Risk factors for nonfatal self-harm and suicide among adolescents: two nested case–control studies conducted in the UK Clinical Practice Research Datalink

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Background: The characteristics of adolescents who die by suicide have hitherto been examined in uncontrolled study designs, thereby precluding examination of risk factors. The degree to which antecedents of nonfatal self-harm and suicide at young age differ remains unknown. **Method:** We delineated two nested case–control studies of patients aged 10–19 years using the Clinical Practice Research Datalink with interlinked hospital and national mortality records. Cases were adolescents who between 1st January 2003 and 31st December 2018 had died from suicide (*N* = 324) – study 1; experienced their first self-harm episode (*N* = 56,008) – study 2. In both studies, cases were matched on sex, age and practice-level deprivation quintile to 25 controls. By fitting conditional logistic regression, we examined how risks varied according to psychiatric diagnoses, prescribed psychotropic medication, patterns of clinical contact and area-level deprivation. **Results:** Suicides occurred more often among boys (66%), but self-harm was more common in girls (68%). Most individuals who self-harmed or died from suicide presented to their GP at least once in the preceding year (85% and 75% respectively). Only a third of cases had one of the examined diagnostic categories recorded. Depression was most strongly associated with elevated risks for both outcomes (self-harm: OR 7.9; 95% CI 7.8–8.2; suicide: OR 7.4; 95% CI 5.5–9.9). Except for autism spectrum disorder, all other diagnostic categories were linked with similar risk elevations for self-harm as for suicide. Whilst self-harm risk rose incrementally with increasing levels of area-level deprivation, suicide risks did not. **Conclusions:** We observed few marked differences in risk factor profiles for nonfatal self-harm versus suicide. As most adolescents who had harmed themselves or died by suicide were known to services in the preceding year, their underlying pathology may not be adequately identified and treated. Our findings highlight the need for a multiagency approach to treatment and prevention. **Keywords:** Adolescence; self-harm; suicide; risk factors; case-control.

Introduction

Self-harm and suicide in young people represent major public health concerns (Hawton, Saunders, & O'Connor, 2012). Individuals who self-harm are at much greater risk of harming themselves again and of subsequently dying by suicide, which is the leading cause of death in the UK between 5 and 19 years of age (Office of National Statistics, 2020). Self-harm and suicide occur as a result of complex interactions among genetic, biological and environmental factors, including sex, socioeconomic position, family dynamics (e.g. parental divorce), adverse childhood experiences (e.g. physical and emotional abuse), interpersonal difficulties, psychological and personality factors (e.g. impulsivity, hopelessness, low self-esteem, etc.) and drug and alcohol misuse (Hawton et al., 2012). Evidence from the United Kingdom, United States of America, Australia and Canada indicate that an increasing number of adolescents have been harming themselves and dying from suicide in recent years, but data from Germany, Japan, Italy and France do not follow this trend (Bould, Mars, Moran, Biddle, & Gunnell, 2019; Morgan et al., 2017; Padmanathan, Bould, Winstone, Moran, & Gunnell, 2020). In common with previous research and consistent with clinical practice in the United Kingdom and elsewhere, when referring to self-harm we have not used terms that imply degree of suicidal intent because self-reported intent is oftentimes transient and unreliable

(National Collaborating Centre for Mental Health, 2012). We use the term nonfatal self-harm to describe any self-harm event that had a nonfatal outcome, and vice versa with fatal self-harm, without making judgements about the degree of suicidal intent in the episode.

Whilst every suicide is an individual tragedy, in absolute terms it is a rare outcome in young people, which renders the study of its aetiology challenging. Studies that have examined risk factors in young persons who engage in nonfatal self-harm, a far more common behaviour, are by contrast abundant in the literature (Chen et al., 2017; Chou, Lin, Sung, & Kao, 2014). Most previous studies that have examined the antecedents of suicide in young people are so-called psychological autopsy studies, in which the prevalence of antecedents (e.g. prior history of bullying) are estimated post-mortem among ascertained suicide cases (Rodway et al., 2016). Although informative to a degree, such studies typically lacked a matched control group in which these characteristics were also examined, which means that relative risks for putative risk factors were not reported. Existing studies that have included matched controls (Brent et al., 1994; Gould et al., 1998; Portzky, Audenaert, & van Heeringen, 2009) have tended to be very small and have, therefore, not been able to establish risks associated with individual psychiatric disorders with an adequate degree of statistical precision. It is therefore unclear how strongly psychiatric illnesses are associated with suicide in young individuals, and whether the strength of these relationships is similar or different between young people who harm themselves nonfatally and those who die by suicide.

We addressed this gap in the evidence base by conducting two separate population-based nested case–control studies in which we examined risks of nonfatal self-harm and suicide associated with psychiatric illnesses diagnosed among adolescents aged 10–19 years who were registered with a general practitioner (GP) in the United Kingdom. We also examined risks associated with clinical and sociodemographic contextual information that is available in routinely collected primary care records, including psychotropic medication prescribed by GPs or practice nurses, frequency of primary care clinical contact and varying neighbourhood deprivation levels.

Method
Data source

We delineated two nested case–control studies from the Clinical Practice Research Datalink (CPRD) Aurum and GOLD datasets. These large longitudinal primary care datasets draw routinely collected information from UK general practices and are broadly representative of the national population in terms of its distributions of sex, age and ethnicity (Herrett et al., 2015; Wolf et al., 2019). In the United Kingdom, approximately 98% of the population is registered with a GP, whose purpose is to provide the first point of contact in the UK healthcare system. Information about treatments received in hospitals and in other parts of the National Health Service (NHS) and private healthcare providers are fed back to patients' primary care records. The Aurum dataset covers approximately 13.0% of the population of England, and GOLD covers roughly 6.9% of the UK population (England, Northern Ireland, Scotland and Wales). We used the April 2020 CPRD GOLD and Aurum release, which contained 18,782,246 and 31,745,393 patients respectively.

The information recorded is similar in the two CPRD datasets, although each uses a different electronic patient record system (Aurum: EMIS Web®; GOLD: Vision®). The datasets contain anonymised patient information pertaining to consultations, diagnoses, drug prescriptions and referrals to other National Health Service (NHS) providers. Clinical information is captured using Read or SNOMED codes which are clinical classification systems developed for primary care (Benson, 2012). All Aurum records, and GOLD records for a subset of patients registered at general practices in England, were linked routinely to Office for National Statistics (ONS) mortality registration records, which contain information about cause of death, and to Hospital Episode Statistics (HES), which provide information regarding patient admission or attendance at hospitals, and to the Index of Multiple Deprivation (IMD) – a composite area-level deprivation measure (Smith et al., 2015).

Population

We identified adolescents aged 10–19 years who had harmed themselves nonfatally or died during the study's observation period, 1st January 2003 to 31st December 2018. Individuals were censored on leaving the study practice or from death from another cause, whichever occurred first (Figure 1). As data are not transferred from patients migrating from one practice to another, we required that individuals had to have been registered at a CPRD practice for a minimum of 12 months before entering the study. This requirement was imposed to reduce the likelihood of including individuals with no exposure information and also to minimise the likelihood of misclassifying prevalent exposure episodes as incident. We identified suicide cases in the ONS mortality register using the following International Classification of Disease version 10 (ICD-10) codes: X60-84, Y10-34 (excluding Y33.9), Y87.0, Y87.2. X-codes are used when a coroner has ruled that the cause of death was suicide; y-codes are applied when the intent is undetermined. We included open verdicts (i.e. y-codes) in order to not underestimate the number of suicides (Linsley, Schapira, & Kelly, 2001; Neeleman & Wessely, 1997) but we did not include Y33.9 because it pertains to adjourned inquests in alleged homicide cases. Index self-harm episodes were identified in CPRD or HES, whichever was the earliest indicated date of occurrence, through clinical Read codes (Appendix S1) and ICD-10 codes respectively. We included HES data pertaining to inpatient admissions and to accident and emergency (A&E) department presentations. For the accident and emergency (A&E) data in the HES dataset, we also used the "aepatgroup" field to identify additional self-harm cases through the "Deliberate self-harm" code. The same set of ICD codes that were used to identify suicide cases were used to identify self-harm episodes in HES.

Measures

We used Read codes to identify diagnoses of attention-deficit hyperactivity disorder (ADHD), anxiety disorders, autism spectrum disorder (ASD), depression and eating disorders. Because there is evidence that general practitioners increasingly use symptom codes (e.g. "low mood") to classify
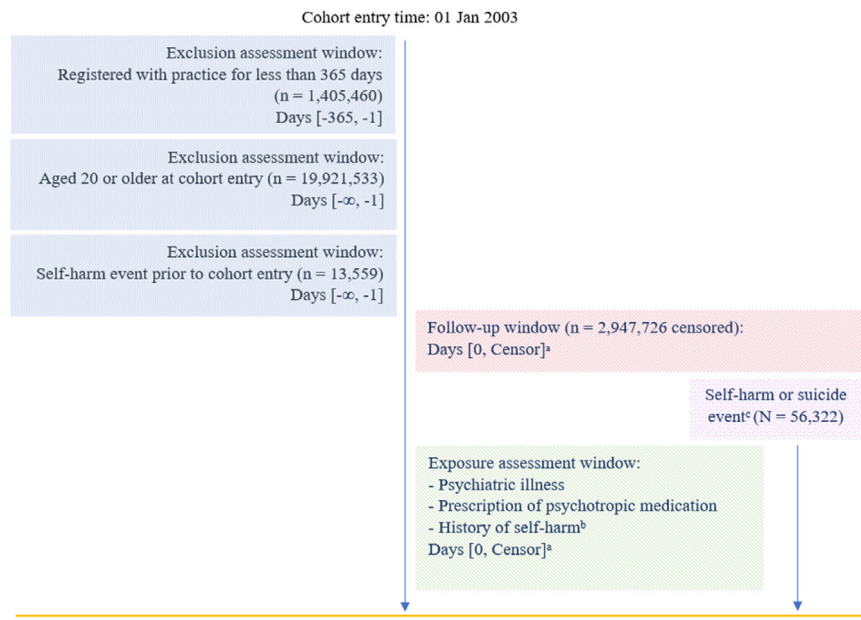
Figure 1 Graphical representation of nested case-control study design. [a]Censoring occurred on leaving the study practice or on the end of the study period, whichever occurred first. [b]Self-harm was only included as an exposure in the suicide case–control study, but not in the self-harm case–control study as incident self-harm episodes ('cases') were examined. [c]Cases were risk-set matched to up to 25 controls on age (±1 year), sex and registered practice. Figure based on template provided in Schneeweiss et al. (2019)

depression and anxiety disorders (John et al., 2015; Sarginson, Webb, Stocks, Esmail, & Garg, 2017), we included symptom codes as well as diagnostic codes (e.g. "depression") when collecting information on exposures. We also used the following ICD-10 codes to identify these psychiatric illnesses in hospital settings: F32-F34, F38 and F39 (depression); F40–43 and F93 (anxiety disorders); F50 (eating disorders); F84 (ASD); F90 (ADHD). In the suicide case–control study, we included self-harm as an exposure using the same ICD-10 and Read codes that we used to identify nonfatal self-harm episodes in the other case–control study. We created code lists for three categories of psychotropic medication: antidepressants, 'other' non-antidepressant types of psychotropic medication, including antipsychotics, anxiolytics, hypnotics, mood stabilisers and stimulants, and a miscellaneous 'any psychotropic medication' category which included all psychotropic medications. Finally, we measured deprivation through the IMD, which provides a composite indicator of deprivation based on information regarding the following seven domains: income, employment, education, skills and training, crime, barriers to housing and services, health and disability and living environment. All code lists were reviewed by three experienced clinical academics in our group: NK: a psychiatrist with specific expertise in self-harm and suicide; SG: a child and adolescent psychiatrist and CCG: a GP with specific expertise in mental health. A full list of Read codes is available in the Supporting Information.

Study design and statistical analyses

In the Aurum and GOLD datasets, we created two nested case–control studies: one in which individuals who had died by suicide were the cases, and another in which individuals with an index nonfatal self-harm episode constituted the cases. The self-harm case–control dataset that was created in Aurum was then appended to the one that was created in GOLD to produce a single case–control study dataset; this step was repeated in building the suicide case–control study dataset. This approach was taken to maximise the number of cases available for analysis and to thereby optimise statistical power. We used a

'bridging' file to identify practices that had migrated between the GOLD and Aurum datasets and removed those practices from the GOLD dataset. Each case was matched with up to 25 controls on sex, age (±1 year) and registered general practice. All suicide cases were matched to 25 controls; 55,883 of 56,008 (98.8%) self-harm cases were matched to 25 controls. The remaining 1.2% (n = 125) of self-harm cases were registered with small general practices, and therefore could not be matched to 25 controls; the mean number of matched controls per case in this small subset was 19 (range: 4–24). Through incidence density sampling, control patients were randomly sampled from the risk-set for each case (Clayton & Hills, 1993). In matching controls to cases on registered general practice, by design we accounted for the potential confounding influences of practice-level deprivation and of local and regional differences in service provision.

We fitted conditional logistic regression models to estimate relative risks as exposure odds ratios (ORs) that were inherently adjusted for by age, sex and practice-level effects in the matched design. These ORs are interpretable as hazard ratios as would have been estimated by a survival analysis conducted on the whole study cohort, in which the nested case–control study was delineated (Clayton & Hills, 1993). We examined the associations among psychiatric diagnoses, type of psychotropic medication prescribed by a GP, patterns of primary care clinical contact and area-level of deprivation and risks for nonfatal self-harm and suicide. As potential confounding influences linked with practice-level deprivation were accounted for in the matched design, the relative risks that we have reported by IMD quintile indicate the independent association with the varying deprivation levels of patients' neighbourhoods.

Results
Suicide

We identified a total of 324 Individuals who had died by suicide, of which two thirds (67%) were boys.

Suicide frequency increased linearly with age, with two thirds of suicides occurring at 17–19 years of age (Table 1). One third of cases were diagnosed with at least one of the examined psychiatric illnesses, compared to 10% of controls. The most common method of suicide was asphyxiation by hanging (68%), followed by poisoning and exposure to a substance (11%) (Table S1). Depression was by far the commonest of the examined conditions among suicide cases, accounting for over a half (54%) of all recorded diagnoses. As can be seen in Table 2, each of the diagnostic categories that we examined was associated with an elevated suicide risk, except for ASD. Among psychiatric illnesses, the association between depression and suicide was the strongest, with a 7-fold elevation in risk observed. However, prior history of self-harm was more strongly associated with suicide than any psychiatric illness: OR 19.8 95% CI 14.8–26.5. Having two or more diagnosed conditions was associated with an approximately doubled suicide risk than having a single diagnosis. Being prescribed any psychotropic drug strongly predicted suicide, especially so within a year of suicide, and particularly if the drug was an antidepressant. Most (70%) individuals presented at least once in the year preceding their death, and risk increased with rising consultation frequency. We did not observe an association between varying neighbourhood deprivation levels and suicide risk. Please see Table S1 for a distribution of suicide cases by ICD10 code.

Nonfatal self-harm

We identified 56,008 adolescents with a nonfatal self-harm episode. Compared to suicide, the sex ratio was reversed; just over two thirds (69%) of these episodes were among girls (Table 1). Individuals who self-harmed also tended to be younger, with almost two thirds (65%) of these cases having their first recorded episode below age 17 (Table 1). The most

common method of nonfatal self-harm was self-poisoning (42%) followed by cutting (12%). However, many episodes were identified via clinical codes that did describe the method (e.g. "[x]intentional self-harm – U2…") (Table S2). The proportion of self-harm cases decreased incrementally as practice-level deprivation decreased; we observed the largest proportion (28%) in the most deprived quintile and the smallest (14%) in the least deprived quintile.

As with suicide, only a third of patients had received a psychiatric diagnosis prior to their index self-harm episode. The associations between the psychiatric illnesses were of a similar magnitude (Table 3) to those that we observed in the suicide case–control set (Table 2). Thus, the rank order for strength of association (magnitude of ORs) across the array of examined conditions was almost the same for self-harm as it was for suicide, although the association between ASD and self-harm risk was statistically significant. Self-harm risk increased incrementally with rising number of prior diagnoses recorded (Table 3); risk was three times greater among adolescents with three or more diagnostic categories compared to one (OR 2.96; 95% CI 2.7–3.2). Self-harm risks among adolescents who had been prescribed psychotropic medication were substantially elevated, but these ORs were somewhat lower than the equivalent values generated from the suicide case–control study. Most (85%) individuals presented in primary care at least once in the preceding year, and self-harm risk increased with rising consultation frequency, but the increase in risk associated with each additional visit was greater compared to suicide. A positive linear relationship was observed between heightened levels of neighbourhood deprivation, independent of practice-level deprivation confounding influences. We examined the associations with diagnostic categories stratified by practice-level deprivation quintile, which revealed a considerably stronger relationship between depression and eating disorders and self-harm risk

Table 1 Distribution of sociodemographic matching variables in the suicide and nonfatal self-harm nested case–control study datasets

	Suicide case–control study				Self-harm case–control study			
	Case (N = 324)	%	Control (N = 8,100)	%	Case (N = 56,008)	%	Control (N = 1,399,356)	%
Age in years								
10–12	7	2	169	2	4,795	8	120,368	8
13–16	107	33	2,674	33	30,097	54	751,354	54
17–19	210	65	5,221	65	21,116	38	526,402	38
Gender								
Girls	108	33	2,700	33	38,558	69	963,326	69
Boys	216	67	5,400	67	17,450	31	436,030	31
Practice-level deprivation quintile								
1 (least deprived)	56	17	1,400	17	8,075	14	201,764	14
2	68	21	1,700	21	9,083	16	227,017	16
3	58	18	1,450	18	10,015	18	250,163	18
4	59	18	1,475	18	13,327	24	333,033	24
5 (most deprived)	83	26	2,075	26	15,508	28	387,379	28

Table 2 Risk factors for suicide estimated as exposure odds ratios (relative risks)

	Case (n = 324)	%	Controls (n = 8,100)	%	Odds ratios	95% CIs
Diagnostic categories						
ADHD	11	3	140	2	2.0	1.1–3.8
Anxiety disorder	38	12	324	4	3.3	2.3–4.8
ASD	7	2	96	1	1.9	0.9–4.1
Depression	77	24	365	5	7.4	5.5–9.9
Eating disorder	9	2	74	1	3.1	1.5–6.3
Any psychiatric illness	104	32	809	10	4.6	3.5–5.9
No. of diagnostic categories						
1	70	22	643	8	3.8	2.9–5.1
2 or more	34	10	166	2	7.7	5.1–11.5
History of self-harm	104	32	210	3	19.8	14.8–26.5
Any psychotropic drug						
Ever prescribed	105	32	751	9	5.1	4.0–6.6
Prescribed in past year	77	24	295	4	9.0	6.7–12.1
Antidepressant						
Ever prescribed	78	24	302	4	9.9	7.3–13.4
Prescribed in past year	64	20	152	2	16.5	11.5–23.6
Other psychotropic drug						
Ever prescribed	56	17	544	7	3.0	2.2–4.1
Prescribed in past year	33	10	173	2	5.3	3.6–7.9
Clinical contacts in past year						
None	97	30	3,853	48	1 (reference)	
1	49	15	1,308	16	1.5	1.1–2.2
2	41	13	889	11	1.9	1.3–2.8
3	27	8	575	7	2.0	1.3–3.1
4	31	10	424	5	3.2	2.1–4.9
5 or more	79	24	1,051	13	3.4	2.4–4.7
Deprivation quintile (Neighbourhood level)						
1 (least deprived)	71	22	1,679	21	1 (reference)	
2	58	18	1,689	21	0.8	0.6–1.2
3	47	14	1,474	18	0.8	0.5–1.2
4	70	22	1,586	20	1.1	0.8–1.7
5 (most deprived)	78	24	1,666	20	1.3	0.8–2.0

among adolescents registered at practices in more affluent localities (Figure 2); depression –-least deprived quintile: OR 9.6, 95% 9.1–10.2; most deprived quintile: OR 6.9 95% CI 6.6–7.2; eating disorders – least deprived quintile: OR 4.1, 95% CI 3.6–4.6; most deprived quintile: OR 2.5 95% CI 2.3–2.8. For the other three diagnostic categories examined, there was no evidence of risk being modified by practice-level deprivation. Side-by-side comparison of the ORs for the associations between the diagnostic categories and self-harm risk, generated in the GOLD and Aurum datasets separately, showed that these two sets of estimates were similar in their magnitude and equal in rank order (Table S3).

Discussion

In this nationally representative study, we conducted a unique examination of risk factors for nonfatal self-harm and suicide side-by-side in two population-based nested case–control studies among adolescents in England.

As with adults, suicide occurs more frequently among males in adolescent populations. Risk also appeared to increase with age; two thirds of individuals in our study were aged 17–19 at the time of their death. Only one third of individuals who died from suicide had received a diagnosis, and these individuals were at considerably heightened risk, especially if they had been diagnosed with depression, or if they were diagnosed with more than one illness. The relatively low proportion of suicide cases with a prior psychiatric diagnosis that we observed is similar to the 35% value reported by Rodway et al. (2016). In their examination of 145 youth suicides in England, these authors had access to a wealth of data, including healthcare records, coroner's reports, criminal justice system reports and child death investigations. The high degree of congruence between our study's result and theirs despite the use of different data sources suggests that our data accurately reflect the true proportion of young suicide cases who had been diagnosed with a psychiatric illness in these populations. We suspect that the low rate of diagnosis primarily is due to a lack of contact with mental health services, rather than an absence of psychiatric illness. Indeed, Rodway et al. (2016) reported that 32% of suicide cases had been in contact with mental health services prior to their death, which is where the majority of psychiatric diagnoses are made. Having two psychiatric diagnoses was associated with a suicide risk that was

Table 3 Risk factors for self-harm estimated as exposure odds ratios (relative risks)

	Case (n = 56,008)	%	Controls (n = 1,399,356)	%	Odds ratios	95% CIs
Diagnostic categories						
ADHD	2,082	4	16,995	1	3.3	3.1–3.4
Anxiety disorder	7,203	13	54,269	4	3.8	3.7–3.9
ASD	1,516	3	16,058	1	2.4	2.3–2.6
Depression	12,366	22	51,731	4	7.9	7.8–8.2
Eating disorder	1,820	3	15,160	1	3.1	3.0–3.2
Any psychiatric illness	19,000	34	131,208	9	5.2	5.1–5.3
No. of diagnostic categories						
1	13,790	25	110,378	8	4.5	4.4–4.6
2	4,502	8	18,811	1	8.9	8.6–9.2
3 or more	708	1	2,019	0.1	13.4	12.3–14.6
Any psychotropic drug						
Ever prescribed	14,285	26	118,454	9	4.0	3.9–4.1
Prescribed in past year	10,288	18	52,578	4	6.1	6.0–6.2
Antidepressant						
Ever prescribed	9,368	17	44,937	3	6.8	6.6–6.9
Prescribed in past year	7,553	14	27,259	2	8.7	8.4–8.9
Other psychotropic drug						
Ever prescribed	7,889	14	85,682	6	2.6	2.5–2.7
Prescribed in past year	4,443	8	29,815	2	4.0	3.8–4.1
Clinical contacts in past year						
None	8,575	15	651,359	47	1 (ref.)	
1	8,910	16	217,544	16	3.3	3.2–3.5
2	7,318	13	148,719	11	4.2	4.0–4.3
3	6,162	11	104,018	7	5.1	5.0–5.3
4	4,940	9	72,849	5	6.0	5.8–6.2
5 or more	20,103	36	204,867	14	9.3	9.0–9.6
Deprivation quintile (Neighbourhood level)						
1 (least deprived)	9,009	16	271,819	19	1 (ref.)	
2	9,289	17	261,022	19	1.2	1.1–1.2
3	10,279	18	260,193	19	1.4	1.3–1.4
4	12,282	22	280,462	20	1.6	1.6–1.7
5 (most deprived)	15,107	27	324,560	23	1.9	1.8–1.9

nearly twice as large than the risk associated with having a single diagnosis; the presence of multiple psychiatric diagnoses may reflect an increased intractability and complexity of an individual's underlying psychopathology. The strongest predictor of suicide was history of nonfatal self-harm, which is consistent with evidence in adults (Hawton et al., 2012). Being prescribed an antidepressant was also substantially associated with an elevated risk for suicide, which is likely explained by confounding by indication in our observational study design. One alternative explanation is that antidepressants may lead to 'activation', a state of hyperarousal and increased impulsivity, that may lead an individual to act on existing suicidal feelings (Luft, Lamy, DelBello, McNamara, & Strawn, 2018). The potential risk of elevated suicidality must nevertheless be weighed against the risk of not medicating these adolescents. Studies of adult populations show that individuals who do not consult their GP in the preceding year are at increased risk of suicide compared to those who consult once (Windfuhr et al., 2016). In our study, not consulting was associated with lowered risk. Whilst adults with mental illnesses may be more likely to conceal their problems, be more socially isolated and refrain from

help seeking, children and adolescents are under the care and responsibility of parents and teachers that may intervene and initiate contact with healthcare professionals. Similarly, neighbourhood deprivation was not associated with an increased risk for suicide, which is contrary to evidence from adult populations (Windfuhr et al., 2016), but one previous UK-based study of 81 youth suicides reported a distribution of individuals across deprivation quintiles that was similar to ours (Wijlaars, Nazareth, Whitaker, Evans, & Petersen, 2013). It may be that suicide in adolescence is caused primarily by severe mental illness that is independent of the risks associated with deprivation, or perhaps by some other determinants that we could not examine.

In the self-harm case–control study, individuals first self-harmed at an earlier age, and were more likely to be female, which is consistent with previous studies from the United Kingdom (Morgan et al., 2017). The strengths of association observed between psychiatric illnesses and risks for nonfatal self-harm and suicide were very similar across the array of diagnostic categories examined. Compared with existing evidence from studies of nonfatal self-harm, the relative risk estimates that we have reported were lower for most psychiatric illnesses
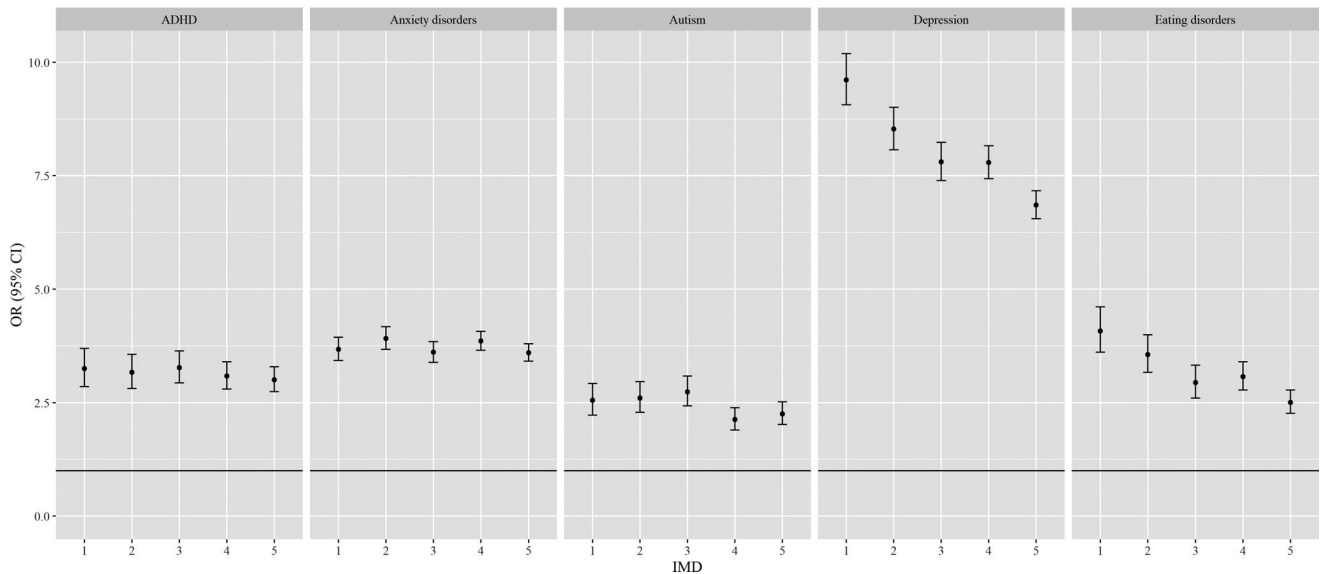
Figure 2 Association between psychiatric disorders and risk of non-fatal self-harm by deprivation quintile

compared to those reported from published studies (Chen et al., 2017; Chou et al., 2014; Fadum, Stanley, Qin, Diep, & Mehlum, 2014), although those previous estimates vary considerably because of differences in study design (e.g. choice of controls), setting population (community, primary care or hospital), definition of self-harm (e.g. self-harm with or without suicidal intent), adjustment of covariates and completeness and accuracy of patient histories. We observed an incremental increase in nonfatal self-harm risk as the number of psychiatric diagnoses increased similar to that observed in the suicide case–control study. Psychotropic medication was associated with self-harm risk, but not as strongly as in the suicide case–control study. Individuals who die by suicide, compared to those who first self-harm, will likely be afflicted by more severe mental illnesses and may, therefore, be more likely to have been issued psychotropic medication. The risk for nonfatal self-harm rose incrementally with increasing clinical consultation frequency, with the increase in risk associated with each additional consultation being greater for self-harm than for suicide. This may be explained by differing help-seeking behaviour between boys and girls. Most adolescents who died by suicide were boys, whereas those who had recorded self-harm episodes were predominantly female. Several studies show that young men are less likely to seek help for mental health problems (Lynch, Long, & Moorhead, 2018). In our study, proportionally fewer self-harm cases (15%) than suicides (30%) did not consult with a GP in the year preceding the index event, which was the refence category for our relative risk estimation. Neighbourhood deprivation was associated with an elevated risk for nonfatal self-harm, but not for suicide, which is somewhat surprising given that studies of adult populations consistently link social

deprivation with elevated suicide risk (Windfuhr et al., 2016). When we stratified our analyses of the associations between diagnostic categories and self-harm by practice-level deprivation quintile, we observed an incremental decrease in relative risk values among adolescents diagnosed with depression or eating disorders as practice-level deprivation levels increased. Because the reference group for the estimated ORs were adolescents without a diagnosis in the same practice-level deprivation quintile, this result most likely illustrates that the relative influence of depression and eating disorders on self-harm risk is less pronounced in more deprived communities where correlated psychosocial risk factors are more prevalent.

Ultimately, comparing adolescents who have harmed themselves nonfatally with those who died by suicide is inherently complicated because future suicides will be preponderant among those individuals who harm themselves nonfatally (Hawton et al., 2012). Whereas most individuals who die by suicide have a history of self-harm (Rodway et al., 2016), the majority of individuals who harm themselves nonfatally do not die from suicide at a later date (Hawton et al., 2015; Hawton & Harriss, 2008). This may also partially explain why we observed multiple similarities in risk factor profiles between the two outcomes.

Strengths and limitations

Suicide during adolescence is an extremely rare outcome, and few available datasets have adequate statistical power for conducting epidemiological studies to examine its risk factors. By combining data from two primary care datasets, we could delineate a large nested case–control study dataset to detect elevations in self-harm and suicide risk linked with specific psychiatric illnesses, primary

healthcare factors and neighbourhood level deprivation. The nature of the CPRD also provided us with a mechanism for circumventing the considerable methodological, ethical, financial and logistical challenges inherent to the recruitment of control subjects to self-harm and suicide cases (Hawton et al., 1998).

Our study was, however, limited in several ways. Despite having a relatively large number of suicide cases for examination, we were nonetheless somewhat constrained by limited statistical power for examining such a rare outcome. Thus, whereas ASD was significantly associated with elevated self-harm risk, it did not significantly predict suicide risk as only seven deaths by suicide were observed in this diagnostic category. Relative risk estimates for less prevalent exposures in our suicide case–control study were therefore less precise when compared to those generated from our self-harm case–control study. Nonetheless, we detected associations for all diagnostic categories examined except for ASD, and the rank ordering of relative risks was almost the same across the two investigated outcomes. Moreover, because we used routinely collected clinical data, we could not estimate associations for a range of other important risk factors, such as bullying or family dynamics (Rodway et al., 2016). Finally, because some self-harm episodes are recorded using free-text instead of clinical Read codes, some self-harm episodes were likely not included in our investigation (Thomas et al., 2013). Similarly, many self-harm events in the community never come to the attention of medical services, and would therefore not be captured in the electronic healthcare records that are held in the CPRD (Geulayov et al., 2018).

Implications

Primary care services are in position to intervene as most adolescents who self-harm or die from suicide have contact with services in the year preceding the initial self-harm episode. Ensuring timely access to effective treatment is a priority as psychiatric illnesses increase the risks of nonfatal self-harm and suicide. Given the detrimental developmental and socioeconomic trajectories associated with self-harm and its strong association with subsequent suicide risk, making available treatments that specifically target self-harm is also important. Evidence from a recent meta-analysis indicates the potential effectiveness of a variety of brief interventions, including 'safety planning', in which patient and clinician collaboratively develop strategies to protect against suicidal thoughts and behaviours (Doupnik et al., 2020). Whilst there currently are no effective self-harm interventions offered in primary care to young people in the United Kingdom (Mughal, Troya, Townsend, & Chew-Graham, 2019), brief interventions such as 'safety planning' could be implemented in primary care. The use of routinely collected information in primary care may also be harnessed

to identify those at risk. For example, emerging evidence from machine learning paradigms has indicated that systems trained on routinely collected clinical data may help clinicians identify individuals at elevated self-harm repetition risk (King et al., 2021; Su et al., 2020).

Self-harm and suicide are implicated with a broad range of antecedents, such as peer and youth–adult relationships (Wyman et al., 2019), bullying, bereavement, academic pressures (Rodway et al., 2016), which emphasise the need for a comprehensive approach to prevention that requires coordination among families, schools, social services and mental health professionals. Evidence from the United States shows that comprehensive community-based programmes that employ multiple strategies, including gatekeeper training, outreach and awareness initiatives and means restriction, can be effective. For instance, counties exposed to the Garrett Lee Smith Memorial Youth Suicide Prevention Program have experienced subsequent reductions in risk of dying by suicide compared to other counties where the initiative was not implemented (Godoy Garraza, Kuiper, Goldston, McKeon, & Walrath, 2019). The observed association between deprivation and self-harm risk also suggests that prevention must target underlying social determinants associated with deprivation, such as barriers to educational achievement, low income, unemployment and crime. Understanding the differing influence of deprivation and its interaction with proximal risk factors on suicide and self-harm risk in young people is a topic for future research.

Given that most children attend school, and because self-harming behaviour and suicidality in adolescence are often precipitated by events that occur in schools, they are increasingly expected to occupy a more prominent role in the identification and treatment of adolescents at heightened risk (Anderson et al., 2019; Rodway et al., 2016; Wasserman et al., 2015). There is some evidence that gatekeeper training, which involves educating teachers and students in identifying warning signs for heightened self-harm and suicide risk, can lead to enhanced knowledge and attitudes, and to increased treatment uptake (Aseltine, James, Schilling, & Glanovsky, 2007). Screening for self-harm symptoms has also been proposed and trialled in school settings, but the evidence that has emerged to date from these studies is equivocal. For instance, one study conducted in seven US high schools found that school-based screening alone successfully identified 34% of all students with mental health needs, which otherwise would have been missed (Scott et al., 2009). However, a recent meta-analysis, which included the aforementioned study by Scott et al. (2009), concluded that the "...heterogeneity of studies, the absence of randomised studies and poor outcome reporting make for a weak evidence-base that only generate tentative conclusions about the effectiveness of school-based identification

programmes" (Anderson et al., 2019). The dynamic nature of risk and the inherent high false-positive rate in predicting rare events (Hawton et al., 2012) are two fundamental impediments to effective screening. Evidence from a large multicentre trial that was conducted in schools in several European countries has showed that a universal, school-based role-playing intervention, which aimed to raise awareness about mental health and risk and protective factors for self-harm, successfully reduced the frequency of subsequent suicidal ideation, compared to schools that were not enrolled in this programme (Wasserman et al., 2015). However, a reduction in frequency of suicide attempts was not evident in either trial arm. Nevertheless, the UK government has in recognition of whole-school approaches pledged that an additional 345,000 children will have access to mental health support via school-based mental health support teams by 2022–2023 (National Health Service, 2020). Future studies will have to examine their potential in reducing risk of self-harm and suicide among adolescents in addition to clinical interventions.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Table S1. Distribution of suicide cases by ICD10 code.
Table S2. Distribution of nonfatal self-harm cases by Read code, ICD10 code and Hospital Episode Statistics Accident and Emergency patient group category.
Table S3. Demographic information and relative risks of self-harm by CPRD dataset (Aurum vs. GOLD).
Appendix S1. Read Codes.

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Key points

- Adolescent suicide has previously been examined in uncontrolled study designs, thereby precluding examination of risk factors.
- Psychiatric illness, prescription of psychotropic medication and frequent use of primary care services were associated with elevated self-harm and suicide risk.
- We noticed few noticeable differences in the risk profile of young people who first self-harm and those who die from suicide.
- Primary care services have an important role to play in intervention and prevention as most adolescents present at least once before they first self-harm or die from suicide.

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