

Review Article

Impulsivity traits and suicide related outcomes: A systematic review and meta-analysis using the UPPS model

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ABSTRACT

Background: The affective, cognitive, and behavioral aspects of impulsivity involved in suicide-related outcomes can be investigated through the UPPS model, which conceptualizes these facets in multidimensional terms related to negative and positive urgency, lack of premeditation and perseverance, and sensation seeking. This systematic review and meta-analysis provided a comprehensive understanding of the role of all facets of impulsivity in the development of suicidal ideation and behaviors.

Methods: We conducted a systematic search on six databases (PsycINFO, PsycARTICLES, PubMed, MEDLINE, Scopus, and Web of Science) until May 5, 2023. Overall, 49 studies met the criteria for systematic review, of which 37 were included in a meta-analysis of data from 17,898 individuals. Additional moderation analyses included age, gender, sample status, country of study conduct, assessment instruments, type of suicide-related outcome, study quality, and research design.

Results: We found significant relationships between aspects of impulsivity and suicide-related outcomes. Specially, affective facets related to impulsivity showed a stronger association with suicidal ideations and attempts than cognitive and behavioral dimensions, recommending the main involvement of emotional aspects-positive and negative-in suicide-related dimensions.

Limitations: The limited number of studies may have negatively impacted the power of moderation analyses. In addition, for most dimensions of impulsivity, the limited number of longitudinal studies did not allow to test the moderating role of research design.

Conclusions: This study supports the role of impulsivity in suicidal ideation and behavior, identifying the affective component of impulsivity as the most involved, providing a significant contribution from a clinical and diagnostic point of view.

1. Introduction

The scientific literature on risk factors for suicide behaviors provides essential contributions about the dimensions involved in developing suicidal tendencies (Beautrais, 2000). Among these, impulsivity plays a central role in developing suicide-related thoughts and behaviors (Gvion et al., 2015).

Impulsivity is a broad and multidimensional construct (Whiteside et al., 2005), encompassing a wide range of behaviors that reflect impaired self-regulation, such as poor planning, responding prematurely before considering consequences, sensation seeking, risk-taking,

inability to inhibit responses, and preference for immediate over delayed rewards. Impulsivity is defined by personality models in various ways. For instance, Cloninger et al. (1993) placed emphasis on the temperamental aspect, considering impulsivity as an aspect of novelty seeking being an automatic response to novel stimuli that occurs as a manifestation of biological tendencies. In contrast, Barratt (1993) stressed behavioral aspects, identifying risk-taking behaviors as manifestations of the impulsive trait. In addition, Whiteside and Lynam (2001) focused on the affective elements and pervasiveness of emotions that may inhibit impulses to engage in problem behaviors. All these perspectives determine a great heterogeneity in the assessments of

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impulsivity.

State of art regarding the link between suicide and impulsivity includes much evidence. Indeed, studies on the relationship between impulsivity and suicide have been conducted with different populations, such as samples composed of college students (Anestis et al., 2011; Bender et al., 2012; Ammerman et al., 2015), clinical samples of patients with borderline personality disorder (Barteček et al., 2019), depression (Szanto et al., 2020), gamblers in psychiatric care (Grall-Bronnec et al., 2012; Mallorquí-Bagué et al., 2018), and samples of military personnel (Martin et al., 2020).

The large body of empirical contributions on the topic has been summarized by systematic literature reviews and meta-analyses that contribute to clarify the relationship between impulsivity and suicide-related outcomes. For instance, Pérez-Balaguer et al. (2022) meta-analyzed data estimating the mediating role of impulsivity in the pathway linking childhood maltreatment and suicidal behavior. The authors found that impulsivity resulting from exposure to traumatic childhood experiences was strongly correlated with suicidal behavior risk, particularly among adolescents and patients with affective disorders. Another valuable meta-analysis has been performed by Liu et al. (2017) who focused on the role of behavioral and cognitive impulsivity. The authors reported a small-to-medium effect size for the relationship between suicide attempts and behavioral impulsivity, and a medium-to-large effect in the case of cognitive impulsivity. However, the literature search was limited to two databases by identifying a pool of studies also restricted by narrow inclusion criteria (e.g., english-language publications). Consistent with these findings, the recent systematic review and meta-analysis by Moore et al. (2022) illuminated the relationship between impulsivity, aggression, and suicidality in the adult population by highlighting the pathways through which impulsivity and aggression may impact suicide risk. Nonetheless, the selection of studies was limited to the adult population, and the literature search was conducted through a single database by performing confirmatory searches.

Although these studies illuminate the link between some impulsivity dimensions and suicide-related outcomes, providing relevant contributions to research in this area, diverse limitations exist. For example, these contributions suffer from the restricted number of consulted databases and the stringent exclusion criteria for the selection of studies (e.g. population, language). Perhaps more importantly, the issues connected to the multidimensional nature of impulsivity have been insufficiently addressed with a limited focus on cognitive and/or behavioral impulsivity.

The impossibility of drawing firm conclusions about the dimensions of impulsivity involved in suicide related outcome has important clinical implications. Knowing which dimensions of impulsivity are more involved than others in the development of suicidal risk would make it possible to improve the quality of preventive and treatment interventions by making them more targeted to the affective, behavioral, or cognitive components of impulsivity underlying suicidal tendencies.

One model that attempts to provide order among the different measures and conceptions of impulsivity, providing us with an opportunity to define which dimensions may contribute most to the development of suicidal behavior, is the Urgency, Premeditation, Perseverance, and Sensation Seeking (UPPS) Model developed by Whiteside and Lynam (2001) and further extended by Cyders et al. (2007).

1.1. The multidimensional model of impulsivity

Based on the Five-Factor Model of Personality (Costa and McCrae, 1990), a study by Whiteside and Lynam (2001) led to the construction of the multidimensional impulsivity assessment tool (UPPS), which presents the dimension of impulsivity in terms of a tendency to act motivated by the experience of a negative valence emotion (Negative urgency) or positive valence emotion (Positive Urgency; Cyders et al., 2007), as a tendency to act without adequate planning and

consideration of consequences (Lack of premeditation), as a tendency to conclude an unrewarded behavior (Lack of perseverance) promptly, and as a tendency to new and stimulating behaviors from the perspective of sensorimotor arousal (Sensation seeking) (Whiteside and Lynam, 2001).

Given the complexity and validity of the model, several studies have investigated the relationship between the cognitive, affective, and behavioral dimensions of impulsivity, as defined by the UPPS model, and suicide. Among them, the systematic literature review by Beach et al. (2021) provided a valuable contribution to collecting the results of studies that examined the UPPS model about suicide-related outcomes in adults. However, the referenced study's theoretical framework for investigating suicide related outcomes is unclear. Consequently, the results of the reported studies refer to generic terms related to suicide risk that contribute to maintaining conceptual confusion regarding this issue. Moreover, to date, despite the large number of studies that have addressed the link between impulsivity and suicide related outcomes, meta-analytic studies on the topic that can provide data on the contribution that the multidimensional construct of impulsivity, according to the UPPS model, can provide in understanding aspects of suicidal ideation and behavior are as yet absent.

1.2. The heterogeneity of the construct of suicide

Suicide is defined as the act of deliberately killing oneself in full knowledge or expectation of the fatality of the outcome. However, the heterogeneity of the construct of suicide could hinder the knowledge of which aspects of the phenomenon are associated with certain risk factors, as such as the multidimensionality of impulsivity can be an obstacle to understanding which individual dimensions are most involved in the development of suicidal tendencies. Indeed, despite the progress of research in this area (Grattan et al., 2019; Hadzic et al., 2020), the lack of a consistent and specific conceptual framework related to suicide that can distinguish the mechanisms involved in the development of suicidal ideations and attempts leads to variable results depending on the theoretical perspective adopted. This issue has been advanced by the work of Klonsky and May (2014), who proposes an "ideation-to-action" framework emphasizing the need to study the mechanisms responsible for ideation distinct from those accountable for attempts. In line with this conceptual proposal, the study by Khazem and Anestis (2016) investigated mechanisms related to suicide by differentiating their role between suicidal ideators and attempters. For example, results regarding the involvement of emotion dysregulation indicated that, compared with controls, both ideators, and attempters sustained higher levels of emotion dysregulation. Still, no significant differences were found between them (Khazem and Anestis, 2016). This result, obtained through adopting a theoretical model capable of distinguishing the mechanisms underlying the ideational and behavioral aspects of suicide related outcomes, draws attention to the lack of studies that have similarly investigated the differential degree of involvement of impulsivity-related facets.

In line with the conceptual and operational proposal of ideation to action (Klonsky and May, 2014), it emerges the need to evaluate the possible moderating effect of the type of suicide investigated about impulsivity, distinguishing between suicidal ideation and suicidal attempt. The link between impulsivity and aspects of suicide has been demonstrated. In particular, it has been found that the affective part of impulsivity is present in individuals with a history of suicide attempts or ideation and not in those who have never thought about suicide and that specific dimensions of impulsivity, such as the cognitive aspect related to premeditation has been purportedly associated with suicide attempt rather than ideation (Klonsky and May, 2010). Thus, it is essential to understand how consideration of the ideational or behavioral aspect of suicide may influence the relationship between suicide and impulsivity.

1.3. The current study

Although the literature demonstrates the link between impulsivity and the development of thoughts and behaviors related to suicide, the lack of conceptual clarity about the multidimensionality of impulsivity and the heterogeneity of suicide hampers the understanding of the dimensions of impulsivity involved distinctly in the ideational and behavioral aspects of suicide. Indeed, even the main theories that conceptualize the involvement of impulsive aspects of suicide do not delineate which dimensions of impulsivity are most involved. For example, in the Interpersonal Theory of Suicide (Joiner, 2005), it is not specified which dimension of impulsivity is referred to in describing the capability of suicide, similarly in the Integrated Motivational-Volitive Model (O'Connor, 2011), it is not specified which dimension is most involved between the lack of premeditation, lack of perseverance, sensation seeking or negative/positive urgency in determining the transition from the formation of the suicidal idea to the suicidal act. This ambiguity in defining the association between the affective, behavioral, and cognitive facets of impulsivity and the dimensions of suicidal ideation and attempts carries significant consequences at both the diagnostic and clinical levels.

This study aims to conduct a systematic review and meta-analysis of empirical data exploring the relationship between impulsivity and suicide. In accordance with literature, specific suicide-related outcomes were selected namely suicide-in the dimensions of ideation and attempts-rather than the associated risk factors. The more specific objectives are (1) to identify the overall effect of the relationship between the UPPS dimensions of impulsivity and suicidal ideation and attempts, (2) to analyze the reported moderating effects about (a) the characteristics of the sample (clinical/not clinical status), (b) the country in which

the study was conducted (c), the type of instruments used to assess suicidal ideation and attempts, (c) the overall quality of the studies reviewed, and (d) the suicide related outcomes (ideation and attempt) examined.

2. Method

Referring to PRISMA guidelines (Moher et al., 2009), a systematic search was carried out. The entire study identification, inclusion, and exclusion (based on the eligibility criteria described below) is represented in the flowchart illustrated in Fig. 1.

2.1. Eligibility criteria

A description of the inclusion and exclusion criteria used is presented in Table 1. The main inclusion criteria were as follows: (1) both constructs of suicide related outcomes and impulsivity must be assessed; (2) impulsivity must be assessed with UPPS instrument; (3) the constructs (or the relationship between them) must be evaluated using quantitative research methods; (4) the constructs must be assessed with validated, reliable, and scientifically recognized instruments; (5) data presented in the articles must be original. Eligibility criteria are described more deeply below.

2.1.1. Types of participants

Concerning the composition of the samples, no age, gender, clinical status, or nationality limit was applied in the selection of studies based on the type of participants. So, the selected studies included all sample types.

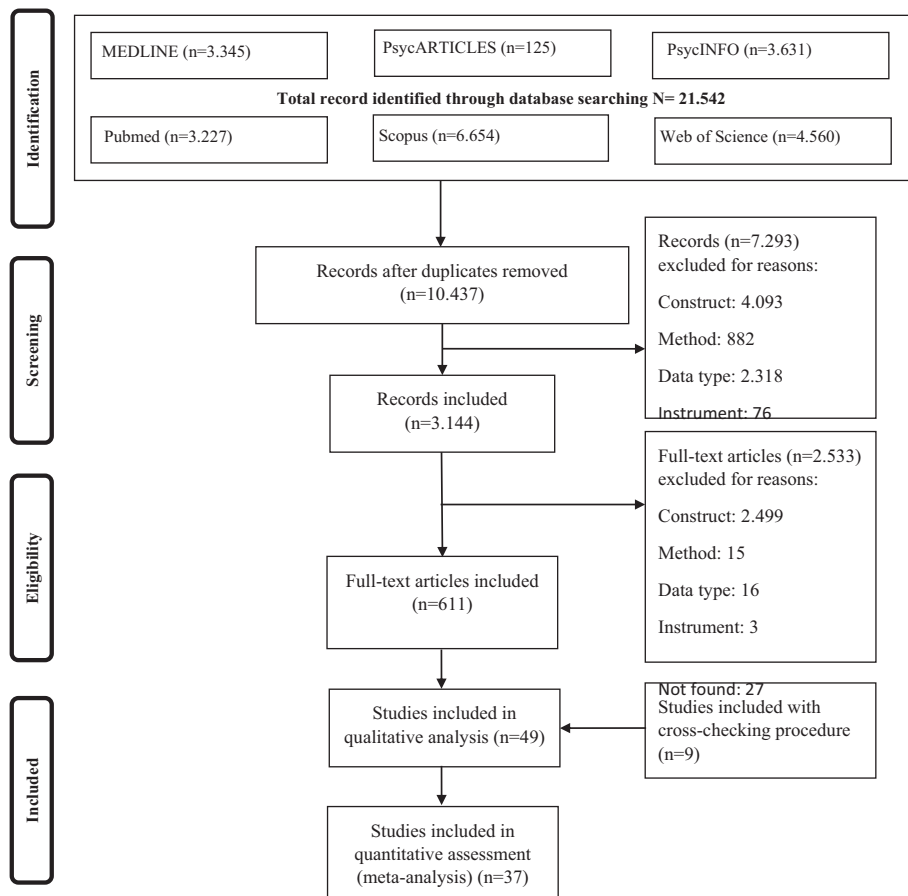


Fig. 1. Flow diagram.

Table 1
Eligibility criteria.

	Inclusion criteria	Exclusion criteria
Construct	Measure of at least one aspect of suicide related outcomes (attempt, ideation) Measure of impulsivity with UPPS instrument Association between suicide related outcomes and impulsivity Comparison between impulsivity levels in groups with and without at least one suicide related outcomes	Unreliable measure of suicidality Unreliable measure of impulsivity Spurious constructs of impulsivity or suicide related outcomes Tasks and physiological measures No estimation of the association between suicide related outcomes and impulsivity and/or the difference in impulsivity levels in groups with and without at least one suicide related outcomes
Method	Quantitative research methods Cross-sectional Longitudinal Experimental	Qualitative research methods Free interviews Focus group Case studies Theoretical articles
Data type	Published Unpublished	Duplicate of original research Conference proceedings Review and meta-analysis Not validated instrument
Instrument	Validated and recognized instruments Single item/question (only for suicide related outcomes) Interviews conducted by an experienced clinician Diagnostic criteria	Single item/question (only for impulsivity)

2.1.2. Outcome measures and comparison types

Regarding suicide related outcomes, all studies that measured this dimension with a validated instrument were included. Also included were studies in which suicide related outcomes was highlighted with a single question (e.g., “Have you ever attempted suicide?” or “Have you ever thought about dying?”) or an interview by an experienced clinician or through a diagnostic criterion of an international nosography (i.e., ICD or DSM-5-TR). If a study compared, in terms of impulsivity, a clinical group in which an aspect related to suicide related outcomes was present, the comparison group consisted of subjects without suicidal aspects or subjects with different suicidal aspects (e.g., suicide attempters vs. suicide ideators).

With regard to the measurement of impulsivity, only studies using the UPPS instrument (Whiteside and Lynam, 2001) and its developments (Cyders et al., 2007; Lynam et al., 2007) were included. Of these studies, those that reported measures obtained by combining the subscales were excluded.

The studies were included in the present systematic review if they reported sufficient data to estimate the quantitative association between the measured values of suicide related outcomes and impulsivity by (1) reporting the bivariate association between these variables and/or (2) reporting descriptive statistics (i.e., sample size, means, and standard deviations) obtained on the UPPS separately for at least a group of individuals displaying suicide related aspects and at least a comparison group.

In case a paper reported that the authors assessed the constructs of interest but without reporting the data, the corresponding author of that work was contacted to request this information.

2.1.3. Study types

To be included, studies had to use a quantitative methodology with no other limitations regarding research design. All studies were included without any limitation as to language or country of conduction. With the aim of including potential unpublished studies, publication in a peer-reviewed journal was not considered as one of the inclusion criteria. Finally, articles that did not contain original research data were not included, such as reviews, meta-analyses, or conference proceedings.

2.2. Search strategy

The following databases were used to conduct the literature search: PsycINFO, PsycARTICLES, PubMed, MEDLINE, Scopus, and Web of Science (all years until May 5, 2023). Search terms for both constructs of suicide related outcomes and impulsivity were assigned to each database. For PsycINFO, PsycARTICLES, MEDLINE, and PubMed, the search terms were used by entering the title and abstract field codes, while for Web of Science and Scopus, no field codes were selected in search terms. A search in PubMed was also conducted using the Mesh terms (see Appendix A). Finally, we searched the grey literature by cross-checking the reference lists of the papers included to find other studies eligible for the meta-analysis.

2.3. Study selection

Using the databases mentioned above, two authors autonomously performed a systematic search of the literature. Through this search, 21,542 records were identified, which were subsequently examined for eligibility. After removing the duplicates, 10,437 records were screened, controlling their title and abstract, resulting in the identification of 3,144 full-text articles to be further and deeper examined. After a careful inspection of these articles, the authors agreed that 611 papers met the inclusion criteria. At this point, for the purposes of the present work, only those studies that used the Negative urgency, (lack of) premeditation, (lack of) Perseverance, and Sensation seeking instrument (UPPS; Whiteside and Lynam, 2001), and its subsequent developments, which include the addition of a scale for Positive Urgency (UPPS-P; Cyders et al., 2007; Lynam et al., 2007) to measure the construct of impulsivity were included. Finally, a cross-checking procedure on the bibliography of each of these articles was applied, with the aim of finding any articles not identified up to this point by the search. At the end of this step, this resulted in a final pool of 49 articles included in the qualitative systematic review work.

Of these 49 papers, 37 were included in the quantitative analysis (meta-analysis), as the data needed to include the other studies could not be retrieved. The entire study selection process is shown in Fig. 1.

2.4. Process of data extraction and coding

A protocol was created to extract and encode the following data categories: (1) characteristics of the publication (i.e., authors, year, country, qualitative assessment); (2) characteristics of the sample (i.e., total size, gender, age, clinical status or composition); (3) methodological characteristics (i.e., research design, suicide related outcomes assessment instruments, suicide related outcomes type); and (4) main results (reported together with the statistical index used in the study). In case a study met all the mentioned inclusion criteria and did not report the effect size measure, available descriptive data and statistics were used to calculate the effect size measure. The influence of moderator variables that could potentially explain the relationship between the observed variables was also examined. Specifically, the candidate moderating variables considered included age, gender, research design, the clinical status of the participants, the type of instrument used to measure suicide related outcomes, the study country, suicide related outcomes type, and quality assessment. These additional analyses were calculated only for those moderator variables that showed sufficient variability (i.e., when they were not excessively homogeneous) and when the number of studies measuring these variables was sufficient. In addition, statistical tests were calculated to assess publication bias. Considering all criteria mentioned above, in the meta-analysis, it was possible to analyze the role of the following moderators:

- a. Clinical status, coded as Clinical or Not clinical (Mixed was coded as Clinical)

- b. Type of instrument used to measure suicide related outcomes, coded as Self-reported or Not self-reported
- c. Country in which studies were conducted, coded as USA or Not USA
- d. Suicide related outcomes type, coded as SA (suicide attempt) or SI (suicide ideation)
- e. Quality assessment
- f. Research design, coded as Cross-sectional or Longitudinal
- g. Age
- h. Gender

Composite measures of suicide (e.g., suicide risk) or merged measures between suicide attempt and ideation were excluded from the analyses. Details on the variables coding and a complete overview of the main information extracted are provided in Appendix B.

2.5. Quality assessment

A modified version of the Newcastle-Ottawa quality assessment Scale (Modesti et al., 2016; Wells et al., 2000), adapted for cross-sectional works, was used to assess the methodological quality of the studies. Specifically, aspects such as selection (e.g., representativeness and size of the sample, response rate, ascertainment of the exposure), comparability (i.e., the existence of matching variables, age, and gender, between clinical and control groups), and outcome (i.e., reliability of measures used and appropriateness of statistical analyses) were evaluated as poor, fair or good. Two authors made independent quality ratings, and disagreements were resolved through discussion and consultation. Fig. 2 summarizes the quality assessment of the studies included in the meta-analysis.

2.6. Statistical analyses

We used the Comprehensive Meta-Analysis (version 3.3) to calculate the pooled ES from the single ES provided by each study. Specifically, only statistical index estimating the pure association between impulsivity dimensions and suicide-related outcomes were used. Therefore, all unadjusted statistical indexes were used (e.g. bivariate coefficient correlation, coefficient of linear regression analyses) whereas spurious associations between variables (e.g., coefficients of multiple linear regression, coefficient of structural equation model) were excluded. Then, statistical indexes were all transformed in r ESs. Lastly, ESs coding was done so that positive associations accounted for a higher level of association between suicide related outcomes and impulsivity constructs.

2.6.1. Calculation of ESs

A random effects model was used in the computation of ESs. The possibility of each study having a separate ES with respect to its

population is taken into account by the random effects model but not by the fixed effects model (Rosenthal, 1995). Moreover, the random effects model seems to be best suited when a set of ESs is significantly heterogeneous (Cooper et al., 1994) and allows unconditional inferences to be made about the population. The estimated variance associated with the effects found was calculated using the Q statistic (Cochran, 1937, 1954), which is a general measure of heterogeneity. In case the measure of variance referring to the Q value is significant, the role of specific moderators can be examined to explain the observed variance. In our study, four categorical moderators (clinical status, type of instrument used to assess suicide-related outcomes, country in which the study was conducted, and type of suicide-related outcomes) were examined, whereas quality assessment, age and gender were examined using a meta-regression technique. Of note, several authors pointed out the problem of interpreting non-significant moderation analyses in case of low statistical power (Hedges and Pigott, 2004). To address this issue, power analyses were performed on a post-hoc basis using the *metapower* package for R for categorical moderators (Griffin, 2021) and following the procedure detailed by Hedges and Pigott (2004) for continuous moderators. Lastly, because a number of moderation effects were planned to be tested, analyses were corrected for multiple testing following the recommendations of Viechtbauer et al. (2015) and using the Knapp and Hartung method (2003).

2.6.2. Publication bias

Duval and Tweedie's (2000) trim-and-fill method was used in the calculation of publication bias tests. This procedure allows an estimate of the number of missing studies—due to publication bias—by including the missing works and providing an estimate of the adjusted ES. This type of analysis is important because, by adjusting the ESs with confidence intervals, it aims to show the average ES in the case where no publication bias is present (Duval and Tweedie, 2000).

3. Results

3.1. Results of the systematic review

A total of 49 articles (reported in Appendix B) exploring the associations between Suicide related outcomes and Impulsivity were considered in the present work. These studies were published in the last 13 years, between 2010 and 2023. Of these, 34 (69 %) were conducted in the United States. With respect to the research design, nine studies (18 %) used a longitudinal approach, while the remaining 82 % were cross-sectional. Regarding the type of sample used, 18 studies (37 %) included a clinical sample, seven (14 %) had a mixed sample, and 24 (49 %) involved community subjects. With respect to studies with a clinical sample, two of them involved patients with a substance use disorder, three subjects with mental health problems in general, two people with physical syndromes, four samples of subjects with previous suicide attempts, and two recruited patients with borderline personality disorder, three involved subjects with mood disorders, two subjects with schizophrenia spectrum disorder and one subject with gambling disorder. The average age of these clinical samples was 33.55, while the percentage of males was 42,9 %. In addition, 34 studies (69 %) used self-report instruments in assessing the dimensions associated with suicide related outcomes, while the remaining 15 studies (31 %) used non-self-report instruments, such as interviews conducted by an expert clinician or criteria from internationally recognized diagnostic manuals. Finally, most of the studies (73,46 %) found an association between at least one of the dimensions of the UPPS instrument and at least one aspect related to suicide related outcomes (ideation or attempt). For details on all these aspects, see Appendix B. The results of the meta-analysis are presented below.

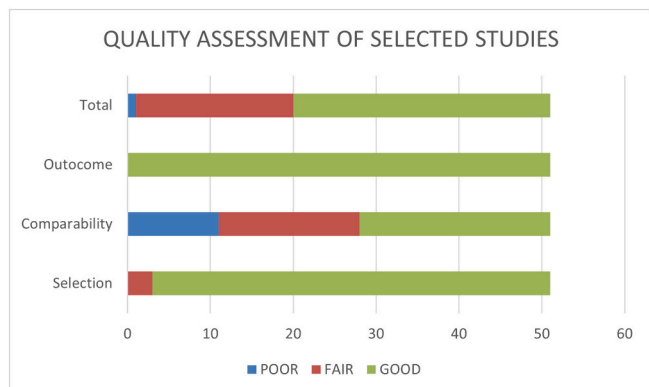


Fig. 2. Qualitative Assessment of selected studies.

3.2. Meta-analysis results

With the aim of understanding which dimensions of impulsivity are most involved in suicide-related attempts and ideations, we conducted several separate meta-analyses on each dimension of impulsivity according to Whiteside and Lynam's (2001) UPPS model and its developments (Cyders et al., 2007; Lynam et al., 2007): lack of perseverance, lack of premeditation, sensation seeking, negative urgency, positive urgency. The entire analysis set comprised 37 papers, including a total of 17,898 individuals. Table 2 presents the results of the analyses with respect to the associations between suicide related outcomes and the subscales of the UPPS instrument, also showing the number of contributions and individuals for each dimension of impulsivity.

3.2.1. Lack of perseverance

A set of 30 contributions that studied the association between lack of perseverance and suicide related outcomes in its attempt and ideation dimensions was included, comprising a total of 11,215 individuals. The results showed a significant mean effect size ($r = 0.18$, $p < .001$). The analyses found that five studies should be added to compensate for the presence of publication bias, and Egger's test (Egger et al., 1997), which quantifies the bias captured by the funnel plot, was consistently significant (CI = 1.52; 5.62). This finding was confirmed and adjusted using Duvall and Tweedie's Trim-and-fill method so that the adjusted effect size value was 0.23, reporting significant results (90 % CI = 0.15; 0.31). For a more detailed analysis, see forest and funnel plots in Figs. 3a and 4a.

The studies showed considerable heterogeneity ($Q = 305.2$; $p < .001$), so we examined the potential moderating role of several covariates: age, gender, country of study conduction, the clinical status of the sample, suicide related outcomes type, instrument used to measure suicide related outcomes and quality assessment. The results showed a moderating effect of the country of study conduction, the clinical status of the sample. Analysis by Group by showed a significant moderation overall effect was observed ($r = 0.17$, 90 % CI = 0.01; 0.34), with studies conducted in the USA reporting a higher effect size ($r = 0.23$, 90 % CI = 0.15; 0.31) compared to others ($r = 0.06$, 90 % CI = 0.03; 0.15). As can be seen, the results of the by group analysis showed that studies conducted outside the US reported a smaller effect size. There were no other significant moderation effects. For details on moderation effects, see Table 3.

3.2.2. Lack of premeditation

A set of 32 contributions that studied the association between lack of premeditation and suicide related outcomes in its attempt and ideation dimensions was included, comprising a total of 15,239 individuals. The results showed a small but significant mean effect size ($r = 0.13$, $p < .001$). Analyses found that seven studies should be added to compensate for the presence of publication bias, and Egger's test was consistently significant (CI = 0.70; 3.91). This finding was confirmed and adjusted

Table 2
Overall results for the associations between suicide related outcomes and UPPS subscales.

	k	N	ES	CI 95 %	z	p
Lack of perseverance	30	11,215	0.18	[0.12; 0.24]	5,49	<0.001
Lack of premeditation	32	15,239	0.13	[0.09; 0.18]	5,40	<0.001
Sensation seeking	25	10,297	0.07	[0.03; 0.12]	3,02	0.003
Positive urgency	18	7102	0.25	[0.19; 0.31]	7412	<0.001
Negative urgency	42	15,667	0.33	[0.27; 0.39]	10,52	<0.001

using Duvall and Tweedie's Trim-and-fill method so that the adjusted effect size value was 0.09, reporting significant results (90 % CI = 0.04; 0.13). For a more detailed analysis, see forest and funnel plots in Figs. 3b and 4b.

The studies showed substantial heterogeneity ($Q = 231.67$; $p < .001$), so we examined the potential moderating role of several covariates: age, gender, country of study conduction, the clinical status of the sample, suicide related outcomes type, instrument used to measure suicide related outcomes and quality assessment. Moderation analyses showed that none of these moderators made significant contributions to the relationship between lack of premeditation and suicide related outcomes. See Table 3 for details on moderation effects.

3.2.3. Sensation seeking

A set of 25 contributions that studied the association between sensation seeking and suicide related outcomes in its attempt and ideation dimensions was included, comprising a total of 10,297 individuals. The results showed a small but significant mean effect size ($r = 0.07$, $p = .003$). The analyses found that four studies should be added to compensate for the presence of publication bias, but Egger's test was not significant (CI = -1.75; 1.84). This finding was confirmed and adjusted by Duvall and Tweedie's Trim-and-fill method so that the adjusted effect size value was 0.10, reporting significant results (90 % CI = 0.05; 0.14). For a more detailed analysis, see forest and funnel plots in Figs. 3c and 4c.

The studies showed modest heterogeneity ($Q = 111.15$; $p < .001$), so we examined the potential moderating role of several covariates: age, gender, country of study conduct, the clinical status of the sample, suicide related outcomes type, instrument used to measure suicide related outcomes and quality assessment. Moderation analyses showed that none of these moderators make significant contributions to the relationship between sensation seeking and suicide related outcomes. For details on moderation effects, see Table 3.

3.2.4. Negative urgency

A set of 42 contributions that studied the association between negative urgency and suicide related outcomes in its attempt and ideation dimensions was included, comprising a total of 15,667 individuals. The results showed a significant mean effect size ($r = 0.33$, $p < .001$). The analyses showed the absence of publication bias. For a more detailed analysis, we showed the forest and funnel plots in Figs. 3d and 4d.

The studies showed considerable heterogeneity ($Q = 554.68$; $p < .001$), so we examined the potential moderating role of several covariates: age, gender, research design, country of study conduct, the clinical status of the sample, suicide related outcomes type, instrument used to measure suicide related outcomes and quality assessment. Moderation analyses showed that none of these moderators make significant contributions to the relationship between negative urgency and suicide related outcomes. See Table 3 for details on moderation effects.

3.2.5. Positive urgency

A set of 18 contributions that studied the association between positive urgency and suicide related outcomes in its attempt and ideation dimensions was included, comprising a total of 7,102 individuals. The results showed a significant mean effect size ($r = 0.25$, $p < .001$). The analyses showed the absence of publication bias. For a more detailed analysis, see forest and funnel plots in Figs. 3e and 4e.

The studies showed modest heterogeneity ($Q = 105.06$; $p < .001$), so we examined the potential moderating role of several covariates: age, gender, country of study conduct, the clinical status of the sample, suicide related outcomes type, instrument used to measure suicide related outcomes and quality assessment. Moderation analyses showed that none of these moderators made significant contributions to the relationship between positive urgency and suicide related outcomes. For details on moderation effects, see Table 3.

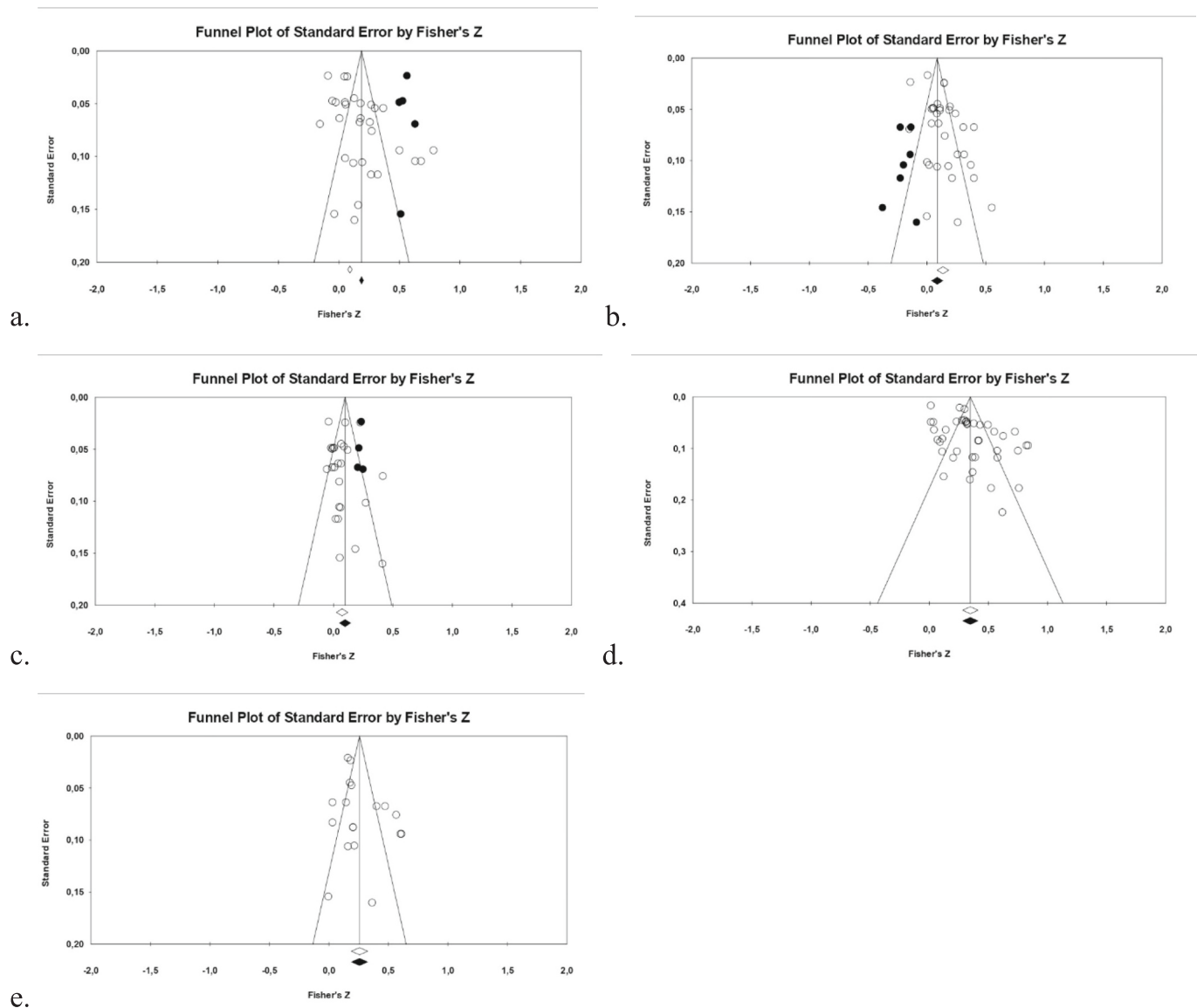


Fig. 4. Funnel plot of publication bias analysis.

addressed this issue reflect the conceptual and empirical confusion arising from the complexity of constructs related to impulsivity and suicide related outcomes. This uncertainty stands as an important limitation to understanding which dimensions of impulsivity are most involved in the outcomes related to suicide ideation and attempt, a topic that needs further clarification.

The main objective of the current study was to fill the gap in the literature by answering the question of which cognitive, affective, or behavioral aspects of impulsivity are most involved in suicidal attempts and ideation. In order to achieve results that reflect the complexity of the impulsivity construct in relation to its multidimensionality, we adopted the theoretical framework of Whiteside and Lynam's (2001) UPPS Model and its developments (Cyders et al., 2007; Lynam et al., 2007), with regard to the facets of impulsivity such as lack of perseverance, lack of premeditation, sensation seeking, negative urgency, positive urgency.

Moreover, regarding the aspect of suicide related outcomes, our study is in line with the framework from ideation to the action proposed by Klonsky and May (2014) in that it supports the distinction between suicide attempts and suicidal ideations and their underlying responsible mechanisms.

With the aim of clarifying which dimensions of impulsivity are most

involved in suicidal tendencies, our study proposed a systematic review of the literature of the last decade concerning the relationship between the facets of impulsivity related to the Whiteside and Lynam (2001) UPPS model and suicide related outcomes and a meta-analysis for assessing the potential moderating role of some key features of the analyzed studies considering publication bias in order to obtain clear, shared and authoritative results on the topic.

4.1. Suicide related outcomes and lack of perseverance

The current study concerning one of the facets referred to the cognitive aspect of impulsivity that we investigated in the link with suicide related outcomes refers to the inability to persevere in goal-directed behavior in the presence of frustration and/or boredom. The results, considering the presence of the publication bias and methods for its correction, showed a positive and significant relationship with the dimensions of suicidal ideation and attempts. Our results appear to be in contrast to the work of Anestis and Selby (2015), who show that a general capacity for persistence can facilitate suicidal behavior by allowing individuals to overcome fear and acute grief in seeking their own death. This explanation would support Joiner's (2005)

Table 3
Moderators of the relationship between suicide related outcomes and UPPS subscales using the Knapp-Hartung adjustment.

Moderator	Lack of perseverance			Lack of premeditation			Sensation seeking			Positive urgency			Negative urgency								
	k	N	ES	CI	k	N	ES	CI	k	N	ES	CI	k	N	ES	CI					
Country (USA)	30	11,215	0.17	[<0.01; 0.34]	32	15,239	0.05	[<0.07; 0.16]	25	10,297	0.03	[<0.07; 0.14]	18	7102	0.07	[<0.12; 0.27]	41	15,667	0.06	[<0.10; 0.22]	
Suicide instrument (Self-report)	30	11,215	-0.08	[<0.24; 0.09]	32	15,239	0.07	[<0.03; 0.17]	25	10,297	0.01	[<0.08; 0.12]	18	7102	0.09	[<0.10; 0.29]	41	15,667	0.02	[<0.12; 0.17]	
Suicide related outcomes (SI)	30	11,215	0.10	[<0.07; 0.26]	32	15,239	-0.01	[<0.11; 0.09]	25	10,297	<-0.01	[<0.11; 0.10]	18	7102	0.09	[<0.09; 0.28]	41	15,667	0.11	[<0.03; 0.25]	
Quality assessment	30	11,215	<0.01	[<0.09; 0.09]	32	15,239	-0.03	[<0.08; 0.02]	25	10,297	<-0.01	[<0.05; 0.04]	18	7102	0.03	[<0.08; 0.14]	41	15,667	-0.02	[<0.09; 0.05]	
Sample status (not clinical)	30	11,215	-0.13	[<0.29; 0.03]	32	15,239	-0.02	[<0.12; 0.09]	25	10,297	-0.04	[<0.14; 0.05]	18	7102	0.01	[<0.18; 0.21]	41	15,667	-0.08	[<0.22; 0.06]	
Age	16	5468	0.01	[<0.01; 0.01]	17	5892	0.01	[<-0.01; 0.01]	17	5660	<0.01	[<-0.01; <0.01]	14	6736	0.01	[<-0.01; 0.01]	30	14,550	<0.01	[<-0.01; <0.01]	
Gender	16	5468	<0.01	[<-0.01; <0.01]	17	5892	<-0.01	[<-0.01; <0.01]	17	5660	<0.01	[<-0.01; <0.01]	14	6736	<-0.01	[<-0.01; <0.01]	28	14,550	<-0.01	[<-0.01; <0.01]	
Research design (Longitudinal)																		41	15,667	0.02	[<-0.52; 0.56]

Interpersonal Theory position that underlying suicidal tendency is a clear intention to die that is pursued through overcoming the distress associated with the imagery of death by persevering through terrifying emotional experiences. In contrast, other authors have found that a lack of perseverance is not an impulsivity-related trait associated with either suicide attempts or ideations (Klonsky and May, 2010). One possible explanation for the different findings on the relationship between the dimensions of suicide related outcomes referred to suicidal ideation and attempts, and the cognitive aspect of lack of perseverance associated with impulsivity may refer to the different ways in which the construct of perseverance has been conceptualized. Indeed, when this link is considered in light of dimensions related to emotion dysregulation and, in particular, the difficulty of maintaining goal-directed behavior when experiencing negative emotional states, our results find solid support in the literature by opening up new research possibilities (Wolff et al., 2019). This could suggest that when viewed as an epiphenomenon of a difficulty regulating emotions, rather than considering only the associated cognitive and behavioral aspects, lack of perseverance as a personality trait could lead to an increased risk of developing suicidal ideations and attempts because it is associated with a sense of perceived ineffectiveness and difficulty making decisions (Chu et al., 2015).

4.2. Suicide related outcomes and lack of premeditation

Another cognitive factor related to impulsivity examined in relation to the dimensions of suicidal ideations and attempts refers to the lack of premeditation. The results, corrected by publication bias, regarding the link between lack of premeditation and suicide related outcomes considered in the dimensions of suicidal ideations and attempts demonstrate a small but positive and significant relationship between the two constructs in line with the literature that shows the involvement of impulsivity, and in particular, the facets related to lack of planning and premeditation, as significantly associated with suicide related outcomes (Abdoli et al., 2022). However, in contrast to the results of studies identifying the impulsive dimension of lack of premeditation as being closely related to suicide attempts (Klonsky and May, 2010), the results of our analysis did not find an influence exerted by the ideation or attempt dimensions of suicide related outcomes in the relationship with the impulsive aspect of lack of premeditation. This result suggests that there are probably other factors that may distinguish individuals with suicidal thoughts from those who enact suicidal behaviors (Klonsky et al., 2021). Indeed, the dimension of premeditation, related to planned thinking about the predictable outcome, is detectable both in suicidal ideas related to thoughts about death and suicide and in suicide attempts related to planning and intention to die. The lack of premeditation does not appear to be a discriminating dimension of suicidal attempts but rather seems to refer to a trait associated with individual vulnerability to suicide (Bloch-Elkouby et al., 2020).

4.3. Suicide related outcomes and sensation seeking

Another facet related to impulsivity studied in relation to the dimensions of suicide related outcomes refers to sensation seeking. Past research has related this trait of impulsivity to the enactment of risk-taking behaviors, including substance abuse (Hughson et al., 2019) and suicidal tendencies, as they are exposed to thrill-seeking experiences that can increase their acquired capacities for suicide attempts because they are less influenced by the negative affective consequences, such as fear, associated with such experiences (Bender et al., 2012). Consistent with this evidence, our results confirm the existence of a small, positive, and significant relationship between the sensation-seeking-related trait of impulsivity and the suicide related outcomes in its dimensions of suicidal ideations and attempts.

4.4. Suicide related outcomes and negative urgency

Another facet examined refers to the affective aspect of impulsivity related to the enactment of impulsive behaviors when experiencing negative emotional states. The results of our analysis demonstrated a positive and significant relationship between negative urgency and suicide related outcomes in the aspects of suicidal ideations and attempts. This result is in line with the data of other work confirming the involvement of the negative affective aspect of impulsivity in relation to suicide related outcomes (Anestis et al., 2012) and shows that suicidal thoughts and behaviors are more frequent in personalities characterized by a high pervasiveness of negative emotions (Brezo et al., 2006).

This finding offers some interesting indications about the involvement of difficulties in regulating emotional states of a negative nature resulting in acting out and in the development of suicidal tendencies. Our results, in line with existing evidence of emotional dysregulation associated with the enactment of impulsive actions in subjects with suicidal ideations and attempts (Hatkevich et al., 2019), recommend the idea that the enactment of impulsive behaviors by subjects with suicidal ideations and attempts may be a consequence of the presence of negative emotional states and of difficulty in modulating their intensity.

4.4.1. Suicide related outcomes and positive urgency

Finally, the last facet considering the affective aspect of impulsivity, refers to the enactment of impulsive behaviors when experiencing positive emotional states. Although research in this area has historically focused on the dysregulation of negative emotions (Carl et al., 2013), findings from recent studies show that the dysregulation of positive emotions may also play an important role in the etiology of mood disorders, such as rumination and dampening of positive emotions in bipolar and depressive disorders (Gilbert et al., 2013) and in particular in suicide ideations and attempts (Weiss et al., 2020). Consistent with findings in the literature, our results demonstrate a positive and significant relationship between the affective facet of impulsivity related to positive urgency and suicide related outcomes in the dimensions of suicidal ideations and attempts. In fact, recent findings have highlighted the involvement of both positive and negative urgency in the development of general violent behaviors and suicide attempts (Ammerman et al., 2015). This finding, consistent with what has been discussed for the dimension of negative urgency, might suggest that it is not so much the emotional connotation, positive or negative in nature, that plays a role in the development of suicidal ideations and attempts, but rather the emotional intensity experienced and not tolerated by the individual. In fact, recent findings on changes in the intensity of emotions following suicidal thoughts have shown that although suicide may be considered the only possible escape route for intolerable emotions (Baumeister, 1990), following suicidal ideation, there is an increased intensity of negative emotions suggesting the presence of a potentially vicious circle between emotional intensity and suicide related outcomes (Al-Dajani and Uliaszek, 2021). An alternative explanation of the role played by the dimension of positive urgency, and thus by the underlying mechanisms of positive emotion dysregulation, in the development of thoughts and behaviors related to suicide may refer to the pathogenic belief of not feeling worthy of the positive emotion experienced and developing a fear of happiness (Gilbert et al., 2014) that can increase tunnel vision and to consider suicide as the only solution (Rodziński et al., 2017). For example, such dynamics can be observed in some psychopathological forms related to mood disorders, such as patients with major depression, where there is a strong resistance to treatment that can be explained by the presence of these beliefs related to unworthiness, fear of happiness, and hopelessness (Baryshnikov et al., 2020).

5. The role of moderators

With the aim of understanding the potential influences that can modulate the relationship between the cognitive, behavioral, and

affective facets of impulsivity and the dimensions of suicide related outcomes, we investigated the facets of suicide related outcomes, the type of instrument used to assess suicide related outcomes and the overall quality of the studies, the characteristics of the sample (age, gender, clinical status), and the study country. Regarding the results of the moderation analyses, some non-significant results should be appreciated with caution. Specifically, we may note that several effect sizes, despite not statistically significant were, from a descriptive point of view, quite consistent. For instance, suicide ideation seemed to be more strongly associated with both lack of perseverance and negative urgency compared to suicide behaviors. Of note, despite several moderation analyses were not statistically significant, these findings may have been impacted by the lack of statistical power in our study (Hedges and Pigott, 2004). For instance, the power to detect a meaningful moderation analysis with our random effect model was low, especially for continuous variables, maybe due to the very low coefficient found. Therefore, more studies are needed to replicate the test of the hypothesis in a future meta-analysis. Moreover, these findings suggests that the results found in this meta-analysis should not stop the investigation of the different associations between dimensions of suicide-related outcomes and impulsivity facets rather than stimulating additional investigation of the question.

5.1. Cognitive aspects of impulsivity and suicide related outcomes

Regarding the moderators related to the link between the cognitive aspects of impulsivity and suicide related outcomes, our results show that for both facets of lack of perseverance and lack of premeditation, the type of suicide related outcomes does not seem to modulate the link, just as the quality of the studies, the type of instrument used to assess suicide related outcomes, and the sample characteristics do not report a significant influence. A factor that influenced the relationship between lack of perseverance and aspects of suicidality is the country in which the study was conducted. In fact, studies conducted in the United States showed a stronger link between lack of perseverance and suicide related outcomes than studies conducted in other countries. This result might suggest that in cultures where the value of perseverance, determination, and achievement is particularly present (such as the US, see Nakitende, 2019), a lack of perseverance is more likely to signal a pathological process such as suicide related outcomes.

5.2. Behavioral aspect of impulsivity and suicide related outcomes

As for the moderators related to the link between the behavioral aspect of impulsivity and suicide related outcomes, our results show that the type of suicide related outcomes examined did not influence the relationship between sensation seeking and suicide related outcomes.

This might suggest that sensation seeking is a trait of impulsivity that does not discriminate ideators from tempters and may play a role in exposing individuals to risky behaviors, such as alcohol use, having an indirect rather than direct involvement with suicidal tendencies (Cole et al., 2019). In addition, the quality of the studies and the type of instrument used to assess aspects of suicide related outcomes have also not been shown to contribute to this relationship, emphasizing that the use of a self-report instrument or other instruments (e.g., single item, diagnostic criteria, psychological autopsy) does not change the magnitude of the link between the two constructs. Finally, neither the characteristics of the sample nor the study country contributed positively or negatively to the magnitude of the relationship between sensation-seeking and suicide related outcomes.

5.3. Affective aspects of impulsivity and suicide related outcomes

The moderators' investigation of the link between the affective aspects of impulsivity and suicide related outcomes showed that the type of suicide related outcome does not seem to influence this relationship

with regard to both negative and positive urgency. This suggests that the affective aspect of impulsivity has a relationship with both suicidal ideation and suicide attempts without being a distinctive component of either dimension. This suggests that, among the various facets of impulsivity, the presence of negative and positive urgency cannot be considered a facet that distinguishes ideators and tempters, in line with what Klonsky and May (2010) have shown (May and Klonsky, 2016). Moreover, the similarity with the impulsive aspect of emotional dysregulation, which indeed reports a significant relationship with both suicidal ideation and suicide attempts (Colmenero-Navarrete et al., 2022), should also be considered when reflecting on the findings that emerged. The research design of the studies with regard to the dimension of negative urgency, the overall quality of the studies, the type of instruments used to assess suicide related outcomes, and the country in which the study was conducted with regard to both dimensions did not report significant influences in the relationship with the dimensions of suicide related outcomes. Regarding sample characteristics, age and gender did not contribute to influence the relationship between affective aspects of impulsivity and suicide-related outcomes. Finally, the clinical status of the sample did not seem to have contributed to the link between suicide-related outcomes and affective dimensions of impulsivity either. This result might suggest the existence of a continuity between normal and pathological aspects in the overall process configuration linking aspects of impulsivity to the dimensions of suicide-related outcomes, with reference to ideation when considered in relation to the facet of positive and negative urgency. However, to obtain more detailed results in this regard, more specific analyses related to the different connotations of the clinical sample should be conducted in greater depth and with a larger number of studies. In this case, one could consider how the different facets of impulsivity interact with psychopathological dimensions (e.g., positive urgency and depression; negative urgency and borderline disorder) and how this has a relevant outcome in the link with suicide related outcomes.

6. Implications from diagnostic and clinical point of views

From a diagnostic perspective, a deeper understanding of the dimensions involved in suicidal behavior. In the section of the DSM-5-TR (2022) describing “Other conditions that may be a focus of clinical attention”, the category “Suicidal behavior” is mentioned, which could be used for individuals who have engaged in self-injurious behaviors characterized by a desire to die. It is specified that evidence of intentionality to end one’s life may be explicit or inferred from behaviors or circumstances. The nature of intentionality and planning of the suicidal act is highly debated (Giotakos, 2022). Therefore, it is essential to know the dimensions of impulsivity involved in suicide ideation, planning and attempts in order to understand the effects of their involvement. Noteworthy, our results do not disentangle the extent by which the lack of premeditation is involved in poor planning of the suicidal act rather than the consequences of the act or both. From this point of view, estimating the association between suicide behaviors and levels of lack of premeditation (i.e., a dimension of the UPPS model) would contribute to the current debate. The findings brought by our meta-analysis, evidencing that a lack of premeditation is significantly associated with suicide-related outcomes, may suggest that planning may not be always characteristic of suicide behaviors, providing a valuable contribution to the consideration proposed by the DSM-5-TR.

Currently, some treatment of impulsivity in patients with suicidal ideations and behaviors will intervene more on the cognitive and behavioral side associated with impulsivity, while others will target mechanisms related to the affective dimension. Among these, for example, Dialectical-Behavioral Therapy (DBT; Linehan, 1993) aims to change the dimensions of impulsivity associated with cognitions to dysfunctional behaviors. In comparison, treatment focused on emotion regulation addresses the strategies for managing negative affect rather than the resulting impulsive behavior (Neto and True, 2011).

Consequently, it is crucial to understand if and which dimensions of impulsivity are most implicated in suicidal ideations and attempts to understand which oriented approaches would be most successful.

7. Limitations and future directions

Although our study has been conducted systematically and rigorously, it is not without limitations. First, the limited number of studies included in the meta-analysis may have adversely affected the power of specific moderators, which in most were found to be non-significant. Because in most cases the Q statistic was significant, this suggest that other moderating variables, not considered in this study, may account for the observed variance. Another explanation is related to the potential lack of statistical power in our moderation analyses. Regarding this point, future studies may want to replicate this meta-analysis on a larger pool of studies or to meta-analyze effect sizes of primary interaction terms. In addition, the small number of studies that used a longitudinal research design did not make moderation analyses possible, with the exception of only one dimension of impulsivity (negative urgency), making it complex to ascertain whether the type of research design could be an influential variable in the relationship between impulsivity and suicide related outcomes. Second, the studies included in the present systematic literature review and meta-analysis study do not represent the largest scientific output related to the different dimensions of impulsivity. In fact, assuming Whiteside and Lynam (2001) UPPS model (Cyders et al., 2007; Lynam et al., 2007), we focused our study on the five affective, cognitive, and behavioral facets of impulsivity by not including in the meta-analytic work the studies investigating composite measures assessed through the revised version of the UPPS, such as deficit conscientiousness (Cole et al., 2019), as a composite measure of lack of premeditation and perseverance, and urgency (Lübbert et al., 2021), as a composite measure of negative and positive urgency. Furthermore, although the facet related to the UPPS model of impulsivity regarding sensation seeking was investigated, our study did not analyze the relationship between suicidal thoughts, suicidal behaviors, and the temperamental aspect related to novelty seeking (Cloninger et al., 1993), also due to the conceptual overlap referred to in literature regarding the common connotations between the dimensions of sensation seeking and novelty seeking. In fact, the definition developed by Zuckerman et al. (1964) of sensation seeking also contains the aspect of novelty seeking to a unidimensional extent. However, future investigations could analyze the involvement of the temperamental aspect of impulsivity in suicide-related outcomes by adopting the three-dimensional temperament model. It might be a focal point to investigate the role played by novelty seeking, harm avoidance and reward dependence in psychopathologies in which these aspects are most implicated in relation to suicidal outcomes. Therefore, further investigations are needed to understand the role of the integrated dimensions of cognitive and affective aspects of impulsivity in suicide related outcomes in its ideation and attempt aspects.

8. Conclusion

The present systematic literature review and meta-analysis, using Whiteside and Lynam’s (2001) UPPS model (Cyders et al., 2007; Lynam et al., 2007) and related emotional, cognitive, and behavioral aspects of impulsivity studied their relations with the broad topic of suicide related outcomes in its dimensions of ideations and attempts, outlining potential new lines of research in this area. The research provides a significant contribution to the discussion of suicidal intentionality inherent in the DSM-5-TR clinical condition definition of Suicidal Behavior by showing that the cognitive dimension of impulsivity referring to lack of premeditation appears to be associated with suicide-related outcomes in terms of both ideations and attempts. This might shed light on one of the features underlying suicidal tendencies in general, that there is not always a rational and decisive premeditation. Considering that negative

and positive urgency are the two facets most closely associated with suicide ideation and attempt allowing for a useful contribution to guidelines for clinical interventions in the field of suicide related outcomes, confirming the relevance of emotion dysregulation in addition to cognitive and behavioral facets in relation to impulsivity traits.

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CRedit authorship contribution statement

Serena Bruno conducted literature search, coded all primary studies, and drafted the manuscript. Gerardo Anconetani conducted literature search, coded all primary studies, and drafted the manuscript. Guyonne Rogier assisted in data analysis and critically reviewed the manuscript. Antonio Del Casale contributed to the design of the study and critical review of the manuscript. Maurizio Pompili contributed to the design of the study and critically reviewed the manuscript. Patrizia Velotti designed the study, guided in data analysis, and critically reviewed the manuscript. All authors contributed to and have approved the final manuscript.

Declaration of competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data availability

The data that support the findings of this study are available on request from the corresponding author.

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Appendices. Supplementary data

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