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 2nd 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 brains 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-analyis 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]; I2=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 cannbis 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-deduplication 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

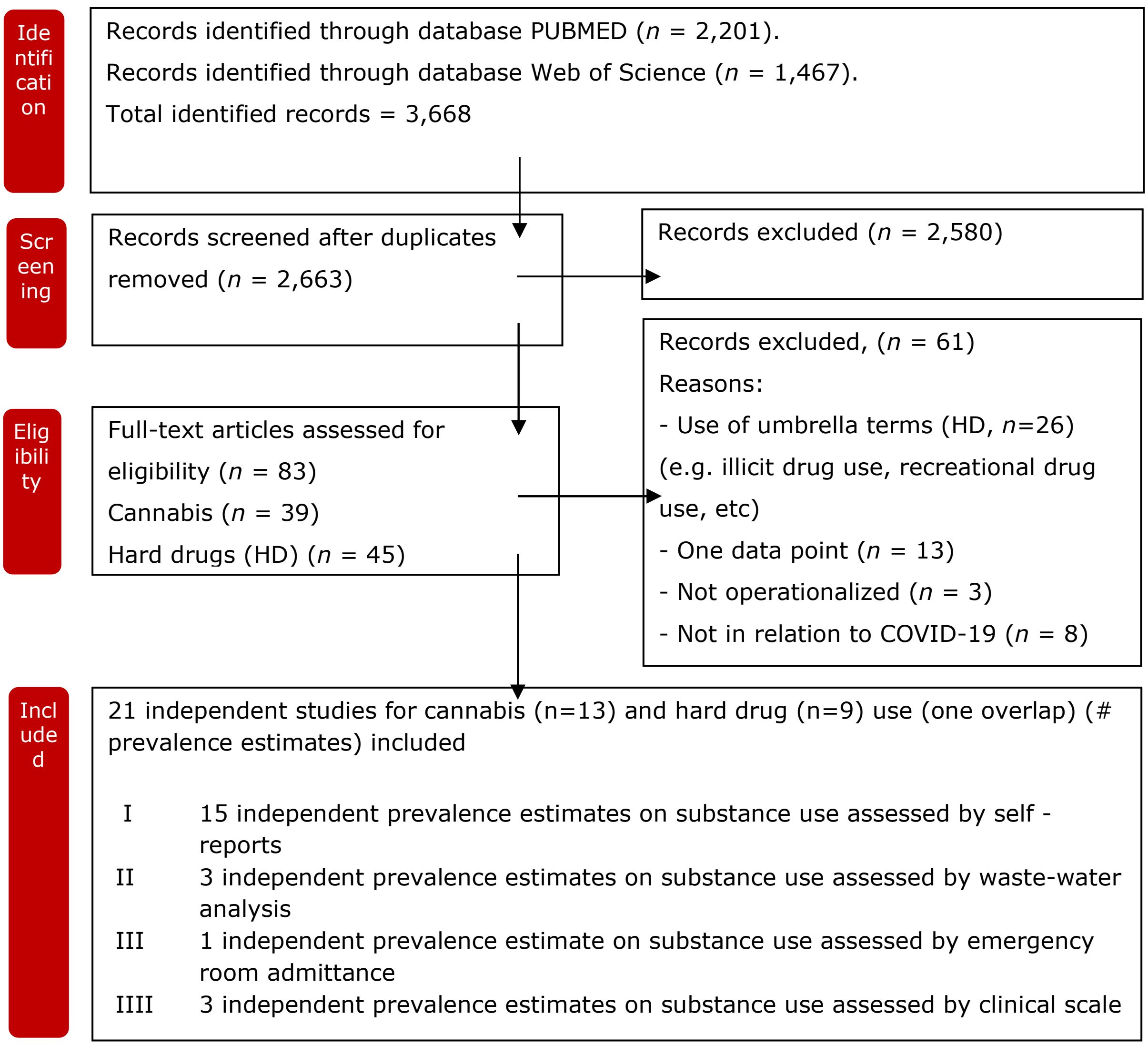


Figure 1. Flowchart on identification, screening and inclusion of eligible publications

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.

Study	N	type of data[a]	age	%female	Country	outcome measure
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

[a]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)[a]	Age	%Female	Country	Outcome measures	Hard drugs analysed[b]
Wainwright, J.J. et all 2020	750000	47.5	52.73	US	Positive urine test results, %	C. F, H, M
McGraw, C. et all 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 all 2021 (injected)	137	41	25.5	UK	Survey results, injected drugs	C, A, H
Croxford, S. et all 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 all 2021	37	56.9	51.2	US	Survey results	C
Palamar et al., 2020	128	23.3	61.7	US	Survey results	C

[a]Average sample size. [b]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[a]	r	Z[b]	p[c]
Cannabis (proportions)	8	0.125	2.12	0.034
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

[a]k = number of studies. [b]Z = Z-score, [c]p = p-value, significant at 0,05

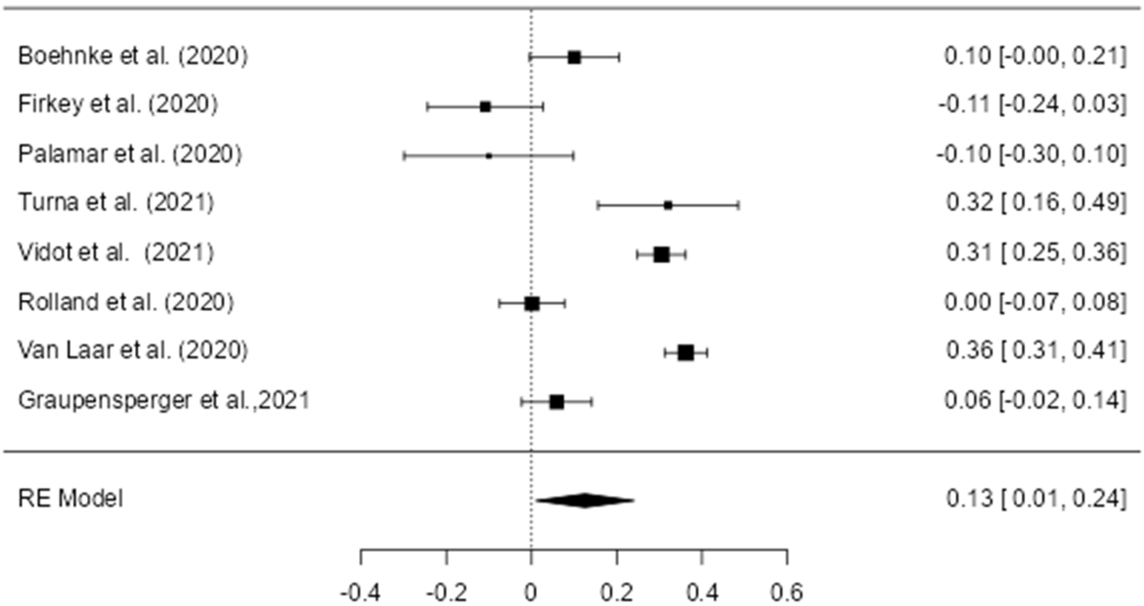
To assess the heterogeneity of the selected data from the population, the I^2 test was used. High levels of between-study heterogeneity in outcome were observed in the analysis on cannabis with proportion based data ($I^2 = 92{,}97\%$, $p = <.001$), cocaine ($I^2 = 99{,}98\%$, $p = <.001$), fentanyl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

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

Drug	I^2[a]	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

[a]Effect sizes used for I^2 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[a]



[a]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.

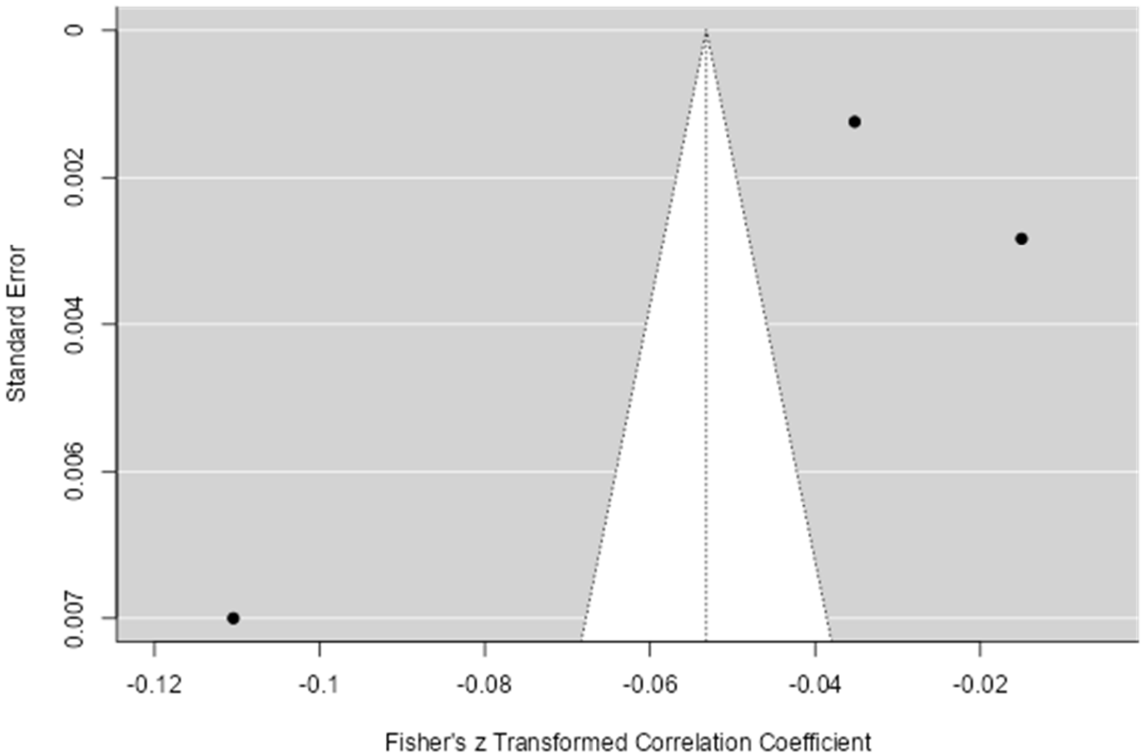
Methodological quality

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

Substance/Moderator	%Female	p	Age	p	Country	p
Cannabis (proportions)	-0,00261	0,479	0,00892	0,139	-0,0812	0,527
Cannabis (md)[b]	-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

[a]Amphetamine, fentanyl and heroin are missing in this table; the amount of included studies was too small to perform moderator analysis with k = 3. [b]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 pattens, 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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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[4]

Class of drugs	Drug name	Description
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[1] (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[2] (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[3] (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

[1] A class of psychoactive drugs that causes hallucinations and changes in perception and consciousness. Adapted from "Hallucinogens DrugFacts," 2021.

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

[3] 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.

[4] All drugs and its sources are put in an adapted table in APPENDIX 2

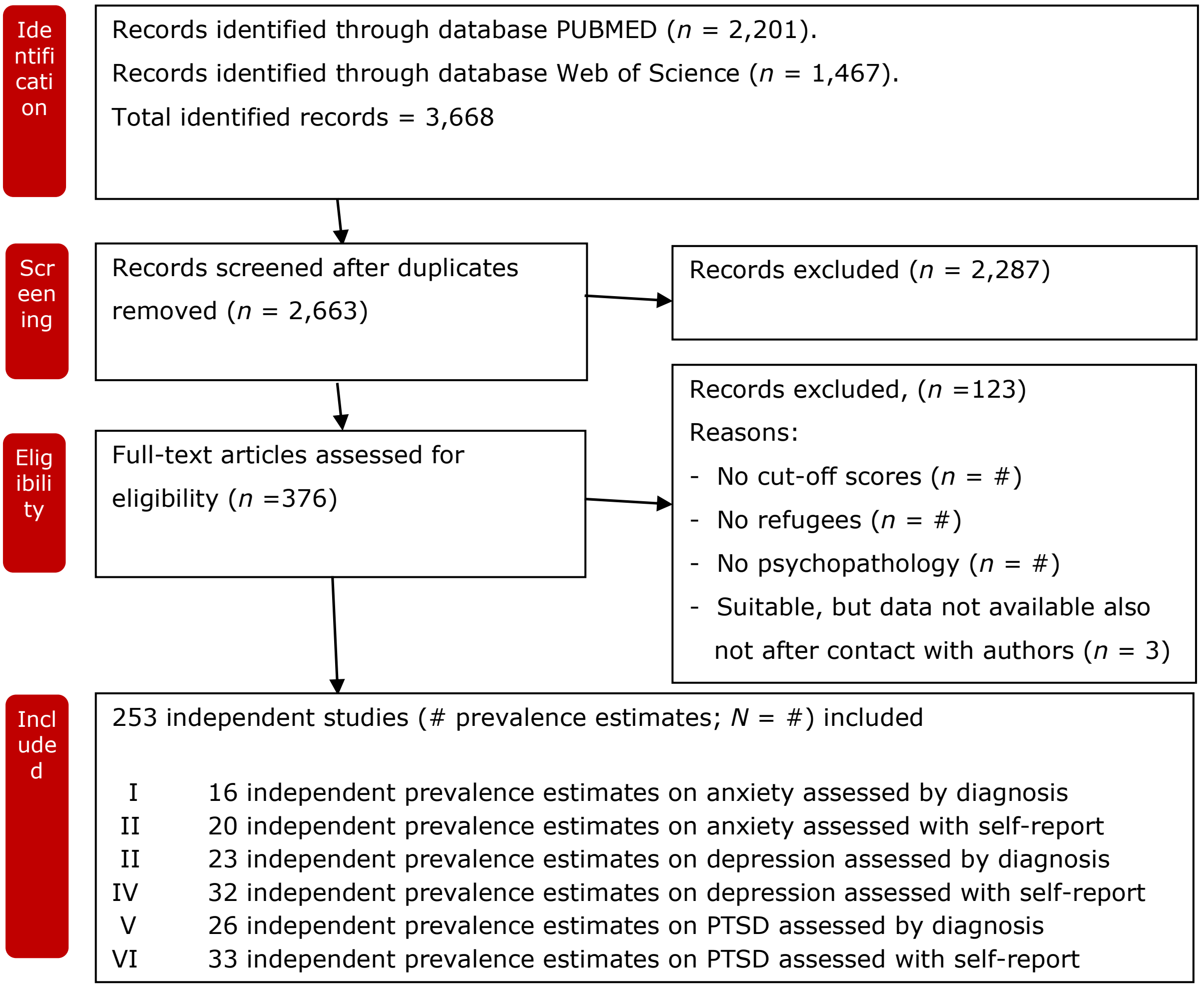
APPENDIX 3

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

Class of drugs	**Drug name**	**Source**
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)

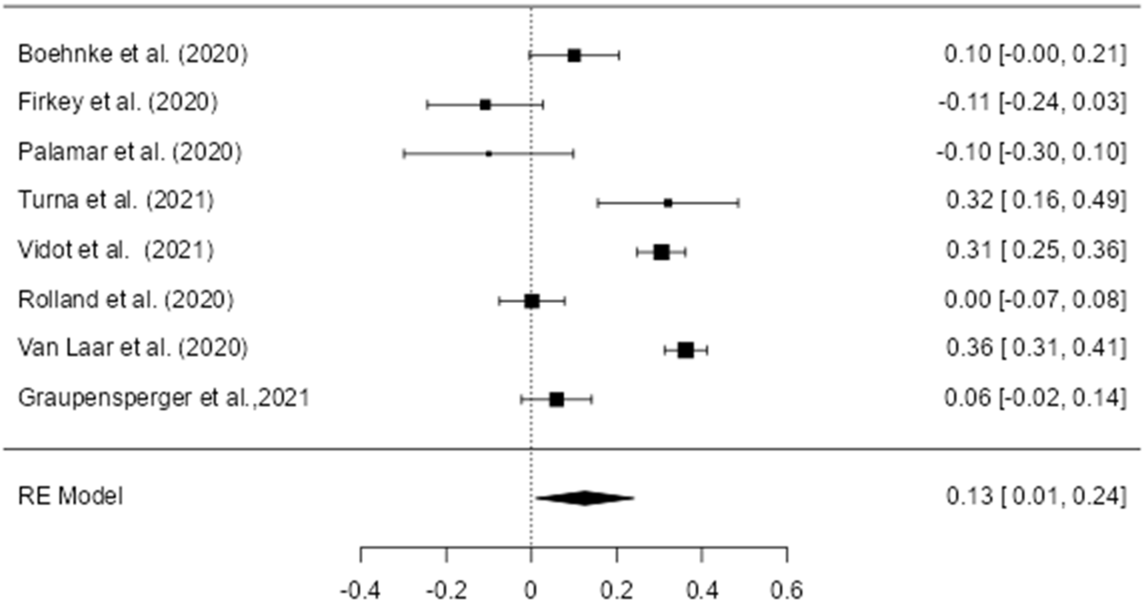


Figure 2: Forest plot illustrating the relation of cannabis use and COVID-19 as a stressor (mean difference data)

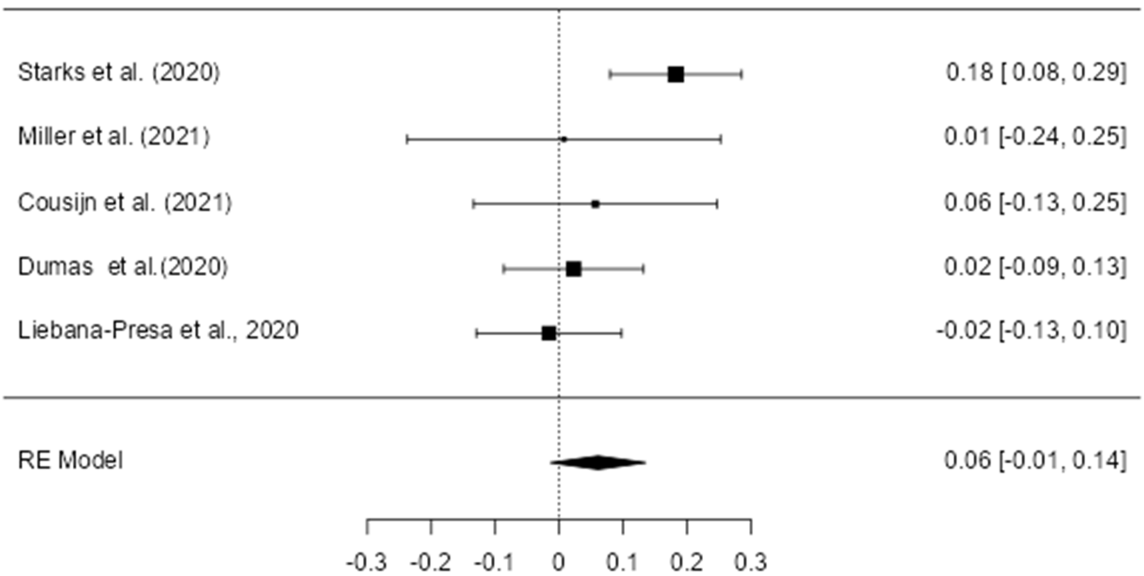


Figure 3: Forest plot illustrating the relation of cocaine use and COVID-19 as a stressor

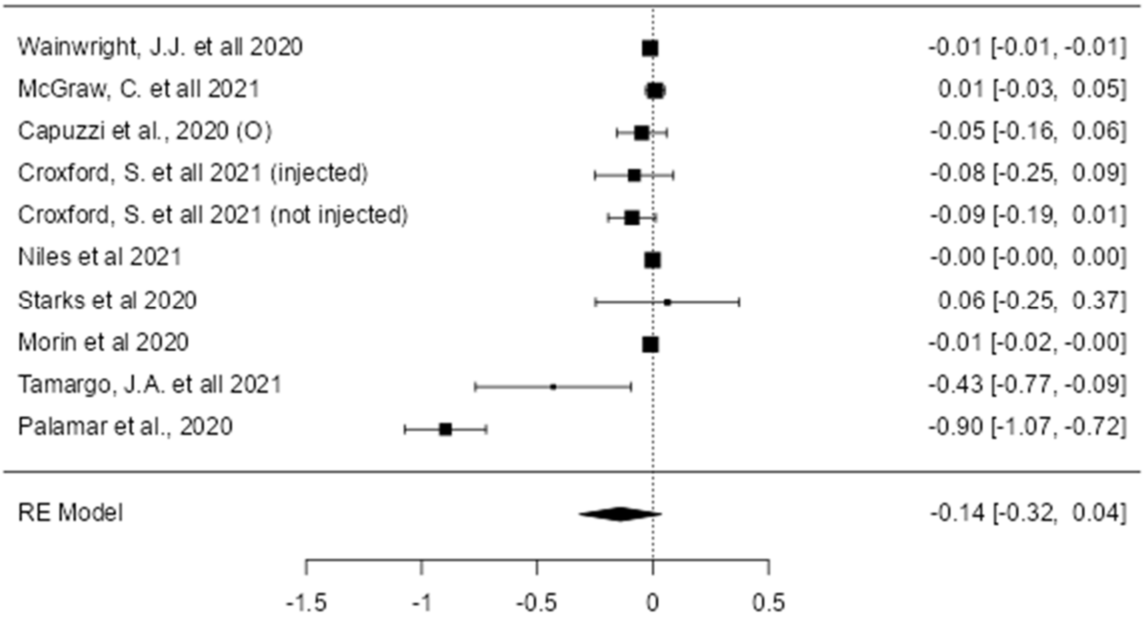


Figure 4: Forest plot illustrating the relation of amphetamine use and COVID-19 as a stressor

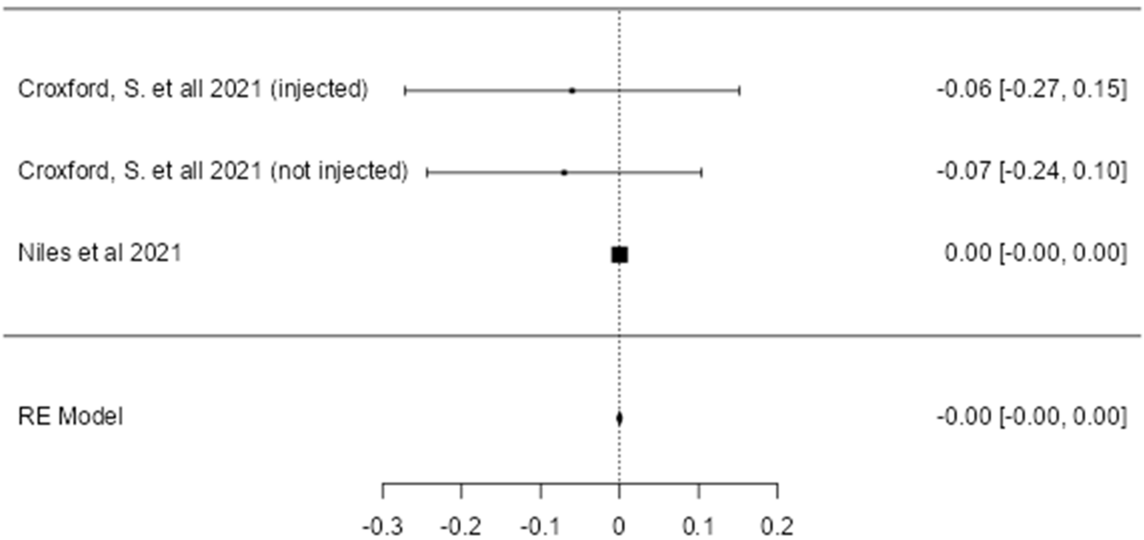


Figure 5: Forest plot illustrating the relation of fentanyl use and COVID-19 as a stressor

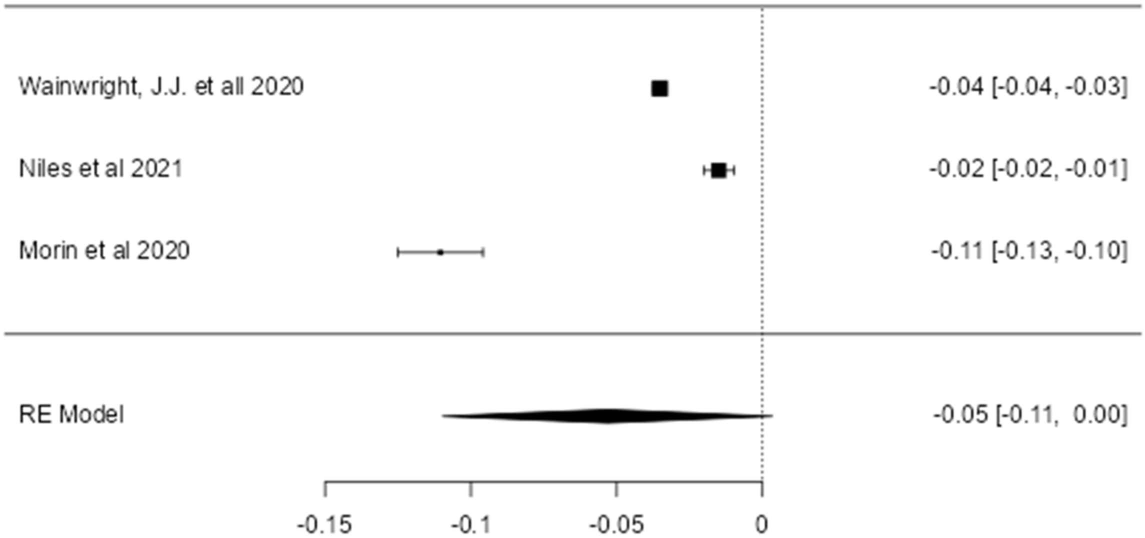


Figure 6: Forest plot illustrating the relation of heroin use and COVID-19 as a stressor

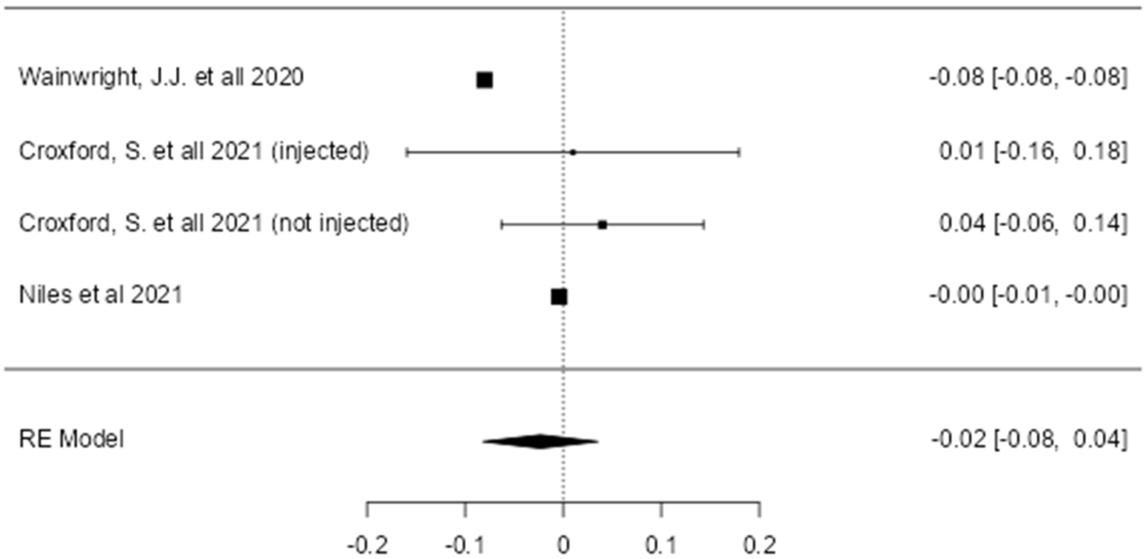
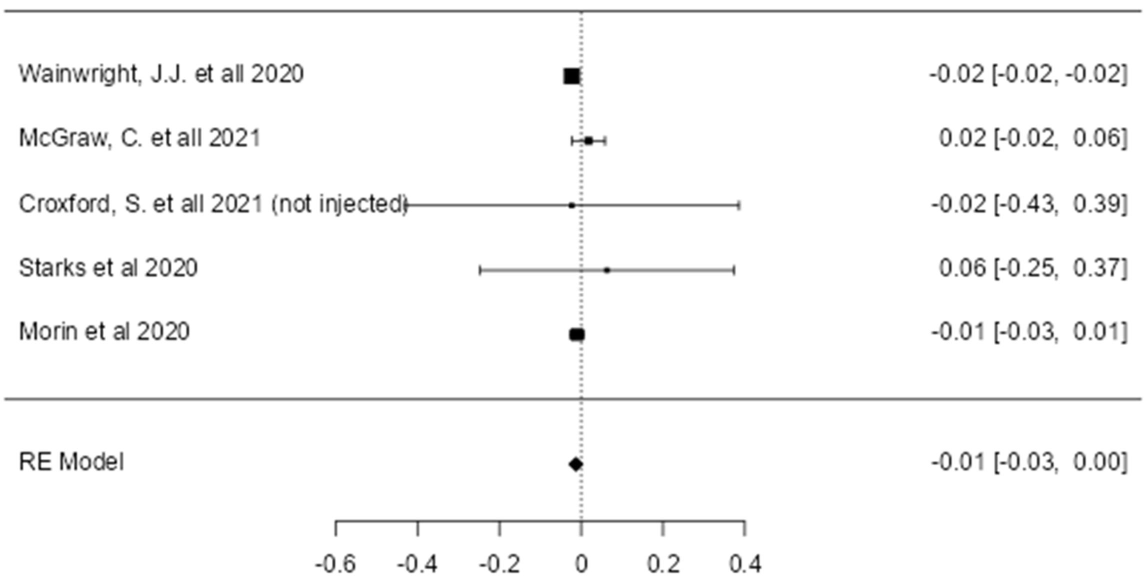


Figure 7: Forest plot illustrating the relation of methamphetamine use and COVID-19 as a stressor



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)

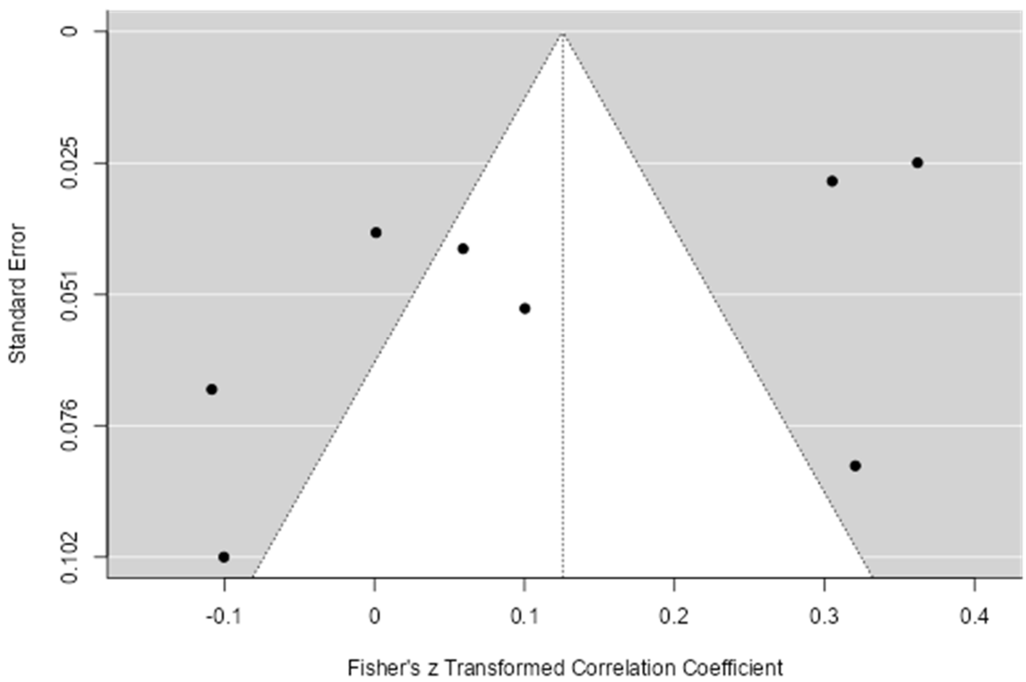


Figure 2: Funnel plot on cannabis use and COVID-19 as a stressor (mean difference data)

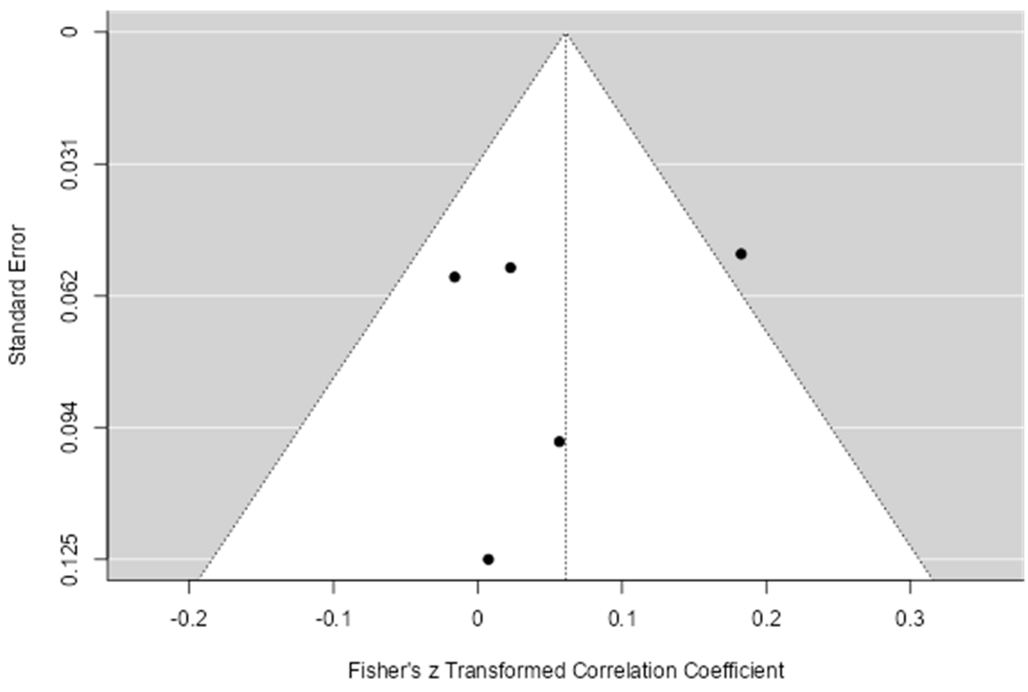


Figure 3: Funnel Plot illustrating possible publication bias in the meta-analysis performed for cocaine use and COVID-19 as a stressor

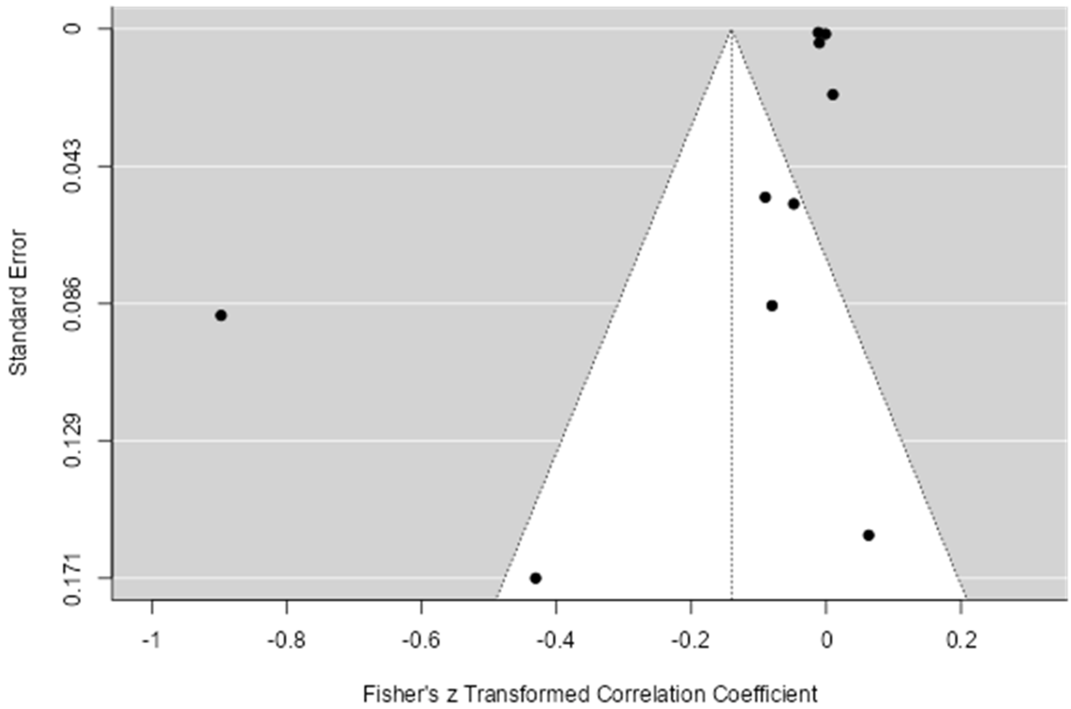


Figure 4: Funnel Plot illustrating possible publication bias in the meta-analysis performed for amphetamine use and COVID-19 as a stressor

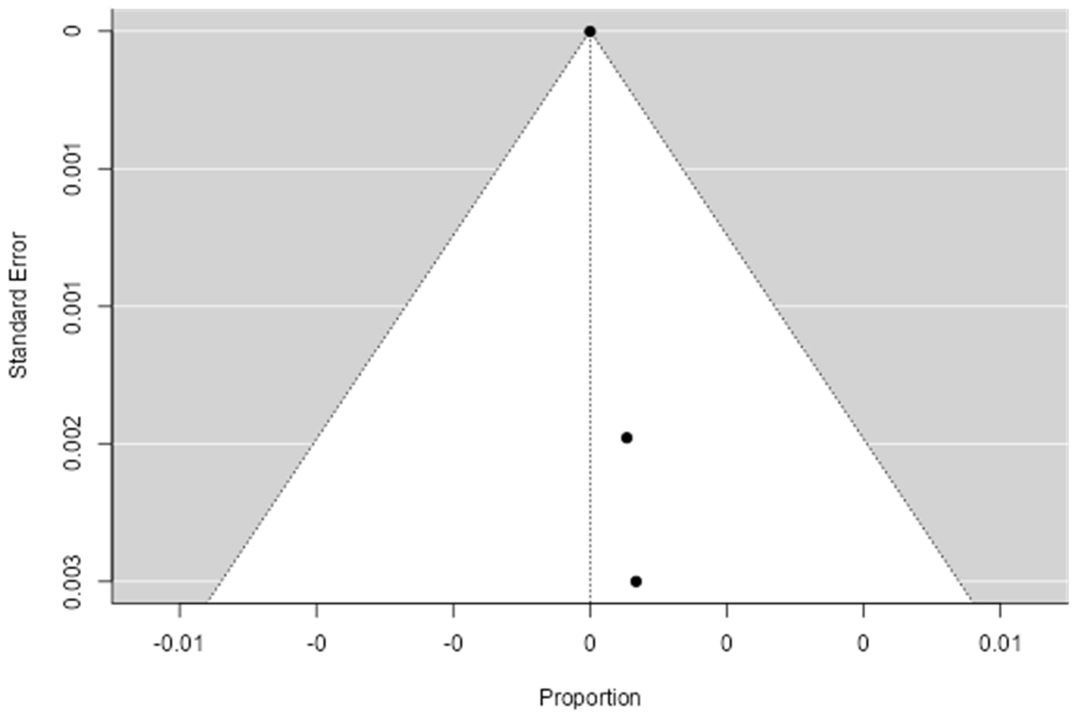


Figure 5: Funnel Plot illustrating possible publication bias in the meta-analysis performed for fentanyl use and COVID-19 as a stressor

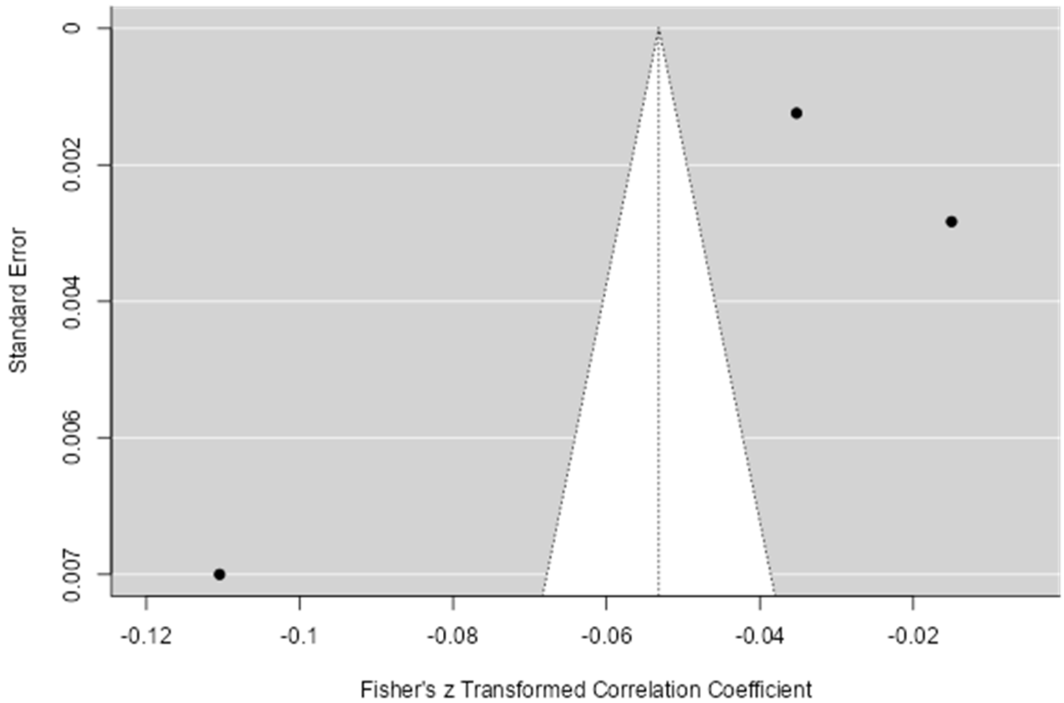


Figure 6: Funnel Plot illustrating possible publication bias in the meta-analysis performed for heroin use and COVID-19 as a stressor

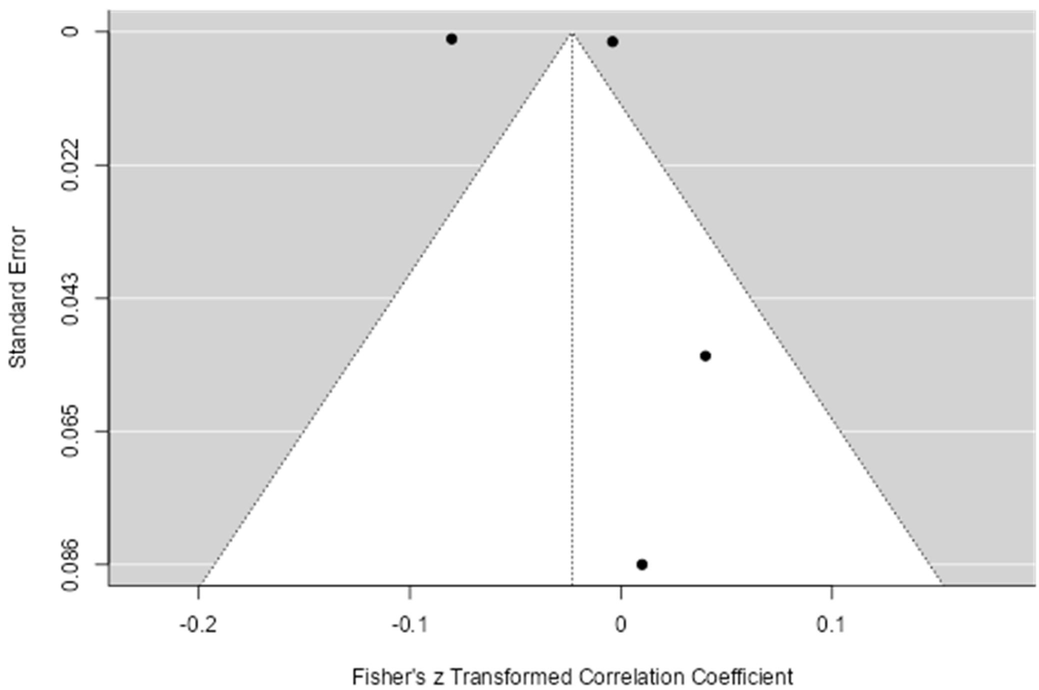


Figure 7: Funnel Plot illustrating possible publication bias in the meta-analysis performed for methamphetamine use and COVID-19 as a stressor