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Suicidal Ideation Assessment in Individuals with Premanifest and Manifest Huntington Disease

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Abstract

Background: Huntington disease (HD) is associated with increased risk of suicide.

Objective: This study compares suicide ideation in HD to the general population, assesses factors associated with increased prevalence of suicidal thoughts, and compares clinician-rated to self-reported assessments of suicidal ideation.

Methods: We examined 496 participants with premanifest or manifest HD. Clinician-rated suicidal ideation was measured using the Problem Behaviors Assessment – short form. Self-reported ideation was measured using two items from the HDQLIFE Concern with Death and Dying item bank. Independent sample *t*-tests were conducted to compare the prevalence of suicidal thoughts between our HD sample and the U.S. population. Logistic regression analyses were used to determine characteristics associated with higher odds of clinically significant suicidal ideation. Kappa agreement coefficients were calculated to evaluate concurrence between clinician-rated and self-reported assessments.

Results: Our sample had a significantly higher occurrence of suicidal ideation (19.76%) and suicidal plans (2.1%) than the general population ($p < 0.0001$). Odds of clinically significant suicidal ideation were 6.8 times higher in females ($p = 0.04$) on the clinician measure, and Hispanic/Latinos had 10.9 times higher odds than non-Hispanics ($p = 0.025$) on the self-report measure. Clinician-rated assessment had fair agreement ($k = 0.2–0.4$) with self-reported

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CONFLICTS OF INTEREST

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assessments, except in early stage HD where there was no overlap in the identification of participants with clinically significant suicidal ideation.

Discussion: Assessment for suicidal ideation and clinically significant suicidal thoughts in HD with a multimodal approach that includes clinician-rated and self-report measures is critical at all stages of the disease.

Keywords

Huntington disease; suicidal ideation; suicide; suicide assessment; comparing methods

INTRODUCTION

Huntington disease is an autosomal dominant, inherited, neurodegenerative disorder associated with an increased risk of suicidal ideation [1, 2]. This increased risk of suicide occurs through all stages of the disease, from the premanifest phase through onset of symptoms and continues as the disease progresses [3]. Opportunities to assess at-risk individuals for suicide and relevant risk factors occur at the time of predictive testing, during clinical care, and during participation in clinical research. The current study sought to evaluate suicide ideation in clinical research participants in the Huntington Disease Health-Related Quality of Life (HDQLIFE) Study [4], and compare the rates of suicidal thoughts and clinically significant ideation to the general population, assess factors associated with an increased risk for suicidal ideation, and compare in-person clinician assessment of suicide ideation with a self-reported online assessment tool.

Huntington disease (HD) affects between 3 and 10 individuals per 100,000 worldwide [5, 6], and causes chorea, cognitive impairment, behavior changes, and psychiatric symptoms [2, 7]. The pathogenic gene mutation is located at 4p16.3 and contains an expanded CAG repeat in exon 1 in individuals with HD [8, 9]. Average diagnosis is in the late 30 s, with the age of onset inversely related to the number of CAG repeats. Symptoms typically emerge gradually, with behavioral and cognitive symptoms commonly occurring years before motor symptoms [10]. Death occurs 15–20 years after symptom onset/diagnosis [2, 11, 12].

George Huntington's original description in 1872 included a "tendency to insanity and suicide" as one of the peculiarities of the disease, and he comments that he was aware of several instances of suicide in affected and at-risk family members [13]. Reported suicide rates vary from 5.7% in affected persons [1] to 7.3% in affected and at-risk participants [14]. Farrer [1] reported that 27.6% of patients had attempted suicide at least once, which exceeds the general US population lifetime prevalence of 1.9–8.7% for suicide attempts [15].

Assessment of suicide risk can occur via an in-person clinical interview or completion of a self-report instrument. While many studies in HD utilize either the Problem Behaviors Assessment-short (PBA-s; 16) or the Columbia Suicide Severity Rating Scale (CSSRS; 17), there is no consensus for which measure should be used, nor are there standardized follow up procedures when someone at high risk is identified.

Additionally, clinician assessment may differ from self-reported suicide ideation. For example, one study found that individuals presenting for their first visit to a clinic for anxiety and depression were more likely to endorse current suicidal ideation on the self-administered questionnaire than the clinician interview [18]. Similarly, a self-report questionnaire also was more likely to reveal increased frequency and severity of suicidal ideation than an in-person clinician interview in individuals with major depressive disorder or bipolar disorder [19]. In contrast, clinicians rated suicide ideation higher than self-report in patients referred from Army hospitals for depression or anxiety [20]. Furthermore, clinician interview assessments of suicidal ideation varied from self-reported suicidal thoughts by 19% in a study of patients admitted to an adult inpatient psychiatric unit that treated primarily mood, anxiety, eating and adjustment disorders [21]. These mixed findings suggest that the mode of assessment (either by self-report or through an in-person interview) may have an impact of how willing an individual is to report suicidal thoughts. Thus, a better understanding of the assessment modality in HD may help inform best practices with regard to suicidal ideation and suicide assessment in these individuals.

The purpose of this paper is to examine suicidal ideation, as well as the impact of assessment modality (in-person versus self-report survey assessment) in HD. Specifically, we hypothesized that the rates of suicidal ideation and clinically significant suicidal ideation in premanifest and manifest HD would exceed that of the general population. In addition, we hypothesized that individuals who are later in the disease process, as well as those with more clinician-rated depression, anxiety and/or anger would exhibit more severe suicidal ideation [22, 23]. We also hypothesized that the demographic differences in the general population (e.g., females have a higher prevalence of suicidal thoughts, but not suicidal plans) [24] also would occur in HD. Finally, we hypothesized that frequency of self-reported suicidal thoughts would be higher than frequency of clinician-rated suicidal ideation.

METHODS

Participants

We examined individuals with either premanifest (gene-positive for the HD CAG expansion and no clinical diagnosis) or manifest HD. Participants had to be at least 18 years of age, able to read and understand English, and have the ability to provide informed consent. Participants were recruited from several HD treatment centers (the University of Michigan, University of Iowa, University of California-Los Angeles, Indiana University, Johns Hopkins University, Rutgers University, Struthers Parkinson's Center, and Washington University), as well as through the National Research Roster for Huntington Disease Patients and Families at Indiana University, existing online medical record data capture systems [25], and the Predict-HD study [26]. All data were collected in accordance to local Institutional Review Boards (IRB) and participants provided informed consent prior to study participation.

HD disease stage

The final item of the Unified Huntington Disease Rating Scale (UHDRS; 27) motor assessment was used to differentiate premanifest from manifest HD. This item indicates the "diagnostic confidence level" on a scale of 0 (no motor abnormalities) to 4 (>99%

confidence that motor abnormalities are unequivocal signs of HD) of the clinician's impression of whether or not the participant has manifest HD. Scores lower than 4 indicate premanifest HD whereas a score of 4 indicates manifest HD. For manifest participants, the UHDRS Total Functional Capacity (TFC) was used to determine HD staging [28]. TFC is a clinician-rated assessment of a participant's ability to maintain a job, manage finances independently, complete chores, accomplish activities of daily living [29], and live at home as opposed to a nursing or chronic care facility. TFC scores range from 0–13 with higher scores indicative of higher functioning. Stage I was defined as individuals with TFC scores ranging from 11–13, and Stage II was defined as individuals with TFC scores ranging from 7–10. Stages III to V were collapsed together into one group, which was defined by a score of 0–6 [28].

Comparisons with the United States average

Rates of suicidal ideation and suicide planning within our sample were compared to published data from reports from the National Survey on Drug Use and Health from the Centers for Disease Control and Prevention [CDC], examining suicidal thoughts in the general population [24]. Respondents were asked whether they had seriously thought about killing themselves at any time during the past 12 months. If participants answered in the affirmative, they were then asked whether they had made any plans to kill themselves and whether they had a suicide attempt. With this information, the CDC article estimates the prevalence of suicidal thoughts and behaviors based on survey data from 8,360 respondents from 2008–2009.

Clinician-rated behaviors and suicidal ideation

Problem Behaviors Assessment – short (PBA-s; 16).—The PBA-s is a clinician-rated measure of behavioral problems based on a semi-structured interview with patients and informants designed specifically for HD. Clinician raters were trained on this measure and required to demonstrate proficiency in its administration. It includes 11 items that examine different aspects of emotion and behavior including depression, suicidal ideation, anxiety, irritability, anger/aggression, apathy, perseverative thinking, obsessive compulsive behaviors, delusions, hallucinations, and disorientation. Clinicians rate each item for severity (rated on a scale of 0 [symptom absent] to 4 [severe] and frequency (rated on a scale of 0 [never/almost never] to 4 [daily/almost daily for most or all of the day]). We examined frequency of suicidal thoughts in premanifest and manifest HD participants compared to the U.S. average, as well as agreement between clinician-rated and self-reported measures. Severity scores were utilized in our assessment of clinically significant individuals, which we defined as participants who had persistent suicidal ideation or have made preparations or an attempt to commit suicide. Participants with ratings of ≥3 for suicide severity were considered clinically significant, defined as severe ideation that includes a plan or prior attempt of suicide. For these participants, additional follow-up questions were asked to determine imminent risk and/or if additional referrals or treatment were warranted. Clinically significant suicidal ideation was coded as a dichotomous variable, either 'Yes' for participants with clinically significant suicidal ideation or 'No' for participants who were not. This variable was compared to the national U.S. estimates of individuals with a suicide

plan, and was also used to measure agreement between clinician-rated and self-reported clinically significant individuals.

Self-reported suicidal ideation

As part of a larger study, participants completed an online survey that examined their health-related quality of life (HRQOL; details reported in 4). This study included two questions that assess suicidal thoughts (these items were administered as part of the HDQLIFE Concern with Death and Dying measure; [30]. The first question read “In the past seven days, how often have you thought about ending your life?” Responses were on a 5-point Likert scale ranging in frequency from ‘Never’ to ‘Always.’ Similar to the clinician-rated measures, self-reported frequency of suicidal thoughts was compared to U.S. estimates. For all responses that were not ‘Never,’ a follow-up question was administered: “Do you intend to act on these thoughts in the near future?” Responses of ‘Yes’ were considered clinically significant (defined below). Clinically significant responses, as determined by the self-report measure, were compared to the U.S. estimate of the prevalence of individuals who have a suicide plan.

Clinically significant suicidal thoughts

Participants who received a severity score greater than or equal to 3 on the suicide-specific question on the PBAs, or who indicated ‘yes’ to the following question on HDQLIFE Concern with Death and Dying, “Do you intend to act on these thoughts in the near future?” were considered clinically significant, and required additional follow-up (as per the suicide assessment protocol associated with this study). The suicide protocol dictated that further questions to establish imminent risk were employed through direct contact (by phone or in-person) between the study investigator or coordinator and participant. Specifically, follow-up questions with regard to suicidal thoughts (including frequency and persistence of these thoughts), details with regard to a plan, identification of future reasons to live, as well as previous history of attempts were queried to determine if there was imminent risk. In all cases of endorsement, the study site investigator was notified, consulted, and follow-up actions documented. In cases where imminent risk was identified the study site investigator made the appropriate referrals following professional standards of conduct, including contacting emergency services if needed.

Analysis plan

Frequency counts for endorsement of the suicide assessment items on the PBA-S and the two self-report suicidal ideation questions from the Concern with Death and Dying measure were calculated using SAS 9.4.

Suicidal ideation prevalence in HD relative to the U.S general population

Four separate independent sample *t*-tests were conducted to compare the prevalence of suicidal thoughts between the CDC’s U.S. average and our sample. The first two *t*-tests compared the proportion of individuals with suicidal ideation between the U.S. population and our measures (i.e., the PBA-s and HDQLIFE survey) of suicide frequency in HD. For these tests, our frequency measures were dichotomized into “no suicide ideation” or “suicide ideation present.” Another *t*-test compared rates of individuals in our cohort with persistent

suicidal ideation and/or plans to act on these thoughts in the future, with rates of individuals within the U.S. population with suicidal thoughts. A final *t*-test compared the proportion of HD participants who were clinically significant based on our measures of suicidal ideation (i.e., PBA-s and HDQLIFE survey) to the proportion of individuals within the U.S. population with a suicide plan.

Demographic risk factors for suicidal ideation in HD

In addition, crude and adjusted logistic regression analyses were used to determine which characteristics relate to higher odds of an individual having clinically significant suicidal ideation. First, we wanted to determine if the demographic factors (i.e., gender, age, race, and ethnicity) related to increased odds of having a suicide plan (CDC Morbidity and Mortality Weekly Report; MMWR) [24] were present in our HD sample. Each of these demographic variables were entered individually into a logistic model with the outcome of clinically significant suicidal ideation. Next, logistic regression models determined if staging and PBA-s total scores of depression, anxiety, and anger/aggression relate to higher odds of clinically significant suicidal ideation. These variables were selected based upon the established relationship between emotional distress and suicidal ideation [22, 23].

Concordance between self-reported and clinician-rated suicidal ideation

Next, a Kappa agreement coefficient [31] was used to evaluate agreement between the frequency of the clinician-rated suicide assessment (i.e., PBA-s), and self-report questions. In addition, Kappa coefficients were used to examine agreement between suicide protocol activation based on the clinician-rated questions, compared to suicide protocol activation based on the self-report questions. A kappa score between 0.81 and 1.00 was considered almost perfect agreement, 0.61–0.80 was considered substantial agreement, 0.41–0.60 was moderate agreement, 0.21–0.40 was deemed fair agreement, and lower than 0.20 indicated no agreement [31, 32]. Paired *t*-tests comparing frequency scores for self-report and clinician rated measures were used to determine whether one measure had a higher average score than the other.

RESULTS

Participants

We examined 496 individuals with either premanifest ($n = 194$) or manifest HD (Stage I $n = 79$; Stage II $n = 113$; and Stage III-V $n = 110$; Table 1). Groups did not differ on gender ($\chi^2_3 = 5.02$, $p = 0.1705$), but, as expected, age differed ($F[3, 492] = 29.31$, $p < 0.0001$). The average age of the premanifest group ($\bar{x} = 42.7$) was nine years younger than the Stage I group ($\bar{x} = 51.1$), 10 years younger than the Stage II group ($\bar{x} = 52.4$), and 13 years younger than the Stage III-V group ($\bar{x} = 54.7$). This finding is expected, as symptoms of HD progress over time [2]. The Stage III-V group included a greater proportion of African Americans than the premanifest and Stage I and Stage II groups (Fisher's Exact = 0.0013), whereas ethnicity did not differ across groups ($\chi^2_6 = 11.10$, $p = 0.09$). Education differed between the four HD groups ($F[3, 490] = 12.21$, $p < 0.0001$), as the pre-manifest group had more years of education than the Stage II and Stage III-V groups. Additionally, the Stage III-V

group had a higher number of CAG repeat lengths than the premanifest group (F[3,381] = 4.93; $p = 0.0023$).

Suicidal ideation prevalence in HD relative to the U.S general population

Published rates of suicidal thoughts in individuals over the age of 18 in the US indicate that approximately 3.7% (95% CI: 3.5, 3.9) of individuals endorse suicidal thoughts and 1% (95%CI: 0.9, 1.1) have a suicide plan [24]. Our self-report measure revealed that 19.76% (95%CI: 16.3, 23.2) of participants endorsed some degree of suicidal thoughts, which exceeded the US average [t(8853) = 35.0186; $p < 0.0001$]. Similarly, our survey indicated that 2.01% (95% CI: 0.8, 3.2) of our sample planned to act on these thoughts in the near future, which is significantly higher than the US average (t[2757] = 427.04; $p < 0.0001$). The clinician rated measure showed a 11.10% (t[8853] = 35.02; $p < 0.0001$) prevalence of suicidal ideation with approximately 2.42% (t[2757] = 425.02; $p < 0.0001$) of participants endorsing intention to act on these thoughts in the near future.

Demographic risk factors for suicidal ideation in HD

For clinician-rated suicidal ideation, females had a 6.8 times (OR = 7.88, 95% CI: 1.01, 61.554; $p = 0.04$; Table 2) greater risk of clinically significant suicidal ideation than males, similar to the U.S. population. However, this finding did not remain significant when controlled for depression, anger and anxiety. None of the other demographic variables (i.e., race, ethnicity, age, or education) significantly related to clinically significant suicidal ideation. Late-stage participants did not have greater risk of clinically significant ideation than either early-stage or premanifest participants. Higher levels of clinician rated depression (OR = 1.47, 95% CI:1.28, 1.70; $p < 0.0001$), anger (OR = 1.30, 95% CI: 1.14, 1.49; $p < 0.0001$), and anxiety (OR = 1.28, 95% CI: 1.13,1.44; $p < 0.0001$) indicated greater risk of clinically significant suicidal ideation. In the adjusted model, clinician-rated depression (OR = 1.44, 95% CI: 1.21,1.71; $p < 0.0001$) was associated with clinically significant suicidal ideation. However, anger/aggression (OR = 1.21, 95% CI: 1.00, 1.46; $p = 0.05$), anxiety (OR = 1.01, 95% CI: 0.87, 1.18; $p = 0.85$) and female gender (OR = 8.21, 95% CI: 0.88, 76.53; $p = 0.06$) did not.

Based upon self-reported suicidal thoughts, ethnicity was the only demographic variable to have an association with clinically significant suicide ideation in our HD group which differs from demographic differences in suicidal ideation in the US population. Participants who identified as Hispanic or Latino had a 10.9 (OR = 10.9, 95% CI: 1.33, 86.88; $p = 0.03$) times higher risk of clinically significant suicidal ideation than non-Hispanics or Latinos. Depression was a significant risk factor of suicidal ideation as well (OR = 1.19, 95% CI: 1.02, 1.38; $p < 0.0001$), but neither anxiety nor anger/aggression were associated with clinical significance. In an adjusted model, both depression (OR = 1.18, 95% CI: 1.01, 1.38; $p = 0.04$) and ethnicity (OR = 9.23, 95% CI: 1.08, 78.53; $p = 0.04$) remained significant.

Concordance between self-reported and clinician-rated suicidal ideation

Clinician-rated suicidal ideation—Overall, 11.10% of all participants had a score higher than 0 (Never) on the suicidal thoughts question of the PBA-s (Table 3). The frequency of suicidal ideation did not differ among the four HD groups (Fisher's Exact $p =$

0.61 Table 3). Overall, we enacted our suicide protocol for 2.27% of the sample based upon the clinician-rated measure(s). Suicide protocol activation also did not differ among the four HD groups (Fisher's Exact $p = 0.66$; Table 3).

Self-reported suicidal ideation—Overall, 19.76% of participants endorsed suicide ideation on the self-report assessments (Table 3). Suicide endorsement did not differ among the four HD groups (Fisher's Exact $p = 0.28$; Table 3). Overall, we enacted our suicide protocol for 1.99% of our study participants based upon the self-report measure(s). The suicide protocol activation did not differ among the four HD groups (Fisher's Exact $p = 0.57$; Table 3).

Comparisons between clinician-rated and self-report measures—Of the five Stage I and three Stage II participants who were clinically significant, four were indicated solely by the clinician measure and four were indicated solely by the self-report measure, with no overlap. This indicates that for Stage I and Stage II individuals, the two measures of clinically significant suicide ideation did not agree ($\kappa = -0.1538$ and -0.0541, respectively; Table 4). The remaining Kappa coefficients indicated that the clinician measure of suicidal ideation and the self-report measure had fair agreement ($\kappa = 0.2–0.4$) for suicide frequency and clinically significant risk. The exception to this was in the premanifest participants, in which there was substantial agreement between the two measures of clinically significant suicidal ideation ($\kappa = 0.6296$; Table 4). Participants typically reported greater frequency of suicidal ideation during the survey than on the clinician measure ($t[495] = -5.02$; $p < 0.0001$).

DISCUSSION

This study confirms that individuals with premanifest and manifest HD have rates of suicidal ideation and having a suicide plan higher than the general population [24]. In fact, rates for self-reported suicidal ideation were more than five times greater than rates in the general population (19.76% in HD relative to 3.7% in the general population). Furthermore, the rate of individuals with HD that had a plan for suicide was two times that of the general population (2.01% in HD relative to 1% in the general population). Findings were similar, although less robust, for clinician-rated suicidal ideation. In this case, clinicians indicated a prevalence rate of 11.10% for suicidal ideation for these same individuals (relative to the 19.76% based on self-report data). These findings are consistent with previous findings of suicidal ideation estimates in this population [33–35]. Clinician-rated measures of suicide plans were comparable to the self-report measures (2.42% for clinician-rated versus 2.01% for self-reported rates), however, for participants in Stage I and Stage II the two measures did not overlap. One explanation could be that the self-reported measure asks about suicide ideation in the past seven days, whereas the clinician-rated measure asks participants about their situation within the past month, which increases the risk for recall bias. The receipt of a clinical diagnosis is an emotionally tumultuous time that may enhance variability of reporting suicidal ideation.

In addition to the general rates for suicidal ideation and suicide plans, we examined different risk factors for clinically significant suicidal ideation. First, findings suggested that females

were more likely than males (6.8% more likely) to report clinician-rated, but not self-reported, clinically significant suicidal ideation. While the finding for clinician-rated risk is consistent with findings in the general population (which also suggest that females have a higher prevalence than males in regards to suicidal thoughts; 24), the absence of this finding for self-reported risk was more surprising.

Second, none of the other demographic factors that relate to risk in the general population were found with clinician-rated risk (i.e., that suicidal thoughts and plans are more prevalent in individuals aged 18–29 [than older participants], in non-Hispanic whites [relative to other races/ethnicities], and in those with a high school education [relative to those with more education. Being Hispanic or Latino related to increased risk with the self-report measure, in contrast to the general population [24]. This unexpected finding seems to contrast with studies that reported lower suicide rates in Hispanics relative national (US) rates for Hispanics, [36] as well as similar rates of lifetime suicide attempt among whites, blacks and Hispanics [37]. To the best of our knowledge, there have been no studies that examined suicidal ideation in Hispanics living with chronic conditions, which may provide a potential explanation for this finding. Given the small number of Hispanic or Latino participants in our study ($n = 12$), further investigation is warranted.

Third, contrary to our hypotheses, disease stage (premanifest, early- or late-HD) did not relate to increased risk of either clinician-rated or self-reported clinically significant suicide ideation. This finding agrees with another study in HD that did not find a relationship between TFC and suicidality [35], but appears inconsistent with other HD literature. Disease stage may not relate to suicidal ideation in HD, however methodological differences between this sample and other studies may explain this discrepancy. First, this study used different measures to assess suicidal ideation. This study employed the PBA-s (a clinician-rated instrument that measures behavior over the last four weeks) and a single self-report item about suicidal thoughts (within the past week), whereas other studies used the BDI-II to assess suicidal thoughts (within the past 2 weeks), the UHDRS assessment of suicidal thoughts and attempts over the past six months, and the C-SSRS which assesses lifetime suicidal thoughts and attempts.

Our findings suggest that other than gender, demographic factors may not play a major role in suicidal ideation in this population. Findings from the National Comorbidity Survey suggest that simply having a chronic illness increases one’s risk of suicidal ideation [38]. In addition, a study conducted within the Mental Health Research Network found that 17 of 19 physical health conditions were associated with an increased risk of suicide and having multiple physical health conditions significantly increased suicide risk [39]. Thus our sample may have been more affected by just having a chronic disease, rather than the severity of their HD (i.e., disease stage). The high risk of suicide in individuals with HD likely reflects the lack of an available cure to this relentlessly progressive condition [1, 2]. Alternatively, individuals with clinically significant suicide ideation may not share their distress either in person or via self-report survey, because they do not want help [40, 41] or to avoid involuntary hospitalization [42, 43]. In addition, clinician-rated risk and self-reported risk yield similar, but not identical, findings; thus further examination of demographic factors such as gender and Hispanic ethnicity warrant further exploration in HD.

As expected clinician-rated depression and anger related to greater risk for clinically significant suicide ideation. Only depression remained a significant risk factor for clinically significant suicidal thoughts whereas other self-reported symptoms did not. The relationship between depression and suicidal ideation in HD resembles the strong relationship found in both the HD population [34, 44] as well as other populations [22, 23, 45]. Also not surprisingly, anger related to suicide risk in HD, as it does in other groups [23, 46]. Interestingly, self-reported risk did not reveal this relationship, perhaps suggesting that those with HD are less apt to share or have less awareness of their own anger.

In general, individuals with HD were more likely to endorse suicidal ideation via self-report than via in-person interview similar to other groups [18, 19]. Finally, although clinician-rated measures reasonably agreed with self-reported suicidal ideation (with substantial agreement for premanifest participants), clinician-rated suicide significance did not agree with self-reported suicide actionable risk. This suggests that these assessment modalities identify different individuals that need intervention. Thus both assessment modalities should be considered to maximize identification of those most likely to engage in a suicide plan.

The current study found that female gender and Hispanic/Latino ethnicity related to an increased occurrence of suicidal ideation in premanifest and manifest HD. Additional factors to consider in evaluating suicide risk in HD (which were not assessed in the current study) include substance dependence, psychiatric history, hopelessness, irritability, emotional distress, sleep disturbance, ego strength, suicidal ideation, history of suicide attempts, unemployment, motor status, and social dysfunction [23, 39, 45, 47–50]. All should be considered when determining best practices for evaluation of suicidal ideation in this population.

Future research should focus on the identification of existing HD suicide risk assessment practices within clinical and research settings. A goal of this research should be to develop formal guidelines for best practices and a standardized assessment for suicide risk in those individuals that are at risk for or have premanifest or manifest HD. The findings from this study would suggest that best practices for assessment of risk should include multiple assessment modalities to ensure that those individuals that are experiencing these thoughts and feelings are identified and provided with appropriate interventions. The goal should be to maximize the identification of those at-risk and thus ensure that all individuals with suicidal ideation are identified, as the potential consequence of not identifying someone is death.

While these findings have important implications for assessing suicidal ideation and clinically significant suicide in HD, we recognize several study limitations. First, we examined thoughts of suicide and suicide plans but did not have consistent data about past history of suicide attempts. A past history of suicide attempt confers a significant risk factor for future attempts in the general population [51], and future work could determine if this holds for HD. In addition, the online and clinician-rated assessments were not identical. The clinician measure provided numerical descriptions for frequency (e.g., once per week, every day) while the online assessment had qualitative options (e.g., rarely, or sometimes). Therefore, participants may have interpreted the online assessment differently from other

participants or the clinician measure. In addition, the demographics of our sample may limit the generalizability of our findings. Our sample was highly educated in comparison to the general population, and was primarily white as evident by the small proportion of African American (1.8%) and Hispanic/Latino (2.4%) participants. While the CDC estimates for suicidal ideation for White, non-Hispanic participants was only slightly above the overall estimate (3.9% compared to 3.7%), the homogenous makeup of our sample must be considered when interpreting our comparisons to the general population. Furthermore, the small proportion of Hispanic participants in our study, as well as the small number of participants who endorsed clinically significant suicide ideation on the survey (N = 10) may have altered the results of the logistic regression model. On the survey, 2 Hispanic participants (17%) had clinically significant suicidal ideation compared to 8 non-Hispanic participants (1.7%), thus a single Hispanic participant who endorses suicidal plans held more weight than a single non-Hispanic participant.

As expected, rates of suicide in HD significantly exceed that in the general population. Furthermore, the typical demographic risk factors for suicidal ideation in the general population were not apparent in this HD sample. Thus, having premanifest or manifest HD warrants increased attention to suicide risk; therefore, clinicians should feel comfortable raising concerns about suicide with their patients to provide or refer to appropriate clinical services. Furthermore, symptoms of depression and anger also should alarm clinicians to further investigate feelings of suicide with their patients. Finally, clinicians should use multiple modes of assessment for suicidal ideation since self-report surveys and in-person interviews identified different individuals with clinically significant suicidal ideation. The threshold for concern should be low to maximize identification of those with suicidal ideation. This extra effort to identify those extremely distressed individuals with greater risk for suicide may save lives.

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ABBREVIATIONS

ADL	Activities of Daily Living
CAG	Cytosine-Adenine-Guanine Trinucleotide DNA repeats
HD	Huntington disease
HDQLIFE	Huntington Disease Health-Related Quality of Life
HRQOL	Health-related Quality of Life
MMWR	Morbidity and Mortality Weekly Report (published by Centers for Disease Control)
PBA-s	Problem Behaviors Assessment-short
TFC	Total Functional Capacity UHDRS Unified Huntington Disease Rating Scale

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Table 1

Demographic Characteristics of Individuals with HD, stratified by disease stage

Variable	Premanifest (N = 194)	Stage I (N = 79)	Stage II (N = 113)	Stage III-V (N = 110)	All (N = 496)
Age (years)					
M(SD)	42.7 (12.1)	51.1 (13.5)	52.4(11.7)	54.7(11.9)	48.9 (13.2)
Gender (%)					
Female	63.9	49.4	58.4	58.2	59.1
Male	36.1	50.6	41.6	41.8	40.9
Race (%)					
White	97.4	96.*2*	98.2	93.6	96.6
African American	0.0	0.0	0.0	6.4	1.8
Other	2.1	3.8	1.8	0.0	1.4
Not Provided	0.5	0.0	0.0	0.0	0.2
Ethnicity (%)					
Not Hispanic or Latino	92.7	89.9	94.7	96.8	93.6
Hispanic or Latino	1,5	6.3	2.7	0.8	2.4
Not Provided	5.9	3.8	2.7	2.4	4
Education (# of years)					
M(SD)	15.9 (2.9)	15.4(3.1)	14.3 (2.5)	14.2 (2.6)	15.1 (2.9)
Marital Status (%)					
Single, Never Married	16.5	16.5	14.3	10.9	14.8
Married	67.0	51.9	54.5	62.7	60.8
Separated/Divorced	13.9	21.5	25.9	22.7	19.8
Widowed	0.0	2.5	3.6	3.7	2.0
Living with Partner	2.6	7.6	1.8	0.0	2.6
CAG Repeats					
M (SD)	42.1 (2.9)	43.4 (4.5)	42.8 (3.3)	44.4 (6.9)	42.8 (4.1)

Table 2

Odds Ratios for Individuals with Clinically Significant Suicidal Ideation

	OR	95% CL	*P*
Clinician-Rated Measure			
Depression	1.44	(1.21, 1.71)	<0.0001
Anger/Aggression	1.21	(1.00, 1.46)	0.05
Anxiety	1.01	(0.87, 1.18)	0.85
Gender	8.21	(0.88,76.53)	0.06
Self-Report Measure			
Depression	1.19	(1.02, 1.38)	0.04
Hispanic or Latino	9.23	(1.08,78.53)	0.04
Ethnicity not Provided	<0.001	(<0.001, >999.99)	0.98

Table 3

Proportions of Suicidal ideation for Clinician Rated and Self-Reported Assessments

	Premanifest (*n* = 194)		Stage I (*n* = 79)		Stage II (*n* = 113)		Stage III-V (*n* = 110)		All (*n* = 496)	
	PBA-s	**Survey**	**PBA-s**	**Survey**	**PBA-s**	**Survey**	**PBA-s**	**Survey**	**PBA-s**	**Survey**
Frequency (%)										
Never	90.2%	85.1%	86.1%	78.5%	88.5%	77.9%	89.1%	75.5%	88.9%	80.2%
Rarely	4.6%	7.7%	10.1%	13.9%	5.3%	13.3%	7.3%	10.0%	6.3%	10.5%
Sometimes	2.6%	3.1%	3.8%	3.8%	4.4%	7.1%	1.8%	7.3%	3.0%	5.0%
Often	2.1%	2.1%	0.0%	1.3%	0.0%	1.8%	0.9%	4.5%	1.0%	2.4%
Always	0.5%	2.1%	0.0%	2.5%	1.8%	0.0%	0.9%	2.7%	0.8%	1.8%
Clinically Significant Suicidal Ideation (% Yes)	1.5%	1.5%	2.5%	3.8%	1.8%	0.9%	3.6%	2.7%	2.4%	2.0%

Table 4

Kappa (k) coefficients comparing agreement between the clinician rated measure and self-report measure

	Frequency	Clinically Significant Suicidal Ideation
Premanifest	0.3214	0.6296
Stage I	0.3850	-0.1538
Stage II	0.1750	-0.0541
Stage III-V	0.3140	0.1818
All	0.2678	0.2031