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Retrospective Study

# Deliberate self-harm among pediatric psychiatric inpatients in China: A single-center retrospective study

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## Abstract

### BACKGROUND

For children and adolescents, deliberate self-harm (DSH) is becoming a mental health problem of concern. Despite several studies on the prevalence and factors of DSH in the world, there is little information on DSH among children and adolescents in China. This study explores the prevalence, types, associated risk factors and tendency of DSH in pediatric psychiatric inpatients in China.

### AIM

To understand the situation of DSH among hospitalized children and adolescents and its related factors.

### METHODS

In this study, we retrospectively studied 1414 hospitalized children and adolescents with mental illness at Xiamen Mental Health Center from 2014 to 2019, extracted the demographic and clinical data of all patients, and analyzed clinical

risk factors of DSH.

## RESULTS

A total of 239 (16.90%) patients engaged in at least one type of DSH in our study. Cutting ( $n = 115$ , 48.12%) was the most common type of DSH. Females ( $n = 171$ , 71.55%) were more likely to engage in DSH than males ( $n = 68$ , 28.45%). DSH was positively associated with depressive disorders [OR = 3.845 (2.196-6.732);  $P < 0.01$ ], female [OR = 2.536 (1.815-3.542);  $P < 0.01$ ], parental marital status [OR = 5.387 (2.254-12.875);  $P < 0.01$ ] and negative family history of psychiatric illness [OR = 7.767 (2.952-20.433);  $P < 0.01$ ], but not with occupation, substance use and history of physical abuse.

## CONCLUSION

Our findings suggest that for patients with depression, females, an abnormal marriage of parents, and no history of mental illness, attention should be paid to the occurrence of DSH.

**Key Words:** Deliberate self-harm; Children; Adolescent; Psychiatric inpatients; Retrospective study

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**Core Tip:** Deliberate self-harm (DSH) is a serious global problem in children and adolescents. Studies have proved that DSH is related to many factors. This study collected a total of 1414 hospitalized case records of children and adolescents under the age of 18 from 2014 to 2019. According to the study, 16.9% of hospitalized children and adolescents had at least one kind of DSH which was associated with gender, depression, parents' marital status and so on. This suggests that we can deal with DSH in children and adolescents from the aspects of relevant influencing factors.

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## INTRODUCTION

Deliberate self-harm (DSH) is an all-embracing term for self-injurious behavior, which can range from the absence of suicidal ideation (the aim is to relieve anxiety, tension and so on) to attempted suicide[1]. In other words, DSH is an act of intentionally harming oneself, regardless of type and real intention (both suicidal and non-suicidal). But with or without suicidal intention, DSH may cause death[2]. Studies have shown that suicide is the second leading cause of death among people aged 15 to 29 around the world[3]. And DSH has attracted much attention as a strong predictor of future suicide attempts[4].

The high incidence of DSH has made it a global public health concern[5]. A previous study found that the lifetime prevalence rate of DSH was 13.7%, and the incidence rate in Western countries was higher than in non-Western countries [5]. Furthermore, the lifetime and annual prevalence of DSH in Asia was the highest among non-western countries[5]. A study in Japan reported that the annual prevalence rate of DSH was 8.4%[6]. In Singapore, two published studies showed that the DSH rates of adolescent psychiatric outpatients were 23.6% and 23.1%, respectively[7,8]. In addition, a study in Hong Kong, China found that about 23.5% of eighth graders had engaged in DSH in the past 12 months[9], but less current relevant study exists in Mainland China related to DSH among juveniles.

Typical behaviors of DSH usually include cutting (with a knife or razor), hitting, burning, scratching, biting or excessively rubbing the skin, and the ultimate goal is to cause themselves to get hurt[10]. Most of the children and adolescents who exhibit DSH behavior, in reality, do not intend to commit suicide but rather channel their negative emotional states such as anxiety and depression[9]. Maybe sometimes they engage in DSH as a way to punish themselves, generate excitement and get the attention of others. Although children and adolescents engage in DSH without suicidal thoughts, this kind of act may lead to death[11]. Moreover, self-harm behavior is easy to have a negative impact on teenagers and imitate each other[8]. People with self-harm behavior have a higher rate of suicide[12], so early identification of DSH influencing factors and intervention may prevent patients from potential suicidal behavior[7]. The study found that interpersonal relationship problems, environmental stress and academic pressure seem to be related factors for DSH among young people in Asia[13]. All of the above factors may contribute to depression, anxiety, conduct disorders and other mental disorders in young people with DSH[14]. And depression, in particular, has been found to be the most common diagnosis among teenagers with DSH[15]. Furthermore, studies from non-western countries have found that there were gender differences in DSH among adolescents, and the prevalence of girls was higher than that of boys, which was consistent with reports in Western countries[7,9,12,13]. In a word, depression, gender, age, social contact or engaged in DSH seem to be the main risk factors for the occurrence of DSH in children and adolescents[16]. At the same time, marginal personality traits or disorders are also a factor that cannot be ignored in the occurrence of DSH behavior[17].

Although there are many studies on DSH around the world, there are few studies on DSH among children and adolescents in hospitalized psychiatric patients in China. In addition, there are few studies in the world to analyze the development trend of DSH in children and adolescents in recent years. So, using a sample of children and adolescent psychiatric inpatients in China, the follow-up study described the prevalence, factors, as well as tendency and different types of DSH behaviors engaged. We investigated primary diagnosis in the prevalence of DSH and explored whether gender, age, substance use, census registration, occupation, parental marital status, family history of psychiatric illness, and history of physical abuse were predictive of DSH. This study expands existing knowledge about the clinical phenomenology in China and allows us to observe the trends of DSH over time.

## MATERIALS AND METHODS

### *Participants and procedures*

A retrospective study was conducted on inpatients with mental illness among children and adolescents in Xiamen Xianyue Hospital, Xiamen Mental Health Center in Fujian, China. Xianyue hospital is a Grade III level A hospital of psychiatric hospital in China, which take on important tasks of medical treatments, teaching and scientific research in Fujian Province and its surrounding provinces and cities, and receive psychiatric patients from all over the country. With the help of the hospital information department, we obtained information of 1414 inpatients under the age of 18 between January 2014 to December 2019. This study was approved by the Ethics Committee of Xiamen Xianyue Hospital (Xiamen, China) and all methods were performed in accordance with the relevant guidelines and regulations. According to the purpose of our study, two professional psychiatrists designed a standardized data collection table to collect basic demographic data and clinical characteristics of patient. And Epidata3.1 was used to record, manage and check the data.

Demographic and clinical characteristics (*e.g.*, age, gender, family history, parental marital status, bad habits) were collected in the clinical history. In order to avoid the error caused by subjective judgment of researchers, statistics were made only based on the records of cases. DSH was defined as the deliberate destruction of one's own body tissue, with or without suicidal intent in this article. Parents were defined as biological parents, and the abnormal marriages of the parents include separation, divorce, remarriage and orphans. The patient's bad habits include smoking, alcohol use, substance dependence and gambling. The data needed to be collected but not recorded in detail in the case is recorded as unknown. In the sample, there were more than 20 main diagnosis types, and some of them had a small proportion or only a few cases in the total sample size, which increased the interference factors of statistical analysis. So on the premise of not affecting the analysis results, these main diagnoses were divided into five groups, and the grouping was as follows: Depression, bipolar disorder, schizophrenia and other primary psychiatric disorder (*e.g.*, schizoaffective disorder, delusional disorder, acute and transient psychotic disorder), neurodevelopmental disorder (*e.g.*, autism, attention deficit hyperactive disorder, tic disorder), other diseases (*e.g.*, anxiety disorder, obsessive-compulsive disorder and organic psychosis). All patients were diagnosed according to ICD-10.

### *Statistical analysis*

The data were analyzed by IBM SPSS Statistics 22.0 software. First of all, descriptive statistics were used to analyze basic demographic data and clinical variables. Then chi-square test and Fisher's exact test were used to compare the demographic and clinical variables between the DSH group and the non-DSH group, and the candidate risk factors for DSH were screened. Finally, multiple Logistic regression analysis was used to further analyze the statistically significant risk factors to test the correlation between the variables and DSH. Inputting variables into the model in turn, selecting the model that is most suitable for hybrid variable control, and identifying the optimal risk factors. We considered *P* value less than 0.05 to be statistically significant.

## RESULTS

### *The demographics and clinical characteristics*

The socio-demographic and clinical characteristics of all samples are shown in Table 1. As shown in Table 1, the number of hospitalized children and adolescents increased year by year from 2014 to 2019. Among the children and adolescents with DSH, female accounted for 71.55%, diagnosed with depression accounted for 63.18%, and 79.50% were students. Most patients with DSH lived with their biological parents (92.05%) and 95.82% had a negative family history of psychiatric illness. Only 1.67% patients who emerged in DSH behavior had a history of physical abuse.

### *Analysis of risk factors related to DSH*

Table 2 analyzes the risk factors of DSH by chi-square test or fisher's accurate test. The results showed that DSH behavior was significantly associated with main diagnosis ( $P < 0.01$ ), gender ( $P < 0.01$ ), occupation ( $P < 0.01$ ), marital status of parents ( $P = 0.02$ ), family history of psychiatric illness ( $P < 0.01$ ) and history of physical abuse ( $P < 0.01$ ). We found no association between DSH and age ( $P = 0.0137$ ), census registration ( $P = 0.405$ ) and bad habits ( $P = 0.184$ ).

### *Further analysis of risk factors related to DSH*

Logical regression analysis is performed based on the results shown in Table 3. Multiple regression analysis revealed four factors related to DSH: Depressive disorders [OR = 3.845 (2.196-6.732);  $P < 0.01$ ], female gender [OR = 2.536 (1.815-3.542);



**Table 1** Sample demographic and clinical characteristics (*n* = 1414)

Characteristic	<i>n</i> (%)
Year	
2014	135 (9.55)
2015	150 (10.61)
2016	184 (13.01)
2017	208 (14.71)
2018	315 (22.28)
2019	422 (29.84)
Main diagnosis	
Depression	427 (30.20)
Bipolar disorder	188 (13.30)
Schizophrenia or other primary psychotic disorder	366 (25.88)
Neurodevelopmental disorder	275 (19.45)
Others	158 (11.17)
Gender	
Male	721 (50.99)
Female	693 (49.01)
Age (yr)	
≤ 12	144 (10.18)
13-18	1270 (89.82)
Census registration	
Rural	890 (62.94)
City	524 (37.06)
Occupation	
Student	970 (68.60)
Employed	17 (1.20)
Not working or studying	427 (30.20)
Marital status of parents	
Normal	1354 (95.76)
Abnormal	60 (4.24)
Family history of psychiatric illness	
Positive	172 (12.16)
Negative	1215 (85.93)
Unknown	27 (1.91)
Substance use	
Yes	26 (1.84)
No	1388 (98.16)
History of physical abuse	
Yes	9 (0.64)
No	1384 (97.88)
Unknown	21 (1.49)
DSH	



Yes	239 (16.90)
No	1175 (83.10)
Types of DSH	
Cutting	115 (48.12)
Scratching	14 (5.86)
Hitting	36 (15.06)
Puncturing	4 (1.67)
Swallow medications	3 (1.26)
Refusing foods	16 (6.69)
Biting	9 (3.77)
Multiple ways	21 (8.79)
Others	6 (2.51)
Unknown	15 (6.28)

DSH: Deliberate self-harm.

$P < 0.01$ ], parental marital status [OR = 5.387 (2.254-12.875);  $P < 0.01$ ] and negative family history of psychiatric illness [OR = 7.767 (2.952-20.433);  $P < 0.01$ ], but not with occupation, substance use. There were no statistically significant differences in age, census registration, and history of physical abuse among patients with or without DSH.

### The trend of DSH from 2014 to 2019

Finally, it is worth emphasizing that from 2014 to 2019, the number of patients in the inpatient department of children and adolescents showed a trend of gradual increase, and the number of inpatients reached a six-year high in 2019. At the same time, the proportion of patients with DSH behavior basically showed an upward trend, although there was a fluctuation in the ratio from 2015 to 2016 (Figure 1).

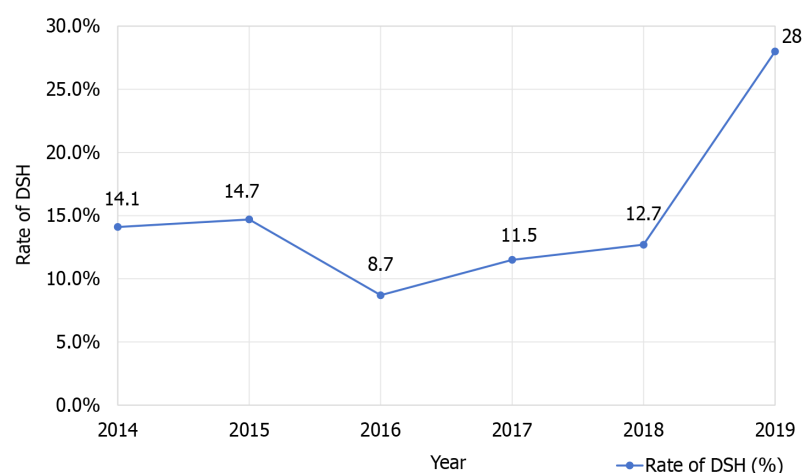


Figure 1 Rate of deliberate self-harm from 2014 to 2019. DSH: Deliberate self-harm.

## DISCUSSION

DSH can cause irreparable damage to the body and even cause accidental death. It is undeniable that people who have committed DSH have a higher risk and tendency to commit suicide[12,18]. Compared with adults, children and adolescents are at high risk of DSH behavior, and they are more vulnerable to imitating DSH to cope with challenges or to obtain a sense of identity from their peer group[19,20]. The primary purpose of this study was to verify the previous research results and further improve the research content. This research studied the DSH behavior among inpatient children and adolescents in China from 2014 to 2019, and explored the influencing factors, incidence and development trend of DSH. This will help to improve the cognition of DSH behavior, understand the vulnerable group of DSH, comprehend the psychology of patients involved in self-harm, then design targeted preventive measures and intervention means for DSH and its related risk factors.

**Table 2 Risk factors of children and adolescents psychiatric in patients with and without deliberate self-harm (*n* = 1414)**

Factors	No. of patients (%)		$\chi^2/Z$	P value
	With DSH	Without DSH		
Main diseases			157.308	< 0.001
Depression	151 (35.36)	276 (64.64)		
Bipolar disorder	4 (2.13)	184 (97.87)		
Schizophrenia or other primary psychotic disorder	33 (9.02)	333 (90.98)		
Neurodevelopmental disorder	34 (12.36)	241 (87.64)		
Others	17 (10.76)	141 (89.24)		
Gender			58.463	< 0.001
Male	68 (9.43)	653 (90.57)		
Female	171 (24.68)	522 (75.32)		
Age (yr)			2.212	0.137
≤12	18 (12.50)	126 (87.50)		
13-18	221 (17.40)	1049 (82.60)		
Census registration			-	0.405 <sup>1</sup>
Rural	151 (16.97)	739 (83.03)		
City	88 (16.79)	436 (83.21)		
Occupation			16.193	< 0.001
Student	190 (19.59)	780 (80.41)		
Employed	1 (5.88)	16 (94.12)		
Not working or studying	48 (11.24)	379 (88.76)		
Marital status of parents			9.725	0.002
Normal	220 (16.25)	1134 (83.76)		
Abnormal	19 (31.67)	41 (68.33)		
Family history of psychiatric illness			27.310	< 0.001
Positive	5 (2.91)	167 (97.09)		
Negative	229 (18.85)	986 (81.15)		
Unknown	5 (18.52)	22 (81.48)		
Substance use			-	0.184 <sup>1</sup>
Yes	7 (26.92)	19 (73.08)		
No	232 (16.71)	1156 (83.29)		
History of physical abuse			-	0.033 <sup>1</sup>
Yes	4 (44.44)	5 (55.56)		
No	234 (16.91)	1150 (83.09)		
Unknown	1 (4.76)	20 (95.24)		

<sup>1</sup>Fisher's exact test.

DSH: Deliberate self-harm.

Among the 1,414 samples in this study, DSH patients accounted for 16.9%, which was lower than the previous study in Singapore and western countries[8,11,21]. The difference in ratio may due to the way of obtaining the sample and the amount of sample size. After all, patients with DSH usually go to the out-patient clinic first, and then decide whether to be hospitalized for further treatment after evaluation. So, in theory, there will be more outpatients than inpatients. In our study, the samples were all from inpatients while the previous research samples were from outpatients, communities or schools, which may be the main reason for the difference. But there is not much difference in the research method and

**Table 3 Multivariate logistic regression analysis of deliberate self-harm behavior**

Factors	P value	OR (95%CI)
Main diseases		
Depression	< 0.001	3.845 (2.196-6.732)
Schizophrenia or other primary psychotic disorder	0.356	0.738 (0.387-1.407)
Bipolar disorder	0.004	0.188 (0.060-0.589)
Neurodevelopmental disorder	0.453	1.283 (0.669-2.460)
Others		1.000
Gender		
Male		1.000
Female	< 0.001	2.536 (1.815-3.542)
Occupation		
Student	0.091	1.398 (0.948-2.063)
Employed	0.847	1.233 (0.146-10.389)
Not working or studying		1.000
Marital status of parents		
Normal		1.000
Abnormal	< 0.001	5.387 (2.254-12.875)
Family history of psychiatric illness		
Yes		1.000
No	< 0.001	7.767 (2.952-20.433)
Unknown	< 0.001	54.444 (5.758-514.780)
History of physical abuse		
No		1.000
Yes	0.088	5.296 (0.783-35.846)
Unknown	0.005	0.020 (0.001-0.312)

content in essence.

Our results are consistent with those of previous studies, suggesting that patients with depression are more likely to conduct DSH behavior[8,11]. It also confirms the findings of some countries in the West and Asia that depression is a high risk factor for DSH[22]. The associations between DSH and gender factors reflected the results of previously published researches[11,23,24], that is, women are more likely to participate in DSH. Our research found that female were about 2.5 times more likely to engage in DSH than males. It suggests that DSH has a stronger association with female. The gender differences in the prevalence of depression and DSH behavior reflect the different responses and coping styles of male and women in the face of emotional distress[8]. As we all know, males are more likely to take external measures to tackle challenges when they run into trouble and setback, while women are more likely to choose internal coping styles of self-suppression, such as self-harm. There is a strong correlation between anxiety and DSH in most studies, but the number of patients who were mainly diagnosed as anxiety disorder in this study was relatively small, so anxiety disorder was not regarded as a separate factor.

In a study conducted in Singapore, no relationship was found between parents' marital status and the occurrence of DSH, and it was speculated that the DSH behavior might be related to family function and quality[11]. Different from the research of Singapore, the occurrence of DSH was associated with the marital status of the parents in this paper. We found the incidence of DSH among children and adolescents whose parents are in normal marriages is lower than that of their parents in abnormal marriages. It is well known that poor family structure (*i.e.*, not living with both biological parents and not having married parents) is commonly associated with depression[25,26], so it's not hard to explain why children from abnormally married families are more likely to conduct DSH behavior. Therefore, parents are advised to manage their own marriages as well as possible to give their children a complete family. The other difference in our study, children and adolescents with no family history of psychiatric illness have a higher incidence of DSH, which is completely different from previous studies. There is a possible explanation: under the influence of traditional Chinese cultural values and beliefs, Chinese people generally believe that "Mianzi" is very important. "Mianzi" represents the social class and dignity of the Chinese social stratum[27]. Unfortunately, the diagnosis of mental illness can cause the "loss of face" to patients and their families. for the sake of preserving the "face", patients and their families are more likely

to conceal the family history of psychiatric illness[28]. Our findings indicated that it is necessary to improve parents' awareness of their children's mental health and enhance their ability to judge abnormal emotion or behavior so as to identify their children's abnormalities timely and accurately and prevent the occurrence of DSH as far as possible.

There was no correlation between DSH and substance uses (*i.e.*, smoking, alcohol use, substance dependence and gambling) in our study, which is different from some studies[8,11,29]. Three possible reasons are as follows. First, children and adolescents are a special group, so they have less chance to develop bad habits during the school year. Next, the patients may deliberately conceal his true information for some reason. Last, under the influence of Chinese traditional culture, females are not allowed to develop substance uses such as smoking and drinking. And DSH behaviors mostly occur in women, which may lead to a low incidence of substance uses in our sample. Therefore, the correlation between DSH occurrence and substance uses cannot be verified. We also studied the relationship between DSH with the age. One researches have shown that the ages between 13 and 18 are the peak of the beginning and end of self-harm, and most studies about DSH mainly focus on adolescents between 12 and 18 years old[30]. But in our study, all children and adolescents under 18 years old were included. And the results showed that there was no statistical significance in the DSH behavior of children under 12 years old and adolescents between 13 and 18 years old, indicating that children and adolescents are equally likely to participate in DSH, and children are also a group that cannot be ignored.

Physical abuse has been proved to be one of the main risk factors for the occurrence of DSH, which has also been verified in a number of literatures[31]. But, the history of physical abuse has not been confirmed to be related to the DSH behavior in this study. Abuse has traditionally been understood as the physical or/and psychological or/and sexual harm inflicted on the victim by others[32,33], without defining the problem whether the victim has a self-abuse. The DSH shown in this study is a kind of self-abuse behavior, and the relationship between DSH and being abused is not clear at present. Therefore, the correlation between DSH and abuse cannot be explained. But a 2013 systematic review on the relationship between maltreatment and adolescent suicidal behavior suggested that abuse, whether sexual or physical, or emotional abuse and neglect, was associated with suicidal ideation and suicide attempts in children and adolescents[34]. A recent study showed the same conclusion: Child maltreatment in the form of emotional abuse may be distinguishing characteristics of female patients with DSH in psychiatric settings[35]. Therefore, it should be theoretically concluded that DSH is associated with physical abuse, but no such correlation was found in this study. There are two possible reasons: First, due to the Chinese people's "Mianzi", as mentioned above, "Mianzi" is very important in the eyes of Chinese people, and some private or difficult things are reluctant to reveal to others[27]. Secondly, for children and adolescents, they may think that things have already happened, it is useless to say, and it is such a private thing (which is also what we often hear children and adolescents express in clinical work). In summary, this study may not reach the same conclusion as before.

The incidence of DSH generally presented an upward trend from 2014 to 2019. However, the DSH ratio decreased from 2015 to 2016, which may be due to the staff adjustment of hospital department and hospitalization standard readjustment of the child and adolescent psychiatric department in Xianyu Hospital in 2015. But the overall upward trend especially from 2016 to 2019 indicate that the physical and mental health of children and adolescents are facing more and more serious challenges.

## CONCLUSION

Important evidence-based findings of Chinese children and adolescents with mental illness were obtained: The positive associations between DSH and female gender, depressive disorders, abnormal parental marital status and negative family history of psychiatric illness suggest that it may be helpful to refine interventions in order to target these factors. In other words, the occurrence of DSH should be controlled from the source. Because children are most exposed to the parents and teachers, families and schools need to pay as much attention as possible to help these special groups actively prevent the occurrence of DSH and take intervention measures to better promote the psychological and physical recovery of children with DSH. At present, many psychiatric hospitals have carried out individual or/and group treatment for children and adolescents who implement DSH, which is considered a better intervention means. At the same time, regular lectures and educations for parents and school teachers on children's physical and mental health are important for the prevention, detection and intervention of DSH behavior. The combination of individual, family, school, hospital and social support is particularly vital in managing children's DSH behavior. Especially within the family and school, recognized as the primary ecological environments for children and adolescents, family education and school education play pivotal roles in fostering the healthy growth of children. Family caregivers should ensure children receive ample emotional support and values, paying close attention to their psychological upbringing. Meanwhile, schools need to create a healthy and joyful learning environment, with a focus on each student's mental health. Strengthening the management of bullying and peer discrimination within schools is also essential. Child and adolescent self-harm has become a public health problem in Asia and even around the world. This study is helpful for us to understand the current situation and trend of DSH behavior in Chinese children and adolescents. However, this is far from enough; we still need to continue in-depth research, expand our understanding of the relationship between DSH and its related risk factors, and improve relevant interventions to help troubled children get rid of the harm to themselves as soon as possible. However, simply paying attention to the severity, treatment options, and intervention effect of DSH cannot improve the current status of DSH, and minimizing the risk factors associated with DSH, such as depression, is the most important goal at present. Furthermore, it has been decades since the relevant research on DSH, but whether these studies can really attract the attention of the family, society, and the country is still something to look forward to.

## ARTICLE HIGHLIGHTS

### Research background

Deliberate self-harm (DSH) in children and adolescents is a serious challenge. Many foreign studies have explored the characteristics and factors of DSH in children and adolescents, but there are few large-scale epidemiological investigations and studies on DSH in China.

### Research motivation

The focus of this study is to explore the characteristics and factors related to DSH in children and adolescents from 2014 to 2019 before the epidemic, which can help us explore ways and measures to prevent DSH in children and adolescents.

### Research objectives

The purpose of this study was to explore the risk factors associated with DSH.

### Research methods

A retrospective study was conducted on 1414 children and adolescents with mental illness who were hospitalized at Xiamen Mental Health Center from 2014 to 2019. chi-square test and Fisher's exact test were used to compare the demographic and clinical variables between the DSH group and the non-DSH group, and the candidate risk factors for DSH were screened. Then, multiple logistic regression analysis was used to analyze the statistically significant risk factors further to test the correlation between the variables and DSH. Inputting variables into the model, in turn, selecting the most suitable model for hybrid variable control and identifying the optimal risk factors.

### Research results

A total of 239 (16.90%) patients engaged in at least one type of DSH in our study. Cutting was the most common type of DSH. Females were more likely to engage in DSH than males. DSH was positively associated with depressive disorders, female, parental marital status and negative family history of psychiatric illness, but not with occupation, substance use and history of physical abuse.

### Research conclusions

The occurrence of DSH should be noted for patients with depression, women, parents with marital abnormalities, and no history of mental illness.

### Research perspectives

Future research should further explore the characteristics and influencing factors of DSH in children and adolescents, including outpatient and hospitalization, and carry out multi-center studies.

## FOOTNOTES

**Co-first authors:** Xing-Zhi Jiang and Huan-Huan Li.

**Co-corresponding authors:** Chen Wang and Zhen-Zhen Yu.

**Author contributions:** Jiang XZ contributed to the study conception and design, drafting manuscript, data analysis and interpretation, critical revision of article for important intellectual content; Li HH contributed to the critical revision of article for important intellectual content; Yu ZZ contributed to the study conception and design, critical revision of article for important intellectual content; Wang C contributed to the study conception and design, drafting manuscript, critical revision of article for important intellectual content. Jiang XZ and Li HH contributed equally to this work as co-first authors. The reasons for designating Jiang XZ and Li HH as co-first authors are threefold. First, the research was performed as a collaborative effort, and the designation of co-corresponding authorship accurately reflects the distribution of responsibilities and burdens associated with the time and effort required to complete the study and the resultant paper. This also ensures effective communication and management of post-submission matters, ultimately enhancing the paper's quality and reliability. Second, the overall research team encompassed authors with a variety of expertise and skills from different fields, and the designation of co-first authors best reflects this diversity. This also promotes the most comprehensive and in-depth examination of the research topic, ultimately enriching readers' understanding by offering various expert perspectives. Third, Jiang XZ and Li HH contributed efforts of equal substance throughout the research process. The choice of these researchers as co-first authors acknowledges and respects this equal contribution, while recognizing the spirit of teamwork and collaboration of this study. In summary, we believe that designating Jiang XZ and Li HH as co-first authors of is fitting for our manuscript as it accurately reflects our team's collaborative spirit, equal contributions, and diversity. Wang C and Yu ZZ contributed equally to this work as co-corresponding authors. The reasons for designating Wang C and Yu ZZ as co-corresponding authors are threefold. First, the research was performed as a collaborative effort, and the designation of co-corresponding authorship accurately reflects the distribution of responsibilities and burdens associated with the time and effort required to complete the study and the resultant paper. This also ensures effective communication and management of post-submission matters, ultimately enhancing the paper's quality and reliability. Second, the overall research team encompassed authors with a variety of expertise and skills from different fields, and the designation of co-corresponding authors best reflects this diversity. This also promotes the most comprehensive and in-depth examination of the research topic, ultimately enriching readers' understanding by offering various expert perspectives. Third, Wang C and Yu ZZ contributed efforts of equal substance throughout the research process. The choice of these researchers as co-corresponding authors acknowledges and respects this equal contribution, while recognizing the spirit of teamwork and collaboration of this study. In summary, we believe that

designating Wang C and Yu ZZ as co-corresponding authors of is fitting for our manuscript as it accurately reflects our team's collaborative spirit, equal contributions, and diversity.

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