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# Risk of severe COVID-19 in patients treated with IBD medications: a French nationwide study

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## Summary

**Background:** Recently, the SECURE-IBD study, based on a physician-reported registry, suggested that thiopurines, either alone or combined with anti-TNF, may increase risk of severe COVID-19.

**Aims:** To compare the risk of severe COVID-19 according to IBD medications in a large and unselected population.

**Methods:** Using the French national health data system, the risks of hospitalisation and of death or mechanical ventilation for COVID-19 from 15 February 2020 to 31 August 2020 in IBD patients were compared according to IBD treatment (immunomodulators and biologics), using multivariable Cox models adjusted for sociodemographic characteristics, budesonide/corticosteroids and aminosalicylates use, and comorbidities.

**Results:** Among 268 185 IBD patients, 600 were hospitalised for COVID-19 and 111 of them died or were mechanically ventilated (including 78 deaths). In multivariable analysis, the risk of hospitalisation for COVID-19 did not differ according to IBD treatment category, with adjusted Hazard Ratios (aHR, unexposed patients used as reference) of 0.94 (95%CI: 0.66-1.35) for immunomodulator monotherapy, 1.05 (0.80-1.38) for anti-TNF monotherapy, 0.80 (0.38-1.69) for anti-TNF combination therapy, 1.06 (0.55-2.05) for vedolizumab and 1.25 (0.64-2.43) for ustekinumab. Similarly, the risk of death or mechanical ventilation for COVID-19 did not differ according to IBD treatment.

**Conclusions:** Immunomodulators and biologics prescribed in patients with IBD do not appear to increase the severity of COVID-19 infection.

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## 1 | BACKGROUND AND AIMS

At the end of 2019, a new form of pneumonia due to a new coronavirus designated as COVID-19 emerged. Approximately, 85 million people contracted the disease and 1.9 million died. Since the start of the pandemic, questions were raised about the safety of immunomodulators and biologics prescribed in patients with IBD. Current recommendations state that IBD medications should not be discontinued, to avoid hospitalisation during the pandemic.[1]

Recently, the SECURE-IBD study showed that compared with anti-TNF monotherapy, thiopurines either alone or combined with anti-TNF were associated with an increased risk of severe COVID-19.[2] This study was based upon a physician-reported registry of 1439 IBD patients with COVID-19. It might have been prone to several biases including differential case reporting according to IBD management.[3]

We aimed to compare the risk of severe COVID-19 according to IBD medications in a large and unselected population.

## 2 | MATERIALS AND METHODS

### 2.1 | Data source

This study was conducted using the French national health data system (SNDS), which contains comprehensive out-patient (reimbursed drugs and procedures) and in-patient (expensive drugs dispensed, procedures performed during hospital stays and diagnoses) information for 99% of the French population (approximately 66 million people).[4] Each person is identified by a unique, anonymous number. Diseases are coded according to the ICD-10, and procedures are coded according to the CCAM (Classification Commune des Actes Médicaux), the French medical classification of clinical procedures. Patients with long-term diseases (LTDs), such as IBD, are reimbursed for their health expenditure, and the diagnosis is recorded in the SNDS. Eligibility for LTDs is established by a national health insurance expert physician at the request of the patient's general practitioner. The LTDs are recorded with ICD-10 codes and the LTD start date (onset of IBD). The SNDS also contains socio-demographic data and, when applicable, the date of death. Within the SNDS, information on drug prescriptions is comprehensive and ascertained.[4]

### 2.2 | Study population

This real-life cohort study included all patients identified with IBD. An individual was considered to have IBD if he/she was eligible for LTD and/or had been hospitalised (including endoscopy) with a diagnosis of IBD between 1 January 2014 and 31 December 2019. This method of identification of IBD patients has already been extensively used before.[5-9]

### 2.3 | Exposure definition

Among IBD patients, IBD drug exposure was computed using drug dispensation (1 month for out-patient drugs except for aminosalicylates [3 months]), drug theoretical coverage (2 months for infliximab, vedolizumab and ustekinumab; and a month or less for every other drugs), plus one month. Thus, exposure to infliximab, vedolizumab or ustekinumab was defined by at least two dispensations between 15 August 2019 and 15 February 2020, including at least one after 15 November 2019. Exposure to adalimumab, golimumab, certolizumab, immunomodulators (thiopurines and methotrexate) was defined by at least two dispensations between 15 October 2019 and 15 February 2020, including at least one after 15 December 2019. Exposure to aminosalicylates was defined by one dispensation between 15 November 2019 and 15 February 2020.

IBD treatment was categorised into six groups: immunomodulator monotherapy, anti-TNF monotherapy, anti-TNF combination therapy (anti-TNF and immunomodulator), vedolizumab (alone or in combination therapy), ustekinumab (alone or in combination therapy) or none of these drugs (subsequently referred to as unexposed patients).

### 2.4 | Follow-up and outcomes

All IBD patients were followed from 15 February 2020 until the onset of a severe COVID-19 outcome including (a) hospitalisation for COVID-19, (b) mechanical ventilation or death during a hospital stay for COVID-19 and (c) death during a hospital stay for COVID-19; or otherwise censored at study end on 31 August 2020.

Information on all hospital stays is integrated into the SNDS (usually in July of the following year). In April 2020, the French government encouraged hospitals to report COVID hospital stays according to an exceptional, fast-track modality (once a week or once a fortnight). Patients who were mechanically ventilated or died formed a subset of all hospitalised patients. During the hospital stay, the date of intubation was not available, and we used the date of hospitalisation for patients who had mechanical ventilation. In patients who died after intubation, the secondary end point was defined as the date of death.

### 2.5 | Statistical analysis

To compare the risk of severe COVID-19 across IBD treatment groups, we performed multivariable Cox models adjusted for age, sex, a deprivation index indicating the socio-economic level of the women's municipality of residence,[4] budesonide/corticosteroids, aminosalicylates, tobacco or alcohol in the previous 5 years, and comorbidities such as obesity, diabetes, anti-hypertensive treatments, lipid-lowering drugs, chronic respiratory diseases, past or present cancer, acute or chronic cardiovascular diseases, chronic end-stage

renal diseases, neurodegenerative diseases, other neurological diseases, psychiatric illnesses.

All tests were two-tailed with a limit of significance of $P < 0.05$. All analyses were performed with SAS® software version 9.4 (SAS Institute).

The French public institution who conducted this study has permanent access to the SNDS database in application of the provisions of articles R. 1461-12 et seq. of the French Public Health Code and deliberation CNIL-2016-316 of the French data protection authority. Therefore, no informed consent is required. This research received no funding. Patients or the public were not involved in any of the design, conduct, reporting or dissemination plans of our research.

## 3 | RESULTS

### 3.1 | Patients

We included 268 185 IBD patients; 17 717 (6.6%) were receiving immunomodulator monotherapy, 38 354 (14.3%) were receiving anti-TNF monotherapy, 5857 (2.2%) were receiving anti-TNF combination therapy, 4125 (1.5%) were receiving vedolizumab, 4468 were receiving ustekinumab (1.7%) and 197 664 (73.7%) were unexposed.

The median age was 50 years (IQR: 37-63) and 52.9% were women. Apart from thiopurines and biologics, 28.6% and 15.1% were prescribed aminosalicylates and corticosteroids respectively. Other baseline characteristics are presented in Table 1.

**TABLE 1** Baseline characteristics (N = 268 185)

| | None (N = 197 664) | Immunomodulator monotherapy (N = 17 717) | Anti-TNF monotherapy (N = 38 354) | Anti-TNF combination therapy[a] (N = 5857) | Vedolizumab (N = 4125[b]) | Ustekinumab (N = 4468[b]) |
|---|---|---|---|---|---|---|
| Age (years), median [IQR] | 53 [39-66] | 48 [36-60] | 41 [30-54] | 41 [29-53] | 46 [33-60] | 42 [32-53] |
| Female gender | 106 415 (53.8) | 8954 (50.5) | 18 897 (49.3) | 2927 (50.0) | 2130 (51.6) | 2652 (59.4) |
| Deprivation index | | | | | | |
| Quintile 1 (less deprived) | 39 638 (20.1) | 3406 (19.2) | 7019 (18.3) | 1096 (18.7) | 732 (17.7) | 815 (18.2) |
| Quintile 2 | 38 712 (19.6) | 3443 (19.4) | 7410 (19.3) | 1149 (19.6) | 803 (19.5) | 858 (19.2) |
| Quintile 3 | 38 322 (19.4) | 3439 (19.4) | 7688 (20.0) | 1126 (19.2) | 864 (20.9) | 931 (20.8) |
| Quintile 4 | 37 367 (18.9) | 3483 (19.7) | 7506 (19.6) | 1146 (19.6) | 830 (20.1) | 862 (19.3) |
| Quintile 5 (more deprived) | 38 201 (19.3) | 3519 (19.9) | 7890 (20.6) | 1187 (20.3) | 845 (20.5) | 931 (20.8) |
| Missing | 5424 (2.7) | 427 (2.4) | 841 (2.2) | 153 (2.6) | 51 (1.2) | 71 (1.6) |
| Tobacco in the previous 5 y | 11 508 (5.8) | 981 (5.5) | 2768 (7.2) | 454 (7.8) | 261 (6.3) | 447 (10.0) |
| Alcohol in the previous 5 y | 3732 (1.9) | 257 (1.5) | 592 (1.5) | 68 (1.2) | 56 (1.4) | 57 (1.3) |
| Obesity | 2069 (1.0) | 151 (0.9) | 323 (0.8) | 64 (1.1) | 48 (1.2) | 48 (1.1) |
| Anti-hypertensive treatments | 47 447 (24.0) | 3523 (19.9) | 5173 (13.5) | 758 (12.9) | 781 (18.9) | 548 (12.3) |
| Lipid-lowering drugs | 27 158 (13.7) | 2002 (11.3) | 2746 (7.2) | 411 (7.0) | 377 (9.1) | 333 (7.5) |
| Chronic respiratory diseases | 15 852 (8.0) | 1191 (6.7) | 2216 (5.8) | 346 (5.9) | 346 (8.4) | 308 (6.9) |
| Present cancer | 7620 (3.9) | 361 (2.0) | 380 (1.0) | 57 (1.0) | 128 (3.1) | 65 (1.5) |
| Cancer under surveillance | 10 155 (5.1) | 486 (2.7) | 715 (1.9) | 95 (1.6) | 183 (4.4) | 123 (2.8) |
| Acute cardiovascular diseases | 1901 (1.0) | 80 (0.5) | 111 (0.3) | 16 (0.3) | 31 (0.8) | 27 (0.6) |
| Chronic cardiovascular diseases | 21 534 (10.9) | 1282 (7.2) | 1852 (4.8) | 259 (4.4) | 394 (9.6) | 236 (5.3) |
| Diabetes | 15 102 (7.6) | 1086 (6.1) | 1457 (3.8) | 260 (4.4) | 273 (6.6) | 168 (3.8) |
| Chronic end-stage renal diseases | 706 (0.4) | 107 (0.6) | 68 (0.2) | 12 (0.2) | 12 (0.3) | 7 (0.2) |
| Neurodegenerative diseases | 2903 (1.5) | 104 (0.6) | 135 (0.4) | 16 (0.3) | 24 (0.6) | 12 (0.3) |
| Other neurological diseases | 3074 (1.6) | 250 (1.4) | 318 (0.8) | 50 (0.9) | 70 (1.7) | 67 (1.5) |
| Psychiatric illnesses | 10 812 (5.5) | 666 (3.8) | 1307 (3.4) | 226 (3.9) | 172 (4.2) | 182 (4.1) |
| Corticosteroids/budesonide use | 29 317 (14.8) | 3163 (17.9) | 5345 (13.9) | 932 (15.9) | 819 (19.9) | 854 (19.1) |
| Aminosalicylates use | 66 467 (33.6) | 4480 (25.3) | 4071 (10.6) | 750 (12.8) | 829 (20.1) | 226 (5.1) |

Abbreviation: IQR, interquartile range.

[a]Combination therapy: exposure to immunomodulators and anti-TNF.

[b]Six patients were exposed to both vedolizumab and ustekinumab.

### 3.2 | Hospitalisation for COVID-19

Overall, 600 patients (0.22%) were hospitalised for COVID-19:32 (0.18%) of those treated with immunomodulator monotherapy, 63 (0.16%) of those treated with anti-TNF monotherapy, seven (0.12%) of those with anti-TNF combination therapy, nine (0.22%) of those with vedolizumab, nine (0.20%) of those with ustekinumab and 480 (0.24%) of those unexposed to these drugs (Table 2). In multivariable analysis, the risk of hospitalisation for COVID-19 did not differ according to IBD treatment category, with adjusted Hazard Ratios (aHR, unexposed patients used as reference) of 0.94 (95% CI: 0.66-1.35) for immunomodulator monotherapy, 1.05 (95% CI: 0.80-1.38) for anti-TNF monotherapy, 0.80 (95% CI: 0.38-1.69) for anti-TNF combination therapy, 1.06 (95% CI: 0.55-2.05) for vedolizumab and 1.25 (95% CI: 0.64-2.43) for ustekinumab. The risk of hospitalisation for COVID-19 also did not differ across the various treatment subgroups (Table 3).

As expected, age >60 years, male gender and comorbidities including diabetes, respiratory, cardiovascular or end-stage renal diseases were associated with an increased risk of hospitalisation for COVID-19 (Table 4). Corticosteroids/budesonide use was also associated with an increased risk of hospitalisation for COVID-19 with an aHR of 1.64 (95% CI: 1.35-1.98), while aminosalicylates use was associated with a lower risk with an aHR of 0.80 (95% CI: 0.67-0.97).

### 3.3 | Death or mechanical ventilation for COVID-19

Death or mechanical ventilation for COVID-19 occurred in two patients (0.01%) with immunomodulator monotherapy, six (0.02%) with anti-TNF monotherapy and 103 (0.05%) in unexposed patients. No death or mechanical ventilation occurred in patients with anti-TNF combination therapy, vedolizumab or ustekinumab (Table 2). In a multivariable analysis, the risk of death or mechanical ventilation for COVID-19 did not differ according to IBD treatment category, with aHR (unexposed patients used as reference) of 0.35 (95% CI: 0.09-1.43) for immunomodulator monotherapy and 0.83 (95% CI: 0.36-1.91) for anti-TNF monotherapy (Table 3).

Corticosteroids/budesonide use was neither associated with an increased risk of death or mechanical ventilation for COVID-19 (aHR 1.37; 95% CI: 0.86-2.19) nor aminosalicylates use (aHR 1.07; 95% CI: 0.71-1.62).

## 4 | DISCUSSION

This population-based, nationwide study based on 268 185 IBD patients, showed that the risk of severe COVID-19 did not differ according to IBD treatment: immunomodulators, anti-TNF alone or in combination therapy, vedolizumab and ustekinumab.

We found an incidence of hospitalisation for COVID-19 per 100 000 IBD patients during COVID-19 first wave of 220 (600/268 185). In population-based studies, this rate over the same period was 80 (15/19 717) in Denmark[10] and 170 (59/34 763) in the Netherlands.[11] These results are consistent with the incidence of hospitalisation for COVID-19 in the general population over the same period: 134 per 100 000 in France,[12] 39 in Denmark[13] and 84 in the Netherlands.[11]

We found that among IBD patients, 19.7% and 9.1% were exposed to biologics and immunomodulators, respectively, leaving 73.7% of patients unexposed at the beginning of year 2020. This rate of unexposed patients is similar to that of a previously published study in France, which found that over a 5-year period between 1 January 2009, and 31 December 2013, 65% of IBD patients remained persistently unexposed, while 22% experienced both periods of non-exposure and exposure to IBD treatments.[6]

The SECURE-IBD study found that, compared with anti-TNF monotherapy, combination therapy and thiopurines were associated with a fourfold increased risk of severe COVID-19.[2] This study also found an increased rate of severe COVID-19 with aminosalicylates use. However, the physician-reported nature of the data might have introduced several biases including over-reporting of cases in patients with closer follow-up (eg, biologic-treated patients), over-reporting of the most serious outcomes and over-reporting of cases that fit a predefined viewpoint (eg, thiopurines are bad; biologics are good).[3] The present study was based on a

**TABLE 2** Severe COVID-19 outcomes in IBD patients, overall and by IBD treatment category (N = 268 185)

| | None (N = 197 664) | Immunomodulator monotherapy (N = 17 717) | Anti-TNF monotherapy (N = 38 354) | Anti-TNF combination therapy[a] (N = 5857) | Vedolizumab (N = 4125[b]) | Ustekinumab (N = 4468[b]) |
|---|---|---|---|---|---|---|
| Hospitalisation for COVID-19, n (%) | 480 (0.24) | 32 (0.18) | 63 (0.16) | 7 (0.12) | 9 (0.22) | 9 (0.20) |
| Mechanical ventilation or death during a hospital stay for COVID-19, n (%) | 103 (0.05) | 2 (0.01) | 6 (0.02) | 0 (0.00) | 0 (0.00) | 0 (0.00) |
| Death during a hospital stay for COVID-19, n (%) | 73 (0.04) | 2 (0.01) | 3 (0.01) | 0 (0.00) | 0 (0.00) | 0 (0.00) |

[a]Combination therapy: exposure to immunomodulators and anti-TNF.

[b]Six patients were exposed to both vedolizumab and ustekinumab.

**TABLE 3** Adjusted hazard ratios[a] [95% confidence interval] of hospitalisation for COVID-19 and of death or mechanical ventilation for COVID-19 associated with IBD treatment category

| | IBD treatment category | | | | |
|---|---|---|---|---|---|
| | Immunomodulator monotherapy | Anti-TNF monotherapy | Anti-TNF combination therapy[b] | Vedolizumab | Ustekinumab |
| Hospitalisation for COVID-19 | | | | | |
| Compared to | | | | | |
| None | 0.94 [0.66-1.35] | 1.05 [0.80-1.38] | 0.80 [0.38-1.69] | 1.06 [0.55-2.05] | 1.25 [0.64-2.43] |
| Immunomodulator monotherapy | | 1.11 [0.73-1.71] | 0.85 [0.37-1.92] | 1.12 [0.53-2.35] | 1.33 [0.63-2.78] |
| Anti-TNF monotherapy | | | 0.76 [0.35-1.66] | 1.00 [0.50-2.03] | 1.19 [0.59-2.40] |
| Anti-TNF combination therapy[b] | | | | 1.32 [0.49-3.56] | 1.57 [0.58-4.21] |
| Vedolizumab | | | | | 1.18 [0.47-2.99] |
| Mechanical ventilation or death during a hospital stay for COVID-19 | | | | | |
| Compared to | | | | | |
| None | 0.35 [0.09-1.43] | 0.83 [0.36-1.91] | [c] | [c] | [c] |
| Immunomodulator monotherapy | | 2.35 [0.47-11.71] | [c] | [c] | [c] |
| Anti-TNF monotherapy | | | [c] | [c] | [c] |
| Anti-TNF combination therapy[b] | | | | [c] | [c] |
| Vedolizumab | | | | | [c] |
| Death during a hospital stay for COVID-19 | | | | | |
| Compared to | | | | | |
| None | 0.59 [0.14-2.41] | 0.81 [0.25-2.62] | [c] | [c] | [c] |
| Immunomodulator monotherapy | | 1.38 [0.23-8.32] | [c] | [c] | [c] |
| Anti-TNF monotherapy | | | [c] | [c] | [c] |
| Anti-TNF combination therapy[b] | | | | [c] | [c] |
| Vedolizumab | | | | | [c] |

[a]Multivariable Cox regression adjusted for age, sex, deprivation index, budesonide/corticosteroids use, aminosalicylates use, tobacco use in the previous 5 y, alcohol use in the previous 5 y, obesity, diabetes, anti-hypertensive treatments, hypolipaemic treatments, chronic respiratory diseases, active cancers, cancers under surveillance, acute cardiovascular diseases, chronic cardiovascular diseases, chronic end-stage renal diseases, neurodegenerative diseases, other neurological diseases, psychiatric illnesses.

[b]Combination therapy: exposure to immunomodulators and anti-TNF.

[c]There was no death or intubation for COVID-19 with anti-TNF combination therapy, vedolizumab or ustekinumab.

nationwide, large and unselected population-based cohort of IBD patients with comprehensive information on drug dispensing and hospitalisations; it is unlikely to be prone to such biases. Two other population-based studies showed no association between the risk of severe COVID-19 and IBD drugs.[14,15] However, in the first one,[14] IBD drugs were not examined separately but rather were grouped into a single group of immune-mediated therapy, and the second one[15] was underpowered; it included only 19 COVID-19 hospitalisations.

This study has some limitations. First, as in previous studies based on data from the SNDS,[5-9] algorithms rather than clinical data were used to identify IBD patients and COVID-19 outcomes. Eighty per cent[5-9] of patients were fully covered for IBD with LTD. LTD is established by a national health insurance expert physician at the request of the patient's general practitioner who certifies that the patient has IBD. The incidence rate of UC and CD observed with this algorithm is in the range of those reported in other European countries.[9] In addition, the SNDS identifies 95% of hospitalisations for COVID-19.[16] Second, some patients may have stopped their treatment after the epidemic onset, by fear of having COVID-19, resulting in exposure misclassification. However, monitoring data on drug use during the pandemic in France suggest that the levels

**TABLE 4** Multivariable Cox model for hospitalisation for COVID-19 (N = 268 185)

| | Hospitalisation for COVID-19 | |
|---|---|---|
| | Adjusted hazard ratios [95% confidence interval] | *P* |
| IBD treatment category | | |
| None | 1 | |
| Immunomodulator monotherapy | 0.94 [0.66-1.35] | 0.75 |
| Anti-TNF monotherapy | 1.05 [0.80-1.38] | 0.73 |
| Anti-TNF combination therapy[a] | 0.80 [0.38-1.69] | 0.56 |
| Vedolizumab | 1.06 [0.55-2.05] | 0.87 |
| Ustekinumab | 1.25 [0.64-2.43] | 0.51 |
| Corticosteroids/ budesonide use | 1.64 [1.35-1.98] | <0.001 |
| Aminosalicylates use | 0.80 [0.67-0.97] | 0.02 |
| Age (years) | | |
| <20 | 0.52 [0.19-1.40] | 0.19 |
| 20-44 | 1 | |
| 45-49 | 1.09 [0.74-1.61] | 0.66 |
| 50-54 | 1.32 [0.93-1.87] | 0.12 |
| 55-59 | 1.37 [0.97-1.94] | 0.08 |
| 60-64 | 1.55 [1.11-2.18] | 0.01 |
| 65-69 | 1.82 [1.30-2.55] | <0.001 |
| 70-74 | 1.55 [1.07-2.23] | 0.02 |
| 75-79 | 2.13 [1.45-3.14] | <0.001 |
| 80-84 | 3.40 [2.35-4.94] | <0.001 |
| 85-89 | 4.31 [2.92-6.37] | <0.001 |
| >89 | 4.16 [2.64-6.56] | <0.001 |
| Female gender | 0.78 [0.66-0.92] | <0.01 |
| Deprivation index | | |
| Quintile 1 (less deprived) | 1 | |
| Quintile 2 | 0.70 [0.54-0.90] | <0.01 |
| Quintile 3 | 0.68 [0.53-0.88] | <0.01 |
| Quintile 4 | 0.72 [0.56-0.93] | 0.01 |
| Quintile 5 (more deprived) | 0.94 [0.74-1.18] | 0.59 |
| Missing | 0.29 [0.13-0.66] | <0.01 |
| Tobacco in the previous 5 y | 0.86 [0.62-1.21] | 0.39 |
| Alcohol in the previous 5 y | 1.10 [0.67-1.80] | 0.71 |
| Obesity | 1.04 [0.49-2.20] | 0.93 |
| Anti-hypertensive treatments | 1.28 [1.05-1.57] | 0.02 |
| Lipid-lowering drugs | 0.96 [0.77-1.19] | 0.70 |
| Chronic respiratory diseases | 1.63 [1.31-2.03] | <0.001 |
| Present cancer | 1.35 [0.99-1.84] | 0.06 |
| Cancer under surveillance | 1.23 [0.94-1.63] | 0.13 |
| Acute cardiovascular diseases | 1.71 [1.16-2.52] | <0.01 |
| Chronic cardiovascular diseases | 1.33 [1.07-1.67] | 0.01 |
| Diabetes | 1.53 [1.22-1.92] | <0.001 |
| Chronic end-stage renal diseases | 4.43 [2.77-7.09] | <0.001 |
| Neurodegenerative diseases | 2.77 [2.05-3.75] | <0.001 |
| Other neurological diseases | 1.81 [1.19-2.73] | <0.01 |
| Psychiatric illnesses | 1.89 [1.47-2.43] | <0.001 |

[a]Combination therapy: exposure to immunomodulators and anti-TNF.

of chronic drug use have remained stable.[17] Furthermore, patients treated with immunomodulators or biologics might have avoided exposure to COVID-19 more cautiously than untreated IBD patients, and this might have resulted in an underestimation of the increased risk associated with these treatments, if any. Third, given the limited number of deaths and mechanical ventilation with thiopurines and biologics, we cannot exclude minor differences between these treatment groups. However, this limited number of deaths and mechanical ventilation is reassuring.

The present study also has a number of major strengths. First, it is based on a large and unselected cohort of patients with IBD. Second, the SNDS includes comprehensive and ascertained information for drug dispensing and hospitalisations. Third, analyses were adjusted for corticosteroids exposure and comorbidities known to be associated with more severe forms of COVID- 19 infections.

In conclusion, in patients with IBD, the risk of severe COVID-19 does not appear to differ according to IBD treatment. Therefore, IBD medications, except corticosteroids, should be maintained during the pandemic, to limit the risk of IBD relapse in the context of healthcare system overload.

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## AUTHORSHIP

*Guarantor of the article*: Rosemary Dray-Spira.

*Author contributions*: Antoine Meyer, Alain Weill, Franck Carbonnel and Rosemary Dray-Spira conceptualised the study; Laura Semenzato involved in acquisition of data and statistical analysis; Antoine Meyer involved in interpretation of data and drafting of the manuscript. All the authors involved in critical revision of the manuscript for important intellectual content and approved the final version of the manuscript.

## ETHICAL APPROVAL

The French public institution that conducted this study has permanent access to the SNDS database in application of the provisions of Articles R. 1461-12 *et seq*. of the French Public Health Code and the French data protection authority decision CNIL-2016-316. Informed consent was therefore not required.

## DATA AVAILABILITY STATEMENT

The authors had access to the SNDS database in application of the provisions of Articles R. 1461-12 et seq. of the French Public Health Code and the French data protection authority decision CNIL-2016-316. Future researchers can request access via the Health data hub: (https://documentation-snds.health-data-hub.fr/introduction/03-acces-snds.html#les-acces-sur-projet).

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