

# The prediction of thoughts of death or self-harm in a population-based sample of female twins

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## ABSTRACT

**Background.** Although suicide is a leading cause of death, few studies have attempted to predict suicidal ideation prospectively using epidemiological samples or multivariate methods.

**Method.** Discrete-time event history analysis was used to model the onset of thoughts of death or self-harm (TD/SH) in a population-based sample of female twins ( $N=2164$ ) using variables from the demographic, psychopathological, childhood adversity, personality and life event domains. Univariate, multivariate-within domain and multivariate-across domain regression analyses were performed.

**Results.** Most variables predicted TD/SH in the univariate analyses. However, the only variables to predict TD/SH independently were obsessive symptoms, childhood sexual abuse, rural residence, unemployment, older age, lifetime history of cocaine misuse and low levels of education, personal religious devotion and altruism, as well as divorce/separation, loss of confidant, assault, job loss and financial problems in the previous month. This final model explained 16% of the variance in TD/SH. Lifetime histories of major depression, panic disorder and alcohol misuse had no significant independent effect.

**Conclusions.** Many variables, from all five domains of risk factors, are associated with the risk of TD/SH, but many of these effects may be mediated by other risk factors. Proximal life events and psychopathology may have more independent effects than other domains. The overall ability of these risk factors to predict TD/SH is modest. We cannot rule out that differences between these analyses and previous reports were due to our use of TD/SH as the dependent variable instead of thoughts of committing suicide *per se*.

## INTRODUCTION

Suicide is one of the leading causes of death worldwide, especially in individuals under the age of 30 (National Center of Health Statistics, 1999). Determining risk factors for suicidal behaviour and developing appropriate interventions is therefore a public health priority. Multiple risk factors for attempted or completed suicide have been reported. These comprise

demographic variables, such as age, sex and marital status (Weissman, 1974; Morgan *et al.* 1975; Sainsbury, 1986; Kessler *et al.* 1999); psychiatric diagnoses, such as major depression, alcohol and drug abuse or dependence and panic disorder (Morgan *et al.* 1975; Black *et al.* 1985a; Rich *et al.* 1986; Johnson *et al.* 1990; Henriksson *et al.* 1993; Beautrais *et al.* 1996; Inskip *et al.* 1998; Kessler *et al.* 1999; Mann *et al.* 1999); temperamental and personality factors (Nordstrom *et al.* 1995; Maser *et al.* 2002); childhood adversity (de Wilde *et al.* 1992; Dinwiddie *et al.* 2000; Molnar *et al.* 2001); and

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proximal stressful life events (SLEs) (Paykel *et al.* 1975; Beautrais *et al.* 1997; Fergusson *et al.* 2000). Although several of these variables would be expected to be correlated with, or to mediate others, only a few studies have used multivariate approaches to examine independent effects across multiple risk domains.

Studies of suicidal behaviour have frequently been based on patient samples. This may represent a more severely ill group, as well as those more likely to seek help and/or come to the attention of mental health providers, especially when comprised of in-patients. However, many patients with suicidal ideation (SI) (Hintikka *et al.* 2001), or who attempt suicide (Beautrais *et al.* 1998a; Barnes *et al.* 2001) never come to clinical attention. Moreover, some suicide victims may not have primary psychiatric diagnoses (Apter *et al.* 1993). Another limitation of clinical studies is that the presence of symptoms of depression or other Axis I disorders may be associated with state-dependent changes in variables from other domains, such as personality traits. For example, neuroticism is increased during depressive episodes, sometimes called the 'state effect' (Hirschfeld *et al.* 1983; Kendler *et al.* 1993). This may be confounded with true trait effects in patients experiencing active symptoms, and thus make it more difficult to infer the direction of causation between predictor variables and suicidality.

These issues underscore the importance of studying epidemiological samples. In recent years, epidemiological studies of suicidal behaviour have benefited from the 'psychological autopsy' method, in which cases of completed suicide are first ascertained and diagnostic, demographic and historical data are obtained post-mortem (Holding & Barraclough, 1975; Rich *et al.* 1988; Runeson, 1989; Apter *et al.* 1991; Marttunen *et al.* 1991; Henriksson *et al.* 1993; Shaffer *et al.* 1996; Appleby *et al.* 1999; Houston *et al.* 2001). Another useful approach has been the record linkage study, in which data from several sources, such as death certificates and patient registries, are linked together (Black *et al.* 1985b; Lewis & Sloggett, 1998; Lawrence *et al.* 2001). Both of these approaches have two important limitations. The first is that they are performed *post hoc* and therefore can be neither prospective nor predictive. Another, more serious limitation is their inability to employ

structured interview algorithms incorporating operationalized diagnostic criteria, or other instruments based on self-report.

Furthermore, it would be advantageous from the standpoint of suicide prevention to intervene at early stages in the causal pathway to the occurrence of suicidal acts, as both planned and unplanned attempts may rapidly follow SI (Kessler *et al.* 1999). The use of either clinical or retrospective epidemiological samples may therefore miss the opportunity to uncover meaningful predictors of SI, which has been addressed in much fewer published studies (Weissman *et al.* 1989, 1999; Cox *et al.* 1994; Statham *et al.* 1998; Vilhjalmsson *et al.* 1998; Kessler *et al.* 1999; Kuo *et al.* 2001; Renberg, 2001; Hintikka *et al.* 2001). As there is currently no consensus in the field these studies have used several different instruments to assess SI, which have used different definitions. They have included single items asking about lifetime history of thinking about 'committing suicide' (Kessler *et al.* 1999; Weissman *et al.* 1999; Kuo *et al.* 2001) to ordinal measures of the intensity of suicidal thoughts (Statham *et al.* 1998; Vilhjalmsson *et al.* 1998; Hintikka *et al.* 2001; Renberg, 2001), which may include thinking that life is not worth living (Hintikka *et al.* 2001; Renberg, 2001).

In this report, we examine the impact of variables in the demographic, psychopathological, personality, childhood adversity and life event domains on thoughts of death or self-harm (TD/SH). We include thoughts of death in this definition, as does criterion A9 of the DSM-III-R and DSM-IV criteria for a major depressive episode, which hold that this phenomenon is equivalent to SI. Furthermore, 'ideas or acts of self-harm' are included in ICD-10 criteria for depressive episode, along with 'ideas or acts of committing suicide'. As such, TD/SH may be very close to the way in which SI is routinely defined by clinicians worldwide although it is not strictly equivalent to SI. We attempted to prevent this definition from being too broad by specifically excluding from it the fear of dying, philosophical or existential preoccupations with death and thoughts of the death of others. Important features of this study are epidemiological ascertainment, the use of structured diagnostic algorithms, multivariate analyses and a prospective design for a majority of the variables examined.

## METHOD

### Subjects

In this report, we included female twins ascertained through the population-based Virginia Twin Registry – formed from a systematic review of all birth certificates in the Commonwealth of Virginia – covering the birth years 1934–1974. Twin pairs became eligible to participate if both members had previously responded to a mailed questionnaire, the response rate to which was 64%. Eighty eight per cent of our sample was first interviewed face-to-face in 1988–1989, an average of 16 months after their first assessment. In this report, we utilize all four waves of interviews, which were completed for 2164 (88%), 1906, (78%) and 1942 (79%), respectively, of the 2440 women to whom the questionnaires were originally sent. After a full explanation of the research protocol, signed informed consent was obtained prior to all face-to-face interviews and verbal assent prior to all telephone interviews. The mean ages of the sample at the first and fourth assessment waves were 29.3 (s.d. = 7.7) and 36.3 (s.d. = 8.3) years, respectively. All assessments were separated by at least 12 months. Zygosity was determined on the basis of a discriminant function of questionnaire responses about physical similarity and blood type developed in this sample (Kendler *et al.* 1992). We will herein refer to the first four interview waves of these female–female twin pairs as FF1 to FF4, respectively.

When interviewing the twins at time 1, we obtained the names and addresses of living biological parents, thus identifying 1698 parents of the 1033 pairs of twins who had both been assessed. Of these, 1472 (90.2%) were interviewed and 160 (9.8%) refused. Of those interviewed, 855 were mothers and 617 were fathers. The majority of these interviews (92.0%) were performed face-to-face.

### Measures

The data used for this study spanned all four waves of assessment. TD/SH in the last year was assessed during each interview wave using a single item. All twins were asked: ‘In the last year, have you had a time lasting at least 5 days, when you thought a lot about death or about harming yourself?’ It was explicitly stated that thoughts of death had to be about the subject’s

own death. The month of onset and offset of that episode were recorded. We implemented a prospective design, in which independent variables were collected at FF1 unless otherwise noted, while TD/SH was assessed at the FF2–FF4 interviews. Demographic and self-report data included years of education, number of siblings, income, marital status, rural *v.* urban residential setting (i.e. size of town or city) and religious affiliation. In this domain, we also included two factors of religiosity – personal devotion and personal conservatism – as described previously (Kendler *et al.* 1997). In addition, religious institutions were assigned ratings according to their degree of fundamentalism. Affiliations were ranked as follows, in order of decreasing conservatism: (1) fundamentalist Protestant, (2) Baptist, (3) Catholic, (4) mainline Protestant, (5) other or unaffiliated. Personality and attitudinal variables were mostly assessed at the first wave, and included neuroticism and extraversion (Eysenck & Eysenck, 1975), altruism and empathy (Casper *et al.* 1980), interpersonal dependency (Hirschfeld *et al.* 1977), locus of control (Peterson *et al.* 1982), mastery (Maddi *et al.* 1979), dispositional optimism (Scheier & Carver, 1985), and the Rosenberg Self-Esteem Scale (Rosenberg, 1965). Novelty-seeking (Cloninger *et al.* 1991) was assessed at FF4.

We examined several variables that we include in the domain of ‘childhood adversity’. First, all subjects were administered the 16-item Parental Bonding Instrument (PBI) (Parker, 1990), reporting on the parenting they had received. As previously described, three factors were derived from this scale: warmth (W), protectiveness (P) and authoritarianism (A) (Kendler, 1996). Childhood sexual abuse was assessed by mailed questionnaire at FF3 using items developed by Martin *et al.* (1993). We include use a narrow definition, in which subjects were positive if there was the occurrence of sexual intercourse, in all analyses herein. Parental loss was defined as either death or separation from a parent prior to age 17. Parental discipline was assessed retrospectively using an adapted and expanded version of the discipline items from the Home Environment Interview (Holmes & Robins, 1988). Twins were asked to rate their mother and father separately. As outlined previously (Wade & Kendler, 2000), factor analysis

identified two meaningful factors, which were called limit-setting (taking away privileges, sending the child to her room and grounding), and physical discipline (scolding or yelling, spanking, slapping, and hitting with a brush, belt, or stick).

As detailed elsewhere (Kendler *et al.* 1995, 1998), in interview sections before those that covered diagnostic criteria for psychiatric illness, we assessed the occurrence over the year prior to interview, to the nearest month, of 11 'personal' SLEs (i.e. events that occurred primarily to the informant). These comprised assault, divorce/separation, major financial problems, serious housing problems, serious illness or injury, job loss, legal problems, loss of confidant, serious marital problems, robbery and serious difficulties at work. We also assessed four classes of 'network' SLEs (i.e. events that occurred primarily to, or in interaction with, an individual in the respondent's social network). These event classes consisted of: (1) serious trouble getting along with an individual in the network; (2) a serious personal crisis of someone in the network; (3) death of an individual in the network; and (4) serious illness of someone in the network. We defined proximal network as the respondent's spouse, child, parent, co-twin, and other non-twin siblings, while distal network comprised all other relationships. The items assessing these events were similar but not always identical over waves. In addition, we lacked an assessment of housing problems at FF1 and network crises at FF2. In wave FF1, we assessed the inter-rater reliability for the occurrence and dating of our SLE categories and found them to be in the good to excellent range, with kappas equalling 0.93 and 0.82, respectively ( $N=53$ ) (Kendler *et al.* 1995). Subjects were coded as positive for these events if they endorsed their occurrence in the last year at any of the four waves.

Lifetime history of the following psychiatric diagnoses was assessed with an adapted version of the Structured Clinical Interview for DSM-III-R (Spitzer *et al.* 1987) at FF1: major depressive disorder (MD), panic disorder, social phobia, agoraphobia, situational phobia, animal phobia, bulimia and alcohol abuse or dependence. DSM-III-R (Spitzer *et al.* 1987) diagnoses of marijuana, sedative, stimulant, cocaine, opiate and hallucinogen abuse or dependence,

and generalized anxiety disorder (GAD), were assessed at FF4. Diagnoses were generated using computerized algorithms. Our criteria for MD differed in one important way from DSM-III-R: we did not include suicidal ideation as one of the nine possible symptoms, of which affected subjects were required to meet five. As this item is also our outcome variable, we did this in order to eliminate trivial associations. Current obsessive and compulsive symptoms were assessed at FF4 using the Padua Inventory (Sanavio, 1988), a self-report questionnaire. As previously described (Jonnal *et al.* 2000), two factors were extracted from this instrument – obsessive and compulsive symptoms. Average number of cigarettes currently smoked per day during the lifetime period when cigarette smoking was at its maximum, were assessed at FF3.

### Statistical analysis

We conducted an event history analysis using a discrete time approach, as previously described (Kendler *et al.* 1998). We examined each 'person month' of observation covered by FF2, FF3 and FF4. These contained information as to which if any SLEs occurred in that month and whether an episode of any syndrome containing suicidal ideation started in that month. Each observation record also included as covariates all of the variables from all other domains. When a twin experienced an episode of any syndrome (defined as any combination of symptoms) that included TD/SH, she was censored from the sample until she was again at risk, having recorded an end to that episode. The risk of having an onset of TD/SH is modelled as the dependent variable in a logistic regression. This method should produce true maximum likelihood estimators without inflating the test statistic or the sample size (Allison, 1982), assuming that each observation is independent. The odds ratios for TD/SH given the predictor variables were calculated from the logistic regression coefficients. In these analyses, we examine only the onset of TD/SH in the month of event occurrence, as prior analyses indicate most of the depressogenic impact of SLEs in this dataset occurs shortly after the SLE (Kendler *et al.* 1998), as has been previously noted with suicide attempts as well (Paykel *et al.* 1975).

Regression analysis was conducted in three steps, as previously described (Kendler, 1996;

Wade & Kendler, 2000): (1) univariate; (2) all independent variables reaching the  $P < 0.005$  level of significance in (1) were entered into a multivariate analysis for each five domains separately (herein referred to as domain-multivariate); and (3) all independent variables in these five analyses reaching the  $P < 0.005$  significance level were entered together into a single multivariate analysis (herein referred to as final-multivariate). Continuous independent variables were standardized with a mean of zero and s.d. of one. All analyses used age and zygosity as covariates. We used the  $P < 0.005$  alpha level to attempt to control for multiple testing. However, it should be noted that these variables are non-independent, and that the domain-multivariate analyses are rigorous in controlling for multiple variables. Regression analysis in steps (1) and (2) were implemented in SAS (SAS Institute, 1999) using the procedure GENMOD. Step (3) was implemented in procedure LOGISTIC, so that the coefficient of multiple determination, or pseudo- $R^2$ , could be calculated. This is a measure of the proportionate reduction in variation in the dependent variable associated with use of the independent variables (Neter *et al.* 1990). We used a  $P$  value of  $< 0.05$  to determine significance in this analysis.

## RESULTS

A total of 73 840 person-months of observation were examined, which contained a total of 206 onsets of episodes of suicidal ideation, reported by 82 subjects (mean number of episodes per subject = 2.51). Results for the multiple regressions examining the separate domains are shown in Table 1. Of the 20 variables in the psychopathology domain, only three – lifetime history of opiate abuse or dependence, bulimia, and animal phobia – did not increase risk of TD/SH in the univariate analyses, and were therefore excluded from the domain-multivariate analysis. In this analysis, lifetime history of cocaine misuse increased risk of TD/SH almost by a factor of three, while one s.d. increase in current obsessive symptoms, compulsive symptoms, and generalized anxiety disorder increased risk by 49%, 65% and 100%, respectively.

All childhood adversity variables increased risk of TD/SH with the exception of paternal

and maternal alcoholism, and paternal MD in the univariate analyses. However, we only had information on parental psychopathology on 1130 subjects (52%), which may have reduced the power to detect significant effects in the domain-multivariate analysis. Of the remaining seven, including maternal MD, that were entered into the multivariate analysis of this domain, only childhood sexual abuse attained statistical significance, increasing risk by 252%.

Eight of the 13 demographic variables reached statistical significance in the univariate analyses. Rural residence and a history of divorce increased risk of TD/SH. More years of education, higher income, current employment (defined as any work for pay) and to a very small extent, social support, were protective factors against it. In the domain-multivariate analysis, rural residence increased risk by 42%, while employment and one s.d. increase in the number of years of education decreased risk by 52% and 25%, respectively. One s.d. increase in age increased risk by 28%.

All measures of personality traits with the exception of extraversion and novelty-seeking were statistically significant in the univariate analyses, but only two – neuroticism and altruism – continued to be significant at the 0.005 level in the domain-multivariate analysis. A score of one s.d. higher on these increased the risk of TD/SH – by 78% and 54% respectively. Altruism was scaled in the inverse direction, i.e. higher scores indicated lower levels of the trait.

All personal SLEs attained statistical significance in the univariate analyses. In the domain-multivariate analysis, five very strongly and significantly predicted TD/SH in the month of their occurrence. Divorce/separation, loss of confidant, assault, job loss and financial problems had RR values of 5.50, 4.46, 21.73, 9.74 and 4.18, respectively. Only two network SLEs reached statistical significance in the univariate analyses – death in the proximal network, and problems getting along with someone in the proximal network. Neither of these reached the  $P < 0.005$  significance level in the domain-multivariate analysis.

The final-multivariate analysis included only variables reaching a significance level of  $P < 0.005$  in the domain-multivariate analyses. In this analysis, variables reaching the  $P < 0.05$

Table 1. *The prediction of thoughts of death/self-harm in a population-based sample of female twins*

Variable	Analysis type					
	Univariate		Domain-multivariate		Final-multivariate	
	RR	95% CI	RR	95% CI	RR	95% CI
<b>Psychopathology</b>						
Alcohol abuse/dependence	<b>1.99</b>	1.39–2.85	1.47	0.93–2.32		
Marijuana abuse/dependence	<b>2.45</b>	1.6–3.74	1.41	0.74–2.66		
Stimulant abuse/dependence	<b>3.3</b>	1.97–5.53	0.97	0.46–2.04		
Sedative abuse/dependence	<b>5.6</b>	3.24–9.69	2.37	1.02–5.52		
Cocaine abuse/dependence	<b>3.65</b>	2.21–6.05	<b>2.95</b>	1.43–6.1	4.68****	2.56–8.56
Opiate abuse/dependence	1.15	0.16–8.2				
Hallucinogen abuse/dependence	<b>4.76</b>	2.11–10.76	0.37	0.12–1.16		
Panic disorder	<b>5</b>	3.34–7.48	1.97	1.06–3.63		
Social phobia	<b>3.34</b>	2.41–4.65	1.45	0.91–2.32		
Agoraphobia	<b>4.23</b>	3.04–5.89	0.71	0.38–1.33		
Animal phobia	2.04	1.39–3				
Situational phobia	<b>2.18</b>	1.55–3.06	0.86	0.53–1.4		
Obsessive symptoms	<b>1.79</b>	1.64–1.95	<b>1.49</b>	1.31–1.7	1.43****	1.22–1.66
Compulsive symptoms	<b>1.93</b>	1.7–2.18	<b>1.65</b>	1.42–1.92	1.08	0.88–1.32
Generalized anxiety disorder	<b>2.78</b>	1.86–4.16	<b>2</b>	1.24–3.22	0.94	0.51–1.75
Bulimia	1.81	0.8–4.1				
Major depression	<b>1.62</b>	1.19–2.19	0.82	0.54–1.23		
Average no. of cigarettes/day (lifetime)	<b>1.38</b>	1.23–1.54	1.17	1–1.37		
<b>Childhood adversity</b>						
Childhood sexual abuse	<b>4.83</b>	3.31–7.04	<b>3.52</b>	2.37–5.23	1.8*	1.06–3.07
Parental loss	<b>1.27</b>	1.13–1.42	1.13	0.98–1.3		
Limit-setting	<b>0.8</b>	0.68–0.93	1	0.82–1.21		
Physical discipline	<b>0.71</b>	0.62–0.82	0.82	0.69–0.98		
Authoritarianism	<b>1.74</b>	1.5–2.02	1.34	1.08–1.66		
Overprotectiveness	<b>0.7</b>	0.6–0.8	0.88	0.72–1.08		
Warmth	<b>1.53</b>	1.34–1.74	1.29	1.07–1.56		
Paternal alcoholism	1.2	0.83–1.74				
Maternal alcoholism	1.39	0.78–2.48				
Paternal major depression	1.65	1.05–2.6				
Maternal major depression	<b>1.86</b>	1.29–2.7	1.14	0.71–1.82		
<b>Demographic</b>						
Years of education	<b>0.6</b>	0.52–0.69	0.75	0.64–0.87	0.92**	0.75–1.13
Number of siblings	1.15	0.99–1.33				
Number of children	1.22	1.04–1.43				
Rural residential setting	<b>1.59</b>	1.37–1.83	<b>1.42</b>	1.22–1.67	1.36**	1.12–1.66
Income	<b>0.76</b>	0.66–0.89	0.95	0.8–1.12		
Married	0.72	0.53–0.99				
Divorced	<b>1.89</b>	1.27–2.82	1.99	1.27–3.11		
Employed	<b>0.49</b>	0.36–0.67	<b>0.48</b>	0.34–0.67	0.57*	0.37–0.87
Protestant	1.19	0.77–1.84				
Catholic	0.72	0.39–1.33				
Personal devotion	<b>0.79</b>	0.68–0.92	<b>0.79</b>	0.68–0.93	0.75*	0.61–0.93
Personal conservatism	<b>1.49</b>	1.26–1.78	1.19	1–1.42		
Social support	<b>0.96</b>	0.94–0.98	0.97	0.95–0.98	1.0	0.98–1.02
Age	<b>1.38</b>	1.20–1.61	<b>1.28</b>	1.07–1.52	1.36*	1.09–1.7
<b>Personality</b>						
Neuroticism	<b>1.83</b>	1.59–2.11	<b>1.78</b>	1.47–2.15	1.33*	1.08–1.64
Extraversion	1.1	0.94–1.3				
Novelty-seeking	1.03	0.87–1.22				
Self-esteem	<b>0.71</b>	0.61–0.82	0.98	0.79–1.22		
Dependency	<b>1.45</b>	1.24–1.69	0.98	0.82–1.18		
Locus of control	1.21	1.03–1.41				
Altruism	<b>1.48</b>	1.26–1.73	<b>1.54</b>	1.33–1.79	1.37**	1.13–1.65
Mastery	<b>0.64</b>	0.55–0.76	0.79	0.63–1		
Optimism	<b>0.7</b>	0.6–0.82	1.08	0.86–1.36		
<b>Stressful life events</b>						
Divorce/Separation	<b>10.3</b>	5.58–19.01	<b>5.5</b>	2.87–10.52	4.38**	1.82–10.58
Marital problems	<b>15.83</b>	8.09–30.98	3.17	1.34–7.51		
Loss of confidant	<b>4.76</b>	2.23–10.16	<b>4.46</b>	2.08–9.56	5.84****	2.62–13.03

Table 1. (cont.)

Variable	Analysis type					
	Univariate		Domain-multivariate		Final-multivariate	
	RR	95% CI	RR	95% CI	RR	95% CI
<i>Illness</i>	3.3	1.36–8.03				
<i>Assault</i>	<b>38.65</b>	12.26–121.83	<b>21.73</b>	6.1–77.43	12.7*	1.71–94.42
<i>Job loss</i>	<b>14.86</b>	6.58–33.57	<b>9.74</b>	4.01–23.67	7.83**	2.42–25.29
<i>Legal problems</i>	4.75	0.66–34.12				
<i>Financial problems</i>	<b>9.63</b>	4.92–18.85	<b>4.18</b>	2–8.76	3.67*	1.45–9.32
<i>Death in proximal network</i>	<b>7.64</b>	2.43–23.97	12.05	3.76–38.6		
<i>Death in distal network</i>	<b>1.49</b>	0.65–3.4	3.25	1.8–5.86		
<i>Illness in proximal network</i>	1.56	0.69–3.53				
<i>Illness in distal network</i>	1.89	0.84–4.28				
<i>Trouble getting along in proximal network</i>	<b>10.19</b>	5.99–17.32	4.9	2.48–9.65		
<i>Trouble getting along in distal network</i>	2.92	1.62–5.24				
<i>Work problems</i>	<b>5.41</b>	2.77–10.59	3.89	1.95–7.76		

All variables significant at the 0.005 level in the univariate analyses were entered into the domain-multivariate analyses. All variables also reaching this level of significance in the domain-multivariate analyses were entered together into the final-multivariate analysis. Independent variables printed in italics were not prospectively measured. In the univariate and domain-multivariate analyses, boldface type indicates  $P < 0.005$ . In the final-multivariate analysis: \*  $P < 0.05$ ; \*\*  $P < 0.005$ ; \*\*\*\*  $P < 0.0001$ .

level of significance included cocaine misuse (RR = 4.68) obsessive symptoms (RR = 1.43), childhood sexual abuse (RR = 1.80), rural residence (RR = 1.36), employment (RR = 0.57) personal devotion (RR = 0.75), age (RR = 1.36) altruism (RR = 1.37), divorce/separation (RR = 4.38), loss of confidant (RR = 5.84), assault (RR = 12.70), job loss (RR = 7.83) and financial problems (RR = 3.67). The estimated pseudo  $R^2$  of this model was 0.16.

## DISCUSSION

In this study, we attempted to predict TD/SH using risk factors from multiple domains. Our aim was to uncover independent effects by controlling for multiple variables from five distinct domains of putative risk factors. We did this by using three sequential levels of regression analysis in the following order: univariate, domain-multivariate and final-multivariate. In this way, we were able to compare a large number of predictor variables as well as compare the relative importance of different domains of risk factors.

Our univariate results support previous studies demonstrating significant associations between SI or attempted or completed suicide and the following psychopathological variables: alcohol (Morgan *et al.* 1975; Fowler *et al.* 1986;

Inskip *et al.* 1998; Vilhjalmsson *et al.* 1998; Mann *et al.* 1999; Kessler *et al.* 1999; Hintikka *et al.* 2001) and substance misuse (Mendelson & Rich, 1993; Kessler *et al.* 1999; Roy, 2001), cigarette smoking (Angst & Clayton, 1998), panic disorder (Weissman *et al.* 1989, 1992; Johnson *et al.* 1990; Korn *et al.* 1997; Kessler *et al.* 1999), GAD (Khan *et al.* 2002) and social phobia (Schneier *et al.* 1992; Kessler *et al.* 1999); the parenting styles of parental control and lack of warmth (Adam *et al.* 1994; Martin & Waite, 1994; Wagner & Cohen, 1994); and the personality trait neuroticism (Nordstrom *et al.* 1995; Mann *et al.* 1999; Maser *et al.* 2002). Previous studies did not control for as many other variables within domains, or for as many other domains, as the current study. Our negative multivariate results for these variables suggests, therefore, that the effects of these variables on SI may not be independent, but rather, mediated by other variables, although this would need confirmation in independent samples.

Both univariate and multivariate results agreed with reports of increased prevalence of SI or suicide attempts in obsessive-compulsive disorder (OCD) (Hollander *et al.* 1996), demographic factors such as rural residential setting (Zacharakis *et al.* 1998; Phillips *et al.* 2002), older age, unemployment and lower educational attainment (Morgan *et al.* 1975; Moscicki,

1997; Beautrais *et al.* 1998*b*; Foster *et al.* 1999), childhood sexual abuse (Dinwiddie *et al.* 2000; Molnar *et al.* 2001), cocaine misuse (Petronis *et al.* 1990; Roy, 2001) and low levels of religiosity, as measured by the personal devotion variable (Martin, 1984; Stack & Lester, 1991). This suggests that these variables have more independent effects.

Univariate results did not support previous reports of increased risk of SI or suicidal acts in bulimia (Favaro & Santonastaso, 1997; Bulik *et al.* 1999), unmarried status (Vilhjalmsson *et al.* 1998; Kessler *et al.* 1999), high levels of impulsivity (through our proxy of novelty-seeking) (Adam *et al.* 1994; Stalenheim, 2001) or non-Catholic religious affiliation (Maris, 1981; Statham *et al.* 1998).

Childhood adversity and personality were the two domains with the fewest variables reaching statistical significance in the final-multivariate model. Only one personality trait – altruism – significantly and independently predicted TD/SH. It was scaled in the inverse direction (i.e. higher scores indicated lower altruism) and modestly increased risk. First discussed as a risk factor by Durkheim in his typology of suicide (Durkheim, 1952), we know of no published studies examining the impact of this personality trait as psychometrically defined on SI or suicidal acts. Childhood sexual abuse was the only childhood adversity variable reaching statistical significance in the domain-multivariate analysis. We found no evidence of independent influences of parental discipline, parental psychopathology, or the personality traits/cognitive styles of extraversion, self-esteem, dependency, locus of control, mastery and optimism on TD/SH.

The domain with the most variables reaching statistical significance in the final-multivariate analysis, as well as that having the largest effect sizes, was SLEs. These results support previous reports that exposure to events such as dissolution of close relationships or marriage, bereavement, traumatic events such as robbery and assault, and work, legal, and financial problems precipitates suicidal acts (Paykel *et al.* 1975; Beautrais *et al.* 1997; Mann *et al.* 1999; Fergusson *et al.* 2000), especially in the month prior to occurrence (Paykel *et al.* 1975).

One of the most unexpected results in this study is the lack of significant independent effects of MD, as it has consistently been reported

to be a risk factor for SI (Statham *et al.* 1998; Vilhjalmsson *et al.* 1998; Kessler *et al.* 1999; Kuo *et al.* 2001; Renberg, 2001) as well as attempted or completed suicide (Morgan *et al.* 1975; Black *et al.* 1985*a*; Beautrais *et al.* 1996; Mann *et al.* 1999; Kessler *et al.* 1999; Kuo *et al.* 2001). This may have been due to our exclusion of the TD/SH criterion in our MD diagnoses. We felt this was necessary to eliminate a non-trivial association between TD/SH and a predictor variable that is in part defined by it. Although this should be addressed in future studies, these results suggest that the effect of depression on future TD/SH is mediated by other variables in the domain-multivariate model.

We were also surprised that panic disorder and misuse of alcohol and other drugs (with the exception of cocaine) did not independently increase risk. Our use of lifetime rather than last year diagnoses as independent variables, but of the presence of TD/SH in the last year as the dependent variable, may also have contributed to negative results, as TD/SH would be expected to have a close temporal relationship with active symptoms of panic or depression, or active substance misuse. However, using last year diagnoses may artefactually elevate other variables, such as temperament, through state effects (Hirschfeld *et al.* 1983; Kendler *et al.* 1993), making it difficult to infer causal influences of these variables on TD/SH. It also would have made it impossible to use a prospective design as implemented in this study. Clearly, further research will be necessary to contextualize these results. The results in the psychopathology domain further suggest that obsessive symptoms may have more independent effects on TD/SH than previously believed. As little is currently known about suicide risk in OCD and other anxiety disorders (Khan *et al.* 2002), more attention should be given to these diagnoses.

With the exception of cocaine misuse (RR=4.68), the effect sizes of variables in domains other than SLEs were modest, with RRs ranging from 0.57–1.80. This contrasts greatly with the effect sizes of SLEs, which ranged from a 267% to almost a 12-fold increase in risk. Part of this may be due to the event-history analysis method, in which TD/SH and life events were measured contemporaneously, whereas other



variables may have been measured prospectively up to several years previously. This could make these prospective variables more susceptible to biased recall. In addition, their effects on TD/SH are more likely to have undergone temporal decay than those of SLEs. Nevertheless, this pattern suggests that 'constitutional' factors, such as psychiatric illness, personality and personal and social history may be less predictive of TD/SH or suicide risk than 'external' factors, such as life events. This should furthermore be placed in the context of the overall modest ability of the variables in the final-multivariate model to predict TD/SH, accounting for 16% of the variance. This underscores the importance of thorough and individualized assessment of suicide risk in patients, including direct enquiry about TD/SH.

The five domains also differed with respect to the independence of the effects of their respective risk factors. SLEs and psychopathological variables had the most independent effects, with, respectively, five out of five and three out of four variables continuing to reach statistical significance when carried forward from the domain-multivariate to the final-multivariate analysis. Of the remaining three domains, only one-half or less of variables reaching statistical significance in the domain-multivariate analyses continued to do so in the final-multivariate analysis. This suggests that the effects on TD/SH of the domains of demographics, personality and childhood adversity are more likely to be mediated by other risk factors, such as psychopathology and SLEs. As we know of no previous work to specifically address this hypothesis, this should be considered tentative, pending confirmation.

The results of this study should be interpreted in the context of the following potentially relevant methodological limitations. First, the validity and reliability of our assessment of TD/SH have not been previously demonstrated. However, although we only used one item, we attempted to eliminate clinically insignificant levels of TD/SH from consideration by requiring that subjects experience thoughts of their own death or self-harm for at least a 5-day period, to be considered positive. This measure is not strictly equivalent to thoughts or impulses to commit suicide, but we believe it is very similar to routine criteria used by most clinicians to

assess SI. Nevertheless, it may include thoughts of death distinct from the wish to die, such as in the context of a life-threatening illness. Secondly, we did not assess lifetime history of suicide attempts, and our results cannot be generalized to the risk of suicidal acts. Negative results, in this study, either univariate or multivariate, do not disconfirm previous studies of the risk of attempted or completed suicide, as it is plausible that at least some variables – e.g. alcohol and drug misuse – may increase the risk of acting on suicidal impulses through mechanisms such as reducing inhibitions, without increasing the risk of TD/SH itself. Thirdly, we could have used other criteria for the inclusion of independent variables into sequentially higher levels of regression analysis. We could have used, for example, cut-offs based on effect size rather than *P* value. *P* values are sensitive to sample size and their use may have led to the exclusion of low-prevalence diagnoses from the final-multivariate analysis. Fourthly, our twin data necessarily consist of correlated observations, i.e. twin pairs, which may result in spuriously low standard errors if not corrected. However, the expansion of our observations to allow for event history analysis (i.e. multiple observations per subject) makes it impossible to use standard generalized estimating equations to control for observations per family. We attempted to minimize the impact of spuriously high significance by employing an alpha level of 0.005 in the univariate and domain-multivariate analyses. Furthermore, the sample size was large, but the cluster size was small (i.e. two twins per family), diminishing the effect of spuriously low standard errors, and as previously described (Kendler *et al.* 1998), twin-pair correlation for the month of a depressive onset in this data was low. Fifthly, a number of subjects had multiple episodes of TD/SH and therefore produced correlated observations and possibly contributed to spuriously low standard errors. We therefore reanalysed the data allowing each subject to have no more than one episode. The regression coefficients in these analyses were outside the 95% CIs of those in the analyses presented here for only 3/68 variables (i.e. 4%, or about what would be expected by chance). Sixthly, some of our measures were retrospective and/or based on lifetime diagnoses, and may have been susceptible to biased recall.

In addition, retrospective measures could be used for the purpose of examining associations, but not of prediction. Seventhly, we only examined main effects in this report, and cannot rule out the presence of interactions among predictor variables. Finally, our sample consisted entirely of Caucasians, and our results cannot be generalized to other ethnic groups.

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