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Dose-response association between psychological distress and risk of completed suicide in the general population

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Introduction

Elevated suicide rates in people with clinical depression, as indexed by hospitalisations or use of psychiatric outpatient services, are well-documented.[1] However, the association between depression across the full range of severity and subsequent suicide risk is unknown. With single cohort studies insufficiently powered to examine this relation, we provide the first pooling of individual-level data from a series of large, general population-based cohort studies.

Methods

Described in detail elsewhere,[2] conducted between 1994 and 2008, sixteen independent, geographically-representative surveys of individuals living in private households were used in the present analyses: the Health Survey for England (N=13) and the Scottish Health Surveys (N=3). Combining these studies resulted in a total of 193,873 participants, 166,606 [86%] of whom had data on age, sex and psychological distress. Study members were linked to the UK National Health Service register for primary and contributing causes of death. Ethical approval was given by the London Research Ethics Council.

Psychological distress was measured using the 12-item General Health Questionnaire (GHQ-12) which contains items principally concerned with symptoms of depression and anxiety. The sensitivity (0.70) and specificity (0.80) against standardized psychiatric interviews is acceptably high.[3] In the present analyses participants were classified according to standard thresholds: asymptomatic (score 0), sub-clinically symptomatic (1-3), symptomatic (4-6), and highly symptomatic (7-12).[2] We used any mention of suicide on the death certificate as our outcome (associations were very similar in analyses using suicide as the underlying cause).

We computed two sets of analyses. First, having used Schoenfeld residuals to ascertain that the proportional hazards assumption had not been violated, we calculated hazard ratios and accompanying 95% confidence intervals for the association between the categories of psychological distress and suicide using Cox proportional hazard models. Having found no evidence of effect modification by sex (p-value for interaction = 0.81), data for men and women were combined. We adjusted hazard ratios for several covariates, the selection of which was based on empirical evidence – in the present dataset, the existing literature,[4] or both – that they are associated with both suicide and psychological distress: socioeconomic position, marital status, frequency of alcohol consumption, smoking status and presence of a somatic long-standing illness. We accounted for between study variation using a shared frailty parameter.[5] Additionally, to allow us to explore inflections in the distress-suicide relation, we used fractional polynomials to estimate the best-fitting dose-response curve for the full distress scale and suicide.

Results

A mean duration of 9.5 years of follow-up (1,581,805 person-years) gave rise to 108 deaths ascribed to suicide. Compared to the asymptomatic group, adjusted hazard ratios (95% confidence intervals), for suicide were raised for participants in the symptomatic (1.83; 0.99-3.39) and highly symptomatic groups (2.43; 1.38-4.27) (p-value for trend < 0.001, table 1). A one standard deviation increase in psychological distress was associated with a 1.29 fold increase (1.12-1.48) in risk of suicide.

Figure 1 shows the best-fitting dose-response curve for psychological distress and suicide. Scores of 2 or more on the distress scale were associated with a step-wise elevation in the risk of suicide.

Discussion

We observed a dose-response relationship between a one-off measure of psychological distress symptom severity and suicide risk in the general population up to 17-years later. That this association was apparent after adjustment for a range of confounding factors, including long-standing illness, suggests other mechanisms underlie the association. One possibility is stressful life experiences combine with a predispositional vulnerability involving multiple neurobiological pathways, such as serotonergic and noradrenergic systems and the ventromedial prefrontal cortex (diathesis-stress model).[6] Our findings raise the question whether health care professionals should pay attention to suicide risk at distress levels lower than current recommendations suggest.

Author contributions

Study concept and design: GDB; Acquisition and preparation of the dataset (including mortality linkage): ES; Statistical analysis: SB; Interpretation of the data: All authors; Drafting of the manuscript: SB and GDB; Critical revision of the manuscript for important intellectual content: All authors. SB had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors saw and agreed on the final manuscript as well as the decision to submit for publication.

Conflicts of Interest and Financial Disclosures

None to declare.

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Table 1 - Hazard ratios (95% confidence intervals) for the relation of psychological distress severity with completed suicide from an individual participant data meta-analysis of 16 general population-based cohort studies

	Number of people at risk	Number of suicide[a] deaths	GHQ-12 score				P-value for trend	1 standard deviation increase in GHQ-12 score[b]
			Asymptomatic (0)	Sub-clinical symptomatic (1-3)	Symptomatic (4-6)	Highly symptomatic (7-12)		
Number of suicide deaths/ Number at risk	166,606	108	52/98,757	25/42,439	14/13,481	17/11,929	--	--
Age- and sex-adjusted	166,606	108	1.00 (ref)	1.13 (0.70,1.83)	2.13 (1.18,3.84)	3.09 (1.78,5.36)	< 0.001	1.38 (1.20,1.58)
Age-, sex- & socioeconomic position	157,306	107	1.00	1.16 (0.72,1.87)	2.00 (1.09,3.68)	3.04 (1.75,5.28)	< 0.001	1.37 (1.20,1.57)
Age-, sex- & frequency of alcohol consumption	165,716	107	1.00	1.11 (0.69,1.79)	2.01 (1.11,3.65)	2.86 (1.64,4.97)	< 0.001	1.35 (1.18,1.55)
Age-, sex- & smoking status	165,060	108	1.00	1.11 (0.69,1.78)	2.03 (1.12,3.67)	2.81(1.61,4.90)	< 0.001	1.34 (1.17,1.54)
Age-, sex- & marital status	166,041	108	1.00	1.10 (0.68,1.77)	1.94 (1.07,3.51)	2.60 (1.49,4.52)	< 0.001	1.32 (1.15,1.51)
Age-, sex- & long-standing illness	166,568	108	1.00	1.19 (0.73,1.92)	2.28 (1.16,4.14)	3.33 (1.91,5.79)	< 0.001	1.41 (1.23,1.61)
Multivariable-adjusted[c]	155,650	106	1.00	1.13 (0.70,1.83)	1.83 (0.99,3.39)	2.43 (1.38,4.27)	0.001	1.29 (1.12,1.48)

[a] Suicide mortality was denoted by any mention of the following events on death certificates (international classification of diseases (ICD) 9th and 10th revisions): ICD-9 suicide and self-inflicted poisoning by solid or liquid substances (E950-E959) and injury undetermined whether accidentally or purposely inflicted (E980-E989), and ICD-10 terrorism (U03.1 and U03.9), intentional self-harm (X60-X84), event of undetermined intent (Y10-Y34), sequelae of intentional self-harm, assault and events of undetermined intent (Y87), and sequelae of unspecified external cause (Y89.9).

[b] Based on sex-specific standard deviations

[c] Multivariable-adjusted effect estimates are adjusted for: age, sex, socioeconomic position (manual, non-manual occupation), marital status (married, other), frequency of alcohol consumption (never, former, occasional, monthly, 1-4 times per week, ≥ 5 times per week), smoking status (non-smoker, current smoker) and presence of a somatic longstanding illness (no, yes; these include neoplasms, diabetes, other endocrine disorders, cerebrovascular disease, myocardial infarction, angina, hypertension, any other heart disease, respiratory diseases and any other non-mental health condition).

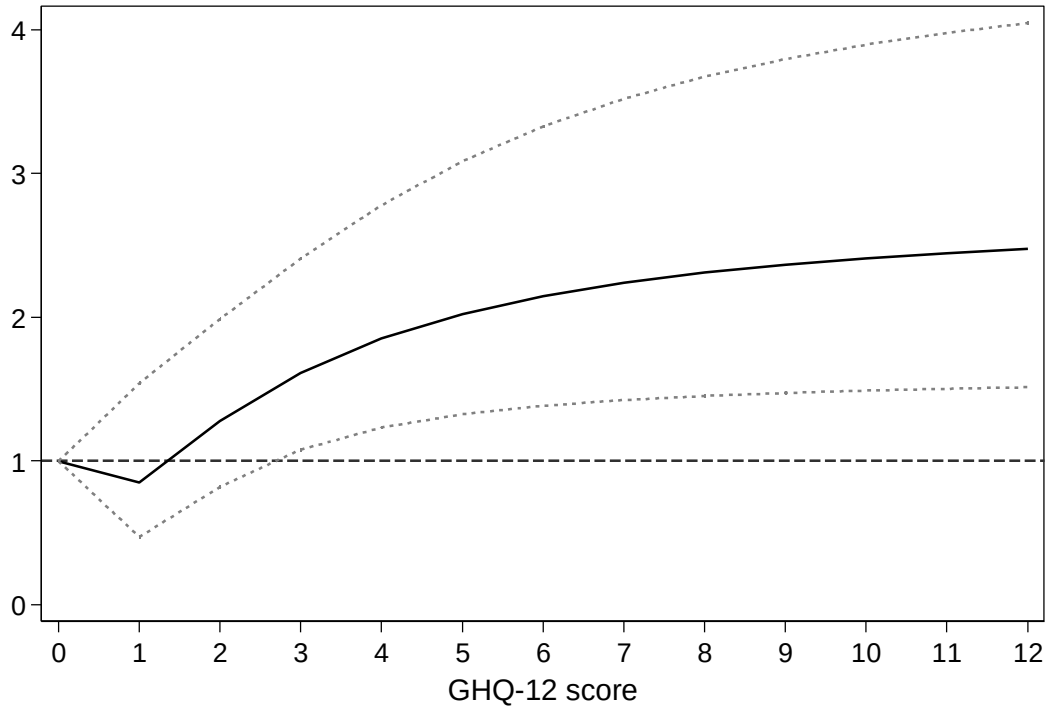

Figure 1 - Dose-response association between psychological distress score and risk of completed suicide (multivariable-adjusted hazard ratios† from an individual participant data meta-analysis of 16 general population-based cohort studies)

The predicted hazard ratio is denoted by a solid black line and the 95% confidence interval by gray dashed lines

† Multivariable-adjusted effect estimates are adjusted for the same covariates as in table 1.