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Corresponding Author: Dr. ela polek, PhD

Corresponding Author's Institution: University College Dublin

First Author: ela polek, PhD

Order of Authors: ela polek, PhD; Sharon Neufeld; Paul Wikinson; Ian M Goodyer; NSPN Consortium; Michelle C St Clair; Gita Prabhu; Ray Dolan; Ed Bullmore; Peter Fonagy; Jan Stochl; Peter B Jones

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We calculated a score on a latent construct Common Mental Distress (the summary measure indexing a broad range of symptoms conventionally seen as components of distinct disorders). We examined the relative prevalence of ST and NSSI over the population distribution of mental distress; we used logistic regressions, IRT and ROC analyses to determine associations between suicide risks and mental distress (in continuous and above-thenorm categorical format); and pathway mediation models to examine longitudinal associations.

Outcomes. We found a dose-response relationship between levels of mental distress and suicide risk. In both cohorts the majority of all subjects experiencing ST (78% and 76%) and NSSI (66% and 71%) had scores on mental distress no more than two standard deviations above the population mean; higher scores indicated highest risk but were, by definition, infrequent. Mental distress contributed to the longitudinal persistence of ST and NSSI.

Interpretation. Universal prevention strategies reducing levels of mental distress in the whole population (in addition to screening) may prevent more suicides than approaches targeting youths with psychiatric disorders.

Replicable associations between common mental distress and suicide risk in young people: implications for clinical practice and population suicide prevention

Ela Polek^{1,7}, Sharon Neufeld¹, Paul Wikinson¹, Ian M. Goodyer¹, NSPN Consortium^{1,2},

Michelle C. St Clair³, Gita Prabhu^{2,8}, Ray Dolan^{2,8}, Ed Bullmore^{1, 5}, Peter Fonagy⁴, Jan

Stochl^{1, 5} & Peter B. Jones^{1, 5, 6}

¹ Department of Psychiatry, University of Cambridge, UK

² Wellcome Centre for Human Neuroimaging, University College London, UK

³ Department of Psychology, University of Bath

⁴ Division of Psychology and Language Sciences, University College London, UK

⁵ NIHR Collaboration for Leadership in Applied Health Research & Care East of England

⁶NIHR Cambridge Biomedical Research Centre

⁷ Tavistock Relationships

⁸ Max Planck UCL Centre for Computational Psychiatry and Ageing Research

Correspondence:

Professor Peter B. Jones, Department of Psychiatry, University of Cambridge, Box 189 Addenbrooke's Hospital, Cambridge CB2 2QQ, UK. (Email: pbj21@cam.ac.uk)

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Key words: suicide risk, suicide prevention, self-injury, suicidal thought, mental distress

Research in context

Evidence before this study

Suicide is the second ranked cause of deaths among 10 to 24 year-olds, worldwide. Prediction and prevention in young people are priorities, but markers of heightened risk such as selfharm and suicidal thought are relatively common, so it is difficult to predict who will ultimately make a serious attempt or die by suicide. The usefulness of clinical risk protocols largely relying on the identification of a depression-related psychiatric diagnosis has been questioned. Indeed, most recent evidence suggests that any symptoms, or any psychiatric diagnosis (particularly multiple diagnoses), when co-ocuring with non-suicidal self-harm predict this risk more accurately.

Added value of this study

To our knowledge, this is the first study examining the relationship between the mental distress (the summary measure indexing a broad range of symptoms conventionally seen as components of distinct disorders) and suicide risk. We found that mental distress was a key predictor of suicide risk and it was related in a dose-response manner to suicidal thought and non-suicidal self-harm in two independent cohorts. Also, mental distress contributed to the longitudinal persistence of suicidal thought and non-suicidal self-harm. Due to the normal distribution of mental distress scores in the population, the majority of high-risk cases came from the above-the-mean, rather than very high ("clinical") range – in line with the *prevention paradox*.

Implications of all the available evidence

Current interventions for preventing suicide focus largely on high-risk individuals or those with psychiatric diagnosis. Our results argue for population-based public health approaches to reduce suicide risk (i.e. interventions aimed at lowering the population mean of mental distress). Focus on the few individuals with the highest levels of mental distress or psychiatric diagnosis will inevitably miss the majority of individuals at risk. Our findings also have major implications for clinical practice: NSSI and ST should never be dismissed or down-played when they occur in young people without clear evidence of psychiatric disorder. NSSI and ST merit a swift professional response regardless of whether or not they occur with other symptoms that take individuals beyond conventional clinical thresholds and trigger traditional clinical risk protocols.

Introduction

Adolescence sees the onset of a range of psychopathology including suicidal thoughts (ST) and non-suicidal self-injury (NSSI)(1) that individually or together convey heightened risk of suicide attempts.(2) Non-suicidal and suicidal self-harm predict completed suicide,(3) the second most common cause of deaths among 10 to 24 year-olds, worldwide.(4) Prediction and prevention in young people are priorities(5) but NSSI (5-42% in community samples)(6) and ST (15-25% in community samples)(7) is common so it is difficult to predict who will ultimately make a serious attempt(8) or die by suicide. Indeed, the usefulness of clinical risk protocols relying on the identification of a psychiatric diagnosis is questionable.(9) The same problems affect public health suicide prevention programmes. A seminal study revealed a high prevalence of false-negatives in prospective identification of suicide.(10) Prevention policies that embrace the whole population might overcome these difficulties but lack theoretical or empirical foundations.(1)

Suicidal thoughts and behaviours are routinely considered as markers of depression (e.g., in DSM-5) but by no means all young people dying by suicide have had a mood disorder.(11) NSSI increases the risk of suicide when occurring in combination with any internalising or externalising symptoms,(12) or with any psychiatric diagnosis,(13) particularly multiple diagnoses.(14) Thus, this risk might be better predicted by multiple symptoms rather than by the presence of a single disorder, such as depression.

Recent studies suggest that a broad range of symptoms conventionally seen as components of distinct disorders are better construed as manifestations of a single, latent dimension distributed within the general population. This dimension has been variously referred to as the p-factor,(15) general psychopathology(16) or, as we prefer here, *common mental distress* (CMD).(17) Parsimonious statistical models with dimensions that encompass low-prevalence phenomena such as psychotic experiences, fit empirical data better than models with distinct disorders.(15) High co-morbidity of psychiatric diagnoses, shared causal factors and treatments, and trans-diagnostic psychological and neural correlates support the validity of a common mental distress concept.(15-18) Suicide risk is related to multiple symptoms or disorders (and thus to higher mental distress scores), not the presence of one specific symptom or disorder, so it is important to understand the nature of dose-response relationships between mental distress and suicide risks. This could guide a clinical response in the face of suicide risk(19) and also shape population-based suicide prevention.

In this study we describe the presence of a mental distress dimension in young people aged 14-26 years and the occurrence of ST and NSSI referred to collectively, hereafter, as suicide risk. We then aimed to test associations between mental distress and suicide risk, and contrast mental distress with specific psychopathological domains, exploring the utility of a summary measure of mental distress. Next, we aimed to answer the following questions:

- 1. What is the prevalence and relative risk of NSSI and ST across the population distribution of mental distress?
- 2. Does mental distress score mediate the persistence of NSSI and ST over time?

We used data from two population-based cohorts with complementary designs and very similar measures. To address the first question we used cross-sectional data from Cohort 1 (used as a discovery sample) and Cohort 2 (used as a stepwise replication sample); to address the second question we used three longitudinal waves of Cohort 1 (see details in Method).

Method

Study Design and Participants

Cohort 1

Participants in the NSPN 2400 Cohort(20) were recruited largely via postal invitations sent through general practitioners and schools in Cambridgeshire and Greater London, UK. Purposive sampling obtained at least 200 males and 200 females in 5 age groups: 14-15, 16-17, 18-19, 20-21, 22-24 years. Three data collections took place a year apart (T1-T3). At T1, 2403 individuals returned questionnaires (average age 18.9 years, SD=3.0; 54% females); at T2, 1815 returned questionnaires (76% response, average age 20.0 years, SD=3.1; 56% female), and 1245 at T3 (52% of baseline; average age 21.0 years, SD=3.1; 59% female). *Cohort 2*

The ROOTS study(21) was used for replication of findings from Cohort 1. Two-stage sampling involved random selection of 27 schools in Cambridgeshire, UK. Eighteen schools agreed to participate; invitations were sent to 14-year-olds randomly selected from class registers and to their parents; 1238 students took part (55% female). Four data collection waves took place: we used data from the third data sweep, when participants were of average age 17.5 years, *SD*=0.3 (N=1074, 56% female; 87% of baseline sample), the closest age to T1 of Cohort 1. Both cohorts comprised predominantly white European (77% in Cohort 1 and 87% in Cohort 2) young people, consistent with the self-ascribed demographics of the two study populations. Written consent from participants age 14 or 15 years was supplemented by written consent from their parent or legal guardian; older participants gave their own written consent. Ethical approval was obtained for Cohort 1 from the National Health Service Research Ethics Service (# 97546) and for Cohort 2 from the Cambridgeshire 2 REC (# 03/302).

Measures

Sociodemographic information was collected using routine methods. (20, 22) The index of multiple deprivation (IMD), a summary measure of socioeconomic status of participants'

residential neighbourhood, is calculated from census information. Psychopathological questionnaires are set out in Table 1. Scores in questionnaires were computed according to published manuals or validation studies (cited in Table 1), standardized to unify their measurement scales.

Table 1

Statistical analysis

Confirmatory bifactor analysis with a maximum likelihood estimator in Mplus 7.4 was used to compute factor scores for the mental distress dimension in the three data sweeps of Cohort 1 and Cohort 2 based on the model validated elsewhere.(23) Next, we imputed all missing data in Cohort 1 using mental distress scores, NSSI and ST variables from the three sweeps, as well as auxiliary variables obtained at T1: centre, sex, age, ethnicity, and IMD. Multiple imputations were computed in R program with MICE package and 54 datasets were generated to equal the percentage of missing data in mental distress, NSSI and ST at T3. Following imputations, the full dataset (N=2403) was used in longitudinal analyses.

To analyse the relationship between age, sex, NSSI, ST and mental distress descriptively, we grouped observations from all 3 time points in Cohort 1_{T1-T3} by age, rather than by data time point. This grouping allowed us to investigate levels of mental distress, NSSI and ST in a broad age range of 14-28 years (note that this also entailed inclusion of the same individuals from consecutive data sweeps (e.g., when an individual was 14, 15 and 16 year old) in the adjacent age groups). The histograms showing percentages of NSSI and ST with Wilson confidence intervals were plotted against the lines representing the means of mental distress with confidence intervals for every age group for both sexes separately (Figure 1).

To prove the principle that NSSI and ST were predicted by multiple psychopathological domains and also by mental distress (which represents a summary of those domains), we used Stata 12 to compute for Cohort 1_{T1} and Cohort 2 data sensitivity / specificity indicator – the area under the curve (AUC – reported in Supplement, Table 1) for NSSI and ST as criteria. We computed a series of logistic regressions, estimating odds ratios (OR) with confidence intervals for each predictor (treated as categorical with the cut-off point above 1SD and then continuous), while we controlled for effects of age and sex (Figure 2).

To answer Question 1, distributions of mental distress scores in both cohorts were plotted against lines representing percentages of subjects reporting NSSI and ST within bands of mental distress expressed as standard deviations (upper panel of Figure 3) and against bar histograms representing NSSI and ST frequencies in both cohorts (lower panel of Figure 3). In addition, NSSI and ST information curves were computed to determine in what range of the mental distress dimension these items are located (see Supplement, Figure 1).

Using Cohort 1_{T1-T3} data to answer Question 2, we examined the longitudinal relationship between mental distress, NSSI and ST (in particular the causal role of mental distress in persistence of NSSI and ST): we computed direct effects and mediation effects (via mental distress_{T2}) of ST_{T1} and NSSI_{T1} on NSSI_{T3} and ST_{T3} in a pathway mediation model with confidence intervals in Mplus 7.4. We computed this model for the total sample (Figure 4) and then for both sexes separately (Supplement, Figure 2) using the Multiple Group Method, so as to test a moderated-mediation model (with mental distress_{T2} as a mediator, and sex as a moderator). Age was a control variable.

Results

Associations of NSSI and ST with demographic and psychopathological variables In both cohorts NSSI and ST were unrelated to ethnicity and socioeconomic status; NSSI was more prevalent in females than males with the biggest sex difference in age groups 15-19 in the pooled NSPN_{T1-T3} datasets. Overall, prevalence of NSSI and ST across age groups mirrored the trend in mental distress levels (Figure 1).

Figure 1

The mental distress score and all conventional psychopathological predictors of NSSI and ST had statistically significant and similar size ORs in logistic regression models (see Figure 2 and Supplement, Table 1).

Figure 2

Prevalence of NSSI and ST in the two cohorts

In Cohort 1 (N=2403) there was no statistically significant change in the prevalence of NSSI (within the last month) over the three time points: in the imputed data 9.3% (n=223) reported NSSI_{T1}, 8.3% (n=199) NSSI_{T2} and 8.2% (n=197) NSSI_{T3}. Similarly, there was no statistically significant change in prevalence of ST (within the last two weeks) over the three time points: 10.1% (n=243) ST_{T1}, 11.4% (n=274) ST_{T2} and 11.7% (n=281) ST_{T3}.

In Cohort 2 (N=1074), 11.7% (n=126) reported lifetime NSSI and 5.4% (n=58) reported ST within the two last weeks. Accuracy and precision of these prevalence estimates was affected by attrition (see *Discussion: limitations*). Attrition in Cohort 2 at T2 and T3 was related to male gender and higher mental distress score at T1 (all p<.05), but unrelated to other demographic variables.

Question 1: Associations of NSSI and ST with mental distress

Next, we focused on absolute risk and the numbers of NSSI and ST events generated by these risk functions. The dose-response curves in the upper panel of Figure 3 show that relative risks of NSSI and ST increased markedly with increasing severity of mental distress, the highest risks being in those with very high scores beyond two standard deviations above the mean. On the other hand, most participants from both cohorts who reported NSSI or ST had

mild (one SD above the mean) to moderate (two SD above the mean) mental distress scores (lower panel of Figure 3). Mental distress was normally distributed so these scores were much more common; only a minority of the total reports came from the few participants with very high mental distress (>2 standard deviations above mean). Thus, the majority of subjects experiencing ST or NSSI (Cohort 1: 78% and 76%; Cohort 2: 66% and 71%, respectively) had mental distress scores within two standard deviations above the population mean: Very high scores indicated highest suicide risk but were rare, so generated the minority of events.

Figure 3

Question 2: Mediating effect of mental distress on suicide risks in Cohort 1 over time Cohort 1 mental distress_{T2} contributed to the longitudinal persistence of NSSI and ST (i.e. $NSSI_{T1}$ predicted $NSSI_{T3}$ directly, and via mediation through mental distress_{T2}. Mental distress_{T2} also completely mediated the longitudinal effect of $NSSI_{T1}$ on ST_{T3} . Moreover, mental distress_{T2} contributed to the longitudinal persistence of ST (i.e. ST_{T1} predicted ST_{T3} directly, as well as via mediating variable – mental distress_{T2}. Overall, mental distress_{T2} was a stronger predictor of $NSSI_{T3}$ and ST_{T3} than the antecedent variables measured at T1 (see Figure 4). There were no significant sex differences in direct and mediation pathways, showing that mediation effects of mental distress_{T2} were not moderated by sex (Supplement, Figure 2). Age_{T1} was not a significant predictor of any variable in the model; the results when age was controlled for were very similar to those without controlling for age (differences in coefficients were in the second decimal place digits).

Figure 4

Discussion

Findings

Depressive phenomena were by no means the only psychopathological domain associated with increased risk of non-suicidal self-injury (NSSI) and suicidal thoughts (ST). Thus, the summery measure *Common Mental Distress* (indexing a broad range of symptoms, which are conventionally seen as components of distinct disorders) with a normal distribution in the population, appeared as a parsimonious and efficient summary that was, itself, a key predictor of suicide risk in both cohorts. NSSI and ST were not confined to participants scoring in the very high, quasi-clinical range of mental distress. Around half of all participants expressing NSSI or ST came from those scoring up to one standard deviation above the mental distress mean in a dose-response manner. The majority expressing these phenomena (two thirds to three quarters) scored within 2SD above the mean (Figure 3).

Regarding medium-term determinants of persistent NSSI and ST we showed (Figure 4) that mental distress_{T2} mediated the persistence of NSSI and ST over two years, independent of gender and age. This mediation operates in two stages: first, ST and NSSI persist because these behaviours are markers for worsening mental distress in the general population. This extends findings in adolescents with depressive disorder, where suicidal thoughts are a predictor of poor outcome. Second, this greater mental distress, itself, increases the risk for further suicidal thoughts and behaviours.

Strengths

Both cohorts were designed on epidemiological principles to capture behavioural and psychological variation in the population during the post-pubertal epoch during which risk for psychopathology accelerates. Replication of the findings in these independent cohorts strengthens confidence in the findings, as does internal consistency between cross-sectional associations found in both cohorts, and longitudinal associations found in Cohort 1.

Limitations

Sample attrition was the main bias in both cohorts. Each retained more young women than men, but socio-economic class played no part in attrition. Cohort 1 is robustly representative of the England and Wales population(20), whereas Cohort 2 under-represents participants with lowest socioeconomic status.(21) However, we have no reason to suppose that our results are specifically modified by socioeconomic status that was unrelated to NSSI, ST and mental distress. If there was a bias, it probably limits power rather than skewing an effect, and is mitigated by replication between the cohorts. We used multiple imputation to minimise this bias.

There was only modest reliability of impulsivity and obsessionality measures, and a skewed measure of conduct problems in Cohort 1. A completely comprehensive range of psychopathological (and behavioural) items was unavailable; we did not have measures of unstable or abnormally elevated mood, addictions, eating disorders or hyperactivity. Thus, our measurement of mental distress focused primarily on internalising rather than externalising symptoms. We broadened our scope far beyond depression, usually the focus of psychological disturbance in suicidality research, but future studies could include a broader range of measures and extend the investigation into clinical populations to improve measurement precision at the highest levels of mental distress.

Implications & Conclusions

Our findings provide a novel evidence that a latent mental distress dimension, conceptually akin to the p-factor, is a useful summary measure of psychopathology in the general population.(17) From a public health and prevention perspective, the fact that rates of NSSI and ST begin to accelerate at levels of mental distress well within a non-clinical range argues strongly for universal interventions overtly aimed at lowering the population mean of mental distress and shifting the curve to the left, alongside targeted approaches and effective clinical services. Strategies concentrated on clinical populations, those with evidence of a psychiatric disorder or other individual markers will miss the majority of individuals experiencing ST or engaging in NSSI because there are so few compared with those at lower risk: the *prevention paradox.(19)*

Defining putative universal interventions to shift the population distribution of mental distress will require careful research that can draw from other areas of medicine such as cardiovascular disease and stroke.(19) Elements have been widely scoped in the USA⁹ and elsewhere, but not for constructs of population health and wellbeing such as mental distress. Many involve decreasing common triggers⁹ or improving young people's abilities to cope with stressors. Delivery systems might include digital platforms that are virtually ubiquitous amongst young people, while schools and colleges are increasingly recognised as contexts for the delivery of such universal interventions.(24) However, the burgeoning importance of social media providing a broad-based and uniquely tailored environment for youth must be considered in suicide prevention strategies as both a toxic and a potentially therapeutic milieu.

Further, our results suggest that psychopathology is generated in a probabilistic manner rather than in diagnostic clusters, with common phenomena concerning depression and anxiety much more likely to occur prior to rarer phenomena such as NSSI, ST or psychotic experiences. Less frequent phenomena begin to co-occur as the severity of psychological disorder (or mental distress) increases, in terms of more mental and behavioural phenomena or symptoms. This begins to yield clusters linked by common items that current diagnostic systems tend to ignore. This is consistent with the co-occurrence of suicidal risk and psychotic experiences seen in other studies of young people,(25) and with the present IRT analysis showing that NSSI and ST are measuring the higher end of mental distress (Supplement, Figure 1). The approach we have followed illustrates the value of moving away

14

from categorical classification and embracing an empirically-rooted, dimensional, hierarchical taxonomy in psychopathology research.(26) Such hierarchical approaches to phenomenological classification had been put forward before(27) or shortly after(28) the publication of DSM-3 and its successor classifications. Hierarchical models merit renewed interest,(29) as they may resolve problems of comorbidity as well as overlapping causes and biological mechanisms for suicide risk and other phenomena.

Our findings also have major implications for clinical practice: NSSI and ST should never be dismissed or down-played when they occur in young people without clear evidence of psychiatric disorder, a logical fallacy because NSSI and ST are *themselves* indicators of higher mental distress. NSSI and ST will usually, but not always occur with other, more common psychopathology and their co-occurrence is a strong risk factor for suicide attempts.(30) Thus, NSSI and ST merit a swift professional response regardless of whether or not they occur with other symptoms that take individuals beyond conventional clinical thresholds and trigger traditional clinical risk protocols. Further studies could explore avenues for the application of screening practices and the development of useful clinical prediction tools(9, 31, 32) along with the population-based approaches advocated above.

Supporting data

Online Supplement is available for this paper. The data and syntaxes utilised for computations reported in this study are deposited in the University of Cambridge Data Repository, with the placeholder DOI <u>https://doi.org/10.17863/CAM.25331</u> available to researchers via <u>openNSPN@medschl.cam.ac.uk</u>.

Contributors

Ela Polek and Peter B. Jones conceptualised the manuscript. Ela Polek analysed the data and drafted the manuscript. Jan Stochl and Sharon Sharon Neufeld provided statistical advice and assistance on data imputations. Peter B. Jones provided senior supervision. All authors read, commented on, and revised the whole report. Ela Polek and Peter B. Jones act as guarantors for the manuscript. The members of the NSPN Consortium took part in the data collection and management.

Declaration of interests

E.P., S.N., I.M.G., J.S. and P.B.J. have no competing interests. E.B., P.F. and PBJ are in receipt of National Institute for Health Research (NIHR) Senior Investigator Awards (NF-SI-0514-10157, and NF-SI-0514-10117. P.F. was in part supported by the NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) North Thames at Barts Health NHS Trust. P.W. has recent/current grant support from NIHR, Cambridgeshire County Council and CLAHRC East of England. P.W. discloses consulting for Lundbeck and Takeda; PBJ discloses consulting for Janssen and Ricordati. E.B. is employed half-time by the University of Cambridge and half-time by GlaxoSmithKline in which he holds stock.

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The funding sources had no role in the design and conduct of the study; collection,

management, analysis, and interpretation of the data; preparation, review, or approval of the

manuscript; and decision to submit the manuscript for publication.

Group Information

NSPN (NeuroScience in Psychiatry Network: http://www.nspn.org.uk/) is a research consortium formed by the University of Cambridge and University College London, launched in November 2012 and supported by Wellcome Trust Award (095844/Z/11/Z). The group includes the following members:

Principal investigators: Edward Bullmore (CI from 01/01/2017)^{1,2,3} Raymond Dolan^{4,5} Ian Goodyer (CI until 01/01/2017)¹ Peter Fonagy⁶ Peter Jones¹

NSPN (funded) staff: Michael Moutoussis^{4,5} Tobias Hauser^{4,5}

Sharon Neufeld¹ Petra Vértes^{1,2} Kirstie Whitaker^{1,2} Gita Prabhu^{4,5} Laura Villis¹ Junaid Bhatti¹ Becky Inkster¹ Cinly Ooi¹ Barry Widmer¹ Ayesha Alrumaithi¹ Sarah Birt¹ Kalia Cleridou⁵ Hina Dadabhoy⁵ Sian Granville⁵ Elizabeth Harding⁵ Alexandra Hopkins^{4,5} Daniel Isaacs⁵ Janchai King⁵ Danae Kokorikou^{5,6} Harriet Mills⁵ Ciara O'Donnell¹ Sara Pantaleone⁵ Aislinn Bowler⁵

Affiliated scientists:

Pasco Fearon⁶ Anne-Laura van Harmelen¹ Rogier Kievit^{4,7}

1 Department of Psychiatry, University of Cambridge, United Kingdom

2 Behavioural and Clinical Neuroscience Institute, University of Cambridge, United Kingdom

3 ImmunoPsychiatry, GlaxoSmithKline Research and Development, United Kingdom 4 Max Planck University College London Centre for Computational Psychiatry and Ageing Research,

University College London, UK

5 Wellcome Centre for Human Neuroimaging, University College London, United Kingdom 6 Research Department of Clinical, Educational and Health Psychology, University College London,

United Kingdom

7 Medical Research Council Cognition and Brain Sciences Unit, University of Cambridge,

United Kingdom

Variables	Measures	Cohorts	
Outcome variables:		$NSPN_{T1-T3}(1)$	ROOTS _{age 17} (2)
Suicidal thoughts (ST)	One item from the MFQ(33): I thought about killing myself. Responses were recoded into a binary format: no ST (original response option <i>Never</i>) and ST (original response options <i>Sometimes</i> or <i>Mostly</i> or <i>Always</i>).	×	×
Non-suicidal self- injury (NSSI)	One question from the Drug, Alcohol and Self-Injury (DASI) questionnaire asking about engaging in self-injury without suicidal intent during the last month. Responses were recoded into a binary format indicating the occurrence of NSSI or lack of thereof.	×	
	One question asking about the occurrence of lifetime NSSI.		×
Predictors:			
Conduct problems	11-item Antisocial Behaviour Questionnaire(23)	×	×
Anxiety	28-item Revised Children's Manifest Anxiety Scale(34)	×	×
Depression	29 items from the 33-item MFQ(33) (all items except for 4 items measuring suicidality)		
Obsessions and compulsions	11-item Revised Leyton Obsessional Inventory(22)	×	×
Distress	10-item Kessler Psychological Distress Scale (K10)(35)	×	×
Psychotic-like	11 items selected from the 74-item Schizotypal Personality Questionnaire (SPQ)(36)	×	
experiences	11 items from the 20-item semi-structured interview from the Diagnostic Interview Schedule for Children-IV(37)		×
Self-esteem	10-item Rosenberg Self-Esteem Questionnaire (*)(38)	×	×
Well-being	14-item Warwick-Edinburgh Mental Well-Being Scale(*)(39)	×	×
Impulsivity	15 items from the 30-item Barratt Impulsiveness Scale(40) selected based on exploratory factor analysis - loadings above .25	×	
Antisocial traits	Total score from the 17-item Antisocial Process Screening Device (APSD)(41)(41)	×	
Schizotypal traits	Total score from the 74-item Schizotypal Personality Questionnaire (SPQ)	×	×

*scales were reversely scored, thus higher scores indicated lower self-esteem and well-being; for all other measures higher score indicates more psychopathology

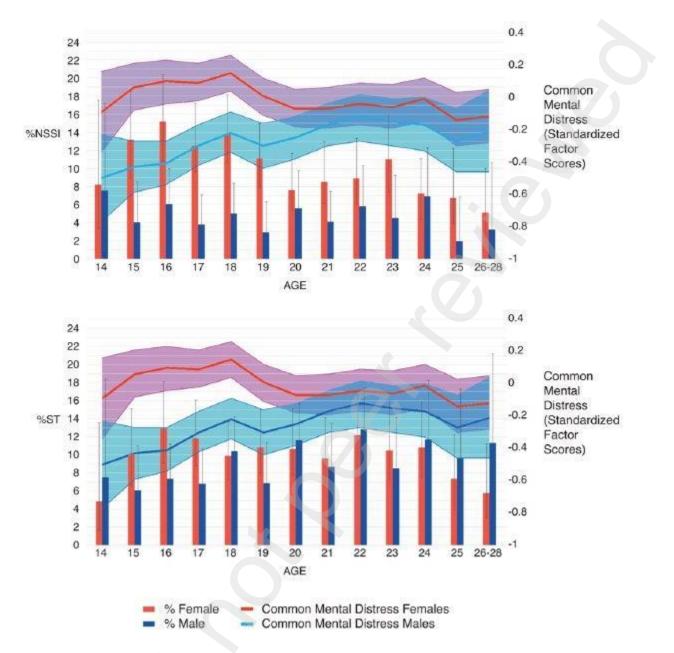


Figure 1. Percentages of non-suicidal self-injury (NSSI), suicidal thoughts (ST) and levels of Common Mental Distress in age groups for both sexes in Cohort 1

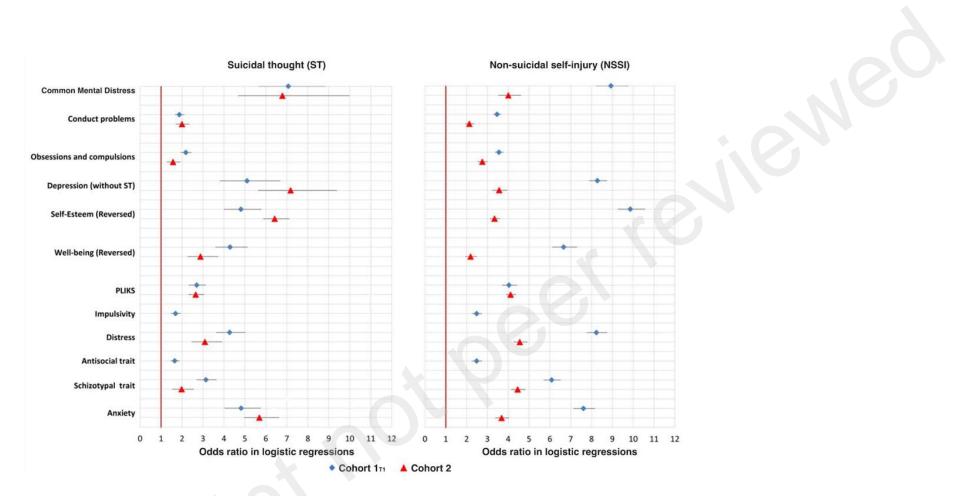
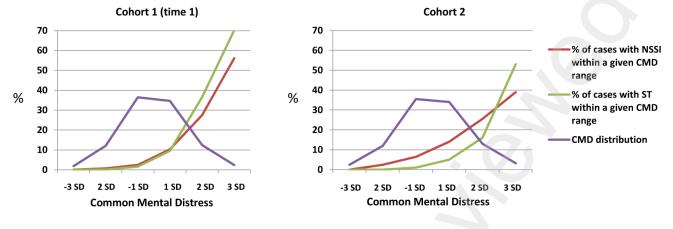


Figure 2: Odds ratio in logistic regressions for suicidal thoughts (ST) and non-suicidal self-harm (NSSI) as outcomes predicted by psychopathological predictors (listed on the left) here treated as a categorical variables with a cut-off point at 1SD; regressions were computed separately for each predictor and effects of age and sex were controlled each regression for in both cohorts.



Dose-response effect of Common Mental Distress on non-suicidal self-harm (NSSI) and suicidal thought (ST)



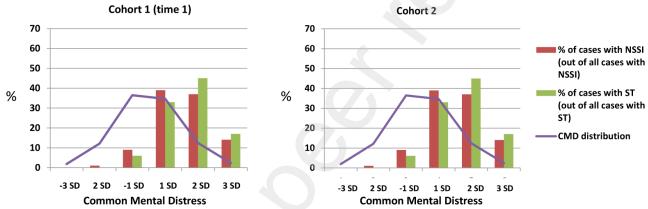


Figure 3: Upper panel shows dose-response effect of Common Mental Distress (CMD) on non-suicidal self-harm (NSSI) and suicidal thought (ST) in Cohort 1 and Cohort 2. Lower panel shows the proportion of total reports in of non-suicidal self-harm (NSSI) and suicidal thought (ST) broken down by standard deviations of Common Mental Distress; these add up to 100% from left to right. The normal population distribution of mental distress is shown by the purple line.

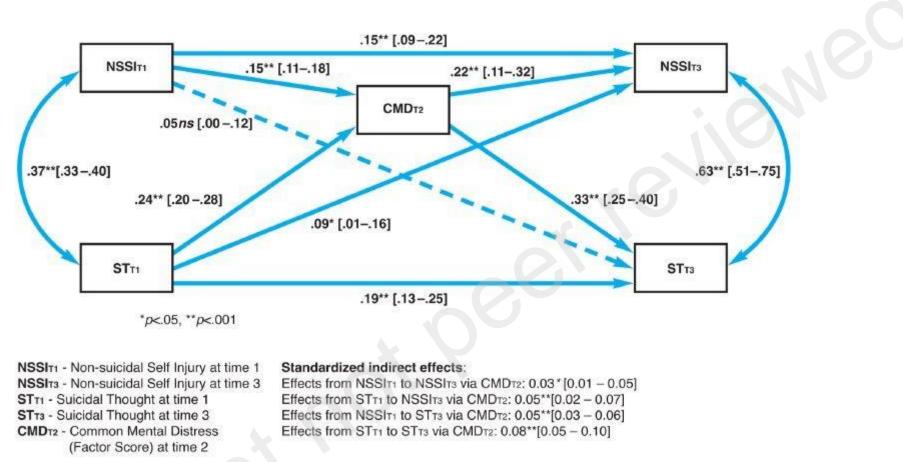


Figure 4: Mediation effect of Common Mental Distress at time 2 in Cohort 2: Standardised pathway coefficients with confidence intervals.

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