

# Neuroticism and suicide in a general population cohort: results from the UK Biobank Project

Eyvyn M. Peters, Ann John, Rudy Bowen, Marilyn Baetz and Lloyd Balbuena

## Background

Neuroticism has often been linked to suicidal thoughts and behaviour.

## Aims

To examine whether neuroticism is associated with suicide deaths after adjusting for known risks.

## Method

UK Biobank participants ( $n = 389\,365$ ) were assessed for neuroticism as well as social, demographic and health-related variables at study entry and followed for up to 10 years. Suicide risk was modelled using Cox regression stratified by gender.

## Results

Neuroticism increased the risk of suicide in both men (hazard ratio (HR) = 1.15, 95% CI 1.09–1.22) and women (HR = 1.16, 95% CI 1.06–1.27). In a subsample who were assessed for mood disorders, neuroticism remained a significant predictor for women (HR 1.25, 95% CI 1.03–1.51) but not for men.

## Conclusions

Screening and therapeutic interventions for neuroticism may be important for early suicide prevention.

## Declaration of interest

None.

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## Personality traits and suicide

Suicide is the culmination of a complex interaction of social, psychological and biological factors. As psychological variables vary from person to person, it is important to identify personality traits that predispose individuals to suicide, acknowledging that personality traits might have biological origins.<sup>1</sup> Neuroticism, broadly defined as the tendency to experience negative emotions in response to stress,<sup>2</sup> has been linked to the full spectrum of suicidal behaviours, although most research has focused on suicidal ideation and non-lethal attempts.<sup>3–13</sup> One study found that knowledgeable informants rated 52 individuals who died by suicide as more neurotic than matched controls.<sup>9</sup> Research has also documented longitudinal associations between suicide and traits similar to neuroticism, such as anxiety, affective instability, self-blame, impulsivity and anger/aggression.<sup>5</sup> To our knowledge, no study has examined the prospective association of neuroticism *per se* and suicide deaths using longitudinal data.

## Neuroticism and social factors

Neuroticism is a distal and non-specific risk factor for suicide – it appears to be more strongly associated with depression and other mental disorders than suicide *per se*.<sup>6,12</sup> Neuroticism is thought to be the common dimension of personality underlying mood and anxiety disorders,<sup>12</sup> both of which independently and additively increase suicide risk.<sup>14</sup> Neuroticism is also closely associated with borderline personality disorder,<sup>15,16</sup> another strong risk factor for suicide.<sup>17</sup> Borderline personality disorder may represent an extreme form of neuroticism,<sup>18</sup> possibly with shared genetic underpinnings, although other personality domains such as agreeableness may be needed to fully describe borderline personality disorder.<sup>16</sup> Neurotic individuals tend to use alcohol,<sup>19</sup> cigarettes<sup>20</sup> and illicit drugs<sup>21</sup> as coping mechanisms, all of which are associated with self-injury and suicide.<sup>22–26</sup> It is possible that using these substances directly makes

users more vulnerable to suicide.<sup>27</sup> Neuroticism has also been linked to poor social and economic outcomes,<sup>28–31</sup> divorce,<sup>32–35</sup> unemployment,<sup>36,37</sup> inadequate social support,<sup>38</sup> area-level deprivation<sup>39,40</sup> and psychiatric disorders,<sup>41,42</sup> all of which are associated with higher suicide risk. Mood instability, defined as rapid and intense mood swings,<sup>43</sup> appears to be a core component of neuroticism that is associated with psychological distress,<sup>44</sup> depression,<sup>45–47</sup> substance use,<sup>48,49</sup> impulsivity<sup>50,51</sup> and suicidality.<sup>52–54</sup>

Our primary objective was to test the hypothesis that neuroticism is a risk factor for suicide. Our secondary objective was to determine whether neuroticism is associated with suicide after adjusting for potential confounders, including mood disorders as well as lifestyle and socioeconomic variables.

## Method

### Sample

This study used data from 389 365 adults aged 40 to 69 years (mean age = 56.9, s.d. = 8.07; % female = 53.8) who participated in the UK Biobank Project (<http://www.ukbiobank.ac.uk>).<sup>55</sup> This particular age group was selected because these people are at proximal risk for developing ageing-related diseases whose risk and preventive factors could be examined.<sup>55</sup> The selection of participants was based on living within 10 miles of assessment centres located in areas of high population density.<sup>56</sup> Potential participants were identified via National Health Service (NHS) registries and contacted by mail. All participants provided written informed consent. Baseline assessments involving questionnaires, physical measurements and collection of biological samples took place at 22 assessment centres across the UK between 2006 and 2010. At baseline assessment, participants granted consent to link their past and future general practice and hospital records, entries in various disease registries, and cause of death should this occur. Ethical approval

for the UK Biobank was granted by the NHS National Research Ethics Service. The UK Biobank approved the current study (application 18046) and granted access to their database. This project also received institutional ethical approval and was conducted in accordance with the Declaration of Helsinki.

## Measures

### Neuroticism

Neuroticism was measured with the 12-item neuroticism subscale from the short form of the revised Eysenck Personality Questionnaire (EPQ-N).<sup>57</sup> From his earliest studies, Eysenck was interested in traits that patients shared and that military commanders could identify in young army recruits unsuitable for service. He later used the term 'emotional instability' to refer to the neurotic characteristics that were applied to young soldiers and people who did not do well psychologically.<sup>58</sup> In the present study, the questionnaire was administered during computerised touchscreen interviews as part of the Biobank baseline assessments. Responses to each item are 'Yes' (coded as 1) or 'No' (coded as 0), which are summed to yield a total score ranging from 0 to 12.<sup>53</sup> This subscale has demonstrated good internal consistency and convergent validity.<sup>57</sup> Cronbach's alpha of the EPQ-N for the present study was 0.84.

### Suicide

Suicide was established through the UK Biobank's linkage with mortality data from the Office of National Statistics.<sup>55</sup> Mortality data are ICD-10 coded for underlying cause based on the death certificates issued by medical practitioners or following a coroner's conclusion of cause of death. We followed the conventional definition of suicide as those where the coroner ruled a death as suicide or having undetermined intent.<sup>59,60</sup> To be specific, suicide was defined as a death with any of the following ICD-10 codes: X60–84, Y10–34 (excluding Y33.9) and Y87.0 (excluding Y87.2). The follow-up period in which suicide deaths were tracked lasted until 2015 for participants in Scotland and 2016 for participants in England and Wales.

### Covariates

We chose to include a number of sociodemographic and lifestyle variables likely to be associated with both neuroticism and suicide: unemployment,<sup>28,32,37,41</sup> community economic deprivation,<sup>30,32,37,39</sup> social support,<sup>31,38</sup> living with a spouse or partner,<sup>32,35,42</sup> living with a child,<sup>32,35,42</sup> cigarette smoking,<sup>20,23,24,26</sup> alcohol use,<sup>19,22,25</sup> and stressful life events in the past 2 years, including getting divorced,<sup>32,33,35</sup> the death of a spouse or partner<sup>61,62</sup> and financial difficulties.<sup>30,32,37,63</sup> Categorical covariates were coded such that the hypothesised risk or protective factor for suicide was coded as 1 (present) and 0 (absent). We had two continuous covariates: age and the Townsend deprivation index. The Townsend index is a small-area measure of economic deprivation that takes into account the prevalence of unemployment, non-ownership of a car, non-ownership of a home and households with more than one person per room.<sup>64</sup>

Lifetime diagnoses for probable mental disorders were available for the subset of 172 000 participants recruited from 2008 to 2010.<sup>65</sup> Major depression was assessed following the items in the Patient Health Questionnaire,<sup>66</sup> whereas the algorithm for diagnosing bipolar disorder followed the Structured Clinical Interview for DSM-IV Axis I Disorders.<sup>67</sup> Following previous work, we used a composite variable with categories ordered by increasing severity: no mood disorder, single major depression episode, recurrent major depression with moderate severity, recurrent major depression with high severity, bipolar disorder type 2 and bipolar disorder

type 1.<sup>65</sup> These categories were formed by assigning each participant to the most severe category for which criteria were met.<sup>65</sup> Treating these DSM diagnoses as a single ordinal variable is consistent with a dimensional concept of mood disorders. Although the DSM follows a categorical approach, dimensional concepts of mood disorders (the bipolar spectrum)<sup>68</sup> and personality disorders (as extremes of normal personality)<sup>69</sup> are gaining acceptance. This alternative understanding – combined with empirical evidence that suicide risk increases from single-episode unipolar depression to recurrent unipolar depression to bipolar depression<sup>70,71</sup> – motivated our decision to use depression as an ordinal variable.

## Analysis

Cox regression modelling was used to assess the prognostic value of candidate risk factors for suicide. The outcome variable was the dichotomous variable suicide or undetermined death (coded as 1) and all other deaths and alive as censored (coded as 0). Our time variable was the number of months between the date of baseline assessment and the date of suicide death or censorship.

Our modelling was done in four steps. First, we created a series of Cox regression models in which a single explanatory variable was entered. Second, all of the covariates (excluding neuroticism) were entered as explanatory variables into a multiple Cox regression model, hereafter referred to as the nested model. Third, neuroticism scores were added to the nested model to create the full model. Finally, we conducted a series of analyses to examine any interactions between neuroticism and the covariates. In all steps, separate regression models for males and females were created. We calculated Harrell's concordance index (C-index) for the univariate, nested and full Cox regression models. The C-index is interpreted as the area under the receiver operating characteristic curve, with 0.5 indicating random guessing and 1.0 indicating perfect discrimination. The advantage of using the C-index for prognostic value is that models are compared on the basis of their ability to distinguish people who committed suicide from those that did not.<sup>72</sup> The proportional hazards assumption for each model was tested by assessing the linearity of Schoenfeld residuals.<sup>73</sup>

In an attempt to differentiate the role of neuroticism from a mood disorder, we created Cox models that included only neuroticism and lifetime mood disorder status. As mentioned earlier, mood disorders were assessed only for later recruits into the UK Biobank Project. Because of drastically reduced suicide deaths among these recruits, the analytic models did not include the rest of the covariates. We likewise calculated the C-index for these Cox models and tested the proportional hazards assumption.

**Table 1** Characteristics of participants dying of suicide versus the rest of the sample, UK Biobank Data

Variable	Mean or percentage (s.e.)	
	Suicide (n = 154)	No suicide (n = 389 211)
Age at study entry, years	55.3 (0.67)	56.9 (0.01)
Female (%)	27.3 (0.04)	53.8 (0.0008)
Neuroticism score	5.90 (0.30)	4.13 (0.005)
Living with a spouse or partner (%)	51.9 (0.04)	73.6 (0.0007)
Living with a child (%)	26.6 (0.04)	35.4 (0.0008)
Able to confide daily in someone close (%)	43.5 (0.04)	54.7 (0.0008)
Unemployed (%)	16.2 (0.03)	7.87 (0.0004)
Community economic deprivation score	-0.06 (0.29)	-1.41 (0.005)
Death of a spouse in the past 2 years (%)	2.60 (0.01)	1.58 (0.0002)
Divorce in the past 2 years (%)	1.30 (0.009)	3.27 (0.0003)
Financial trouble in the past 2 years (%)	15.6 (0.03)	12.2 (0.0005)
Smoking cigarettes daily or more (%)	18.2 (0.03)	7.64 (0.0004)
Drinking alcohol daily or more (%)	26.0 (0.04)	21.0 (0.0007)

**Table 2** Univariate Cox regression models of suicide, UK Biobank data

Variable	Males			Females		
	HR (95% CI)	s.e.	Z	HR (95% CI)	s.e.	Z
Neuroticism	1.19 (1.13–1.26)	0.03	6.75***	1.17 (1.07–1.28)	0.05	3.49***
Age	0.98 (0.96–1.00)	0.01	-2.05*	0.98 (0.94–1.01)	0.02	-1.27
Living with a spouse	0.26 (0.18–0.38)	0.05	-7.13***	0.70 (0.37–1.30)	0.22	-1.13
Living with a child	0.67 (0.44–1.01)	0.14	-1.90	0.64 (0.32–1.26)	0.22	-1.29
Able to confide daily	0.57 (0.39–0.83)	0.11	-2.96**	0.83 (0.45–1.52)	0.26	-0.61
Unemployed	3.09 (1.90–5.00)	0.76	4.57***	1.39 (0.55–3.55)	0.66	0.70
Economic deprivation	1.16 (1.10–1.22)	0.30	5.61***	1.06 (0.97–1.17)	0.05	1.28
Death of a spouse	2.48 (0.79–7.81)	1.45	1.55	1.24 (0.17–9.01)	1.25	0.21
Divorce	0.56 (0.14–2.26)	0.40	-0.81	–	–	–
Financial difficulty	1.29 (0.77–2.16)	0.34	0.97	1.49 (0.66–3.37)	0.62	0.97
Smoking	2.91 (1.85–4.57)	0.67	4.64***	1.44 (0.52–4.05)	0.76	0.70
Alcohol use	1.18 (0.79–1.78)	0.25	0.82	1.01 (0.45–2.28)	0.42	0.03

\*  $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

## Results

During the follow-up period, more than twice as many men as women died by suicide as women (112 v. 42). The difference between proportions for men (0.062%) and women (0.020%) was statistically significant ( $z = 6.61$ ,  $P < 0.001$ ). Table 1 presents descriptive statistics for participants who died by suicide compared with the rest of the cohort.

### Univariate models

Among men, high neuroticism, younger age, unemployment, living in an economically deprived community and daily smoking were associated with suicide. On the other hand, living with a spouse and having someone to confide in daily were inversely related to suicide. In all univariate models for men, neuroticism best discriminated suicides from the rest of the cohort (C-index = 0.66, 95% CI 0.60–0.72). Among women, only high neuroticism scores were associated with suicide (C-index = 0.63, 95% CI 0.54–0.72). None of the 42 women who died by suicide had been divorced. As such, a hazard ratio (HR) could not be estimated and divorce was dropped from all subsequent models for women. Univariate results are presented in Table 2.

### Bivariate models

#### Interaction effects

Among men, we found a significant interaction between neuroticism and daily confiding (HR = 1.13, s.e. = 0.06,  $P = 0.025$ ) such that at lower levels of neuroticism, daily confiding decreased

suicide risk, whereas at higher levels of neuroticism, daily confiding increased suicide risk. None of the other covariates had significant interactions with neuroticism. We found no significant interactions with neuroticism among females.

#### Post hoc models

Given the pattern of univariate results for men, we examined two bivariate models *post hoc*. To determine whether daily confiding was independent of living with a spouse, we performed a Cox regression that included both variables. This model showed that living with a spouse remained significant (HR = 0.28, s.e. = 0.06,  $P < 0.001$ ), whereas daily confiding did not (HR = 0.83, s.e. = 0.17,  $P = 0.36$ ). To determine whether living in an economically deprived area was independent of unemployment, we entered both variables in a Cox regression model simultaneously. Both economic deprivation (HR = 1.13, s.e. = 0.03,  $P < 0.001$ ) and unemployment (HR = 2.13, s.e. = 0.56,  $P = 0.004$ ) remained significant.

### Multiple variable models

#### Males

In the nested model, the effects of economic deprivation, living with a spouse and smoking were statistically significant; unemployment was marginally significant ( $P = 0.08$ ). When neuroticism was added, living in a deprived area, living with a spouse, smoking and neuroticism significantly explained suicide. The C-index for the nested model was 0.72 (95% CI 0.66–0.78), which increased to 0.75 (95% CI 0.69–0.81) with the addition of neuroticism in the full model (Table 3).

**Table 3** Multiple variable Cox regression models of suicide (males), UK Biobank data

Variable	Nested model			Full model		
	HR (95% CI)	s.e.	Z	HR (95% CI)	s.e.	Z
Neuroticism	–	–	–	1.15 (1.09–1.22)	0.03	5.21***
Age	0.98 (0.96–1.00)	0.01	-1.56	0.99 (0.96–1.01)	0.01	-1.08
Living with a spouse	0.35 (0.22–0.56)	0.08	-4.39***	0.36 (0.23–0.58)	0.09	-4.29***
Living with a child	1.00 (0.61–1.62)	0.24	0.00	1.04 (0.64–1.69)	0.26	0.16
Able to confide daily	0.84 (0.56–1.26)	0.17	-0.84	0.99 (0.66–1.48)	0.95	-0.06
Unemployed	1.61 (0.94–2.76)	0.44	1.75	1.33 (0.21–2.18)	0.37	1.04
Economic deprivation	1.07 (1.01–1.14)	0.03	2.40*	1.07 (1.01–1.13)	0.03	2.21*
Death of a spouse	1.29 (0.40–4.14)	0.77	0.42	1.22 (0.38–3.92)	0.73	0.33
Divorce	0.32 (0.08–1.31)	0.22	-1.59	0.30 (0.07–1.22)	0.22	-1.68
Financial trouble	0.74 (0.43–1.29)	0.23	-0.72	0.64 (0.37–1.11)	0.19	-1.59
Smoking	1.84 (1.14–2.97)	0.45	2.48*	1.79 (1.11–2.90)	0.44	2.38*
Alcohol use	1.32 (0.87–1.99)	0.28	1.31	1.30 (0.86–1.96)	0.27	1.25

\*  $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

**Table 4** Multiple variable Cox regression models of suicide (females), UK Biobank Data

Variable	Nested model			Full model		
	HR (95% CI)	s.e.	Z	HR (95% CI)	s.e.	Z
Neuroticism	–	–	–	1.16 (1.06–1.27)	0.05	3.15**
Age	0.96 (0.92–1.00)	0.20	–1.83	0.97 (0.93–1.01)	0.02	–1.61
Living with a spouse	0.88 (0.44–1.75)	0.31	–0.36	0.85 (0.43–1.69)	0.30	–0.47
Living with a child	0.47 (0.22–1.01)	0.18	–1.93	0.49 (0.23–1.05)	0.19	–1.84
Able to confide daily	0.87 (0.47–1.62)	0.28	–0.44	1.04 (0.55–1.96)	0.34	0.13
Unemployed	1.22 (0.47–3.19)	0.60	0.41	1.04 (0.40–2.74)	0.51	0.09
Economic deprivation	1.03 (0.94–1.14)	0.05	0.65	1.03 (0.93–1.14)	0.05	0.54
Death of a spouse	1.21 (0.16–9.17)	1.25	0.18	1.14 (0.15–8.63)	1.18	0.13
Divorce	–	–	–	–	–	–
Financial trouble	1.24 (0.53–2.93)	0.54	0.49	1.04 (0.44–2.47)	0.46	0.09
Smoking	1.14 (0.40–3.31)	0.62	0.25	1.07 (0.37–3.10)	0.58	0.13
Alcohol use	1.06 (0.40–3.30)	0.44	0.14	1.06 (0.47–2.39)	0.44	0.13

\*  $P < 0.05$ , \*\*  $P < 0.01$ , \*\*\*  $P < 0.001$ .

## Females

In the nested model, having a child in the home became marginally significant ( $P = 0.05$ ). In the full model, this association became nonsignificant, whereas neuroticism remained significant. The C-index index for the nested model was 0.65 (95% CI 0.56–0.74), increasing to 0.67 (95% CI 0.60–0.74) with the addition of neuroticism in the full model (Table 4).

## Models with both neuroticism and mood disorder diagnoses entered together

In the subset of participants assessed for mental disorders, there were only 14 suicide deaths (0.03%) among males and 12 among females (0.02%). Accordingly, we performed a Wald test to determine whether it was justified to treat clinical diagnosis as a continuous variable. Doing so would avoid having imprecise estimates owing to low suicide numbers in some categories. The Wald test showed that having five ordered categories did not result in a better statistical fit ( $\chi^2 = 2.68$ , d.f. = 4,  $P = 0.44$ ); therefore, using the continuous variable was justifiable.

Among males, the association of neuroticism with suicide became nonsignificant when mood disorder status was entered. The opposite pattern was found among females – neuroticism remained significantly associated with suicide, although mood disorder status was not (Table 5). The C-index for the model was 0.71 (95% CI 0.56–0.86) for males and 0.81 (95% CI 0.64–0.98) for females. Note that these models are not comparable to the earlier ones because of sampling differences.

## Proportionality of hazards testing

We tested the proportionality assumption for each variable in all regression models by plotting residuals against time. We also performed global tests for the multiple regression models. A violation of proportionality indicates that the hazard associated with a given covariate is not constant with time. We found no violations of proportionality except for daily smoking in the full model for

women ( $\chi^2 = 4.62$ , d.f. = 1,  $P = 0.03$ ). On further examination, we found that this resulted from a single outlier. Removing this observation did not substantially change the coefficient estimates.

## Discussion

We found that neuroticism was a risk factor for suicide among men and women in a large sample of UK residents followed for up to 10 years. To our knowledge, we are the first to report a link between neuroticism and suicide deaths, as opposed to attempts or ideation. This is consistent with previous research reporting associations of neuroticism with suicidal ideation and attempts.<sup>3–8,10,11,13</sup> In addition, we found that among men, living with a spouse was associated with lower suicide risk, whereas daily smoking and living in an economically deprived area increased suicide risk.

Among women, but not men, the association of neuroticism with suicide remained significant after accounting for mood disorder diagnoses. This is consistent with a cross-sectional study reporting an association of neuroticism with increased suicidality (i.e. ideation, past attempts and intent), in women only, which controlled for depression.<sup>4</sup> Neuroticism may represent an intermediate phenotype that is on the same genetic or developmental pathway as depression and suicide.<sup>74–76</sup> A recent meta-analysis that included data from the UK Biobank found multiple candidate genes for neuroticism,<sup>77</sup> one of which also appears to differentiate people with depression who die by suicide versus other causes.<sup>78</sup> Further research in this area is needed, as the genetic basis of neuroticism is not completely understood,<sup>79,80</sup> nor is the relationship between neuroticism and depression.<sup>12,79–81</sup>

Mental illness is thought to be a stronger risk factor for suicide among women compared with men.<sup>50,81,82</sup> Our results suggest that neuroticism may be a more important predictor of suicide in women than lifetime mood disorder diagnosis. It is important to point out, however, that the participants were not necessarily suffering from a mood disorder at the time of assessment. Interestingly, our results suggest the opposite pattern for men, in whom

**Table 5** Multiple variable Cox regression models with neuroticism and mood disorder diagnoses as explanatory variables of suicide, UK Biobank 2008–2010 participants

Variable	Males			Females		
	HR (95% CI)	s.e.	Z	HR (95% CI)	s.e.	Z
Neuroticism	1.08 (0.92–1.27)	0.09	0.95	1.25 (1.03–1.51)	0.12	2.31*
Mood disorder <sup>a</sup>	1.61 (1.12–2.34)	0.30	2.54*	1.48 (0.97–2.27)	0.32	1.83

<sup>a</sup> Ordinal variable treated as continuous with levels: 0 = no mood disorder, 1 = single major depression episode, 2 = recurrent major depression with moderate severity, 3 = recurrent major depression with high severity, 4 = bipolar disorder type 2, and 5 = bipolar disorder type 1.

\*  $P < 0.05$ .



neuroticism may be less relevant to suicide after taking into consideration the presence of a lifetime mood disorder diagnosis. However, the effect sizes were small when both mood disorders and neuroticism were entered simultaneously. It is tempting to posit depression as a mediating variable in the relationship between neuroticism and suicide for men, although our data did not allow us to identify a temporal relationship between neuroticism and depression. There is overlap between the symptoms of depression and the content of neuroticism questionnaires,<sup>12,79–81</sup> but a diagnosis of depression includes symptoms related to sleep, appetite and energy, which could impair overall function more than the dysphoria experienced by neurotic individuals. Socioeconomic factors are thought to be more strongly associated with suicide in men,<sup>33,34,42,63,82,83</sup> this may explain why neuroticism became nonsignificant when mood disorders were added to the model. This gender difference needs to be replicated in other larger studies, and our interpretations should currently be considered only speculative.

The interaction between neuroticism and daily confiding among men is counterintuitive, and would be best considered tentative until replicated. It is also difficult to know the clinical significance of a small hazard ratio based on a somewhat vague social support variable – particularly in contrast to, for example, the smoking and neuroticism variables, which are more quantifiable. A possible, albeit speculative, interpretation is that neurotic individuals are more likely to become dependent and excessively seek reassurance, ultimately straining relationships and leading to rejection.<sup>84–89</sup> Neurotic individuals also tend to negatively interpret social interactions<sup>90,91</sup> and may lash out angrily in response to perceived criticism and rejection.<sup>84,89</sup> Neurotic men might also consider suicide as an altruistic act to rid their partners of the burden of themselves. These maladaptive patterns of social interaction could explain how more social contact could exacerbate emotional distress, isolation and, ultimately, suicide risk.

Men are thought to be at greater risk for suicide than women if they are unmarried or become divorced,<sup>33,34,42,82,83</sup> consume alcohol,<sup>82,83</sup> or experience unemployment and economic hardships.<sup>63,82,83</sup> Our results are partially consistent with these findings, as unemployment, community economic deprivation, and living with a spouse or partner were all associated with suicide risk in men but not women. In the multiple regression models, the association of unemployment with suicide became nonsignificant, whereas that of economic deprivation remained significant. It is possible that unemployment, as assessed at study entry, changed in the succeeding months, whereas economic conditions at an area level were more enduring and may be a better index of economic and health inequality. Our alcohol use variable was not associated with suicide in either gender, possibly because it only assessed the number of days per week in which participants consumed alcohol, which may not adequately represent disordered patterns of alcohol use that increase suicide risk. Recent divorce or the death of a spouse was also not associated with suicide in men, possibly because the UK Biobank participants were aged 40 to 69, whereas previous studies have suggested that separation in early adulthood<sup>61,62</sup> is what increases suicide risk.

Cigarette smoking was associated with suicide in men but not women. By comparison, two meta-analyses found increased rates of suicide in smokers of both genders,<sup>23,24</sup> whereas an older study found that only male smokers were more likely to have previously attempted suicide.<sup>26</sup> It is likely that smoking is simply a marker for underlying psychopathology, part of an intercorrelated pattern of high-risk behaviours related to suicide, but it is also possible that the toxins contained in cigarettes may biologically predispose people toward suicide.<sup>27</sup> This topic requires further research with regard to parameters such as the number of cigarettes smoked and the effect of other tobacco products.

The main strength of this study was the linkage of deaths from suicide with a large cohort of participants while controlling for other relevant sociodemographic risk factors. The main limitation was that clinical psychiatric diagnoses were available for a smaller subset. With a much lower number of suicide deaths in this subset, we could not examine the effects of other variables together with both neuroticism and depression. Another limitation was the restricted age range of the participants. For this reason, our findings are most relevant to middle- and older-aged individuals. Future research will need to replicate our results with samples from other age groups to determine generalisability across the lifespan. We were also unable to control for other aspects of personality. We do not believe that that this would have a huge influence on our results, because neuroticism appears to be the personality trait most strongly associated with suicidality.<sup>5,13</sup> Neuroticism may interact with other personality risk factors for suicide (e.g. impulsivity), although there is some evidence against this hypothesis.<sup>13</sup>

Neuroticism has important public health implications.<sup>92,93</sup> It is relatively easy to administer self-rated neuroticism scales, and our results suggest that this could potentially be incorporated into suicide prevention strategies for both men and women. Given the stability of neuroticism compared with depression,<sup>12</sup> neuroticism may be a more accurate marker of chronic rather than acute suicide risk. This could be useful, for example, in the assessment of longer-term suicide risk among psychiatric patients whose symptoms have otherwise remitted. Our results suggest that this may be particularly useful for female patients with a history of a mood disorder. Interventions targeting neuroticism may be important for early suicide prevention.

**Evyn M. Peters**, MD, Department of Psychiatry, University of Saskatchewan, Saskatoon, SK, Canada; **Ann John**, MD FFPH, Swansea University Medical School and the Farr Institute, Swansea, Wales, UK; **Rudy Bowen**, MD CM FRCPC, **Marilyn Baetz**, MD FRCPC, **Lloyd Balbuena**, PhD, Department of Psychiatry, University of Saskatchewan, Saskatoon, SK, Canada

**Correspondence** Lloyd Balbuena, Department of Psychiatry, University of Saskatchewan, Saskatoon, SK S7N0W8, Canada. E-mail: [lloyd.balbuena@gmail.com](mailto:lloyd.balbuena@gmail.com)

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