









PSYCHOLOGY AND PSYCHIATRY

NOVEL-RESULT

# Adverse childhood experiences and craving: Results from an Italian population in outpatient addiction treatment

Claudio Russo<sup>1,2</sup> , Natale Salvatore Bonfiglio<sup>3</sup> , Eva Orlando<sup>1</sup> , Giuseppe Falcone<sup>1</sup> , Lucia Iuliano<sup>1</sup>, Antonietta Grandinetti<sup>1</sup>, Carmine Acconcia<sup>1</sup>, Adriana Napoletano<sup>1</sup>, Giada Conte<sup>1</sup>, Barbara Landi<sup>1</sup>, Giovanni Truono<sup>1</sup>, Marco D'Alto<sup>1</sup>, Maria Pietronilla Penna<sup>4</sup>  and Antonio De Luna<sup>1</sup> 

<sup>1</sup>Department of Addictions, Azienda Sanitaria Locale Salerno, Salerno, Italy, <sup>2</sup>Department of Medicine, Surgery and Dentistry, Salerno Medical School, University of Salerno, Salerno, Italy, <sup>3</sup>IRCCS Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy, and <sup>4</sup>Department of Pedagogy, Psychological Sciences and Philosophy, University of Cagliari, Cagliari, Italy

**Corresponding authors:** Claudio Russo and Eva Orlando; Emails: [clrusso@unisa.it](mailto:clrusso@unisa.it); [spec.orlandoe@aslsalerno.it](mailto:spec.orlandoe@aslsalerno.it)

(Received 12 April 2023; Revised 25 April 2023; Accepted 03 May 2023)

## Abstract

**Background:** Despite the growing interest in addiction research, which demonstrates the potential predictive role of adverse childhood experiences (ACEs), little is known about their impact on the psychological symptoms of craving.

**Methods:** After reviewing the relevant diagnostic criteria for addiction and comorbid mental disorders along with routinely collected clinical and service-use data, 208 outpatients were assessed on the study protocol. Following the recruitment phase, nominal and ordinal data were analyzed using nonparametric methods.

**Results:** Most of the outpatients reported ACEs (89.1%) and experienced cravings (73.4–95.7%). A positive association between ACEs and either intention and preplanning ( $r = .14, p < .05$ ) or lack of control ( $r = .15; p < .05$ ) of the craving behavior was found.

**Conclusion:** Craving behavior in addiction remains a subject of debate. Although correlation analyses showed significant associations between reported ACEs and measures of craving, they were relatively small.

**Keywords:** addiction; childhood adversity; comorbidity; craving; Italy

## Introduction

In recent decades, adverse childhood experiences (ACEs) have been associated with negative health outcomes in early adolescence and adulthood (Boullier & Blair, 2018; Felitti et al., 1998; Flaherty et al., 2013; Hughes et al., 2017). Further to the developmental impact of ACEs on children's behavior and their social competence (Clarkson Freeman, 2014; Manly et al., 1994), a growing literature has found that the lived experience of ACEs can lead to long-term effects on the mental health of adults and the onset of chronic diseases (Boyce et al., 2012; Edwards et al., 2003; Sonu et al., 2019).

In addiction research, child maltreatment and genetic factors have been linked to cigarette and marijuana use (Azimi & Connolly, 2022), and ACEs have accounted for issues with illicit drug use in one-half to two-thirds of cases (Dube et al., 2003). A modeling study showed that more than half of heroin and crack cocaine use was tied to ACEs (Bellis et al., 2014). Another study by Hodgins et al. (2010) tied the experience of childhood maltreatment to the likelihood of experiencing a gambling problem.

Furthermore, ACEs have been associated with an increased likelihood of binge drinking among adults (Crouch et al., 2018).

Substance craving is a core symptom of substance use disorders (SUDs), namely an uncontrolled desire which may be linked to one's intentional use of substances, including self-regulation failure, diminished self-efficacy regarding substance abstinence, and affective response patterns (Sayette, 2016). Different models have relied on theoretical and empirical investigations involving in-depth explanations of craving and focusing on the autonomous reactions, or analyzing one's biological imbalance and brain activity (Danese et al., 2009; Koban et al., 2023; Skinner & Aubin, 2010).

Hence, the appearance of craving can be linked to the severity of addiction, including the comorbid conditions and behaviors (Hormes, 2017). As Stalcup et al. (2006) noted, the clinical management of craving requires four domains of analysis, namely environmental cues, stress-related conditions, mental impairment, and physical withdrawal.

In clinical terms, substance craving may persist over time in patients with SUDs, during either the progression or early remission of the disorder. The timeframe required for detecting an early remission of SUDs ranges from 3 to 12 months, although the symptoms of craving may still be present (Hasin et al., 2013).

## Objectives

For this study, we investigated the role of ACEs on craving measures and collected clinical and patient-reported data from a sample of outpatients undertaking routine addiction treatment.

## Methods

### *Sample and procedure*

A sample of 208 outpatients ranging from 18 to 65 years old participated in this study. Participants were recruited between the period February and August of 2021 from five distinct addiction service centers that receive public funding from the Italian National Health System and offer free admission and healthcare services in the Salerno area, South Italy. All participants were administered questionnaires by trained psychologists as part of an individualized, routine clinical support plan for addiction and received no compensation for their participation. While the data collection and assessment were undergoing, a total of 125 patients were excluded from the study based on prior medical evaluations or by having already completed their treatment. A group of independent physicians supported the data collection, aiding in cross-referencing the information on diagnosis, comorbidity, and pharmacotherapy.

### *Measures*

The Adverse Childhood Experiences International Questionnaire (ACE-IQ) is a retrospective and self-reported measure of childhood adversities developed by the World Health Organization (WHO, 2018). A set of demographic information is followed by a total of 13 categories concerning adverse or stressful events during the first 18 years of one's life.

The Substance Craving Questionnaire (SCQ-NOW) is a self-reported measure of craving that has been validated for substance use and gambling disorder, with Cronbach's alpha ranging from 0.70 to 0.89 (Bonfiglio et al., 2019). Adapted from the original version of a cocaine craving questionnaire by Tiffany et al. (1993), it is composed of 45 items grouped into five dimensions. Each dimension is the sum of nine items, measuring the following factors: (1) desire to use a substance (DES); (2) intention to use a substance and preplanning (INT); (3) anticipation of positive outcomes (ANP); (4) anticipation of relief from substance withdrawal symptoms, or negative mood (ANR); (5) lack of control over substance use (LCO).

### Data analysis

A preliminary data screening was performed to detect missing or invalid data. The patient characteristics were analyzed alongside the collected data from the subscales of the ACE-IQ and the SCQ-NOW. For analytical purposes, the mean and standard deviation of each continuous variable was noted, and the assumption of normality for each variable was examined by visual inspection and the Kolmogorov–Smirnov test.

The cut-off score or mean value of the SCQ-NOW referred to the validation results as reported by Bonfiglio et al. (2019). The scores were presented as the average of the summed items and dichotomized. A score below the mean value on each subscale was referred to as “absent craving.” Conversely, a score equal to or above the mean value was referred to as “experienced craving.” Likewise, two dimensions of exposure, namely experience of childhood adversity vs. no experience of childhood adversity, were dichotomized from the ACE-IQ subscales.

Chi-square tests, Fisher’s exact method, and Spearman rank correlations were used to analyze categorical variables. A bivariate regression analysis was used to establish the strength of the association between the subscales of the SCQ-NOW and the ACE-IQ. The demographic characteristics and other clinical information were expressed by covariates and examined with the counts and percentages across the SCQ-NOW subscales and the ACE-IQ total score.

After adjusting for potential confounding variables, all variables with a *p*-value less than .05 were combined from the bivariate analysis and entered a multivariate logistic regression model (Kirkwood & Sterne, 2010). The final model was assessed using the Hosmer–Lemeshow goodness-of-fit test. Lastly, the adjusted odds ratios (aOR) were used to estimate the occurrence of experienced craving with a 95% confidence interval, given the exposure to at least one experience of childhood adversity.

Data analysis was performed using the IBM SPSS Statistics software, Version 24 (IBM Corp., Armonk, NY, USA) and Jasp 0.15 (Jasp Team, 2020).

### Results

The patient characteristics are presented in Table 1.

A consistent amount of exposure to ACEs and craving (89.1% and between 73.4 and 95.7%, respectively) was reported (Table 2).

Specifically, 56% of outpatients met the ANR threshold and presented no familiarity with mental disorders, while 57.2% reported ACEs and no familiarity with addiction. Among those reporting ACEs, 59.2% were not presenting comorbid mental disorders, including 20.4% of outpatients that were below the ANR threshold and 47.8% that were above it. The identification of this clinical subgroup indicated that when comorbid mental disorders were absent, ANR was more experienced.

In Figure 1, statistically significant correlations between the ACE-IQ total score and the SCQ-NOW subscales are shown, including significant associations across the demographic and clinical characteristics.

In terms of service use, significant negative correlations between either the number of sessions of psychological intervention or psychotherapy ( $r = -.23$ ;  $p = .02$ ) or the duration of psychological therapies in days ( $r = -.18$ ;  $p = .017$ ) and the ACE-IQ total score were found. Furthermore, statistically significant negative correlations were found between either the number of sessions of psychological intervention or psychotherapy ( $r = -.26$ ;  $p = .001$ ) or the duration of psychological therapies in days ( $r = -.27$ ;  $p = .001$ ) and the ANR subscale. A statistically significant negative correlation was also found between the number of months individuals were enrolled in addiction services and the ANR subscale score ( $r = -.20$ ;  $p = .004$ ).

The group of outpatients for which the severity of addiction was either moderate (aOR = 2.47; 95% CI: 0.89, 6.82) or severe (aOR = 5.05; 95% CI: 1.06 16.1) were, respectively, 2.47 and 5.05 times more likely to report high ANR scores compared to the group of outpatients with a low severity addiction. Additionally, the ANR score was 1.15 times higher for the group of outpatients reporting ACEs

**Table 1.** Patient Characteristics

Variable	Level	N (%)
Sex	Male	176 (84.6)
	Female	32 (15.4)
Age	38.96 (10.78) Mean (Standard Deviation)	
Civic status	Cohabiting	35 (16.8)
	Divorced/separated	28 (13.5)
	Single	83 (39.9)
	Married	46 (22.1)
	Other	16 (7.7)
Level of education	Up to primary school	16 (7.7)
	Secondary school	178 (85.6)
	Bachelor's degree	4 (1.9)
	Master's degree	9 (4.3)
	No answer	1 (.5)
Employment status	Employed	71 (34.1)
	Unemployed	67 (32.2)
	Self-employed	52 (25)
	Other	18 (8.7)
Nationality	Italian	199 (95.7)
	Other	9 (4.3)
DSM-5 diagnosis	Gambling disorder	28 (13.5)
	Alcohol use disorder	31 (14.9)
	Substance use disorder	149 (71.6)
Addiction	Gambling	28 (13.5)
	Alcohol	31 (14.9)
	Cocaine	51 (24.5)
	Opioids	87 (41.8)
	Cannabis	11 (5.3)
Pharmacological treatment of addiction	Total	96 (46)
	Sodium Oxybate <sup>a</sup>	11 (11.5)
	Methadone <sup>a</sup>	69 (71.8)
	Buprenorphine/naloxone <sup>a</sup>	14 (14.6)
	Other <sup>a</sup>	2 (2.1)
Severity of addiction	Mild	18 (8.7)
	Moderate	121 (58.2)
	Severe	66 (31.7)
	Missing	3 (1.4)
Remission	Early	34 (16.3)

Table 1. Continued

Variable	Level	N (%)
	Sustained	42 (20.2)
	No	129 (62)
	Missing	3 (1.4)
Multiple addictions	Yes	143 (68.7)
	No	65 (31.3)
Mental health comorbidity	Yes	64 (30.8)
	No	137 (65.9)
	Missing	7 (3.4)
Pharmacological treatment of mental disorders	Yes	49 (23.6)
	No	151 (72.6)
	Missing	8 (3.8)
Familiarity with addiction <sup>b</sup>	Yes	67 (32.2)
	No	141 (67.8)
Familiarity with mental disorders <sup>b</sup>	Yes	41 (19.7)
	No	166 (79.8)
	Missing	1 (0.5)
Use of addiction services (months enrolled)	70.9 (97.4) Mean (Standard Deviation)	
Number of sessions (psychological intervention or psychotherapy)	10.2 (14.8) Mean (Standard Deviation)	
Duration of sessions in days (psychological intervention or psychotherapy)	175.3 (366) Mean (Standard Deviation)	

Note. DSM-5: *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*.

<sup>a</sup>The percentage is calculated within the subgroup on pharmacological treatment of addiction.

<sup>b</sup>Familiarity equals clinical information or individual's awareness of relatives/significant others with addiction or mental disorders.

(aOR = 1.15; 95% CI: 0.98, 1.33). The final model ( $X^2 = 13.03$ ;  $p = .005$ ) indicated a high sensitivity (.96) and low specificity (.11).

## Discussion

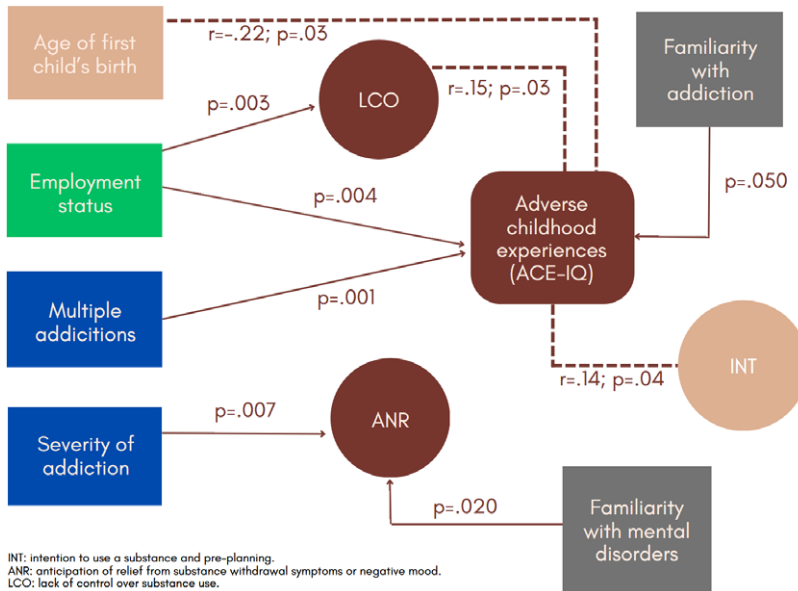
Previous research evidence has suggested that the occurrence of childhood adversities is a potential source of toxic stress (Oral et al., 2016), in which stress reactivity (Groh et al., 2020) and a prolonged state of exposure may trigger the toxic effects later in life (Shonkoff et al., 2012).

The ACE-IQ total score (Mean: 3.01; SD: 2.32) revealed distinctive features that were consistent with previous findings (Garland et al., 2019), as shown in the pioneering study of Felitti et al. (1998).

In the present study, we found small and positive associations between either the LCO or the INT and the ACE-IQ total score, along with a small and negative association between the ACE-IQ total score and the age of first child's birth. As a significant association between the ANR and the severity of addiction emerged, the results from the final model were collateral to previous evidence on the intergenerational transmission of behavioral risks resulting from ACEs (Schickedanz et al., 2018). Not surprisingly, a significant association between the familiarity with mental disorders and the ANR was also tied to the severity of addiction.

**Table 2.** Observed range, mean and standard deviation (SD) for ACE-IQ and SCQ-NOW

ACE-IQ	N (%)	Female/male	Observed range	Mean (SD)	Kolmogorov–Smirnov		
					SStatistic	df	Sig.
Physical abuse	17 (8.2)	7/10					
Emotional abuse	31 (15)	11/20					
Sexual abuse	29 (14)	10/19					
Substance use of a household member	33 (15.9)	8/25					
Incarceration of a household member	24 (11.6)	6/18					
Mental illness of a household member	37 (17.9)	10/27					
Domestic violence	98 (47.3)	21/77					
Parental separation or divorce	108 (52.2)	22/86					
Emotional neglect	96 (46.4)	13/83					
Physical neglect	18 (8.7)	3/15					
Bullying	14 (6.8)	5/9					
Community violence	47 (22.7)	8/39					
Collective violence	72 (34.8)	7/65					
Total score			0–13	3.01 (2.32)	0.164	207	<.001
<b>SCQ-NOW</b>							
Desire to use a substance (DES)			9–51	32.25 (6.40)	0.233	207	<.001
Intention to use a substance (INT)			9–53	30.53 (6.02)	0.215	207	<.001
Anticipation of positive outcomes (ANP)			9–47	30.34 (6.79)	0.203	207	<.001
Anticipation of relief (ANR)			9–49	28.88 (8.93)	0.113	207	<.001
Lack of control (LCO)			9–54	32.88 (7.48)	0.096	207	<.001



**Figure 1.** Adverse childhood experience and craving

Following the recruitment of 208 study participants, we analyzed a larger population of outpatients in routine addiction treatment at different levels of morbidity, chronicity, and severity, even when the criteria for exploratory and confirmatory factor analyses were not met. The main study limitation is that data analyses were performed on a limited sample with statistical significance that was determined at  $p < .05$ . Incidentally, we used retrospective estimates of ACEs which were tied to single self-reported measures of current craving. Therefore, the occurrence of overlapping physical or mental health issues will be a necessary step to validate our results with the ones from different socio-cultural settings and therapeutic contexts, as well as to benefit from the analysis of dissimilar measures for ACEs and craving at multiple points in time.

## Conclusions

The main results extended the measures of craving in relation to the experience of ACEs and provided new evidence on cognitive, emotional, and automatic cravings in addiction (cf. Flaudias et al., 2019). Our pattern of analysis was consistent with the most recent findings from Romero-Sanchiz et al. (2022), in which urge and desire for cannabis were linked to craving following experimental exposure to trauma reminders. In particular, the duration of addiction treatment and the self-reported childhood adversities (Hughes et al., 2017; Kelly-Irving & Delpierre, 2019) contributed to explore the underlying mechanisms of ANR and more generally of psychological craving, compared to the self-medication attempts (Khantzian, 1997), biological imbalance (Wise, 1988), cue reactivity (Limbrick-Oldfield et al., 2017), and emotional states (Wilson, 2022). Drawing on findings from the craving literature, the lack of control or pre-planning, the intention to use substances, the occurrence of multiple addictions, a variable employment status, or familiarity with addiction were found significantly associated with the experience of childhood adversities.

**Open peer review.** To view the open peer review materials for this article, please visit <http://doi.org/10.1017/exp.2023.12>.

**Data availability statement.** Data are available upon reasonable request due to privacy or other restrictions.

**Authorship contribution.** Conceptualization, Methodology, Investigation, Data Curation, Project administration, Writing—Original Draft, Writing—Review and Editing (C.R. and E.O.; equally contributed). Conceptualization, Formal analysis, Writing—Original Draft, Writing—Review and Editing (N.S.B.). Conceptualization, Data Curation, Visualization (G.F., L.I.,

A.G., C.A. and A.N.; equally contributed). Data Curation, Project administration (G.C., B.L., G.T., and M.D.; equally contributed). Conceptualization, Writing—Original Draft (M.P.P.). Visualization, Supervision (A.D.L.).

**Funding statement.** This work received partial financial support from the Campania regional plan for addiction prevention and recovery (grant number 86/2016).

**Competing interest.** The authors have no conflict of interest to declare that is relevant to the content of this article.

**Ethical standard.** The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all patients for being included in the study.

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**Cite this article:** Russo C, Bonfiglio NS, Orlando E, Falcone G, Iuliano L, Grandinetti A, Acconcia C, Napoletano A, Conte G, Landi B, Truono G, D'Alto M, Penna MP, De Luna A (2023). Adverse childhood experiences and craving: Results from an Italian population in outpatient addiction treatment. *Experimental Results*, *4*, e11, 1–13. <https://doi.org/10.1017/exp.2023.12>

# Peer Reviews

## Review 1: Adverse childhood experiences and craving: results from an Italian population in outpatient addiction treatment

Reviewer: Dr. Robert Lundin 

Deakin University, Burwood, Australia, 3125

Date of review: 18 April 2023

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**Conflict of interest statement.** Reviewer declares none.

### Comment

Comments to the Author: Thank you for addressing the requested changes. I am satisfied this has been completed.

### Score Card

#### Presentation



Is the article written in clear and proper English? (30%)

4/5

Is the data presented in the most useful manner? (40%)

4/5

Does the paper cite relevant and related articles appropriately? (30%)

4/5

#### Context



Does the title suitably represent the article? (25%)

4/5

Does the abstract correctly embody the content of the article? (25%)

4/5

Does the introduction give appropriate context? (25%)

4/5

Is the objective of the experiment clearly defined? (25%)

4/5

#### Analysis



Does the discussion adequately interpret the results presented? (40%)

4/5

Is the conclusion consistent with the results and discussion? (40%)

4/5

Are the limitations of the experiment as well as the contributions of the experiment clearly outlined? (20%)

4/5

## Review 2: Adverse childhood experiences and craving: results from an Italian population in outpatient addiction treatment

Reviewer: Dr. Varun Thirayan 

Waikato DHB Laboratory, Hamilton, New Zealand, 3240

Date of review: 21 April 2023

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**Conflict of interest statement.** Reviewer declares none.

### Comment

Comments to the Author: EXP-23-0016

22.4.23

Abstract “Most of the outpatients reported ACEs and experienced cravings.” Recommend include percentage in brackets.

ACE-IQ – this is used in the abstract but the acronym should be written in full when first used. Perhaps include what survey you used in the methods part of abstract.

“A positive association between the ACE-IQ total score and either intention and pre-planning (INT) or lack of control (LCO) of the craving behaviour was found.” - was this finding statistically significant? If so mention this e.g.  $p < 0.05$ .

“Craving behaviour in addiction remains a subject of debate. “ – I don’t believe this can be written in your conclusion as nothing in your results suggests this.

“Although correlation analyses showed significant associations between reported ACEs and craving, they were relatively small. “ – to say this, you need to quantify how small in your results.

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The introduction still does not explain why you want to investigate the link between ACE and cravings. Lines 34-37 you mention different models have been used to explain cravings – but you do not say what they found or if there is controversy e.g. in the abstract you mention it is a subject of debate, but your introduction does not highlight the aspects of this debate which is important for the reader to be aware of to justify your objective.

In summary your intro is conveying to me: ACE is related to mental health problems. ACE is associated with substance use. Craving is associated to substance use and severity of addiction. Craving has various domains. Craving can persist even after substance use stops. – why does this justify your objective?

Is it important to be aware that more severe ACE could potentially be a predictor for greater cravings when attempting to stop SUD and the need for more support to be put in place? Is there controversy in the literature about this? Has this not been investigated before? This is important to discuss in your intro in my opinion.

Line 102 – I would not give a range % for the craving, give one % instead of 73.4-95.7 since you already mentioned you dichotomised the data.

Table 2 – are there missing values in the ACE-IQ section of Kolmogorov-smirnov? I see a large empty part of the table. If values are not relevant to ACE-IQ, may be worth putting a dash or n/a?

Line 105 to 110: The SCQNOW mean for each variable is found and shown in table 2. This is to help you say whether the person scored positive or negative in that particular variable. Yet, you only talk about INR? What about results from DES ANP LCO and INT? If nothing is relevant, state this.

e.g. Are you trying to say: Of the patients with no familiarity with mental disorders, SCQ-NOW threshold was met for ANR (56%), DES (%), ANP (%), LCO (%), and INT (%). Of patients with no familiarity with addiction, threshold was met for .... Etc.

Line 107, you say “among those reporting ACEs”. – in the methods you do not mention what the cut off for this is. Does scoring for 1 variable in ACE mean it is positive for ACE? Please make this clear in methods.

It would be useful if you could show results that a greater number of positive variables in ACE may increase scores in ANR DES ANP LCO or INT (Please check with your statistician about this).

Are you focusing only on ANR because you are looking at craving? If so you may want to mention in your methods that this is what you are looking at and specify why only ANR? However, consider that all factors of SQCNOW are a measure of cravin so you need to justify clearly why only ANR is discussed.

For my knowledge: Does “familiarity with addiction” mean, the patient is aware and has insight that they have an addiction?

In methods, line 52. What is the inclusion criteria for participant inclusion from the addiction service centres? Anyone receiving any form of treatment at the service centre? Are all participants assumed to an addiction as per DSM? I would make this clear in the methods since in the results you have said some are “not familiar with addiction” suggesting the participant did not think they had an addiction, yet to the service we are identifying they have an addiction based on ?DSM criteria.

Line 116: does this mean the more sessions of therapy and longer duration in therapy, the lower the ACE-IQ score? Does this mean, people with less ACE engaged better in services? If so, consider revision of the sentence structure e.g. there was a positive correlation between ACE and therapy duration etc. Currently it reads backwards i.e. the more therapy a person has the lower their ACE (yet ACE occurred historically).

Line 119: consider sentence revision. Are you trying to convey greater frequency of therapy and greater duration were associated with lower ANR?

Line 134: quote the ACEIQ scores from the other studies to show the comparison.

Line 139: avoid using the word “small”. What does this mean? That the p value is <0.05?

Line 139: do you mean “maternal” age of first child’s birth ? i.e. older the mother when first child is born, the less ACE? Consider sentence structure.

Line 124 and 140: in the methods you did not say how “severity of addiction” was found.

Line 144: unclear what this sentence means

Line 147-8:  $p < 0.05$  is considered statistically significant, remove this as a limitation.

Line 149-152: unclear what this sentence means or why it is relevant to your results. Are you trying to say a limitation is that your study did not consider physical health comorbidities or cultural contexts? Table 1 has 30.8% comorbid mental health issues so you did record this.

Line 154: In your conclusion, why are you referencing Flaudias 2019 paper? It is meant to be your conclusion based on your own findings, not Flaudias.

Line 156-158 put in your discussion, not conclusion. This referenced paper talked about urge and desire but you made limited note of DES variable in your findings.

Your whole “conclusion” section should be revised. Some of what you mention could go in your “discussion” but your conclusion section should have your overall summary and conclusion of your results and key take home message.

There are 14 authors mentioned on this paper. I would suggest you collaborate to improve this manuscript. The results are important but significant revision of manuscript is required in my opinion.

Note to editor: does a statistician need to check if the appropriate tests have been used? E.g. In the methods the Kolmogorov-smirnov test was used to assess normality for each variable. Is this appropriately used in table 2 for the ACE-IQ?

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## Score Card

### Presentation



Is the article written in clear and proper English? (30%)

2/5

Is the data presented in the most useful manner? (40%)

2/5

Does the paper cite relevant and related articles appropriately? (30%)

2/5

### Context



Does the title suitably represent the article? (25%)

5/5

Does the abstract correctly embody the content of the article? (25%)

2/5

Does the introduction give appropriate context? (25%)

1/5

Is the objective of the experiment clearly defined? (25%)

2/5

### Analysis



Does the discussion adequately interpret the results presented? (40%)

1/5

Is the conclusion consistent with the results and discussion? (40%)

1/5

Are the limitations of the experiment as well as the contributions of the experiment clearly outlined? (20%)

1/5