


# Incidence of inpatient cases with mental disorders due to use of cannabinoids in Germany: a nationwide evaluation

Maximilian Gahr <sup>1</sup>, Julia Ziller<sup>1</sup>, Ferdinand Keller<sup>2</sup>, Rainer Muche<sup>3</sup>, Ulrich W. Preuss<sup>4</sup>, Carlos Schönfeldt-Lecuona<sup>1</sup>

<sup>1</sup> Department of Psychiatry and Psychotherapy III, University of Ulm, Ulm, Germany

<sup>2</sup> Department of Child and Adolescent Psychiatry and Psychotherapy, University of Ulm, Ulm, Germany

<sup>3</sup> Institute of Epidemiology and Medical Biometry, University of Ulm, Ulm, Germany

<sup>4</sup> Department of Psychiatry, Psychotherapy and Psychosomatics, University Hospital Halle (Saale), Halle, Germany

**Correspondence:** Maximilian Gahr, Department of Psychiatry & Psychotherapy III, University Hospital of Ulm, Leimgrubenweg 12-14, 89075 Ulm, Germany, Tel: +49 (0) 731 500 61552, Fax: +49 (0) 731 500 61412, e-mail: [maximilian.gahr@uni-ulm.de](mailto:maximilian.gahr@uni-ulm.de)

**Background:** Quantitative (e.g. increasing recreational cannabinoid use) and qualitative (e.g. increasing availability and use of synthetic cannabinoids and cannabis preparations with increased tetrahydrocannabinol content) changes in cannabinoid use may be associated with changes in the prevalence of cannabinoid-related mental and behavioural disorders and, accordingly, changes in the need for medical care. We aimed to investigate if there are changes in the number of inpatient cases (ICs) due to cannabinoid-related disorders in Germany. **Methods:** Data were obtained from the Federal Statistical Office of Germany (Destatis) and comprised type and number of hospital main diagnoses (according to ICD-10) of all ICs in Germany in the period 2000–18. Linear trend analysis of absolute and relative annual frequencies (AFs) of ICs with diagnoses related to the use of cannabinoids (DRUCs), and, as controls, alcohol-related psychiatric disorders and schizophrenia-spectrum disorders was performed. **Results:** Absolute AFs of ICs with DRUCs increased statistically significantly ( $P < 0.0001$ , trend analysis) in Germany between 2000 and 2018 and corresponding relative AFs increased considerably (4.8-fold increase when comparing 2000 and 2018). Specifically, absolute AFs of ICs with cannabinoid intoxications ( $P < 0.0001$ ), harmful use ( $P = 0.0005$ ), dependence syndrome ( $P < 0.0001$ ), withdrawal state ( $P < 0.0001$ ), psychotic disorders ( $P < 0.0001$ ) and residual and late-onset psychotic disorder ( $P < 0.0001$ ) statistically significantly increased. Absolute AFs of schizophrenia-spectrum disorders slightly, but statistically significantly decreased ( $P = 0.008$ ), and alcohol dependence did not statistically significantly change ( $P = 0.844$ ). **Conclusions:** Our evaluation demonstrates increasing numbers of ICs with mental and behavioural disorders due to use of cannabinoids in Germany and emphasizes the need for adequate prevention of such disorders.

## Introduction

Cannabis is the worldwide most commonly used drug apart from alcohol, tobacco and caffeine.<sup>1</sup> It is predominantly used for recreational purposes,<sup>2</sup> but it is also important in various spiritual contexts and traditional medicines.<sup>3</sup> In the last years, the medical use of cannabinoids, namely cannabis and some of its psychoactive ingredients, particularly tetrahydrocannabinol (THC) and cannabidiol, is increasingly studied in both physical illness<sup>4</sup> and psychiatric disorders.<sup>5</sup> The use of cannabinoids, however, is associated with several health concerns: Acute use is associated with psychiatric (e.g. anxiety, mood changes, psychotic symptoms and cognitive impairment)<sup>6,7</sup> and cardiovascular complications<sup>8</sup> and even deaths.<sup>9</sup> Chronic use is associated with respiratory diseases,<sup>7</sup> reduced (left prefrontal) cortical thickness, especially when chronic cannabis use starts in adolescence,<sup>10</sup> reduced hippocampal volume,<sup>11</sup> impaired cognitive functioning<sup>12</sup> and cannabinoid use disorders (e.g. formerly substance abuse and dependence).<sup>13</sup> The effects of cannabis use on the development and course of psychotic disorders, however, are still discussed controversially.<sup>14,15</sup> In several countries an increase in the use of cannabinoids, particularly among younger people, was observed.<sup>16–21</sup> Moreover, the respective legal frameworks have changed significantly (e.g. approval of medical cannabis<sup>22</sup> and legalization of cannabinoid use<sup>19,23</sup>). In addition, potentially more harmful cannabinoid preparations (e.g. synthetic cannabinoids<sup>6</sup> and

cannabis derived from special breedings and/or genetically engineered cannabis plants with an increased THC content<sup>24</sup>) are increasingly used. Considering the risks associated with cannabinoid use the above-mentioned quantitative and qualitative changes in cannabinoid use and changes of the legal framework may be associated with changes in the incidence of mental and behavioural disorders due to cannabinoid use and, accordingly, changes in the need for psychiatric care. However, quantitative changes of in- and/or outpatient health care procedures in patients with disorders related to the use of cannabinoids are insufficiently studied. Information on trends in health care with regard to specific disorders is necessary for planning and implementation of adequate preventive measures. While some studies on the impact of cannabinoid use on health care in the USA are available,<sup>25–29</sup> no such studies are available in Germany. Therefore, we performed a nationwide evaluation of the annual types and numbers of diagnoses of inpatient cases (ICs) in Germany.

## Methods

### Ethical approval

The study and its procedures were approved by the ethics committee of the University of Ulm.

### Period of data collection

The data evaluated in the present study were requested on 22 November 2020 and received on 27 November 2020.

### Database

The data analyzed in the present study were obtained from the Federal Statistical Office of Germany ['Statistisches Bundesamt' (Destatis)], which is a federal authority of Germany and reports to the Federal Ministry of the Interior (<https://www.destatis.de>). Destatis is responsible for collecting, processing, presenting and analysing statistical information concerning various aspects (e.g. economy, environment, society, health-related topics, etc.). The aim of Destatis is providing independent, objective and highly qualitative statistical information. In the area of health care, Destatis conducts diagnostic statistics for hospitals. Hospitals in Germany are obliged by law to annually report data on all performed inpatient treatments [according to Section 21 of the German Hospital Fees Act ('Krankenhausentgeltgesetz')]. Data products of Destatis are available to the public free of charge.

### Data

We requested absolute annual frequencies (AFs) of all (any diagnosis) and diagnosis-related ICs treated in Germany in the years 2000–18. (Electronic health care data from Destatis is available as of 2000. At the time of the database query, data referring to 2019 were not yet available.) Data regarding day-clinic, outpatient and rehabilitation treatments were not available. In the data obtained from Destatis inpatient treatments with any type of financing were considered, meaning that inpatient treatments of self-payers and inpatient treatments at the expense of statutory and private health insurance companies are included. In the data processing of Destatis, every new hospital admission that causes an inpatient treatment generates a new case. Therefore, in the present study, a 'case' was defined as every new hospital admission of a patient causing inpatient treatment (excluded: day-clinic, outpatient and rehabilitation treatments) in Germany between 2000 and 2018. Individual/case-specific or individual aggregated data were not available. The absolute AFs of all ICs (any diagnosis) and ICs with any of the following hospital main diagnoses (HMDs, i.e. the diagnosis which is the main reason for the respective inpatient treatment) of chapter V (F00–F99) of the 10th revision of The International Statistical Classification of Diseases and Related Health Problems (ICD-10) in relation to cannabinoids (ICD-10 F12), and alcohol (ICD-10 F10) as a control condition, were obtained: F1x.0: acute intoxication, F1x.1: harmful use, F1x.2: dependence syndrome, F1x.3: withdrawal state, F1x.4: withdrawal state with delirium, F1x.5: psychotic disorder, F1x.6: amnesic syndrome, F1x.7: residual and late-onset psychotic disorder, F1x.8: other mental and behavioural disorders and F12.9: unspecified mental and behavioural disorders. Alcohol-related mental and behavioural disorders were used as a control condition, as they are quantitatively the most important substance-related disorders in Germany and thus well suited as indicators for quantitative and qualitative changes of treatment approaches of substance-related disorders over time (e.g. gradual transfer from the inpatient to the outpatient setting or vice versa). In addition, the diagnostic categorization of patients with psychotic disorders and comorbid use of psychoactive substances is frequently difficult, particularly in patients with comorbid cannabinoid use, and thus these patients may be classified differently ['genuine' psychotic disorder (F20–F29) vs. intoxication (F1x.0) vs. withdrawal state with delirium (F1x.4) vs. substance-related psychotic disorder (F1x.5)]. Furthermore, diagnostic classification of patients featuring psychotic symptoms may change over time. Therefore, a further control condition was established by additionally obtaining the absolute AFs of cases with the following HMDs associated with 'psychotic symptoms': schizophrenia, schizotypal and delusional disorders

(ICD-10 F20–F29) (=schizophrenia-spectrum disorders). The annual numbers of cases of any of the HMDs related to F20–F29 were added and the thus obtained cumulative absolute AFs of schizophrenia-spectrum disorders were used for data analysis. Diagnoses related to the use of cannabinoids (DRUCs) were defined as all diagnoses of ICD-10 F12.0-9. Absolute AFs of cases with DRUCs as HMDs were calculated by adding up the absolute AFs of cases with each of the diagnoses of ICD-10 F12.0-9.

### Data analysis

Relative AFs of ICs with each of the above-mentioned HMDs were calculated based on the proportion of the absolute annual number of ICs with the respective HMD of the annual number of all cases (any HMD) and expressed as a percentage. Regression analysis assuming a linear trend was performed for the absolute AFs of cases with mental and behavioural disorders due to cannabinoid and alcohol use, and schizophrenia-spectrum disorders with statistical analysis system (SAS) 9.4 (SAS Institute Inc.). To control for the generally increasing AF of ICs in Germany an identical regression analysis was performed for the relative AFs of inpatient cases with DRUCs. Slope coefficients were considered significant at  $P < 0.05$ . For the comparison of the relative AFs of ICs with DRUCs over time, a trend line was fitted based on a linear course for explanatory purposes (see [figure 1](#)).

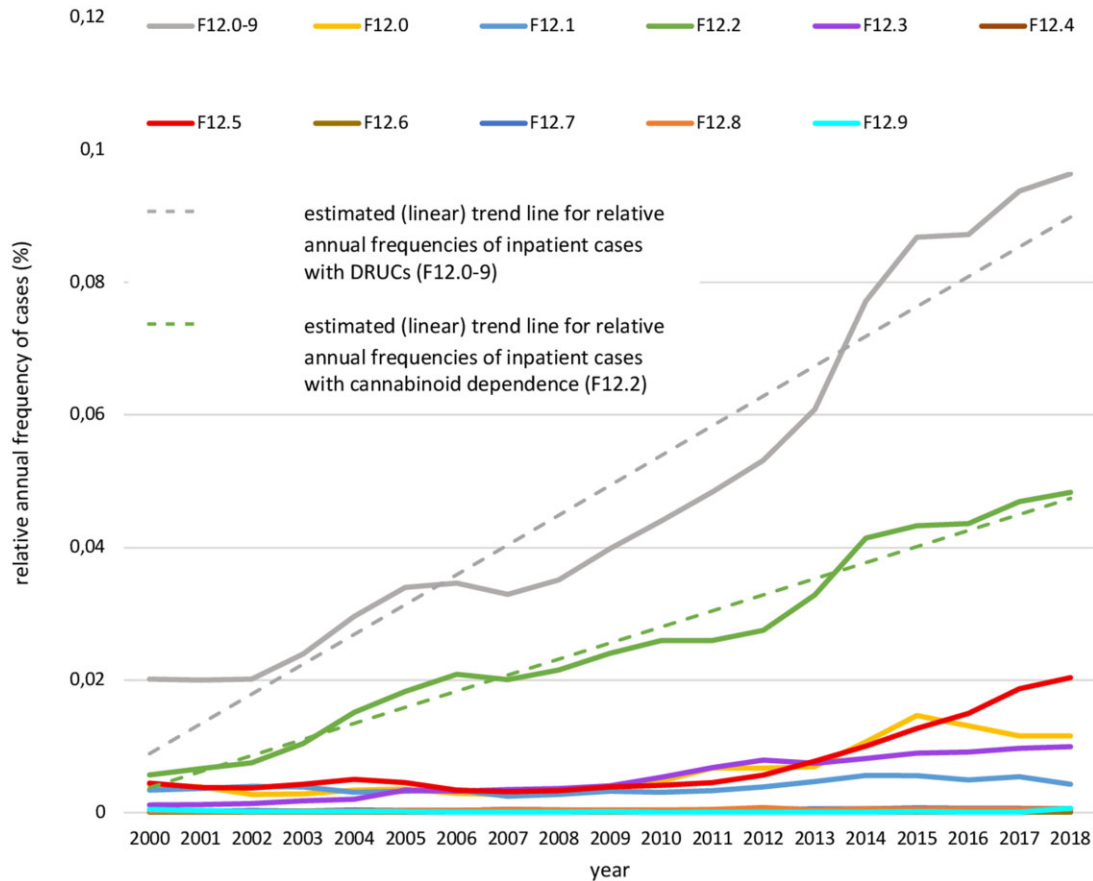
## Results

### Inpatient cases with DRUCs

Absolute (and relative) AFs of ICs with DRUCs (F12.0-9) and several other specific HMDs related to the use of cannabinoids increased during the observation period (see [tables 1 and 2](#); [figure 1](#)). There was a 4.8-fold increase of the relative AF of ICs with DRUCs when comparing 2000 and 2018. The relative AFs of cases with cannabinoid intoxications (2.8-fold increase when comparing 2000 and 2018), harmful use (1.3-fold increase), cannabinoid dependence (8.5-fold increase), cannabinoid withdrawal state (8.3-fold increase), cannabinoid-related psychotic disorders (4.5-fold increase), cannabinoid-related residual and late-onset psychotic disorders (3.0-fold increase) and other mental and behavioural disorders due to use of cannabinoids (2.0-fold increase) also increased during the observation period (see [table 2](#) and [figure 1](#)). Trend analysis revealed a statistically significant increase of relative and absolute AFs of ICs with DRUCs during 2000 and 2018 (see [table 3](#)). Specifically, the absolute AFs of ICs with cannabinoid intoxications, harmful use of cannabinoids, cannabinoid dependence, withdrawal state, psychotic disorders due to cannabinoid use, residual and late-onset psychotic disorders and other mental and behavioural disorders due to use of cannabinoids statistically significantly increased during 2000 and 2018 as shown by trend analysis. [Table 3](#) presents the detailed results of the trend analysis in regards to each evaluated disorder.

### Control conditions

Trend analysis demonstrated a small, but statistically significant increase of absolute AFs of mental and behavioural disorders due to alcohol use (ICD-10 F10.0-9), whereas the corresponding relative AFs decreased (0.9-fold decrease) when comparing 2000 and 2018 and absolute AFs of ICs with alcohol dependence did not statistically significantly change (see [table 3](#)). (Between 2000 and 2018 the range of the relative annual frequencies of all alcohol-related psychiatric disorders was 1.5–1.9%. Alcohol-related disorders (ICD-10 F10.0-9) and alcohol dependence (ICD-10 F10.2) were continuously among the most frequent disorders causing inpatient treatments in Germany between 2000 and 2018, considering both only psychiatric (any HMD of ICD-10 F0-99) and all inpatient treatments (any HMD): range of share of F10.0-9 and F10.2 between 25.4% and



**Figure 1** Relative annual frequencies of inpatient cases with hospital main diagnoses related to the use of cannabinoids (DRUCs) (ICD-10 F12.0-9).

**Table 1** Absolute and relative annual frequencies of all cases (any diagnoses) and inpatient cases with mental and behavioural disorders due to cannabinoid use

Year	All inpatient cases	Absolute (and relative frequency) of inpatient cases with DRUC, <i>n</i> (%)
2000	16 864 324	3392 (0.02)
2001	17 259 596	3452 (0.02)
2002	17 398 538	3509 (0.02)
2003	17 313 222	4151 (0.024)
2004	17 233 624	5107 (0.03)
2005	17 033 775	5789 (0.034)
2006	17 142 476	5932 (0.035)
2007	17 568 576	5790 (0.033)
2008	17 937 101	6297 (0.035)
2009	18 231 569	7251 (0.04)
2010	18 489 998	8145 (0.044)
2011	18 797 989	9099 (0.048)
2012	19 082 321	10 142 (0.053)
2013	19 249 313	11 708 (0.061)
2014	19 632 764	15 153 (0.077)
2015	19 758 261	17 148 (0.087)
2016	20 063 689	17 495 (0.087)
2017	19 952 735	18 710 (0.094)
2018	19 808 687	19 091 (0.096)

DRUC (ICD-10 F12.0-9).

30.39%, respectively, 15.06–11.0% when considering only psychiatric HMDs, and 1.861–1.511% resp. 0.819–0.655% when considering all HMDs). Trend analysis indicated a slight, but statistically significant decrease of absolute AFs of schizophrenia, schizotypal and delusional disorders (ICD-10 F20–29) (see table 3); the corresponding relative AFs also decreased when comparing 2000 and

2018 (0.8-fold decrease). Absolute AFs of all ICs (due to any HMDs) in Germany increased during the observation period (see table 1), however, also the relative AFs of ICs with DRUCs statistically significantly increased as shown by trend analysis (see table 3).

## Discussion

We evaluated AFs of HMDs of German ICs during the period 2000–18 and found a steady and statistically significant increase of the absolute and relative AFs of cases that received an inpatient treatment caused by DRUCs. In particular, the absolute AFs of cannabinoid intoxications, harmful use, dependence, withdrawal state, psychotic disorders (as well as residual and late-onset psychotic disorders and other mental and behavioural disorders due to use of cannabinoids) statistically significantly increased during the observation period. In the same period, the absolute AFs of ICs with schizophrenia, schizotypal and delusional disorders slightly, but statistically significantly decreased. Absolute AFs of ICs with alcohol-related psychiatric disorder slightly, but statistically significantly increased, whereas the corresponding relative AFs decreased and absolute AFs of alcohol dependence did not statistically significantly change. Our data do not allow to clarify these changes. However, several factors might have contributed to this development: First of all, considering that the use of cannabinoids is associated with the risk of the development of several psychiatric disorders<sup>30</sup> an increasing overall prevalence of cannabinoid use may increase the prevalence of cannabinoid-related mental and behavioural disorders. Over the last years, the prevalence of cannabinoid use has significantly increased in several countries,<sup>16,17,19,20</sup> also in Germany.<sup>18,21</sup> The reasons for this development are insufficiently understood. There is, however, some evidence suggesting that medical marijuana

Table 2 Absolute and relative annual frequencies of inpatient cases with specific mental and behavioural disorders due to cannabinoid use according to ICD-10 F

Year	Absolute (and relative) annual frequencies of inpatient cases with cannabinoid-related mental and behavioural disorders									
	F12.0 (acute intoxication), n (%)	F12.1 (harmful use), n (%)	F12.2 (dependence syndrome), n (%)	F12.3 (withdrawal state), n (%)	F12.4 (withdrawal state with delirium), n (%)	F12.5 (psychotic disorder), n (%)	F12.6 (amnestic syndrome), n (%)	F12.7 (residual and late-onset psychotic dis- order), n (%)	F12.8 (other mental and behavioural disorder), n (%)	F12.9 (unspecified mental and be- havioural dis- order), n (%)
2000	711 (0.0042)	575 (0.0034)	959 (0.0057)	195 (0.0012)	28 (0.00017)	751 (0.0045)	7 (0.00004)	39 (0.0002)	46 (0.0003)	81 (0.00048)
2001	670 (0.0039)	634 (0.0037)	1139 (0.0066)	207 (0.0012)	27 (0.00016)	656 (0.0038)	3 (0.00002)	36 (0.0002)	31 (0.0002)	49 (0.00028)
2002	479 (0.0028)	695 (0.0040)	1312 (0.0075)	242 (0.0014)	10 (0.00006)	653 (0.0038)	6 (0.00003)	54 (0.0003)	34 (0.0002)	24 (0.00014)
2003	496 (0.0029)	674 (0.0039)	1804 (0.0104)	304 (0.0018)	10 (0.00006)	745 (0.0043)	4 (0.00002)	45 (0.0003)	45 (0.0003)	24 (0.00014)
2004	592 (0.0034)	532 (0.0031)	2613 (0.0152)	355 (0.0021)	11 (0.00006)	863 (0.0050)	3 (0.00002)	67 (0.0004)	43 (0.0002)	28 (0.00016)
2005	607 (0.0036)	554 (0.0033)	3113 (0.0183)	580 (0.0034)	9 (0.00005)	778 (0.0046)	11 (0.00006)	56 (0.0003)	59 (0.0003)	22 (0.00013)
2006	503 (0.0029)	580 (0.0034)	3577 (0.0209)	553 (0.0032)	10 (0.00006)	579 (0.0034)	2 (0.00001)	55 (0.0003)	56 (0.0003)	17 (0.00010)
2007	476 (0.0027)	434 (0.0025)	3527 (0.0201)	611 (0.0035)	9 (0.00005)	555 (0.0032)	2 (0.00001)	83 (0.0005)	78 (0.0004)	15 (0.00009)
2008	515 (0.0029)	492 (0.0027)	3867 (0.0216)	654 (0.0036)	5 (0.00003)	600 (0.0033)	4 (0.00002)	71 (0.0004)	70 (0.0004)	19 (0.00011)
2009	672 (0.0037)	586 (0.0032)	4382 (0.0240)	743 (0.0041)	4 (0.00002)	704 (0.0039)	3 (0.00002)	56 (0.0003)	78 (0.0004)	23 (0.00013)
2010	883 (0.0048)	562 (0.0030)	4808 (0.0260)	986 (0.0053)	8 (0.00004)	756 (0.0041)	3 (0.00002)	63 (0.0003)	67 (0.0004)	9 (0.00005)
2011	1268 (0.0067)	622 (0.0033)	4886 (0.0260)	1276 (0.0068)	9 (0.00005)	844 (0.0045)	7 (0.00004)	75 (0.0004)	97 (0.0005)	15 (0.00008)
2012	1288 (0.0067)	734 (0.0038)	5249 (0.0275)	1514 (0.0079)	6 (0.00003)	1085 (0.0057)	4 (0.00002)	95 (0.0005)	146 (0.0008)	21 (0.00011)
2013	1340 (0.0070)	903 (0.0047)	6324 (0.0329)	1426 (0.0074)	12 (0.00006)	1499 (0.0078)	2 (0.00001)	105 (0.0005)	77 (0.0004)	20 (0.00010)
2014	2089 (0.0106)	1101 (0.0056)	8125 (0.0414)	1608 (0.0082)	13 (0.00007)	1977 (0.0101)	6 (0.00003)	117 (0.0006)	103 (0.0005)	14 (0.00007)
2015	2895 (0.0147)	1105 (0.0056)	8560 (0.0433)	1775 (0.0090)	25 (0.00013)	2507 (0.0127)	6 (0.00003)	142 (0.0007)	108 (0.0005)	25 (0.00013)
2016	2624 (0.0131)	988 (0.0049)	8748 (0.0436)	1831 (0.0091)	17 (0.00008)	3007 (0.0150)	6 (0.00003)	137 (0.0007)	114 (0.0006)	23 (0.00011)
2017	2312 (0.0116)	1085 (0.0054)	9368 (0.0470)	1936 (0.0097)	16 (0.00008)	3731 (0.0187)	3 (0.00002)	123 (0.0006)	120 (0.0006)	16 (0.00008)
2018	2288 (0.0116)	846 (0.0043)	9571 (0.0483)	1971 (0.0100)	9 (0.00005)	4034 (0.0204)	10 (0.00005)	116 (0.0006)	116 (0.0006)	130 (0.00066)

**Table 3** Linear trend analysis of absolute and relative annual frequencies of evaluated inpatient cases with specific hospital main diagnoses treated between 2000 and 2018

Evaluated data	Hospital main diagnosis (ICD-10 code)	B	P-value	Adjusted R-square	
Absolute annual frequencies	Mental and behavioural disorders due to cannabinoid use (F12.0-9)	Acute intoxication (F12.0)	125.4	<0.0001	0.715
		Harmful use (F12.1)	27.8	0.0005	0.490
		Dependence syndrome (F12.2)	500.0	<0.0001	0.961
		Withdrawal state (F12.3)	112.2	<0.0001	0.959
		Withdrawal state with delirium (F12.4)	-0.19	0.542	-0.035
	Mental and behavioural disorders due to alcohol use (F10.0-9)	Psychotic disorder (F12.5)	161.2	<0.0001	0.639
		Amnesic syndrome (F12.6)	0.06	0.611	-0.043
		Residual and late-onset psychotic disorder (F12.7)	5.4	<0.0001	0.817
		Other mental and behavioural disorders due to use of cannabinoids (F12.8)	5.2	<0.0001	0.773
		Unspecified mental and behavioural disorder (F12.9)	0.2	0.890	-0.058
		All mental and behavioural disorders due to cannabinoid use (F12.0-9)/DRUCs	937.3	<0.0001	0.903
		Dependence syndrome (F10.2)	39.4	0.844	-0.056
		All mental and behavioural disorders due to alcohol use (F10.0-9)	2654.5	0.002	0.394
Schizophrenia, schizotypal and delusional disorders (F20-F29)	-315.6	0.008	0.308		
Relative annual frequencies	All mental and behavioural disorders due to cannabinoid use (F12.0-9)/DRUCs	0.0045	<0.0001	0.911	

B, slope coefficient (unstandardized).

legislation and legalization of recreational cannabis use in several states of the USA has increased the use of cannabis (and emergencies related to the use of cannabis<sup>31</sup>) and may increase the prevalence of cannabinoid use disorders.<sup>23,32</sup> Therefore, the possibility to prescribe cannabinoids under certain conditions at the expense of the statutory health insurances in Germany as of March 2017<sup>22</sup> and the long-standing political debates in Germany about legalization/decriminalization of recreational cannabis use may have affected the attitude of the general population towards the use of cannabinoids and indirectly increased the use of cannabinoids in Germany. Secondly, synthetic cannabinoids and illicit cannabinoid preparations derived from special breedings and/or genetically engineered *Cannabis sativa* plants with higher and occasionally extremely high content of THC are increasingly used in Germany in the last decades.<sup>18</sup> Synthetic cannabinoids feature a higher affinity to the cannabinoid receptor type 1 (CB<sub>1</sub>),<sup>33</sup> are more potent<sup>34</sup> and are associated with greater toxicity<sup>35</sup> in comparison to preparations of wild *C. sativa*. Apart from an increase in cardiovascular emergencies,<sup>8</sup> also psychiatric emergencies, particularly psychoses,<sup>6,36</sup> were reported in association with the use of synthetic cannabinoids. Moreover, it is discussed that synthetic cannabinoids are associated with an increased risk of dependence.<sup>34</sup> Therefore, the increasing use of synthetic cannabinoids and cannabinoid preparations derived from special breedings and/or genetically engineered *C. sativa* plants may have contributed to the increasing AFs of ICs with DRUCs as HMDs in our evaluation.

### Limitations

Several limiting factors have to be considered when interpreting our results. Most important, we have analyzed cases and not individual data. Taken into account that chronicity and relapse are characteristics of substance use disorders, it is very likely that a proportion of the evaluated annual ICs with DRUCs refers to a lower number of individuals who were treated repeatedly in the respective year. In this context, it has to be considered that there were significant changes of the system for the remuneration of hospital services in Germany during the observation period towards a standardized remuneration system: The German Diagnosis-Related Groups system

was established in 2003 in the German hospital sector for physical illnesses, and in 2017, a similar 'flat-rate payment system' was implemented in Germany for inpatient mental health care services ('Pauschalierendes Entgeltsystem Psychiatrie und Psychosomatik'). Both hospital reimbursement systems provide implicit monetary incentives for a reduction of the duration of inpatient treatments, which may increase the annual number of inpatient treatments per individual, particularly in substance use disorders. Therefore, we cannot distinguish between an increase in repeat admissions and cases with DRUCs. Secondly, trend analyses were estimated for a specific time period (2000–18) and adding frequencies of future years may change the results. In addition, linear trend lines were not fitting well in the two control conditions, as there were some ups and downs in the course of the case frequencies. Furthermore, the absolute frequency of all ICs increased during the observation period (1.17-fold increase when comparing 2000 and 2018). Therefore, the increasing AFs of ICs with DRUCs may be interpreted as a result of an overall increase of ICs in Germany. However, the relative AFs of ICs with DRUCs also considerably and significantly increased during the observation period as shown by trend analysis, which speaks in favour of an increase of ICs with DRUCs independent of the overall increase of all ICs. Another important aspect is missing data on corresponding outpatient cases and factors that determine in- or outpatient treatment and non-initiation/absence of treatment. For instance, there are political efforts in Germany to prioritize outpatient care and to gradually transfer the quantitative focus of mental health care to the outpatient setting. Against this background the increasing relative AFs of ICs with DRUCs are unexpected. Corresponding data on outpatient cases would have allowed to further explain the trends regarding ICs found in our study. Moreover, since we did not evaluate outpatient treatment data, the increasing frequencies of ICs with DRUCs in Germany must not be considered as increasing overall numbers of patients with DRUCs. Missing case-specific data (e.g. gender, age, comorbidities, etc.) impede the interpretation of our findings. These data would have facilitated to partly explain the trends found in our study. Finally, validity and reliability of clinical diagnoses is limited,

which particularly applies to mental and behavioural disorders. Therefore, the psychiatric diagnoses evaluated in our study are ambiguous and have to be interpreted with caution.

## Conclusions

Our evaluation suggests that hospital admissions and inpatient treatments of patients with mental and behavioural disorders due to use of cannabinoids have significantly increased in Germany between 2000 and 2018. Although we are not able to clarify the causes of the observed trends, our results emphasize the need for adequate prevention of mental and behavioural disorders due to use of cannabinoids.

## Acknowledgements

We thank Destatis for providing the data evaluated in this study.

## Funding

No funding was received for this study.

**Conflicts of interest:** The authors declare that they do not have any conflicts of interest including financial, consultant, institutional and other relationships.

## Key points

- Inpatient treatments of patients with mental and behavioural disorders due to use of cannabinoids have significantly increased in Germany between 2000 and 2018.
- Possible reasons for the detected increase are changes in the legal framework concerning the use of cannabinoids, particularly 'medical cannabis', and increasing availability and use of synthetic cannabinoids and cannabis preparations with increased THC content. Changes of the German hospital reimbursement system may also play a role.
- Although we are not able to clarify the causes of the observed trends, our results emphasize the need for adequate prevention of cannabinoid-related mental and behavioural disorders.

## References

- 1 Substance Abuse and Mental Health Services Administration. *Results from the 2018 National Survey on Drug Use and Health: Detailed tables*. Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, 2019. Retrieved from: <https://www.samhsa.gov/data/>.
- 2 Osborne G, Fogel C. Understanding the motivations for recreational marijuana use among adult Canadians. *Subst Use Misuse* 2008;43:539–72; discussion 573–9, 585–7.
- 3 Mathre M. *Cannabis in Medical Practice: A Legal, Historical, and Pharmacological Overview of the Therapeutic Use of Marijuana*. Jefferson, North Carolina and London: McFarland & Company, Inc. Publishers, 1997.
- 4 Whiting P, Wolff R, Deshpande S, et al. Cannabinoids for medical use: a systematic review and meta-analysis. *JAMA* 2015;313:2456–73.
- 5 Black N, Stockings E, Campbell G, et al. Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis. *Lancet Psychiatry* 2019;6:995–1010.
- 6 Hobbs M, Kalk N, Morrison P, Stone J. Spicing it up – synthetic cannabinoid receptor agonists and psychosis – a systematic review. *Eur Neuropsychopharmacol* 2018;28:1289–304.
- 7 Hall W, Solowij N. Adverse effects of cannabis. *Lancet* 1998;352:1611–6.
- 8 Pacher P, Steffens S, Haskó G, et al. Cardiovascular effects of marijuana and synthetic cannabinoids: the good, the bad, and the ugly. *Nat Rev Cardiol* 2018;15:151–66.
- 9 Drummer O, Gerostamoulos D, Woodford N. Cannabis as a cause of death: a review. *Forensic Sci Int* 2019;298:298–306.
- 10 Albaugh M, Ottino-Gonzalez J, Sidwell A, et al. Association of cannabis use during adolescence with neurodevelopment. *JAMA Psychiatry* 2021;78:1–11.
- 11 Yücel M, Lorenzetti V, Suo C, et al. Hippocampal harms, protection and recovery following regular cannabis use. *Transl Psychiatry* 2016;6:e710.
- 12 Scott J, Slomiak S, Jones J, et al. Association of cannabis with cognitive functioning in adolescents and young adults: a systematic review and meta-analysis. *JAMA Psychiatry* 2018;75:585–95.
- 13 Hasin D, Kerridge B, Saha T, et al. Prevalence and correlates of DSM-5 cannabis use disorder, 2012–2013: findings from the National Epidemiologic Survey on Alcohol and Related Conditions-III. *Am J Psychiatry* 2016;173:588–99.
- 14 Hill M. Perspective: be clear about the real risks. *Nature* 2015;525:S14.
- 15 Murray R, Di Forti M. Cannabis and psychosis: what degree of proof do we require? *Biol Psychiatry* 2016;79:514–5.
- 16 Hasin D, Shmulewitz D, Sarvet A. Time trends in US cannabis use and cannabis use disorders overall and by sociodemographic subgroups: a narrative review and new findings. *Am J Drug Alcohol Abuse* 2019;45:623–43.
- 17 Hasin D. US epidemiology of cannabis use and associated problems. *Neuropsychopharmacology* 2018;43:195–212.
- 18 Orth B, Merkel C. In: BzGA-Forschungsbericht, editor. *Der Cannabiskonsum Jugendlicher und junger Erwachsener in Deutschland. Ergebnisse des Alkoholsurveys 2018 und Trends*. Köln: BZGA-Forschungsbericht, 2019.
- 19 Zuckermann A, Battista K, Bélanger R, et al. Trends in youth cannabis use across cannabis legalization: data from the COMPASS prospective cohort study. *Prev Med Rep* 2021;22:101351.
- 20 Hasin D, Walsh C. Trends over time in adult cannabis use: a review of recent findings. *Curr Opin Psychol* 2021;38:80–5.
- 21 Seitz N, Lochbühler K, Atzendorf J, et al. Trends in substance use and related disorders-analysis of the Epidemiological Survey of Substance Abuse 1995 to 2018. *Dtsch Arztebl Int* 2019;116:585–91.
- 22 Cremer-Schaeffer P, Knöss W. Cannabis for medical purposes-the law of March 2017 and its history. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2019;62:801–5.
- 23 O'Connell M, Levy S, Shrier LA, Harris SK. Trends in cannabis-related attitudes and behaviors among cannabis – using adolescents and young adult outpatients following medical cannabis legalization. *Subst Abuse* 2021;1–8.
- 24 Zoorob M. The frequency distribution of reported THC concentrations of legal cannabis flower products increases discontinuously around the 20% threshold in Nevada and Washington state. *J Cannabis Res* 2021;3:6.
- 25 Mazumder S, Khan MTF, Bhuiyan MAN, Kiser H. Historical trends of admitted patients by selected substances and their significant patient's level factors. *Addict Behav* 2020;109:106478.
- 26 Wipfler K, Simon T, Katz P, et al. Increase in cannabis use among adults with rheumatic diseases: results from a 2014–2019 US observational study. *Arthritis Care Res* 2021. doi: 10.1002/acr.24752.
- 27 Matson TE, Carrell DS, Bobb JF, et al. Prevalence of medical cannabis use and associated health conditions documented in electronic health records among primary care patients in Washington State. *JAMA Netw Open* 2021;4:e219375.
- 28 Matson TE, Lapham GT, Bobb JF, et al. Cannabis use, other drug use, and risk of subsequent acute care in primary care patients. *Drug Alcohol Depend* 2020;216:108227.
- 29 Lapham G, Lee A, Caldeiro R, et al. Frequency of cannabis use among primary care patients in Washington State. *J Am Board Fam Med* 2017;30:795–805.
- 30 Volkow N, Baler R, Compton W, Weiss S. Adverse health effects of marijuana use. *N Engl J Med* 2014;370:2219–27.
- 31 Wang G, Davies S, Halmo L, et al. Impact of marijuana legalization in Colorado on adolescent emergency and urgent care visits. *J Adolesc Health* 2018;63:239–41.
- 32 Yuan M, Kanellopoulos T, Kotbi N. Cannabis use and psychiatric illness in the context of medical marijuana legalization: a clinical perspective. *Gen Hosp Psychiatry* 2019;61:82–3.

- 33 Koller V, Zlabinger G, Auwärter V, et al. Toxicological profiles of selected synthetic cannabinoids showing high binding affinities to the cannabinoid receptor subtype CB1. *Arch Toxicol* 2013;87:1287–97.
- 34 Cannaert A, Storme J, Franz F, et al. Detection and activity profiling of synthetic cannabinoids and their metabolites with a newly developed bioassay. *Anal Chem* 2016;88:11476–85.
- 35 Abouchedid R, Ho JH, Hudson S, et al. Acute toxicity associated with use of 5F-derivations of synthetic cannabinoid receptor agonists with analytical confirmation. *J Med Toxicol* 2016;12:396–401.
- 36 Armenian P, Darracq M, Gevorkyan J, et al. Intoxication from the novel synthetic cannabinoids AB-PINACA and ADB-PINACA: a case series and review of the literature. *Neuropsychopharmacology* 2018;134:82–91.