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### ► To cite this version:

M. Lacaud, A. Leclerc, F. Marguet, M. Faisant, P. Lesueur, et al.. Impact of Covid-19 pandemic on neuro-oncology multidisciplinary tumor board in the pre-vaccine era: the Normandy experience. *Neurochirurgie*, 2023, 69 (3), pp.101429. <10.1016/j.neuchi.2023.101429>. <hal-04060458>

**HAL Id: hal-04060458**

**<https://normandie-univ.hal.science/hal-04060458v1>**

Submitted on 31 Mar 2025

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## **Impact of Covid-19 Pandemic on Neuro-Oncology Multidisciplinary Tumor Board in the Pre-Vaccine Era: the Normandy experience.**

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1     **Impact of Covid-19 Pandemic on Neuro-Oncology Multidisciplinary Tumor Board in the Pre-**  
2                                   **Vaccine Era: the Normandy experience.**

3

4     **Key words**

5     Primary brain tumor, neuro-oncology, COVID 19, Sars-Cov2, multidisciplinary tumor board

6

7     Article type: Research Article

8     Word counts: 1924 words

9     Number of Figure: 4

10    Number of Table: 2

11    Number of References: 17

12    Abstract Yes

13

14    **Data availability**

15    Data are available on request.

16

17    **Funding**

18    No funding

19

20 **HIGHLIGHTS**

- 21 • COVID19 pandemic in the pre-vaccination era did not influence the activity of  
22 multidisciplinary tumor board in neuro-oncology.
- 23 • Neurosurgical, chemotherapy, or radiation therapy activities were maintained for patients with  
24 primary malignant brain tumor.
- 25 • The proportion of patients with tumor resection was greater during the lockdown phases.

26

27 **ABSTRACT**

28 **Introduction**

29 The COVID19 pandemic had a strong impact on the healthcare system, particularly in oncology. Brain  
30 tumor are usually revealed by acute and life threatening symptoms. We wanted to evaluate the  
31 possible consequences of the COVID19 pandemic in 2020 on the activity of neuro-oncology  
32 multidisciplinary tumor board in a Normandy region (France).

33 **Methods**

34 A descriptive, retrospective, multicenter study was conducted in the four referent centers (two  
35 university hospitals and two cancer centers). The main objective was to compare the average number  
36 of neuro-oncology patients presented per multidisciplinary tumor board per week between a pre-  
37 COVID19 reference period (period 1 from December 2018 to December 2019) and the pre-vaccination  
38 period (period 2 from December 2019 to November 2020).

39 **Results**

40 Across Normandy, 1540 cases were presented in neuro-oncology multidisciplinary tumor board in  
41 2019 and 2020. No difference was observed between period 1 and 2: respectively 9.8 per week versus  
42 10.7,  $p=0.36$ . The number of cases per week also did not significantly differ during the lockdown  
43 periods: 9.1/week versus 10.4 during the non-lockdown periods,  $p=0.26$ . The only difference observed  
44 was a higher proportion of tumor resection during the lockdown periods: 81.4% ( $n=79/174$ ) versus  
45 64.5% ( $n=408/1366$ ),  $p=0.001$ .

46 **Conclusion**

47 The pre-vaccination era of the COVID19 pandemic did not impact the activity of neuro-oncology  
48 multidisciplinary tumor board in the Normandy region. The possible consequences in terms of public  
49 health (excess mortality) due to this tumor location should now be investigated.

50

51 **1. INTRODUCTION**

52 The coronavirus disease 2019 (COVID19) pandemic resulted in a significant disruption of the  
53 healthcare system worldwide specially during the pre-vaccine era. Lockdown, health distancing  
54 measures as well as the reorganization of hospital care supply particularly impacted the standard of  
55 care of non-COVID patients. Among them, the specific impact on patients suffering from cancer was  
56 significant due to potential delay in diagnosis and treatment [1]; and to recommendations for the  
57 isolation of cancer patients deemed to be at risk of severe forms[2]. This impact is particularly true for  
58 cancers covered by national screening programs screened and/or not symptomatic cancers in the initial  
59 phase, such as breast or colorectal cancers.

60 There is probably heterogeneity in access to diagnosis depending on the initial symptoms. With  
61 around 5500 to 6000 new cases per year in France[3], primary brain tumors are revealed by acute  
62 symptoms such as seizure, intracranial hypertension and neurological deficit. The initial clinical  
63 presentation usually requires rapid management in reference centers as university hospitals and cancer  
64 centers. Several guidelines in neuro-oncology adapted to the COVID19 pandemic were published back  
65 in 2020[4,5]. For example, guidelines recommended to maintain tumor resection in selected situation  
66 such as malignant tumor in young and/or fit patients.

67 Tumor resection is known to be crucial for histomolecular diagnosis[6] and for prognosis in common  
68 malignant tumor such as high-grade glioma[7]. Tumor molecular characterization is also required for  
69 adjuvant treatment decision, for example *MGMT* promoter methylation for elderly patients[8] or *IDH*  
70 mutant glioma[9].

71 The impact on neurosurgical activity along the initial phase of the COVID19 pandemic is not clearly  
72 established[10][11]. In this context, we conducted a descriptive study during the COVID19 pandemic  
73 on the activity in neuro-oncology in Normandy region (France) for BRAIN tumor diagnosis:  
74 COVIBRAIN study. The main objective was to compare the activity in neuro-oncology  
75 MultiDisciplinary Tumor board meeting (MDT) between the pre-COVID19 period and the initial  
76 phase of the COVID19 epidemic before the vaccination.

77

78 **2. PATIENTS AND METHODS**

## 79           **2.1. Study Design and Data collection**

80 COVIBRAIN study was an observational, retrospective, and multicenter study. Four centers were  
81 included: two university hospitals (Charles Nicolle University Hospital at Rouen and Côte de Nacre  
82 University Hospital at Caen) and two cancer centers (Henri Becquerel at Rouen and François Baclesse  
83 at Caen). Data were collected from institutional database between December 2018 and December  
84 2020. Patients were selected using the centralized neuro-oncology MDT. All adult patients (i.e. 18  
85 years of age or older) suffering from suspected and/or histologically confirmed primary brain tumor  
86 were included. Patients suffering from brain metastases were not included. For each presented case at  
87 the MDT the following data were collected: patient demographics (sex, age), initial or follow-up  
88 management, details on surgery procedure (biopsy or surgery), non-surgical therapeutic  
89 recommendations (radiochemotherapy, chemotherapy alone, radiotherapy alone, best supportive care,  
90 follow-up). Newly-diagnosed primary brain tumors along the studied period were collected using  
91 neuropathology data files. Non-surgical treatments were also collected: chemotherapy (molecule,  
92 number of administration) and radiotherapy. The regional incidence of SARS-CoV-2, the number of  
93 hospitalized patients in intensive care and the total number of hospitalizations due to this infection  
94 were obtained from the French national database.

## 96           **2.2. Objectives**

97 The main objective of COVIBRAIN study was to compare the number of patients presented at MDTs  
98 for a primary brain tumor from december 1st 2019 to november 30th 2020 (period 2) to a control  
99 period from december 1st 2018 to november 30th 2019 (period 1).

100 Secondary objectives were to compare: i) the number of newly-diagnosed patients for a primary brain  
101 tumor based on neuropathology cases between the period 1 and period 2; ii) the number of delivered  
102 treatments (chemotherapy and radiotherapy) between the above-mentioned periods.

103 We also conducted an exploratory analysis of the number of patients presented at MDTs between the  
104 two lockdown periods in France (from march 17th 2020 to may 11th 2020 and from october 30th 2020  
105 to december 15th 2020) compared to the non-lockdown periods.

106 Finally, we investigated the association between the number of hospitalized patients due to SarsCov2  
107 infection and the number of cases presented in neuro-oncology MDT per week.

108

### 109 **2.3. Statistical Analysis**

110 To meet the primary and secondary objectives, comparisons of proportions were performed with chi-  
111 square test or the exact Fisher test as appropriate. The alpha risk threshold was set at 5%. Figures and  
112 analyses were performed in RStudio version 1.2.1335 (RStudio, Inc.) using the ggpubr package.

113

## 114 **3. RESULTS**

### 115 **3.1. Multidisciplinary Tumor Board Meeting**

116 During the period from december 2018 to november 2020, 1540 cases were discussed in MDT in the  
117 four included centers: 735 within the period 1 (non Covid period) and 805 within the period 2 (Covid  
118 period) (Table 1). No difference was observed between the two periods as regard to population  
119 characteristics or tumor histology. As expected, glioma and malignant or refractory meningioma were  
120 the most represented tumors: respectively 73.3% (n=1129/1540) and 13.2% (n=204/1540) in the entire  
121 population. Mean number of cases per MDT per week was similar between the two periods: 9.8 in the  
122 period 1 and 10.7 in the period 2, p=0.36 (Figure 1a and Table 1).

123 During the lockdown periods, 174 cases were presented and no difference in the number of cases per  
124 week was observed between lockdown and non-lockdown periods: respectively 9.1 cases/week *versus*  
125 10.4, p=0.26 (Figure 1b).

126 The only observed difference was a higher proportion of tumor resection during the lockdown periods:  
127 81.4% (n=79/174) versus 64.5% (n=408/1366), p=0.001. When considering the calendar year, no  
128 difference was observed between 2019 and 2020 (Figure 1c). Within the year 2020, the only  
129 significant decrease of number of MDT cases was observed in October, as compared to October 2019  
130 (Figure 2). This difference, although not significant, was observed when comparing the 2020 overall  
131 mean number of cases to the mean per month (Supplementary Figure A). A slight and opposite  
132 correlation was observed (coefficient correlation=0.17, p=0.002) between the number of cases per  
133 week and the number of patients hospitalized for a Sars-Cov2 infection (Figure 3).

134 Regarding newly and histomolecular confirmed diagnosis (by resection or biopsy), no difference was  
135 observed between the two periods: 480 new cases during period 1 and 494 new cases during period 2.  
136 Repartition by histomolecular subtypes shows no significant difference (Figure 4).

137

### 138 **3.2. Treatments Decision**

139 No difference in the MDT decision was observed between the period 1 and the period 2 (Table 2).

140 About radiotherapy, we did not find any modification in proposed radiation-fraction or technique,  
141  $p=0.896$ . As an example, 21 patients had a short course radiotherapy during period 1 and 18 patients  
142 during period 2,  $p=0.414$ .

143 Regarding chemotherapy treatments, no difference was observed between the two periods,  $p=0.822$ .

144 Interestingly, proposition for inclusion in clinical trials was continued due to the maintenance of  
145 clinical research in oncology.

146 Finally, we explored the impact of COVID19 on the volume of oncologic treatments for a primary  
147 brain tumor and administered during the two periods. The number of radiotherapy sessions in the two  
148 main centers in Normandy (François Baclesse center and Henri Becquerel center) did not change, nor  
149 has the quantity of chemotherapy delivered by the hospital pharmacy at the Henri Becquerel center  
150 (Supplementary Figure B).

151

## 152 **4. DISCUSSION**

153 COVIBRAIN study showed that the COVID19 pandemic did not impact MDT activity in neuro-  
154 oncology in 2020 compared to 2019 in Normandy. Non-significant monthly variations were observed  
155 and appear to be related to the number of hospitalizations for Sars-Cov2 infection. These results are  
156 the first described in France on the specific population of patients suffering from primary brain tumor.

157 The data presented are exhaustive on a French region representing 5% of the French metropolitan  
158 population. These results are in line with the similar comparative experience in a New York center:  
159 133/166 patients (80%) were managed at their center from a primary brain tumor in 2020 *versus*

160 90/112 patients (80%) in 2019[12]. However, the study conducted in 18 English centers showed a  
161 significant reduction in the number of cases presented in MDT per week between March 23 and April  
162 20, 2020 *versus* February 2020 (baseline) with an average of 15.3 patients *versus* 21.2 respectively,  
163  $p=0.0005$ [11]. This difference can be explained by the choice of the studied period. In COVIBRAIN  
164 study, we explored the overall annual impact of the pandemic on neuro-oncology activity. Our results  
165 showed possible monthly variation, but comparison was not possible due to lack of statistical power. It  
166 would be interesting to perform a national-based analysis of the number of cases presented per week  
167 while studying the correlation with the hospital pressure related to COVID19.

168 Regarding all tumor localizations in another Occitania region (France), Grosclaude et al[13] observed  
169 a significant reduction of 23% in the number of cases presented at MDT when comparing 2019 and  
170 2020; with a peak of decrease at 33% during the third week following the first lockdown. Our  
171 exploratory results did not find any significant impact of lockdown periods on the average number of  
172 cases presented in neuro-oncology MDT. The particularity of the tumor location with acute  
173 neurological deficit could partially explained those findings. Ashkan et al showed in a single-center  
174 study conducted in UK that the overall number of patients referred for neurosurgical emergencies  
175 decreased between before and during the COVID19 pandemic. Concerning the oncological causes as  
176 well as the proportion of neurosurgical interventions due to brain tumor, the proportions of patients  
177 were stable during the COVID19 period: respectively 13.9% *versus* 11.4% before COVID19 and  
178 17.9% *versus* 14.7%[14]. This stability in oncological neurosurgical activity was also observed in  
179 other centers[10,15]. The proportion of patients who underwent tumor resection did not vary in our  
180 study: 68.7% in period 2 *versus* 64.1% in period 1,  $p=0.23$ . These results are in line with those found  
181 in other centers[10,16]. Surprisingly, we observed a higher proportion of tumor resection during the  
182 lockdown period: 81.4% ( $n=79/174$ ) *versus* 64.5% ( $n=408/1366$ ),  $p=0.001$ . This difference is possibly  
183 explained by the best accessibility to the operating room during the period of lockdown in the studied  
184 centers.

185 Overall, COVIBRAIN study confirms that neurosurgical activity for a primary brain tumor was  
186 maintained during the COVID19 pandemic, both quantitatively and qualitatively. This findings

187 highlight the non-follow-up of the recommendations proposing to postpone neurosurgery in selected  
188 situations: newly diagnosed low-grade glioma or high grade glioma in elderly and/or frail  
189 patients[4,5]. MDT activity was also maintained during the entire epidemic period within the studied  
190 centers using virtual technology, as also described in Germany[17]. The impact of the COVID19 on  
191 neuro-oncological MDT should be investigated in regions with higher prevalence of SarsCov2  
192 infection, such as the *Grand Est* or the *Ile-De-France* regions in France.

193 Finally, COVIBRAIN study did not explore the consequences of the COVID19 pandemic on the  
194 public health in neuro-oncology. The delay in oncological care beyond neurosurgery, the difficulty of  
195 access to healthcare structures, particularly for supportive care, SarsCov2 intercurrent infections may  
196 have generated a significant reduction in survival during the pandemic period.

197 No difference in therapeutic decisions in MDT was observed in COVIBRAIN study. Nowadays, it  
198 would be interesting to assess the overall clinical consequences of the pandemic on the population of  
199 patients with a primary brain tumor in the Normandy region.

200

## 201 5. CONCLUSION

202 The number of cases presented to the neuro-oncology MDT did not vary significantly between the pre-  
203 COVID19 period and the initial phase of the pandemic in Normandy. Despite the hospital pressure of  
204 the pandemic on the care structures, the activity of neuro-oncology management was maintained. This  
205 maintenance was probably possible during 2020 thanks to the non-explosion of the number of  
206 hospitalized patients due to SarsCov2. The consequences in terms of survival in this specific  
207 population should now be explored, in particular to investigate the possible impact of the delay within  
208 the care pathway of the patients.

209

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265

## 266 **Acknowledgments**

267 The authors thank Dr. Jean Rouvet (Cancer Center Henri Becquerel) and Mrs. Dany Corban (Rouen  
268 University Hospital) for their help in collecting data.

269

## 270 **Disclosure of Interest**

271 All the authors report no disclosure.

272

## 273 **Abbreviations**

274 COVID19: Coronavirus-disease 2019

275 MDT: Multidisciplinary tumor board meeting

276 MGMT: O6-Methylguanine DNA Methyltransferase

277 TMZ: temozolomide

278 RT: radiotherapy

279

## 280 **Figure Legend**

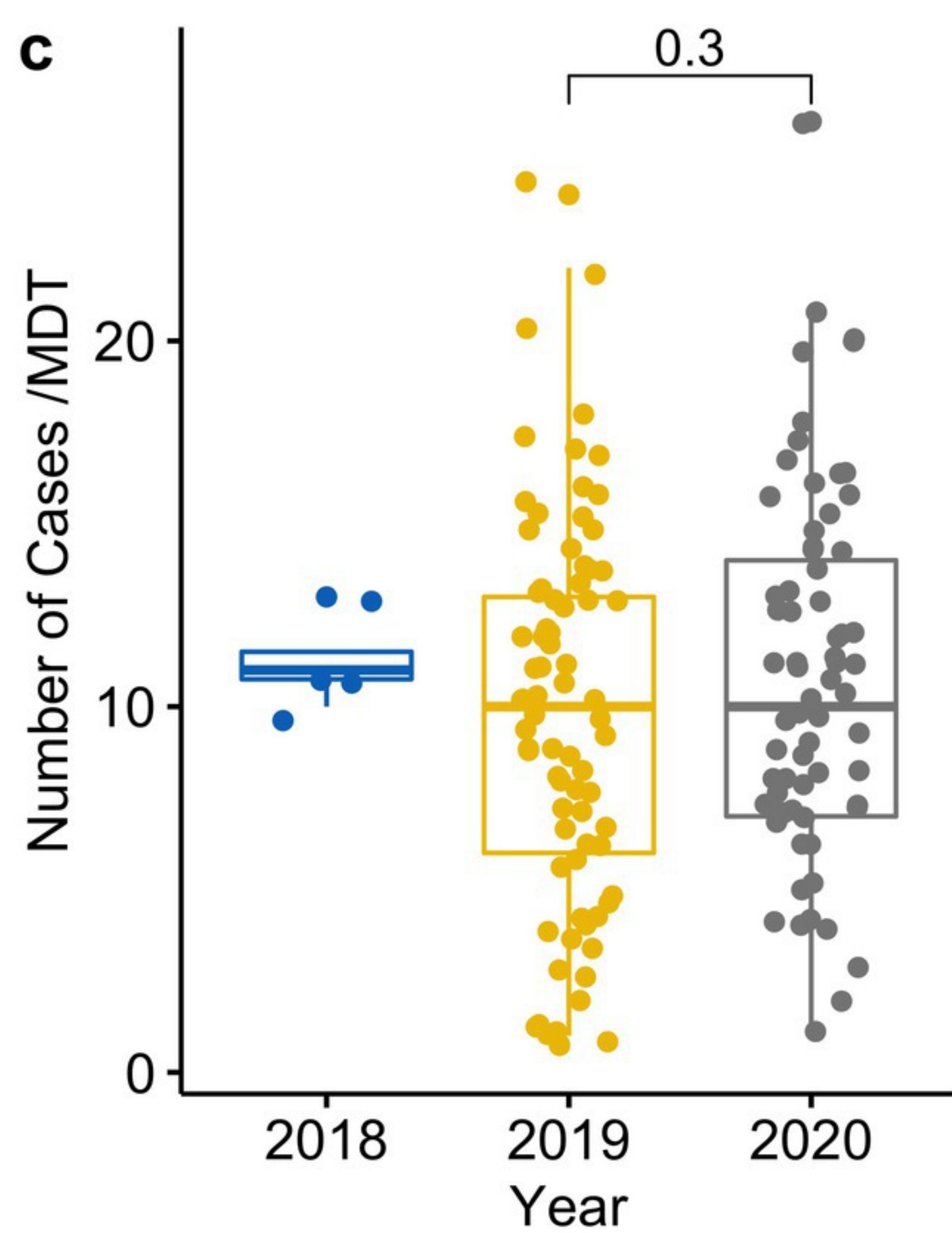
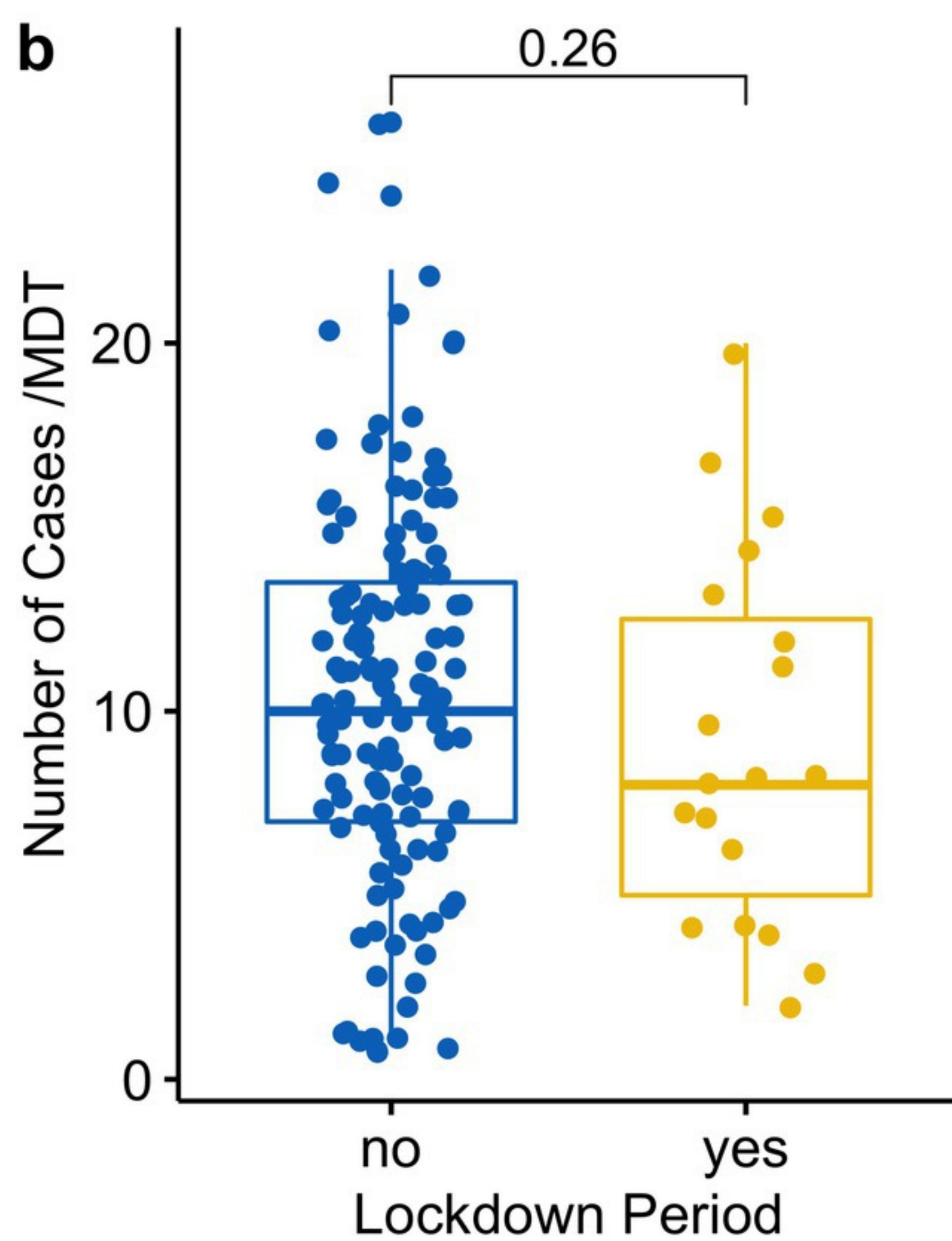
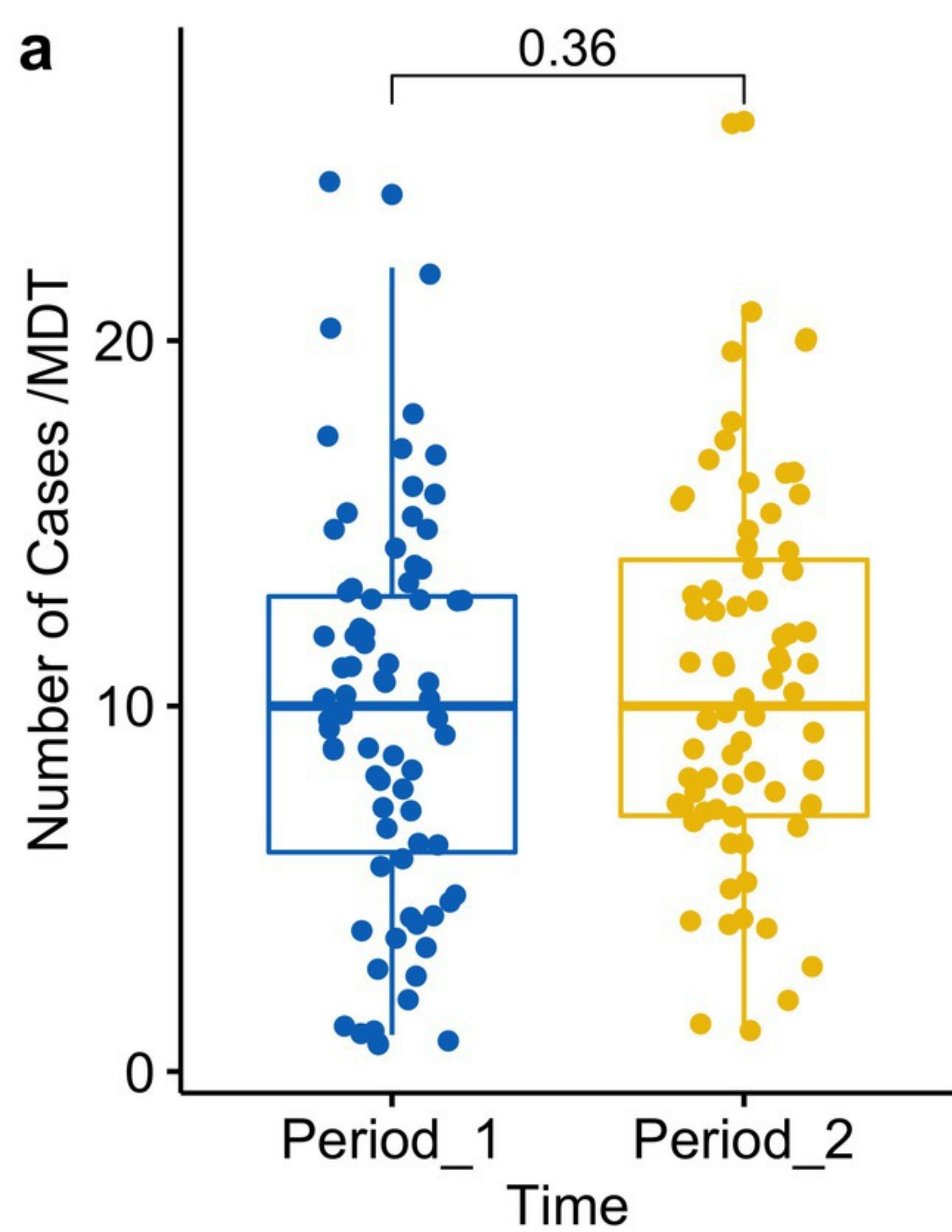
281 **Figure 1.** Comparison of cases per week per MDT in Normandy between period 1 (december 1st 2018  
282 to november 30th 2019) and period 2 (from december 1st 2019 to november 30th 2020) (a); between  
283 lockdown periods and non lockdown period (b); and per year.

284 MDT: multidisciplinary tumor board meeting.

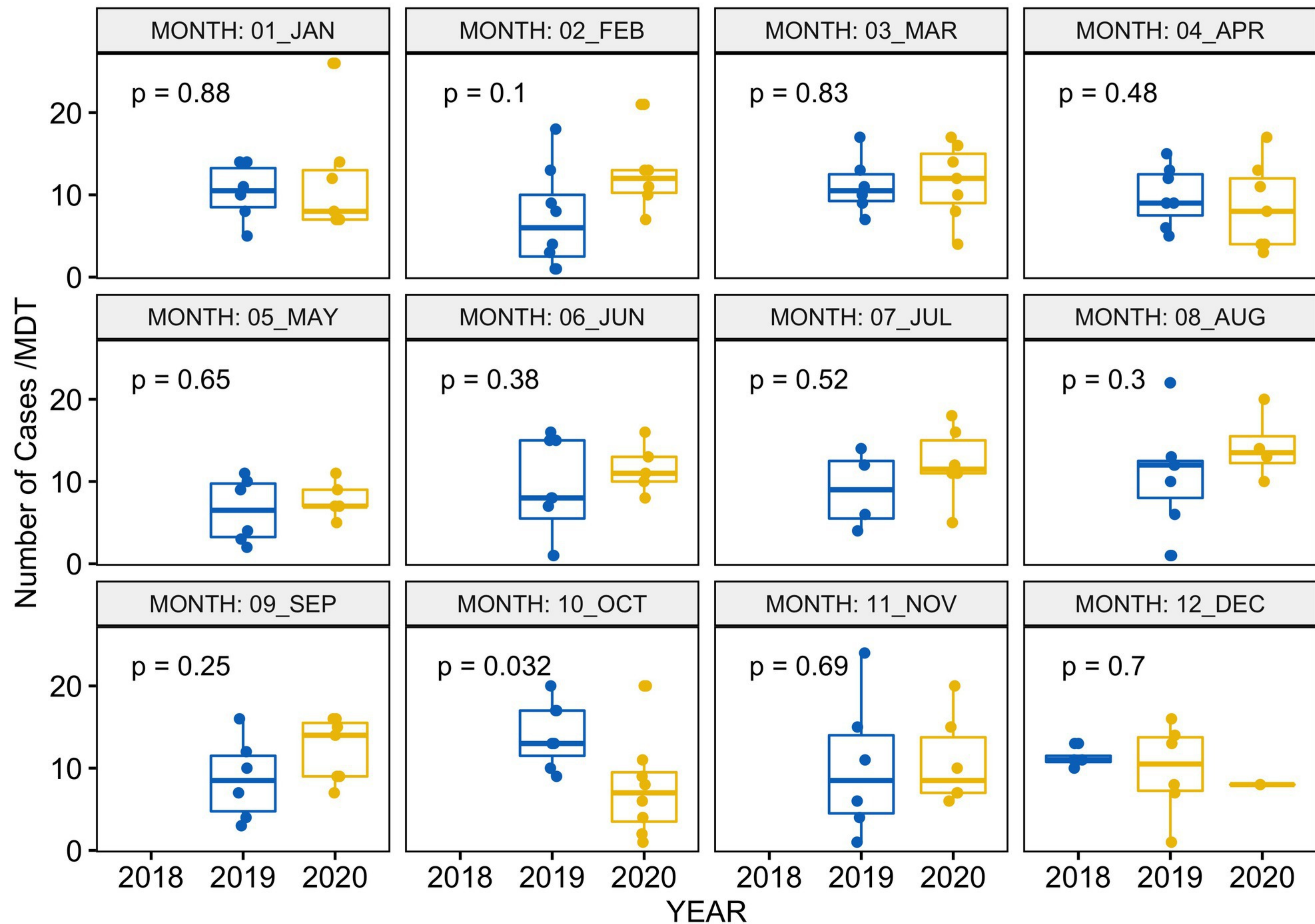
285 **Figure 2.** Comparison of cases presented at the neuro-oncology MDT in Normandy per month  
286 between 2019 and 2020.

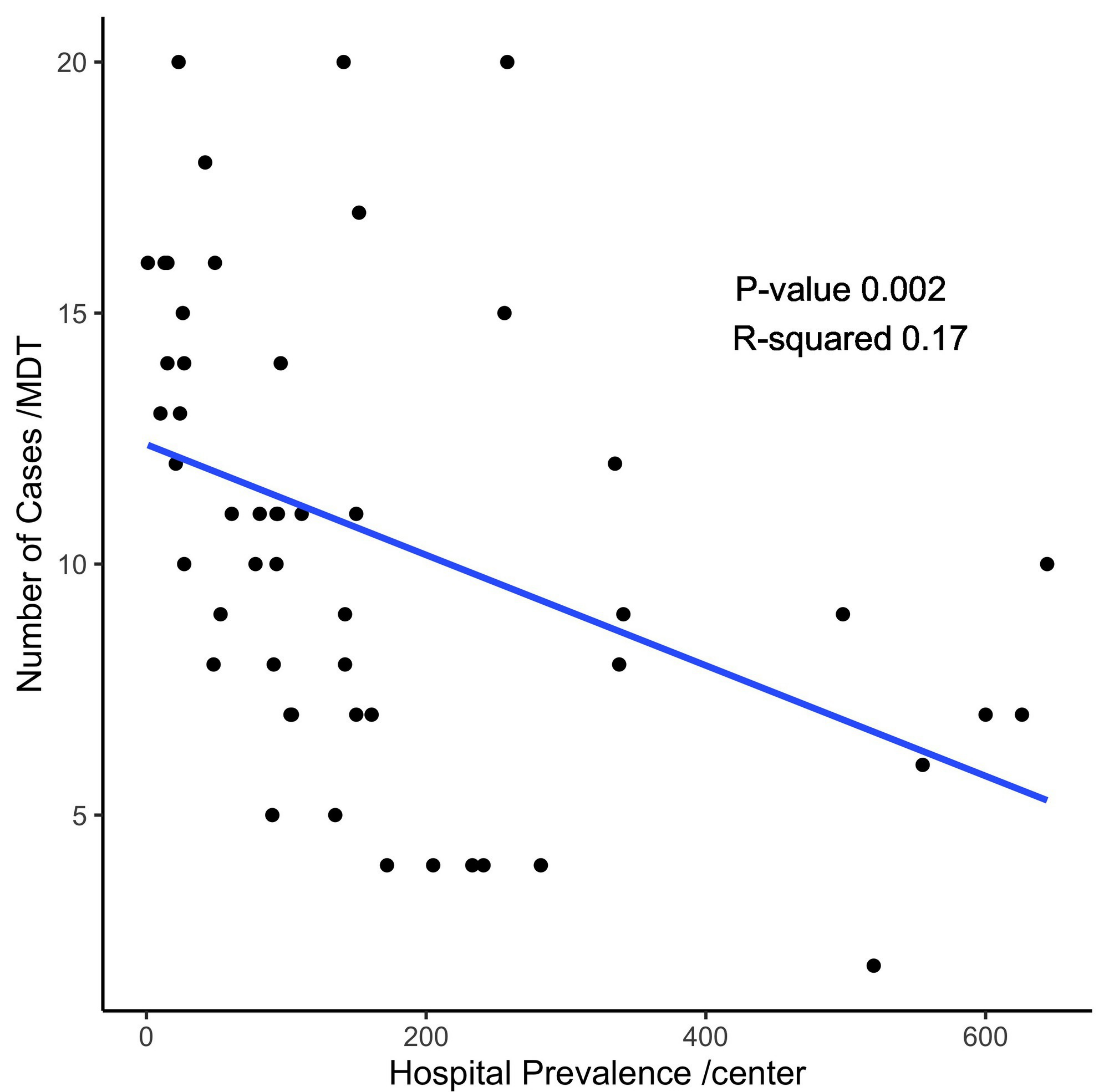
287 **Figure 3.** Linear regression of the number of cases per week as a function of the concomitant number  
288 of hospitalized patients for a SarsCov2 infection.

289 **Figure 4.** Repartition and comparison of histomolecular newly-diagnosed cases between period 1 and  
290 period 2 per tumor typr.

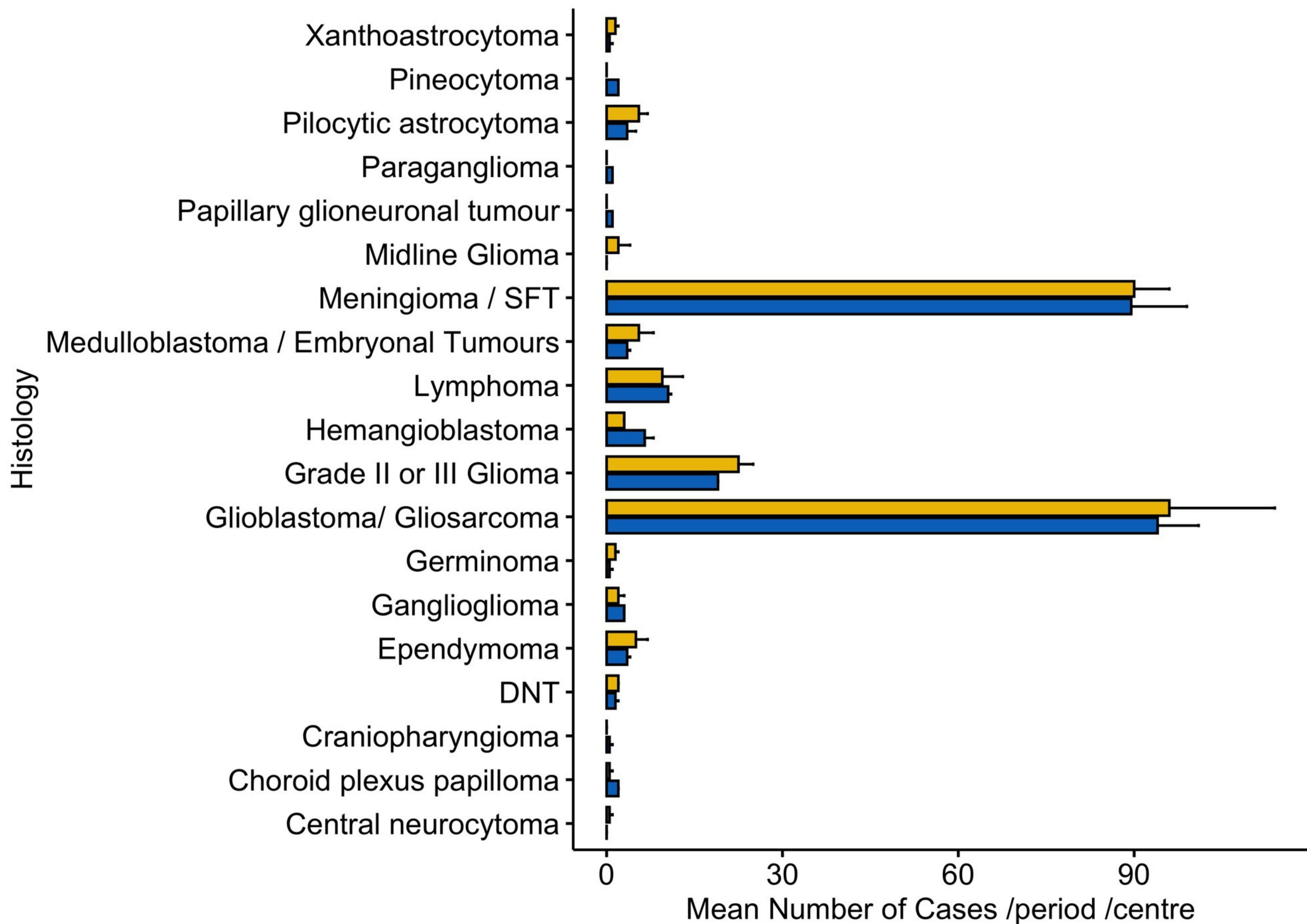


Time  Dec 2018 > Nov 2019  Dec 2019 > Dec 2020





Period ■ Dec 2018 > Nov 2019 ■ Dec 2019 > Dec 2020



**Table 1. Characteristics of the patients' cases discussed during studied period - COVIBRAIN study (2019-2020).**

Data were collected between December 1st 2018 to November 30th 2019 (Period 1) and December 1st 2019 to November 30th 2020 (Period 2)

	<b>Period 1</b>	<b>Period 2</b>	<b>p</b>
<b>n</b>	735	805	
<b>Gender = men (%)</b>	388 (52.8)	440 (54.7)	0.494
<b>Age (mean (SD))</b>	58.3 (15.79)	59 (14.83)	0.339
<b>Number of MDM per week (mean (SD))</b>	9.8 (5.19)	10.7 (4.99)	0.36
<b>Type of MDM (%)</b>			0.44
Initial	286 (38.9)	303 (37.6)	
Follow up	437 (59.5)	502 (62.4)	
Unknown	12 (1.6)	0 (0.0)	
<b>Tumor resection (%)</b>	200 (64.1)	287 (68.7)	0.225
<b>Histology (%)</b>			0.193
Astrocytic/oligodendroglial tumors	528 (71.8)	601 (74.7)	
Choroid plexus tumors	2 (0.3)	1 (0.1)	
Cranial nerves tumors	5 (0.7)	1 (0.1)	
Embryonal tumors	8 (1.1)	3 (0.4)	
Ependymal tumors	12 (1.6)	12 (1.5)	
Germ cell tumors	1 (0.1)	2 (0.2)	
Lymphomas	18 (2.4)	18 (2.2)	
Meningiomas	102 (13.9)	102 (12.7)	
Mesenchymal tumors	7 (1.0)	12 (1.5)	
Neuronal/glioneuronal tumors	9 (1.2)	4 (0.5)	
Other astrocytic tumors	2 (0.3)	4 (0.5)	
Other gliomas	0 (0.0)	3 (0.4)	

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Other/ unknown	16 (2.2)	9 (1.1)
Sellar region	25 (3.4)	33 (4.1)

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**Table 2. Comparison of the number of delivered treatments between the period 1 and the period 2 - COVIBRAIN study (2019-2020).**

	<b>Period 1</b>	<b>Period 2</b>	<b>p</b>
<b>n</b>	735	805	
<b>Radiotherapy = yes (%)</b>	269 (36.6)	291 (36.1)	0.896
<b>Type of radiotherapy (%)</b>			0.414
Protontherapy	42 (15.6)	44 (15.1)	
Short-course radiotherapy	21 (7.8)	18 (6.2)	
Standard-course radiotherapy	190 (70.6)	219 (75.3)	
Stereotactic radiotherapy	16 (5.9)	10 (3.4)	
<b>Chemotherapy = yes (%)</b>	424 (57.7)	470 (58.4)	0.822
<b>Temozolomide</b>	222 (52.4)	230 (48.9)	0.435
RT/TMZ + TMZ protocol	149 (35.1)	152 (32.3)	
TMZ monotherapy	69 (16.3)	74 (15.7)	
TMZ + anti-VEGF	2 (0.5)	4 (0.9)	
TMZ + topotecan	2 (0.5)	0 (0.0)	
<b>Nitrosourea</b>	82 (19.3)	90 (19.1)	0.48
Nitrosourea monotherapy	35 (8.3)	38 (8.1)	
Nitrosourea + anti-VEGF	31 (7.3)	40 (8.5)	
PCV regimen	16 (3.8)	12 (2.6)	
<b>Anti -VEGF monotherapy</b>	51 (12.0)	73 (15.5)	
<b>Platine based regimen</b>	26 (6.1)	26 (5.5)	0.24
Platine + anti-VEGF	7 (1.7)	11 (2.3)	

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Platine monotherapy	19 (4.5)	15 (3.2)
<b>Other chemotherapy</b>	31 (7.3)	30 (6.4)
<b>Targeted therapy</b>	1 (0.2)	3 (0.6)
<b>Clinical trial</b>	5 (1.2)	8 (1.7)

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