



## Risk of self-harm in physically ill patients in UK primary care

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### ABSTRACT

**Objective:** To examine self-harm risk across the adult age range in patients diagnosed with various physical illnesses using the General Practice Research Database – a broadly representative sample of all people registered with a family practice in the United Kingdom.

**Methods:** We conducted a large nested case–control study sampled from the whole primary care cohort. During 2001–2008 we studied 2306 cases of self-harm and 46,120 age and gender-matched controls without such an episode recorded. Relative risks were estimated against reference patients with none of the examined physical illnesses. Additionally, we assessed confounding by recorded depression, effect modification by gender and multi-morbidity effects.

**Results:** Risk was significantly elevated in relation to any of the physical illnesses (male OR 1.35, 95% CI 1.18–1.54; female OR 1.62, 95% CI 1.40–1.86). For both genders combined, risk was raised with each specific illness. Effects sizes were consistently larger in women. Adjustment for recorded depression explained much of the elevated risk, but not so in women with asthma, back pain, diabetes, epilepsy or hypertension. Raised risk was seen in younger adults and during middle age, but not among older people. There was a dose–response relationship with increasing number of physical illnesses, and in women this was independent of depression. **Conclusion:** Heightened risk was seen with a variety of physical illnesses. The findings indicate a need for tackling psychological distress and reducing self-harm risk in physically ill patients who attend primary healthcare services for non-psychiatric reasons, particularly so for women and younger and middle aged adults.

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### Introduction

In recent years there has been heightened interest in investigating the links between physical illness, mental illness, and suicidal behaviour [1]. However, the exact nature of these associations remains unclear from previous research, due to methodological limitations; for example, inadequate sample sizes, reliance on self-reported morbidity data, and incomplete adjustment for psychiatric disorder [2,3]. Higher risk of completed suicide in physically ill elderly people has been studied extensively [4–8], but there have been far fewer investigations of suicide among younger people affected by physical ill health [9]. This is pertinent because physical illness of some kind is present in most suicide cases that occur at age 50 years and older [10]. It is, however, also important to examine non-fatal suicidal outcomes separately in younger adults [11]. As well as being far more common overall than

completed suicide, self-harm occurs more frequently at younger age and with a higher female to male ratio [12]. It is also an especially strong predictor of completed suicide [13], and so suicide prevention initiatives require a profound understanding of the whole suicidal process.

In this paper, we seek to answer the following research questions:

1. What is the relative risk of self-harm linked with physical illness *per se*?
2. How does relative risk vary between different types of major physical illnesses experienced by primary care patients across the whole adult age range?
3. How do the effect sizes vary according to gender, age and number of physical illnesses diagnosed?
4. How much of any increased risks observed can be explained by clinical depression as detected by healthcare services?

We expected to find elevated risks in physically ill patients across the broad range of physical illnesses examined. More specifically, and in line with the findings of our recent study of completed suicide risk in the same study population [14], we anticipated that relative risk

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would be higher in women than in men, and that there would be a gradient in rising risk with a greater number of physical illnesses.

## Methods

### Description of the study dataset

Our nested case-control study was derived from routinely collected primary care records in the General Practice Research Database (GPRD) [15,16], the world's largest population-based longitudinal primary care data source. We have utilised this source to conduct a similar study on completed suicide [14]. The methods of the study reported here are almost identical to those used previously, except for the examination of a different outcome. Although practices providing data to the GPRD were not randomly sampled from all practices nationally, the database provides a broadly representative sample of all people registered with a family practice, which applies to virtually every UK resident. The September 2010 version we analysed contained around 10.6 million complete patient records from 593 family practices. The GPRD routinely records all primary care consultations with registered patients, including detailed and complete clinical coding for symptoms, diagnoses, treatment (including prescribed medication), and referral to other forms of National Health Service care and to other healthcare providers. Prior to the creation of our bespoke study dataset, the Independent Scientific Advisory Committee of the GPRD granted ethical approval. Consent from individual patients is not required for these studies.

We initially identified recorded episodes of self-harm that occurred between January 1, 2001 and December 31, 2008, among patients registered at GPRD practices and with at least 2 full years of 'up-to-standard' GPRD clinical data. We applied a stringent case definition, by including Read coding descriptions that included the terms 'suicide and self-inflicted,' 'suicide and self-harm,' 'para-suicide' or 'attempted suicide.' Our previous nested case-control study of completed suicide in the GPRD identified 873 cases [14]. During the same study period (calendar years 2001–2008) we initially identified a total of 2478 patients with a first episode of suicidal behaviour. These included 172 people who died at their first recorded episode. Our intention was to ensure that our two studies examined mutually exclusive outcomes (completed suicide and non-fatal self-harm), and so we excluded these deceased individuals from the second study that we report here.

### Physical diseases and clinical depression

We examined the following major physical illnesses that either place a heavy burden on UK primary care services [17], or are indicated in the literature as being likely correlates of clinical depression or suicidality: cancer, coronary heart disease, hypertension, stroke, diabetes, asthma, chronic obstructive pulmonary disease (COPD), osteoarthritis, osteoporosis, back pain and epilepsy. We identified them using Read and OXMIS (Oxford Medical Information System) coding, which are widely used hierarchical coding systems in UK primary care [18]. Recent validation showed that ICD-9 codes for indentifying multiple physical diseases can be readily translated for examination in the GPRD [19]. Two of the co-authors of the current paper previously examined the impact of national schemes to incentivise family practitioners to improve their quality of care [20]. They conducted an extensive consensus-development process with experienced academic family practitioners to identify valid codes denoting major illnesses in the GPRD and other national routinely collected datasets. We applied their validated coding ranges.

The same approach was used to identify patients diagnosed with depression that pre-dated the first recorded act of self-harm. These were all classified as 'depression positive' patients unless their record clearly indicated that their condition had remitted, to achieve comprehensive adjustment in the multivariate models. For controls, it was

necessary for relevant physical illness or depression to have been diagnosed prior to the matched case's recorded first self-harm episode, to achieve equivalence of measurement between cases and controls and thus preclude information bias. The detailed lists of Read / OXMIS codes used are available on request from the corresponding author.

### Study design and statistical analyses

Our nested case-control study was sampled from a nationally representative cohort of adult primary care patients at risk of a first recorded episode of self-harm. The identified self-harm cases were matched individually to living controls with no record of self-harm by gender and age in years at the date of the case's first recorded episode. Twenty controls were selected from the age, gender and time-specific risk set of each case, to maximise power for precise effect estimation with physical illnesses of low prevalence [21]. We calculated exposure prevalence among cases and controls separately, and generated conditional logistic regression models to estimate relative risks as exposure odds ratios across both genders. These models were adjusted inherently for gender and age in the matched design. We then fitted gender interaction terms, and formally tested their significance. The incidence density sampling in the nested case-control design meant that the odds ratios were interpretable as hazard ratios (relative risks) as would be derived from survival analysis of the whole cohort [22]. All analyses were conducted using Stata statistical software version 11.2 (StataCorp: College Station, TX).

## Results

### Demographic characteristics of self-harm cases and controls

In total we examined 2306 cases and 46,120 age and gender-matched controls (males: 1259 cases, 25,180 controls; females: 1047 cases, 20,940 controls). Age at first episode of self-harm ranged from 17 to 87 years (median: 38 years; interquartile range, IQR: 27–49 years). The median age at first episode was higher in cases diagnosed with any of the 11 physical illnesses (45 years) compared to those with none of the 11 assessed illnesses (35 years); Wilcoxon rank-sum test:  $P < 0.001$ . Fig. 1 is a boxplot showing the median, interquartile range and complete range in age at first episode across the specific physical illnesses. Relatively young median ages for onset of this behaviour were seen in patients with asthma (median: 32 years; IQR: 22–45 years), epilepsy (median: 39.5 years; IQR: 33–45 years) and back pain (median: 40 years; IQR 33–49 years), reflecting the younger peak ages for the occurrence of these conditions.

### Relative risk irrespective of age and gender

These results are shown in Table 1. In patients diagnosed with any of the assessed physical illnesses, we observed an almost 50% elevated risk of self-harm. This effect was reduced, but risk remained significantly raised with adjustment for previous or concurrent clinical depression. Against the generic reference group of people without any of the assessed illnesses, we estimated odds ratios in relation to each of the specific conditions listed in Table 1. A significantly higher risk was found in 9 of the 11 conditions, with the unadjusted odds ratios ranging from 1.30 for hypertension to 2.35 for epilepsy. After adjustment for recorded depression, elevated risk remained statistically significant for just 3 conditions: asthma, back pain and epilepsy. These three illnesses had relatively young age of onset for self-harm, as shown in Fig. 1. For any of the physical diseases assessed, this adjustment explained 57% of the elevated risk of self-harm; for the specific illnesses, the percent of raised risk explained ranged from less than a half (46%) for epilepsy to 100% for osteoarthritis.

### Relative risk by gender

As noted beneath Table 1, in the unadjusted models there were significant gender interactions with diabetes ( $\chi^2$  8.2, 1 d.f.,  $P = 0.004$ ), hypertension ( $\chi^2$  4.9, 1 d.f.,  $P = 0.03$ ) and back pain ( $\chi^2$  4.0, 1 d.f.,  $P = 0.05$ ). The effect sizes for these 3 conditions were significantly greater in women than in men (Table 2). Many of the gender-specific unadjusted odds ratios reported in the second table were significantly raised, but no male effects remained significant after adjusting for depression. By contrast, the following adjusted female effects were significant: any of the assessed physical illnesses, asthma, back pain, diabetes, epilepsy and hypertension. For any of the physical illnesses, adjustment for depression explained 66% of the elevated risk of self-harm in men and 50% of the raised risk in women. Epilepsy was linked with the highest relative risks, in both men and women separately, and in all patients irrespective of gender.

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