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Risk of non-fatal self-harm and premature mortality in the three years following hospitalization in adolescents and young adults with an eating disorder: A nationwide population-based study

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Abstract

Introduction: Eating disorders (ED) are associated with high rates of suicide attempts and premature mortality. However, data in large samples of adolescents and young adults are limited. This study aims to assess the risk of self-harm and premature mortality in young people hospitalized with an ED.

Methods: Individuals aged 12 to 25 years old hospitalized in 2013–2014 in France with anorexia nervosa and/or bulimia nervosa as a primary or associated diagnosis were identified from French national health records. They were compared to two control groups with no mental disorders, and with any other mental disorder than ED. The main outcomes were any hospitalization for deliberate self-harm and mortality in the 3 years following hospitalization. Logistic regression models were used.

Results: This study included 5,452 patients hospitalized with an ED, 14,967 controls with no mental disorder, and 14,242 controls with a mental disorder other than an ED. During the three-year follow-up, 13.0% were hospitalized for deliberate self-harm (vs. 0.2 and 22.0%, respectively) and 0.8% died (vs. 0.03 and 0.4%). After adjustment, hospitalization with an ED was associated with more self-harm hospitalizations (hazard ratio [HR] = 46.0, 95% confidence interval [32.3–65.3]) and higher all-cause mortality (HR = 12.6 [4.3–37.3]) relative to youths without any mental disorder; less self-harm hospitalizations (HR = 0.5 [0.5–0.6]) but higher mortality (HR = 1.6 [1.0–2.4]) when compared to youths with any other mental disorder.

Conclusion: Young patients hospitalized with an ED are at high risk of self-harm and premature mortality. It is urgent to evaluate and implement the best strategies for post-discharge care and follow-up.

Public significance: We found that the risk of being hospitalized for a suicide attempt is 46 times higher and mortality 13 times higher than the general population in

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adolescents and young adults during the 3 years following hospitalization with an eating disorder. Eating disorders are also associated with a 1.5 higher risk of premature mortality relative to other mental disorders. This risk is particularly high in the 6 months following hospitalization. It is therefore crucial to implement careful post-discharge follow-up in patients hospitalized for eating disorders.

KEYWORDS

adolescent, anorexia nervosa, bulimia nervosa, eating disorders, epidemiology, mortality, suicide, suicide attempt, young adults

1 | INTRODUCTION

Eating disorders (ED), including anorexia nervosa (AN) and bulimia nervosa (BN), are severe psychiatric disorders. They mainly begin during adolescence and early adulthood, affect nine females for one male, and their overall prevalence is 8.6% among females and 4% among males (Solmi et al., 2021; Treasure et al., 2015). Some authors described ED as complex “metabolo-psychiatric” disorders (Duriez et al., 2019; Watson et al., 2019) as these disorders result from various biopsychosocial mechanisms. Moreover, they combine a large number of severe physical consequences affecting the whole body through undernutrition and overnutrition, and risky compensatory behaviors (purging, use of laxatives, excessive physical activity), and comorbid mental disorders including mood and anxiety disorders, alcohol and substance abuse, obsessive-compulsive disorders, neurodevelopmental or personality disorders. The financial costs of ED were estimated at \$64.7 billion in 2018–2019 in the USA (Streatfeild et al., 2021).

ED are associated with high premature mortality (Arcelus et al., 2011; Preti et al., 2011). Mortality in ED is partly due to starvation-related health problems, notably in AN, but also to suicide (Selby et al., 2010). Approximately one in five premature deaths in patients with AN is due to suicide, and suicide-related standardized mortality ratios are 18.1 in AN and 7.5 in BN (Arcelus et al., 2011). The longest follow-up study of mortality in ED to date enrolled 246 patients with a median follow up of 20 years (Franko et al., 2013). In this study, the standardized mortality ratio was 4.4 (95% CI = 2.4–7.3) for lifetime AN, and 2.3 (95% CI = 0.3–8.4) for BN with no history of AN. Among 16 deaths, the four suicide deaths were all in patients with AN. When all mental disorders are considered, both all-cause and suicide-related mortality are among the highest in AN (Chesney et al., 2014). However, data focusing on young people are much more limited. Mortality in adolescents and young adults was addressed only in one study: within a sample of 13,240 patients aged 15–24 followed for 1 year after discharge, the standardized mortality ratio was 11.5 (95% CI = 6.0–17.0) for AN and 4.1 (95% CI = 0–8.7) for BN (Hoang et al., 2014).

Self-harm is also prevalent in ED, may it be with or without intent to die. ED, even at subthreshold levels, have been associated to high rates of suicide attempt histories (Ahn et al., 2019; Forcano et al., 2009; Lipson & Sonnevile, 2020; Paul et al., 2002). A recent

large study estimated the suicide attempt prevalence at 24.9% for all subtypes of AN, 15.7% for restrictive subtype of AN, 44.1% for binge/purge subtype of AN, and 31.4% for BN (Udo et al., 2019). It is established that a history of suicide attempt is a major risk factor of subsequent suicide death (Fazel & Runeson, 2020). Individuals can also engage in non-suicidal self-injurious behaviors without suicidal intent (Kostro et al., 2014). Again, the prevalence is high: a review of the existing literature showed that the reported occurrence of non-suicidal self-injuries in ED ranged between 25.4% and 55.2% (Svirko & Hawton, 2007). The prevalence is higher in individuals with BN than in individuals with AN (Ahrén-Moonga et al., 2008; Claes et al., 2015; Cucchi et al., 2016).

Several limitations of previous studies have to be underlined. First, most studies on mortality in ED have focused on AN (Arcelus et al., 2011) and only a few studies have investigated mortality in BN (Crow et al., 2009; Franko et al., 2013). Second, estimates of the suicidal risk in adolescents and young adults are lacking even though suicide is the second leading cause of death among young people worldwide (Mokdad et al., 2016). Adolescence is also the time period corresponding to the development of the symptomatic period of ED (Solmi et al., 2021), and early care is critical for improved long-term outcomes (Treasure & Russell, 2011). Third, available data on self-harm and mortality in ED mainly come from monocentric studies in tertiary care centers in Finland (Suokas et al., 2013), Germany (Fichter & Quadflieg, 2016), England (Cliffe et al., 2020) or the USA (Franko et al., 2013), while national population-based studies are more limited (e.g. in England [Hoang et al., 2014], Denmark [Zerwas et al., 2015], and Sweden [Yao et al., 2016]). Fourth, due to the relative rarity of suicide (but also of premature mortality at this age), knowledge about prevalence and risk factors for suicide mortality during adolescence or early adulthood necessitates large sample sizes. The quantification of suicidal risk in specific populations is important for the adoption of targeted prevention and harm reduction measures (Mandelli et al., 2019). National registries give information about rare events. Large and exhaustive population-based studies are essential to provide more reliable estimates of the risk of suicide in individuals with ED. Recent data is also necessary as improved knowledge and changes in clinical practices may have altered risk factors.

The present study aims to examine mortality and severe (here defined as hospitalized) self-harm in adolescents and young adults with AN and BN using data from French national hospital registries.

The objective of this study was to assess the risks of premature mortality, including from suicide and other causes (natural, accident, undetermined), and hospitalizations for self-harm in adolescents and young adults with an ED hospitalization during the 2013–2014 period as compared to two control groups: (i) individuals with no history of ED or any mental disorders and (ii) individuals with a history of mental disorders but not ED. We hypothesized that the rates of these negative outcomes would be increased in youths with an ED when compared with both control groups.

2 | METHODS

2.1 | Study design

This is a nationwide retrospective cohort study of all adolescents and young adults aged 12–25 years and hospitalized with an AN or BN diagnostic code in mainland France between January 1, 2013, and December 31, 2014. A fixed follow-up period of 3 years following the index hospitalization was defined, as well as a retrospective period from 2008.

This study was approved by the National Committee for data protection (registration number: DR 2019-021). Patients' written consent was not required for this study.

2.2 | Data extraction

We extracted data from the French National Health data system, called *Système National des Données de Santé* (SNDS), which ensures individual linkage between various databases and anonymization of data. It covers 99% of the French population (Bezin et al., 2017). From birth to death and from all private clinics and public hospitals, these databases collect individual data for care consumption from hospital discharge abstracts (private and public hospitals, medicine, surgery and psychiatric departments), healthcare consultations, reimbursed drugs (for outpatients only), chronic disease compensation, and specific causes of death. Information for the causes of death is based on death certificates completed by physicians and forensic institutes. Hospital diagnoses, chronic diseases and causes of death are recorded using the International Classification of Diseases 10th edition (ICD-10) codes.

The authors had access to all data from the French national health data system (SNDS) regarding the eligible population according to the protocol.

2.3 | Population

Young people aged 12–25 years in 2013–2014 were identified from the diagnosis codes F50.0 or F50.1 for AN, and F50.2 or F50.3 for BN as the main, related or associated diagnoses. In the rare event of a double diagnosis code (AN and BN) during the same hospital stay, we only took into account the diagnosis of AN.

The first hospitalization mentioning an ED in 2013 or 2014 was considered as the *index hospitalization*. Patients who died during the index hospitalization were excluded. This population was named “youths with ED”.

A first control group was selected from a sampling of 5% of the French 12 to 25-year-old population recorded in the French national health data system that was drawn (Figure S1). This group was composed of adolescents and young adults for whom no hospitalization mentioning an ED or any other mental disorder, or any outpatient psychotropic drug reimbursement were identified between 2008 and 2014. We considered that the “youths without any mental disorder” were included in the study on January 1, 2013.

A second comparison group (“youths with any other mental disorders”) was selected from our previous study (Jollant, Goueslard, et al., 2022) (Figure S1). It comprised all patients aged 12–24 hospitalized for a mental disorder, with the exception of any ED, in 2008–2014.

2.4 | Outcomes

Each adolescent and young adult included in this study was followed-up for a three-year period after inclusion using information obtained from the SNDS. Follow-up ranged from inclusion (index hospitalization for youths with ED or January 1, 2013, for both control groups) to December 31, 2016.

Youths with ED were followed-up for a median of 1096 days from the day of inclusion.

The first main outcome of interest was any hospitalization for self-harm identified with at least one main and/or associated diagnosis code X60 to X84 recorded on the discharge abstract.

The second outcome of interest was mortality, with causes of deaths classified as suicide, accident, natural, or undetermined causes. While data for mortality were available for the whole 3-year period for all participants, causes of death were only available until December 31, 2015. Therefore, for cause of death only, the follow-up period ranges from one to 3 years depending on the date of index hospitalization.

2.5 | Confounding variables

The following variables were extracted and analyzed for all people included in the study: age (categorized as 12–15, 16–18, 19–21, or 22–25 years), sex (male/female), and past history (during the period from 2008 to inclusion date) of hospitalization for ED, self-harm, somatic disease, psychiatric disorder and/or history of outpatient drug reimbursement (according to the Anatomical Therapeutic Chemical [ATC] classification system) (See Supplemental material for all codes used). We have also extracted all hospitalizations for physical or mental disorders and outpatient drug reimbursement occurrence during the 3-year follow-up period. Of note, information relative to medication use during hospitalization is not currently available.

2.6 | Statistical analyses

Individual characteristics, somatic or psychiatric comorbidities and drug reimbursement are presented as proportions. All comparisons between youths with ED and the two control groups were first made using a Pearson χ^2 test or Fisher exact test, as appropriate. Then, survival analyses using a Cox proportional hazards regression model were performed to explore the association between a hospitalization with an ED and subsequent hospitalizations for self-harm or all-cause mortality, after adjustment for confounding variables. Individuals were followed until hospitalization for self-harm, death or the end of the follow-up period, whichever came first.

We also compared adolescents with or without a history of hospitalization for ED in the “youths with ED” group.

The results are reported as adjusted hazard ratios (HRs) and 95% confidence intervals (CI). The statistical significance threshold was set at <0.05 for all analyses.

SAS 9.4 software was used for the analyses.

3 | RESULTS

3.1 | Population characteristics

In 2013–2014, in France, 5452 youths were hospitalized with a code for AN or BN in the discharge abstract, including 4,234 with AN (77.7%) and 1374 with BN (25.2%) (Table 1). 93.6% of patients were females and 50.5% were aged 12–18 years. A fraction of 25.4% of patients had already been hospitalized for an ED between 2008 and their inclusion in the study. As expected, when compared to youths without any mental disorder, we found that youths with ED had high rates of past hospitalizations (prior to the index hospitalization) for somatic and psychiatric disorders, self-harm and psychotropic medication reimbursement (Table 1).

Details about somatic and mental disorders, in the past and during follow-up, can be found in Table S1. Almost all categories of disorders were increased in youths with ED vs. controls. The most frequent somatic disorders in the past and during follow-up among youths with ED were endocrine and digestive disorders, and injury, poisoning and certain other consequences of external causes. The most frequent comorbid mental disorders were depression, stress-related disorders, and personality disorders before and after the index hospitalization, and substance abuse during follow-up. Overall, rates of hospitalization for both mental disorders (50.3 vs. 9.4%; $p < .0001$) and somatic disorders (68.9 vs. 0.9%; $p < .0001$) during follow up were higher in youths with ED as compared to youths without any mental disorders at inclusion.

Details about the three groups are found in Table 1.

3.2 | Hospitalization for self-harm during follow-up

During follow-up, youths with ED were more likely to be hospitalized for subsequent self-harm than youths without any mental disorder

(13.0 vs. 0.2%, $p < .0001$). These rates were slightly higher in BN (19%) than in AN (14%). Self-harm occurred mostly once (59.2%) or twice (19.2%) in youths with ED (and only once in youths without any mental disorder). In youths with ED, there was not a significant difference in rates of hospitalization for self-harm at 3 years between patients with a history of hospitalization for ED and those for whom it was the first hospitalization (13.7% vs. 12.8%; $p = .4$).

The risk of hospitalization for self-harm at 3 years was increased in youths with ED as compared to youths without any mental disorder: global unadjusted HR = 61.4, 95% CI (43.5–86.6); in AN: unadjusted HR = 9.2, 95% CI (7.9–10.8); and in BN: unadjusted HR = 7.1, 95% CI (6.1–8.3). Logistic analysis with adjustment for sex, age, a history of hospitalization for self-harm (prior to index hospitalization), and somatic disorder, showed that a hospitalization for ED remained associated with subsequent admission for self-harm (adjusted HR = 46.0, 95% CI [32.3–65.3]). In this model, a history of hospitalization for somatic disorders (HR = 1.3, 95% CI [1.1–1.5]), for self-harm (HR = 3.2, 95% CI [2.7–3.9]), a younger age (under 16: HR = 1.8, 95% CI [1.4–2.2]; 16 to 18: HR = 1.4, 95% CI [1.1–1.7]) and being female (HR = 1.8, 95% CI [1.2–2.6]) significantly increased the risk of subsequent hospitalization for self-harm.

Relative to youths with any other mental disorder, youths with ED had lower unadjusted rates than (13.0 vs. 21.9%, $p < .0001$). The risk of hospitalization for self-harm at 3 years was decreased in youths with ED compared to youths with any other mental disorder: global unadjusted HR = 0.6, 95% CI (0.5–0.6); in AN: unadjusted HR = 0.6, 95% CI (0.5–0.6); and in BN: unadjusted HR = 0.9, 95% CI (0.8–1.0). Analysis showed that a hospitalization for ED was associated with less subsequent admission for self-harm (aHR = 0.5, 95% CI [0.5–0.6]), after adjustment for sex, age, a past history of hospitalization for self-harm, psychiatric disorders (excluding eating disorder), somatic disorders. In this model, a history of hospitalization for self-harm (aHR = 2.9, 95% CI [2.6–3.2]) or for somatic disorder (aHR = 1.2, 95% CI [1.1–1.3]), a younger age (under 16: aHR = 1.5, 95% CI [1.3–1.7]; 16–18: 1.3, 95% CI [1.2–1.4]; 19–21: 1.1, 95% CI [1.0–1.3]) and being a woman (2.1, 95% CI [1.7–2.5]) significantly increased the risk of subsequent hospitalization for self-harm.

The corresponding survival curves are presented in Figure 1. The median duration between the index hospitalization and the first hospitalization for self-harm was 204 days (1–1095) in patients vs. 380 days (0–1096) in youths with any other mental disorder vs. 447 (41–1093) youths without any mental disorder. Among youths with ED who were subsequently hospitalized for self-harm ($n = 708$), 11.4% of the hospitalizations for self-harm occurred within the first month following discharge from the index hospitalization, 47% during the first 6 months (183 days), and three-quarters within 15 months (457 days).

3.3 | Mortality during follow-up

Young people hospitalized with an ED were more likely to die during the 3 years of follow-up than youths without any mental disorder (0.8% vs. 0.03%, respectively; $p < .0001$), mainly from a natural cause

TABLE 1 Characteristics at time of index hospitalization and outcome variables in youths with an eating disorder in 2013–2014 in France, as compared to youths without any mental disorder and youths with any mental disorder other than an eating disorder.

	Youths with an eating disorder (n = 5452)	Youths without any mental disorder (n = 14,967)	p value	Youths with any other mental disorder (n = 14,242)	p value
	n (%)	n (%)		n (%)	
At index hospitalization					
Age (years)					
12–16	1112 (20.4)	3238 (21.6)	.003	3091 (21.7)	1
16–18	1641(30.1)	4705 (31.4)		4485 (31.5)	
19–21	1350 (24.8)	3653 (24.4)		3751 (26.3)	
22–25	1349 (24.7)	3371 (22.5)		2915 (20.5)	
Sex					
Male	350 (6.4)	982 (6.6)	1	992 (7.0)	1
Female	5102 (93.6)	13,985 (93.4)		13,250 (93.0)	
Type of eating disorder at index hospitalization					
Anorexia nervosa	4234 (77.7)	–	–	–	–
Bulimia nervosa	1374 (25.2)	–	–	–	–
Past history of hospitalization for					
Eating disorder	1385 (25.4)	0		0	
Self-harm	644 (11.8)	11 (0.1)	–	1167 (8.2)	<.0001
Mental disorder	1937 (35.5)	0	–	6667 (46.8)	<.0001
Somatic disorder	2510 (46.0)	1425 (9.5)	<.0001	4733 (30.8)	<.0001
Past psychotropic medication reimbursement	2861 (52.5)	0	–	5057 (35.5)	<.0001
During follow-up					
Self-harm hospitalization	708 (13.0)	34 (0.2)	<.0001	3137 (22.0)	<.0001
Mortality	41 (0.8)	4 (0.03)	<.0001	59 (0.4)	.003
Cause of death ^a					
Natural	18 (54.6)	^b		9 (15.3)	.003
Suicide	10 (30.3)	^b		27 (45.8)	.04
Accident	^b	^b		9 (15.3)	–
Undetermined or missing	^b	^b		13 (22.0)	–

^aData only available until December 31, 2015.

^bNot reported as it was lower than N = 5.

(0.3% vs. 0.01%) or suicide (0.2% vs. 0%). In youths with ED, 41 died including 35 with AN (0.8%) and 8 (0.6%) with BN. Among those with a known cause of death, 18 patients with an ED died from a natural cause (54.6% of deaths), and 10 from suicide (30.3%). In youths with ED, mortality was higher at 3 years for those with a history of hospitalization for ED compared to first ED hospitalization (1.2% vs. 0.6%; $p = .03$).

At 3 years, the unadjusted HR for all-cause mortality following a hospitalization with an ED was 28.2, 95% CI (10.1–78.8) relative to youths without any mental disorder, AN: unadjusted HR = 13.4, 95% CI (6.7–27.1); and in BN: unadjusted HR = 3.0, 95% CI (1.4–6.4). Analysis with adjustment for sex, age, past history of self-harm, and of somatic disorder showed that hospitalization for an ED was

associated with higher subsequent death (aHR = 12.6, 95% CI [4.3–37.3]). In this model, a history of a somatic disorder (aHR = 5.4, 95% CI [2.5–12.0]) was associated with an increased risk. The risk of death was decreased for female patients (aHR = 0.3, 95% CI [0.1–0.8]) and younger people (under 16: aHR = 0.2, 95% CI [0.1–0.8]; 16–18: aHR = 0.5, 95% CI [0.2–1.0]), while a history of self-harm was not significant.

These analyses could not be conducted for suicide separately due to the small number of suicides in the studied population.

Relative to youths with any other mental disorder, youths with an ED had higher mortality in the 3 years period following the index hospitalization (0.8 vs. 0.4%, $p = .003$). Death occurred more often from natural cause (54.6 vs. 15.3%; $p = .003$) and less often from suicide

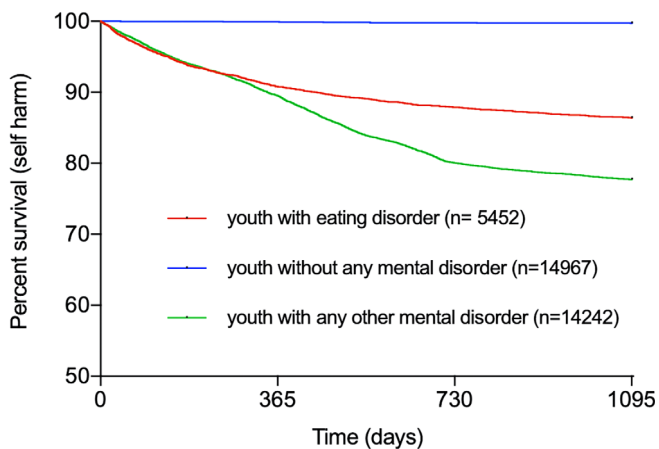


FIGURE 1 Survival curves for hospitalization for self-harm during the 3 years following index hospitalization in youths with an eating disorder in 2013–2014 in France, in youths without any mental disorders and in youths with any other mental disorders than eating disorder.

(30.3 vs. 45.8%; $p = .04$). At 3 years, the unadjusted HR for all-cause mortality following a hospitalization with an ED was 1.8, 95% CI (1.2–2.7), AN: unadjusted HR = 2.0, 95% CI (1.3–3.0); and in BN: unadjusted HR = 1.2, 95% CI (0.6–2.4). After adjustment for sex, age, past history of self-harm, psychiatric disorder, and somatic disorder, hospitalization for ED was associated with higher subsequent death (aHR = 1.6, 95% CI [1.0–2.4]). In this model, a history of hospitalization for somatic disorders (aHR = 2.7, 95% CI [1.7–4.3]) or psychiatric disorders (aHR = 1.8, 95% CI [1.1–2.9]) were associated with an increased risk of death. The risk of death was decreased for younger age (under 16: aHR = 0., 95% CI [0.1–0.5]; 16–18: aHR = 0.4, 95% CI [0.2–0.7]) while it was not significant for sex and a history of self-harm.

The corresponding survival curves are presented in Figure 2. Within 3 years of hospitalization for ED, the median duration between index hospitalization and death was 464 days (14–1081) vs. 635 days (111–1094) in youths with any other mental disorder vs. 556 (520–1041) youths without any mental disorder. Around 50% percent of deaths occurred during the first 16 months following discharge.

4 | DISCUSSION

Our study based on a nationwide cohort of more than 5400 adolescents and young adults aged 12 to 25 years suffering from an ED found significantly increased risks of hospitalization for self-harm in the 3 years following hospitalization for an ED when compared to youths without any mental disorder. However, this risk was decreased when compared to youths with any other mental disorder than ED. Moreover, premature mortality was increased in youths with ED as compared to youths without any mental disorder but also to youths hospitalized with any other mental disorders, mainly from natural causes. In youths with ED, approximately 1 in 10 were hospitalized for self-harm and 1 in a 100 died during the follow-up period. These risks remained significant when controlling for previous psychiatric

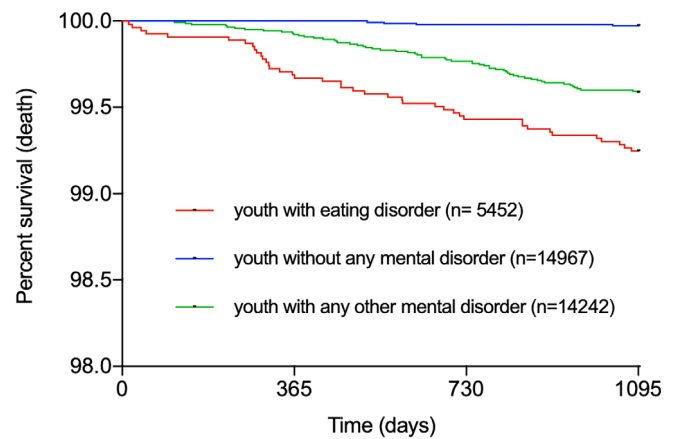


FIGURE 2 Survival curves for premature mortality during the 3 years following index hospitalization in youths with an eating disorder in 2013–2014 in France, in youths without any mental disorders and in youths with any other mental disorders than eating disorder.

and somatic disorders, which are highly frequent in anorexia and bulimia nervosa. Indeed, high rates of all categories of disorders were found in this population in both the years preceding the index hospitalization and during the three-year follow-up, confirming the particular fragility of patients with ED and the high level of comorbidities even at a young age.

The risk factors significantly associated with a risk of self-harm during follow-up in individuals hospitalized for ED were a younger age, being female, and having a history of a mental disorder or of self-harm. This aligns with previous reports in other populations (Jollant, Goueslard, et al., 2022). However, hospitalization with an ED remained a significant and major risk factor of subsequent self-harm beyond these classical risk factors. The early months after discharge is a high-risk period, and half of the hospitalizations for self-harm occurred within 6 months of discharge. Rates were slightly higher in BN than in AN. These observations concur with the existing literature according to which self-harm is prevalent in ED (Smithuis et al., 2018; Svirko & Hawton, 2007) particularly BN (Ahrén-Moonga et al., 2008; Claes & Vandereycken, 2007; Cucchi et al., 2016). The causes of this over-representation of suicidality in AN binge-eating/purging type and BN is uncertain (Leppanen et al., 2022; Rania et al., 2021). Higher levels of emotion dysregulation and impulsivity may play a role independently of depressive comorbidity.

It is worth noting, however, that a lower risk of self-harm hospitalization was found when youths with an ED were compared to youths with a hospitalization for any other mental disorder. This was found for both AN and BN. Some mental disorders found in this control group may more often lead to self-harm. We previously reported that the most frequent mental disorder categories at the time of the index hospitalization among those with a subsequent self-harm hospitalization were mood disorders, neurotic and stress-related disorders and personality disorders (Jollant, Goueslard, et al., 2022).

All-cause mortality was significantly higher in youth hospitalized with an ED than in both an age-matched sample of youths without any mental disorders and youths with any other mental disorder.

Excess mortality affects both BN and AN in comparison to youths without any mental disorder but is found only in AN in comparison to youths with any other mental disorder. Of note, a previous hospitalization for ED may also be associated with an increased risk of premature mortality suggesting that those with more hospitalization are at increased risk. Additional risk factors were a history of comorbid somatic and mental disorders, while a younger age and being a female were associated with lower mortality.

Natural causes accounted for 55% of identified causes of death in youths with an ED, and suicide for 30%. It should be highlighted here that causes of death, and notably suicide, may be underestimated in the present study (contrary to mortality) for several reasons. First, the follow-up period for this outcome could not be extended to 3 years for many patients since data were only available until December 15, 2015 at time of analyses (though all patients had a minimum of one-year follow-up for cause of death and 3 years for mortality). Second, suicide is largely miscoded worldwide, as shown by several studies, usually replaced by accidents and undetermined causes. Death from natural causes occurred in 0.3% of patients hospitalized for an ED within 16 months post-discharge in our study. This is considerably more than the general population, which at this young age was only 0.01%. Regarding suicide, our findings are in line with previous studies showing an increased risk in patients with an ED, especially AN (Arcelus et al., 2011; Cliffe et al., 2020b; Franko & Keel, 2006; Smith et al., 2018). The largest meta-analysis found that 20% of deaths in patients suffering from AN were due to suicide (Arcelus et al., 2011).

It should be highlighted that higher mortality in youths with ED was also found in the comparison with youths hospitalized for any other mental disorder. This confirms the previously reported particular excess mortality of ED among mental disorders (Hoang et al., 2014; Jollant, Goueslard, et al., 2022). This was mainly related to more natural causes, while suicide was less often found in ED as compared to patients with other mental disorders. The reported association between mortality risk and a history of hospitalization for a somatic disorder suggests a preponderant role of somatic complications related to more frequent undernutrition in subjects suffering from AN.

Our results highlight the importance of high-quality follow-up after hospitalization for ED, especially the first few months after discharge, which is a high-risk period. A similar period of risk is seen in other psychiatric conditions (Cooper et al., 2005; Hawton et al., 2015; Jollant, Goueslard, et al., 2022; Vuagnat et al., 2020). Follow-up is therefore essential to prevent relapse and maintain gains, especially in young people (Clark Bryan et al., 2022). One study showed that mortality among female patients with AN in Sweden had decreased dramatically in recent years, which may be related to the introduction of specialized care units (Lindblad et al., 2006). In France, 8% of private and public hospitals are identified as managing patients with ED and there are 70 specialized ED hospitalization units. Six administrative regions out of 13 have an “expert center” combining care, research and teaching on EDs (Document: Rapport FFAB—DGOS sur l'offre de soins TCA en France, n.d.). Moreover, new national clinical guidelines

for BN and binge eating disorders (Boulimie et hyperphagie boulimique: Repérage et éléments généraux de prise en charge, n.d.) were published in 2019. Though more still needs to be done, we hope these recent changes will curb the negative outcomes reported here. The mismatch between the supply and demand of specialist care may lead to premature discharge from inpatient care and insufficient planning of aftercare (Bulik, 2021; Walsh et al., 2021), which may have contributed to these adverse outcomes. Also, the failure of the French health service to commission psychotherapy, which is recommended as aftercare for a year by some guidelines (e.g., NICE), may have also increased the risk of these adverse consequences.

While our study has several strengths (exhaustive data, national scale, large sample size), some limitations have to be considered. First, our study does not present data for binge eating disorder because it was not well coded in the database we used. The future ICD-11 will include coding for this specific disorder. Second, our data do not allow for the analysis of subtypes of AN (binge/purge and restrictive). A switch in these behaviors has been identified as a periods of high risk (Foulon et al., 2007). Third, death by suicide remains a rare event, so making statistical inferences was not possible: with zero events in our first control group, we could not calculate a hazard ratio or perform statistical analyses. Fourth, we focused on young people and therefore excluded late-onset and chronic forms of ED. Mortality increases with age and therefore probably with the duration of the disorder. One of the few long term follow-up studies found that a long duration of illness was associated with poor psychosocial functioning and a heightened mortality risk (Franko et al., 2013). Fifth, our results have to be interpreted with caution as they are based on treated (and hospitalized) samples while EDs often go undetected in the community. A study conducted in France and involving 1493 students (mean age 20.1 SD 1.9) showed that subjects with possible signs of ED were more likely to renounce consulting a health professional (Tavolacci et al., 2020). In a Finnish cohort, only 32% of patients with ED were actually diagnosed (Silén et al., 2021). Similarly, up to 40% of people who attempt suicide do not present to hospitals, especially young people (Jollant, Hawton, et al., 2022).

In conclusion, our results confirm the high risk of hospitalized self-harm and premature mortality, mostly from natural causes, in the 3 years following a hospitalization for ED. These results suggest that transition after care should be carefully planned and delivered.

AUTHOR CONTRIBUTIONS

Philibert Duriez: Methodology; writing – original draft; writing – review and editing. **Karine Goueslard:** Conceptualization; data curation; formal analysis; methodology; writing – review and editing. **Janet Treasure:** Writing – review and editing. **Catherine Quantin:** Conceptualization; formal analysis; funding acquisition; methodology; project administration; supervision; validation; writing – review and editing. **Fabrice Jollant:** Conceptualization; funding acquisition; methodology; project administration; supervision; validation; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

This administrative data is only available through request from the French National System of Health Data ("Système National des Données de Santé," SNDS), which manages this sensitive information (<https://www.snds.gouv.fr/SNDS/Accueil>) and cannot be shared. Analysis outcomes can be obtained upon request immediately following publication for investigators whose proposed use of the data has been approved by an independent review committee ("learned intermediary") identified for this purpose. Purpose notably includes individual participant data meta-analysis. Proposals should be directed to the corresponding author.

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SUPPORTING INFORMATION

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