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Title: All-cause mortality after non-fatal self-poisoning: a cohort study

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Keywords: self-harm; self-poisoning; mortality; natural causes of death; physical illness

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Abstract: Background. Suicide has been repeatedly shown to have greatly increased incidence after non-fatal self-harm but far less is known about early death from other causes. The present study's aim was to describe mortality and risk factors concerning all causes of death after non-fatal self-poisoning. Methods. A prospective cohort study of 976 patients who attended the Emergency Department in Nottingham, UK during a nine-month period in 1985-86. Information on deaths was obtained for 16 years following an episode of self-poisoning, from the records of the Office for National Statistics. Results. The observed:expected ratio for all-cause mortality was 2.2. Deaths due to diseases of the digestive and respiratory systems were respectively 4.4 and 2.9 times more frequent than expected. The risk for accidents was 6-fold and for probable suicides 17-fold compared to the risk in the general population. The main risk factor for subsequent deaths from natural causes was increasing age. Conclusions. The findings of this study suggest that patients who survive self-poisoning have an increased risk of death from natural and unnatural causes. The findings point towards the need for more effective clinical management and preventive initiatives.

ABSTRACT

Background. Suicide has been repeatedly shown to have greatly increased incidence after non-fatal self-harm but far less is known about early death from other causes. The present study's aim was to describe mortality and risk factors concerning all causes of death after non-fatal self-poisoning.

Methods. A prospective cohort study of 976 patients who attended the Emergency Department in Nottingham, UK during a nine-month period in 1985-86. Information on deaths was obtained for 16 years following an episode of self-poisoning, from the records of the Office for National Statistics.

Results. The observed:expected ratio for all-cause mortality was 2.2. Deaths due to diseases of the digestive and respiratory systems were respectively 4.4 and 2.9 times more frequent than expected. The risk for accidents was 6-fold and for probable suicides 17-fold compared to the risk in the general population. The main risk factor for subsequent deaths from natural causes was increasing age.

Conclusions. The findings of this study suggest that patients who survive self-poisoning have an increased risk of death from natural and unnatural causes. The findings point towards the need for more effective clinical management and preventive initiatives.

Keywords:

Self-harm, self-poisoning, mortality, natural cause of death, physical illness, risk factors.

INTRODUCTION

Self-harm is an important issue for healthcare services. Rates of non-fatal self-harm are around their highest ever level with an estimate of 220,000 episodes dealt with by general hospitals in the UK each year [13]. Self-harm is one of the commonest reasons for medical admission to hospital, the commonest reason for females and the second commonest for males. Self-harm, especially when repetitive, is responsible for substantial health service costs [28]. Of all self-harm episodes resulting in hospital attendance, over 80% involve self-poisoning [13].

Many studies have focused on the association between self-harm and subsequent suicide (for example, [18, 27]), revealing a high rate of suicide after self-harm that has been estimated to be more than 60 times the general population rate [15]. The estimated rate of death by suicide after self-harm varies between studies, depending mainly on differing patient populations and follow-up times, but it is high; a systematic review estimated that more than 6 per cent of patients attending hospital due to self-harm will have died by suicide after ten years [23].

Although there have been numerous research reports that examine the relation between self-harm and subsequent suicide, much less attention has been paid to the risk of death from causes other than suicide. There is evidence to suggest that physical illness is associated with excess risk of suicide [11, 30] and attempted suicide [5]. A 10-year follow-up study in Denmark investigated mortality for patients admitted to hospital after self-poisoning [21]; many more deaths than expected were due to natural causes comprising respiratory, neurological, digestive, neoplasm and alcohol-related conditions. A study in Oslo followed up patients treated for self-poisoning for a 10-year period and

found suicide, heart disease, opiate abuse, and accidents to be the commonest causes of death [9]. A systematic review and meta-analysis found a raised incidence of early death from natural causes [19]. Similar results were found more recently in follow-up studies conducted in Austria, Australia and Finland among patients who had attended hospital because of self-poisoning or attempted suicide; in each case there were clear excesses of deaths due to natural and unnatural causes [1, 2, 22]. On the other hand, a Canadian study found that patients admitted to inpatient psychiatric care following a suicide attempt were significantly less likely than the population in general to die of natural causes [17].

The only comparable UK study to have considered the relation between self-harm and subsequent death due to reasons other than suicide is from Oxford [16]. The study sample comprised all patients attending the general hospital in Oxford over a period of 20 years from 1978 to 1997, following them up for an average of 13 years – to the end of 2000. The study observed a higher than expected death rate from natural causes, particularly from respiratory, circulatory, neurological, endocrine, digestive, skin and musculoskeletal conditions. Deaths due to accidents were also more frequent than expected, and homicides were more frequent among males. The Oxford study is particularly interesting because it used larger sample sizes and longer follow-up periods than did the previous research cited.

Our investigation set out to corroborate or refute earlier findings about excess mortality following non-fatal episodes of self-harm by following-up for 16 years a rather different cohort: one that was assembled in a very short inception period (less than one year), and from a large city that is more typical of urban England. The aims of the present study are: 1) to determine the subsequent

mortality rates and causes of death in patients who had previously attended the Emergency Department because of non-fatal self-poisoning, 2) to examine the risk factors for subsequent non-suicidal deaths, and 3) to determine any possible differences between those who died by natural causes and those who were alive in the follow-up period. Findings on the increased risk of suicide in these patients have previously been published [25].

METHOD

Study population and sample

The cohort comprises 976 consecutive patients aged 14 years or over who attended a large Emergency Department in Nottingham as a consequence of self-poisoning over nine months during 1985-1986. The Emergency Department was the only one serving the city and adjacent population of over 600,000. Nottingham is a large city, its surrounding urban area being the seventh largest in the UK, with a socio-demographic profile typical of UK metropolitan areas. The index self-poisoning episode was defined as the first attendance at the Emergency Department because of self-poisoning during the study period from November 1985 to July 1986. National data on population and cause-specific mortality were obtained from the Office for National Statistics.

Definition of self-harm and self-poisoning

For the purpose of this report the definition of self-harm is intentional self-poisoning or self-injury, irrespective of motivation or degree of suicidal intent [15]. Self-poisoning is defined as the intentional ingestion of more than the prescribed amount of any drug, whether or not there is evidence that the act

was intended to result in death. The definition also includes intentional poisoning with non-ingestible substances and intentional overdoses of recreational drugs [13].

Patient Characteristics

The study patients were identified round the clock by Emergency Department clerical staff, and the clinical staff in the Emergency Department collected information on a research checklist while the patients were in the emergency room. Checklists asked about potential risk factors for the seriousness of the index episode as a suicide attempt and for the likelihood of adverse outcome in the medium to long term. Items included past mental health service contact, previous self-harm, living arrangements, and social and medical status. In addition data were collected about demographic variables, and about alcohol consumption around the time of the self-poisoning [24, 25].

Follow-up

The identifying particulars of patients from the 1985-1986 cohort were passed on to the Office for National Statistics (ONS) who ascertained whether the people were alive or dead at the end of 2002, some 16-17 years after attendance at the Emergency Department because of self-harm [25]. In the case of those who were deceased, ONS provided a copy of the death certificate, which includes the ICD-10 coding for the causes of death [32].

After careful examination of all death certificates it was decided that only the primary causes of death recorded would be used for this study. Secondary causes were either further descriptions of primary causes or they were not related to death. The natural causes of death were grouped as follows: neoplasms (ICD-10: C00-D48), diseases of the circulatory system (I00-I99),

diseases of the respiratory system (J00-J99), diseases of the digestive system (K00-K93), diseases of the genitourinary system (N00-N99), and deaths from all other causes. The unnatural causes of death were: accidents (S00-T98, V01-X59, Y40-Y98) and probable suicides (X60-X84, Y10-Y43). The category of probable suicides includes deaths recorded by coroners as suicides (X60-X84) or open verdicts (Y10-Y43). It is standard practice to combine open verdicts with suicides, as it has been suggested that suicide mortality is underestimated when suicide is used alone [4].

Statistical Analyses

Mortality rates, for all causes and for cause-specific deaths in the study population compared to the general population, were calculated using mid-year populations for England and Wales. The total of person-years at risk were calculated according to gender and 10-year age bands, with the exception of the last two intervals which ranged from 45 to 59 years and 60 and over – because of the right skewed age pattern seen in self-poisoning. Individuals aged 14 years and under were excluded due to age-group inconsistencies of the Office for National Statistics data. The expected number of deaths was obtained by multiplying the person-years at risk by the national rate. Standardised mortality ratios (SMRs) were calculated by dividing the observed numbers of death by the expected numbers.

For the comparison of patients who were alive with those who had died, non-parametric two-tailed tests (Mann Whitney U test) were used in comparisons of metric variables, and two-tailed chi-squared tests when comparing proportions. We looked for predictors of subsequent death, analyzing the variables collected from Emergency Department records and the clinicians' checklists.

Survival analysis was conducted to create a Kaplan-Meier survival graph for assessing the survival time for each gender.

Using the variables that proved to have a statistically significant association with subsequent mortality, Cox's proportional hazards regression models were used to determine any independent predictors of death due to natural causes. Cases with missing variables were excluded. When Cox regression could not include all possible risk factors, because of insufficient outcome events, logistic regression analyses were used, in which case the final model identifies any additional variables but it does not take into account the time of follow-up. For selecting the model all variables were entered in one block, using the Enter method of regression. Hazard ratios and odds ratios are reported with 95% confidence intervals (95% CI). Goodness of fit for the final models was acceptable ($P < 0.001$). The data were analysed using SPSS version 16.0.

Ethical Approval

Ethical approval was received from the Faculty Research Ethics Committee (Faculty of Development and Society) of Sheffield Hallam University and the Nottingham (National Health Service) Research Ethics Committee.

RESULTS

Study sample

During the nine months of recruitment (1985-1986), 976 people attended the Emergency Department as a result of 1091 episodes of self-poisoning. 591 (61%) of those were female and 384 (39%) were male. The median age of the sample was 27 years, range 14 to 86, interquartile range 20 to 39 years.

Young adults made up most of the sample, with 84% (*n* = 815) under the age of 45 years.

Mortality

The Office for National Statistics was able to trace 912 (93%) of the 976 people. Individuals not traced were similar to those traced in terms of age and gender. 157 out of 912 people (17%) had died by the end of the follow-up period (at least 16%, 157/976, of the original cohort); 84 of the 591 women (14%), and 73 of the 384 men (19%). From those traced, 125 died by causes other than probable suicide (80% of the deaths). The median time to death, following the index episode of self-poisoning, for those who died by natural causes or accidents was 9.8 years for males (*n* = 52) and 7.2 years for females (*n* = 73). Survival analysis (Figure 1) shows that the risk of death is similar for each gender (logrank test, $x^2 = 0.17$, P = 0.68; Hazard ratio 0.92, 95% CI 0.62 to 1.37).

Figure 1 about here

Causes of death

The causes of death, by gender are shown in Table 1. By the end of 2002, 99 people had died from natural causes, 17 died by accidents, 32 died from probable suicides, and in 9 cases the cause was unknown or unspecified but we found no indications that the death was due to probable suicide. In the natural causes of death, the standardized mortality ratio (SMR) was highest for digestive diseases, at ratios between four- and five-fold for each gender. A high observed to expected ratio was also found for respiratory diseases, with ratios around 3. Very high mortality was observed for accidents, with female

SMR 7.6, and male SMR 5.3. As expected, from the findings reported previously about suicides [25], the SMR for suicide pointed towards a huge excess of probable suicides following non-fatal self-poisoning: in females SMR around 20 and in males 16.

Age-specific mortality

Table 1 also shows mortality ratios from all causes across 5 age bands. The mortality ratio from all causes was 1.96 (95% CI 1.5-2.4) for females and 2.43 (95% CI 1.9-3.0) for males. In the females, the excess of deaths was greatest (around 9-fold) between 25 and 34 years of age, for the males aged between 35 and 44 years (around 8-fold).

Table 1 about here

Patients who died by causes other than suicide, compared with patients who were alive

A number of differences were observed between patients who died either by natural cause or accident (that is, non-suicidal deaths) and patients who were alive at the end of follow-up. Differences that are not statistically significant are not reported here. As expected, patients who died in the follow-up period were significantly older at the time of index attendance than were patients who remained alive: median age at index episode of those who were alive at follow-up was 24 years (interquartile range 19 to 34 years), while median age at index of those who died during the follow-up period was 59 years (48 to 71), ($U = 11879$, $P < 0.001$).

Patients who had died showed an excess of a number of characteristics (Table 2). At the point of the index episode those who died but not by suicide were

much more likely than those who remained alive to be suffering from serious physical illness, and to be living alone – both factors that are closely associated with increasing age. They were also much more likely to have had psychiatric care, admission to a psychiatric unit, and previous self-harm. At the time of the episode of index attendance at the emergency department, those who subsequently died from causes other than suicide were more likely to have attended hospital during the working day, and to have ingested psychotropic drugs (rather than analgesics and a range of other medications) or non-ingestible substances. They were also much more likely to be drowsy or unconscious. It is also clear that there was a higher than expected non-suicidal mortality among patients who went on to repeat self-harm in the year following the index episode.

Table 2 about here

All of the above findings held true whether deaths designated as due to accidents were included or not with deaths from natural causes (Table 2).

Risk Factors for deaths from natural causes

In the regression models, the outcome was death from natural causes; we did not create a model for the outcome of natural and accidental deaths combined. A number of relations between single variables and mortality were observed, although Cox's proportional hazards regression model showed only one variable to have a clear effect when the factors were considered together: increasing age at the time of attendance because of self-harm (hazard ratio = 1.1 per year, 95% CI 1.09 -1.12).

The data were re-analysed using logistic regression in order to identify any other important variables. Again, only increasing age was found to independently predict death by natural causes (odds ratio = 1.13 per year, 95% CI 1.10 -1.16). The effects of the other variables that were significant with univariate analysis (Table 2) were not confirmed in the regression model.

DISCUSSION

This prospective cohort study, with its sample consisting of mainly young adults, showed high mortality with 17% of them dead by 16 years later. Overall, mortality was double the expected rate found in the general population. Females between the ages of 25 and 34 years had the highest excess of non-suicidal deaths with a standardised mortality ratio of about 9, while women aged 45 to 59 years had a standardised mortality ratio of over 5. The risk pattern was slightly different for males, whose highest excess of deaths was at 35 to 44 years (more than 7 times that of the general population), with a high risk also between the ages of 25 and 34 (standardised mortality ratio around 6).

Around 80% of all deaths were from natural causes or accidents, with most of the males having died within ten years and most of females by seven years. The overall risk of death during follow-up was similar for both genders.

As expected, the mortality was very high from probable suicide – around 16 to 20 times the expected rate. The mortality rate was, however, higher than expected even after the deaths by suicide were set aside. Excess risk of death was highest for accidents, but deaths from a range of natural causes were also substantially more frequent than expected in the general population. For

example, people who self-poisoned had more than four times the general population risk of dying from digestive diseases and they were around three times as likely to die from diseases of the respiratory system.

The people who died by natural causes or accidents showed a number of differences from those who were alive at the end of follow-up. First, as expected, they were older at the time of attendance at the Emergency Department than were the sample of people who were still alive 16 years later. They were also more likely to be living alone and to be suffering from a serious illness at the time of overdose. Those who had died also showed strong associations with previous and subsequent self-harm, and with past psychiatric history. At the time of the index attendance, people who later died were more often showing impaired consciousness, were more likely to have attended the emergency department during the working day, and more likely to have ingested psychotropic drugs or non-ingestibles.

The present study has a number of strengths. First, the study sample included all patients attending the emergency department because of self-poisoning. Many studies of outcome after self-harm have a filter based on physical or psychiatric severity; for example, samples are drawn only from patients assessed by the mental health team, or are even restricted to those admitted to the mental health unit. Second, the use of national rather than local mortality data resulted in high ascertainment of survival or death, with only 6% untraced. Third, Nottingham has a socio-demographic profile typical of UK metropolitan areas and the study findings are thereby likely to be relevant to other places. A limitation of this study is that not all possible associations have been examined due to few deaths in some categories of cause of death. Sample size also meant that we were largely unable to identify independently predictive

variables - partly due to inconsistent recording of data by the emergency department staff at the time of the original hospital attendance for self-poisoning.

Our findings are broadly in line with previous research. High overall mortality after self-harm has been reported by other studies [8, 21, 10, 31]. The importance of physical illness at the time of self-harm was also evident in a cohort of young people [14]. Our study further shows that physical illness is a risk factor for subsequent death among people who have previously overdosed. Unfortunately, we do not have the data needed to examine whether the illness present when individuals self-harmed is similar to the type of illness which caused subsequent death.

An excess of deaths due to natural causes has been found in previous studies of self-harm [14, 26]. In particular, our findings are closely congruent with those from a large cohort study based on 20 years of episodes of non-fatal self-harm in Oxford, which found more than the expected number of deaths due to respiratory diseases, digestive disorders, and accidents [16]. An excess of digestive causes of death was also found in a Danish study [21]. Respiratory disorders are associated with long-term disability and it may well be the presence of disability in those with respiratory disorders that links with self-harm [7]. Our method of data collection from emergency department records meant that we were unable to determine whether people who died from digestive or respiratory diseases had self-poisoned with medicines used in their treatment for these disorders.

The significant excess of accidental deaths points to a number of possible interpretations including excessive risk-taking behaviour and the

consequences of mental disorder and associated treatment; but there is also a possible misclassification of deaths that represent probable suicide. In the UK and elsewhere, studies that have scrutinised certification of deaths with a verdict of misadventure or accident found some that were deemed probable suicides [6, 3]. A small number of suicides may be missed because the death was not subject to a coroner's investigation; researchers in Sheffield, UK examined clinicians' ability to recognise reportable deaths using fictitious case histories and some clinicians failed to recognize probable suicides [29].

Emergency department records are ideal for ensuring that all patients attending the hospital, not just those admitted or subjected to specialist consultations, are included in analyses. These case records, however, typically contain little information about patients' physical and mental health beyond that needed for the management of the acute episode of poisoning. Consequently, it is not possible to make many robust assertions from these data about why mortality – from suicide, accident and natural causes – is so much higher among people who have self-poisoned than in the general population. In particular, neither the present study nor other published work sheds much light on the reasons for an excess of deaths from natural causes. Our multivariate analysis points towards no useful factors that can be modified either by clinicians or through public health initiatives. Even the single variable analyses show only relations between early death and background factors that cannot realistically be modified, such as living alone, and having a history of physical or psychiatric illness. All the features of the non-fatal episode of self-poisoning that emerged as relevant – ingesting non-ingestible substances or prescribed psychotropic medicines, attending during the day-time, and being rendered drowsy or unconscious – are likely to be largely explained by age.

The current context for care and aftercare following hospital attendance due to self-harm is of uncertainty about how best to deliver the most effective service. The Cochrane review of interventions is inconclusive [12] and NICE guidelines in England are based entirely on good practice points because the clinical evidence from studies of good quality is unavailable [20]. People attending hospital because of self-harm, more than a quarter of a million each year in the UK, have a poor outcome as judged by non-fatal repetition, suicide, accident and natural causes. The present study is an indication of how important it is to move forwards towards an evidence based approach to assessment, treatment and follow-up.

Fig. 1 Death from any cause according to gender: Kaplan-Meier curves represent time from the first episode during study period to death.

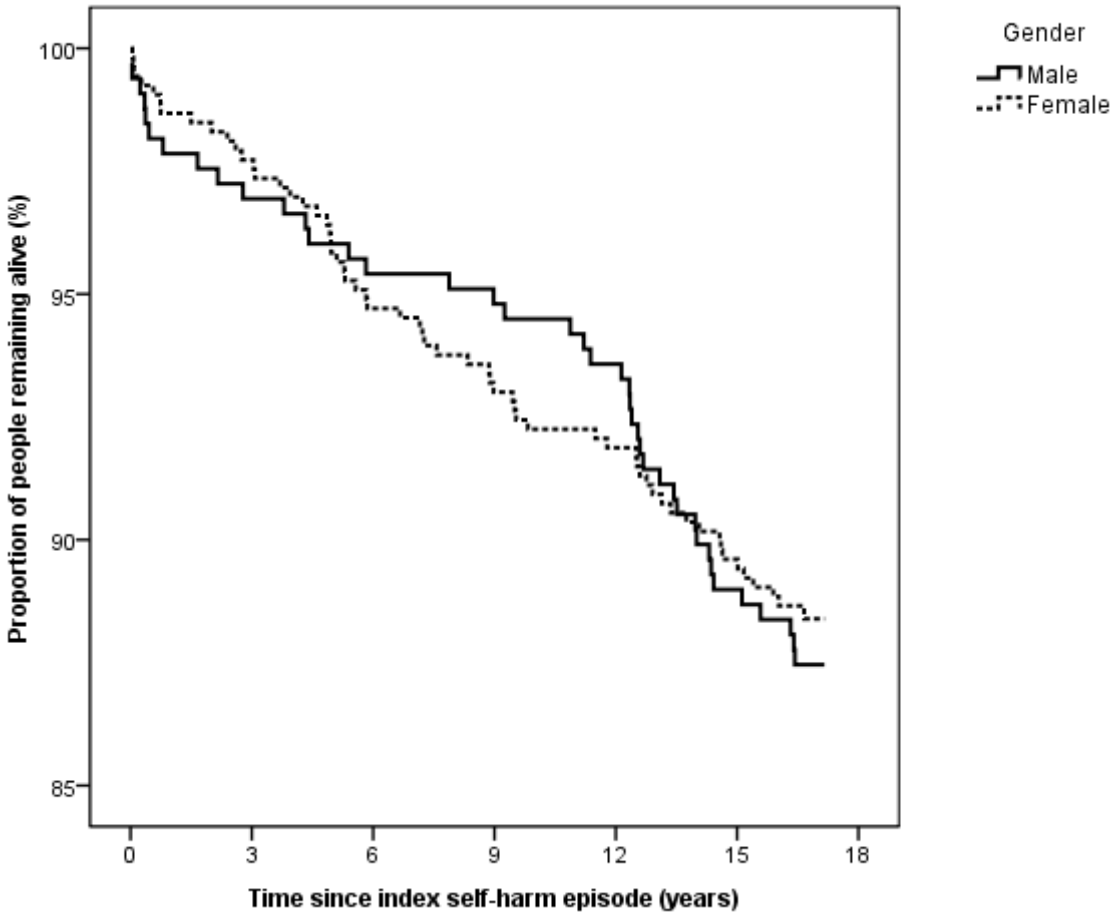

Table 1 Cause-specific and age-specific mortality ratios, by gender.

	Females			Males			Both	
	Number who died (N=84)	SMR	(95% CI)	Number who died (N=73)	SMR	(95% CI)	SMR	(95% CI)
Cause of Death								
Neoplasm	12	1.15	0.6-1.9	8	1.05	0.5-2.0	1.11	0.7-1.7
Circulatory	20	1.17	0.7-1.8	14	1.22	0.7-2.0	1.19	0.8-1.6
Respiratory	18	2.69	1.6-4.1	13	3.24	1.8-5.4	2.90	2.0-4.1
Digestive	7	4.16	1.8-8.2	5	4.91	1.8-10.9	4.44	2.4-7.5
Genitourinary	1	1.85	0.1-9.1	1	3.36	0.2-16.5	2.38	0.4-7.9
Accidents	8	7.60	3.5-14.4	9	5.32	2.6-9.8	6.19	3.7-9.7
Probable suicides	11	19.82	10.4-34.4	21	15.84	10.1-23.8	17.01	11.8-23.7
All ages	84	1.96	1.5-2.4	73	2.43	1.9-3.0	2.15	1.8-2.5
15-24	4	2.97	0.9-7.1	2	1.13	0.1-3.7	1.93	0.7-4.0
25-34	8	8.97	4.1-17.0	11	5.71	3.0-9.9	6.74	4.1-10.3
35-44	4	2.45	0.7-5.9	15	7.61	4.4-12.2	5.28	3.2-8.0
45-59	17	5.40	3.2-8.4	15	4.93	2.8-7.9	5.17	3.6-7.2
60+	51	1.42	1.0-1.8	30	1.40	0.9-1.9	1.41	1.1-1.7

SMR: Standardised Mortality Ratio; CI: Confidence Interval

Table 2 Relation between patient characteristics and mortality, separately examining deaths from natural causes only and deaths that combine natural causes with accident and misadventure verdicts.

	Death from natural causes		Death from natural cause or accident/misadventure	
	Proportion who died if risk factor present; not present (values are numbers of deaths/people at risk)	Difference between proportions (95% confidence interval)	Proportion who died if risk factor present; not present (values are numbers of deaths/people at risk)	Difference between proportions (95% confidence interval)
Characteristics pre-dating index episode:				
Serious illness	29/87 (33%); 37/493 (8%)	25.8% (16.4 to 36.4)	32/90 (36%);46/502 (9%)	26.4% (16.9 to 36.9)
Live alone	26/119 (22%); 49/538 (9%)	12.7% (5.7 to 21.3)	31/124 (25%); 59/548 (11%)	14.2% (6.9 to 22.9)
Previous self-harm	40/236 (17%); 24/380 (6%)	10.6% (5.5 to 16.3)	48/244 (20%); 30/386 (8%)	11.9% (6.4 to 17.8)
Psychiatric history	41/226 (18%); 24/367 (7%)	11.6% (6.2 to 17.5)	50/235 (21%); 29/372 (8%)	13.5% (7.8 to 19.6)
Previous psychiatric admission	30/122 (25%); 31/452 (7%)	17.7% (10.4 to 26.3)	33/125 (26%); 40/461 (9%)	17.7% (10.2 to 26.4)
Characteristics of the episode				
Attend during day (0800-1600)	43/228 (19%); 58/624 (9%)	9.6% (4.4 to 15.5)	52/237 (22%); 72/638 (11%)	10.7% (5.2 to 16.8)
Drowsy rather than alert	68/387 (18%); 34/470 (7%)	10.3% (5.9 to 14.9)	81/400 (20%); 44/480 (9%)	11.1% (6.4 to 15.9)
Poisoned with psychotropic drugs or non-ingestibles	74/375 (20%); 28/482 (6%)	13.9% (9.5 to 18.6)	88/389 (23%); 37/491 (8%)	15.1% (10.4 to 19.9)
Subsequent episodes of self-harm				
Repeated within 1 year of index episode	18/100 (18%); 84/757 (11%)	6.9% (0.15 to 15.8)	22/104 (21%); 103/776 (13%)	7.9% (0.67 to 17.0)

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Conflict of interest statement None

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