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

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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. It is predominantly used for recreational purposes, but it is also important in various spiritual contexts and traditional medicines. 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 and psychiatric disorders. 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) and cardiovascular complications and even deaths. Chronic use is associated with respiratory diseases, reduced (left prefrontal) cortical thickness, especially when chronic cannabis use starts in adolescence, reduced hippocampal volume, impaired cognitive functioning and cannabinoid use disorders (e.g. formerly substance abuse and dependence). The effects of cannabis use on the development and course of psychotic disorders, however, are still discussed controversially. In several countries an increase in the use of cannabinoids, particularly among younger people, was observed. Moreover, the respective legal frameworks have changed significantly (e.g. approval of medical cannabis and legalization of cannabinoid use). In addition, potentially more harmful cannabinoid preparations (e.g. synthetic cannabinoids and cannabis derived from special breedings and/or genetically engineered cannabis plants with an increased THC content) 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, 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.
**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.

**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...
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, 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, also in Germany. The reasons for this development are insufficiently understood. There is, however, some evidence suggesting that medical marijuana...
### Table 2 Absolute und relative annual frequencies of inpatient cases with specific mental and behavioural disorders due to cannabinoid use according to ICD-10 F

| Year | 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 disorder), n (%) | F12.8 (other mental and behavioural disorder), n (%) | F12.9 (unspecified mental and behavioural disorder), 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)                     | 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)                     | 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 (0.0002)                     | 31 (0.0002)                                 |
| 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)                                 |
| 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)                                 |
| 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)                     | 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)                     | 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)                     | 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)                     | 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)                     | 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)                     | 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)                     | 9 (0.00005)                                 |
| 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)                                |
| 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)                                 |
| 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)                                |
| 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)                                |
| 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)                    | 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)                    | 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)                    | 130 (0.00066)                               |
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) and may increase the prevalence of cannabinoid use disorders. Therefore, the possibility to prescribe cannabinoids under certain conditions at the expense of the statutory health insurances in Germany as of March 2017 and the longstanding political debates in Germany about legalization/discrimination 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. Synthetic cannabinoids feature a higher affinity to the cannabinoid receptor type 1 (CB1), are more potent and are associated with greater toxicity in comparison to preparations of wild C. sativa. Apart from an increase in cardiovascular emergencies, also psychiatric emergencies, particularly psychoses, 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. 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 cases with DRUCs. Secondly, trend analyses were estimated for a specific time period (2000–18) and adding frequencies of future cases with DRUCs. 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.

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