Thoughts of death and suicidality among patients with cancer: Examining subtypes and their association with mental disorders

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Abstract
Objective: Cancer is associated with an increased risk for completed suicide. We explored subtypes of thoughts of death, death wishes, suicidal ideation and behavior and their association with mental disorders and demographic and disease-related characteristics.

Methods: We studied 2,141 cancer patients with the standardized Composite International Diagnostic Interview-Oncology (CIDI-O). Assessment included 4-weeks-prevalences of thoughts of death, wish to die, suicidal ideation, suicide plans, and lifetime suicide attempts. We further assessed 4-weeks-prevalences of mood, anxiety, adjustment, somatoform, substance use, and disorders due to general medical condition. We conducted latent class analyses (LCA).

Results: The LCA identified three classes with distinct patterns of suicidality. Class 1 (89.0% of the sample) showed no suicidality. Class 2 (6.9%) was characterized by thoughts of death without suicidal ideation. Class 3 (4.1%) was characterized by thoughts of death, suicidal ideation, and suicide plans. Death wishes occurred in both classes 2 and 3. Classes 2 and 3 were associated with a significantly higher risk for any mental disorder (OR from 4.22, adjustment disorder, to 10.20, mood disorders, p < 0.001) compared to class 1. Patients with mental disorders were equally likely in classes 2 and 3. Patients with incurable cancer were significantly more likely in class 2, and less likely in class 3.

Conclusions: Cancer patients with suicidal ideation are not distinctly characterized by mental disorders. Further study of concepts that consider problematic adjustment to the cancer stressor such as death anxiety and demoralization may contribute to understand psychological distress underlying subtypes of thoughts of death and suicidality in cancer.

KEYWORDS
cancer, death wishes, latent class analysis, mental disorders, suicidal ideation and behavior, suicidality, thoughts of death
Cancer is associated with an increased risk for completed suicide.\textsuperscript{1-3} Zaorsky et al.\textsuperscript{4} recent register study confirmed a 4.4-fold increased rate of death by suicide drawing on representative data from over 8 million cancer patients. While the 0.154\% rate of deaths by suicide shows that completed suicide is nonetheless a rare event in patients with cancer, this is not the case for suicidal ideation. The systematic review of Kolva et al.\textsuperscript{5} indicates widely ranging suicidal ideation prevalences between 0.7\% and up to 46.3\% among individuals with cancer. Although the one-item assessments used in many included studies do not respect the heterogeneity of suicide-related thoughts and omit suicidal behaviors, the state of research enheartens further detailed investigation.

Manifestations of thoughts of death and suicidality\textsuperscript{1} in cancer may range on a continuum from death acceptance over death wishes, with or without a desire to hasten death, to actual suicide plans.\textsuperscript{6,7} Especially death wishes in advanced cancer patients can have different meanings and degrees of suicidal intent. Qualitative interview studies have subtyped their meanings and functions.\textsuperscript{8,9} The wish to die may for example express a sense of letting go, a hypothetical exit plan to assure control in case the situation is perceived as unmanageable, or current intolerable despair and suffering.\textsuperscript{10} The nature of the cancer stressor and its association with existential fears of uncertainty, functional impairments, loss of autonomy, uncontrollable suffering, burdening others, or being left alone,\textsuperscript{11} can make it difficult to distinguish suicidal ideation and behavior from other adjustment reactions in patients with cancer. Much of the distress underlying suicidal ideation and plans (e.g. requests for physician-assisted suicide) is directed towards a hypothetical future state where suffering may become intolerable.\textsuperscript{6} The complexity of suicide-related phenomena in cancer raises interest in their typology.

In non-cancer samples, latent class analyses have identified subtypes of self-injurious thoughts and behaviors.\textsuperscript{12} The heterogeneous suicide indicators used interfere with cross-study comparisons, yet results often showed a major large class without suicidal ideation and behavior, and smaller classes that were distinguished by suicidal ideation and plans alone vs. individuals who had attempted suicide.\textsuperscript{13,14}

The known association between mental disorders and an increased risk for suicidal ideation has been confirmed in cancer samples.\textsuperscript{15-17} Other risk factors for suicidal ideation in cancer patients include a higher physical symptom burden, living alone and advanced cancer (stage IV),\textsuperscript{3} while findings have been inconsistent for sex and age. This pattern deviates from the risk factors for completed suicide in cancer: younger age, male sex, white race, and early stage cancer.\textsuperscript{4}

There has, to our knowledge, been no attempt so far to classify suicidality profiles among patients with cancer using quantitative methods. The main goal of the present study is to (1) identify subtypes characterized by specific features of suicidality in a mixed sample of patients with cancer that is representative for all tumor entities in Germany. Such subtypes can be determined by latent class analysis. We applied this method to explore whether the patterns of thoughts of death and suicidality endorsed by individuals with cancer form distinct subgroups.\textsuperscript{2} We further aimed to investigate (2a) how the resulting classes were characterized by demographic and disease-related patient variables, and (2b) their association with mental disorders.

2 | METHODS

2.1 | Participants and procedures

We analyzed data from an epidemiological cross-sectional study.\textsuperscript{19,20} Patients were recruited while receiving oncological treatments from oncological inpatient clinics at acute care hospitals, specialized outpatient cancer care facilities, and cancer rehabilitation centers across Germany. Exclusion criteria were age younger than 18 or older than 75 years, severe cognitive or physical impairment, and language barrier. All patients provided written informed consent. Participants were screened with the Patient-Health-Questionnaire-9 (PHQ-9). Patients with sum scores $\geq$9 were further assessed by a standardized diagnostic interview for mental disorders. Patients with sum scores <9 were randomly assigned to the interview. All statistical analyses were weighted to control for the oversampling of patients with PHQ-9 scores $\geq$9. All patients completed a set of self-report questionnaires.\textsuperscript{20} The research ethics committees of the local medical association in each study center approved this study (reference numbers 2768, 61/09, 244/07, S-228/2007, 50155039, 107/07, 200-2007).

Of 5889 eligible patients, 4020 (68\%) agreed to participate in the study. As reported elsewhere,\textsuperscript{19} non-participants were younger, but did not differ in sex. 1202 patients (30\%) screened $\geq$9 on the PHQ-9 and were assigned to the standardized interview (CIDI-O), of which 903 (75\%) completed the interview. 2818 patients (70\%) screened <9 on the PHQ-9, of which 1508 (54\%) were randomly assigned to the CIDI-O. Among these, 1238 (82\%) completed the interview. In total, 2141 patients completed the CIDI-O and were analyzed in this study.

A detailed overview of demographic and disease-related sample characteristics as well as descriptive information about study variables is given in the supplement, table S1.

2.2 | Measures

Demographic data were collected by a standardized questionnaire. Disease-related characteristics were obtained from medical charts. Incurable cancer was defined by stage IV diagnosis for solid tumors and evaluation of curative vs. palliative treatment intent by the attending physician in hematological cancers.

We used the standardized computer-assisted Composite International Diagnostic Interview for Oncology (CIDI-O) to assess the 4-weeks prevalence of thoughts of death, death wishes, suicidal ideation and
suicidal behavior, as well as mental disorders. Assessment included the following questions as part of the depression section: In the past 4 weeks, did you have a period of two weeks or more, when you 1) thought a lot about death, 2) had the wish to die, 3) felt so low you thought about committing suicide, 4) made a suicide plan? Question 5) asked individuals whether they had ever attempted suicide. The interview further assessed the 4-weeks prevalence of the following mental disorders: disorders resulting from general medical condition (organic mood disorders and organic anxiety disorder), substance use disorders (dependence and abuse of alcohol), mood disorders (unipolar and bipolar), anxiety disorders (including acute and post-traumatic stress disorder; without obsessive compulsive disorder), somatoform disorders, and eating disorders. The CIDI-Oncology further enables diagnosis of adjustment disorders in response to specific cancer-related stressors. In accordance with DSM-IV criteria, an adjustment disorder was diagnosed where distress was problematic, out of proportion to the clinical setting, causing impairment, no other axis I disorder was present, and symptoms did not persist for longer than 6 months.

We used the physical problem list of the Distress Thermometer (DT) to assess the presence of 21 common physical symptoms in cancer patients. The total physical symptom count (possible range from 0 to 21) was used as a measure of physical symptom burden.

### 2.3 Statistical methods

We calculated descriptive statistics including means, standard deviations, and frequencies for demographic and disease-related characteristics.

We used latent class analyses to define subtypes of suicidality as implemented in R package depmixS4. The latent class model was calculated from the five suicidality items assessed by the structured CIDI-interview as indicator variables. We determined the solution with an optimum number of classes by examining the following indices: loglikelihood value, Akaike’s information criterion, Bayesian information criterion, likelihood ratio value, and entropy value.

We then determined the extent to which mental disorders as well as demographic and disease-related characteristics differed in frequency across classes using multinomial regression analyses. Odds ratios (ORs) quantify the odds for having a mental disorder among members of the respective class compared to members of the reference class. We first conducted a bivariate multinomial regression analyses, where the association of each predictor with class membership was tested separately. We then performed a multivariate regression analysis with simultaneous entry of all demographic, disease, and disorder-related patient characteristics as predictors of class membership. This analysis determines the contribution of each predictor under control of the remaining variables in the model.

Analyses were weighted to control for the oversampling of patients with PHQ-9 depression scores ≥9. Missing values occurred in 0.1% of responses for the self-report measure of physical symptoms and were person mean-imputed. We used R version 3.6.1 for all analyses.

### 3 RESULTS

#### 3.1 Subtypes of thoughts of death and suicidality: latent class analysis

A three-class solution yielded the best fit (see supplement Table S2) with lowest AIC and BIC values. The loglikelihood and likelihood ratio values were similar for three-, four-, and five-class solutions, but improved markedly from the two-class to the three-class solution. The entropy value of 0.82 suggests adequate latent class separation.

Table 1 and Figure 1 show the pattern of item endorsement probabilities for thoughts of death, death wishes, suicidal ideation and behaviors for all three classes. Of the total sample, 1905 (89%) individuals were assigned to class 1, 148 (6.9%) were assigned to class 2, and 88 (4.1%) were assigned to class 3. Class 1 was characterized by zero probability for all items and hence labeled "No Suicidality". In class 2, labeled "Thoughts of Death", the probability for frequent thoughts of death in general or one’s own death was 0.79, and 0.18 for a wish to die over the past 4 weeks. Class 3, "Suicidal Ideation", was characterized by a high probability of thoughts of suicide (0.97). Most members in class 3 also endorsed a wish to die (0.77) and thoughts of death (0.80). There was a moderate probability for suicide plans (0.36) and suicide attempts (0.14) in class 3.

Association of thoughts of death and suicidality subtypes with sociodemographic and disease-related characteristics.

Table 2 presents differences in sociodemographic and disease-related characteristics across the three latent classes. Odds ratios indicate whether members of class 2 and class 3 were more or less likely to carry the respective characteristic compared to the reference group class 1.

Members of class 2 (thoughts of death) as well as class 3 (suicidal ideation) were significantly younger, more often female and less often married compared to class 1 (no suicidality). Classes 2 and 3 were also characterized by longer time since diagnosis, and a higher number of physical symptoms. Education was better in class 2.

Illness prognosis however showed a notably divergent pattern across the three classes. While incurable disease was significantly more frequent in class 2 (OR = 1.39, 95% CI 1.10 to 1.87), it was significantly less frequent in class 3 (OR = 0.48, 95% CI 0.29 to 0.81). Tumor entity distribution showed relatively low differences across classes, except for those attributable to sex (breast cancer, prostate cancer, and gynecological cancer).

Table 3 shows case numbers and prevalence rates of mental disorders across the three classes. Members of both class 2 (thoughts of death) and class 3 (suicidal ideation) were significantly more likely to suffer from a mental disorder compared to members of class 1 (no suicidality), with odds being 4.2 (adjustment disorders,
TABLE 1 Probabilities for endorsement of suicide items across latent classes

|                  | Class 1                  | Class 2                  | Class 3                  |
|------------------|--------------------------|--------------------------|--------------------------|
|                  | No Suicidality (n = 1905)| Thoughts of Death (n = 148)| Suicidal Ideation (n = 88) |
|                  | 89.0%                    | 6.9%                     | 4.1%                     |
| 1) Frequent thoughts of death | 0.00                     | 0.79                     | 0.80                     |
| 2) Wish to die   | 0.00                     | 0.18                     | 0.77                     |
| 3) Suicidal ideation | 0.00                     | 0.00                     | 0.97                     |
| 4) Suicide plans | 0.00                     | 0.00                     | 0.36                     |
| 5) Suicide attempt | 0.00                     | 0.00                     | 0.14                     |

Note: Structured clinical interview questions: In the past 4 weeks, did you have a period of two weeks or more, when you 1) thought a lot about death, 2) had the wish to die, 3) felt so low you thought about committing suicide, 4) made a suicide plan? 5) Have you ever attempted suicide?

Figure 1 Probability profile of thoughts of death, death wishes, suicidal ideation and behavior across the latent classes. Structured clinical interview questions: In the past 4 weeks, did you have a period of two weeks or more, when you 1) thought a lot about death, 2) had the wish to die, 3) felt so low you thought about committing suicide, 4) made a suicide plan? 5) Have you ever attempted suicide?

To our knowledge, this is the first study to conduct a latent class analysis of thoughts of death and suicidality in a large representative sample of cancer patients with mixed tumors. We found three subtypes with distinct patterns. While thoughts of death, death wishes, suicidal ideation and behavior did not occur in most participants (89%, class 1), a distinction emerged between individuals who were primarily concerned with thoughts of death (6.9%, class 2) and those who additionally contemplated suicide over the past 4 weeks (4.1%, class 3). The relationship between thoughts of death, death wishes, suicidal ideation, and suicidal behavior has been little studied in patients with cancer. Consistent with the subtypes resulting in the present study, Walker et al.\textsuperscript{26} found that not all cancer patients who reported death wishes had thoughts of committing suicide. Coherent with the literature in non-cancer samples, we found that only a subgroup of patients with such suicidal ideation report suicide.
The absence of any thoughts of death and suicidality in 89% of the sample may be explained by the wording of the interview question which explicitly asked individuals whether they had thought "a lot about death" over a period of at least two weeks or more. Transient thoughts of death might have occurred more frequently in our sample but were not captured by the interview question.

Individuals in class 2 had frequent thoughts of death over at least two weeks. Such thoughts may relate to a variety of subjective experiences in the context of living with a life-threatening disease. The extent of distress related to thoughts of death was not assessed in the present study and may vary across individuals. Participants with frequent thoughts about death may have been concerned with fear of death and dying, fear of cancer recurrence or progression, or worry about consequences for caregivers (death-related distress). The association of class 2 with incurable cancer supports this idea. On the other hand, thoughts of death in cancer patients may also indicate less distressing attempts to cope, accept and prepare.

### Table 2: Frequency of demographic and disease-related characteristics across latent classes, bivariate associations

|                | Class 1 No Suicidality (n = 1905) | Class 2 Thoughts of Death (n = 148) | Class 3 Suicidal Ideation (n = 88) |
|----------------|----------------------------------|-------------------------------------|-----------------------------------|
|                | N (% of class 1) | N (% of class 2) | OR* | 95% CI | N (% of class 3) | OR* | 95% CI |
| Age < 40       | 100 (5.3)        | 14 (9.4)         | 1.87*** | 1.17 to 2.98 | 6 (6.5)         | 1.25 | 0.62 to 2.50 |
| Age ≥ 70       | 327 (17.2)       | 16 (10.7)        | 0.58* | 0.38 to 0.89 | 9 (10.1)        | 0.54* | 0.31 to 0.95 |
| Female sex     | 906 (47.5)       | 86 (57.9)        | 1.52** | 1.16 to 1.99 | 67 (76.8)       | 3.66*** | 2.45 to 5.46 |
| Married/cohabiting | 1562 (82.0)   | 109 (73.7)       | 0.62** | 0.44 to 0.86 | 53 (60.7)       | 0.34*** | 0.23 to 0.50 |
| High school/university education | 598 (31.4) | 64 (43.3) | 1.67*** | 1.28 to 2.19 | 33 (37.7)       | 1.32 | 0.93 to 1.88 |
| Incurable cancer | 430 (22.5)    | 42 (28.8)        | 1.39* | 1.10 to 1.87 | 11 (12.3)       | 0.48* | 0.29 to 0.81 |
| Recurrent cancer | 376 (19.7)    | 38 (25.3)        | 1.38* | 1.01 to 1.88 | 18 (21.0)       | 1.08 | 0.71 to 1.64 |
| Inpatient treatment** | 849 (44.5) | 58 (39.5)       | 0.81 | 0.62 to 1.07 | 29 (32.6) | 0.60** | 0.42 to 0.87 |
| <12 Months since first diagnosis | 1224 (64.2)   | 73 (49.2)        | 0.54*** | 0.40 to 0.73 | 46 (52.6) | 0.62* | 0.43 to 0.90 |
| Physical symptom count, mean (SD)** | 5.21 (3.63) | 7.63 (3.87) | 1.17*** | 1.13 to 1.22 | 7.80 (3.94) | 1.19*** | 1.13 to 1.24 |
| Breast cancer  | 369 (19.3)       | 38 (26.2)        | 1.48* | 1.09 to 2.01 | 30 (34.1)       | 2.15*** | 1.50 to 3.10 |
| Prostate cancer | 340 (17.9)      | 14 (9.0)         | 0.46*** | 0.29 to 0.72 | 5 (5.8)         | 0.28*** | 0.14 to 0.58 |
| Colorectal cancer | 253 (13.3)   | 22 (14.6)        | 1.11 | 0.76 to 1.63 | 5 (10.1) | 0.74 | 0.42 to 1.29 |
| Lung cancer    | 169 (8.9)        | 12 (8.2)         | 0.91 | 0.56 to 1.48 | 7 (8.0)         | 0.89 | 0.47 to 1.67 |
| Gynecologic cancer | 152 (8.0)    | 13 (8.6)         | 1.08 | 0.67 to 1.74 | 13 (14.5) | 1.95** | 1.20 to 3.20 |
| Hematologic cancer | 139 (7.3)     | 14 (9.4)         | 1.33 | 0.84 to 2.10 | 9 (10.1) | 1.44 | 0.81 to 2.54 |
| Stomach/esophageal cancer*** | 77 (4.0) | 5 (3.4)         | -    | -    | 2 (2.2) | -    | -    |
| Kidney/urinary tract cancer*** | 73 (3.8) | 3 (2.1) | -    | -    | 1 (0.7) | -    | -    |
| Head and neck cancer*** | 57 (3.0) | 6 (3.9) | -    | -    | 3 (2.9) | -    | -    |
| Bladder cancer*** | 44 (2.3) | 4 (2.6) | -    | -    | 2 (2.9) | -    | -    |
| Pancreatic cancer*** | 46 (2.4) | 3 (1.7) | -    | -    | 1 (1.4) | -    | -    |
| Malignant melanoma*** | 34 (1.8) | 3 (2.1) | -    | -    | 0 (0.0) | -    | -    |

Abbreviations: CI, confidence interval; OR, odds ratio.

*Class 1 is the reference group for odds ratios, interpretation: the OR of 1.87 for example indicates that the odds of being in class 2, compared to class 1, is 1.87 times higher for patients younger than 40 years than for those 40 years or older.

**Acute oncologic inpatient treatment (excluding rehabilitation inpatients).

***Possible range: 0-21.

Interpretation for OR: with every additional physical symptom, the odds of being in class 2, compared to class 1, increase by 1.17.

No ORs calculated due to low n in classes 2 and 3.

*p < 0.05, **p < 0.01, ***p < 0.001.
with cancer. Pervasive thoughts of death may become overwhelming and require adequate intervention in multiprofessional cancer care. In previous studies, death-related distress (fear of death, fear of dying in pain, worry about close others, fear of being a burden) was further associated with the wish to die in a subgroup of patients with advanced cancer. The present results in hits regard were yet mixed and depended on class-membership: in class 2, thoughts of death occurred mostly without death wishes, whereas in class 3, thoughts of death occurred mostly together with death wishes.

Class 3 comprised all participants with suicidal ideation over the preceding 4 weeks (4.1%). While this rate is higher compared to the 2.0% rate in the general population, suicidal ideation was relatively low despite serious medical illness. Earlier work has also linked major illness to a higher risk for suicidal ideation, but ORs were generally small and ranged between 1 and 2. The observable burden of illness, its symptoms, and prognosis may not function as simple explaining factors for suicidal ideation in cancer patients, consistent with the lower frequency of suicidal ideation in patients with incurable cancer in the present study. Psychological factors may significantly affect individuals’ adaptation capacities when facing severe illness.

### 4.1 Clinical implications

The present results suggest that the increase in severity of suicidality from class 2 to 3 does not coincide with an increase in severity or frequency of mental disorders. Since all phenomena assessed in the present study (including recent thoughts of death, death wishes, suicidal ideation, suicide plans, and lifetime suicide attempts) were associated with a substantially higher risk for mental disorders, they require clinical evaluation for underlying psychological distress. Despite comparable frequency of mental disorders, the individual nature of distress may be quite different across classes 2 and 3 and require further exploration along with the severity of suicidal ideation. The presence of suicidal ideation requires further systematic evaluation and crisis interventions. The substantial co-occurrence of thoughts of death, death wishes and suicidal ideation in class 3 might reflect the clinical challenge to differentiate these phenomena in each patient.

In line with previous studies on suicidal ideation, younger age, female sex, living alone, and a higher physical symptom burden were risk factors in the present study. Health care professionals should nonetheless be aware of a higher vulnerability in better educated patients and outpatient settings. Inpatient treatment may provide some protection through increased social interactions and availability of psychosocial support. It is notable that breast cancer was associated with a higher risk for suicidal ideation despite good
prognosis. This effect may be linked to the gender discrepancy in both cancer and general population studies with women being at higher risk for suicidal ideation and attempts and men at higher risk for completed suicides.\(^4\)

4.2 | Conceptual implications

From a conceptual perspective, the present pattern of mental disorders across classes did not contribute to distinguish patients in class 2 (thoughts of death) from those in class 3 (suicidal ideation). While a higher burden might have been expected in class 3 compared to class 2, the frequency of mental disorders was almost equal in both classes. Previous studies suggest a significant association of higher levels of hopelessness and demoralization with death wishes as well as suicidal ideation in patients with cancer.\(^5,36,38\) Individuals in class 3 might be characterized by higher levels of hopelessness and demoralization which are not reflected by current diagnostic criteria for mental disorders. To better distinguish the psychology of individuals in classes 2 and 3, the contribution of concepts such as death anxiety, sense of dignity, and demoralization may be of interest to future work.\(^39\)

4.3 | Study limitations

Given the changes in diagnostic criteria in a number of mental disorders in the DSM-5 and presumably in the ICD-11, our prevalence estimates of mental disorders have to be interpreted with some caution. Moreover, a substantial number of patients withdrew from completing the CIDI after being assigned to it, and our sample is biased toward younger age, a higher level of education, and inpatient rehabilitation setting, thus limiting the generalizability of our findings. We did not assess severe mental disorders including schizophrenia spectrum disorders and obsessive-compulsive disorder which may be linked to an increased risk for suicidality. Further research is needed on this understudied group. The association of suicidal ideation with mood disorders may further be somewhat overestimated because suicidal ideation and behaviour is also a diagnostic criterion for the latter. Although analyses were weighted to account for oversampling of individuals with PHQ-9 scores ≥ 9, the sampling procedure may have led to a higher association. The interpretation of the results is limited to 4-weeks-prevalences and does not capture previous suicidality and mental disorders. Moreover, there was no clinical assessment of suicide risk and requests for euthanasia or physician-assisted suicide.

5 | CONCLUSION

The present study assessed a broader range of suicidal ideation and behavior than many previous studies in cancer. Future studies could improve class differentiation by a more detailed assessment of thoughts of death, death wishes, and suicidal ideation, and the extent to which these are pervasive. While the present mixed sample enabled us to analyse differences between patients with early and advanced stage cancer, a larger subsample of patients with advanced and terminal cancer might be required to identify subtypes including pervasive thoughts of death and death wishes as suggested by qualitative studies. This work provides valuable quantitative support for distinct patterns of thoughts of death and suicidal ideation in patients with cancer.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualization and design: SV, AM, UK; Analysis and interpretation of data: All authors; Data curation: SV, AM; Drafting and critical revision: All authors; Final approval of the version to be published: All authors; Accountable for all aspects of the work: All authors; Supervision: AM, UK; Project administration: AM; Funding acquisition: AM, UK.

DATA AVAILABILITY STATEMENT

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

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ENDNOTES

1. We use the term ‘suicidality’ to simplify the text when referring to the phenomena of death wishes, suicidal ideation, suicide plans, and suicide attempts combined. We acknowledge that this term does not reflect the complex characteristics related to each of these phenomena.
2. Latent class analysis is a technique which clusters similar response profiles on a set of symptoms into distinct classes. The categorization is statistically implemented by an algorithm that minimizes the association across symptoms, given the mathematical condition that class membership causes associations between symptoms.\(^16\)

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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