

UNIVERSITÀ DEGLI STUDI DELL'INSUBRIA

DOTTORATO DI RICERCA

**MEDICINA CLINICA E SPERIMENTALE E MEDICAL HUMANITIES
- XXXV CICLO**



**ASSESSING MENTAL PAIN AS A PREDICTIVE FACTOR OF
SUICIDE RISK IN A CLINICAL SAMPLE OF PATIENTS
WITH PSYCHIATRIC DISORDERS**

Docente Guida: Chiar.ma Prof.ssa Camilla Callegari
PhD Student: Dr.ssa Giulia Lucca



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Overall the Candidate did a good work on a very important topic in the field of Psychiatry. Understanding how to better identify people at risk for suicidal behavior is crucial for suicide prevention. The real world setting and the use of reliable assessment tools represent strengths of her research.

I would suggest the revision of some minor issues before admitting the thesis to the discussion:

Check for typos (e.g. page 4 "Psychach", title on page 29: "Matherials")

Page 29: consider specifying what you mean by "emergency therapeutic intervention" .

Page 32: you mention the Psychache Scale - PAS, but a few lines below you mention the Pain Attitudes Scale (PAS): please clarify.

Page 34: you describe the laboratory tests included in the assessment, but there seems to be no explanation/reference to support your choice. Please consider adding at least a couple of references. You actually mention some in the discussion session, which could be updated (the most recent one you mention is from a 2019 study).

Page 47: please note that sometimes you mention "SA" for suicide attempt, sometimes "AS" : maybe it would be easier to choose one and use it consistently in the text.

I think that in the conclusion section there is too much focus on the possibility to use the scales in the primary care setting, while this topic has not been previously introduced or discussed, and it was not even included in the study objectives. I would then suggest to target the conclusions more on what the study actually achieved, suggesting only in the end the issue of primary care as a further, possible development.

Novara, 15/01/2024

Patrizia Zeppego



www.regione.piemonte.it/sanita



Firmato digitalmente da Patrizia ZeppegoData:
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RISPOSTA AL REVISORE 1

Gent.ma prof.ssa Zeppegno,

la ringrazio per la revisione e per gli spunti di approfondimento forniti.

Ho provveduto a correggere gli errori di battitura e ad approfondire i temi da lei indicati al fine di renderli più completi e comprensibili per la lettura.

Ho aggiornato la letteratura rispetto al tema dei parametri laboratoristici rendendo la descrizione introduttiva più mirata a quanto di nostro interesse.

Ho rielaborato le conclusioni per renderle più aderenti agli scopi del lavoro, come da sua indicazione.

La ringrazio ancora e spero che il lavoro possa essere un punto di partenza per futuri cambiamenti positivi nel panorama della prevenzione suicidaria.

Cordialmente,

Dottorando

dott.ssa Giulia Lucca



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La Candidata ha provveduto a rivedere il proprio lavoro secondo le indicazioni fornite. Non ho ulteriori osservazioni.

La tesi può essere ammessa alla discussione davanti alla Commissione che assegnerà il titolo di Dottore di Ricerca.

Patrizia Zepegno



Verona, 20/02/2024

Dear Committee,

please find below my comments on the PhD thesis of the candidate Dr. Giulia Lucca.
I remain available for any further inquiry.

With best regards

Dr. Giovanni Ostuzzi, MD, PhD

Department of Neuroscience, Biomedicine, and Movement, University of Verona

Revision on the thesis "Assessing mental pain as a predictive factor of suicide risk in a clinical sample of patients with psychiatric disorders" by Dr. Giulia Lucca

Thank you for the opportunity of revising this interesting piece of work, and sorry for the delay in sending my comments.

This thesis deals with the interesting topic of the association between suicide behavior and mental pain. Data retrieved are surely of clinical interest, however some relevant methodological issues should be highlighted. Further, the formal presentation of methods and results can be notably improved.

Abstract (p. 4-5)

"[...] described as an unbearable subjective experience to which the person wishes to end by any means, including death". Remove "to".

"The works conducted so far". I would suggest "Available literature on this topic".



“Mental pain is a measurable parameter through psychometric scales ...”. I would suggest
“Mental pain is a construct that can be measured through ...”.

“...and to propose the measurement of the same as a large-scale screening tool”. Considering
that we are in the background section, I suggest against suggesting such relevant implication at
this point.

“The sample, representative of the main psychiatric diagnoses carried out in accordance with
the DSM-V-TR, consists in 179 adult patients, recruited at psychiatric services of Varese”. I
suggest: “The sample consists in 179 adult patients, recruited at psychiatric services of Varese,
and suffering from the main psychiatric diagnoses according to the DSM-V-TR”. Maybe DSM-5-
TR is more accurate. I would suggest also briefly explain which diagnoses are included.

“[...] As occurred in the follow-up period were detected and they were related to the levels of
mental pain, measured at the baseline”. I would stop the sentence after “detected”. Afterwards,
I suggest providing some more details on the statistical approach used to assess the possible
association between mental pain and risk of suicide.

“...a lesser risk...” → a lower risk

“...Increases the probability [...]”, I would add “of AS”.

I see you alternate the use of “,” and “.” for numbers with decimal figures. Please amend this
throughout the text to make the style consistent.

“A significant association was found between suicide attempts and antipsychotic therapy [...]”.
In which direction is the association, is treatment a protective factor? I assume it is, but this
should always be clear.

“A previous AS is related with an increased probability of carrying out a new AS ($p < 0,05$)”. It
would be interesting to assess whether there is a cumulative effect, ie, if the risk increases with
the number of previous suicide attempts.

“Regarding biological markers, [...]”. Did you measure any specific biomarker in your cohort? If
so, this should be mentioned in the Methods section.

“...were searched for, [...]”. I would stop the sentence here.

“[...] while no clear association with mental pain scales was identified at 12 months, several
scales (C-SSRS, BDI, BHS, PAS) were statistically significant at 6 months in detecting patients
with a higher suicide risk ($p < 0,05$)”. According to the Methods, I figured that you assessed the



number of events at 12 months only, while here it looks like you assessed AS at 6 months as well. Please clarify in the Methods section.

“...and characteristics of good applicability even in contexts other than psychiatric, proving suitable to be used as potential tools...”. I would amend “providing suitable”. Put it this way, it looks like your study showed that these rating scales have “characteristics of good applicability”, but this is not what you looked for. You might provide some reasoning why you believe these tools might be feasible and in which contexts to contribute to suicide prevention.

Introduction

In general, the Introduction contains many important background information, and the references are generally up-to-date.

p. 16: I notice that the terms DSM-5-TR and DSM-V-TR are both use. Please revise for consistency.

p. 24 “Tabella 2: Commonalities of suicide”. I would suggest using the original wording in English rather than translating to Italian.

Materials and Methods

p. 29: “[...] through the administration of the following evaluation scales of the levels of depression, anxiety, hopelessness and mental pain)”. I would remove “following” (no rating scales’ names are reported thereafter) and remove the final bracket.

“The aim was to calculate any correlation [...]”. I would suggest “to assess”. In general, this sentence is rather long.

“[...] to deepen the association between socio-demographic [...] with suicide risk [...]”. If I understand correctly, we probably want to deepen the knowledge on this association.

“Complete suicides were considered, or suicidal attempts [...]”. This sentence might reflect some of the issues that I outlined below.

I have some concerns on how the objectives are described:

“The objectives of this study are as follows:

1. To assess the relationship between levels of mental pain and history of suicide attempts.
2. To evaluate the existing relationship between severity of mental pain and suicide attempt, independently from the symptomatic condition of the individuals.



3. To assess whether incorporating biochemical markers can enhance the accuracy of suicide risk screening.”

Point 2 and point 1 are broadly overlapping. The only apparent difference is that the objective “2” takes into account the symptoms of psychopathology, arguably through a statistically adjusted model, while objective “1” considers only the “raw” association.

As it is formulated, objective “3” seem to suggest that you used a model to predict suicide risk which includes the assessment of biochemical markers and then verified the accuracy of this prediction. As far as I understand, you rather explored the possible association between risk of suicide and biochemical markers.

In addition to the objectives of the study, I would expect primary and secondary outcomes to be detailed. The “association between mental pain and suicide attempts” might mean different things. I understand that you will use “mental pain” as a continuous outcome, but this should be specified along with the rating scale on which you primarily rely to measure this variable.

In general, I strongly advise to make a list of primary and secondary outcomes.

Further, I strongly advise to be more precise in the wording. Objectives 1 and 2 refer to “suicide attempts” only (therefore, no complete suicides and no suicide ideation), while objective 3 refers to “suicide risk”. Are you referring to a broad/inclusive definition of suicide? In this case, the term “suicidal behavior” (which include ideation, attempt, and death by suicide) should be advised.

p. 30: Sample. Do you mean that they were referred to the UOP of Varese from the CPS and the specialized outpatient clinic? Please rephrase to increase clarity.

“[...] homogeneous in clinical and sociodemographic characteristics”. This consideration pertains to the results/discussion sections.

p. 30: Tools. If understand correctly, such tools were administered only at baseline, and not at follow-up, as the information on suicidal behavior was derived from clinical records and from the psychiatrist in charge for the case. Is this correct? I strongly suggest making this clear in the text.

p. 33: I suggest to specify that biological markers were collected under ordinary clinical routine, so to make clear that participants did not undergo laboratory assessments which were not consistent with normal practice.



p. 34: Statistical analysis. The main limitation here is that you performed only univariate binary analyses. At least for the primary outcome I suggest to set up a multivariable model in order to adjust for possible confounders (age, sex, symptoms of depression and anxiety, previous suicide attempts, duration of disease, type of core diagnosis, etc.).

p. 34: If I understand correctly, the study was not formally submitted to the local Ethics Committee? Apart from signing an informed consent, did the participants sign also a privacy consent to allow an anonymous use of their data for scientific purposes?

Results

I think that the main issue here is that you describe a number of variables and analyses, without giving preference to one over another, while one would expect the primary outcome to be addressed first.

In general, I noticed that sometimes you reported decimal separated by a comma and some other times by a point. Please revise and make consistent throughout the text.

Tables look a bit blurred. Can you insert the table within the text, rather than an image?

p. 36: I would suggest including a table with the main socio-demographic variables.

P. 37: Table 3: I suggest to re-order diagnoses according to their frequency. If you use acronyms, there should be a legend in the caption or as a footnote.

p. 38: “[...] incongruous ingestion of drugs [...]”. It might worth specify “prescribed” drugs, or “medications”, as opposed to “psychoactive substances”.

Figure 8: Interesting that no significant differences between groups emerged according to the HAM-D, while the BDI-II shows some differences. Some reasoning about this point should be included in the discussion.

Discussion

p. 45: “This longitudinal study aimed to evaluate the role of mental pain in predicting effective suicide attempt and its interactions with other sociodemographic, clinical, and psychometric factors, [...]”. I think that the binary analysis actually prevents from exploring such interactions, which a multivariable model might address.

In this section, the candidate discusses each variable that has been analyzed, providing references from available literature. I suggest to maintain a more consistent structure



throughout the text, discussing whether an association, or a lack of association is in line with what we already know from available evidence. Thereafter, known or novel theoretical grounds might be discussed. It seems to me that the sentence “further research is needed” is too widely used, while for at least some variables we might have a rather relevant amount of evidence.

The Discussion mirrors the major problem of the Results, which is that the primary objective of the study is not prioritized.

p. 47: I see many typos and grammatical errors, including excessively articulated sentences. Please revise the whole text to improve written English and rephrase were needed.

“In this study, the suicide risk was also assessed over time, specifically in the 6 and 12 months following patient recruitment”. The 12-months follow-up is mentioned only in the Abstract and in the Discussion, while it does not appear in the Methods section. Please revise.

p. 47: “[...] the tools listed above (C-SSRS, BDI, BHS, PAS) were statistically significant [...]”. Please be more precise, e.g. the score obtained at the tools was statistically associated with [...]

p. 48: “Regarding biochemical markers, no significant association with suicide was found, mainly due to the difficulties in retrieving tests result that were univocally related to the suicide attempt”. This sentence is of unclear interpretation, please consider rephrasing.

In this last paragraph, I do not seem to discuss the results of your analysis, i.e. whether you found that those individuals attempting suicide were at higher risk of showing altered biomarkers.

p. 48: “[...] self-administered scales were more statistically significant than HAM-A and HAM-D [...]”. Again here, the wording is imprecise. How can a rating scale be more statistically significant than another?

In general, the paragraph on limitations and strengths is too short, while it should stimulate a thorough critical appraisal of results. This should be expanded and developed according to the various issues raised above.

p. 49: “The results of this study suggest that the scores obtained from the C-SSRS, BHS, BDI-II, PAS, and OMMP scales can be useful tools for primary care physicians [...]”. I am not convinced that results from this study point in this direction. The study was conducted in a specialized setting, so the main implications should regard this environment, although possible applications to primary care can be hypothesized and their pros and cons discussed. According



to my clinical experience, such a set of rating scales pertain more to specialized setting rather than primary care, where colleague might lack expertise in this field, and might find simpler instruments more appropriate.

Among major shortcomings, please consider what discussed above throughout the revision.

Additionally, I would highlight the following methodological issues:

- Adverse childhood events have not been evaluated, although there is strong literature in support of their possible role as predictors of both mental pain and suicide behaviors. This should be discussed among limitations;
- The statistical analysis consists in binary regressions, but a multivariate analysis was not performed
- You describe the study design as longitudinal. Can you be more precise? It seems to me that this is a cohort study, as you identify exposed individuals (or rather the degree of exposure to mental pain) and follow them up for 6 months. The conceptual issue here is that there is not a clear temporal "starting point" for this exposure. You measure this exposure at baseline, but it is not clear since when individuals have been exposed. If you should conduct a multivariate analysis, an adjustment for illness duration might be relevant, as this might be reasonably considered as proxy of the duration of mental pain;
- One might argue that I could have formulated a hypothesis on the primary outcome, such as how do expect mental pain to increase the risk of suicide attempt? To what extent? As there is literature on this matter, one might even attempt a calculation of the sample size required to detect the expected effect.



RISPOSTA AL REVISORE 2

Gent.mo prof. Ostuzzi,

la ringrazio per la revisione e per gli spunti di approfondimento forniti. Passo ora a rispondere punto per punto ai suoi commenti, alcuni dei quali applicabili, altri no.

Abstract (p. 4-5)

"[...] described as an unbearable subjective experience to which the person wishes to end by any means, including death". Remove "to". *Fatto*

"The works conducted so far". I would suggest "Available literature on this topic". "Mental pain is a measurable parameter through psychometric scales ...". I would suggest "Mental pain is a construct that can be measured through ...". *Fatto*

"...and to propose the measurement of the same as a large-scale screening tool". Considering that we are in the background section, I suggest against suggesting such relevant implication at this point. *Aggiunto una sezione obiettivi*

"The sample, representative of the main psychiatric diagnoses carried out in accordance with the DSM-VTR, consists in 179 adult patients, recruited at psychiatric services of Varese". I suggest: "The sample consists in 179 adult patients, recruited at psychiatric services of Varese, and suffering from the main psychiatric diagnoses according to the DSM-V-TR". Maybe DSM-5-TR is more accurate. *Fatto, ho tolto "main" in quanto fuorviante. Ogni diagnosi, purchè codificata secondo il DSM5TR è, infatti, stata inclusa.*

I would suggest also briefly explain which diagnoses are included. "[...] As occurred in the follow-up period were detected and they were related to the levels of mental pain, measured at the baseline". I would stop the sentence after "detected". Afterwards, I suggest providing some more details on the statistical approach used to assess the possible association between mental pain and risk of suicide. *Ho aggiunto la descrizione della statistica come da lei suggerito e ho modificato la frase da lei indicata. Togliera completamente tempo possa far perdere ai lettori il senso del lavoro.*

"...a lesser risk..." à a lower risk " *Fatto*

...Increases the probability [...]", I would add "of AS". *Fatto*

I see you alternate the use of "," and "." for numbers with decimal figures. Please amend this throughout the text to make the style consistent. *Fatto*

"A significant association was found between suicide attempts and antipsychotic therapy [...]". In which direction is the association, is treatment a protective factor? I assume it is, but this should always be clear. *No, il contrario, per questo è stato scritto "è stata riscontrata un'associazione tra terapia antipsicotica e*



TS". Ho aggiunto "assumption" sperando di renderlo più chiaro. Ho preferito non scrivere che la terapia antipsicotica aumenta il rischio in quanto non sarebbe corretto, tuttavia, credo sia ridondante dare spiegazioni sull'interpretazione del risultato nell'abstract, che sono invece rimandate al testo (sezione discussione).

"A previous AS is related with an increased probability of carrying out a new AS. It would be interesting to assess whether there is a cumulative effect, ie, if the risk increases with the number of previous suicide attempts. *Sono pienamente d'accordo, tuttavia la numerosità campionaria è troppo limitata (i pz con TS al follow up di 12 mesi sono solo 26).*

"Regarding biological markers, [...]" . Did you measure any specific biomarker in your cohort? If so, this should be mentioned in the Methods section. *Fatto*

"...were searched for, [...]" . I would stop the sentence here. *Ho modificato l'intera frase, togliendo la parte statistica, già chiarita nella sezione metodi.*

"[...] while no clear association with mental pain scales was identified at 12 months, several scales (C-SSRS,BDI, BHS, PAS) were statistically significant at 6 months in detecting patients with a higher suicide risk ($p < 0,05$)". According to the Methods, I figured that you assessed the number of events at 12 months only, while here it looks like you assessed AS at 6 months as well. Please clarify in the Methods section. *Fatto.*

"...and characteristics of good applicability even in contexts other than psychiatric, proving suitable to be used as potential tools..." . I would amend "proving suitable". Put it this way, it looks like your study showed that these rating scales have "characteristics of good applicability", but this is not what you looked for. You might provide some reasoning why you believe these tools might be feasible and in which contexts to contribute to suicide prevention. *Ho modificato la frase rispondendo solo all'obiettivo del lavoro e lasciando il resto alla parte conclusiva del testo.*

Introduction

In general, the Introduction contains many important background information, and the references are generally up-to-date.

p. 16: I notice that the terms DSM-5-TR and DSM-V-TR are both use. Please revise for consistency. *Fatto*

p. 24 "Tabella 2: Commonalities of suicide". I would suggest using the original wording in English rather than translating to Italian. *Trattasi di testo copiato da altro autore (Shneidman) e dunque non modificabile.*

Materials and Methods

p. 29: "[...] through the administration of the following evaluation scales of the levels of depression, anxiety, hopelessness and mental pain)". I would remove "following" (no rating scales' names are reported thereafter) and remove the final bracket. *Ha ragione, era un refuso, tolto*

"The aim was to calculate any correlation [...]" . I would suggest "to assess". In general, this sentence is rather long *fatto*

“Complete suicides were considered, or suicidal attempts [...]”. This sentence might reflect some of the issues that I outlined below *ok*

I have some concerns on how the objectives are described: “The objectives of this study are as follows: 1. To assess the relationship between levels of mental pain and history of suicide attempts. 2. To evaluate the existing relationship between severity of mental pain and suicide attempt, independently from the symptomatic condition of the individuals. 3. To assess whether incorporating biochemical markers can enhance the accuracy of suicide risk screening.” Point 2 and point 1 are broadly overlapping. The only apparent difference is that the objective “2” takes into account the symptoms of psychopathology, arguably through a statistically adjusted model, while objective “1” considers only the “raw” association. As it is formulated, objective “3” seem to suggest that you used a model to predict suicide risk which includes the assessment of biochemical markers and then verified the accuracy of this prediction. As far as I understand, you rather explored the possible association between risk of suicide and biochemical markers. In addition to the objectives of the study, I would expect primary and secondary outcomes to be detailed. The “association between mental pain and suicide attempts” might mean different things. I understand that you will use “mental pain” as a continuous outcome, but this should be specified along with the rating scale on which you primarily rely to measure this variable. In general, I strongly advise to make a list of primary and secondary outcomes. Further, I strongly advise to be more precise in the wording. Objectives 1 and 2 refer to “suicide attempts” only (therefore, no complete suicides and no suicide ideation), while objective 3 refers to “suicide risk”. Are you referring to a broad/inclusive definition of suicide? In this case, the term “suicidal behavior” (which include ideation, attempt, and death by suicide) should be advised.

Obiettivi riformulati in modo più chiaro

p. 30: Sample. Do you mean that they were referred to the UOP of Varese from the CPS and the specialized outpatient clinic? Please rephrase to increase clarity. *Riformulata*

“[...] homogeneous in clinical and sociodemographic characteristics”. This consideration pertains to the results/discussion sections. *Ok*

p. 30: Tools. If understood correctly, such tools were administered only at baseline, and not at follow-up, as the information on suicidal behavior was derived from clinical records and from the psychiatrist in charge for the case. Is this correct? I strongly suggest making this clear in the text *fatto*

p. 33: I suggest to specify that biological markers were collected under ordinary clinical routine, so to make clear that participants did not undergo laboratory assessments which were not consistent with normal practice *fatto*

p. 34: Statistical analysis. The main limitation here is that you performed only univariate binary analyses. At least for the primary outcome I suggest to set up a multivariable model in order to adjust for possible confounders (age, sex, symptoms of depression and anxiety, previous suicide attempts, duration of disease, type of core diagnosis, etc.). *Non applicabile per numerosità campionaria ridotta. Come spiegarlo allo statistico che si è occupato delle analisi, introducendo altre variabili la numerosità del campione con è sufficiente e vengono violati gli assunti della regressione. Su sua indicazione l'ho comunque aggiunto nei limiti.*

p. 34: If I understand correctly, the study was not formally submitted to the local Ethics Committee? Apart from signing an informed consent, did the participants sign also a privacy consent to allow an anonymous use of their data for scientific purposes? *Si, la frase dove è specificato è la seguente: "signing of an informed consent for the use of data anonymously for research purposes", nei criteri di inclusione. L'ho riportato nuovamente nella parte sulla protezione dei dati per maggiore chiarezza e completezza.*

Results

I think that the main issue here is that you describe a number of variables and analyses, without giving preference to one over another, while one would expect the primary outcome to be addressed first. In general, I noticed that sometimes you reported decimal separated by a comma and some other times by a point. Please revise and make consistent throughout the text. *Fatto*

Tables look a bit blurred. Can you insert the table within the text, rather than an image? *Fatto*

p. 36: I would suggest including a table with the main socio-demographic variables. *Ho preferito riportare in tabella solo le variabili statisticamente significative, per non appesantire eccessivamente il lavoro con troppe tabelle non essenziali. I riferimenti sono comunque presenti nel testo.*

P. 37: Table 3: I suggest to re-order diagnoses according to their frequency. If you use acronyms, there should be a legend in the caption or as a footnote. *Fatto.*

p. 38: "[...] incongruous ingestion of drugs [...]". It might be worth specifying "prescribed" drugs, or "medications", as opposed to "psychoactive substances". *Fatto.*

Figure 8: Interesting that no significant differences between groups emerged according to the HAM-D, while the BDI-II shows some differences. Some reasoning about this point should be included in the discussion. *È già presente nel testo della discussione, al quale si rimanda.*

Discussion

p. 45: "This longitudinal study aimed to evaluate the role of mental pain in predicting effective suicide attempt and its interactions with other sociodemographic, clinical, and psychometric factors, [...]". I think that the binary analysis actually prevents from exploring such interactions, which a multivariable model might address. *Vedere risposta sopra. Ho comunque chiarito il limite nell'apposita sezione.*

In this section, the candidate discusses each variable that has been analyzed, providing references from available literature. I suggest to maintain a more consistent structure throughout the text, discussing whether an association, or a lack of association is in line with what we already know from available evidence. Thereafter, known or novel theoretical grounds might be discussed. It seems to me that the sentence "further research is needed" is too widely used, while for at least some variables we might have a rather relevant amount of evidence. *Tolte le ripetizioni*

The Discussion mirrors the major problem of the Results, which is that the primary objective of the study is not prioritized. *Gli obiettivi sono stati riformulati*



p. 47: I see many typos and grammatical errors, including excessively articulated sentences. Please revise the whole text to improve written English and rephrase were needed. *Ok*

“In this study, the suicide risk was also assessed over time, specifically in the 6 and 12 months following patient recruitment”. The 12-months follow-up is mentioned only in the Abstract and in the Discussion, while it does not appear in the Methods section. Please revise. *Avevo omissso un dettaglio importante che ho ora inserito sperando di aver reso il tutto più chiaro.*

p. 47: “[...] the tools listed above (C-SSRS, BDI, BHS, PAS) were statistically significant [...]”. Please be more precise, e.g. the score obtained at the tools was statistically associated with [...] *ok*

p. 48: “Regarding biochemical markers, no significant association with suicide was found, mainly due to the difficulties in retrieving tests result that were univocally related to the suicide attempt”. This sentence is of unclear interpretation, please consider rephrasing. *Fatto*

In this last paragraph, I do not seem to discuss the results of your analysis, i.e. whether you found that those individuals attempting suicide were at higher risk of showing altered biomarkers. *Ho rielaborato il concetto per renderlo più chiaro.*

In general, the paragraph on limitations and strengths is too short, while it should stimulate a thorough critical appraisal of results. This should be expanded and developed according to the various issues raised above *ok*

p. 49: “The results of this study suggest that the scores obtained from the C-SSRS, BHS, BDI-II, PAS, and OMMP scales can be useful tools for primary care physicians [...]”. I am not convinced that results from this study point in this direction. The study was conducted in a specialized setting, so the main implications should regard this environment, although possible applications to primary care can be hypothesized and their pros and cons discussed. According to my clinical experience, such a set of rating scales pertain more to specialized setting rather than primary care, where colleague might lack expertise in this field, and might find simpler instruments more appropriate. *Non era da intendersi tutta la batteria di test ma solo le scale autosomministrate risultate significative, ho cercato di rendere più chiaro il concetto e spostato nelle conclusioni.*

Among major shortcomings, please consider what discussed above throughout the revision. Additionally, I would highlight the following methodological issues: - Adverse childhood events have not been evaluated, although there is strong literature in support of their possible role as predictors of both mental pain and suicide behaviors. This should be discussed among limitations; *essendo la proposta di lavoro quella di fornire strumenti di screening, escludo che una tematica tanto delicata possa essere affrontata nel breve spazio di una visita somministrando questionari dedicati. Questa affermazione deriva dall'esperienza diretta di reclutamento di pazienti per un altro studio a cui il nostro centro ha partecipato in passato e che ha prodotto nei pazienti uno stato di disagio psichico laddove tale indagine non era giustificato da motivi clinici. Nelle cartelle dei Servizi dell'U.O. questo dato non è, purtroppo, riportato in anamnesi e va dunque chiesto esplicitamente al momento della valutazione. Tuttavia, potrebbe essere utile considerarlo tra i fattori di rischio anamnestici, qualora il clinico ne fosse a conoscenza. Inserisco comunque queste considerazioni nella sezione limiti.*



The statistical analysis consists in binary regressions, but a multivariate analysis was not performed. *Non applicabile. Vedere risposta sopra. Inserito nei limiti.*

You describe the study design as longitudinal. Can you be more precise? It seems to me that this is a cohort study, as you identify exposed individuals (or rather the degree of exposure to mental pain) and follow them up for 6 months. The conceptual issue here is that there is not a clear temporal "starting point" for this exposure. You measure this exposure at baseline, but it is not clear since when individuals have been exposed. If you should conduct a multivariate analysis, an adjustment for illness duration might be relevant, as this might be reasonably considered as proxy of the duration of mental pain; *Il dolore mentale non è un disturbo psichiatrico codificato come può esserlo il disturbo depressivo maggiore o il disturbo d'ansia, ma piuttosto una condizione esistenziale. Non è quindi possibile stabilire un inizio o una fine a meno che i pazienti non vengano sottoposti a dei test di misurazione regolarmente, cosa che non viene fatta abitualmente nella pratica clinica. Dunque, non si può parlare di "individui esposti" al dolore mentale e il campione non è stato selezionato in base alla presenza/assenza di dolore mentale (che non è possibile stabilire a priori basandosi soltanto sulla base dell'impressione clinica). Rispetto al secondo punto (mutivariata), rimando alle precedenti risposte rispetto al medesimo quesito.*

One might argue that I could have formulated a hypothesis on the primary outcome, such as how do expect mental pain to increase the risk of suicide attempt? To what extent? As there is literature on this matter, one might even attempt a calculation of the sample size required to detect the expected effect. *Credo che questo, per quanto interessante, avrebbe allontanato dallo scopo principale del lavoro, ovvero fornire un metodo il più semplice, rapido e pragmatico possibile (dunque applicabile nel real world) per identificare i pazienti a rischio suicidario da indirizzare a percorsi di prevenzione mirata. Un approfondimento di questo tema potrebbe essere lo spunto per un altro lavoro ma ci terrei che il presente rimanga il più possibile fedele all'obiettivo clinico da cui è nato.*

La ringrazio per gli innumerevoli spunti di miglioramento forniti, credo che ora l'elaborato si presenti notevolmente migliorato. Ha inoltre fornito suggerimenti interessanti per altri lavori futuri e la ringrazio anche per questo.

Cordialmente,

Dottorando

dott.ssa Giulia Lucca



UNIVERSITA
di VERONA

Dipartimento
di **NEUROSCIENZE,
BIOMEDICINA E MOVIMENTO**



Verona, 06/03/2024

Dear Committee,

the candidate Dr. Giulia Lucca replied to all the comments I provided and made extensive amendments to the manuscript of the PhD thesis.

I believe that the work is now sufficiently improved to undergo the thesis defense. I remain available for any further inquiry.

With best regards

Dr. Giovanni Ostuzzi, MD, PhD

Department of Neuroscience, Biomedicine, and Movement, University of Verona

A mio marito

A mia madre

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ABSTRACT

Background: Suicide is one of the main causes of death globally. According to modern suicidology, the greatest risk factor would be represented by high levels of mental pain, described as an unbearable subjective experience which the person wishes to end by any means, including death. Available literature on this topic have highlighted a relationship between suicidal ideation and mental pain, but no study has yet clarified the clinical link between mental pain and the risk of a concrete attempted suicide (AS). Mental pain is a construct that can be measured through psychometric scales of simple and rapid use and therefore potentially usable also by non-psychiatrist specialists.

Purpose of the study: primary objective of this work is to establish whether the measurement of mental pain is actually predictive of SA and to propose the measurement of the same as a large-scale screening tool.

Materials and methods: The sample consists of 179 adult patients, recruited at the psychiatric services of Varese, and suffering from psychiatric diagnoses coded according to the DSM-5-TR. After obtaining informed consent, patients were evaluated at the T₀ through the collection of socio-demographic and clinical data and through the administration of the following psychometric tools, aimed at evaluating the presence of mental pain, hopelessness, anxiety, depression and suicidal ideation: Psychache Scale (PAS), Orbach Mental Pain questionnaire (OMMP), Beck Hopelessness Scale (BHS), Hamilton Depression Rating Scale (Ham-D), Hamilton Anxiety Rating Scale (Ham-A), Columbia Severity Rating Scale (S-CSSRS). After 6 month (T₁) and 12 months (T₂), through the analysis of the hospital and territorial databases, The AS occurring in the follow-up periods were recorded and were then correlated to the parameters collected at baseline, using Cramer's V test, linear regression for the quantitative dependent variables and binary logistic regression for the dichotomous qualitative dependent variables. The quantitative variables were processed with the Kolmogorov Smirnov test to evaluate normality; the variables found to be non-parametric were then analyzed with the Mann Whitney and Kruskal Wallis tests. Furthermore, laboratory data from blood tests of patients with AS were compared with those of the general population.

Results: During the T₁ follow-up period 24 out of 179 subjects made an AS, while only two attempted suicide at the second follow-up (T₂). For this reason, only the first follow-up (T₁) was taken into consideration for analyses. For all the variables investigated, the two groups of AS and non-AS patients were then compared. Regarding the socio-demographic variables, only the employment status presents a statistically significant difference between AS and non-AS patients ($p < 0,001$). Marital status appears to be protective compared to other conditions (unmarried, divorced and widowed; $p < 0,05$). Regarding age, gender, education level, medical conditions or family history of mental illness, no statistically significant association was found with AS. No statistically significant differences were observed for primary psychiatric diagnosis. The absence of comorbidities is associated to a lower risk of AS ($p < 0,05$). While the presence of substance abuse history increases the probability of AS ($p < 0,001$). A significant association was found between suicide attempts and assumption of antipsychotic therapy ($p < 0,05$) and mood stabilizer therapy ($p < 0,05$), while no significant association was found for antidepressant and anxiolytic therapy. A

previous AS is related with an increased probability of carrying out a new AS ($p < 0,05$). Regarding biological markers, no statistically significant indicators of suicide attempt were found. However, most of the patients showed altered biochemical results at the routine tests done after the suicide attempt. Regarding association between the analyzed scales and attempted suicide, subjects who attempted suicide during the follow-up period show higher scores at all the psychometric scales; however, only the BDI-II, PAS, BHS and C-SRSS scores achieved statistical significance. No clear association with mental pain scales was identified at 12 months, while several scales (C-SSRS, BDI, BHS, PAS) were statistically significant at 6 months in detecting patients with a higher suicide risk ($p < 0,05$).

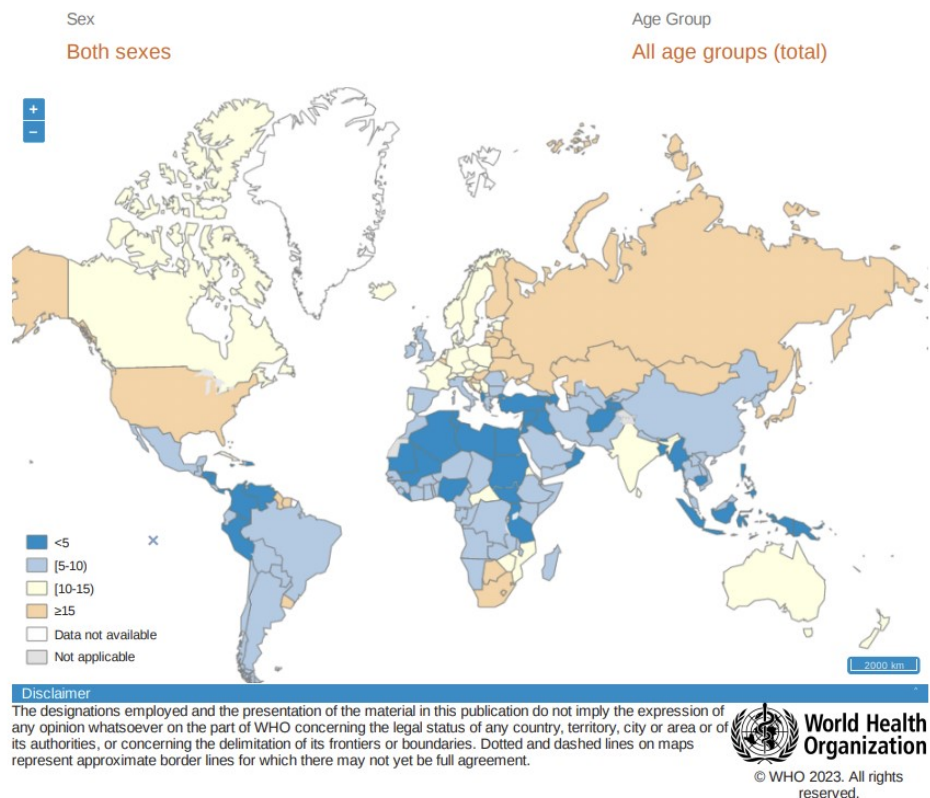
Discussion: Among all the evaluation tools BDI-II, BHS and PAS showed a good predictivity of suicide risk, especially in short term (6 month) and characteristics of good applicability. This makes them potentially useful tools as a method of screening for suicide risk in psychiatric outpatients.



1. INTRODUCTION

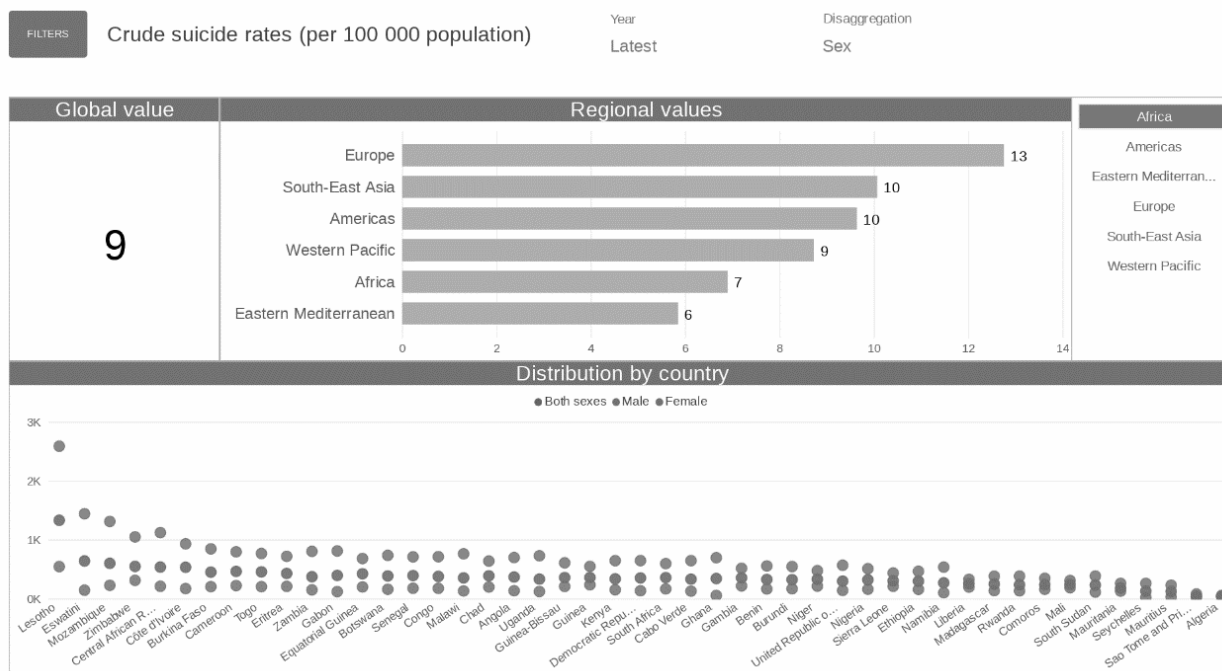
1.1. SUICIDE EPIDEMIOLOGY

As of today, data from the World Health Organization (WHO) shows that in a year there are almost 700.000 suicides globally, whereas suicide attempt are 20 times more frequent. Suicide is the 18th leading cause of death, but the fourth one among 15-29 years-olds globally (WHO 2021).



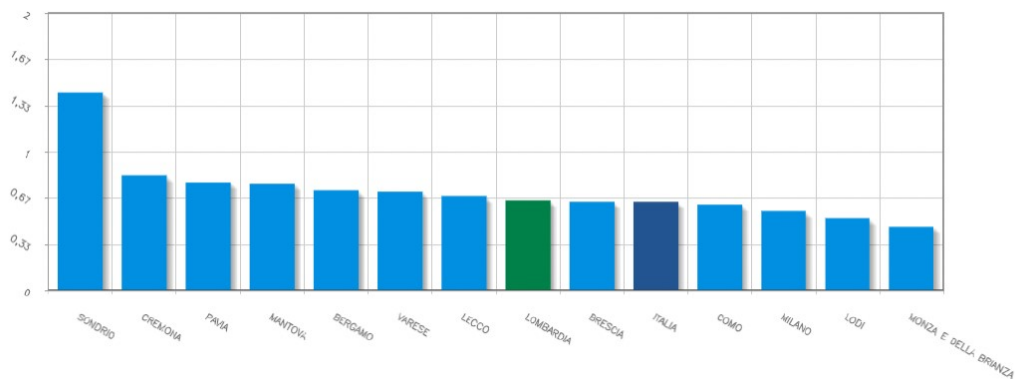
[Fig.1] crude suicide rates per 100 000 population (WHO 2021)

[Fig.1] and [Fig.2] show suicide rates globally, as of the last WHO data. 79% of suicides occurs in low and middle income and the 60% occurs in Asia; data relative to many countries are only an estimate, as not all countries have a national system for registering deaths. Moreover, literature from those countries seems lacking and it is difficult to elaborate precise epidemiological estimation (Guzman et al., 2019).



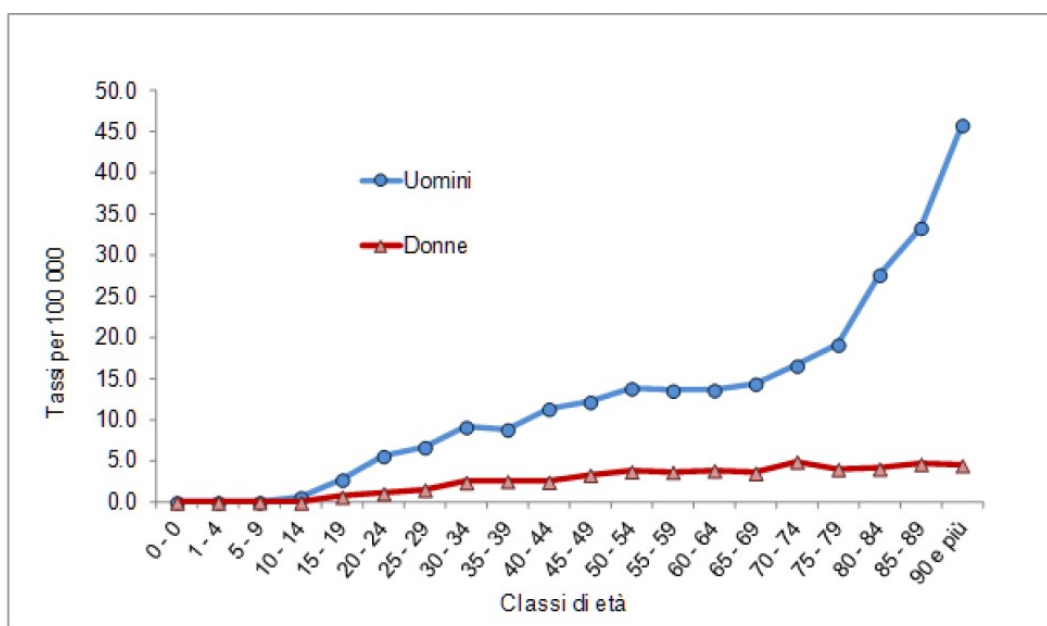
[Fig.2]: global suicide rates (WHO 2021)

As for Europe (UE), 13 death every 100 000 inhabitant are suicides. Lower standardized mortality rates were registered in Cyprus (4 per 100 000); Greece, Malta, Italy, UK, Spain and Slovakia have registered relatively low results, inferior to 8 deaths per 100.000. Between countries of the European Free Trade Association (EFTA) and candidates a low result was found in Turkey (2 per 100 000). In Lithuania there's a high incidence of 26 per 100 000, two times UE average. Suicide rates in Europe have been progressively decreasing, probably due to the efforts made in prevention programs. According to ISTAT estimates, the decrease in the suicide rate in Italy from 1995 to today is around 14% (going from 8.1 to 6.3 per 100,000 inhabitants), a reason for hope for the future, but also demonstrating how a constant commitment on the subject is still necessary. Rates increase with age, from 0.7/100.000 in adolescents to 10.6/100.000 in the elderly, with 4 times higher rates in males. Highest rates have been found in the northern region in Italy, whereas the lowest rates are found in Southern Italy. However, Sardinia is an exception for the insular area since its mortality rate for suicide is one of the highest in the country (ISTAT, 2016). These differences may be in part due to socio-cultural differences: the protective value of family and the strength of relationships represent one of the most important resources against the vulnerability showed when the social net collapses (EpiCentro, 2017). On the other hand, a wide social net translates in a better integration and a lower sense of loneliness, discouraging self-harm in the individual. Nevertheless, in regions affected by lower income and higher job insecurity, the average suicide age is lower and this is alarming; moreover, discrepancies in the socio-sanitary services is to be considered. [Fig.3] shows mortality rates for suicide in 2015, as for the *Annuario Statistico Regionale*, in the provinces of Lombardy.



[Fig.3]: Mortality rates for suicide in Lombardy in 2015 (Annuario Statistico Regionale)

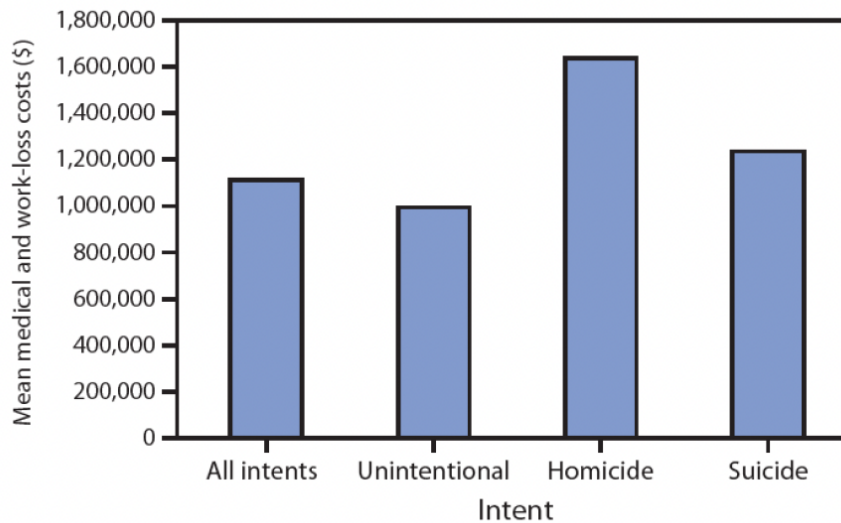
Suicide is a phenomenon in which differences in gender and age are prevalent: as for WHO data for the year 2012, almost 800.000 people killed themselves and the global rate (standardized to the global population) is 11,4 per 100.000, with higher values, 15,0, for males in contrast with the 8,0 in females. Similarly, in Italy, death by suicide (almost 4000, 4,7 per 100000) shows differences related to gender (7,6 for males and 1,9 for females), while age shows increasing results with the increasing age (1,4 suicides per 100000 in people up to 24 years old, 10,4 in over 65). [Fig.4] shows suicide rates for gender and age in Italy, as for the year 2010.



[Fig.4]: suicide rates in Italy in 2010 (ISTAT)

As it is stated in the DSM-5-TR (APA, 2022), suicidal behavior disorder varies in prevalence and form across sex and gender. On average, suicides are about twice as common in men compared to women, although the prevalence ratio varies by country and cultural context. Estimates also vary because the intent of self-harm behaviors is not always clearly measured; however, suicidal behavior that does not result in death is more common in women than in men. Men generally use more violent methods such as gunshots and hanging, whereas less violent means such as self-poisoning are more common in women. The frequency of suicidal behaviors is higher in women (i.e., the average number of suicide attempts for a woman is generally higher than the average number for a man), but this could be

explained by the more frequent use of less lethal methods among women. Suicide rates among individuals who identify as transgender are high, and transgender individuals are also at higher risk for suicidal behavior than cisgender individuals (DSM-5-TR). Other risk factors for suicide may be low economic and socio-cultural level. A systematic review (Li et al., 2011) showed how a lower socioeconomic standard represents an independent risk factor for suicide, meaning even after having corrected for the presence of psychiatric illness; another work highlighted how a low level of instruction is a risk factor per se, even after correction for gender and age (Kim et al., 2016). As for the methods, hanging and suffocation (48,9%), precipitation (19,2%), and firearms (11,3%) have been the most frequent. Precipitation is the main method used by man over 65 years old, whereas younger patients are more inclined to jump from moving objects. Women most frequently choose precipitation, then hanging, drowning and poisoning (Eurostat 2016). An interesting work made by WHO showed how methods differ geographically: pesticide poisoning is very common in Asia and Latin America; drugs intoxication in the UK and northern Europe; hanging is most frequent in Oriental Europe and firearms in the US. In cities such as Beijing and Hong Kong, the most frequent method is precipitation (Ajdacic-Gross et al., 2008). There are also discrepancies between suicide and attempted suicide with the chosen method: hanging and stabbing are more frequent in complete suicides, whereas drug abuse is more frequent in attempted suicides (Lim et al, 2014). As for failed attempt, it seems that the chosen method can predict a subsequent complete attempt: a research, made in 2010, which compared methods for attempted suicides and complete suicides, showed that people who survived hanging and suffocation had a higher chance to try again and succeed; most of the subsequent complete suicides used the same method (Runeson et al, 2010). As for ISTAT data relative to year 2013, almost half the suicide happened at home. The share is higher if suicide is associated with mental illness (57%). In a considerable number of cases there are relevant comorbidities: mental illness in 13% and physical illnesses in 6% respectively. As for ISTAT almost one suicide in 5 may be attributed to these comorbidities, even if the association is not to be considered cause-effect (ISTAT, 2013). Frequency of the most relevant comorbidities is higher with age and in women (27% in women, 16% in men) and most are represented by relevant physical illnesses. As for the most frequently related mental illnesses, depression, psychosis, drug addiction, anxiety disorders, personality disorders, DCA and PTSD (Bachmann, 2018). In these researches, conducted between 2011 and 2013, of 2401 death from suicides, in 737 cases relevant physical illnesses have been found; between these, 288 presented also a mental illness (mostly depression). Moreover, in 1664 cases, there was only a mental illness reported, mainly depression or anxious disorder. In women there is a higher prevalence of mental illness in suicides in the age range 35-64 (23%, 12% in man) and in the range above 65 years old (20% versus 10%). 30% of suicides in association with physical illnesses take place in institutions (ISTAT, 2013). Suicide and attempted suicide have an enormous impact on families and friends of the victim, but there is also an economical cost for individuals, families, communities, states and institutions. These includes medical costs and loss of income for families. WHO and International Association for Suicide Prevention (IASP) in order to raise awareness on the phenomenon state that natural calamities and terrorists' attacks and all the war fought around the world cannot compare to the tragedy the suicide phenomenon consists at an international level. More than 97% of this cost is due to a loss in productivity, 3% is medical costs. The total cost of suicides and attempted suicides is estimated to be around \$93.5 billion (Shepard et al., 2015). [Fig.5] shows the socio-economic costs for cause of death in 2013: in the US we can see the elevated economic impact of suicide, more so if compared to other causes of violent death (Florence et al., 2015).



[Fig.5]: Costs of suicide in year 2013 in the USA

1.2 ETIOPATHOGENESIS OF THE SUICIDAL PHENOMENON – INTERPRETATIVE MODELS AND RISK FACTORS

Until recently, suicidal behavior wasn't included as a nosographic entity inside the Diagnostic and Statistical Manual of Mental Disorder. But this changed with the new edition, the DSM-5-TR, which added the phenomenon under the chapter *Suicidal Behavior Disorder* (criteria listed below). Moreover, DSM-5-TR contains a new text section for each diagnosis, "Association With Suicidal Thoughts or Behavior," when such information is available in literature. The information included is based on studies demonstrating associations of suicidal thoughts or behavior with a given diagnosis. These changes are quite belated but very necessary, since suicidal behavior is a reality very closely connected with the world of mental illness, as we'll discuss in another paragraph. It is possible that we've got this addition only with this new edition because even in the scientific landscape there is no agreement on the etiopathogenesis: from neuro-biological hypothesis, to more sociological ones. An hypothesis is that suicidal behavior is a highly complex phenomenon in its genetic, epigenetic and psychosocial aspects (Lennon, 2019).

1.2.1 BIOLOGICAL FACTORS

Neuroimaging and EEG

Functional and structural neuroimaging studies in adults that attempted suicide suggest that there can be anomalies in the volume of grey matter in cortical regions, as well as differences in neuronal circuits of the prefrontal cingulate gyrus and anterior-dorsal cingulate gyrus as compared to results in the control group affected from affective disorder without suicide attempt and as compared to healthy control (Martin et. Al, 2015). A recent systematic review (Bani-Fatemi et al., 2018), reviewed 45 scientific papers that inquired on the possibility of neuroimaging alteration in suicidal individuals. There have been reports of association of suicidal disorder and anomalies in the temporal and

frontal cortex. Some works identified anomalies in the EEG of patients with suicidal ideation as compared to healthy controls, mostly in the electric activity in the fronto-central cerebral region (Lee et al, 2017). In a study on patient with major depressive disorder (Dolsen et al., 2018) found, using EEG analysis during sleep, an increase in activity in rapid frequency, a decrease in delta activity and an increase on alpha-delta sleep in patients with suicidal ideation. This result was later confirmed with statistical correction for age, gender, depression and insomnia. This result may inquire that an overactivity of the CNS during sleep may be related to suicidal ideation.

Biological markers

Biological markers have been studied in the last decades as a potential red flag for suicidal behavior disorder. The research methods for biological markers range from brain morphological analyzes and autoradiographic methods to evaluate the functionality of brain receptors, up to the most recent molecular, genetic and epigenetic analyses. However, the quickest, simplest and cheapest method is certainly the dosages of markers in plasma or in cerebrospinal fluid (CSF). Focusing attention on these latter methods, we can observe how one of the first systems to have been investigated is the serotonergic one. In particular, decreased concentrations of 5-HT or 5- HIAA in the plasma have been reported in suicidal patients and it would appear that plasma 5-HT levels are not influenced by different psychiatric diagnoses (Kim & Lee, 2015). Similarly, several works have demonstrated that, although the platelet count does not differ between patients with suicidality and controls (both healthy and depressed), in patients with suicidality the platelet concentration of serotonin appeared to be reduced (Roggenbach et al., 2007). Another widely studied system is the Hypothalamic-pituitary-adrenal (HPA) axis. Basal plasma and CSF cortisol levels have been reported to be higher in individuals who attempted suicide, compared with healthy controls or depressed nonattempters (Chatzittofis et al., 2013; Jokinen & Nordstrom, 2009; Jokinen et al., 2010, O'Connor et al., 2020), while, nonsuppression in the dexamethasone suppression test (DST) significantly predicted future suicide in follow-up studies of depressed individuals and in previous attempters (Coryell & Schlessner, 2001; Jokinen & Nordstrom, 2008). With respect to neurotrophic factors it has been demonstrated how low levels of brain-derived neurotrophic factor (BDNF), both peripheral and cerebral, were correlated with suicidal behaviors in depressed patients (De Simone et al., 2022). Respect to lipid metabolism, it was been reported a significant associations between low serum cholesterol and suicide; in particular, risk of death by suicide was found to be more than 6-fold higher in individuals with serum total cholesterol levels in the lowest quartile, compared with those in the highest quartile (Ellison & Morrison, 2001). Baek and colleagues (Baek et al., 2014) further noticed significant differences in triglyceride levels between recent attempters and lifetime attempters with MDD. A recent meta-analysis (Li et al., 2020) demonstrated that lower concentrations of total cholesterol (TC) and LDL-cholesterol (LDL-C) were associated with attempted suicide in patient affected by major depressive disorder (MDD). This indicates that TC and LDL-C may be useful as biological markers for predicting whether MDD patients may attempt suicide. This finding is confirmed by other authors (Zhou et al., 2021). In the last decade, increasing attention has been devoted to the correlation between mental disorders and the inflammatory system. Black and Miller (2015), conducted a Meta-Analysis about the relation between suicidality and Cytokines and Chemokines levels. They found that cerebrospinal fluid levels of IL-8 were significantly decreased in patients with suicidality versus control subjects ($p < 0.05$). Furthermore, in vitro IL-2 production by peripheral blood mononuclear cells was significantly decreased in patients with suicidality compared with both patients without

suicidality and healthy controls ($p < 0.01$) and cerebrospinal fluid levels of IL-8 were significantly decreased in patients with suicidality versus control subjects ($p < 0.05$). The authors supported the possibility of distinguishing patients with suicidality from people without, by investigating these elements (Black & Miller, 2015). High levels of IL-6 appear to correlate with a greater risk of suicide (Fernández-Sevillano et al, 2022). Katon and co. described the biological profile of patients with increased suicide how characterized by increased levels of IL-6, lymphocytes, monocytes, WBC and PMN significantly impacted suicide risk, with the latter two inferring the strongest influence. The cytokine IL-8 was, instead, independently and negatively associated with increased suicide risk (Keaton et al., 2019). Elevated levels of C-reactive protein have also been identified as correlated with both high-lethality suicide attempts (Aguglia et al., 2022) and a lower response to antidepressants (Gasparini et al., 2022). Recent interest has been directed at other factors potentially promoting depression and suicide, such as low vitamin D levels (Somoza-Moncada et al., 2023; Mohammadi et al., 2023) and folic acid (Liwinski et al., 2023; Li et al., 2024), alteration of thyroid hormones (Tolosa et al., 2021) and PTH and calcium homeostasis (Ruljancic et al., 2013; Steardo et al., 2020). Most of the research has focused on values for which it is necessary to carry out accurate second-level investigations and therefore not very useful as risk predictive factors in daily clinical practice. Furthermore, many findings are common to different mental disorders and therefore not very specific and not very usable as predictive factors for suicidal risk (Franklin et al., 2016).

Genetic and Epigenetic factors

In a study that inquired about suicide in twins (Roy, 1995), it was observed that the concordance rate was higher in the sample of monozygotic twins compared to the dizygotic ones. Genomic analysis identifies some loci as potentially implied, inter alia the gene that codified for tryptophan hydroxylase (TPH) and the gene that codified for serotonin transporter 5 (5-HTTLPR) (Anguelova et al, 2003; Cuortet et al., 2004). Some polymorphism in the promoter region 5-HTTLPR seems to be involved in a higher vulnerability to suicidal risk in patients that were abused during childhood (Roy et al, 2007). The serotonergic system is the most studied one, both for suicidal ideation and impulsivity and aggressive behavior. Reduced level in 5-HIAA, final product of serotonin metabolism, found in the liquor of dead subjects may suggest a correlation between reduced activity in serotonergic system and suicidal tendencies (Sadkowsky et al., 2013). Moreover, the noradrenergic pathway showed alteration in suicidal subjects: low levels of noradrenalin metabolite in liquor have been found in depressed patients, in hetero-aggressive subjects and in complete suicides (Placidi et al., 2001). Epigenetically, two of the most relevant mechanism have been inquired: DNA methylation and histone acetylation, in order to highlight if there were changes related to childhood trauma (major trauma, abuse, neglect). Both major trauma, sexual and physical abuse, and neglect have been related to modification in genic expression and with elevated suicidal risk. A study identified a significant correlation between childhood sexual abuse and suicidal ideation, as well as an indirect correlation with increased pathologic anxiousness and psychological abuse in childhood (Yong-Chun Bahk et al., 2017). Childhood trauma correlates with suicidal ideation in both patients affected by mental illness and those who are not affected, but in a study (Roy & Janal, 2004) was found that female sex, childhood trauma, and a family history of suicidal behavior are each independent, and non-interacting, risk factors for attempting suicide. Additionally, female sex and high

childhood trauma are independent risk factors for both an early onset of first attempting suicide and for making more attempts. This was later confirmed by another study (Xie et al, 2018). Perroud et al. (2008) identified in a polymorphism a single functional nucleotide of gene BDNF (Val66Met) a correlation between childhood trauma and suicidal ideation in a sample of Caucasian ethnicity patients; in particular, sexual abuse in childhood was associated with attempted violent suicides in adult age in individual Val/Val and in individuals Val/Met or Met/Met, highlighting how trauma had a bigger impact in a pre-existing genetic vulnerability. Roy et al (2010) demonstrated how genes that regulate the hypothalamus pituitary adrenal axis (HPA) are implied in a correlation between childhood trauma a suicidal risk, suggesting how childhood trauma and FKBP5 may interact to increase the risk of suicidal behavior disorder. Gene silencing may therefore lead to an inadequate stress response from glucocorticoid receptors. Subsequent alteration of the hypothalamus pituitary adrenal axis may lead to a disfunction of cortisol activity, the main hormone in stress response. In a study on mice, McGowan and al. (2009) demonstrated how epigenetic state of the gene promoter of glucocorticoids receptor is regulated by parental care in the first stages of postnatal development and is susceptible to pharmacological intervention in the adult mouse.

1.2.2 PSYCHOSOCIAL FACTORS

The psychosocial risk factors for suicide are related to the individual's interactions with both the family context (abuse, loss, conflict) and the environmental context (Lee & Jung, 2006). Among the most important risk factors for suicide are traumatic events in childhood and adolescence, as well as the early loss of a parent or significant figure. If the loss of a parent occurred through suicide, the risk is increased (Paolucci et al., 2001; Christoffersen et al., 2003). The presence of conflicts, lack of family warmth, and disturbed relationships between parents and children are also associated with possible psychopathological conditions and increased suicide risk in childhood, adolescence, and adulthood (Kim, 2002). Similarly, episodes of bullying and exclusion from peer groups are important risk factors, especially in adolescence (Klomek et al., 2009). Stressful life events often precede suicides and suicide attempts, up to 80% of cases (Kolves et al., 2006). Among these, the loss of one's home, job or academic failure, unemployment, financial difficulties, the loss of important relational figures, or loss of health appear to be among the main risk factors that can catalyze suicidal ideation. The suicide of a family member is considered a high-risk factor for suicide, even in adulthood (Kim et al., 2006; Lee & Jung, 2006; Wilcox et al., 2010). Expanding the scenario from individual risk factors to socioeconomic ones, historically there has been a correlation between the typical consequences of economic crises (such as increased unemployment rates) and increased suicide rates. The correlation is difficult to demonstrate, but some examples that are reported occurred during the Great Depression in the United States, where the number of suicides increased while those caused by other illnesses decreased; even in Asia, in the last years of the decade, a large number of suicide cases were reported during the Asian economic crisis. In recent years, there has been an increase in requests for help from unemployed people with suicidal thoughts due to the economic crisis (Norström & Grönqvist, 2015). Recent studies have also linked factors such as isolation and unemployment, occurring during the current COVID-19 pandemic, to the increased rate of suicides that occurred during the lockdown and that still occur (Kawohl & Nordt, 2020; McIntyre RS, Lee, 2020). In summary, individual psychosocial risk factors such as trauma, loss, and family conflict, along with socioeconomic factors such as unemployment and

economic crises, are associated with increased risk of suicide. Social integration plays a decisive role, both at the level of the individual (for example, think of lonely elderly people) and at the cultural and ethnic level. Migration, with the consequent loss of one's cultural and relational context and the general social, cultural, economic, and health precariousness that results, represents a potentially risky condition for the development of depression and suicidal ideation. A recent systematic review, conducted by an Italian group (Forte, Buscajoni et al., 2019), analyzed literature on suicides in ethnic minorities from 1980 to 2017: some of the studies considered reported lower rates of suicide attempts, while others suggested higher rates of suicidal behavior and deaths among immigrants compared to the native population. Moreover, a positive correlation was found between suicidal behavior and specific countries of origin. For example, for women from Asian countries or sub-Saharan Africa, the risk of suicide appeared higher than other ethnic groups. The same study identified the following as risk factors for suicidal behavior among migrants and ethnic minorities: language barriers, concern for the family left behind in the country of origin, and separation from them, while lack of information on the health system, loss of status and social network, as well as levels of acculturation, were identified as possible precipitating factors of suicidal behavior. Overall, the results suggest that specific populations of migrants and ethnic minorities present a higher risk of suicidal behavior than native populations, as well as a higher risk of death by suicide. Non-trivial are also the phenomena of emulation, widespread especially among young people, known as "suicide epidemics" or the "Werther effect". In fact, the dissemination of suicide through media channels leads to an increase in suicides in the immediately following period, especially if the suicide has a high media impact, such as with well-known or famous individuals (Stack, 2003; Ju Ji et al., 2007; Bakst et al., 2019). Even if a suicide epidemic did not arise after all in relation to Goethe's novel (Jan Thorson et al., 2003), a quantitative review of 293 findings (Steven Stack, 2000) measuring the presence of either an entertainment or political celebrity suicide were 14.3 times more likely to find a copycat effect than studies that did not. Studies based on real stories as opposed to fictional stories were four times more apt to uncover an imitation effect. The medium of coverage was a significant predictor of copycat effects with televised stories being 82 percent less likely to affect suicide than newspaper-based stories. Some evidence was found for period effects, and stories were linked more often to the incidence of suicide attempts than suicide completions. In year 2017, linked with the release of Netflix television series *13 Reasons Why*, there was an increase in suicides among adolescents in the USA (Arendt et al., 2019; Niederkrotenthaler et al., 2019). Religion has been thought to be a protective factor against suicidal behavior, since most condemn it as a punishable sin, inter alia Christianity and Islam. A systematic review made in 2016 (Lawrence et al, 2016) analyzing 89 articles made in the last decade, with a goal of identifying what specific dimensions of religion are associated with specific aspects of suicide. It was found that religious affiliation does not necessarily protect against suicidal ideation but does protect against suicide attempts. Whether religious affiliation protects against suicide attempts may depend on the culture-specific implications of affiliating with a particular religion, since minority religious groups can feel socially isolated. After adjusting for social support measures, religious service attendance is not especially protective against suicidal ideation, but does protect against suicide attempts, and possibly protects against suicide. A study about depression in Chinese university student (Lew et al., 2019) found that the students' major risk factors for suicide were depression, anxiety, stress, and hopelessness, and the students' minor risk factors included orientation to happiness and coping mechanism (including self-distraction, self-blame and substance use). Notably, the presence of meaning in life had a positive effect on preventing suicide and acted as a protective factor, which suggests that it is important to identify risk factors as well as protective factors

relevant to the target population group in order to increase the effectiveness of counseling and suicide prevention programs. *Hopelessness* has been studied for long in the cognitive behavioral model as a predictive factor for suicide and suicidal tendencies. A recent study analyzed various coping styles, distinguishing between problem-focused coping (active coping, planning, interruption of maladaptive activities, concurrent activities, search for instrumental social support), emotion-focused coping (search for emotional social support, positive reinterpretation, acceptance, refuge in religion), and maladaptive coping styles (mental disengagement, behavioral disengagement, impulsivity, superstitious, negative, useless thinking, tobacco and substance use). The study found that patients hospitalized after a suicide attempt had a higher frequency of maladaptive coping styles (Bazrafshan et al., 2014). Conversely, the presence of good adaptation skills and high levels of resilience would appear to be protective against suicidal ideation even in the presence of high levels of anxiety and depression (Jung-Ah Min et al., 2015). The presence of valid levels of self-esteem also represents a balancing factor between stressful life events and suicidal risk (Johnson et al., 2010).

1.2.3 ENVIRONMENTAL FACTORS

In individuals with comorbid depression and alcoholism, greater serotonergic impairment may be associated with higher risk of completed suicide (Sher, 2004). Dopaminergic dysfunction may play an important role in the pathophysiology of suicidal behavior in alcoholism. Brain damage and neurobehavioral deficits are associated with alcohol use disorders and may contribute to suicidal behavior in persons with alcohol dependence or abuse. Aggression/impulsivity and alcoholism severity affect risk for suicide among individuals with alcoholism. Weaker gun state laws are associated with higher rates of suicide secondary to firearms (Alban et al., 2018), since it grants easier access to a mean of self-harm which is more associated to complete attempt and worse injuries. How having access to an “easy” mean of self-harm is correlated to an higher suicide rate of suicide was also shown in a study about British gas conversion: Between 1963 and 1975 the annual number of suicides in England and Wales showed a sudden, unexpected decline from 5,714 to 3,693 at a time when suicide continued to increase in most other European countries. This appears to be the result of the progressive removal of carbon monoxide from the public gas supply. Accounting for more than 40 percent of suicides in 1963, suicide by domestic gas was all but eliminated by 1975. (Clarke and Mayhew, 1988). A similar case was seen in the decrease of suicide by precipitation from the Duke Ellington bridge (O’Carroll, 1994): after the implementation of effective barriers, the number of suicides halved.

1.2.4 SUICIDE AND MENTAL ILLNESS

The new entity “Suicidal Behavior Disorder” has the following proposed criteria as per DSM-5-TR:

Proposed Criteria

- A. Within the last 24 months, the individual has made a suicide attempt.
Note: A suicide attempt is a self-initiated sequence of behaviors by an individual who, at the time of initiation, expected that the set of actions would lead to his or her own death. (The “time of initiation” is the time when a behavior took place that involved applying the method.)
- B. The act does not meet criteria for nonsuicidal self-injury—that is, it does not involve self-injury directed to the surface of the body undertaken to induce relief from a negative feeling/cognitive state or to achieve a positive mood state.
- C. The diagnosis is not applied to suicidal ideation or to preparatory acts.
- D. The act was not initiated during a state of delirium or confusion.
- E. The act was not undertaken solely for a political or religious objective.

Specify if:

Current: Not more than 12 months since the last attempt.

In early remission: 12–24 months since the last attempt.

[Fig.6]: *Suicidal Behavior Disorder proposed criteria (DSM-5-TR)*

The essential feature of Suicidal Behavior Disorder is a suicide attempt, which is a behavior undertaken with some intent to die, regardless of whether it leads to injury or medical consequences. Factors that influence the medical consequences of a suicide attempt should not be considered in assigning the diagnosis. Determining the degree of intent can be challenging, but markers of risk include degree of planning, the individual's mental state at the time of the behavior, recent discharge from inpatient care, or recent discontinuation of a mood stabilizer or antipsychotic medication. At least one suicide attempt must have been made for the criteria to be met, and the behavior should not have been initiated during a state of delirium or confusion. Currently, there are no clinical instruments or biomarkers that can predict suicidal behavior with sufficient accuracy to be useful at the patient level (DSM-5-TR). Suicidal behavior disorder is seen in the context of a variety of mental disorders, most commonly Bipolar Disorder, Major Depressive Disorder, Schizophrenia, Schizoaffective Disorder, Anxiety Disorders (in particular, Panic Disorders associated with catastrophic content and PTSD flashbacks), Substance Use Disorders (especially alcohol use disorders), Borderline Personality Disorder, Antisocial Personality Disorder, Eating Disorders, and Adjustment Disorders (DSM-5-TR). A meta-analysis of cohort and case-control studies that assessed suicidal ideation as determinant for completed suicide in both psychiatric and non-psychiatric adults (Hubers et al., 2018) stated that assessment of suicidal ideation is a priority in psychiatric patients. Expression of suicidal ideation in psychiatric patients should prompt secondary prevention strategies to reduce their substantial increased risk of suicide. An increased risk of suicide has been reported for psychiatric patients (Wasserman 2021). In several world regions, an underlying psychiatric disorder is reported in up to 90% of people who die from suicide, though this rate seems to be considerably lower in low- and middle-income countries (Vijayakumar, L. (2004). In a meta-analysis by Knipe and colleagues (Knipe et al., 2019), a mood disorder (e.g. Bipolar disorder and Major depressive disorder) was identified in 25% of people who died by suicide. Most of the psychiatric conditions associated with suicidality are mood disorders, alcohol and substance use disorders, borderline personality disorder, and schizophrenia. Comorbidity between different disorders is frequently associated with a higher suicide risk. A history of suicide attempts, feelings of hopelessness, impulsivity and aggression, adverse childhood experiences, severe psychopathology, and somatic disorders are common risk factors for suicide among psychiatric patients. Stressful

life events and interpersonal problems, including interpersonal violence, are often triggers. A comprehensive and repeated suicide risk assessment represents the first step for effective suicide prevention. Particular attention should be paid during and after hospitalization, with the first days and weeks after discharge representing the most critical period. Pharmacological treatment of mood disorders and schizophrenia has been shown to have an anti-suicidal effect. A significant reduction of suicidal thoughts and behavior has been reported for cognitive behavioral therapy and dialectical behavior therapy. Brief interventions, including psychoeducation and follow-ups, are associated with a decrease in suicide deaths (DSM-5-TR). Wasserman and colleagues (Wasserman et al., 2012) found in a study that an underlying psychiatric disorder is a major risk factor for completed suicide. Among affective disorders, Bipolar Disorder carries the highest risk of suicide, yet not all bipolar patients commit or even attempt suicide during their illness. While the general suicide risk factors also apply for Bipolar Disorders, there are several disease-specific risk factors as well which should be taken into account when evaluating suicide risk in case of patients (Gonda et al., 2012). Several research studies have indicated that suicide attempts are common in adolescents with SUD (substance use disorder), and that substance use is common in those seeking treatment for suicidal behavior. Vajda and Steinbeck in a retrospective review (Vajda and Steinbeck, 2000) of 112 adolescents (13–20 years old) who presented after a suicide attempt at an emergency department, found that 35% met the criteria for an alcohol use disorder and 27% met criteria for an SUD at the time of the attempt. Moreover, the study found that a diagnosis of alcohol abuse increased the risk of a repeat suicide attempt threefold, while a diagnosis of illicit drug abuse increased the risk of a repeat suicide attempt fourfold in the subsequent 12 months.

1.2.5 SUICIDE AND SOMATIC ILLNESS

Multiple pieces of evidence have shown that the risk of suicide is greater in patients with severe, disabling, and/or chronic somatic illnesses compared to the general population. It is reasonable to hypothesize that the idea of taking one's life may seem better than facing life in conditions of marked discomfort, pain, disability, and with the prospect of having to depend on others even for the most common daily tasks (Goodwin, Marusic et al., 2003; Balestrieri, 2013). The diseases that literature has identified as most frequently associated with suicidal behavior are epilepsy, multiple sclerosis, Huntington's chorea, AIDS, peptic ulcer, and cancer. However, other conditions may also be related to suicidal ideation, such as migraine, diabetes, and psoriasis in younger subjects (Balestrieri, 2013) and cardiovascular, pulmonary, and prostate diseases in older ones (Quan et al., 2002). In most cases, patients with somatic illnesses who attempt suicide also present concomitant psychiatric symptoms (Berman & Pompili, 2011; Balestrieri, 2013). In other words, it can be said that the correlation between severe somatic diseases and suicidal ideation is present in conjunction with other factors; however, the presence and severity of somatic pathology seem to represent an independent risk factor. Other extrinsic risk factors not to be overlooked include poor social or family support, financial difficulties and access to care, and poor consideration by healthcare professionals of actual and/or perceived distress (Kishi et al., 2001). Nevertheless, it is likely that, even in all these cases, other factors, essentially intrinsic, may play a role (e.g. personality and temperamental traits or pathological localization, as in the case of temporal epilepsy or brain tumors, etc.). COVID-19 is a systemic disease that can affect various organs of the body, not just the respiratory system. The available literature on suicide during the COVID-19 pandemic is limited to

mainly case reports. Fear of contamination, poor care for COVID-19 patients, financial hardship, lockdown, self-isolation, alcohol withdrawal, lack of access to educational resources, and stigma were the reasons reported for suicide. A systematic review (Farooq et al., 2021) showed that the pooled prevalence of suicidal ideation was 12.1%, but evidence was not consistent across studies. The prevalence of suicidal ideation was higher in the general population (11.5%) than what has been generally reported in literature. Factors such as loneliness and physical distancing measures appeared to be important contributory factors to suicidal ideation, but the evidence was not consistent across studies (Bryran et al., 2020). Evidence has shown that suicide rates in high-income and upper-middle-income countries have remained largely unchanged or declined in the early months of the COVID-19 pandemic (Pirkis et al., 2021). The long-term effects of social isolation on suicide rates are not fully understood. Although the literature is still lacking with regards to the correlation between COVID-19 infection and suicide, the correlation between COVID-19 and the development of psychiatric disorders has already been demonstrated. A cohort study published in *The Lancet Psychiatry* in 2022 (Taquet et al., 2022) showed that the risk of mood and anxiety disorders tends to decrease after two months from infection, while the risk of cognitive deficits, psychosis, and dementia remains high even after two years. SARS-CoV-2 virus can cause direct and indirect neuronal damage leading to neurovirulence (Han et al., 2021).

1.3 SUICIDE PREVENTION

Universal Prevention Plans

Multiple strategies have been studied in order to prevent suicide, mostly in adolescents and young adults since it is the second cause of death between age 15-24 at global level (WHO). In a 10-year systematic review (Zalsman et al., 2016) in the multitude of prevention strategies analyzed, some have been found having a better outcome than others. In particular, there are strong evidences that restricting access to lethal means (guns mostly) is associated with a decrease in suicide. The same as been found about pharmacological intervention such as antidepressants (both in adults and in children, with the drug of choice being an SSRI (fluoxetine). Lithium has been found effective in reducing the risk of suicide in people with mood disorders. Case studies have found electroconvulsive therapy a rapid relief of suicidal thought and therefore it should be considered in the early stages of the illness. Data support about the efficacy of psychotherapies is lacking. Follow-up in people who have attempted suicide is strongly recommended by data. Community and family-based intervention are not effective in preventing suicide in severely ill mental patients but should be considered in adolescent, since it is shown a promising effect on suicidal ideation. Plans with or without focus on specific populations (school, communities, etc.) have several advantages compared to the ones directed to the individual. Participation is usually higher since, for example, every student is involved in sessions for understanding the problematics. These plans may have an effect in subjects already at risk that subsequently know how to ask for help.

- **Events for the community:** these are some examples: *Chooselife Plan* (Scotland) a ten years' national strategy and action plan to prevent suicide in Scotland. The strategy includes a target to reduce suicide by 20% by 2013 and progress towards this target can be viewed in the statistics section of the website. It involves advertisement in cabs, undergrounds, and stadiums, with messages such as: "Suicide: don't hide it, talk it";

Race for Life (Italy), was a running event meant to raise awareness and promoted by IASP International Association for Suicide Prevention, that was held the 10th of September, World day for Suicide prevention.

- **Environmental prevention:** noteworthy initiatives involve interventions aimed at protecting bridges and tall buildings, which unfortunately are often used for jump suicides. In general terms, the programs of various governments have provided for the installation of barriers or safety nets to make it more difficult to lean out, as well as the placement of nets to prevent impact with the ground (Beautrais 2001; Bennewith, Nowers et al., 2007; New York State Bridge Authority 2008; O'Carroll and Silverman 1994). The effectiveness of these measures is demonstrated by various interventions: the installation of a safety net at the Bern Muenster Terrace in Switzerland eliminated suicides from this location (and there is no evidence that individuals have replaced it with another less protected site) (Reisch and Michel 2005). Conversely, the removal of safety barriers at the Grafton Bridge in Auckland, New Zealand, had led to a five-fold increase in the number of suicides from this location (Beautrais, 2001): the new installation of barriers then discouraged potential suicides, again without apparent replacement with another location (Beautrais and Gibb, 2009). These same authors have described similar evidence for several other places where protective barriers have been installed. In addition to protective barriers, it has been observed that placing signs on bridges (but also near subway and railway tracks) that indicate telephone numbers or boxes containing a phone that allows direct contact with teams responsible for assisting people in crisis has reduced the number of suicides in those areas (Pompili, 2013).
- **Internet and mass media:** Evidence continues to amass on the significant impact of media coverage on suicide. Research literature on the impact of news reports of nonfictional suicides as well as fictional suicide stories is reviewed in order to determine the nature and scope of the influence of the mass media on suicide. This is what is called the Werther Effect. Recommendations are presented for the reporting of suicide stories, which may minimize the risk of imitative suicides. The media's positive role in educating the public about risks for suicide and shaping attitudes about suicide is emphasized (Gould, 2001). On the internet, there are several sites that offer notion and advise for suicidal people (www.prevenireilsuicidio.it, www.suicidology.org, www.befrienders.org e www.prevenireilsuicidio.it), providing also numbers that can be called for support. On the other hand, it is quite easy to find sites that encourage suicide, as it was shown in recent research (C. De rosa et al., 2022), with vast majority of the websites providing information on how to commit suicide and promote or encourage suicide if searched for it. Only few sites have preventive or deterrence information. The pro-suicide websites appear first in search results and, therefore, are more accessible.

Selective prevention plans

- **Prevention plans in schools:** both intended to educate teachers and caregivers (Beautrais et al 2007), and to screen students for potential risk, with screening programs such as the Teen Screening Program. Deserves mentioning also the plan CARE (Care, Assess, Respond, Empower) and SOS (Signs of Suicide) (Pompili, 2013).

- ***Prevention in Family Medicine:*** usually the family doctor is the first specialist a person in need tends to contact (Luoma et al., 2002). Since it might be difficult for a family doctor to assess and respond the suicidal behavior of a patients, it might be advisable having professional connection with a psychiatrist (Pompili, 2013).
- ***Centers for suicide prevention and helplines:*** the first center for prevention was based in Los Angeles and founded in the fifties by Shneidman, Farberow and Litman. In Italy there's a center of reference in Rome, directed by prof. M. Pompili (Pompili, 2013). Usually there are also dedicated helplines that are available 24/7, assuring anonymity and a non-judgmental listening medium (Letster, 2010).

1.4 ASSESSING SUICIDAL RISK

In the assessment of suicidal risk, American Psychiatric Association (APA, 2003), states that professionals usually use two screening instruments: the Ask Suicide-Screening Question tool or the Columbia-Suicide Severity Rating Scale, but, as it was suggested by Craig Bryan, PsyD, ABPP, who directs the Suicide Prevention Program at The Ohio State University College of Medicine, these tools may ask the wrong questions. “The traditional approach is to think about suicidal ideation as the gateway to suicidal behaviors,” said Bryan, author of *Rethinking Suicide: Why Prevention Fails, and How We Can Do Better* (Oxford University Press, 2021). “But there's increasing recognition that there are different trajectories toward suicide.” Some people may progress through the sequence in a matter of hours; others may not follow the sequence at all. Maurizio Pompili, who directs the prevention services at national level in Italy, suggested that the following mental scheme may be a valid way to assess red flags for suicidal risk for the clinician (*Table 1*).

Valutazione del rischio di suicidio
<ul style="list-style-type: none"> • Identificare i vari fattori che contribuiscono alla crisi suicidaria; • Condurre una valutazione psichiatrica completa, identificando i fattori di rischio e fattori di protezione distinguendo quelli modificabili e quelli non modificabili; • Chiedere direttamente sul suicidio; • Determinare il livello di rischio: basso, medio, alto; • Determinare il luogo e il piano terapeutico; • Indagare l'ideazione suicidaria presente e passata così pure intenti, gesti o comportamenti suicidari; indagare sui metodi usati; determinare il livello di hopelessness, anedonia, sintomi ansiosi, motivi per vivere, abuso di sostanze, ideazione omicida; • Segnali d'allarme: esprimere sentimenti suicidi o riferirsi al tema del suicidio; disfarsi di cose di valore, sistemare affari in sospeso, fare un testamento; segni di depressione: umore triste, alterazione delle abitudini del sonno e dell'appetito; cambiamento di comportamento (scarso rendimento scolastico o lavorativo); comportamento ad alto rischio (<i>high-risk behavior</i>); aumento del consumo di alcol o droghe; perdita di interesse nell'aspetto esteriore; isolamento sociale; sviluppare un piano specifico per il suicidio.
Porre attenzione ai segnali che denotano rischio di suicidio imminente:
<ul style="list-style-type: none"> • parlare del suicidio o della morte • dare segnali verbali come "Magari fossi morto" o "Ho intenzione di farla finita" oppure segnali meno diretti come "A che serve vivere?", "Ben presto non dovrai più preoccuparti di me" e "A chi importa se muoio?" • isolarsi dagli amici e dalla famiglia • esprimere la convinzione che la vita non ha senso e non ha speranza; • disfarsi di cose care; • mostrare un miglioramento improvviso e inspiegabile dell'umore dopo essere stato depresso; • trascurare l'aspetto fisico e l'igiene <p>Con riferimento, agli anziani, ma non esclusivamente ad essi:</p> <ul style="list-style-type: none"> • mettere da parte farmaci • comprare armi • esprimere un improvviso interesse oppure perdere un interesse per la religione
<ul style="list-style-type: none"> • trascurare attività quotidiane di routine • fissare un appuntamento medico anche per sintomi lievi <p>Con riferimento ai giovani ma non esclusivamente ad essi:</p> <ul style="list-style-type: none"> • cambiamenti di umore improvvisi e cambiamenti di personalità • indicazioni di problemi di salute, escoriazioni, ferite, faccia contusa a causa di abusi o percosse nell'ambito di frequentazioni; • improvviso deterioramento dell'aspetto fisico • autolesionismo • reiterazione di discorsi di morte e violenza • problemi alimentari associati a cambiamenti repentini di peso (a parte quelli associati a diete sotto controllo medico) • problematiche dell'identità di genere • depressione

Table 1: *Suicidal Risk Assessment – italian version (Pompili, 2013)*

It is useful to openly investigate with the patient not only the themes related to suicidal ideation but also the motivations underlying it: ask what life means to the person in question, if there is something that interests them, what they think will happen to them in the next 24 hours, the next month, if they have plans for the future, if they have resources (friends, family) that can support them. The patient's expectations regarding death and the chosen method (lethality) can also help distinguish people with a higher risk. A history of attempted suicide represents the main risk factor, but symptoms and signs such as aggression, directed violence, impulsivity, lack of hope, agitation,

psychological anxiety, fear, apprehension, anhedonia, insomnia, and panic attacks are frequently associated with suicidal risk. One of the key elements in studying suicidal behavior is the definition of "suicide attempt": under this label, in fact, a series of behaviors are included that, in most cases, differ from the real meaning of the term. According to the definition of the World Health Organization (WHO), a suicide attempt is "an unusual act with a non-fatal outcome, in which an individual deliberately initiates an unusual behavior, without the intervention of others, in order to cause harm to oneself or ingests a substance in excess of the prescribed dose to cause physical consequences" (WHO, Working Group on Preventive Practices in Suicide and Attempted Suicide, 1986). The fact that suicide attempts often include non-lethal methods and have a non-fatal outcome leads to the erroneous belief that these are manipulative gestures or requests for attention. However, this interpretation leads clinicians to not take the assessment of suicide risk seriously in these patients. In analyzing the spectrum of suicide, we observe at one extreme the action without the intention to die and at the opposite extreme the lethal intention that results in death (suicide attempt). In this context, it becomes necessary to distinguish the real intention behind the gesture: those who actually wanted to die and survived against their will (the chosen method of suicide did not work as expected, chance external interventions), from those who did not really have the intention of dying (think of patients who take high amounts of sedatives to sleep, and who may then experience unforeseen complications due to various interactions, sometimes with fatal outcomes). In this perspective, "suicide attempt" should be reserved for those who really wanted to die but survived due to unforeseen circumstances. However, even with this definition, we have a very heterogeneous population ranging from mild to very serious outcomes, all classified as "suicide attempts". To this definition, an analysis of the lethality of the gesture should be associated, distinguishing between "low lethality suicide attempts" and "high lethality suicide attempts". In an attempt to clarify the classification and nomenclature, guidelines were drawn up (Silverman, Berman et al., 2007a; Silverman, Berman et al., 2007b) proposing two categories:

- Suicidal gesture
- Suicide attempt

The first definition includes those people who make gestures whose lethality is too low to refer to a properly defined suicide attempt (for example, patients who increase the dosage of drugs they are already taking by 3-4 tablets, patients who take 2 or 3 aspirins, etc.). These individuals are still dealing with a problem and present a disturbed state, but they do not plan to die. The suicide attempt, on the other hand, according to the new nomenclature, is defined as "a potentially harmful behavior with a non-lethal outcome for which there is, both implicitly and explicitly, the intention to die." If the intention to die is present, a distinction is made between:

- Suicide attempt type I (no injuries)
- Suicide attempt type II (with injuries)

regardless of the severity of the injury or the lethality of the method. What makes the distinction, therefore, is the presence of intention and not the outcome of the act.

1.5 PSYCHACHE AND SUICIDE PREVENTION

1.5.1 THE DEFINITION OF PSYCHACHE

Breakthrough in understanding the suicidal mind was made by Edwin Shneidman, father of Suicidology, with the assessment of the importance of the concepts of Psychache and Hopelessness (Shneidman 1993). Comparing farewell letters written by suicide victims and fake farewell letters, he understood that it wasn't only diagnosis and context making the difference between the two, but also psychache, or mind's torment. Shneidman (1996) coined the term "psychache" to describe this pain: "Psychache is the hurt, anguish, or ache that takes hold in the mind ... the pain of excessively felt shame, guilt, fear, anxiety, loneliness, angst, dread of growing old or of dying badly". Shneidman identifies the roots of psychache in shame, guilt, anger, loneliness, despair, all of them originating by neglected psychological needs. This leads the suicide victim to think of the suicidal act as the only remedy. Shneidman defines suicide as a sort of "multidimensional malaise" to become a "self-induced annihilation" for those individuals who, having first "defined an issue" view this act as "the best solution" to their predicament (Shneidman, The Definition of Suicide, 1985). Shneidman also identified common elements in at least 95% of suicides and named them "Commonalities of suicide" (Shneidman, 1996), shown in the following *Table 2*.

Tabella 2: Commonalities of Suicide" (Shneidman, 1996)

Lo scopo del suicidio è trovare una soluzione; non si tratta mai di un atto afinalistico
Il fine del suicidio è quello della cessazione della coscienza, ovvero della sofferenza
Lo stimolo al suicidio è il dolore psicologico e la volontà di sfuggirgli
Lo <i>stressor</i> comune nei suicidi si riferisce ai bisogni psicologici insoddisfatti
Lo stato emotivo dei soggetti suicidi è riferibile all'hopelessness-helplessness
Lo stato cognitivo tipico del soggetto suicida è caratterizzato da costrizione mentale e ambivalenza
L'azione tipica dei suicidi è la fuga (da qualcosa di angosciante)
L'atto interpersonale tipico dei soggetti suicidi è la comunicazione dell'intenzione

1. The common **purpose** of suicide is **to seek a solution**: A suicidal person is seeking a solution to a problem that is "generating intense suffering" within him or her.
2. The common **goal** of suicide is **cessation of consciousness**: The anguished mind of a suicidal person interprets the end of consciousness as the only way to end the suffering.
3. The common **stimulus** of suicide is **psychological pain**: Shneidman calls it "psychache," by which he means "intolerable emotion, unbearable pain, unacceptable anguish."
4. The common **stressor** in suicide is **frustrated psychological needs**: A suicidal person feels pushed toward self-destruction by psychological needs that are not being met (for example, the need for achievement, for nurturance or for understanding).
5. The common **emotion** in suicide is **hopelessness-helplessness**: A suicidal person feels despondent, utterly unsalvageable.
6. The common **cognitive state** of suicide is **ambivalence**: Suicidal people, Shneidman says, "wish to die and they simultaneously wish to be rescued."
7. The common **perceptual state** in suicide is **constriction**: The mind of a suicidal person is constricted in its ability to perceive options, and, in fact, mistakenly sees only two choices—either continue suffering or die.
8. The common **action** in suicide is **escape**: Shneidman calls it "the ultimate egression (another word for *escape*) besides which running away from home, quitting a job, deserting an army, or leaving a spouse ... pale in comparison."
9. The common **interpersonal act** in suicide is **communication of intention**: "Many individuals intent on committing suicide ... emit clues of intention, signals of distress, whimpers of helplessness, or pleas for intervention."
10. The common **pattern** in suicide is **consistent with life-long styles of coping**: A person's past tendency for black-and-white thinking, escapism, control, capitulation and the like could serve as a clue to how he or she might deal with a present crisis.

[Fig. 7]: Shneidman 'Commonalities of Suicide' and Italian translation (Shneidman, 1996)

The subject feels a sense of *psychological constriction*, a tunnel vision that reduces solutions normally available. Subsequently, an ambivalence in the cognitive state manifests with only two options: a solution (almost magical) or an ending. Suicide is more understandable not as a desire for death, that is life's ending, but as an annihilation of the cognitive state, and, therefore, of pain (Pompili, 2008b). Suicide is the result of an inner dialogue that usually happens over a span of years: the mind scans over all of the possible solutions for its own psychache. Suicide appears as a solution and, initially, the mind discards it; eventually, having all the other options failed, the mind accepts suicide firstly as a possible solution, then as the only one. The subject wants to live, but psychache is unbearable and suicide is the only mean to escape it. Shneidman says in his work that suicide is not a choice for death, but a departure from psychache, which gives the process a underlying sense of hope. opposed to the mere desire for death (Shneidman 1996). This implies that by reducing psychache the suicidal ideation may disappear, and the subject would therefore choose life (Shneidman 2004). Shneidman states that the origin of psychache lies in the frustration of psychological needs (love and belonging, self-actualization, key-relationships, ect.) and also, that psychache is inherently different from depression and sadness, and comes with its own characteristics. In addition, mental pain is a condition that is different from depression or sadness and has its own set of characteristics:

- **Persistence:** although mental pain can have an acute onset, this sensation is long-lasting and requires a considerable amount of time before it can possibly be resolved. During this time, the intensity of the painful condition can fluctuate (Meerwijk et al., 2013).
- **Irreversibility:** the individual experiences the sensation of having lost something or being faced with an inevitable negative change, to which they cannot find a solution (Orbach et al., 2003).
- **Unsustainability:** the individual cannot endure such a condition for an extended period of time. In this regard, Shneidman introduced the concept of the pain threshold, stating that the capacity to tolerate psychological pain, and therefore to increase one's threshold of tolerance, is an individual characteristic. The consequences of prolonged exposure to mental pain can lead to extreme solutions, such as suicide (Shneidman, 1999).
- **Incommunicability:** the individual experiencing mental pain is unable to describe the condition they are in with their own words, and therefore cannot communicate it to others (Fleming, 2006). The presence of alexithymic personalities and individuals with limited emotional expressive capacity is believed to be an additional risk factor for suicide, according to some authors (Levi et al., 2008; Horesh et al., 2012).

1.5.2 CLINICAL IMPLICATIONS OF PSYCHACHE

Correlation between psychache and suicidal ideation is found frequently in new studies. Psychache has been found a statistically significant predictor of suicidal ideation in both inpatients and outpatients. For example, several studies on students (Flynn & Holden, 2007; Holden, Mehta et al., 2001; Troister & Holden, 2010a; Troister & Holden, 2010b; You, Song et al., 2014) assessing the weight of psychache, depression and hopelessness on suicidal ideation and behavior. The general outcome of those studies was that suicide was more correlated with psychache, which was found more predictive of suicidal behavior than depression, hopelessness, coping mechanism and one's purpose in life (DeLisle & Holden, 2009; Pereira, Kroner et al., 2010). The same results were found in studies on non-clinical samples. Patterson et al. have tested the correlation between psychache and suicidal ideation in 97 homeless patients and compared it with depression, hopelessness and life's purpose. The best predictor of suicidal behavior was still found to be mental pain (Patterson & Holden, 2012). Similar outcome was obtained in a study by Mills et al. on a sample of inmates (Mills, Green, Reddon, 2005). In a clinical environment, 88 psychiatric inpatients were interviewed by using the *Psychological Pain Assessment Scale* (PPAS), (Shneidman, 1999), and there was a significant statistical correlation between the score obtained through the PPAS and the risk of suicide assessed by clinical interview. However, there wasn't a correlation between PPAS score and previous suicide attempts (Pompili, Lester et al., 2008). In a sample of 67 patients with major depressive disorder with a recent attempted suicide, 61 with previous suicide attempts and 62 without history of suicide attempts, Olié (Olié et al., 2010) found that that elevated levels of psychache were significantly related to a recent suicidal event and history of suicide attempts, compared to those without history of suicide attempts. Moreover, psychache was proportional to the levels of intensity and frequency of suicidal ideation. Mehmet and colleagues (Mehmet, Emin et al., 2019), for example, conducted a study on a sample of 113 patients with schizophrenia, of which 50 had a history of attempted suicide. Only scores on the Psychache Scale (PAS) and the Alexithymia Scale (TAS) showed a statistically significant correlation with suicidal ideation, as evaluated by the Beck Scale for Suicidal Ideation (BSSI), even after statistical regression analysis. Demirkol and colleagues (Demirkol, Namlı et al., 2019), instead, conducted a cross-sectional

study on patients with obsessive-compulsive disorder (OCD), recruiting a sample of 67 patients with OCD and comparing them to 63 patients without OCD. Again, the only scale that showed a significant correlation with a history of attempted suicide was the Psychache Scale (PAS). Recently, Berdarelli and colleagues (Berardelli, Sarubbi et al., 2019) evaluated a clinical sample of 291 patients admitted to a psychiatric ward and suffering from depressive disorder, bipolar disorder, and schizophrenia, subjecting them to the Psychological Pain Assessment Scale (PPAS) for the assessment of mental pain and the Mini International Neuropsychiatric Interview (MINI) for the assessment of suicidal ideation and diagnostic definition. The authors identified a significant association between current mental pain and the worst mental pain ever experienced with a high suicide risk. The authors also report that the correlation between mental pain and suicide risk is higher for mood disorders than for schizophrenia and concludes that the evaluation of psychache appears to be a useful tool for predicting suicide risk and should be used routinely to identify and treat suicide risk in clinical practice. Moreover, it is interesting to note that even in the few prospective studies that have been conducted on the subject, mental pain plays a crucial role in predicting changes in suicidal ideation, compared to other variables. Troister and colleagues (Troister & Holden, 2012) conducted a two-year prospective study on university students at high risk of suicide (history of attempted suicide or high scores on suicidal ideation scales at baseline), testing the following parameters at time zero and after two years: depression; hopelessness; psychache; suicidal ideation. The authors demonstrated how the only parameter that predicted changes in suicidal ideation was mental pain. The authors also showed, through regression analysis, that the parameters of depression and hopelessness only had statistical significance in relation to variations in mental pain. More recently, Montemarano and colleagues found similar results in a four-year follow-up. Interestingly, even when considering shorter follow-ups of five months or even three and ten weeks, mental pain was the only parameter capable of predicting a change in suicidal ideation. This suggests that the use of scales that investigate levels of psychache may be a clinically valid screening tool, both in the short and long term, in the field of suicide prevention. There is a clear correlation between mental pain and suicide risk, both in clinical and non-clinical samples, and this correlation seems to be independent of the presence and type of associated psychiatric diagnosis. However, most studies on the subject consider samples selected based on high suicide risk (due to a positive history of attempted suicide or high scores on suicidal ideation intensity measurement scales). While it is certain that a positive history of attempted suicide is one of the main suicide risk factors, it is also possible that other factors may play an equally determining role, and from the scientific literature analyzed so far, mental pain seems to represent a risk factor in its own right. Given the possibility of quantifying levels of mental pain through relatively simple and quick psychometric tools, it is very useful, for the purposes of prevention, to understand whether investigating mental pain at a clinical level can be a valid tool that helps healthcare professionals in assessing suicide risk and thus guides them towards correct identification and management of high-risk patients. Based on these considerations, we will present a longitudinal study. The study aims to understand if the proposed tools can be integrated into the routine diagnostic evaluation of patients at risk of suicide.

2. MATERIALS AND METHODS

2.1 STUDY DESIGN

This is a longitudinal, observational study: 179 patients were recruited between October 2020 and October 2022. The patients were recruited at the university hospital of Varese (Azienda Socio-Sanitaria Territoriale Sette Laghi), on the occasion of a check-up visit at the psychiatric outpatients care services, of Varese, Azzate and Arcisate and at the outpatients clinic for anxiety and depression, fulfilling the following inclusion criteria: over 18 years of age; presence of a psychiatric illness diagnosed following the diagnostic criteria of the Statistical Diagnostic Manual of Mental Disorders, Fifth Edition (DSM-5-TR); signing of an informed consent for the use of data anonymously for research purposes. Minor age and the presence of a cognitive or linguistic barrier that compromised the understanding of the study were considered exclusion criteria. Subjects suffering from major neuropsychiatric pathologies such as epilepsy, intellectual disabilities or genetic syndromes with psychiatric correlates, patients suffering from conditions that did not allow completing the evaluation such as linguistic problems, severe dyslexia, poor knowledge of the Italian language were excluded from the study. At baseline, sociodemographic, clinical and psychometric data were collected which were subsequently correlated with suicidal behaviors assessed at follow-up. Complete suicides were considered, or suicidal attempts that led to access to the emergency room requiring observation for at least 24 hours, or subsequent hospitalization, or which were followed by an emergency therapeutic intervention, such as gastric lavage or urgent surgical stitching. Attempts which did not lead to access to emergency services, but which were described as objectively anti-conservative by the referring clinicians and reported in the patient's clinical documentation were also considered. After 6 months (T₁) and 12 months (T₂) from the date of recruitment, the hospital (PORTALE) and territorial (PSYCHE) databases and medical records were analyzed with the aim of underlining any suicides or attempted suicides that occurred during the follow-up period.

3.2 STUDY OBJECTIVES

The objectives of this study are as follows:

1. Evaluate the association between levels of mental pain measured at baseline and the risk of suicide or AS during follow-up.
2. Deepen knowledge of the correlation between sociodemographic, clinical and laboratory parameters with the risk of suicide or attempted suicide.

2.3. SAMPLE

Patients were recruited from the Psychiatry Unit (U.O.P) of Varese, during a check-up visit, from the psychosocial centers (CPS) of Varese, Azzate, and Arcisate, and from the specialized "Anxiety and Depression" outpatient clinic of the Hospital of Circolo and Fondazione Macchi of Varese. The sample consists of a group of n=179 patients.

2.4 INCLUSION AND EXCLUSION CRITERIA

Recruitment was conducted with the following inclusion criteria:

- Presence of a psychiatric diagnosis made following the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR).
- Age > 18 years.
- Signature of an informed consent form.

The exclusion criteria were:

- Age < 18 years.
- Presence of neurocognitive deficits compromising the understanding of the evaluation tools.
- Presence of linguistic barriers compromising the understanding of the evaluation tools.
- Refusal to sign informed consent.

2.5 ASSESSMENT TOOLS

The baseline assessment was conducted during a psychiatric follow-up visit and using the following tools:

1. Patient Anamnesis Form
2. Columbia Suicide Severity Rating Scale (C-SSRS)
3. Beck Depression Inventory-II (BDI II)
4. Beck Hopelessness Scale (BHS)
5. Hamilton Depression Rating Scale (HDRS or HAM-D)
6. Hamilton Anxiety Rating Scale (HAM-A)
7. Psychache Scale (PAS)
8. Mental Pain Questionnaire (OMMP)

Patient Anamnesis Form

This form collected, through direct questioning of the patient, verification of information with the treating physician, and review of medical records and databases, the main information about the patient's life and clinical history. The collected information includes sociodemographic data (marital status, education, profession, living situation) as well as clinical data (psychiatric diagnosis, age of onset, number of hospitalizations, current therapy, previous therapy, previous suicide attempts). Information on substance abuse and any comorbid medical diagnoses was also collected.

Suicide Columbia Severity Rating Scale - C-SSRS (Posner et al., 2011)

The scale is divided into four parts: the first assesses the severity of suicidal ideation (on a 5-point scale, where 1 = wish to be dead, 2 = non-specific active suicidal ideation, 3 = suicidal ideation including methods, 4 = suicidal intent, and 5 = active suicidal intent with specific plan and means); it is a structured interview designed to evaluate suicidal behavior and ideation. The scale consists of four parts: the first part assesses the presence and severity of suicidal ideation, and includes five questions about frequency, intensity, controllability, deterrents, and reasons. The total score of this subscale ranges from 0 to 5, with a higher

number indicating more intense ideation and greater suicide risk. The second part is the "intensity of ideation" subscale, which includes 5 questions about frequency, duration, controllability, deterrents, and reasons. The total score of this subscale ranges from 2 to 25, with a higher number indicating more intense ideation and greater suicide risk. The third part is the behavior subscale, which is evaluated on a nominal scale that includes actual attempt, interrupted attempt, failed attempt, and preparatory behavior. The fourth and final part is the subscale that assesses the lethality of actual attempts and is evaluated on a 6-point scale (ranging from 0 = no physical harm or very minor physical harm, e.g. superficial scratches, to 5 = death), as well as the potential lethality if the attempt did not result in actual harm (0 = behavior that is unlikely to cause injury; 1 = behavior that can cause injury, but is unlikely to cause death; 2 = behavior that can cause death despite available medical care). The C-SSRS has demonstrated good validity and high sensitivity and specificity in evaluating suicidal behavior (Posner et al., 2011). The "alert responses" are the 4th and 5th items in the "suicidal ideation" section, which relate to the past 30 days (4 = Have you had these thoughts and some intention of carrying them out? 5 = Have you started to organize or have you already organized the details of how to kill yourself? Do you intend to carry out this plan?) and the 6th item in the "suicidal behavior" section, which relates to the past 90 days (6 = Have you done anything to attempt suicide or prepare to kill yourself, such as hoarding pills, obtaining a gun, giving away valuable objects, or writing a suicide note?). The guidelines for using the scale warn that in case of an affirmative response to these items, prompt engagement with psychiatric services is necessary.

Beck Depression Inventory-II (BDI II)

The second scale mentioned is the Beck Depression Inventory-II (BDI II), which aims to estimate the presence and intensity of depressive traits through 21 guided response questions. The items of the scale are constructed according to the diagnostic criteria of major depressive episode of the DSM-IV. Each item consists of a list of four statements organized in order of increasing severity (from 0 to 3) and referring to the past two weeks. The questionnaire evaluates the presence of the following depressive symptoms: sadness, pessimism, sense of failure, loss of pleasure, guilt, feelings of punishment, loss of self-esteem, self-criticism, suicide, crying, agitation, loss of interest, indecision, sense of worthlessness, loss of energy, sleep, irritability, appetite, concentration, fatigue, and libido. The BDI-II has been structured to provide a single overall score that can range from 0 to 63, and which allows for different degrees of depression to be distinguished: minimal (0-13), mild (14-19), moderate (20-28), and severe (29-63).

Beck Hopelessness Scale - BHS (Beck et al., 1974)

Hopelessness is a psychological construct underlying various mental disorders and refers to the cognitive patterns that have a negative expectation towards the future. "Desperate" individuals believe that nothing will work in their favor, that they will never succeed in life, that their important goals will not be achieved, and their problems will never be solved. This definition of hopelessness corresponds to the third component of the negative triad of Aaron T. Beck's cognitive model of depression, composed of a negative view of oneself, a negative view of the present, and a pessimistic view of the future. This instrument assesses the feelings and expectations regarding the subject's future and loss of volitional drive through 20 statements with dichotomous response (True/False). Scores between zero and 3 are considered physiological; scores between 4 and 8 are mild; scores between 9 and 14 are considered moderate, while scores > 14 are considered severe. A score higher than 9 is still considered a high suicide risk according to the results of a study on hospitalized patients, which showed that a score of 9 (or more) on the BHS scale exposed patients to an 11 times higher suicide risk than those who had a score lower than 9 (Beck et al., 1990). Other studies have also demonstrated the clinical utility of this scale in identifying suicide risk (McMillan et al., 2007; Klonsky et al., 2012); however, more recent evidence has shown the superiority of mental pain scales over BHS in predicting suicide risk (Troister et al., 2015).

Hamilton Depression Rating Scale - HDRS or HAM-D (Hamilton, 1960)

Among the hetero-evaluation scales, it is the most commonly used in clinical practice, to the point of being considered a reference parameter in most studies on depression. The version we used consists of 21 items. Items are graded, some at 3 (0-2) and others at 5 (0-4) levels of severity referring to the main depressive symptoms: depressed mood, feelings of guilt, suicide, early insomnia, middle insomnia, late insomnia, work and interests, psychomotor retardation, agitation, psychic anxiety, somatic anxiety, gastrointestinal somatic symptoms, general somatic symptoms, genital somatic symptoms, hypochondria, weight loss, insight, diurnal variation, depersonalization and derealization, paranoid symptoms, obsessive and compulsive symptoms. The assessment criteria are, for the most part, the result of the integration between the objective observation of signs by the administrator and the subjective exposure of symptoms, although the severity criterion mainly refers to objective aspects. Scores are calculated as follows: < 7: absence of depression; 8-17: mild depression; 18-24: moderate depression; > 25: severe depression.

Hamilton Anxiety Rating Scale - HAM-A (Hamilton, 1959)

Widely used in clinical practice and often administered in conjunction with the HAM-D, it consists of 14 items that assess both psychic and somatic anxiety. The administration mode is similar to that of the HAM-D. Each item is scored on a scale from 0 (not present) to 4 (severe), with a total score range of 0-56 (<17: mild; 18-24: mild to moderate; >25: severe).

Psychache Scale - PAS (Holden, Mehta et al., 2001)

Shneidman (1999) was the first to attempt to operationalize mental pain, measuring frustration of vital needs and the disturbance associated with this state. Holden and colleagues (2001), in order to test Shneidman's theory of suicide, developed the Psychache Scale (PAS) by considering the definition of psychache. There are several studies that confirm this theoretical model (Berlim et al., 2003; Mills et al., 2005; Holden et al., 2001). The Psychache Scale consists of 13 items in total and is a self-administered scale. Nine elements are evaluated on a 5-point Likert scale ranging from "never" to "always". Four other elements, which reflect the intensity of pain, are evaluated on a 5-point Likert scale ranging from "strongly disagree" to "strongly agree". The total score is obtained by adding the scores of the items, resulting in a total score between 13 and 65. The PAS is typically considered a unidimensional scale (Holden et al., 2001; Mills et al., 2005), with good psychometric properties, as reported by several studies involving samples of subjects with different characteristics. The internal consistency is above 90% (Holden et al., 2001; Mills et al., 2005; Pereira et al., 2010; Campos & Holden, 2015). The PAS has been found to be able to distinguish those who attempt suicide from those who do not (Holden et al., 2001), as well as statistically predicting a person's tendency to commit suicide, even after controlling for depression and hopelessness variables (Troister & Holden, 2012; Pereira et al., 2010; DeLisle & Holden, 2009; Berlim et al., 2003; Holden et al., 2001). Through the use of PAS, it has been possible to deduce that depression, hopelessness, and psychache constitute three distinct dimensions, although they are strongly correlated with each other (DeLisle & Holden, 2009; Troister & Holden, 2013) and that each of them contributes uniquely to predicting suicidal ideation. The PAS is a fast, sensitive tool primarily aimed at measuring the frequency of the painful phenomenon in order to assess the role of psychache as a proximal cause of suicide, rather than quantifying mental pain itself.

Orbach & Mikulincer Mental Pain Scale - OMMP (Orbach and colleagues, 2003a)

Orbach and colleagues (2003a) define mental pain as a set of subjective experiences characterized, in particular, by the individual perception of negative changes in oneself. Mental pain proves to be a multidimensional phenomenon that involves cognitive, emotional, and psychic aspects. This conceptualization of mental pain allows it to be considered as a common existential condition and not exclusively involved in psychopathological processes (Orbach et al., 2003a). This definition, while showing some similarities with those provided by Shneidman, as stated by the author himself, also takes into consideration other aspects, never examined before, among which are the irreversibility of pain, freezing (conditioned immobility), emotional flooding, self-

alienation, and disturbance. Therefore, compared to PAS, which evaluates mental pain as a unidimensional construct correlated with suicidal ideation, the Orbach & Mikulincer Mental Pain Scale (OMMP) evaluates mental pain as a multidimensional construct. The self-evaluating questionnaire OMMP is composed of 44 items, grouped into 9 factors: in addition to those already mentioned, it includes loss of control, narcissistic wounds, need for external support, and inner emptiness. Both a total score and a score for each individual factor are provided. Each item is rated on a 5-point Likert scale, ranging from "strongly disagree" to "strongly agree." The higher the score, the higher the level of mental pain. Compared to PAS, the OMMP adds experiential qualities to the definition of mental pain, specifically the irreversibility of pain, freezing, alienation, disturbance, and need for others. The scale has demonstrated good concurrent validity compared to the PAS and has been able to distinguish between subjects who exhibit suicidal behavior and those who do not. However, it is not able to differentiate between fatal and non-fatal suicide attempts (Orbach et al., 2003a; Orbach et al., 2003b; Conrad et al., 2009; Gvion et al., 2014; Levi et al., 2008; Shelef et al., 2015). The internal consistency of the different factors ranges from .72 to .95 (Levi et al., 2008; Shelef et al., 2015), while the total consistency is over .89 (Gvion et al., 2014; Shelef et al., 2015).

BIOLOGICAL MARKERS

As emerges in the introductory section, the analysis of the literature revealed a lack of works showing a correlation between suicidal risk and alterations in routine laboratory parameters. For this reason we also wanted to include in the analyzes the laboratory tests normally used in the clinical practice of emergency room visits or hospital admissions to highlight any correlations between their alterations and an increased risk of suicide. We have collected those biological markers that are most frequently associated in the literature with major depression or suicide risk and which are normally analyzed as a screening at each hospital access. No additional laboratory tests were required. Taking these two parameters into account, we included the following laboratory tests in the assessment: white blood cells count, ESR (erythrocyte sedimentation rate), CRP (C-reactive Protein), total serum calcium, total cholesterol and TSH (thyroid-stimulating hormone).

2.6 STATISTICAL ANALYSIS

Descriptive statistics were reported as mean and standard deviation for continuous variables or frequency and percentage for qualitative variables. Statistical significance was defined with a p-value ≤ 0.05 . All statistical analyses were performed using SPSS Statistics software (IBM SPSS Statistics for Windows, Version 28.0; IBM Corp., Armonk, New York, USA). Kolmogorov-Smirnov Test was used to assess distribution. To evaluate the difference in scores of a non-parametric quantitative variable in a parametric qualitative variable with two modes, the Mann-Whitney U test was used. To evaluate the difference in scores of a parametric quantitative variable in a qualitative variable with two modes, the Students' T-test for independent samples was used. To evaluate the dependence of one or more independent variables on a binary qualitative dependent variable, the binary logistic regression model was used. To evaluate the association between two qualitative variables, the Chi-square test was used. When necessary (when more than 20% of values were less than or equal to 5 and/or there was the presence of values less than 1) and to obtain a better interpretation of the data, Cramer's V test was used to verify the association between variables.

2.7 DATA PROTECTION

The present study did not involve any additional costs and did not represent an obstacle to the usual clinical activities. The processing of personal, demographic, and clinical data is solely for scientific research purposes, and the dissemination of the results will only occur in anonymous and/or aggregated form for scientific purposes. Access to such data is protected by the responsible party of this research. The material is and will be used exclusively for scientific research purposes, never for profit and/or commercial purposes. Clinicians were trained to administer the psychometric scales. All personally sensitive information contained in the database used for this study was previously de-identified according to the Italian legislation (D.L. 196/2003, art. 110, -24 July 2008 art. 13). Since data were made anonymous and unidentifiable, the Provincial Health Ethical Review Board (Ethics Committee of Insubria – Azienda Socio Sanitaria Sette Laghi, Varese, Italy) consulted prior to the beginning of the study, has confirmed that, since the study consists in a longitudinal investigation, it does not need approval process from the Board. The authorization to process the data in anonymous form was included in the informed consent signed by the patients. The study was carried out in accordance with the Declaration of Helsinki (with amendments) and Good Clinical Practice.

3. RESULTS

3.1 SAMPLE CHARACTERISTICS

Sociodemographic data

The sample consists of 64 males and 114 females, for a total of 178 patients. The majority of patients are between the ages of 30 and 69, with a higher percentage between the ages of 50 and 59 (23,5%). 44% of the total sample are single, 36% are married, 15,4% are divorced, and 4,6% are widowed. Regarding education, 7,4% of the sample has an elementary school diploma, 33% has a middle school diploma, 48,3% has a high school diploma, while 11,4% have a university degree. Regarding employment, 33,7% are unemployed, 4% have occasional work, 38,3% have stable work, 19,4% are retired, and 4% are disabled.

Clinical data

Clinical data regarding familiarity with psychiatric disorders, 48,3% of the sample has no significant familiarity, 16,7% has familiarity with depressive disorder, 13,8% with anxiety disorder, 6,9% with substance use disorder, and 12,6% have familiarity with multiple psychiatric disorders. Only one patient has familiarity with an eating disorder (ED) and only two with a psychotic spectrum disorder. Regarding comorbidity with somatic disorders, the data is distributed as follows: 54,0% of patients have no physical comorbidity, 12,1% have comorbidity with cardiovascular diseases, only one patient has comorbidity with gastrointestinal disorders, 5,2% have comorbidity with neurological disorders, 5,2% with endocrine disorders, 1,7% with infectious diseases, 1,7% have comorbidity with autoimmune disorders, 1,7% with rheumatological disorders, only one patient with orthopedic disorders, 1,7% with gynecological disorders, while 14,4% of the total sample has multiple comorbidities. **Table 3** shows data on the main psychiatric diagnosis and psychiatric comorbidities, expressed as frequency (n) and percentage (%).

Table 3: Frequency of the main psychiatric diagnosis in the sample listed in order of frequency

Main Psychiatric Diagnosis	n (%)	Psychiatric Comorbidity	n (%)
Personality Disorder (PD)	69 (39,4)	None	132 (75,9)
Major Depressive Disorder (MDD)	46 (26,3)	MDD	11 (6,3)
Attachment Disorder (AD)	21 (12)	OCD	1 (0,6)
Bipolar Disorder 1 (BD1)	10 (5,7)	PAD	1 (0,6)
Psychotic Spectrum Disorder (PSD)	9 (5,1)	PSD	4 (2,3)
Generalized Anxiety Disorder (GAD)	6 (3,4)	SUD	9 (5,2)
Panic Attack Disorder (PAD)	3 (1,7)	PD	5 (2,9)
Bipolar Disorder 2 (BD2)	3 (1,7)	ED	7 (4,0)
Obsessive Compulsive Disorder (OCD)	2 (1,1)	Disability	3 (1,7)
Eating Disorder (ED)	1 (0,6)	Unknown	5 (2,8)
Total	179 (100,0)	Total	179 (100,0)

SUD=Substance Use Disorder

The onset age of the main psychiatric disorder is between 10 and 59 years, with no patient starting before the age of 10; 6 patients starting after 60 years, and 6 patients starting after 70. Most onsets occurred between 10 and 19 years (48,27%). Regarding psychiatric pharmacological therapy, 8,6% of the total sample does not take any pharmacological therapy, 19,5% are on monotherapy, and 71,8% are on polytherapy. Furthermore, 26,4% of the sample is also undergoing treatment with non-psychiatric drugs. Regarding substance abuse, 10.34% of the sample has a positive history of alcohol abuse, 6,3% has a history of abuse of substances other than alcohol (a single substance), while 13,8% have a history of poly-substance abuse. Regarding the use of substances at the time of recruitment, the total sample is distributed as follows: 73,5% do not present substance abuse; 10,3 abuse alcohol, 5,2% abuse a substance other than alcohol, and 10,9% have poly-substance abuse. Suicidal ideation and suicidal behavior in the total sample are showed in **Table 4**. The data are reported as frequency (n) and percentage (%).

Table 4: Suicidal ideation and history of AS

Lifetime Suicidal Ideation	n(%)	Current Suicidal Ideation	n(%)	History of AS	n(%)
Never	87 (50)	Never	118 (67,8)	No	93 (53,4)
Ideation without planning	23 (13,2)	Ideation without planning	23 (13,2)	Yes	81 (46,6)
Ideation with planning	64 (36,8)	Ideation with planning	35 (20,1)		

AS= Attempted Suicide

Of the 26 new suicide attempts, 53,8% (14) involved incongruous ingestion of medicines or toxic substances, 19,2% (5) involved a mix of substances, 15,4% (4) involved defenestration, and 11,5% (3) involved self-inflicted wounds.

4.2 SAMPLE ANALYSIS

In the first follow up (6 months) 24 patients attempted suicide. In the second follow up (12 months) 2 patients underwent AS. Due to this low number of second follow-ups, only T₁ was taken into consideration for the statistical analyses, which from now on, will generally be defined as "follow up".

In this study, the association between marital status and suicide attempts (AS) within a six-month period was investigated. Gender was also evaluated, but no significant differences were found. The contingency table revealed that among single individuals, 15 out of 77 (19,5%) attempted suicide compared to 4 out of 63 (6,3%) married individuals. The chi-squared test showed no significant association between marital status and SA ($\chi^2 = 2,74$, $p =$

0,097), although a trend was observed. However, when combining data for unmarried, divorced and widowed, the results are significant, both for the association between married individuals and absence of suicide attempt and for those who are not married, or are divorced, or widowed and a new suicide attempt, with a percentage of 6,3% new attempts in married individuals against a percentage of 17,9% in those who are not currently married ($\chi^2 = 4,51$, $p = 0,03$). Education level was also evaluated, but no significant differences were found between the groups. The association between employment status and suicide attempt was also investigated. The contingency table shows that for unemployed individuals, there were 47 cases without suicide attempts and 12 cases of suicide attempts (20,3%). In contrast, for employed individuals, there were 63 cases without suicide attempts and 4 cases of suicide attempts (6,0%). The chi-square test yielded a value of 22,28, with an asymptotic significance of $<0,001$ and a Cramer's V of 0,357, with an approximate significance of $<0,001$, indicating a statistically significant association between employment status and suicide attempt. Regarding family history of mental illness, the contingency table did not reveal any significant association between the variable and the outcome ($\chi^2 = 10,83$, $p = 0,09$). Regarding medical conditions, no statistically significant association was found with suicide attempt. Significant differences based on the primary psychiatric diagnosis wasn't found, however, patients with a primary diagnosis of Personality Disorder, showed a higher rate of AS compared to other diagnoses, with 21,7% new suicide attempts, although the chi-square test did not reach statistical significance ($\chi^2 = 11,47$, $p = 0,322$). The analysis of comorbidities showed interesting results in those who had no comorbidity, with 9,8% new suicide attempts, compared with the Substances Use Disorder (SUD) group who had a 44,4% of the sample perform a AS with a bilateral asymptotic significance of 0,02 and a Cramer's V of 0,34. These findings suggest that the absence of comorbidities may be associated to a lesser risk of suicide attempt, while the presence of SUD or disability may increase the probability. In the analysis of the association between age and suicide attempt, no significant differences were found. However, an interesting finding was observed in the group of patients over 60 years of age ($n=48$), where none had a new suicide attempt. Similarly, this trend was replicated by the fact that in the association between age of onset and suicide attempt, no significant differences were found. However, an interesting finding was observed in the group of patients over 40 years of age ($n=57$), where only one individual had a new suicide attempt within 6 months. A significant association was found between suicide attempts and antipsychotic therapy ($\chi^2=9,9$, $p=0,02$) and mood stabilizer therapy ($\chi^2=10,0$, $p=0,02$), while no significant association was found for antidepressant and anxiolytic therapy. A significant association between substance abuse history and suicide attempt at follow-up was found, with 112 "no" and 9 "yes" (7,4%) in those without history of substance abuse and 39 "no" and 14 "yes" (26,4%) in those with history of substance abuse, with a $\chi^2 = 11,57$, and a p-value of $<0,001$ and a Cramer's V of 0,26. Similarly, a significant association between current substance use and new suicide attempt at follow-up with a chi-square of 21,98 and $p < 0,001$, with a Cramer's V of 0,35. Among the 128 subjects who do not abuse substances, 8 AS at follow-up, while among the 19 subjects who abuse multiple substances, 6 attempted suicide. The group of patients with a suicide attempt made during the follow-up period, have a significantly 32% higher percentage of previous suicide attempts compared to the control group ($p=0,005$). Regarding lifetime suicidal ideation calculated with the C-SRSS score, a notable association was found between never having had suicidal ideation and not attempting suicide at follow up (8,0% new suicide attempts), and having had suicidal ideation with a plan and attempting suicide at follow up (25,0% new suicide attempts), while the association of ideation without a plan was also associated with not attempting suicide (23=no, 0=yes). The Pearson chi-square had a value of 12,27 and a *p value* of 0,001, while the Cramer's V was 0,28. Current suicidal ideation using the C-

SRSS had similar results. Among the subjects without current suicidal ideation, 9 out of 116 AS within 6 months (7,8%). For those with suicidal ideation without a plan, 2 out of 23 (8,7%) attempted suicide within 6 months, while for those with current suicidal ideation with a plan, 13 out of 35 (37,1%) attempted suicide within 6 months. The association between these variables and the new suicide attempt was statistically significant with a chi-square value of 20,10 and a *p-value* <0,001, and a Cramer's V of 0,34. With the binary regression model it was found that with the C-SSRS Lifetime Suicidal Ideation Score, those who had suicidal ideation with any degree of planning were associated with a new suicide attempt in 6 months, with a $\text{Exp(B)}=5$ showing that a unitary increase of the score was associated with an increase of 5 times in the risk of suicide ($R^2\text{Nagelkerke} = 0,121$, $p<0,001$). Moreover, the results were consistent with the C-SRSS Current Suicidal Ideation, with an $\text{Exp(B)}=6,9$ and $R^2=0,164$ and $p=0,001$. In the next **Table 5** and **Table 6**, a summary of the significant ($p<0,05$) associations between anamnestic factors and new suicide attempts is shown.

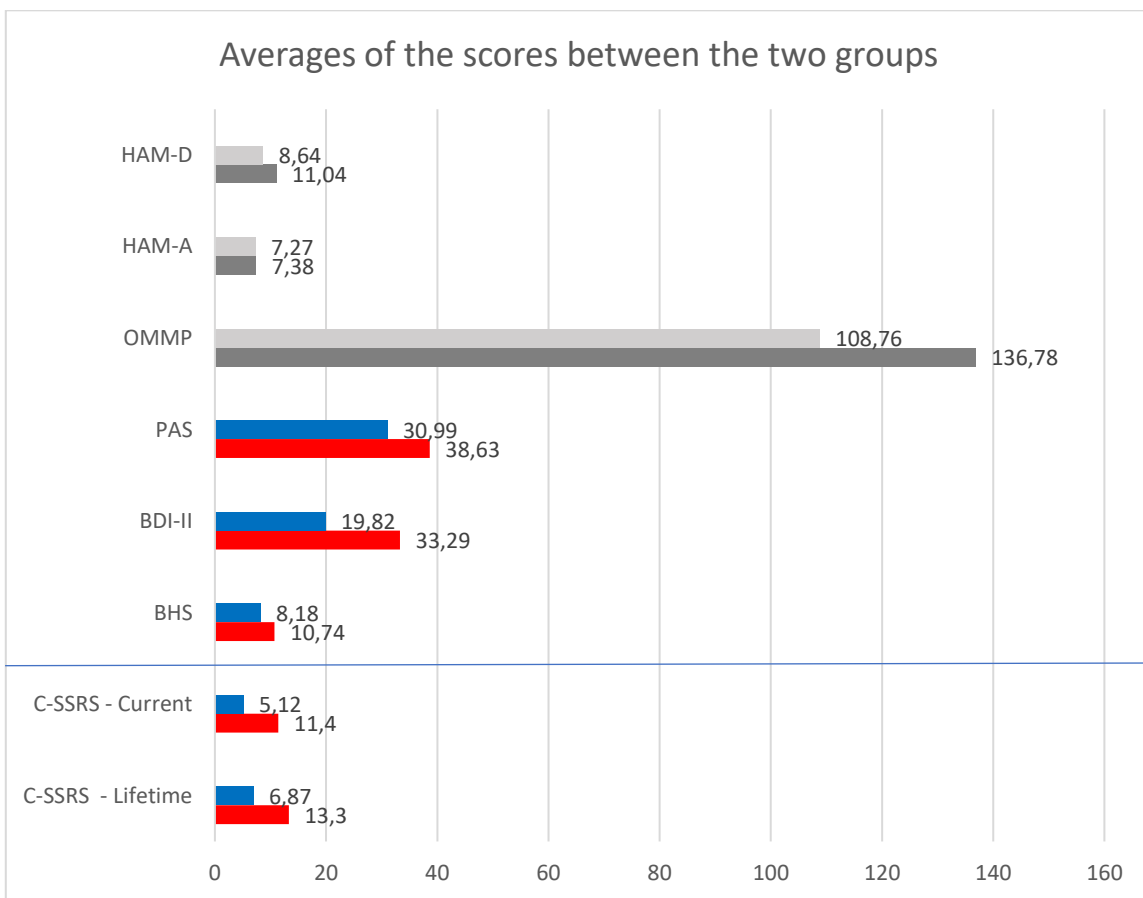
Table 5: Socio-demographic and clinical variables with statistical significance ($p<0,05$).

	No new AS	New AS	<i>p</i>	V
Employment				
Unemployed	79,7	20,3	< 0,001	0,357
Employed	94,0	6,0		
Invalid	57,1	42,9		
Comorbidity				
None	90,2	9,8	0,002	0,337
Disability	33,3	66,7		
Substance Abuse Disorder	55,6	44,4		
Antipsychotic				
None	93,3	6,7	<0,001	0,461
Quiapine	47,1	52,9		
Mood stabilizers				
None	91,9	8,1	0,002	0,240
Any stabilizer	74,0	26,0		
History of drug abuse				
None	92,6	7,4	0,002	0,297
Substance Poly-abuse	70,8	29,2		
Current drug abuse				
None	93,8	6,3	<0,001	0,355
Substance Poly-abuse	68,4	31,6		
without planning	91,3	8,7		
with planning	62,9	37,1		

Table 6: difference in incidence of suicidal attempts in patients with and without a history of previous suicidal attempt.

Previous AS	% No new AS	% new AS	<i>p</i>	<i>V</i>
No	58,6	26,9	0,005	0,224
Yes	41,4	73,1		

Regarding association between the analyzed scales and attempted suicide at 6 months, subjects who attempted suicide during the follow-up period show higher scores at all the psychometric scales; however, only the BDI-II, PAS, BHS and C-SRSS scores achieved statistical significance. **Fig.8** and **Table 7** show the averages of scales' scores, considering the coefficients of statistical significance.



[Fig.8]: Averages of the psychometric scales' scores associated with the risk of new SA. Grayed out - insignificant ones ($p > 0,05$); colored out – the scores with p value $< 0,05$, red indicates the scores for those who attempted suicide at the time of the follow-up, in blue those who did not. C-SSRS is the control scale.

Table 7: Averages of psychometric scales' scores associated with the risk of new SA and differences between the two groups.

Scales	Mean score ±DS New AS	Mean score ±DS No new AS	Mean difference	<i>p</i>	
C-SSRS - Lifetime	13,36±10,73	6,87±8,58	6,49	0,007	Control scale
C-SSRS - Current	11,41±7,56	5,12±7,90	6,28	<0,001	Control Scale
BHS	10,74±6,02	8,18±5,55	2,55	0,047	Hoplessness
BDI-II	33,29±13,77	19,82±13,88	13,47	<0,001	Depression
PAS	38,63±14,78	30,99±13,77	7,64	<0,01	Psychache
OMMP	136,78±31,60	108,76±39,96	28,02	>0,05	Psychache
HAM-A	7,38±5,29	7,27±5,59	0,10	>0,05	Depression
HAM-D	11,04±7,25	8,64±6,74	2,38	>0,05	Anxiety

Using binary logistic regression, predictive models of suicide risk were searched for and are reported in **Table 8**. High mean scores obtained in C-SRSS, BHS, BDI-II, PAS and OMMP scales increase the likelihood of making a suicide; in particular, the increase of one unit in the total score on the BDI-II scale translates into a probability greater than 6,4% of attempting a new suicide ($p < 0,001$), this being the score with the highest R^2 Nagelkerke, a measure of fit of the model used in logistic regression. ($R^2=0,169$); similarly, increases of the C-SSRS - Current score ($p < 0,001$) by one unit corresponds to a 8,9% greater risk of incurring a new SA; the increase of one unit in the scale score C-SSRS - Lifetime ($p = 0,002$) results in a probability of making a new SA greater than 7,4%; the increase of one unit in the scale score BHS ($p = 0,04$) results in a probability of making a new SA greater than 8,1%; the increase of one unit in the scale score PAS ($p = 0,015$) results in a probability of making a new SA greater than 3,8%; while the OMMP scale showed no significant difference between those who attempted suicide in 6 months and those who didn't, the increase of one unit in the scale score OMMP ($p = 0,002$) results in a probability of making a new SA greater than 1,8%. **Table 9** summarizes these results.

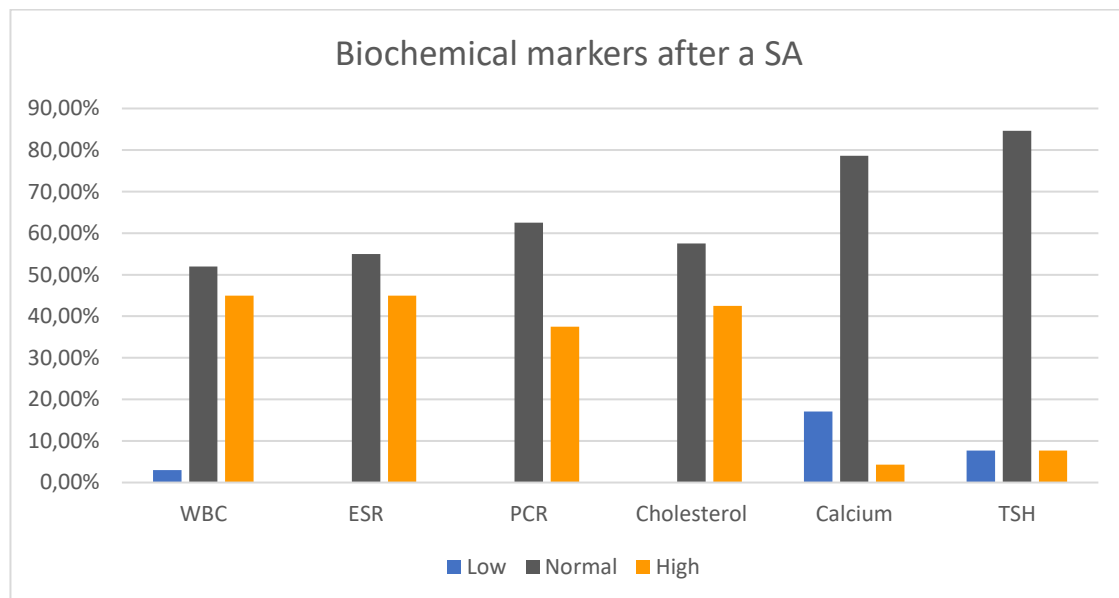
Table 8: Binary regression model between psychometric scales and predictive risk of incurring a new AS

Scales	R² Nagelkerke	Exp(B)	p	
C-SSRS - Intentisty (Lifetime)	0,096	1,074	0,002	Control Scale
C-SSRS - Intensity (Current)	0,115	1,089	<0,001	Control Scale
C-SSRS – Ideation (Lifetime)	0,121	4,905	<0,001	Control Scale
C-SSRS – Ideation (Current)	0,164	6,876	<0,001	Control Scale
BHS	0,042	1,081	0,044	Hoplessness
BDI-II	0,169	1,064	<0,001	Depression
PAS	0,061	1,038	0,015	Psychache
OMMP	0,102	1,018	0,002	Psychache
HAM-A	0,000	1,004	0,928	Anxiety
HAM-D	0,024	1,047	0,112	Depression

Table 9: increase in suicidal risk for each point of increase in score on the scales considered, measured through binary logistic regression.

Scales	Increase in suicide risk (%)	<i>p</i>	
C-SSRS (Lifetime)	7,4	0,002	Control Scale
C-SSRS (Current)	8,9	<0,001	Control Scale
BHS	8,1	0,044	Hoplessness
BDI-II	6,4	<0,001	Depression
PAS	3,8	0,015	Psychache
OMMP	1,8	0,002	Psychache

Regarding biological markers, no statistically significant indicators of suicide attempt were found. However, most of the patients showed altered biochemical results at the routine tests done after the SA. In particular, for inflammation markers, 45% had high WBC, 45% had high ESR and 37,5% had high CRP. 42,5% of the sample had a high cholesterol count, only 4,3% had high calcium and 7,7% had high TSH.



[Fig. 9]: Values of biochemical markers assessed at time of the suicide attempt.

WBC = 4.30-11.00 [$10^9/L$]; ESR = 0-15 [mm]; CRP = 0,0-5,0 [mg/L]; Cholesterol = <200 [mg/dL]; Total Calcium = 8.8-10.2 [mg/dL]; TSH = 0,4-4 [$\mu U/ml$]

4. DISCUSSION

4.1 RESEARCH DISCUSSION

According to suicide research over the past 20 years, the greatest risk factor for suicide is not psychiatric diagnosis but levels of psychological pain or "psychache," described as a subjective experience of intolerable distress that the person wishes to end by any means available, including physical death (Shneidman 1993; 2005). Therefore, suicide prevention efforts are shifting towards early recognition and treatment of this pain, so that the individual can see his quality of life improve and therefore choose to live (Pompili, 2013). Several studies have found a statistically significant association between high levels of mental pain and a history of suicide attempts, both in clinical samples (Orbach et al, 2003b; Flamenbaum & Holden, 2007; Levi et al., 2008; Pereira et al, 2010; Troister & Holden, 2010; Patterson & Holden, 2012; DeLisle & Holden, 2009) and non-clinical samples (Lester, 2000; Holden et al., 2001; Leenaars & Lester, 2004). In the few prospective studies published so far, it has also been shown that the initial intensity of psychological pain is associated with the intensity of suicidal ideation measured both in the short term (weeks, months) and in the long term (2 years, 4 years), but, as yet, no studies have actually correlated mental pain with suicide or suicidal attempts (Troister & Holden: 2012; 2013, 2018; 2020; Sajatovic et al., 2016). This longitudinal study aimed to evaluate the role of mental pain in predicting effective suicide or suicide attempt and its interactions with other sociodemographic, clinical, and psychometric factors, in order to better understand the potential applicability of its measurement as a screening method in the context of suicide prevention.

Regarding the first objective we can say that from this work a significant correlation emerges between high levels of mental pain and the risk of attempting suicide in the following months. The results showed that not only mental pain, but also high levels of hopelessness and depressive symptoms are associated with the risk of AS in the following months. The results also showed that high levels of mental pain, hopelessness and depressive symptoms are associated not only with a history of AS but also with the risk of AS in the following months. Total scores measured by the PAS, BDI-II, C-SSRS and BHS scales were significantly higher in the group with a AS during the follow up than in those without and the binary regression model made possible to highlight how as the score on these scales increases, the risk of AS also increases. Among these, however, only PAS, BDI-II and BHS seem to have the characteristics of simplicity and speed of use which make them more applicable in a screening contexts. HAM-A and HAM-D scale did not seem to be related to suicide risk, despite various evidence showing that high levels of anxiety and depression are a risk factor and that anxiety disorders are associated with an increase in suicide risk (Nepon et al., 2010). This discrepancy could be explained both in terms of diagnostic sampling, i.e. a prevalence of Panic Disorder (Katz et al., 2011), and intrinsic limitations of the evaluation tool. Pathological anxiety is a complex phenomenon not adequately estimated, in its subjective dimensions and experience (therefore properly symptomatic), by a scale that focuses on the evaluation mainly on clinical signs (thus objectivable). The OMMP score wasn't significantly associated with new AS, although high were found in that group. Moreover, it was found to be significant, when analyzed with a regression model. This was also found in literature were a new form of the scale (OMMP-8) was found a more viable option, although more research should be completed prior to adoption (Casanova et al, 2021).

In this study, the suicide risk was also assessed over time, specifically in the 6 and 12 months following patient recruitment. The low number of AS at 12 months (only two patients) made it impossible to proceed with a statistical comparison. Some of the tools used in this work (C-SSRS, BDI, BHS, PAS) were statistically significant at 6 months in detecting patients with a higher suicide risk. This can be interpreted as an important clinical finding, indicating that mental pain may be an indicator of suicide risk in the short term, while it may lose validity over time, although confirmation can only be obtained by extending the sample in order to have an adequate number of patients for statistical analyzes even at 12 months. Anyway, this finding has important clinical implications, as it highlights the potential value of using mental pain scales to assess suicide risk in specific time periods.

Regarding the second objective, deepening knowledge on the correlation between sociodemographic and clinical variables with suicide risk, we can analyze our findings here.

Regarding sociodemographic data, the characteristics that appeared to be more represented in those who attempted suicide was being unemployed or invalid, whereas being employed was positively associated with less percentage of AS, which is a tendency that is found in other studies among the literature (Milner et al., 2016). The main reason for the absence of work in the people in our sample was represented by the presence of a mental disability such as to limit if not abolish the ability to work. There are several reasons why disability may be associated with suicide risk. One is that individuals with disabilities might face significant challenges in their daily lives, including physical limitations, social isolation, and financial difficulties. These challenges can lead to feelings of hopelessness, helplessness, and despair, which are known risk factors for suicide. Another factor is the presence of co-occurring mental health conditions, such as depression or anxiety, which are more common among individuals with disabilities. These conditions can contribute to suicidal ideation and behavior (Hawton et al., 2013). No significant associations were found with gender, age, education level, and marital status, although being unmarried seemed to have a tendency towards an increased risk of AS. This data has also been found in other works (Masocco et al., 2008). This finding might be due to an increased feeling of loneliness, and the hypothesis that marriage leads to greater social integration and more supportive social networks may be applicable.

As for clinical data, our findings suggest that the absence of comorbidities may be associated to a lesser AS risk, while the presence of SUD or disability may increase it. The association between alcohol use disorder and suicidal risk can be explained both by an individual predisposition to impulsive and maladaptive behaviors and by a worsening of executive functions induced by chronic alcohol use with consequent loss of the ability to self-regulate emotions and the development of maladaptive copings which, in turn, increase suicidal risk. In addition, job loss, social isolation and loss of family relationships associated with alcohol dependence, further contribute to increase the risk of AS (Rizk et al., 2021). Similarly, chronic use of opioids and other substances can cause changes in the brain's neurobiology that result in heightened negative emotions, further contributing to the risk of suicide or AS and perpetuating ongoing opioid use. Another clinical risk factor for AS found in our sample is, in fact, the presence of substance abuse, past or present. This finding is consistent with numerous other scientific evidence on the subject (Pompili, Serafini et al., 2012; Yuodelis-Flores, Ries, 2015). Substance abuse is associated with suicide for several reasons. Firstly, some substances like alcohol and psychoactive substances, are known to impair judgment, increase impulsivity and reduce inhibitions, making it more likely for individuals to engage in risky behaviors, including self-harm or suicide attempts (Isaacs et al., 2022). Secondly, substance abuse often co-occurs with other psychiatric disorders, such as depression,

anxiety, and personality disorders, which also increase the risk of suicide (Hag Lee et al., 2017). Thirdly, substance abuse can lead to social, financial, and interpersonal problems, which can further exacerbate feelings of hopelessness and despair, contributing thus to suicidal ideation and suicidal behavior. Additionally, also substances' withdrawal, including alcohol withdrawal, cause intense emotional distress, thus increasing suicide risk, during the withdrawal period (Gupta et al., 2019). Finally, substance abuse can interfere with effective treatment for mental health conditions, making more difficult to manage the underlying psychiatric symptoms that contribute to suicidal ideation and behavior (Venkatakrishnan et al., 2006).

The increased use of polypharmacy in those who had a suicide attempt, compared to those who hadn't, may be due to more severe and complex psychopathological conditions, including comorbidity with more than one mental disorder. In fact, the presence of a more serious clinical picture and the co-presence of multiple diagnoses, lead clinicians to a greater use of therapeutic combinations. However, using multiple medications at the same time can cause several challenges, for example it makes harder to determine if a medication is causing a particular side effect or if it is due to the underlying condition. Furthermore, drug interactions, not always carefully evaluated or investigated, can cause irritability or agitation and these are known factors associated with suicidal behavior (Boghos et al., 2013). Regarding the use of antipsychotics, the explanation appears more controversial: other authors have found that the use of antipsychotics seems to represent a risk factor to SA (Ruengorn, Sanichwankul et al., 2012). There are two important issues related to bipolar disorder that are often overlooked in research studies. The first issue is that patients with bipolar disorder frequently do not adhere to their treatment plan, which can affect their risk of suicide or AS (Sajatovic et al., 2009). The second issue is the significant risk of suicide or AS associated with psychotropic withdrawal, especially if the withdrawal is rapid (Cosci et al., 2020). Furthermore, add-on therapy with second generation antipsychotics is often used in resistant forms of depression and therefore prescribed in the most serious clinical conditions. It is therefore possible to interpret this data not so much in the form that the antipsychotic in itself increases the risk of suicide, but rather that the antipsychotic is more easily prescribed in forms of resistant or bipolar depression, more easily associated with suicide risk in itself.

Regarding biochemical markers, no significant association with suicide was found. This may be at least partly due to the fact that not all cases of AS were subjected to routine blood tests and therefore the sample size was small and not homogeneous. Almost none of the patients without a suicide attempt had blood tests done so it was not possible to compare the two groups. The comparison of the laboratory values was then compared to the values of the general population. Levels of WBC, ESR and CRP were higher than normal in respectively 45%, 45% and 37,5% of the sample, a finding that is consistent with what is seen in literature. For example, Katon and co. described the biological profile of patients with increased suicide how characterized by increased levels of IL-6, lymphocytes, monocytes, WBC and polymorphonuclear white blood cells (PMN) significantly impacted suicide risk, with the latter two inferring the strongest influence (Keaton et al., 2019). Elevated levels of C-Reactive Protein have also been identified as correlated with both high-lethality suicide attempts (Aguglia et al., 2022) and a lower response to antidepressants (Gasparini et al., 2022). Total calcium and TSH were in normality range in most of the patients, as only 4,3% had high calcium levels and only 7,7% had high TSH levels. Surely the introduction of laboratory tests among the screening methods, are a topic of growing interest and deserve further investigation in the future.

4.2 LIMITATIONS

A limitation, common to all surveys using self-administered instruments (or in any case concerning emotional and subjective dimensions) is the possibility of confusing information due to patients' reticence, shame or fear of consequences. Still, the fact that the self-administered scales were statistically significant, while the scales administered by the clinician are not (HAM-A and HAM-D). This data shows how subjective self-evaluation of mental distress is more reliable than external evaluation.

Another factor that represented a major limitation is the small sample size. Firstly, because it did not allow statistical analyzes to be carried out at 12 months but only at 6 months. Secondly because it did not make it possible to use multivariable regression to estimate suicide risk. The introduction of other independent variables with the available sample size would have violated the regression axioms themselves. This, however, did not make it possible to correct the correlation between scale scores and suicide risk for other confounding variables such as sociodemographic factors, diagnosis, comorbidity or previous AS. Our results are aligned with some works (Orbach et al, 2003b; Flamenbaum & Holden, 2007; Levi et al., 2008; Pereira et al, 2010; Troister & Holden, 2010; Patterson & Holden, 2012; DeLisle & Holden, 2009), but not with other studies (Lester, 2000; Holden et al., 2001; Leenaars & Lester, 2004), thus confirming the need to reproduce the study on a larger sample.

The collection of blood test values was limited by the fact that patients who did not enter hospital at baseline or during the follow-up did not have blood tests performed. In this way it was not possible to include in the analyzes any of the patients from the group who did not attempt suicide during follow-up and only a fraction of those who have attempted it. The comparison was therefore made with the values of the general population but this represents a significant limit to the interpretation of the results as it is not possible to correct for confounding factors.

Finally, some variables potentially useful in predicting increased suicide risk were not analyzed. An example is the presence of childhood trauma, which in the literature seems related to both an increase in levels of mental pain and an increased risk of suicidal ideation (Pompili et al., 2022). We chose not to consider this variable as it is not included in the anamnestic collection routinely registered in the medical record and it seemed to the authors to be a too delicate topic to be addressed in the space of a single check-up visit. This, however, subtracts an important risk factor to consider when estimating suicide risk.

4.3 CONCLUSION AND FUTURE PERSPECTIVES

The results of this study suggest that scores obtained from the C-SSRS, BHS, BDI-II, PAS and OMMP scales may be useful tools for assessing suicidal risk in psychiatric outpatients. It would be useful to broaden the sample also for a more accurate temporal risk stratification, for example by evaluating the short-term (within 1 month) or longer-term risk. Furthermore, the study of other environmental and biological screening factors seems to be of primary importance, in order to identify a target population with an increased risk to be directed to targeted treatment pathways. From this point of view, the data relating to changes in inflammation or hormone levels seem to be a promising investigation area.

A key point is that the correlation between scale scores and suicidal risk proved to be independent of psychiatric diagnosis. We therefore hope to involve a greater number of people in this research in the future, including not only

patients belonging to psychiatric services, but also the general population with the help of general practitioners. This is particularly important since primary care physicians are often the first point of contact for patients seeking mental health care, and they may not have access to specialized psychiatric services or resources. By identifying patients at increased risk of suicide using some of these scales, primary care physicians and general practitioner can provide targeted prevention and treatment interventions in order to reduce the risk of suicide in their patient population (Luoma et al., 2002; Gunnell et al., 2003).



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BHS – Beck Hopelessness Scale

Adattamento italiano a cura
di Maurizio Pompili et al.

QUESTIONARIO

Nome e cognome _____ Sesso: M F Età _____
Occupazione _____ Scolarità _____
Data della prova _____

ISTRUZIONE

Il presente questionario si compone di 20 affermazioni. Per favore legga le affermazioni attentamente una alla volta. Sel'affermazione descrive i suoi atteggiamenti nell'ambito della settimana passata (oggi compreso) segni con una X la casella nella colonna Vero accanto all'affermazione. Se l'affermazione non descrive i suoi atteggiamenti segni con una X la casella nella colonna falso accanto all'affermazione. Si accerti di leggere ogni affermazione attentamente. Grazie.

	VERO	FALSO
1. Vedo il futuro con speranza ed entusiasmo	<input type="checkbox"/>	<input type="checkbox"/>
2. Potrei arrendermi perché non posso migliorare le cose per me	<input type="checkbox"/>	<input type="checkbox"/>
3. Quando le cose vanno male mi consola sapere che non può durare così in eterno	<input type="checkbox"/>	<input type="checkbox"/>
4. Non posso immaginare quello che sarà della mia vita tra 10 anni	<input type="checkbox"/>	<input type="checkbox"/>
5. Ho abbastanza tempo per realizzare le cose che desidero fare	<input type="checkbox"/>	<input type="checkbox"/>
6. Nel futuro mi aspetto di riuscire in quello che mi interessa di più	<input type="checkbox"/>	<input type="checkbox"/>
7. Il mio futuro mi sembra buio	<input type="checkbox"/>	<input type="checkbox"/>
8. Mi aspetto di ottenere dalla vita più cose buone rispetto alla persona media	<input type="checkbox"/>	<input type="checkbox"/>
9. Semplicemente non riesco ad avere buone occasioni e non c'è motivo per cui ci riesca in futuro	<input type="checkbox"/>	<input type="checkbox"/>
10. Le mie esperienze passate mi hanno preparato bene per il futuro	<input type="checkbox"/>	<input type="checkbox"/>
11. Se guardo avanti vedo solo situazioni spiacevoli piuttosto che piacevoli	<input type="checkbox"/>	<input type="checkbox"/>
12. Non mi aspetto di ottenere ciò che voglio veramente	<input type="checkbox"/>	<input type="checkbox"/>
13. Quando guardo al futuro mi aspetto di essere più felice di adesso	<input type="checkbox"/>	<input type="checkbox"/>
14. Semplicemente le cose non vanno come io desidero che vadano	<input type="checkbox"/>	<input type="checkbox"/>
15. Ho una grossa fede nel futuro	<input type="checkbox"/>	<input type="checkbox"/>
16. Non ottengo mai ciò che desidero, quindi è sciocco desiderare alcunché	<input type="checkbox"/>	<input type="checkbox"/>
17. È molto inverosimile che nel futuro io ottenga una vera soddisfazione	<input type="checkbox"/>	<input type="checkbox"/>
18. Il futuro mi sembra vago e incerto	<input type="checkbox"/>	<input type="checkbox"/>
19. Posso aspettarmi che arrivino bei tempi piuttosto che brutti	<input type="checkbox"/>	<input type="checkbox"/>
20. È inutile provare ad ottenere ciò che voglio perché probabilmente non ci riuscirò	<input type="checkbox"/>	<input type="checkbox"/>

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Scala del Dolore Mentale

Mental Pain Scale (OMMP), Orbach et al., 2003

Per favore, indichi il numero che meglio descrive il suo accordo come le seguenti affermazioni :

- 1 Totalmente in disaccordo
- 2 In disaccordo
- 3 Per certi versi d'accordo
- 4 D'accordo
- 5 Particolarmente d'accordo

1. Nessuno si interessa a me	1	2	3	4	5
2. Sono completamente impotente	1	2	3	4	5
3. Mi sento sconvolto emotivamente/ Sento una forte agitazione emotiva dentro di me	1	2	3	4	5
4. Non posso fare nulla/ Non sono capace di fare niente	1	2	3	4	5
5. Andrò in pezzi/ crollerò	1	2	3	4	5
6. Sono spaventato dal future/ Ho paura del futuro	1	2	3	4	5
7. Sono rifiutato da tutti	1	2	3	4	5
8. Mi sento in balia di tanti sentimenti/ Sono schiacciato da tanti sentimenti	1	2	3	4	5
9. Sono completamente annientato	1	2	3	4	5
10. Ho perso qualcosa che non troverò ma più	1	2	3	4	5
11. Mi sento intorpidito e privo di vita	1	2	3	4	5
12. Mi sento abbandonato e solo	1	2	3	4	5
13. Non ho il controllo sulla mia vita	1	2	3	4	5
14. I miei sentimenti cambiano in continuazione	1	2	3	4	5
15. Mi sento estraneo a me stesso	1	2	3	4	5
16. Gli altri mi odiano	1	2	3	4	5

17. Sento che non sono più quello di una volta	1	2	3	4	5
18. Sono inutile/ Non ho nessun valore	1	2	3	4	5
19. Mi sento paralizzato	1	2	3	4	5
20. Non riesco a concentrarmi	1	2	3	4	5
21. Non riesco a fidarmi di me	1	2	3	4	5
22. Le situazioni difficili non cambieranno mai	1	2	3	4	5
23. Mi sento come se non fossi reale	1	2	3	4	5
24. Ho difficoltà a pensare	1	2	3	4	5
25. Ho bisogno del supporto di altre persone	1	2	3	4	5
26. Il mondo è cambiato per sempre	1	2	3	4	5
27. Mi sento confuso	1	2	3	4	5
28. Non ho controllo su ciò che sta accadendo dentro me	1	2	3	4	5
29. Non sarò mai capace di ridurre la mia sofferenza	1	2	3	4	5
30. La mia vita si è fermata	1	2	3	4	5
31. Non so cosa aspettarmi dal futuro	1	2	3	4	5
32. Qualcosa nella mia vita è stato danneggiato per sempre	1	2	3	4	5
33. C'è incertezza rispetto alla mia vita e a me stesso	1	2	3	4	5
34. Non sarò mai più la stessa persona	1	2	3	4	5
35. I miei sentimenti sono fortemente altalenanti	1	2	3	4	5
36. Non ho il controllo della situazione	1	2	3	4	5
37. Voglio essere lasciato da solo	1	2	3	4	5
38. Non ho obiettivi per il futuro	1	2	3	4	5

39. Non ho desideri	1	2	3	4	5
40. Non ho voglia di parlare con gli altri	1	2	3	4	5
41. Non riesco a trovare un senso alla mia vita	1	2	3	4	5
42. Non riesco a stare da solo	1	2	3	4	5
43. Non posso cambiare ciò che mi sta succedendo	1	2	3	4	5
44. Il dolore non cesserà mai	1	2	3	4	5

Psychache Scale (PAS), Holden et al., 2001

Le seguenti affermazioni si riferiscono alla sua sofferenza psicologica, NON al suo dolore fisico. Cerchiando il numero appropriato indichi quanto di frequente si presentano le seguenti condizioni.

1= mai 2= a volte 3= spesso 4= moto spesso 5= sempre

	mai	a volte	spesso	molto spesso	sempre
1. Provo dolore psicologico	1	2	3	4	5
2. Provo tormento interiore	1	2	3	4	5
3. Il mio dolore psicologico sembra essere peggiore di qualsiasi dolore fisico	1	2	3	4	5
4. Il mio dolore mi fa venire voglia di urlare	1	2	3	4	5
5. Il mio dolore rende la mia vita cupa	1	2	3	4	5
6. Non riesco a capire perché soffro	1	2	3	4	5
7. A livello psicologico mi sento malissimo	1	2	3	4	5
8. Soffro perché mi sento	1	2	3	4	5
9. La mia anima è tormentata/la mia anima soffre/ Soffro nell'anima	1	2	3	4	5

Gentilmente continui il questionario utilizzando la seguente scala:

1= fortemente in disaccordo 2= in disaccordo 3= incerto/non so

4= d'accordo

5= fortemente

d'accordo

	fortemente in disaccordo	In disaccordo	Incerto/non so	d'accordo	fortemente d'accordo
10. Non riesco più a sopportare il dolore	1	2	3	4	5
11. A causa del mio dolore, la mia condizione è insostenibile	1	2	3	4	5
12. Il mio dolore mi sta distruggendo	1	2	3	4	5
13. Il mio dolore influisce su tutto ciò che faccio/ Il mio dolore psicologico influenza qualsiasi cosa	1	2	3	4	5

BDI – II

Istruzioni

Il presente questionario consiste di 21 gruppi di affermazioni. Per favore legga attentamente le affermazioni di ciascun gruppo. Per ogni gruppo scelga quella che meglio descrive come lei si è sentito nelle ultime due settimane (incluso oggi). Faccia una crocetta sul numero corrispondente all'affermazione da lei scelta. Se più di un'affermazione dello stesso gruppo descrive ugualmente bene come lei si sente, faccia una crocetta sul numero più elevato per quel gruppo. Non scelga più di un'affermazione per ciascun gruppo, inclusa la domanda 16 (“Sonno”) e la domanda 18 (“Appetito”). È importante ricordare che non ci sono risposte giuste o sbagliate. Non si soffermi troppo su ogni affermazione. La prima risposta è spesso la più accurata. Grazie.

1. Tristezza

0. Non mi sento triste.
1. Mi sento triste per la maggior parte del tempo.
2. Mi sento sempre triste.
3. Mi sento così triste o infelice da non poterlo sopportare.

2. Pessimismo

0. Non sono scoraggiato riguardo al mio futuro.
1. Mi sento più scoraggiato riguardo al mio futuro rispetto al solito.
2. Non mi aspetto nulla di buono per me.
3. Sento che il mio futuro è senza speranza e che continuerà a peggiorare.

3. Fallimento

0. Non mi sento un fallito.
1. Ho fallito più di quanto avrei dovuto.
2. Se ripenso alla mia vita riesco a vedere solo una serie di fallimenti.
3. Ho la sensazione di essere un fallimento totale come persona.

4. Perdita di piacere

0. Traggo lo stesso piacere di sempre dalle cose che faccio.
1. Non traggio più piacere dalle cose come un tempo.
2. Traggo molto poco piacere dalle cose che solitamente mi divertivano.
3. Non riesco a trarre alcun piacere dalle cose che una volta mi piacevano.

5. Senso di colpa

0. Non mi sento particolarmente in colpa.
1. Mi sento in colpa per molte cose che ho fatto o che avrei dovuto fare.
2. Mi sento molto spesso in colpa.
3. Mi sento sempre in colpa.

6. Sentimenti di punizione

- 0. Non mi sento come se stessi subendo una punizione.
- 1. Sento che potrei essere punito.
- 2. Mi aspetto di essere punito.
- 3. Mi sento come se stessi subendo una punizione.

7. Autostima

- 0. Considero me stesso come ho sempre fatto.
- 1. Credo meno in me stesso.
- 2. Sono deluso di me stesso.
- 3. Mi detesto.

8. Autocritica

- 0. Non mi critico né mi biasimo più del solito.
- 1. Mi critico più spesso del solito.
- 2. Mi critico per tutte le mie colpe.
- 3. Mi biasimo per ogni cosa brutta che mi accade.

9. Suicidio

- 0. Non ho alcun pensiero suicida.
- 1. Ho pensieri suicidi ma non li realizzerei.
- 2. Sento che starei meglio se morissi.
- 3. Se mi si presentasse l'occasione, non esiterei ad uccidermi.

10. Pianto

- 0. Non piango più del solito.
- 1. Piango più del solito.
- 2. Piango per ogni minima cosa.
- 3. Ho spesso voglia di piangere ma non ci riesco.

11. Agitazione

- 0. Non mi sento più agitato o teso del solito.
- 1. Mi sento più agitato o teso del solito.
- 2. Sono così nervoso o agitato al punto che mi è difficile rimanere fermo.
- 3. Sono così nervoso o agitato che devo continuare a muovermi o fare qualcosa.

12. Perdita di interessi

- 0. Non ho perso interesse verso le altre persone o verso le attività.
- 1. Sono meno interessato agli altri o alle cose rispetto a prima.
- 2. Ho perso la maggior parte dell'interesse verso le altre persone o cose.
- 3. Mi risulta difficile interessarmi a qualsiasi cosa.

13. Indecisione

0. Prendo decisioni come sempre.
1. Trovo più difficoltà del solito nel prendere decisioni.
2. Ho molte più difficoltà nel prendere decisioni rispetto al solito.
3. Non riesco a prendere nessuna decisione.

14. Senso di inutilità

0. Non mi sento inutile
1. Non mi sento valido e utile come un tempo.
2. Mi sento più inutile delle altre persone.
3. Mi sento completamente inutile.

15. Perdita di energia

0. Ho la stessa energia di sempre.
1. Ho meno energia del solito.
2. Non ho energia sufficiente per fare la maggior parte delle cose.
3. Ho così poca energia che non riesco a fare nulla.

16. Sonno

0. Non ho notato alcun cambiamento nel mio modo di dormire.

- 1a. Dormo un po' più del solito.
- 1b. Dormo un po' meno del solito.

- 2a. Dormo molto più del solito.
- 2b. Dormo molto meno del solito.

- 3a. Dormo quasi tutto il giorno.
- 3b. Mi sveglio 1-2 ore prima e non riesco più ad addormentarmi.

17. Irritabilità

0. Non sono più irritabile del solito.
1. Sono più irritabile del solito.
2. Sono molto più irritabile del solito.
3. Sono sempre irritabile.

18. Appetito

0. Non ho notato alcun cambiamento nel mio appetito.

- 1a. Il mio appetito è un po' diminuito rispetto al solito.
- 1b. Il mio appetito è un po' aumentato rispetto al solito.

- 2a. Il mio appetito è molto diminuito rispetto al solito.
- 2b. Il mio appetito è molto aumentato rispetto al solito.

- 3a. Non ho per niente appetito.
- 3b. Mangerei in qualsiasi momento.

19. Concentrazione

0. Riesco a concentrarmi come sempre.
1. Non riesco a concentrarmi come al solito.
2. Trovo molto difficile concentrarmi per molto tempo su qualsiasi cosa.
3. Non riesco a concentrarmi su nulla.

20. Fatica

0. Non sono più stanco o affaticato del solito.
1. Mi stanco e mi affatico più facilmente del solito.
2. Sono così stanco e affaticato che non riesco a fare molte delle cose che facevo prima.
3. Sono talmente stanco e affaticato che non riesco più a fare nessuna delle cose che facevo prima.

21. Sesso

0. Non ho notato alcun cambiamento recente nel mio interesse verso il sesso.
1. Sono meno interessato al sesso rispetto a prima.
2. Ora sono molto meno interessato al sesso.
3. Ho completamente perso l'interesse verso il sesso.

HAMILTON RATING SCALE FOR ANXIETY (HAM-A)

Cognome e Nome _____	Età _____	PUNTEGGIO GLOBALE
Codice Paziente _____	Valutatore _____	Data di valutazione _____
Istruzioni: Riportare nell'apposita casella il punteggio attribuito a ciascun item.		
Punteggio: 0 = assente 1 = lieve 2 = moderato 3 = grave 4 = molto grave		
1. ANSIA		<input style="width: 50px; height: 20px;" type="text"/>
Preoccupazioni, previsioni pessimistiche, paura del futuro, irritabilità		
2. TENSIONE		<input style="width: 50px; height: 20px;" type="text"/>
Senso di tensione, facile stancabilità, trasalimenti, facilità al pianto, tremiti, sensazione di irrequietezza, incapacità a rilassarsi		
3. PAURE		<input style="width: 50px; height: 20px;" type="text"/>
Del buio, degli estranei, di essere lasciato solo, degli animali, del traffico, della folla		
4. INSONNIA		<input style="width: 50px; height: 20px;" type="text"/>
Difficoltà ad addormentarsi, sonno interrotto, sonno non riposante e senso di stanchezza al risveglio, sogni, incubi, terrori notturni		
5. SFERA INTELLETTIVA		<input style="width: 50px; height: 20px;" type="text"/>
Difficoltà a concentrarsi, riduzione della memoria		
6. UMORE DEPRESSO		<input style="width: 50px; height: 20px;" type="text"/>
Perdita di interessi, incapacità a trovare piacere negli hobbies, depressione, risveglio precoce, alternanza diurna		
7. SINTOMI SOMATICI		<input style="width: 50px; height: 20px;" type="text"/>
Dolori muscolari, senso di stiramento, irrigidimento, contrazioni cloniche, denti serrati, vocetremula, aumento del tono muscolare		
8. SINTOMI SOMATICI (ORGANI DI SENSO)		<input style="width: 50px; height: 20px;" type="text"/>
Ronzii auricolari, visione confusa, vampi di caldo e di freddo, senso di debolezza, sensazioni di bucare		
9. SINTOMI CARDIOVASCOLARI		<input style="width: 50px; height: 20px;" type="text"/>
Tachicardia, palpitazioni, dolori al petto, pulsazioni vasali, senso di svenimento		
10. SINTOMI RESPIRATORI		<input style="width: 50px; height: 20px;" type="text"/>
Senso di peso o di costrizione al torace, senso di soffocamento, sospiri, dispnea		
11. SINTOMI GASTROINTESTINALI		<input style="width: 50px; height: 20px;" type="text"/>
Difficoltà a deglutire, flatulenza, dolori addominali, pirosi, senso di pienezza, nausea, vomito, borborigmi, meteorismo, perdita di peso, stipsi		
12. SINTOMI GENITOURINARI		<input style="width: 50px; height: 20px;" type="text"/>
Pollachiuria, stimolo alla minzione, amenorrea, menorragie, comparsa di frigidità, ejaculatio praecox, perdita della libido, impotenza		
13. SINTOMI A CARICO DEL SISTEMA NERVOSO AUTONOMO		<input style="width: 50px; height: 20px;" type="text"/>
Secchezza delle fauci, rossore, pallore, tendenza a sudare, vertigini, cefalea, piloerezione		
14. COMPORTAMENTO DEL SOGGETTO DURANTE L'ESAME		<input style="width: 50px; height: 20px;" type="text"/>
Agitato, irrequieto, va avanti e indietro, tremore alle mani, fronte corrugata, faccia tirata, sospiri o tachipnea, pallore del volto, deglutizioni, ecc.		

HAMILTON RATING SCALE FOR DEPRESSION (HAM-D)

Cognome e Nome _____ Et  _____ **PUNTEGGIO GLOBALE** _____

Codice Paziente _____ Valutatore _____ Data di valutazione _____

ISTRUZIONI GENERALI: scegliere per ciascun item il punteggio che meglio caratterizza il paziente e riportarlo nella casella a destra dell'item stesso.

1- UMORE DEPRESSO

(Sentimento di tristezza, mancanza di speranza, sentimento di incapacit  e di inutilit )

- | | |
|---|---|
| 0 = Assente | 3 = Comunica questi sentimenti con messaggi non verbali, cio  attraverso l'espressione del volto, la voce e la tendenza al pianto |
| 1 = Manifesta questi sentimenti solo se interrogato | 4 = Il paziente manifesta quasi esclusivamente questi sentimenti mediante messaggi sia verbali che non verbali |
| 2 = Esprime spontaneamente questi sentimenti | |

2 – SENTIMENTI DI COLPA

- | | |
|--|--|
| 0 = Assenti | 3 = L'attuale malattia   una punizione. Deliri di colpa |
| 1 = Autoaccusa, pensa di aver deluso la gente | 4 = Ode voci di accusa o di denigrazione e/o ha esperienze allucinatorie visive a contenuto minaccioso |
| 2 = Idee di colpa o ripensamenti su errori passati o su azioni peccaminose | |

3 – SUICIDIO

- | | |
|--|--|
| 0 = Assente | 3 = Idee o gesti di suicidio |
| 1 = Pensa che la vita non valga la pena di essere vissuta | 4 = Tentativi di suicidio (<i>ogni serio tentativo deve essere valutato '4'</i>) |
| 2 = Vorrebbe essere morto e pensa alla possibilit  di suicidarsi | |

4 – INSONNIA INIZIALE

- 0 = Nessuna difficolt  ad addormentarsi
 1 = Lamenta di avere talvolta difficolt  ad addormentarsi (p. es., gli occorre pi  di mezz'ora)
 2 = Ha sempre difficolt  ad addormentarsi

5 – INSONNIA CENTRALE

- | | |
|---|--|
| 0 = Nessuna difficolt  | 2 = Si sveglia durante la notte - segnare '2' se si alza dal letto (<i>a meno che non sia per urinare</i>) |
| 1 = Lamenta di essere diventato irrequieto durante la notte | |

6- INSONNIA RITARDATA

- 0 = Nessuna difficolt 
 1 = Si risveglia precocemente (nelle prime ore del mattino), ma si riaddormenta
 2 =   incapace di addormentarsi se si alza dal letto

7- LAVORO E INTERESSI

- 0 = Nessuna difficolt 
 1 = Pensieri o sentimenti di incapacit , facile affaticabilit  o debolezza nelle attivit  (lavoro o hobby)
 2 = Perdita di interesse per le attivit  - lavoro o hobby - sia riferite direttamente dal paziente, sia espresse mediante atteggiamenti, indifferenza, indecisione ed incertezza (*sente che deve sforzarsi per lavorare*)
 3 = Dedicava un minor tempo alle attivit  o   inefficiente
 4 = Ha cessato di lavorare a causa della malattia

8 – RALLENTAMENTO

(Ideazione e linguaggio rallentati; ridotta capacit  a concentrarsi; diminuita attivit  motoria)

- | | |
|---|-----------------------------------|
| 0 = Pensiero e linguaggio normali | 3 = Colloquio difficile |
| 1 = Lieve rallentamento durante il colloquio. | 4 = Stato di arresto psicomotorio |
| 2 = Evidente rallentamento durante il colloquio | |

9 – AGITAZIONE

- | | |
|--|---|
| 0 = Assente | 3 = Si muove continuamente, non riesce a stare seduto |
| 1 = Irrequietezza | 4 = Si torce le mani, si morde le unghie, si tira i capelli, si morde le labbra |
| 2 = Gioca con le mani, con i capelli, ecc. | |

10 – ANSIA PSICHICA

- | | |
|--|---|
| 0 = Assente | 3 = Atteggiamento apprensivo evidente dalla mimica e dal linguaggio |
| 1 = Tensione soggettiva ed irritabilit  | 4 = Manifesta spontaneamente paure |
| 2 = Preoccupazioni per questioni di poco conto | |

11 – ANSIA SOMATICA			<input type="text"/>
<i>ASPETTI SOMATICI DELL'ANSIA</i>			
Gastrointestinali: secchezza delle fauci, meteorismo, indigestione, diarrea, crampi, eruttazione; Cardiovascolari: palpitazioni, cefalea; Respiratori: iperventilazione, sospiri; Genito-urinari: pollachiuria; Sudorazione			
0 = Assente	2 = Moderata	4 = Invalidante	
1 = Lieve	3 = Notevole		
12 – SINTOMI SOMATICI GASTROINTESTINALI			<input type="text"/>
0 = Assenti			
1 = Perdita dell'appetito, ma si lamenta senza essere stimolato o aiutato dal personale. Senso di peso all'addome.			
2 = Difficoltà ad alimentarsi senza lo stimolo o l'aiuto del personale. Richiede o ha bisogno di lassativi o di farmaci per i disturbi gastrointestinali			
13 – SINTOMI SOMATICI GENERALI			<input type="text"/>
0 = Assenti			
1 = Pesantezza agli arti, alla schiena o alla testa. Mal di testa, mal di schiena, dolori muscolari. Perdita di energia e facile affaticabilità			
2 = Se i sintomi sono molto evidenti segnare '2'			
14 – SINTOMI GENITALI			<input type="text"/>
<i>(Sintomi quali: perdita della libido, disturbi mestruali)</i>			
0 = Assenti	1 = Lievi	2 = Gravi	
15 – IPOCONDRIA			<input type="text"/>
0 = Assente			
1 = Polarizzazione sul proprio corpo			
2 = Preoccupazioni per la propria salute			
3 = Frequenti lamentele, richieste di aiuto, ecc.			
4 = Deliri ipocondriaci (ferma convinzione di avere una malattia somatica, senza che ve ne siano i motivi)			
16 – PERDITA DI PESO (segnare A o B)			<input type="text"/>
<i>A – SECONDO IL PAZIENTE O FAMILIARI</i>			
0 = Nessuna perdita di peso			
1 = Probabile perdita di peso associata alla presente malattia			
2 = Evidente perdita di peso			
3 = Non valutata			
<i>B – VALUTAZIONE OBIETTIVA ESEGUITA PERIODICAMENTE</i>			<input type="text"/>
0 = Meno di 500 g in una settimana			
1 = Più di 500 g in una settimana			
2 = Più di 1 Kg in una settimana			
3 = Non valutata			
17 – INSIGHT			<input type="text"/>
0 = Riconosce di essere depresso e ammalato			
1 = Riconosce di essere ammalato, ma attribuisce la responsabilità alla cattiva alimentazione, al clima, al superlavoro, a malattie infettive, al bisogno di riposo.			
2 = Nega decisamente di essere ammalato			
18 – VARIAZIONI DIURNE			<input type="text"/>
<i>A – INDICARE SE I SINTOMI SONO PIÙ GRAVI AL MATTINO O ALLA SERA</i>			
0 = Nessuna variazione			
1 = Più gravi al mattino			
2 = Più gravi alla sera			
<i>B – SE PRESENTI, VALUTARE L'ENTITÀ DELLE VARIAZIONI</i>			<input type="text"/>
0 = Assenti			
1 = Lievi			
2 = Gravi			
19 – DEPERSONALIZZAZIONE E DEREALIZZAZIONE			<input type="text"/>
<i>(Per es., sentimenti di irrealtà, idee di negazione)</i>			
0 = Assente			
1 = Lieve			
2 = Moderata			
3 = Grave			
4 = Invalidante			
20 – SINTOMI PARANOIDEI			<input type="text"/>
0 = Assenti			
1 = Sospettosità			
2 = Idee di riferimento			
3 = Deliri di riferimento o di persecuzione			
21 – SINTOMI OSSESSIVI E COMPULSIVI			<input type="text"/>
0 = Assenti			
1 = Lievi			
2 = Gravi			

SCALA DELLA COLUMBIA UNIVERSITY PER LA VALUTAZIONE DELLA GRAVITÀ DEL RISCHIO DI SUICIDIO (C-SSRS)

Lifetime-Recent

Versione 14/01/09

***Posner, K.; Brent, D.; Lucas, C.; Gould, M.; Stanley, B.; Brown, G.; Fisher, P.; Zelazny, J.;
Burke, A.; Oquendo, M.; Mann, J.***

Declinazione di responsabilità:

Questa scala di valutazione deve essere usata da persone che sono state addestrate per somministrarla. Le domande contenute nella Scala della Columbia University per la valutazione della gravità del rischio di suicidio (C-SSRS) sono suggerimenti per l'approfondimento. La determinazione della presenza di ideazione o comportamento suicidari dipende fondamentalmente dal giudizio della persona che somministra la scala.

*Le definizioni degli eventi relativi a comportamento suicidario in questa scala di valutazione si basano su quelle utilizzate nel **The Columbia Suicide History Form**, sviluppato da John Mann, MD e Maria Oquendo, MD, Conte Center for the Neuroscience of Mental Disorders (CCNMD), New York State Psychiatric Institute, 1051 Riverside Drive, New York, NY, 10032. (Oquendo M. A., Halberstam B. & Mann J. J., Risk factors for suicidal behavior: utility and limitations of research instruments. In M.B. First [Ed.] Standardized Evaluation in Clinical Practice, pp. 103 -130, 2003.)*

Per le ristampe della C-SSRS contattare Kelly Posner, Ph.D., New York State Psychiatric Institute, 1051 Riverside Drive, New York, New York, 10032; per informazioni e richieste di formazione professionale contattare posnerk@nyspi.columbia.edu

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IDEAZIONE SUICIDARIA		
<i>Porre le domande 1 e 2. Se la risposta ad entrambe è negativa, passare alla sezione "Comportamento suicidario". Se la risposta alla domanda 2 è "sì", porre le domande 3, 4 e 5. Se la risposta alle domande 1 e/o 2 è "sì", compilare la sezione qui sotto "Intensità dell'ideazione".</i>	Nel corso della vita: periodo in cui il soggetto ha avuto più tendenze suicide	Ultimo Mese
1. Desiderio di essere morto/a Il soggetto ammette di avere pensieri che riguardano il desiderio di essere morto o non più vivo oppure vorrebbe addormentarsi e non svegliarsi più. Ha desiderato di essere morto/a o di potersi addormentare e non svegliarsi più? Se sì, descriva:	Sì No <input type="checkbox"/> <input type="checkbox"/>	Sì No <input type="checkbox"/> <input type="checkbox"/>
2. Pensieri suicidari attivi non specifici Pensieri generici non specifici di voler mettere fine alla propria vita/di suicidarsi (ad es. "Ho pensato di uccidermi") senza pensieri sui modi di uccidersi/sui corrispondenti metodi, sull'intenzione o sul piano durante il periodo di valutazione. Ha pensato veramente di uccidersi? Se sì, descriva:	Sì No <input type="checkbox"/> <input type="checkbox"/>	Sì No <input type="checkbox"/> <input type="checkbox"/>
3. Ideazione suicidaria attiva con qualsiasi metodo (nessun piano) senza l'intenzione di agire Il soggetto ammette di avere pensieri di suicidio e ha pensato ad almeno un metodo durante il periodo di valutazione. Questo è diverso da un piano specifico con dettagli sul tempo, sul luogo o sul metodo (ad es. ha pensato al metodo per uccidersi, ma senza un piano specifico). Sono incluse le persone che dicono: "Ho pensato di prendere un'overdose di farmaci, ma non ho mai fatto un piano specifico su quando, dove o come lo farei veramente.....e non lo porterei mai a termine". Ha pensato a come potrebbe farlo? Se sì, descriva:	Sì No <input type="checkbox"/> <input type="checkbox"/>	Sì No <input type="checkbox"/> <input type="checkbox"/>
4. Ideazione suicidaria attiva con qualche intenzione di agire, senza un piano specifico Pensieri suicidari attivi di uccidersi con il soggetto che dichiara di avere <u>qualche intenzione di metterli in pratica</u> , al contrario di "Ho questi pensieri ma certamente non farei niente in tal senso". Ha avuto questi pensieri e qualche intenzione di metterli in pratica? Se sì, descriva:	Sì No <input type="checkbox"/> <input type="checkbox"/>	Sì No <input type="checkbox"/> <input type="checkbox"/>
5. Ideazione suicidaria attiva con un piano specifico e con intenzione Pensieri di uccidersi con dettagli di un piano completamente o in parte organizzato e con il soggetto che ha qualche intenzione di realizzarlo. Ha iniziato ad organizzare o ha già organizzato i dettagli di come uccidersi? Ha intenzione di realizzare questo piano? Se sì, descriva:	Sì No <input type="checkbox"/> <input type="checkbox"/>	Sì No <input type="checkbox"/> <input type="checkbox"/>
INTENSITA DELL'IDEAZIONE		
<i>I seguenti aspetti dovrebbero essere valutati per la tipologia di ideazione più grave (cioè, in base alle risposte qui sopra da 1 a 5, dove 1 sta per la meno grave e 5 per la più grave). Chiedere in quali momenti il soggetto ha sentito di avere più tendenze suicide.</i> Nel corso della vita - Ideazione più grave: Tipologia n° (1-5) _____ Descrizione dell'ideazione _____ Ultimo mese - Ideazione più grave: Tipologia n° (1-5) _____ Descrizione dell'ideazione _____	Più grave	Più grave
Frequenza Quante volte ha avuto questi pensieri? (1) Meno di una volta la settimana (2) Una volta la settimana (3) 2-5 volte la settimana (4) Ogni giorno o quasi ogni giorno (5) Molte volte al giorno	_____	_____
Durata Quando ha questi pensieri quanto tempo durano? (1) Passeggeri - pochi secondi o pochi minuti (4) 4-8 ore/la maggior parte della giornata (2) Meno di 1 ora/un po' di tempo (5) Più di 8 ore/persistenti o continui (3) 1-4 ore/molto tempo	_____	_____
Controllabilità Se voleva/vuole, riusciva/riesce a smettere di pensare ad uccidersi o a voler morire? (1) Riesce facilmente a controllare i pensieri (4) Riesce a controllare i pensieri con molta difficoltà (2) Riesce a controllare i pensieri con poca difficoltà (5) Non riesce a controllare i pensieri (3) Riesce a controllare i pensieri con qualche difficoltà (0) Non cerca di controllare i pensieri	_____	_____
Deterrenti Ci sono delle cose - qualcuno o qualcosa (ad es. la famiglia, la religione, il dolore della morte) - che le hanno impedito di voler morire o di mettere in atto i suoi pensieri di suicidarsi? (1) I deterrenti le hanno certamente impedito di tentare il suicidio (4) I deterrenti molto probabilmente non gliel'hanno impedito (2) I deterrenti gliel'hanno probabilmente impedito (5) I deterrenti non gliel'hanno certamente impedito (3) È incerto/a che i deterrenti gliel'abbiano impedito (0) Non pertinente	_____	_____
Motivi dell'ideazione Che tipo di motivi aveva per pensare di voler morire o di uccidersi? Era per mettere fine al dolore o al modo in cui si sentiva (in altre parole, non riusciva a continuare a vivere con quel dolore o nel modo in cui si sentiva) o era per attirare l'attenzione, per vendetta o per suscitare una reazione da parte degli altri? O entrambe le cose? (1) Esclusivamente per attirare l'attenzione, per vendetta o per suscitare una reazione da parte degli altri. (4) Soprattutto per mettere fine al dolore (non poteva continuare a vivere con quel dolore o nel modo in cui si sentiva). (2) Soprattutto per attirare l'attenzione, per vendetta o per suscitare una reazione da parte degli altri. (5) Esclusivamente per mettere fine al dolore (non poteva continuare a vivere con quel dolore o nel modo in cui si sentiva). (3) Sia per attirare l'attenzione, per vendetta o per suscitare una reazione da parte degli altri, che per mettere fine al dolore. (0) Non pertinente	_____	_____

COMPORTEMENTO SUICIDARIO (Segni tutto ciò che è pertinente, purché si tratti di eventi separati; deve porre le domande su tutte le tipologie)		Nel corso della vita		Ultimi 3 mesi	
Tentativo concreto: Un atto potenzialmente autolesivo commesso con almeno qualche desiderio di morire <i>in seguito a tale atto</i> . Il comportamento era stato pensato in parte come metodo per uccidersi. L'intenzione non deve essere necessariamente del 100%. Se c'è qualsiasi intenzione/desiderio di morire associato all'atto, allora può essere considerato un tentativo concreto di suicidio. Non devono prodursi necessariamente lesioni o danni fisici , ma basta che ci sia la possibilità di lesioni o danni fisici. Se una persona preme il grilletto mentre ha la pistola in bocca, ma la pistola è rotta e perciò non si determina una lesione, questo è considerato un tentativo. Intenzione implicita: anche se un individuo nega l'intenzione/il desiderio di morire, lo si può dedurre clinicamente dal comportamento o dalle circostanze. Per esempio, da un atto altamente letale che chiaramente non è un incidente, non si può dedurre altra intenzione se non quella di suicidarsi (ad es. colpo di pistola alla testa, lanciarsi dalla finestra da un piano alto). Inoltre, se una persona nega l'intenzione di morire, ma pensa che quello che ha fatto poteva essere letale, si può dedurre comunque l'intenzione. Ha tentato il suicidio? Ha fatto nulla per farsì del male? Ha fatto qualcosa di pericoloso che avrebbe potuto causare la sua morte? Che cosa ha fatto? Ha _____ come modo per mettere fine alla sua vita? Voleva (anche solo un po') morire quando ha _____? Stava tentando di mettere fine alla sua vita quando ha _____? Oppure pensava che sarebbe potuto/a morire quando ha _____? Oppure l'ha fatto semplicemente per tutt'altre ragioni/senza NESSUNA intenzione di uccidersi (come ad esempio, per alleviare lo stress, per sentirsi meglio, per suscitare comprensione o per far succedere qualcos'altro)? (Comportamento autolesivo senza intenzione suicida) Se sì, descriva:		Sì No <input type="checkbox"/> <input type="checkbox"/> N° totale di tentativi	Sì No <input type="checkbox"/> <input type="checkbox"/> N° totale di tentativi		
Il soggetto ha manifestato un comportamento autolesivo non suicidario?		Sì No <input type="checkbox"/> <input type="checkbox"/>	Sì No <input type="checkbox"/> <input type="checkbox"/>		
Tentativo interrotto: Quando la persona viene fermata (da una circostanza esterna) dall'iniziare l'atto potenzialmente autolesivo (<i>se non fosse stato per quello, si sarebbe attuato un tentativo concreto</i>). Overdose di farmaci: la persona ha in mano delle pillole, ma le viene impedito di ingerirle. Una volta che abbia ingerito delle pillole, questo diventa un tentativo piuttosto che un tentativo interrotto. Spararsi: la persona ha la pistola puntata contro se stessa, ma qualcuno gliela toglie o le viene in qualche modo impedito di premere il grilletto. Una volta premuto il grilletto, anche se la pistola non spara, si tratta di un tentativo. Buttarsi: la persona è pronta a buttarsi, ma viene presa e portata via dal bordo. Impiccarsi: la persona ha il cappio attorno al collo, ma non si è ancora impiccata e le viene impedito di farlo. Le è mai capitato di iniziare a fare qualcosa per mettere fine alla sua vita, ma qualcuno o qualcosa glielo ha impedito prima che lei potesse farlo veramente? Se sì, descriva:		Sì No <input type="checkbox"/> <input type="checkbox"/> N° totale di tentativi interrotti	Sì No <input type="checkbox"/> <input type="checkbox"/> N° totale di tentativi interrotti		
Tentativo fallito: Quando una persona inizia a mettere in atto un tentativo di suicidio, ma si ferma prima di aver effettivamente dato inizio ad un comportamento autolesivo. Gli esempi sono simili a quelli dei tentativi interrotti, ma in questo caso il soggetto si ferma da solo, invece di essere fermato da qualcos'altro. Le è mai capitato di iniziare a fare qualcosa per mettere fine alla sua vita e di essersi fermato/a prima di averlo fatto veramente? Se sì, descriva:		Sì No <input type="checkbox"/> <input type="checkbox"/> N° totale di tentativi falliti	Sì No <input type="checkbox"/> <input type="checkbox"/> N° totale di tentativi falliti		
Comportamenti o atti preparatori: Atti o preparativi per mettere in atto un tentativo di suicidio imminente. Questo può includere qualsiasi cosa che vada oltre la verbalizzazione o l'ideazione, come ad esempio procurarsi il necessario per il metodo specifico (ad es. comprare le pillole, acquistare una pistola) o prepararsi a morire tramite suicidio (ad es. regalando le proprie cose, scrivendo un biglietto di addio). Ha fatto qualche cosa per mettere in atto un tentativo di suicidio o per prepararsi a uccidersi (come mettere da parte le pillole, procurarsi una pistola, regalare oggetti di valore o scrivere un biglietto di addio)? Se sì, descriva:		Sì No <input type="checkbox"/> <input type="checkbox"/>	Sì No <input type="checkbox"/> <input type="checkbox"/>		
	Data del tentativo più recente:	Data del tentativo con la più alta probabilità di esito letale:	Data del primo tentativo:		
Effettiva letalità/danni fisici: 0. Nessun danno fisico o danni fisici molto lievi (ad es. graffi superficiali). 1. Danni fisici lievi (ad es. eloquio rallentato, ustioni di primo grado, lieve sanguinamento, slogature). 2. Danni fisici moderati, necessaria l'assistenza medica (ad es. cosciente ma assonnato/a, parzialmente reattivo/a, ustioni di secondo grado, sanguinamento dai vasi sanguigni principali). 3. Danni fisici abbastanza gravi; necessario il ricovero ospedaliero e probabilmente la terapia intensiva (ad es. stato comatoso con riflessi intatti, ustioni di terzo grado su meno del 20% del corpo, forte perdita di sangue con possibilità di recupero, fratture importanti). 4. Danni fisici gravi; necessari il ricovero ospedaliero e la terapia intensiva (ad es. stato comatoso senza riflessi, ustioni di terzo grado su più del 20% del corpo, forte perdita di sangue con instabilità dei segni vitali, danni gravi a organi vitali). 5. Morte	Inserire il codice	Inserire il codice	Inserire il codice		
Letalità potenziale: rispondere solo in caso di letalità effettiva=0 Tentativi concreti che avrebbero condotto a esiti letali pur in assenza di conseguenti danni fisici (gli esempi seguenti, in assenza di effettivi danni fisici, avevano una letalità potenzialmente molto elevata: mettersi la pistola in bocca e premere il grilletto ma la pistola non spara, cosicché non provoca danni fisici; stendersi sui binari con un treno in arrivo ma spostarsi prima di essere investiti). 0 = Comportamento che difficilmente causerà lesioni 1 = Comportamento che può causare lesioni, ma che difficilmente può causare la morte 2 = Comportamento che può causare la morte nonostante le cure mediche disponibili	Inserire il codice	Inserire il codice	Inserire il codice		

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