substance use habits (Chiappini, Guirguis, John, Corkery, & Schifano, 2020). Pandemics seem to increase general worry, depression, and stress (Coughlin, 2012). These increased mental health problems during a pandemic can lead to increased substance use in order to cope (Coughlin, 2012). For instance, Mallet, Dubertret, & le Strat (2021b) found indications for an increase in the prevalence of substance use disorders during lockdowns. With (certain) drug use becoming more mainstream and legalized, one can only wonder how this pandemic has influenced substance (mis)use. For instance, new contexts such as virtual raves and happy hours report increased substance use (Palamar & Acosta, 2020). The information provided here paints a grim image of the global, all-encompassing pandemic caused by the COVID-19 virus. However, the exact relationship between the COVID-19 pandemic and substance use remains unclear at the time.

### **Theoretical framework of addiction**

To grasp the importance of this research and why substance abuse during a pandemic is in great need to be assessed, the topic of substance addiction is introduced. Over the years, substance addiction, or drug addiction, has become a clinically recognized, neuropsychiatric disorder (Zou et al., 2017). In the DSM-5 (the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition) there are 10 different classes of drugs specified that all have in common that when taken (in excess), direct activation of the brains reward system occurs (American Psychiatric Association & Association, 2013). A substance use disorder is a

bundle of cognitive, behavioural and physiological symptoms that incentivize continued use of the drug, even when there are negative consequences. Changes in the brain's structure occur when an individual becomes addicted. When the drug is not taken anymore, withdrawal symptoms can become triggered. Both a physiological tolerance and a psychological need to use the substance again, coined as the term craving, can develop (Zou et al., 2017).

The negative aspects of being addicted to a drug are widely varied but often severe. Drug addiction can in the long-term lead to physical health problems (Harris, Mowbray, & Solarz, 1994). Damage can occur to the various bodily systems such as the cardiovascular and respiratory system, but also organs such as the kidneys and the liver can be negatively affected (Stein, 1999). Not only is long-term substance abuse associated with negative health problems, mental health seems to also suffer under these drug taking habits. Substance use disorders seem comorbid with psychiatric conditions, as found by (Schuckit, 2006). Furthermore, substance abuse is associated with anxiety and depression (Kranzler & Liebowitz, 1988). Even very severe psychological problems, such as being suicidal, are associated with substance abuse (Rowan, 2001). Additionally, drug users are at risk of dying to an overdose. Substance abuse also influences and changes the brain; the effects and release patterns of neurotransmitters are altered, making it difficult to quit. It can take years for the activity of these neurotransmitter to return to a normal state. This makes the years after quitting, due to the altered neurotransmitter activity, feel very pleasure derived (Lingford-Hughes, 2005).

### **Prior research**

When investigating the current literature there seem to be a limited amount of meta-analysis investigating this topic. In research from Acuff, Strickland, Tucker, and Murphy (2021) changes in alcohol consumption were investigated and in turn, a non-significant mean

was found in their meta-analysis. Other studies investigated substance use as a risk factor for COVID-19 as a disease. For instance, according to a meta-analysis from Patanavanich and Glantz (2020), smoking is a risk factor of the progression of COVID-19 (OR 1.91, 95% confidence interval [CI] 1.42-2.59,  $p = 0.001$ ). In the meta-analysis by Vai et al. (2021) an increased mortality risk was found among COVID-19 patients with a substance use disorder (OR 2.00 [95% CI 1.58-2.54];  $I^2=92.66\%$ ). Individual studies seem to differ in their findings. In the research of Cousijn, Kuhns, Larsen, and Kroon (2021) cannabis use was found to have increased due to the COVID-19 lockdown. Other research suggests that cannabis use has mostly stayed consistent (Donovan & Portman, 2021). Similar to cannabis use during the pandemic, the relationship between COVID-19 and hard drug use is also unclear. For example, it has been reported that deaths during the COVID-19 pandemic due to methamphetamine and cocaine increased, while deaths due to heroin decreased (Manchikanti et al., 2021). Another article suggests that heroin, cocaine and MDMA use decreased during lockdown, and then increased to its normal levels when the lockdown was lifted again (Gili et al., 2021). In line with this, Palamar, Le, and Acosta (2020) found that most of their sample reported decreased cocaine, ecstasy/MDMA/Molly or LSD use, but not for all. Hence, there seems to be discourse about the relationship of COVID-19 and substance use, with some articles stating it has increased, but other research stating it has decreased, and other literature concluding there was no significant effect to be found between the two. After extensive literature search, the most common drugs found in the relevant research were classified. To get a clear overview of what (types of) drugs will be investigated, a table was created and put in Appendix 2. It would be immensely valuable for the broad field of clinical psychology to get a get overview of substances and its respective habits use during the COVID-19 pandemic, also in the face of possible future pandemics.

Substance use can be measured at different levels. Self-reports, sale figures, urine drug screening results and wastewater analysis all assess levels of substance use. Furthermore, admittance to emergency & trauma rooms, hospitals and ambulances can also provide insight on this topic. The literature seems to suggest an increased severity and frequency of admission to this type of care. As an example, during the pandemic, increased alcohol related trauma room presentations were found by Devarakonda et al. (2020). In addition, Shreffler, Shoff, Thomas, and Huecker (2021) found an increase in drug-related overdoses in the context of an emergency department. The different ways to assess use/misuse may contribute to the differences in outcomes when it comes to substance use in the face of COVID-19.

### **Research objectives**

This review and meta-analysis assess the potential associations between the stressor COVID-19 and substance (ab)use. The objective is to find an overarching and summarizing effect of whether cannabis and hard drug use has increased, decreased, or stayed the same during this pandemic relative to use prior to the COVID-19 pandemic. Kumar et al. (2021) state there is a concerning lack of research regarding the different substances' consumption in the context of COVID-19. Tying into this, the current meta-analysis aims to look at a broad range of different substances and its consumption. The proposed analyses will provide an overall effect-size for the stressor COVID-19 and cannabis, cocaine, heroin, fentanyl, methamphetamine, XTC/MDMA and amphetamine use. Possible effect moderators such as gender, age and nationality will be investigated. At this moment in time, no such analysis has been done before. The following research question was formulated:

- What is the relationship between the COVID-19 pandemic and recreational cannabis/hard drugs use?



To answer this research question, the following hypothesis were formulated:

- $H_0$ : The COVID-19 pandemic has no effect on recreational cannabis/hard drug use.
- $H_1$ : The COVID-19 pandemic has a positive effect on recreational cannabis/hard drug use.

## **METHOD**

### **Search strategy**

A systematic search was conducted in both PubMed and Web of Science. To select the relevant articles, a search string was created and adapted to each individual database (see Appendix 1). Articles from 2020 up until April 2nd, 2021 were selected. In the PubMed database the search string found 2201 results. In the Web of Science database 1467 results were found. After de-duplication using Bookends, a reference manager, 2668 unique articles were left of the total 3668 (<https://www.sonnysoftware.com/>). The articles were put in Rayyan, a piece of systematic review software (<https://www.rayyan.ai/>). Then, with a double blind on, each article was in- or excluded by reading the title and the abstract of the article by two different individuals. After completing the first selection, conflicting articles were looked at again to decide whether it met the in- and exclusion criteria that are specified below.

### **In- and exclusion criteria**

To select relevant articles, in- and exclusion criteria were formulated. Articles were included when: 1. original data reported on at least one moment of measurement; 2. relevant substances were present; 3. in relation to COVID-19. In the articles reporting the increase/decrease in percentages or prevalence's, both an increase and a decrease needed to be reported, otherwise a true percentage of increase could not be calculated. Original data means that actual research was conducted, with for instance, open-ended surveys or the use of an instrument. This means that articles such as reviews and commentaries will not be included, because there is no original data being gathered in these. The articles could have been published in English, Dutch, German, Arabic, Spanish, Greek or Turkish.

## Data extraction

The data consisted of three different types: mean differences, prevalence differences and percentage differences. Data on mean differences are characterized by the measurement of the absolute difference between two groups in the research design. An example relating to this meta-analysis is the mean difference among participants using cannabis operationalized in grams used per week, among two different groups; before and during covid. Differences in prevalence look at how many individuals among a population have used a drug in a certain timeframe, for instance, a wastewater analysis investigating the number of cocaine users during 2019 as opposed to 2020. Differences in percentage look at the number of users in a sample increasing or decreasing their substance use during a certain time period. This difference is calculated by subtracting the percentage of decreasing users from the increasing users, creating a so-called *true* increase in a percentage. Each of these types of data was converted into a standardized Pearson correlation coefficient  $r$ . Prevalence and percentages were pooled, resulting in the proportion-based data. In addition to the relevant substances and its increase or decrease of use, data on various demographics were also extracted. These variables were the average age of the sample, the percentage of females in the sample (gender distribution) and the country in which the study was performed. These three variables were entered into the meta-analysis model to be investigated as potential moderators, either as continuous (age, %female) predictors or as categorical (country) predictors. Each selected article was individually read and relevant data was extracted with using the pre-defined criteria list as formulated above.

## Outcome measures

In this meta-analysis, the outcome variable (standardized Pearson correlation coefficient,  $r$ ) was the change in cannabis and hard drug use. In studies with multiple

measurement points, an odds ratio will be the effect size used to compare two different means with a 95% confidence interval. For studies with one measurement point (did you increase substance use in the pandemic? y/n), a population proportion with a 95% confidence interval was used.

### **Statistical analyses**

Data-analysis was conducted with jamovi, an open-source statistical analysis platform (version 1.8.0, standard version plus the “MAJOR” meta-analysis module). The data was pooled in a random effects meta-analysis. This model assumes that each study has a different estimation of the actual, true effect. A fixed effects model however, assumes there is one common, fixed effect for all works of research. The random effects model is a better fit for meta-analysis with high levels of (expected) heterogeneity between their included studies (Borenstein, Hedges, Higgins, & Rothstein, 2010). Additionally, the results apply beyond the included studies, making it generalizable to the population, whereas a meta-analysis with a fixed-effects model estimates the effect for just the included studies. (Tufanaru, Munn, Stephenson, & Aromataris, 2015).

The methodological quality of the meta-analysis was investigated by evaluating possible publication bias. Additionally, to assess the heterogeneity of the selected data from the population, the  $I^2$  test was used. This test measured the variation in the outcomes reported in the included articles. This statistic gave insight to how much of the variation is due to heterogeneity as opposed to chance (Higgins, 2003). The data its heterogeneity was considered *low* if the  $I^2$  value falls in the range of 25-50%.  $I^2$  values of 50-75% were viewed as *moderate*, while values above 75% were deemed *high* in heterogeneity (Higgins, 2003, as cited in Bueno-Notivol et al., 2021). Variables that were used to explain potential heterogeneity (and lack thereof) of the data include: age, %female and country of assessment.

This was explored by performing multiple moderator analysis, also in the data-analysis program mentioned earlier; jamovi. Possible publication bias was assessed by means of visual inspection of funnel plots and the Egger's test, with p values smaller than 0.05 indicating publication bias (95% confidence interval) (Lin & Chu, 2017).

## RESULTS

Figure 1 shows the process of literature search and in/exclusion in the form of a flowchart. Of the 23 articles included in the analysis, 13 articles were used for the analysis on cannabis use. Of those 13, 8 were used in the analysis for proportions and 5 were used in the analysis for mean differences. Out of the previously mentioned 23 included articles, 10 were used in the different analysis for hard drug use, with each drug having its own respective amount of research papers. There are differences among the papers in which hard drugs were and were not examined.

Figure 3. Flowchart on identification, screening and inclusion of eligible publications

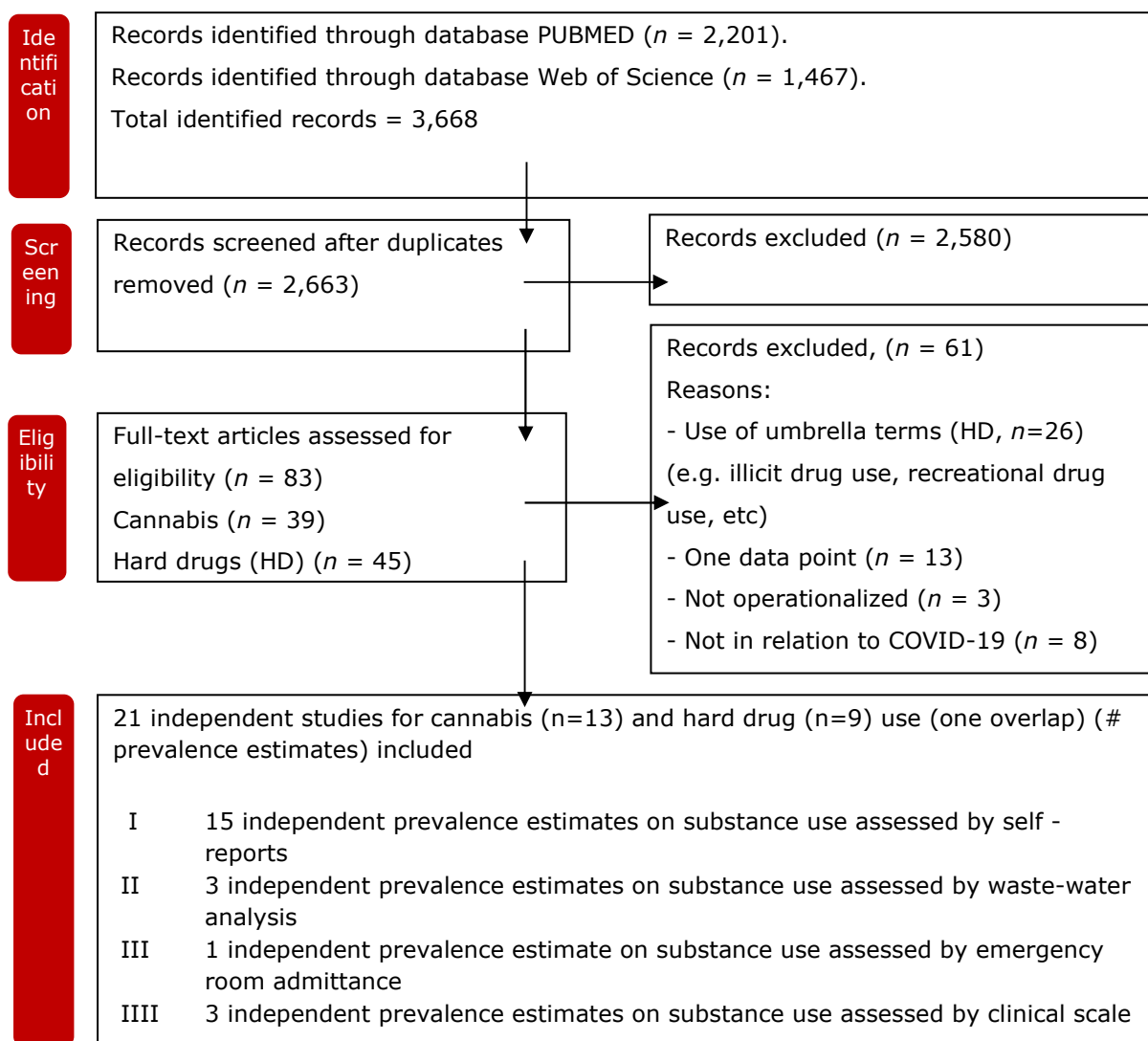


Figure 1. Flowchart on identification, screening and inclusion of eligible publications

An overview of the studies used for the cannabis analysis and hard drug analysis is provided in Table 1 and 2 with their respective demographics. Sample sizes ranged from 67 to 1563 for the articles on cannabis use, and from 37 to 750.000 for the articles on the various hard drugs. Among both the articles included for cannabis and hard drug use, average age ranged from 14 to 61.7 and gender distribution ranged from 0% female to 76.4%. Country of assessment greatly varied, with the US being the biggest source of research.

**Table 1:** Characteristics of included studies and samples reporting on changes in Cannabis use.

<b>Study</b>	<b>N</b>	<b>type of data<sup>a</sup></b>	<b>age</b>	<b>%female</b>	<b>Country</b>	<b>outcome measure</b>
Starks et al. (2020)	365	1	40.53	0	US	Self-reported consumption
Miller et al. (2021)	67	1	35.11	46.3	US	CUDIT-R score
Cousijn et al. (2021)	109	1		67.4	Netherlands	Use in days/week, grams/month
Dumas et al.(2020)	324	1	16.68	76.4	Canada	Frequency of use
Liebana-Presa et al., 2020	300	1	14	62	Spain	Habits of use questionnaire
Boehnke et al. (2020)	353	2	37	55.5	US	% of users from sample
Firkey et al. (2020)	212	2	22.09	50.5	US	% of users from sample
Palamar et al. (2020)	100	2	23.03	61.7	US	% increase/decrease consumption
Turna et al. (2021)	145	2	40.04	82	US	% increase/decrease consumption
Vidot et al. (2021)	1202	2	47.2	46.9	US	% increase/decrease consumption
Rolland et al. (2020)	667	2	47.7	52.1	Europe	% increase/decrease consumption
Van Laar et al. (2020)	1563	2	32.7	33.7	Europe	% increase/decrease consumption
Graupensperger et al.,2021	572	2	25.14	60.8	US	% increase/decrease consumption

<sup>a</sup>Type of data: 1=mean differences, 2= proportions

**Table 2:** Characteristics of included studies and samples reporting on changes in hard drugs.

Study	N (average) <sup>a</sup>	Age	%Female	Country	Outcome measures	Hard drugs analysed <sup>b</sup>
Wainwright, J.J. et al 2020	750000	47.5	52.73	US	Positive urine test results, %	C, F, H, M
McGraw, C. et al 2021	2381	40	27.5	US	Trauma room admission blood/urine drug tests	C, M
Capuzzi et al., 2020	338	44.05	49.6	Italy	Clinical characteristics of subjects admitted to psychiatric ER rooms	C
Croxford, S. et al 2021 (injected)	137	41	25.5	UK	Survey results, injected drugs	C, A, H
Croxford, S. et al 2021 (not injected)	365	41	25.5	UK	Survey results, non-injected drugs	C, A, H, M
Niles et al 2021	387471	60	57.5	US	Positive urine test results, %	C, A, F, H
Starks et al 2020	43	40.53	0	US	Survey results	C, M
Morin et al 2020	52393	-	-	Canada	Positive urine test results, %	C, F, M
Tamargo, J.A. et al 2021	37	56.9	51.2	US	Survey results	C
Palamar et al., 2020	128	23.3	61.7	US	Survey results	C

<sup>a</sup>Average sample size. <sup>b</sup>Harddrugs respectively: C=cocaine, A=amphetamine, F=fentanyl, H=heroin, M=methamphetamine

## Meta-analysis

The results of the meta-analysis for each drug are shown in table 3. The meta-analysis reporting on changes in cannabis use with proportion-based data showed a significant increase ( $k = 8, Z = 2.12, p = 0.034$ ). The other meta-analysis done for cannabis with regard to mean differences found no significant increase ( $k = 5, Z = 1.60, p = 0.110$ ). As for the different meta-analysis done for the various hard drugs, namely cocaine ( $k = 10, Z = -1.55, p = 0.121$ ), amphetamine ( $k = 3, Z = -0.0227, p = 0.982$ ), fentanyl ( $k = 3, Z = -1.84, p = 0.065$ ), heroin ( $k = 4, Z = -0.775, p = 0.438$ ) and methamphetamine ( $k = 5, Z = -1.50, p = 0.134$ ), none found any significant increase. Figure 1 shows a forest plot of the significant analysis on COVID-19 related changes in cannabis use. This figure describes the relationship between COVID-19 as a stressor and cannabis use per individual study included in the meta-analysis. The other forest plots can be found in Appendix 4.



**Table 3: Results of the meta-analysis per drug**

Drug	k <sup>a</sup>	r	Z <sup>b</sup>	p <sup>c</sup>
Cannabis (proportions)	8	0.125	2.12	<u>0.034</u>
Cannabis (mean differences)	5	0.0609	1.60	0.110
Cocaine	10	-0.140	-1.55	0.121
Amphetamine	3	1.30e-6	-0.0227	0.982
Fentanyl	3	-0.0532	-1.84	0.065
Heroin	4	-0.0232	-0.775	0.438
Methamphetamine	5	-0.0128	-1.50	0.134

<sup>a</sup>k = number of studies. <sup>b</sup>Z = Z-score, <sup>c</sup>p = p-value, significant at 0,05

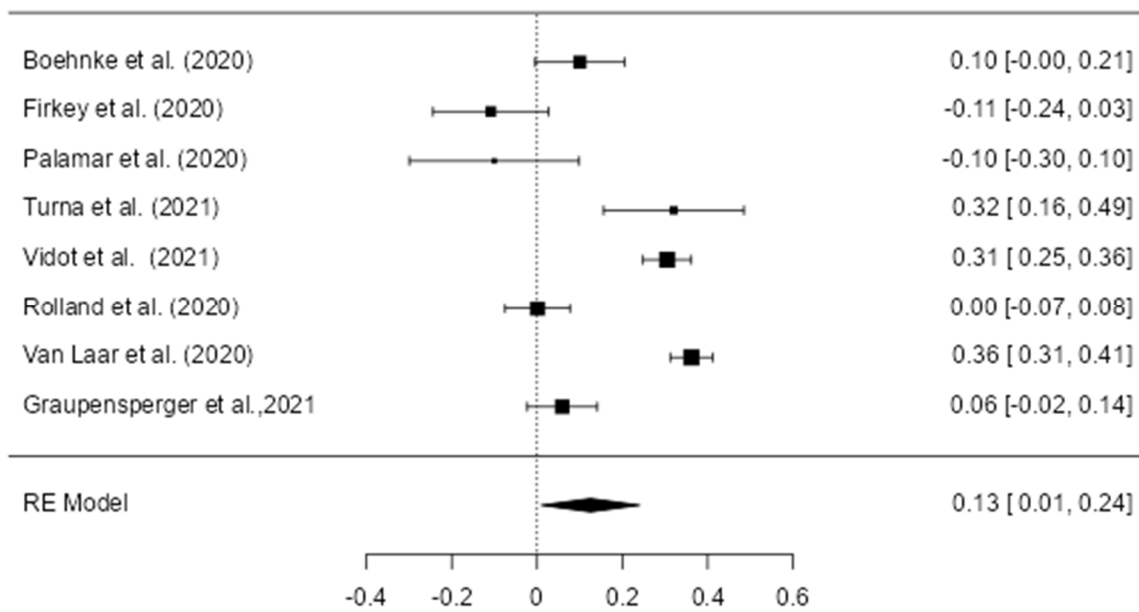
To assess the heterogeneity of the selected data from the population, the I<sup>2</sup> test was used. High levels of between-study heterogeneity in outcome were observed in the analysis on cannabis with proportion based data (I<sup>2</sup> = 92,97%, p = <.001), cocaine (I<sup>2</sup> = 99,98%, p = <.001), fentanyl (I<sup>2</sup> = 99,7%, p = <.001) and heroin (I<sup>2</sup> = 99,76%, p = <.001). The data used in the analysis on methamphetamine (I<sup>2</sup> = 52,28%, p = 0,175) contained moderate levels of heterogeneity. Lastly, the mean difference analysis for cannabis (I<sup>2</sup> = 33,86%, p = 0,101), and the analysis for amphetamine (I<sup>2</sup> = 0%, p = 0,627) both contain low amounts of heterogeneous data.

**Table 4: Assessment of the heterogeneity in the study data used, classified per drug**

Drug	I <sup>2</sup> <sup>a</sup>	p	Heterogeneity
Cannabis (proportions)	92,97%	< .001	High
Cannabis (mean differences)	33,86%	0.101	Low
Cocaine	99,98	< .001	High
Amphetamine	0%	0.627	Low
Fentanyl	99,7	< .001	High
Heroin	99,76	< .001	High
Methamphetamine	52,28	0.175	Moderate

<sup>a</sup>Effect sizes used for I<sup>2</sup> are 25%-50% = low, 50%-75% = moderate and +75% = high in regards to the amount of heterogeneity present in the data (Higgins, 2003, as cited in Bueno-Notivol et al., 2021).

**Figure 1: Forest plot illustrating the relation of cannabis use and COVID-19 as a stressor per study<sup>a</sup>**



<sup>a</sup>On the left we see each study followed by its result (the black box) with a 95% confidence interval (the line going through the box). The bigger the box, the bigger the sample size of the study. On the right is the 95% confidence interval given in numbers. The vertical line provides a line for the null effect, the value where there would be no effect between the variables. The horizontal axis represents the scale for the statistic, in this case the odds ratio. RE Model stands for Random-Effects model. The diamond shape at the bottom represents the point estimate combined with its 95% confidence interval.

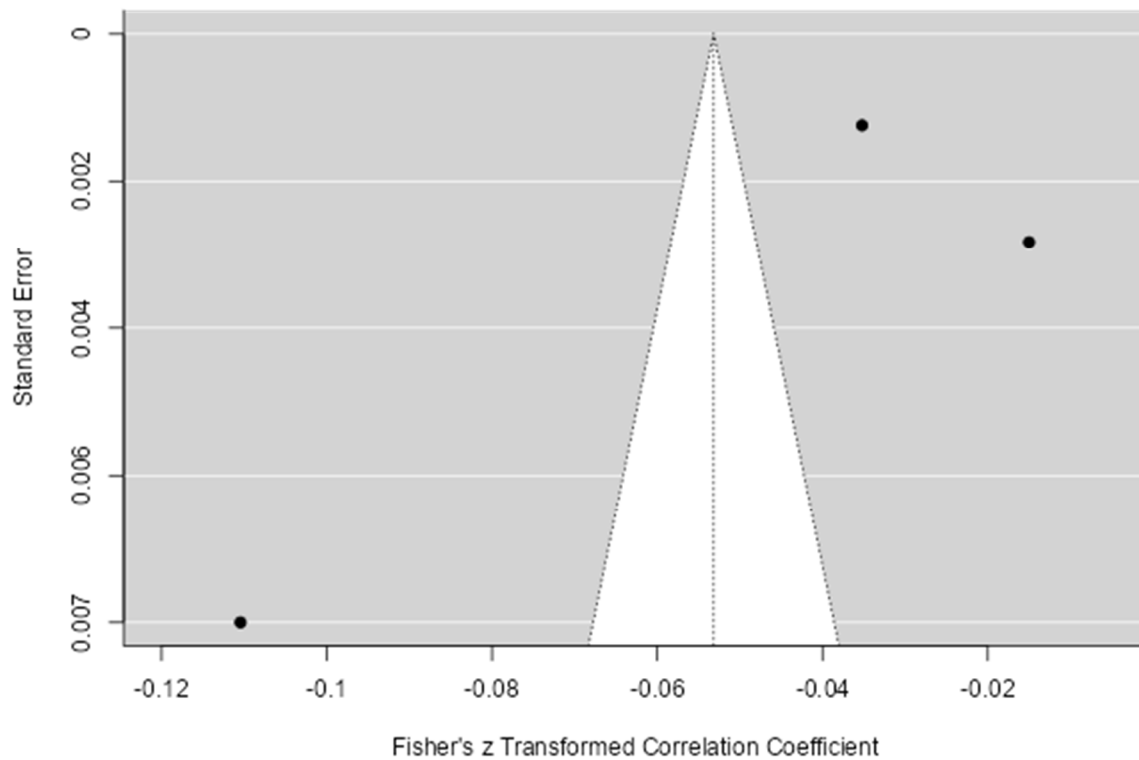
### Methodological quality

Only the analysis on fentanyl proved significant amounts of publication bias (Egger's value = -2,140,  $p = 0,032$ ). Table 5 provides these results. Figure 2 shows an asymmetrical funnel plot, with all three studies falling outside of the triangle. Funnel plots for the other substances' assessment on publication bias can be found in Appendix 5.

**Table 5: Assessment of publication bias of the study data used, classified per drug**

Drug	Egger's value	p
Cannabis (proportions)	1.846	0.065
Cannabis (mean differences)	-0.584	0.559
Cocaine	-1.274	0.203
Amphetamine	-0.952	0.341
Fentanyl	-2.140	0.032
Heroin	0.971	0.331
Methamphetamine	1.923	0.054

**Figure 2: Funnel Plot of the meta-analysis done on fentanyl use**



The white triangle outlined by the dotted lines indicate the spread in which there would be no publication bias present. The black dots represent the individual studies used in the meta-analysis.

### Moderator analysis

In this meta-analysis, we investigated the moderator's percentage of females in the sample, the average age of the sample and the country of assessment. In the analysis done for mean differences, two significant moderators were found (gender,  $p = 0,011$  and age,  $p =$

0,01). This suggests that the relation between COVID-19 and cannabis use was affected by gender and/or age, but not by country of assessment. These same moderators were also found in the analysis done for methamphetamine (gender,  $p = 0,041$  and age,  $p = 0,043$ ), again suggesting the relation of COVID-19 and methamphetamine use was affected by gender and/or age, but not by country of assessment. No other moderators were found significant, suggesting that the relation of COVID-19 and cannabis use (proportion based data), cocaine use and heroin use were not affected by age, gender of country of assessment.

**Table 6: Assessment of moderator analysis for the meta-analysis classified per drug**

<b>Substance/Moderator</b>	<b>%Female</b>	<b>p</b>	<b>Age</b>	<b>p</b>	<b>Country</b>	<b>p</b>
Cannabis (proportions)	-0,00261	0,479	0,00892	0,139	-0,0812	0,527
Cannabis (md) <sup>b</sup>	-0,00234	<u>0,011</u>	0,00659	<u>0,01</u>		
Cocaine	-0,00771	0,132	0,0157	0,07	0,0627	0,464
Heroin	-0,002	0,398	-6.03e-4	0.899	0,0719	0,28
Methamphetamine	-0,0016	<u>0,041</u>	-0,00549	<u>0,043</u>	-0,00169	0,916

<sup>a</sup>Amphetamine, fentanyl and heroin are missing in this table; the amount of included studies was too small to perform moderator analysis with  $k = 3$ . <sup>b</sup>cc = mean differences

The substances that did not warrant enough works of research that fit the pre-defined criteria for a meta-analysis are XTC/MDMA, LSD and (recreationally used) benzodiazepines. Palamar et al. (2020) report a 63,2 decrease of XTC use. Reinstadler et al. (2021) found an 28,46% decrease for MDMA use. As for LSD, Palamar et al. (2020) found a 56% decrease. Prevalence of benzodiazepines went from 9,0% to 8,6% as found by Niles et al. (2021) and stayed the same at 15% as reported by McGraw, C. et al. (2021).

## DISCUSSION

We found a positive relationship between COVID-19 and cannabis use by pooling the proportion based data, representing the numbers of users (8 studies with a total of 4814 participants). The effect size found was 0.125, which indicates that COVID-19 explains about 1,56 percent of the variance in outcomes. There was no effect found when pooling the data investigating mean differences, which represent the amount of use (5 studies with a total of 1165 participants). This suggests that COVID-19 did not significantly influence the amount of cannabis used before and during the pandemic's restrictions. No significant effects were found for any of the hard drugs investigated, suggesting that COVID-19 did not alter the number of users of these particular drugs, namely cocaine, amphetamine, fentanyl, heroin and methamphetamine.

In this meta-analysis, a distinction was made between the soft drug cannabis and various hard-drugs; cocaine, amphetamine, fentanyl, heroin and methamphetamine. It was originally hypothesized that the stress, isolation and decreased mental health caused by the pandemic would lead to an increase in substance use to cope. However, no effect was found for any of the hard drugs investigated as opposed to one effect found among the two meta-analyses performed for cannabis use. First of all, the observed associations could possibly be explained by the type of drug and its availability. The push for legalisation for cannabis all around the world has led to this drug's availability to be on the rise, being sold recreationally in many American states, Canada and a handful of European countries (Hammond et al., 2020; Bahji & Stephenson, 2019; Smart & Pacula, 2019). While it might be harder to obtain certain drugs during a lockdown because they are illegal, this might not be the case for cannabis. This is supported by research from Gili et al. (2021b). They found that the state-imposed measures led to significant changes in substance use patterns, with users switching to the drugs that were more easily available. This provides a possible explanation to why we

found an effect for cannabis use, but not for the multiple hard drugs investigated. Another possible explanation for the difference in findings between cannabis and hard drug use could be the decreased social contexts in which these drugs are typically used. During the COVID-19 pandemic lockdowns and quarantines, social contexts decreased (Hwang, Rabheru, Peisah, Reichman, & Ikeda, 2020). It is important to note that substance use is less of an individual, isolated phenomenon, but more of an interpersonal, social process, as described by Kadushin, Reber, Saxe, & Livert (1998). Over the years, biopsychosocial models have emerged to investigate what factors drive substance use and how to prevent and treat the addiction that might follow (Miller, 2013). Substance use is strongly linked to interpersonal use and the social systems which it emerges in and gets encouraged by (Marlatt, 1992; Sutherland & Shepherd, 2001). With social contexts decreasing during the pandemic, it is possible that many individuals were simply less in contact with these substances, and thus were not inclined as much to use them. To build upon this, Roberts et al., (2021) state that individuals could have faced less social pressure or answerability to use drugs during the pandemic because there were simply fewer social situations for this to occur. These factors could explain these findings because less experienced users fail to encounter the drug because of the decreased social contexts, and more experienced users simply continue their old drug using habits.

### **Strengths and limitations**

A strength of this meta-analysis is the reliability of the types of included studies, namely the inclusion of urine drug screening works of research. These studies provide an accurate, reliable way of measurement as urine drug results are found to be highly effective (Kelly, 1988; Schwartz, 1988; Moeller, Lee, & Kissack, 2008). In contrast to the objective urine drug tests are the more subjective self-report surveys. In the context of substance abuse

however, these measurements seem more than adequate in their reliability (Darke, 1998) and validity (O'Farrell, Fals-Stewart, & Murphy, 2003; Winters, Stinchfield, Henly, & Schwartz, 1990). When looking at urine drug screen test results compared to self-report test results, there are high levels of concordance between these two (Wilcox, Bogenschutz, Nakazawa, & Woody, 2013). This reliability is accompanied by big sample sizes, ranging from well over 50.000 to 750.000, further emphasizing these articles as highly relevant in their inclusion. This provides reason to believe that the influence of the COVID-19 pandemic on hard drug use is much smaller as initially thought. The COVID-19 pandemic was described as detrimental to the well-being of people and that maladaptive coping patterns, such as substance abuse, seemed very likely (Avena, Simkus, Lewandowski, Gold, & Potenza, 2021). Models of negative reinforcement of substance use predicted that the increase in stress could lead to increased substance use (Rogers, Shepherd, Garey, & Zvolensky, 2020). COVID-19 was described as a big negative influence on stress, isolation, unemployment and mental health problems which in turn could lead to an increased substance use (Coughlin, 2012). For existing drug users, the many social and economic changes were thought to certainly worsen during this period, and increase substance use (Ornell et al., 2020). After our findings, these expectations on the increase of substance use seem less relevant now.

This meta-analysis also has its limitations. Firstly, heterogeneity differed greatly among the data for each of the meta-analysis. Only the data used in the analysis for cannabis (mean differences), amphetamine and methamphetamine were concluded to be homogenous. These low amounts of heterogeneity are not a limitation on its own, but unfortunately, the meta-analysis that were deemed to consist of heterogenous data did not correspond with any significant moderator analysis. This means that their heterogeneity could not be explained by moderator analysis in this work of research. To build upon this, articles that used admittance to ER rooms (or similar) as an outcome measure like mentioned in the introduction, did not

fit the criteria for this meta-analysis. While this could have possibly influenced the difference in outcomes as a moderator, it could not be investigated in this meta-analysis due to a lack of fitting data. The second limitation is the number of studies used for some of the analysis. The meta-analysis done on amphetamine and fentanyl only included 3 studies each. This makes it difficult to provide any conclusive, unbiased evidence of a true effect as statistical power remains low. A third limitation is the difference in significance between the two cannabis meta-analysis. The distinction, and thus two meta-analysis, needed to be made because of the different types of data available. The data consisted of three different types: mean differences, prevalence differences and percentage differences. Data on mean differences are characterized by the measurement of the absolute difference between two groups in the research design. Differences in prevalence look at how many individuals among a population have used a drug in a certain timeframe. Differences in percentage look at the number of users increasing or decreasing their substance use during a certain time period. Prevalence and percentages were pooled, resulting in the proportion-based data. The other data related to mean differences. Both analyses were positive, meaning they share the direction of the effect, but only one of the analyses proved significant. This is not a problem per say, but it does raise questions about why one analysis is significant and the other one not. Perhaps it is due to a difference in power, as the non-significant mean difference meta-analysis has 5 studies included as opposed to 8, and a total of 1165 participants as opposed to the 4814 total participants for the proportion based meta-analysis. This inconsistency in significance makes it difficult to provide a comprehensive claim on what the influence of COVID-19 on cannabis use is.



## **Theoretical and practical consequences of results**

By combining multiple studies and their sample sizes into one effect, the meta-analyses done have provided a valuable addition to the research field. Their results are more representative and reliable than any of the individual works of research published. By creating a summarizing effect of all these individual studies, the actual relationship between COVID-19 and substance was better identified. By using the random effects model for the meta-analysis, the results found apply well beyond the included studies, making it highly generalizable to the broader population. The two meta-analyses performed on cannabis use included 13 studies in total and had a total sample size of close to 6.000 participants. Additionally, the inclusion of the urine drug screening results in the meta-analysis performed for the multiple hard drugs, came with massive sample sizes ranging from 50.000 to well over 750.000, making the results found incredibly reliable. All these factors together make for results that can be applied to the general public, providing highly practical findings. Substance use was affected by COVID-19, but not with the detrimental force that was initially hypothesized. This means that on a more theoretical note, it remains relatively unclear at the time why these findings are rather mild. Some theories have been presented to explain it, but none with great confidence. Consequently, in the clinical field of psychology, it might be better to invest more (of the limited) resources in alleviating mental health problems such as depression, anxiety, feelings of isolation and stress as opposed to problems with substance (ab)use, which showed to be less reactive than initially imagined.

## **Recommendations for future research**

With the COVID-19 pandemic dwindling down sooner or later, it would be immensely valuable to repeat the meta-analysis with the undoubtedly newly added relevant research. This meta-analysis only included articles from 2020 up until April 2nd, 2021. The

amount of relevant research would only have increased with the following years, providing bigger sample sizes and more diverse data on substances to be investigated. It is also immensely valuable to look at what the levels of substance use will be when the pandemic's restrictions cease to exist. Additionally, to investigate which factors influence the relationship between COVID-19 and substance use, future experimental research could also prove to be immensely valuable. Variables such as the illegal/legal status per country/state and drug availability (proposed as possible explanations for the effects found in the discussion) could be used in this research design.

## CONCLUSION

We conducted two meta-analyses investigating the relationship between COVID-19 and cannabis use. An increase in the number of cannabis users was found among the sample before and during COVID-19 ( $k = 8$ ,  $N = 4814$ ,  $Z = 2.12$ ,  $p = 0.034$ ). No difference was found in the amount of cannabis used at the two different time points ( $k = 5$ ,  $N = 1165$ ,  $p = 0.110$ ). We also conducted multiple different meta-analysis for various hard drugs, namely cocaine, amphetamine, fentanyl, heroin and methamphetamine. There were no significant changes in the number of hard drug users during the COVID-19 pandemic relative to before its restrictions; cocaine ( $k = 10$ ,  $N = 1193293$ ,  $p = 0.121$ ), amphetamine ( $k = 3$ ,  $N = 387973$ ,  $p = 0.982$ ), fentanyl ( $k = 3$ ,  $N = 1189864$ ,  $p = 0.065$ ), heroin ( $k = 4$ ,  $N = 1138243$ ,  $p = 0.438$ ) and methamphetamine ( $k = 5$ ,  $N = 387973$ ,  $p = 0.134$ ). These results come despite the inclusion of urine drug screening results, which come with large sample sizes, making these results very reliable. This suggests that the influence of COVID-19 on substance use is smaller than we initially thought. Consequently, in the clinical field of psychology, it might be better to invest more (of the limited) resources in alleviating mental health problems such as depression, anxiety, feelings of isolation and stress as opposed to problems with substance (ab)use, which showed to be less reactive than initially imagined.

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## REFERENCES

- Acuff, S. F., Strickland, J. C., Tucker, J. A., & Murphy, J. G. (2021). Changes in alcohol use during COVID-19 and associations with contextual and individual difference variables: A systematic review and meta-analysis. *Psychology of Addictive Behaviors*. <https://doi.org/10.1037/adb0000796>
- Adderall Oral: Uses, Side Effects, Interactions, Pictures, Warnings & Dosing - WebMD. (n.d.). Retrieved June 24, 2021, from <https://www.webmd.com/drugs/2/drug-63163/adderall-oral/details>
- American Psychiatric Association, & Association, A. P. (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5®)*. Zaltbommel, Netherlands: Van Haren Publishing.
- Avena, N. M., Simkus, J., Lewandowski, A., Gold, M. S., & Potenza, M. N. (2021). Substance Use Disorders and Behavioral Addictions During the COVID-19 Pandemic and COVID-19-Related Restrictions. *Frontiers in Psychiatry*, *12*. <https://doi.org/10.3389/fpsy.2021.653674>
- Bahji, A., & Stephenson, C. (2019). International Perspectives on the Implications of Cannabis Legalization: A Systematic Review & Thematic Analysis. *International Journal of Environmental Research and Public Health*, *16*(17), 3095. <https://doi.org/10.3390/ijerph16173095>
- Borenstein, M., Hedges, L. V., Higgins, J. P., & Rothstein, H. R. (2010). A basic introduction to fixed-effect and random-effects models for meta-analysis. *Research Synthesis Methods*, *1*(2), 97–111. <https://doi.org/10.1002/jrsm.12>
- Bueno-Notivol, J., Gracia-García, P., Olaya, B., Lasheras, I., López-Antón, R., & Santabárbara, J. (2021). Prevalence of depression during the COVID-19 outbreak: A

- meta-analysis of community-based studies. *International Journal of Clinical and Health Psychology*, 21(1), 100196. <https://doi.org/10.1016/j.ijchp.2020.07.007>
- Capuzzi, E., di Brita, C., Caldiroli, A., Colmegna, F., Nava, R., Buoli, M., & Clerici, M. (2020). Psychiatric emergency care during Coronavirus 2019 (COVID 19) pandemic lockdown: results from a Department of Mental Health and Addiction of northern Italy. *Psychiatry Research*, 293, 113463. <https://doi.org/10.1016/j.psychres.2020.113463>
- Chiappini, S., Guirguis, A., John, A., Corkery, J. M., & Schifano, F. (2020). COVID-19: The Hidden Impact on Mental Health and Drug Addiction. *Frontiers in Psychiatry*, 11, 1–4. <https://doi.org/10.3389/fpsyt.2020.00767>
- Coughlin, S. S. (2012). Anxiety and Depression: Linkages with Viral Diseases. *Public Health Reviews*, 34(2). <https://doi.org/10.1007/bf03391675>
- Cousijn, J., Kuhns, L., Larsen, H., & Kroon, E. (2021a). For better or for worse? A pre–post exploration of the impact of the COVID-19 lockdown on cannabis users. *Addiction*, 1–12. <https://doi.org/10.1111/add.15387>
- Cousijn, J., Kuhns, L., Larsen, H., & Kroon, E. (2021b). For better or for worse? A pre–post exploration of the impact of the COVID-19 lockdown on cannabis users. *Addiction*, 116(8), 2104–2115. <https://doi.org/10.1111/add.15387>
- Cousijn, J., Kuhns, L., Larsen, H., & Kroon, E. (2021c). For better or for worse? A pre–post exploration of the impact of the COVID-19 lockdown on cannabis users. *Addiction*, 116(8), 2104–2115. <https://doi.org/10.1111/add.15387>
- Croxford, S., Emanuel, E., Ibitoye, A., Njoroge, J., Edmundson, C., Bardsley, M., . . . Phipps, E. (2021). Preliminary indications of the burden of COVID-19 among people who inject drugs in England and Northern Ireland and the impact on access to health and

- harm reduction services. *Public Health*, 192, 8–11.  
<https://doi.org/10.1016/j.puhe.2021.01.004>
- Czeisler, M., Lane, R. I., Petrosky, E., Wiley, J. F., Christensen, A., Njai, R., . . . Rajaratnam, S. M. (2020). Mental Health, Substance Use, and Suicidal Ideation During the COVID-19 Pandemic — United States, June 24–30, 2020. *MMWR. Morbidity and Mortality Weekly Report*, 69(32), 1049–1057.  
<https://doi.org/10.15585/mmwr.mm6932a1>
- Darke, S. (1998). Self-report among injecting drug users: A review. *Drug and Alcohol Dependence*, 51(3), 253–263. [https://doi.org/10.1016/s0376-8716\(98\)00028-3](https://doi.org/10.1016/s0376-8716(98)00028-3)
- Depressants - Alcohol and Drug Foundation. (n.d.). Retrieved June 24, 2021, from <https://adf.org.au/drug-facts/depressants/>
- Devarakonda, A. K., Wehrle, C. J., Chibane, F. L., Drevets, P. D., Fox, E. D., & Lawson, A. G. (2020). The Effects of the COVID-19 Pandemic on Trauma Presentations in a Level One Trauma Center. *The American Surgeon*, 000313482097371.  
<https://doi.org/10.1177/0003134820973715>
- Donovan, K. A., & Portman, D. G. (2021). Effect of COVID-19 Pandemic on Cannabis Use in Cancer Patients. *American Journal of Hospice and Palliative Medicine*®, 1–4.  
<https://doi.org/10.1177/1049909121999784>
- Dumas, T. M., Ellis, W., & Litt, D. M. (2020a). What Does Adolescent Substance Use Look Like During the COVID-19 Pandemic? Examining Changes in Frequency, Social Contexts, and Pandemic-Related Predictors. *Journal of Adolescent Health*, 67(3), 354–361. <https://doi.org/10.1016/j.jadohealth.2020.06.018>
- Dumas, T. M., Ellis, W., & Litt, D. M. (2020b). What Does Adolescent Substance Use Look Like During the COVID-19 Pandemic? Examining Changes in Frequency, Social

- Contexts, and Pandemic-Related Predictors. *Journal of Adolescent Health*, 67(3), 354–361. <https://doi.org/10.1016/j.jadohealth.2020.06.018>
- The Effects of PCP vs LSD | Tacoma, WA. (2019, August 27). Retrieved June 24, 2021, from <https://www.bayviewrecovery.com/rehab-blog/pcp-vs-bsd/>
- Fentanyl DrugFacts. (2021, June 10). Retrieved June 24, 2021, from <https://www.drugabuse.gov/publications/drugfacts/fentanyl>
- Field, A. P., & Gillett, R. (2010). How to do a meta-analysis. *British Journal of Mathematical and Statistical Psychology*, 63(3), 665–694. <https://doi.org/10.1348/000711010x502733>
- Firkey, M. K., Sheinfil, A. Z., & Woolf-King, S. E. (2021). Substance use, sexual behavior, and general well-being of U.S. college students during the COVID-19 pandemic: A brief report. *Journal of American College Health*, 1–7. <https://doi.org/10.1080/07448481.2020.1869750>
- Gili, A., Bacci, M., Aroni, K., Nicoletti, A., Gambelunghe, A., Mercurio, I., & Gambelunghe, C. (2021a). Changes in Drug Use Patterns during the COVID-19 Pandemic in Italy: Monitoring a Vulnerable Group by Hair Analysis. *International Journal of Environmental Research and Public Health*, 18(4), 1967–1978. <https://doi.org/10.3390/ijerph18041967>
- Gili, A., Bacci, M., Aroni, K., Nicoletti, A., Gambelunghe, A., Mercurio, I., & Gambelunghe, C. (2021b). Changes in Drug Use Patterns during the COVID-19 Pandemic in Italy: Monitoring a Vulnerable Group by Hair Analysis. *International Journal of Environmental Research and Public Health*, 18(4), 1967. <https://doi.org/10.3390/ijerph18041967>
- Goldstein, R. Z., & Volkow, N. D. (2002). Drug Addiction and Its Underlying Neurobiological Basis: Neuroimaging Evidence for the Involvement of the Frontal



Cortex. *American Journal of Psychiatry*, 159(10), 1642–1652.

<https://doi.org/10.1176/appi.ajp.159.10.1642>

Graupensperger, S., Fleming, C. B., Jaffe, A. E., Rhew, I. C., Patrick, M. E., & Lee, C. M.

(2021). Changes in Young Adults' Alcohol and Marijuana Use, Norms, and Motives From Before to During the COVID-19 Pandemic. *Journal of Adolescent Health*,

68(4), 658–665. <https://doi.org/10.1016/j.jadohealth.2021.01.008>

Hallucinogens DrugFacts. (2021, June 9). Retrieved June 24, 2021, from

<https://www.drugabuse.gov/publications/drugfacts/hallucinogens>

Hammond, D., Goodman, S., Wadsworth, E., Rynard, V., Boudreau, C., & Hall, W. (2020).

Evaluating the impacts of cannabis legalization: The International Cannabis Policy Study. *International Journal of Drug Policy*, 77, 102698.

<https://doi.org/10.1016/j.drugpo.2020.102698>

Harris, S. N., Mowbray, C. T., & Solarz, A. (1994). Physical Health, mental Health, and

Substance Abuse Problems of Shelter Users. *Health & Social Work*, 19(1), 37–45.

<https://doi.org/10.1093/hsw/19.1.37>

Heroin - Alcohol and Drug Foundation. (n.d.). Retrieved June 24, 2021, from

<https://adf.org.au/drug-facts/heroin/>

Higgins, J. P. T. (2003). Measuring inconsistency in meta-analyses. *BMJ*, 327(7414), 557–

560. <https://doi.org/10.1136/bmj.327.7414.557>

Holland, K. M., Jones, C., Vivolo-Kantor, A. M., Idaikkadar, N., Zwald, M., Hoots, B., . . .

Houry, D. (2021). Trends in US Emergency Department Visits for Mental Health, Overdose, and Violence Outcomes Before and During the COVID-19 Pandemic.

*JAMA Psychiatry*, 78(4), 372. <https://doi.org/10.1001/jamapsychiatry.2020.4402>

- Hwang, T. J., Rabheru, K., Peisah, C., Reichman, W., & Ikeda, M. (2020). Loneliness and social isolation during the COVID-19 pandemic. *International Psychogeriatrics*, 32(10), 1217–1220. <https://doi.org/10.1017/s1041610220000988>
- Ismael, F., Zaramella, B., Battagin, T., Bizario, J. C. S., Gallego, J., Villela, V., . . . Castaldelli-Maia, J. M. (2021). Substance Use in Mild-COVID-19 Patients: A Retrospective Study. *Frontiers in Public Health*, 9. <https://doi.org/10.3389/fpubh.2021.634396>
- Kadushin, C., Reber, E., Saxe, L., & Livert, D. (1998). The Substance Use System: Social and Neighborhood Environments Associated with Substance Use and Misuse. *Substance Use & Misuse*, 33(8), 1681–1710. <https://doi.org/10.3109/10826089809058950>
- Kelly, K. L. (1988). The Accuracy and Reliability of Tests for Drugs of Abuse in Urine Samples. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, 8(5), 263–276. <https://doi.org/10.1002/j.1875-9114.1988.tb04082.x>
- Kranzler, H. R., & Liebowitz, N. R. (1988). Anxiety and Depression in Substance Abuse: Clinical Implications. *Medical Clinics of North America*, 72(4), 867–885. [https://doi.org/10.1016/s0025-7125\(16\)30749-0](https://doi.org/10.1016/s0025-7125(16)30749-0)
- Kumar, N., Janmohamed, K., Nyhan, K., Martins, S. S., Cerda, M., Hasin, D., . . . Khoshnood, K. (2021). Substance use and substance use disorder, in relation to COVID-19: protocol for a scoping review. *Systematic Reviews*, 10(1). <https://doi.org/10.1186/s13643-021-01605-9>
- Lee, Y. H. (2019). Strengths and Limitations of Meta-Analysis. *The Korean Journal of Medicine*, 94(5), 391–395. <https://doi.org/10.3904/kjm.2019.94.5.391>
- Liébana-Presa, C., Martínez-Fernández, M. C., Benítez-Andrades, J. A., Fernández-Martínez, E., Marqués-Sánchez, P., & García-Rodríguez, I. (2020). Stress, Emotional

- Intelligence and the Intention to Use Cannabis in Spanish Adolescents: Influence of COVID-19 Confinement. *Frontiers in Psychology*, *11*.  
<https://doi.org/10.3389/fpsyg.2020.582578>
- Lin, L., & Chu, H. (2017). Quantifying publication bias in meta-analysis. *Biometrics*, *74*(3), 785–794. <https://doi.org/10.1111/biom.12817>
- Lingford-Hughes, A. (2005). Human brain imaging and substance abuse. *Current Opinion in Pharmacology*, *5*(1), 42–46. <https://doi.org/10.1016/j.coph.2004.10.002>
- Mallet, J., Dubertret, C., & le Strat, Y. (2021a). Addictions in the COVID-19 era: Current evidence, future perspectives a comprehensive review. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *106*, 110070.  
<https://doi.org/10.1016/j.pnpbp.2020.110070>
- Mallet, J., Dubertret, C., & le Strat, Y. (2021b). Addictions in the COVID-19 era: Current evidence, future perspectives a comprehensive review. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *106*, 110070.  
<https://doi.org/10.1016/j.pnpbp.2020.110070>
- Manchikanti, L., Vanaparthi, R., Atluri, S., Sachdeva, H., Kaye, A. D., & Hirsch, J. A. (2021). COVID-19 and the Opioid Epidemic: Two Public Health Emergencies That Intersect With Chronic Pain. *Pain and Therapy*, 1–8. <https://doi.org/10.1007/s40122-021-00243-2>
- Marijuana DrugFacts. (2021, June 7). Retrieved June 24, 2021, from <https://www.drugabuse.gov/publications/drugfacts/marijuana>
- Marlatt, G. A. (1992). Substance abuse: Implications of a biopsychosocial model for prevention, treatment, and relapse prevention. *Psychopharmacology: Basic Mechanisms and Applied Interventions.*, 131–162. <https://doi.org/10.1037/10114-004>

- McAlonan, G. M., Lee, A. M., Cheung, V., Cheung, C., Tsang, K. W., Sham, P. C., . . . Wong, J. G. (2007). Immediate and Sustained Psychological Impact of an Emerging Infectious Disease Outbreak on Health Care Workers. *The Canadian Journal of Psychiatry, 52*(4), 241–247. <https://doi.org/10.1177/070674370705200406>
- McGraw, C., Salottolo, K., Carrick, M., Lieser, M., Madayag, R., Berg, G., . . . Bar-Or, D. (2021). Patterns of alcohol and drug utilization in trauma patients during the COVID-19 pandemic at six trauma centers. *Injury Epidemiology, 8*(1). <https://doi.org/10.1186/s40621-021-00322-0>
- MDMA (Ecstasy/Molly). (2021, June 7). Retrieved June 24, 2021, from <https://www.drugabuse.gov/drug-topics/mdma-ecstasymolly>
- Mental Health Considerations During a Pandemic Influenza Outbreak. (2009). *The Internet Journal of Rescue and Disaster Medicine, 9*(1). <https://doi.org/10.5580/1481>
- Meth vs. Coke. (n.d.). Retrieved June 24, 2021, from <https://www.drugrehab.com/addiction/drugs/crystal-meth/meth-vs-coke/>
- Miller, K., Laha-Walsh, K., Albright, D. L., & McDaniel, J. (2021). Cannabis use during the COVID-19 pandemic: results from a longitudinal study of Cannabis users. *Journal of Substance Use, 27*(1), 38–42. <https://doi.org/10.1080/14659891.2021.1885517>
- Miller, P. M. (2013). *Principles of Addiction: Comprehensive Addictive Behaviors and Disorders, Volume 1* (1st ed.). San Diego, California: Elsevier.
- Moeller, K. E., Lee, K. C., & Kissack, J. C. (2008). Urine Drug Screening: Practical Guide for Clinicians. *Mayo Clinic Proceedings, 83*(1), 66–76. <https://doi.org/10.4065/83.1.66>
- Morgan, C. J. A., & Curran, H. V. (2011). Ketamine use: a review. *Addiction, 107*(1), 27–38. <https://doi.org/10.1111/j.1360-0443.2011.03576.x>

- Morin, K. A., Acharya, S., Eibl, J. K., & Marsh, D. C. (2021). Evidence of increased Fentanyl use during the COVID-19 pandemic among opioid agonist treatment patients in Ontario, Canada. *International Journal of Drug Policy*, *90*, 103088. <https://doi.org/10.1016/j.drugpo.2020.103088>
- Niles, J. K., Gudin, J., Radcliff, J., & Kaufman, H. W. (2021). The Opioid Epidemic Within the COVID-19 Pandemic: Drug Testing in 2020. *Population Health Management*, *24*(S1), S-43. <https://doi.org/10.1089/pop.2020.0230>
- O'Farrell, T. J., Fals-Stewart, W., & Murphy, M. (2003). Concurrent validity of a brief self-report Drug Use Frequency measure. *Addictive Behaviors*, *28*(2), 327–337. [https://doi.org/10.1016/s0306-4603\(01\)00226-x](https://doi.org/10.1016/s0306-4603(01)00226-x)
- Ornell, F., Moura, H. F., Scherer, J. N., Pechansky, F., Kessler, F. H. P., & von Diemen, L. (2020). The COVID-19 pandemic and its impact on substance use: Implications for prevention and treatment. *Psychiatry Research*, *289*, 113096. <https://doi.org/10.1016/j.psychres.2020.113096>
- Palamar, J. J., & Acosta, P. (2020). Virtual raves and happy hours during COVID-19: New drug use contexts for electronic dance music partygoers. *International Journal of Drug Policy*, 102904. <https://doi.org/10.1016/j.drugpo.2020.102904>
- Palamar, J. J., Le, A., & Acosta, P. (2020a). Shifts in Drug Use Behavior Among Electronic Dance Music Partygoers in New York During COVID-19 Social Distancing. *Substance Use & Misuse*, *56*(2), 238–244. <https://doi.org/10.1080/10826084.2020.1857408>
- Palamar, J. J., Le, A., & Acosta, P. (2020b). Shifts in Drug Use Behavior Among Electronic Dance Music Partygoers in New York During COVID-19 Social Distancing. *Substance Use & Misuse*, *56*(2), 238–244. <https://doi.org/10.1080/10826084.2020.1857408>

- Patanavanich, R., & Glantz, S. A. (2020). Smoking Is Associated With COVID-19 Progression: A Meta-analysis. *Nicotine & Tobacco Research*, 22(9), 1653–1656. <https://doi.org/10.1093/ntr/ntaa082>
- Pinkham, A. E., Ackerman, R. A., Depp, C. A., Harvey, P. D., & Moore, R. C. (2020). A Longitudinal Investigation of the Effects of the COVID-19 Pandemic on the Mental Health of Individuals with Pre-existing Severe Mental Illnesses. *Psychiatry Research*, 294, 113493. <https://doi.org/10.1016/j.psychres.2020.113493>
- Roberts, A., Rogers, J., Mason, R., Siriwardena, A. N., Hogue, T., Whitley, G. A., & Law, G. R. (2021). Alcohol and other substance use during the COVID-19 pandemic: A systematic review. *Drug and Alcohol Dependence*, 229, 109150. <https://doi.org/10.1016/j.drugalcdep.2021.109150>
- Rogers, A. H., Shepherd, J. M., Garey, L., & Zvolensky, M. J. (2020). Psychological factors associated with substance use initiation during the COVID-19 pandemic. *Psychiatry Research*, 293, 113407. <https://doi.org/10.1016/j.psychres.2020.113407>
- Rolland, B., Haesebaert, F., Zante, E., Benyamina, A., Haesebaert, J., & Franck, N. (2020). Global Changes and Factors of Increase in Caloric/Salty Food Intake, Screen Use, and Substance Use During the Early COVID-19 Containment Phase in the General Population in France: Survey Study. *JMIR Public Health and Surveillance*, 6(3), e19630. <https://doi.org/10.2196/19630>
- Rowan, A. B. (2001). Adolescent substance abuse and suicide. *Depression and Anxiety*, 14(3), 186–191. <https://doi.org/10.1002/da.1065>
- Schuckit, M. A. (2006). Comorbidity between substance use disorders and psychiatric conditions. *Addiction*, 101, 76–88. <https://doi.org/10.1111/j.1360-0443.2006.01592.x>

- Schwartz, R. H. (1988). Urine Testing in the Detection of Drugs of Abuse. *Archives of Internal Medicine*, 148(11), 2407.  
<https://doi.org/10.1001/archinte.1988.00380110059012>
- Shreffler, J., Shoff, H., Thomas, J. J., & Huecker, M. (2021). Brief Report: The Impact of COVID-19 on Emergency Department Overdose Diagnoses and County Overdose Deaths. *The American Journal on Addictions*, 1–4. <https://doi.org/10.1111/ajad.13148>
- Smart, R., & Pacula, R. L. (2019). Early evidence of the impact of cannabis legalization on cannabis use, cannabis use disorder, and the use of other substances: Findings from state policy evaluations. *The American Journal of Drug and Alcohol Abuse*, 45(6), 644–663. <https://doi.org/10.1080/00952990.2019.1669626>
- Starks, T. J., Jones, S. S., Sauermilch, D., Benedict, M., Adebayo, T., Cain, D., & Simpson, K. N. (2020a). Evaluating the impact of COVID-19: A cohort comparison study of drug use and risky sexual behavior among sexual minority men in the U.S.A. *Drug and Alcohol Dependence*, 216, 108260.  
<https://doi.org/10.1016/j.drugalcdep.2020.108260>
- Starks, T. J., Jones, S. S., Sauermilch, D., Benedict, M., Adebayo, T., Cain, D., & Simpson, K. N. (2020b). Evaluating the impact of COVID-19: A cohort comparison study of drug use and risky sexual behavior among sexual minority men in the U.S.A. *Drug and Alcohol Dependence*, 216, 108260.  
<https://doi.org/10.1016/j.drugalcdep.2020.108260>
- Stein, M. D. (1999). MEDICAL CONSEQUENCES OF SUBSTANCE ABUSE. *Psychiatric Clinics of North America*, 22(2), 351–370. [https://doi.org/10.1016/s0193-953x\(05\)70081-2](https://doi.org/10.1016/s0193-953x(05)70081-2)
- Stimulants - Alcohol and Drug Foundation. (n.d.). Retrieved June 24, 2021, from <https://adf.org.au/drug-facts/stimulants/>

- Sutherland, I., & Shepherd, J. P. (2001). Social dimensions of adolescent substance use. *Addiction*, 96(3), 445–458. <https://doi.org/10.1046/j.1360-0443.2001.9634458.x>
- Tamargo, J. A., Martin, H. R., Diaz-Martinez, J., Trepka, M. J., Delgado-Enciso, I., Johnson, A., . . . Baum, M. K. (2021). COVID-19 Testing and the Impact of the Pandemic on the Miami Adult Studies on HIV Cohort. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, 87(4), 1016–1023. <https://doi.org/10.1097/qai.0000000000002680>
- Thabane, L., Mbuagbaw, L., Zhang, S., Samaan, Z., Marcucci, M., Ye, C., . . . Goldsmith, C. H. (2013). A tutorial on sensitivity analyses in clinical trials: the what, why, when and how. *BMC Medical Research Methodology*, 13(1), 2–8. <https://doi.org/10.1186/1471-2288-13-92>
- Tufanaru, C., Munn, Z., Stephenson, M., & Aromataris, E. (2015). Fixed or random effects meta-analysis? Common methodological issues in systematic reviews of effectiveness. *International Journal of Evidence-Based Healthcare*, 13(3), 196–207. <https://doi.org/10.1097/xeb.0000000000000065>
- Turna, J., Zhang, J., Lamberti, N., Patterson, B., Simpson, W., Francisco, A. P., . . . Ameringen, M. V. (2021a). Anxiety, depression and stress during the COVID-19 pandemic: Results from a cross-sectional survey. *Journal of Psychiatric Research*, 137, 96–103. <https://doi.org/10.1016/j.jpsychires.2021.02.059>
- Turna, J., Zhang, J., Lamberti, N., Patterson, B., Simpson, W., Francisco, A. P., . . . Ameringen, M. V. (2021b). Anxiety, depression and stress during the COVID-19 pandemic: Results from a cross-sectional survey. *Journal of Psychiatric Research*, 137, 96–103. <https://doi.org/10.1016/j.jpsychires.2021.02.059>
- Vai, B., Mazza, M. G., Delli Colli, C., Foiselle, M., Allen, B., Benedetti, F., . . . de Picker, L. J. (2021). Mental Disorders and Risk of Covid-19 Related Mortality, Hospitalization



- and Intensive Care Unit Admission: A Systematic Review and Meta-Analysis. *SSRN Electronic Journal*. <https://doi.org/10.2139/ssrn.3832645>
- van Bortel, T., Basnayake, A., Wurie, F., Jambai, M., Koroma, A. S., Muana, A. T., . . . Nellums, L. B. (2016). Psychosocial effects of an Ebola outbreak at individual, community and international levels. *Bulletin of the World Health Organization*, *94*(3), 210–214. <https://doi.org/10.2471/blt.15.158543>
- van Laar, M. W., Oomen, P. E., van Miltenburg, C. J. A., Vercoulen, E., Freeman, T. P., & Hall, W. D. (2020). Cannabis and COVID-19: Reasons for Concern. *Frontiers in Psychiatry*, *11*. <https://doi.org/10.3389/fpsyt.2020.601653>
- Vidot, D. C., Islam, J. Y., Marlene Camacho-Rivera, Harrell, M. B., Rao, D. R., Chavez, J. V., . . . Messiah, S. E. (2020). The COVID-19 cannabis health study: Results from an epidemiologic assessment of adults who use cannabis for medicinal reasons in the United States. *Journal of Addictive Diseases*, *39*(1), 26–36. <https://doi.org/10.1080/10550887.2020.1811455>
- Wainwright, J. J., Mikre, M., Whitley, P., Dawson, E., Huskey, A., Lukowiak, A., & Giroir, B. P. (2020). Analysis of Drug Test Results Before and After the US Declaration of a National Emergency Concerning the COVID-19 Outbreak. *JAMA*, *324*(16), 1674. <https://doi.org/10.1001/jama.2020.17694>
- What are benzodiazepines? (2021, April 1). Retrieved June 24, 2021, from <https://www.mind.org.uk/information-support/drugs-and-treatments/sleeping-pills-and-minor-tranquillisers/about-benzodiazepines/>
- What are the short-term effects of cocaine use? (2021, June 13). Retrieved June 24, 2021, from <https://www.drugabuse.gov/publications/research-reports/cocaine/what-are-short-term-effects-cocaine-use>

- Wilcox, C. E., Bogenschutz, M. P., Nakazawa, M., & Woody, G. (2013). Concordance between self-report and urine drug screen data in adolescent opioid dependent clinical trial participants. *Addictive Behaviors*, *38*(10), 2568–2574.  
<https://doi.org/10.1016/j.addbeh.2013.05.015>
- Winters, K. C., Stinchfield, R. D., Henly, G. A., & Schwartz, R. H. (1990). Validity of Adolescent Self-Report of Alcohol and Other Drug Involvement. *International Journal of the Addictions*, *25*(sup11), 1379–1395.  
<https://doi.org/10.3109/10826089009068469>
- Zou, Z., Wang, H., D'Oleire Uquillas, F., Wang, X., Ding, J., & Chen, H. (2017). Definition of Substance and Non-substance Addiction. *Advances in Experimental Medicine and Biology*, 21–41. [https://doi.org/10.1007/978-981-10-5562-1\\_2](https://doi.org/10.1007/978-981-10-5562-1_2)

## APPENDIX

### Appendix 1

Search string Web of Science:

(ALL = (covid OR covid-19 OR coronavirus OR "corona virus" OR SARSCoV-2 OR "severe acute respiratory syndrome coronavirus 2") AND ALL = ("Alcohol-Related Disorders" OR Alcohol\* OR Prescription Drug\* OR substance use OR substance misuse OR substance abuse OR opioid OR Opiate OR Heroin OR Opium OR Cannabis OR Marijuana OR Cocaine OR sedatives OR tranquilizers OR major tranquilizers OR Amphetamine OR Tobacco OR Nicotine OR benzodiazepines OR psychoactive OR psychotropic OR psychopharmacology OR psychiatric medication\* OR anticonvulsant\* OR antidepressant\* OR antipsychotic\* OR anxiolytic\* OR recreational drug\* OR stimulant medication\* OR self-medication OR mental health drug\* OR anti-anxiety medication\* OR sleep aid)) AND ((PY=="2021" OR "2020") AND DT=="ARTICLE" OR "EARLY ACCESS")) NOT (DT=="REVIEW" OR "LETTER" OR "EDITORIAL MATERIAL"))

Search string PubMed:

((((covid OR covid-19 OR coronavirus OR "corona virus" OR SARSCoV-2 OR "severe acute respiratory syndrome coronavirus 2") AND ("Alcohol-Related Disorders"[Mesh] OR Alcohol OR Prescription Drugs OR substance use OR substance misuse OR substance abuse OR substance-related disorders OR SubstanceRelated Disorders OR Opioid-Related Disorders OR Opiate OR Opioid OR Prescription Opiate OR Prescription Opioid OR Opiate Overdose OR Heroin OR Opium OR Cannabis OR Marijuana OR Cocaine Hydrochloride OR Cocaine-Related Disorders OR sedatives OR tranquilizers OR major tranquilizers OR Amphetamine OR Tobacco OR Nicotine OR benzodiazepines OR psychoactive OR psychotropic OR psychopharmacology OR "psychiatric medications" OR anticonvulsant\* OR antidepressant\*

OR antipsychotic\* OR anxiolytic\* OR recreational drug\* OR stimulant medication\* OR self-medication OR mental health drug\* OR anti-anxiety medication\* OR sleep aid)) AND  
(("2020"[Date - Publication] : "2021"[Date - Publication])) NOT ("comment"[Publication Type] OR "editorial"[Publication Type] OR "letter"[Publication Type] OR "review"[Publication Type] OR "systematic review"[Publication Type] OR "meta analysis"[Publication Type])

## APPENDIX 2

### *Classification of drugs originally included in the meta-analysis<sup>4</sup>*

<b>Class of drugs</b>	<b>Drug name</b>	<b>Description</b>
Cannabis/Marijuana (soft drug)		A psychoactive drug originating from the Cannabis plant.
Benzodiazepines (hard drug)		A class of psychoactive drugs that is used as sedative medication since it slows and lowers brain function. Examples include Ativan, Valium and Xanax
Hallucinogens <sup>1</sup> (hard drug)	LSD	This hallucinogenic drug alters thoughts, feelings, and awareness such as visual or auditory hallucinations
	PCP (Phencyclidine)	Similar to LSD, but less intense and also classed as a stimulant or pain reliever.
	Ketamine	Used as in high doses as anesthesia, in lower doses it shares its effects with other hallucinogens and causes hallucinations
Depressants <sup>2</sup> (hard drug)	Heroin	An opioid (define in notes) that is highly addictive and causes great euphoria
	Fentanyl	A very powerful opioid that is used as pain medication or as a recreational drug, more potent than heroin, causing the same effects
Stimulants <sup>3</sup> (hard drug)	Adderal (Mydayis)	A stimulant that improves focus and reduces impulsivity
	Cocaine	An addictive stimulant that gives energy, makes the individual talkative and mentally alert
	Methamphetamine (Speed)	A strong stimulant that is similar in effects to cocaine, but lasts longer, with speed being a less intense version
	XTC	A stimulant/psychoactive drug that increases energy but also causes altered sensations, hence being classed as both a stimulant and hallucinogen

<sup>1</sup> A class of psychoactive drugs that causes hallucinations and changes in perception and consciousness. Adapted from "Hallucinogens DrugFacts," 2021.

<sup>2</sup> A class of drugs that reduce arousal and stimulation by slowing down brain activity. Adapted from "Depressants - Alcohol and Drug Foundation" n.d.

<sup>3</sup> A class of drugs that increases energy, makes the individual more alert and awake, by speeding up brain activity. Adapted from "Stimulants - Alcohol and Drug Foundation," n.d.

<sup>4</sup> All drugs and its sources are put in an adapted table in APPENDIX 2

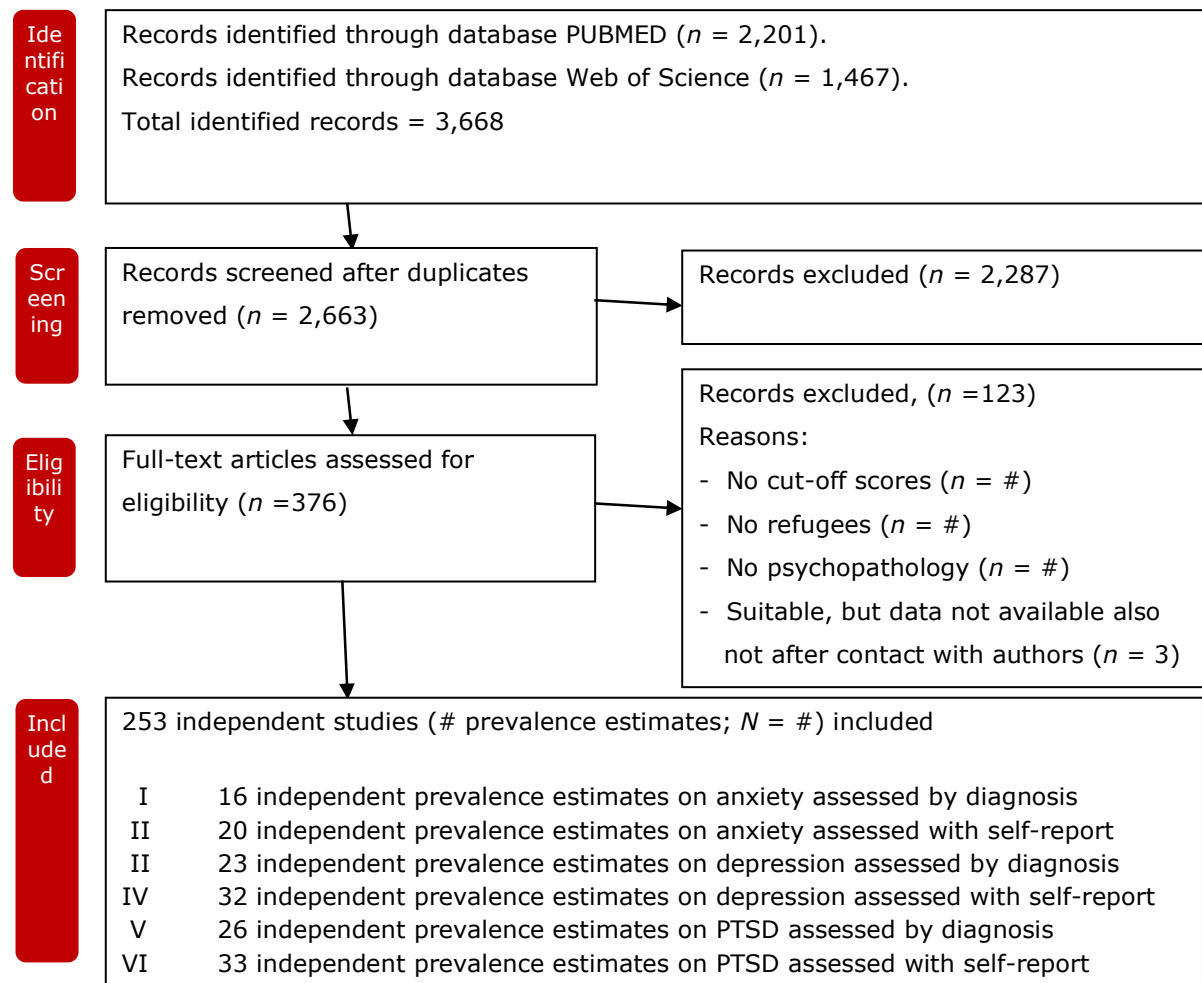
## APPENDIX 3

### *Classification of drugs included in the meta-analysis and its sources*

<b>Class of drugs</b>	<b>Drug name</b>	<b>Source</b>
Cannabis/Marijuana (soft drug)		("Marijuana DrugFacts," 2021)
Benzodiazepines (hard drug)		("What are benzodiazepines?," 2021)
Hallucinogens (hard drug)	LSD	("The Effects of PCP vs LSD   Tacoma, WA," 2019)
	PCP (Phencyclidine)	("Hallucinogens DrugFacts," 2021)
	Ketamine	(Morgan & Curran, 2011)
Depressants (hard drug)	Heroin	("Heroin - Alcohol and Drug Foundation," n.d.)
	Fentanyl	("Fentanyl DrugFacts," 2021)
Stimulants (hard drug)	Adderal (Mydayis)	("Adderall Oral: Uses, Side Effects, Interactions, Pictures, Warnings & Dosing - WebMD," n.d.)
	Cocaine	("What are the short-term effects of cocaine use?," 2021)
	Methamphetamine (Speed)	("Meth vs. Coke," n.d.)
	XTC	("MDMA (Ecstasy/Molly)," 2021)

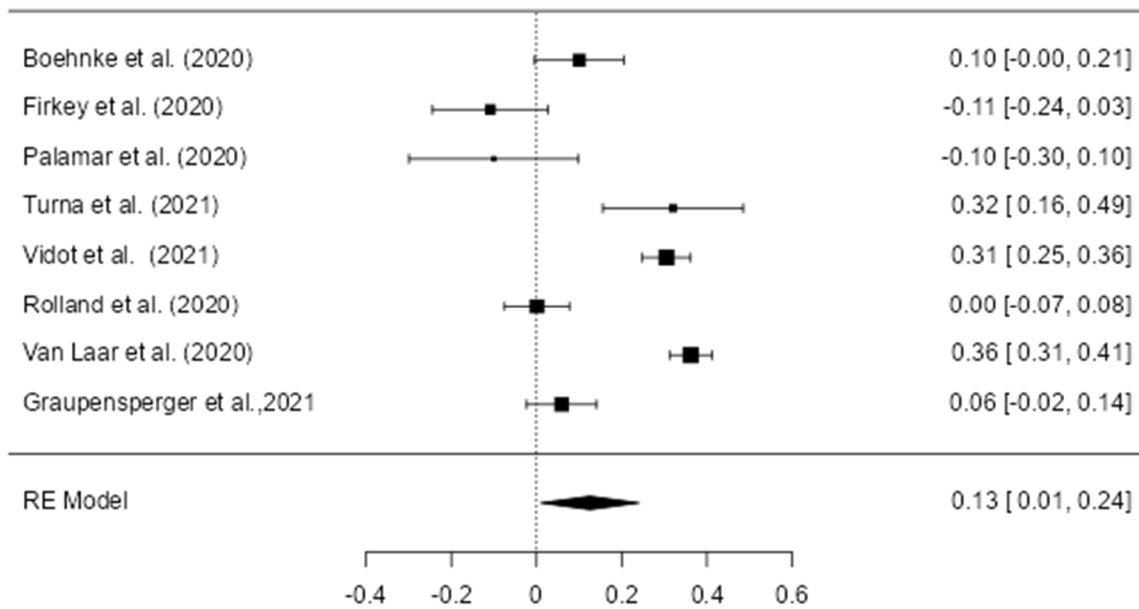
## APPENDIX 4

Figure 3. Flowchart on identification, screening and inclusion of eligible publications

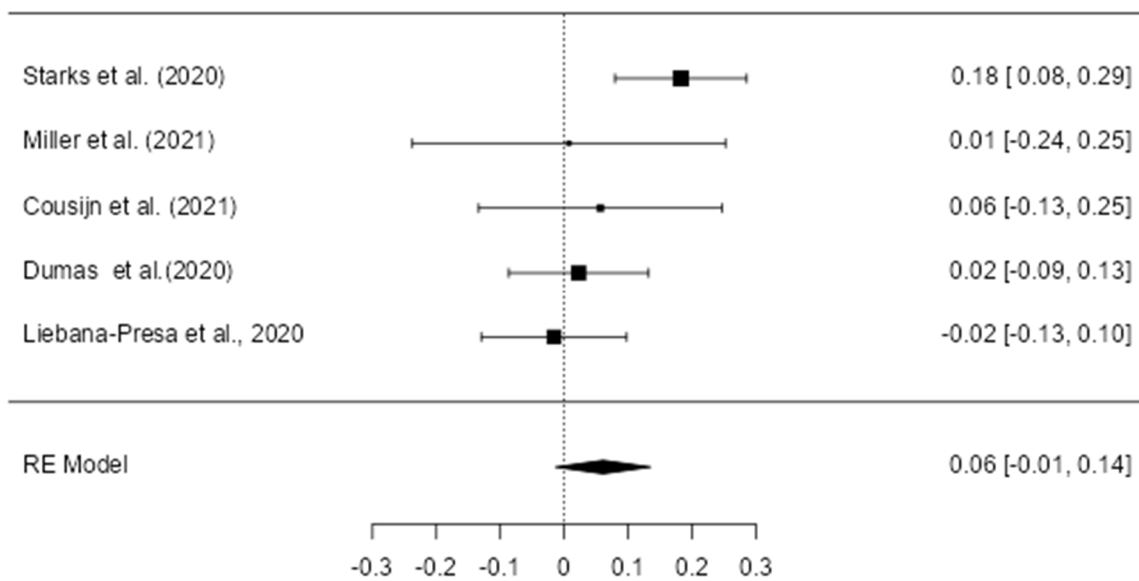


APPENDIX 5

**Figure 1: Forest plot illustrating the relation of cannabis use and COVID-19 as a stressor (proportion based data)**

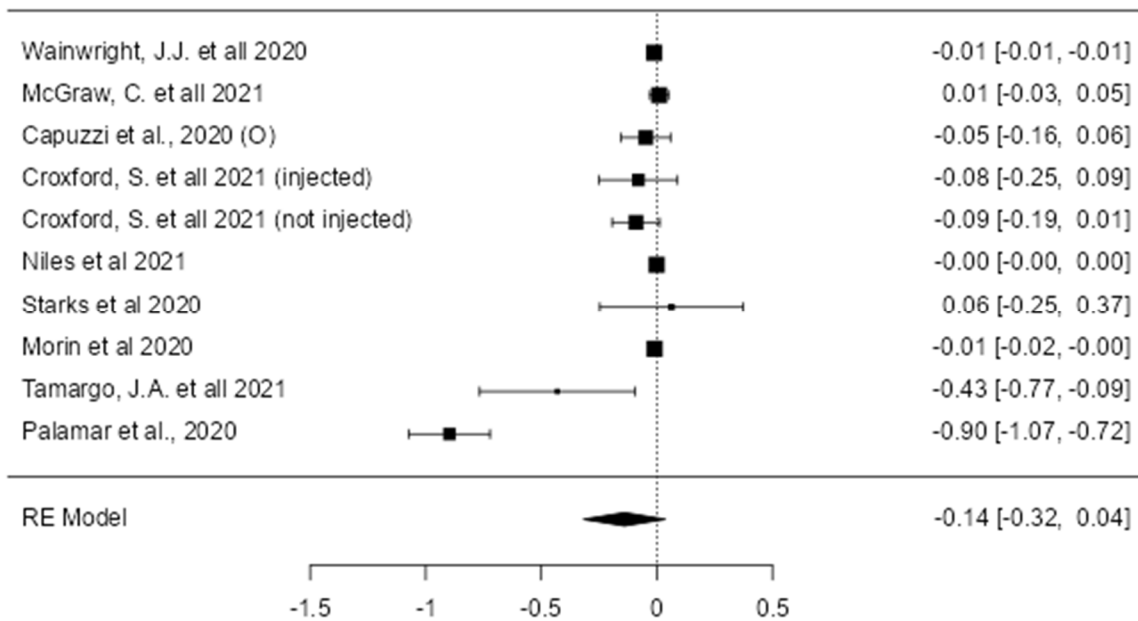


**Figure 2: Forest plot illustrating the relation of cannabis use and COVID-19 as a stressor (mean difference data)**

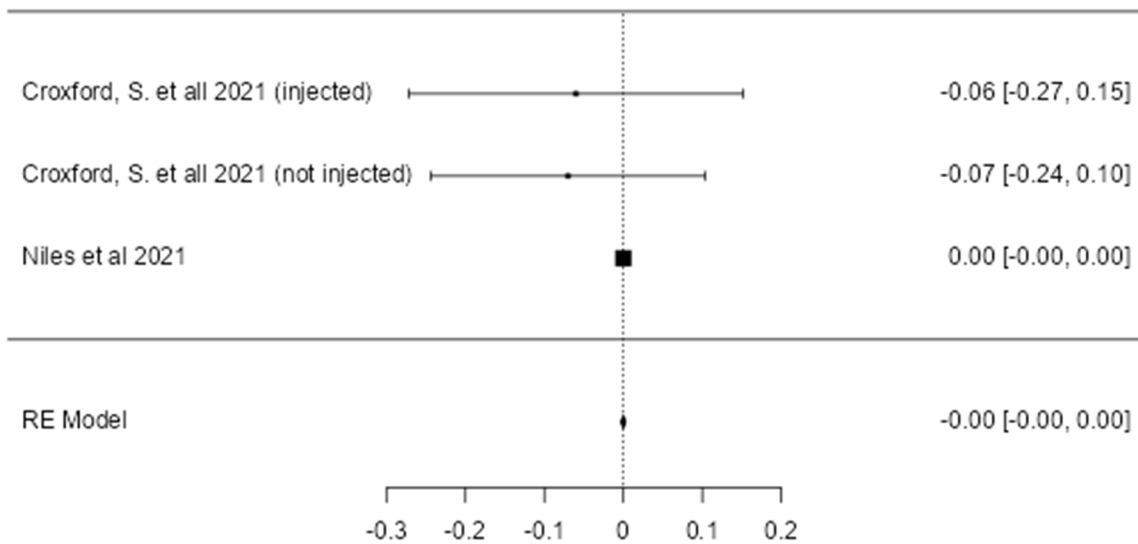




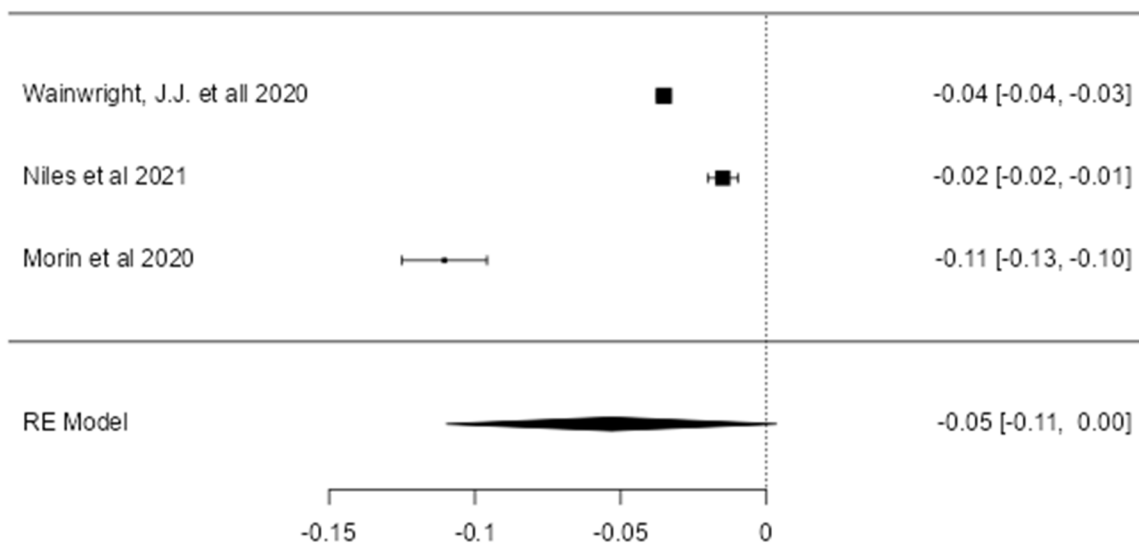
**Figure 3: Forest plot illustrating the relation of cocaine use and COVID-19 as a stressor**



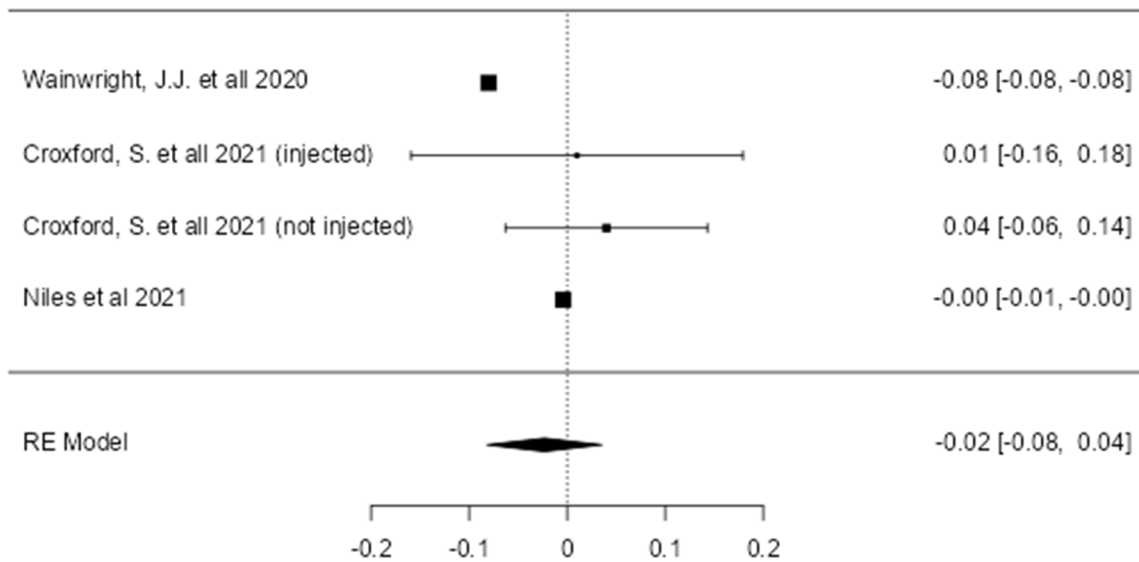
**Figure 4: Forest plot illustrating the relation of amphetamine use and COVID-19 as a stressor**



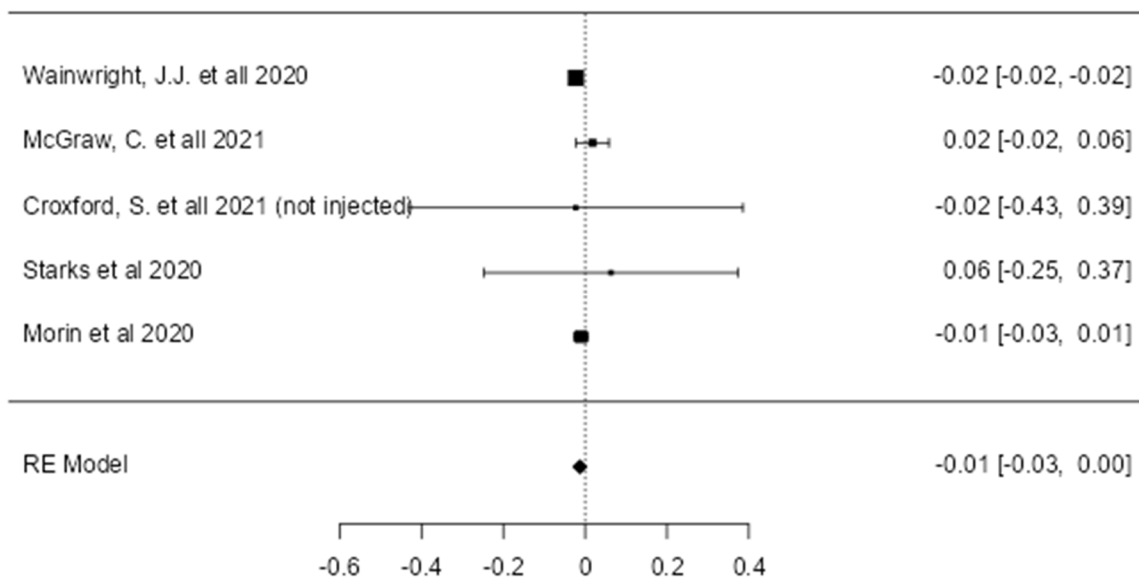
**Figure 5: Forest plot illustrating the relation of fentanyl use and COVID-19 as a stressor**



**Figure 6: Forest plot illustrating the relation of heroin use and COVID-19 as a stressor**

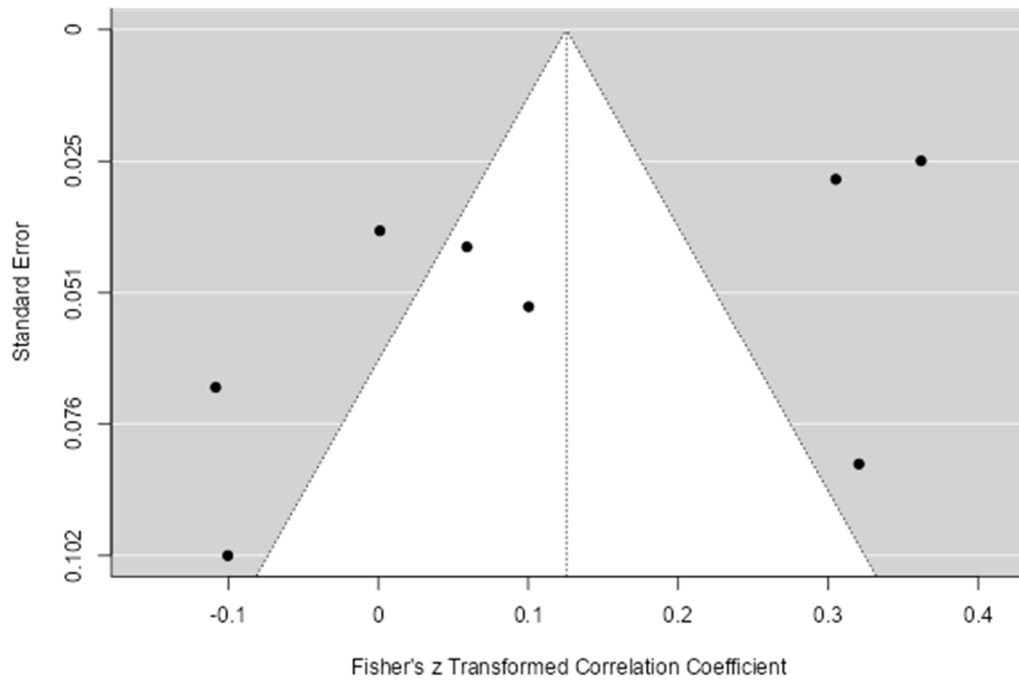


**Figure 7: Forest plot illustrating the relation of methamphetamine use and COVID-19 as a stressor**

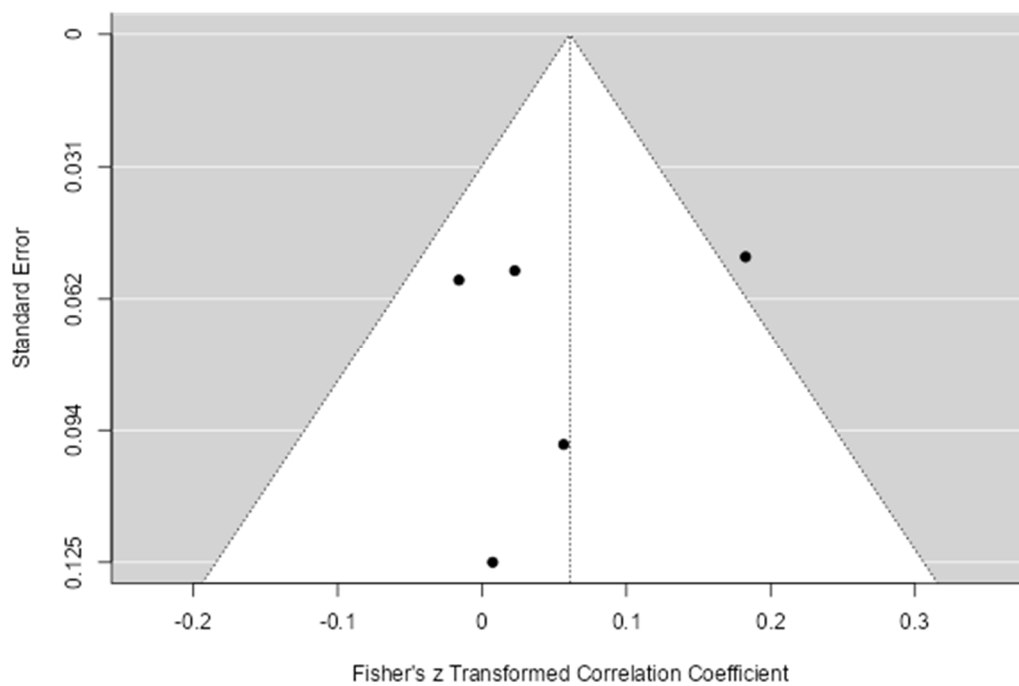


APPENDIX 6

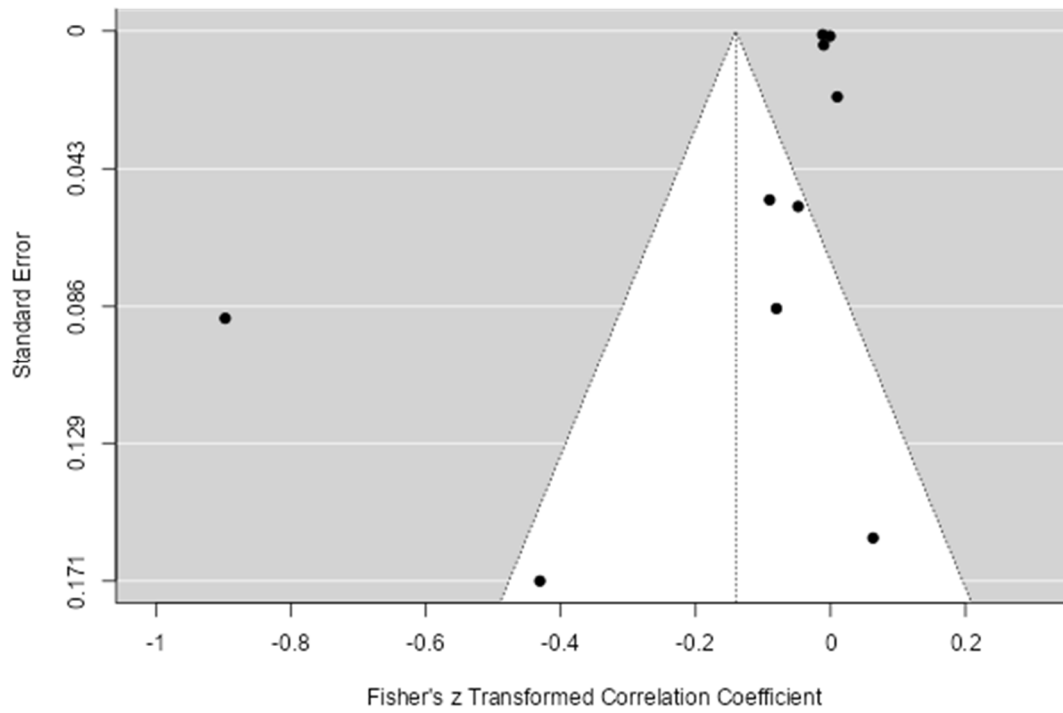
**Figure 1: Funnel Plot illustrating possible publication bias in the meta-analysis performed for cannabis use and COVID-19 as a stressor (proportion based data)**



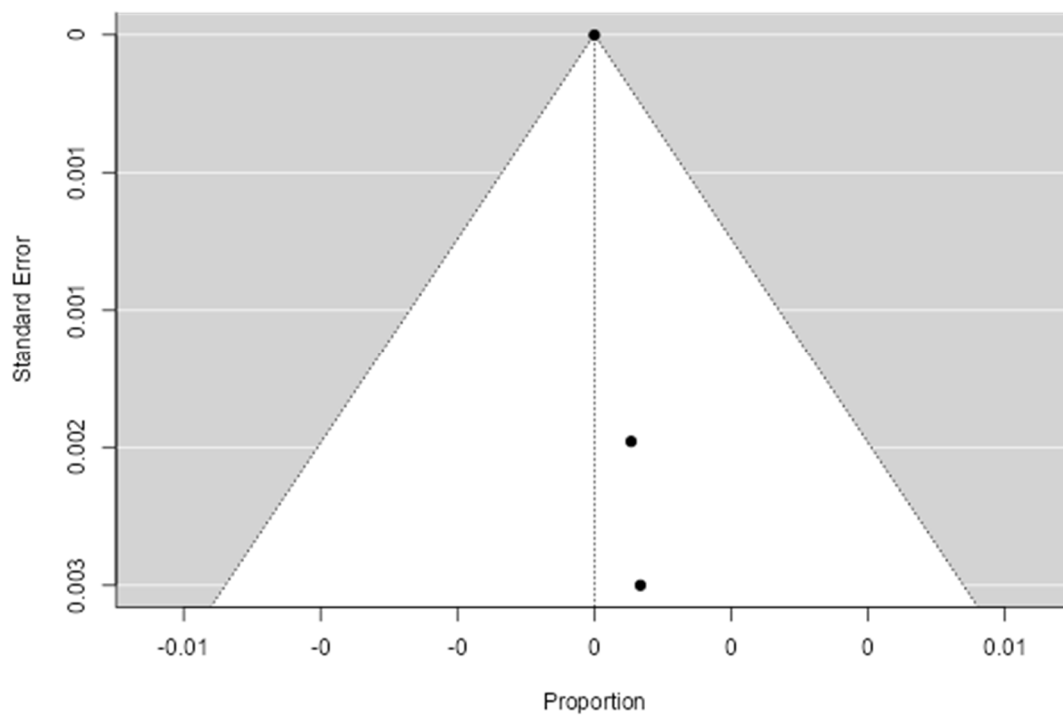
**Figure 2: Funnel plot on cannabis use and COVID-19 as a stressor (mean difference data)**



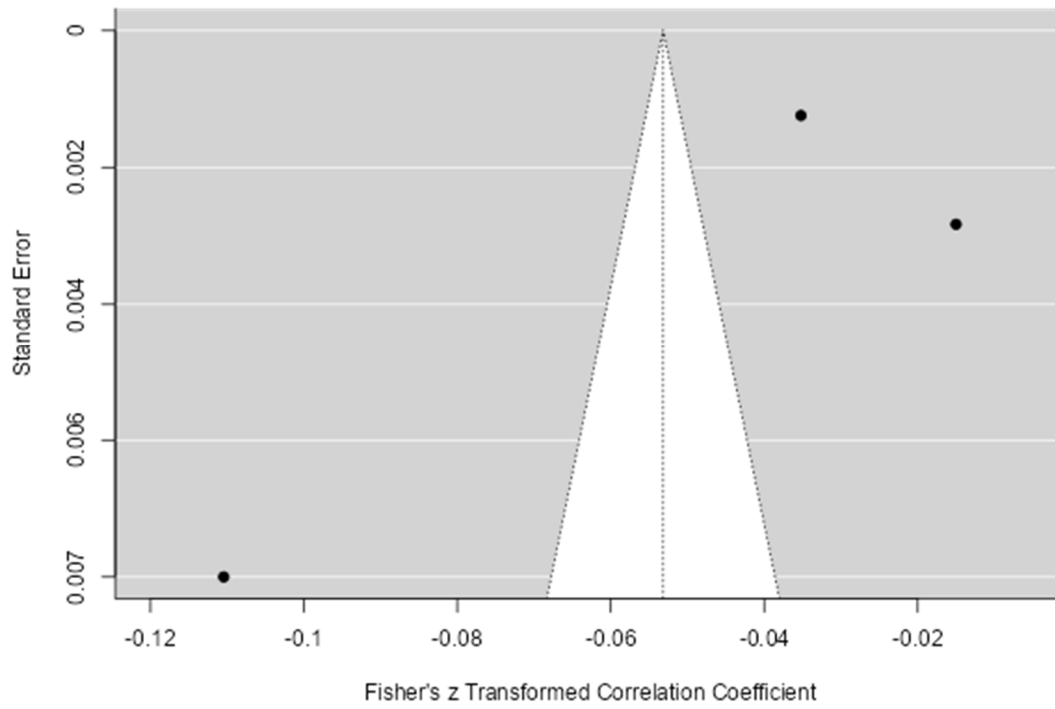
**Figure 3: Funnel Plot illustrating possible publication bias in the meta-analysis performed for cocaine use and COVID-19 as a stressor**



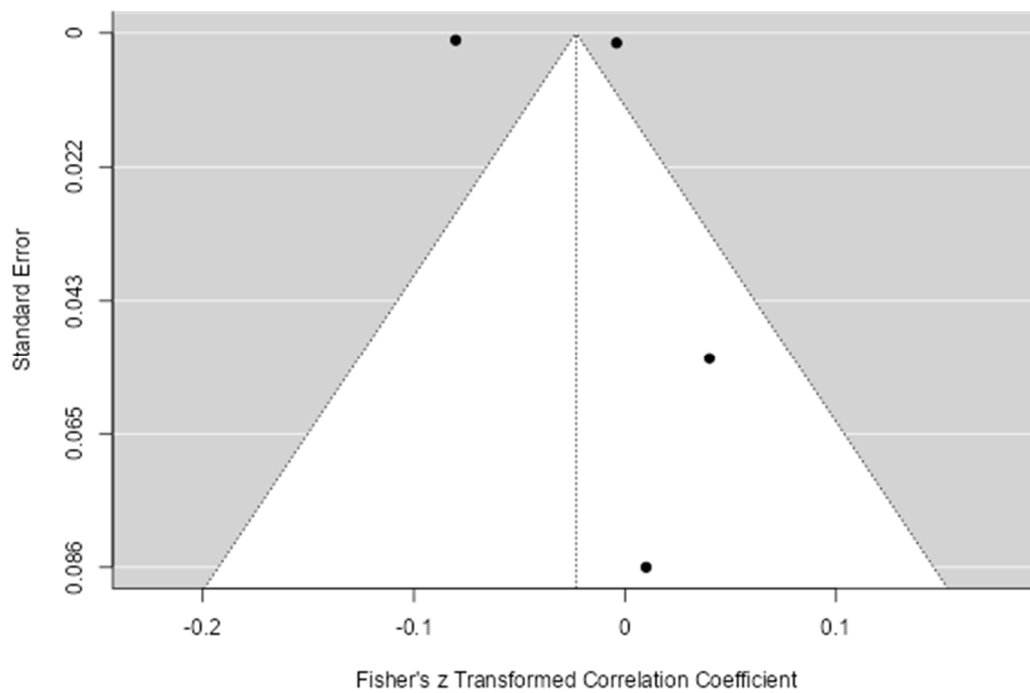
**Figure 4: Funnel Plot illustrating possible publication bias in the meta-analysis performed for amphetamine use and COVID-19 as a stressor**



**Figure 5: Funnel Plot illustrating possible publication bias in the meta-analysis performed for fentanyl use and COVID-19 as a stressor**



**Figure 6: Funnel Plot illustrating possible publication bias in the meta-analysis performed for heroin use and COVID-19 as a stressor**



**Figure 7: Funnel Plot illustrating possible publication bias in the meta-analysis performed for methamphetamine use and COVID-19 as a stressor**

