

Maintenance therapy with infliximab or vedolizumab in IBD is not associated with increased SARS-CoV-2 seroprevalence: UK experience in the 2020 pandemic

We read with great interest the recent publication from Ungaro and colleagues,¹ reporting the latest data from the Surveillance Epidemiology of Coronavirus Under Research Exclusion (SECURE-IBD) registry. These data, while raising concerns regarding the use of thiopurine and corticosteroid therapy in the SARS-CoV-2 pandemic, also provide valuable reassurance that monotherapy with anticytokine therapies, in particular those directed against tumour necrosis factor (TNF), are not associated with adverse outcomes in patients with IBD developing COVID-19. It has been postulated that anticytokine therapies may ameliorate or abrogate the 'cytokine storm' associated with severe COVID-19,² with anti-IL6 strategies now approved for use.³

We have assessed the SARS-CoV-2 antibody seroprevalence in patients with IBD, receiving either intravenous anti-TNF therapy, or anti-integrin therapy, during the first wave of the pandemic in the UK.

Sera from 640 patients attending for maintenance infliximab or vedolizumab infusions between April and June 2020 at the John Radcliffe Hospital (Oxford, UK) and Royal London Hospital (London, UK) were tested using the Abbott SARS-CoV-2 IgG assay. Adults (180) and paediatric (56) patients were included from London. Demographic and clinical data are summarised (online supplemental tables 1, 2). Key differences between the Oxford and London adult cohorts included ethnicity, smoking, comorbidities, disease type, concomitant thiopurines and biologic; in our data set, patients attending Royal London Hospital had significantly greater evidence for deprivation than Oxford (deprivation score 4 (3–6.3) vs 8 (6–9.3), $p < 0.001$). Seroprevalence data were compared with available data from a contemporaneous healthy healthcare worker (HCW) study in Oxford⁴ and from a Public Health England seroprevalence study in unselected paediatric patients attending the Royal London Children's Hospital.

We report no increase in overall SARS-CoV-2 seropositivity in patients

with IBD on biologics compared with controls. 12/404 (3.0%) patients tested positive for SARS-CoV-2 antibodies in Oxford. A higher seroprevalence rate was reported in London patients, 13/180 (7.2%) for adults ($p \leq 0.0001$ vs Oxford patients) and 7/56 (12.5%) for children (table 1). Seroprevalence rates in adult IBD cohorts were lower than rates reported in local healthy controls. Seroprevalence in all Oxford HCW of 10.6% and in non-patient facing HCW (6.1%)⁴ were higher than in patients ($p < 0.00001$ and $p < 0.0154$, respectively). Seroprevalence rates of the London paediatric control group were comparable to patients, 13.6% (54/396, median age 13.0 years (8.1–16.0), male 49%).

On univariate analyses, there were no associations of SARS-CoV-2 positive patients with baseline characteristics, including ethnicity or deprivation status or concomitant thiopurine use (table 1, online supplemental table 3). In Oxford, a trend towards lower seropositivity was observed in patients on infliximab versus vedolizumab (1.1% vs 4.4%); only two anti-TNF treated patients were seropositive (table 1). These trends were not observed in adults or children in London. Concomitant budesonide or 5-aminosalicylic acid use was associated with higher seropositivity rates, although statistical significance was not reached.

These seroprevalence data, the first reported from the UK during the pandemic, and the first analysis of a paediatric cohort undergoing biological therapies, complement the SECURE-IBD registry data, and also seroprevalence data from Germany⁵ and Italy.^{6,7} Together, these data sets provide substantial confidence to clinicians and patients in continuing biological therapy as monotherapy.

Further data are keenly anticipated, with respect to susceptibility, severity of outcome, durability of serological response and effects on vaccination efficacy—these are the subjects of prospective analysis, both nationally in the UK-based CLARITY study⁸ and internationally by the SECURE-IBD and ICARUS-IBD Consortia.⁹ Results from these ongoing studies will be available within the next year and will be of great interest to clinicians and patients.

Colleen GC McGregor ,¹ Alex Adams ,¹ Ross Sadler,² Carolina V Arancibia-Carcamo,¹ Rebecca Palmer,¹ Tim Ambrose,¹ Oliver Brain,¹ Alissa Walsh,¹ Paul Klenerman,¹

Simon PL Travis ,¹ Nicholas M Croft ,^{3,4} James O Lindsay,^{3,4} Jack Satsangi¹

¹Translational Gastroenterology Unit, NIHR Oxford Biomedical Research Centre, Oxford University Hospitals NHS Foundation Trust, University of Oxford, Oxford, UK

²Department of Laboratory Immunology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK

³Centre for Immunobiology, Blizard Institute, Queen Mary University of London, London, UK

⁴Departments of Gastroenterology and Paediatric Gastroenterology, Royal London Hospital, Barts Health NHS Trust, London, UK

Correspondence to Dr Colleen GC McGregor, Translational Gastroenterology Unit, NIHR Oxford Biomedical Research Centre, Oxford University Hospitals NHS Foundation Trust, University of Oxford, Oxford OX3 9DU, UK; colleen.mcgregor@ndm.ox.ac.uk

Twitter Colleen GC McGregor @ColleenMcGreg15

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Table 1 (A). Overall SARS-CoV-2 seroprevalence per cohort. (B). Seropositivity versus biologic and IBD diagnoses. (C). Seropositivity versus concomitant thiopurine therapy (D). Univariable relationships between clinical, socioeconomic and demographic factors with SARS-CoV-2 seropositivity

A:	Oxford* n=404	London n=180	London (paediatric)† n=56	
Overall seroprevalence	3.0% (12)	7.2% (13) ‡	12.5% (7)§	
B: Oxford	CD	UC	IBD-U	Total
IFX	1/105 (1.0%)	1/66 (1.5%)	0/3 (0.0%)	2/176‡ (1.1%)
VDZ	4/82 (4.9%)	6/144 (4.2%)	0/1 (0.0%)	10/228¶ (4.4%)
Total	5/187 (2.7%)	7/210 (3.3%)	0/4 (0.0%)	12/404 (3.0%)
London	CD	UC	IBD-U	Total
IFX	6/85 (7.1%)	2/31 (6.5%)	0/2 (0.0%)	8/118 (6.8%)
VDZ	2/21 (9.5%)	2/40 (5.0%)	1/1 (100%)	6/62 (8.1%)
Total	8/106 (7.5%)	4/71 (5.6%)	1/3 (33.3%)	13/180 (7.2%)
London (Paediatric)	CD	UC	IBD-U	Total
IFX	3/29 (10.3%)	3/16 (18.8%)	0/3 (0.0%)	6/48 (12.5%)
VDZ	0/0 (0.0%)	1/7 (4.2%)	0/1 (0.0%)	1/8 (4.4%)
Total	3/29 (10.3%)	4/23 (17.4%)	0/4 (0.0%)	7/56 (12.5%)
C: Concomitant thiopurine	Oxford n=101	London n=71	London (Paediatric) n=49	
Azathioprine	1/84 (1.2%)	2/59 (3.4%)	6/43 (14.0%)	
6-mercaptopurine	0/17 (0.0%)	1/12 (8.3%)	0/6 (0.0%)	
D:	Oxford	London	London (Paediatric)	
Parameter	OR (95% CI)	P value	OR (95% CI)	P value
Age	0.99 (0.96 to 1.03)	0.78	1.01 (0.97 to 1.04)	0.61
Sex (male)	1.80 (0.47 to 8.32)	0.39	6.68 (0.95 to 291.9)	0.06
Weight	1.02 (0.99 to 1.05)	0.19	1.00 (0.96 to 1.03)	0.98
Deprivation	0.95 (0.75 to 1.24)	0.68	1.01 (0.80 to 1.25)	0.91
UC diagnosis	1.60 (0.40 to 7.58)	0.55	0.66 (0.14 to 2.50)	0.57
VDZ	3.98 (0.83 to 37.85)	0.08	1.20 (0.30 to 4.40)	0.77
Concomitant thiopurine	0.27 (0.01 to 1.87)	0.31	0.44 (0.07 to 1.79)	0.25
Concomitant 5-ASA	3.39 (0.82 to 12.83)	0.05	0.35 (0.01 to 2.55)	0.47
Comorbidity	0.22 (0.01 to 1.54)	0.19	4.59 (1.17 to 17.44)	0.01

All ORs for univariable logistic regression are given with calculated 95% CIs in parentheses. F=fishers test, otherwise logistic regression, all P values uncorrected (extended analyses online supplemental table 3). *Control data: seroprevalence in all Oxford HCW 987/9311 (10.6%) and in non-patient facing HCW (administrative staff) 78/1289 (6.1%) were higher ($p<0.00001$ and p value 0.0154, respectively) (χ^2 with Yates correction, acknowledging not stratified for confounders).

†Control data: seroprevalence rates of the London paediatric control group were comparable at 54/396 (13.6%).

‡Oxford versus London (adult) seroprevalence $p\leq 0.001$.

§London adult versus London paediatric seroprevalence p value 0.2696.

¶Including one 'NA' for diagnoses, †including two 'NAs' for diagnoses.

5-ASA, 5-aminosalicylic acid; CD, Crohn's disease; IBD-U, IBD-unclassified; IFX, infliximab; Thiopurine, azathioprine or 6-mercaptopurine; UC, ulcerative colitis; VDZ, vedolizumab.

Ethics approval Samples from Oxford patients were collected as a project (ref ORB 20/A054) under the ethical approval of the Oxford Radcliffe Biobank, a research tissue bank that has a favourable opinion from the Oxford C South Central REC, with reference 19/SC/0173. Samples from London patients were collected as a project under the ethical approval of the Digestive Disease Bioresource, Barts Health NHS Trust, a research tissue bank that has a favourable opinion from the Bromley REC, reference 15/LO/2127.

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ORCID iDs

Colleen GC McGregor <http://orcid.org/0000-0002-4090-0375>

Alex Adams <http://orcid.org/0000-0001-9364-8540>

Simon PL Travis <http://orcid.org/0000-0002-2690-4361>

Nicholas M Croft <http://orcid.org/0000-0002-1519-6435>

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Supplementary material

Supplementary Table 1: Demographic, socioeconomic and clinical characteristics

	Oxford n=404		London (Adult) n=180		London (Paediatric) n=56	
Median age (IQR)	44.0 (29.0-60.0)		31.5 (23.0-44.2) ****		14.8 (12.7-16.3)	
Sex (Male) (n, %)	214 (53.0)		119 (66.1) **		32 (57.1%)	
Median weight (kg) (IQR)	74 (64.0-88.0)		67.5 (59.0-78.0) ****		53.6 (44.8-66.1)	
Median deprivation score[†] (IQR)	8 (6.0-9.3)		4 (3.0-6.3) ****		4 (2.8-7.0)	
Ethnicity						
White	349 (86.4)		74 (41.1) ****		14 (25.0)	
Asian	14 (3.5)		63 (35.0) ****		13 (23.2)	
Black	3 (0.7)		11 (6.1) ***		7 (12.5)	
Mixed	3 (0.7)		0 (0.0)		2 (3.6)	
Other	5 (1.2)		10 (5.6) **		1 (1.8)	
Unstated	30 (7.4)		21 (11.7)		19 (33.9)	
Smoking status						
Current (n, %)	41 (11.7)		8 (4.4) **			
Ex-smoker (n, %)	114 (32.6)		12 (6.7) ****			
Disease						
Crohn's disease (CD) (n, %)	188 (46.5)		106 (58.9) **		29 (51.8)	
Ulcerative colitis (UC) (n, %)	211 (52.5)		71 (39.4) **		23 (41.1)	
IBD-U (n, %)	4 (1.0)		3 (1.7)		4 (7.1)	
Median disease duration, yrs (IQR)	10 (5.0-18.0)		8.5 (4.8-15.2)		3.3 (2.1-5.9)	
Comorbidity (n, %)	116 (28.7)		32 (17.8) **		5 (8.9)	
Medication (n, %)						
Infliximab	176 (43.6)		118 (65.6) ****		48 (85.7)	
Vedolizumab	228 (56.4)		62 (34.4) ****		8 (14.3)	
Concomitant medication						
Prednisolone	12 (3.0)		8 (4.4)		6 (10.7)	
Budesonide	6 (1.5)		2 (1.1)		0 (0.0)	
Steroid	18 (4.5)		10 (5.6)		6 (10.7)	
5-ASA	73 (18.1)		33 (18.3)		18 (32.1)	
Thiopurine	101 (25.0)		71 (39.4) ***		49 (87.5)	
	IFX (n=88)	VDZ (n=13)	IFX (n=64)	VDZ (n=7)	IFX (n=43)	VDZ (n=6)
Azathioprine	73 (83.0)	11 (84.6)	54 (84.4)	5 (71.4)	37 (86.0)	6 (100.0)
6-mercaptopurine	15 (17.0)	2 (15.4)	10 (15.6)	2 (28.6)	6 (14.0)	0 (0.0)
MTX	12 (3.0)		9 (5.0)		0 (0.0)	
MMF	12 (3.0)		0 (0.0) *		0 (0.0)	

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P values denote comparison of Oxford vs. London (adult): *P ≤ 0.05, **P ≤ 0.01, ***P ≤ 0.001, ****P ≤ 0.0001, non-significant otherwise

† Deprivation score: Derived from the English Indices of Multiple Deprivation (IMD), the score classifies relative deprivation per area. A score of 1 = Most deprived, 10 = Least deprived

IBD-U: Inflammatory Bowel Disease-Unclassified, COPD: Chronic obstructive pulmonary disease, CVD: Cerebrovascular disease, 5-ASA: 5-aminosalicylic acid, MTX: Methotrexate, MMF: Mycophenolate mofetil, IFX: Infliximab, VDZ: Vedolizumab

Supplementary Table 2: Demographic characteristics of control groups

	Oxford [†] Non-patient facing HCW (Administrative staff)			Oxford [†] HCW			London [§] (Paediatric)
	All	Seropositive	Seronegative	All	Seropositive	Seronegative	All
n	1289	78	1211	9311	987	8324	396
Median age (IQR)	45.0 (32.3-55.4)	45.1 (33.4-56.1)	45.0 (32.2-55.4)	38.8 (29.8-48.8)	39.2 (29.5-49.0)	38.7 (29.9-48.8)	13.0 (8.1 – 16.0)
Gender (n, %)							
M	197 (15.3)	9 (4.6)	188 (95.4)	2545	296 (11.6)	2249 (88.4)	194 (49.0)
F	1087 (84.3)	68 (6.3)	1019 (93.7)	6744	689 (10.2)	6055 (89.8)	202 (51.0)
Prefer not to say	3 (0.2)	0 (0.0)	3 (100.0)	19	2 (10.5)	17 (89.5)	-
Trans	2 (0.2)	1 (50.0)	1 (50.0)	3	0 (0.0)	3 (100.0)	-
Ethnicity (n, %)							
White	1082 (84.0)	65 (6.0)	1017 (94.0)	6544 (70.3)	563 (8.6)	5981 (91.4)	-
Asian	102 (7.9)	11 (10.8)	91 (89.2)	1670 (17.9)	261 (15.6)	1409 (84.4)	-
Black	43 (3.3)	1 (2.3)	42 (97.7)	364 (3.9)	70 (19.2)	294 (80.8)	-
Chinese	4 (0.3)	0 (0.0)	4 (100.0)	99 (1.1)	8 (8.1)	91 (91.9)	-
Mixed	39 (3.0)	0 (0.0)	39 (100.0)	231 (2.5)	30 (13.0)	201 (87.0)	-
Other	12 (1.0)	1 (8.3)	11 (91.7)	251 (2.7)	39 (15.5)	212 (84.5)	-
Unstated	7 (0.5)	0 (0.0)	7 (100.0)	152 (1.6)	16 (10.5)	136 (89.5)	-
HCW: Healthcare worker, Trans: Transgender							
† Source data: Eyre DW et al. <i>Elife</i> 2020;9.							
§ Source data: Public Health England, National Paediatric Seroprevalence study, Royal London Children's Hospital							

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Supplementary Table 3: *Extended univariable relationships between clinical, socioeconomic and demographic factors with SARS-CoV-2 seropositivity. All statistics show 95% confidence intervals in parentheses. F=fishers test, otherwise logistic regression, all p values uncorrected*

	Oxford		London (Adult)		London (Paediatric)	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Biologic						
Vedolizumab (VDZ) ^F	3.98 (0.83-37.85)	0.08	1.20 (0.30-4.40)	0.77	1.00 (0.02-10.54)	1
Infliximab (IFX) ^F	0.25 (0.03-1.20)	0.08	0.83 (0.23-3.38)	0.77	1.00 (0.09-52.49)	1
Demographics						
Age	0.99 (0.96-1.03)	0.78	1.01 (0.97-1.04)	0.61	0.90 (0.67-1.24)	0.5
Sex (Male) ^F	1.80 (0.47-8.32)	0.39	6.68 (0.95-291.99)	0.06	0.52 (0.07-3.46)	0.45
Weight	1.02 (0.99-1.05)	0.19	1.00 (0.96-1.03)	0.98	0.99 (0.94-1.04)	0.66
Deprivation	0.95 (0.75-1.24)	0.68	1.01 (0.80-1.25)	0.91	0.87 (0.58-1.19)	0.42
Current smoker ^F	0.75 (0.02-5.51)	1	1.90 (0.04-16.94)	0.46	-	-
Ethnicity						
White	0.78 (0.16-7.54)	0.67	0.89 (0.22-3.23)	1	0.47 (0.01-4.46)	0.67
Asian	2.64 (0.06-20.92)	0.35	0.81 (0.18-3.07)	1	2.86 (0.36-20.12)	0.33
Black	0.00 (0.00-83.87)	1	0.00 (0.00-5.44)	1	1.19 (0.02-13.05)	1
Mixed	0.00 (0.00-83.87)	1	-	-	7.48 (0.09-636.53)	0.24
Other	0.00 (0.00-38.81)	1	3.57 (0.33-21.30)	0.16	0.00 (0.00-271.84)	1
Clinical						
Disease UC ^F	1.60 (0.40-7.58)	0.55	0.66 (0.14-2.50)	0.57	2.08 (0.31-15.77)	0.43
Disease duration	1.00 (0.95-1.05)	0.88	1.00 (0.91-1.06)	0.97	1.03 (0.72-1.39)	0.86
Comorbidities						
All comorbidity ^F	0.22 (0.01-1.54)	0.19	4.59 (1.17-17.44)	0.01	0.00 (0.00-8.44)	1
Cancer ^F	0.00 (0.00-30.39)	1	9.65 (0.74-94.17)	0.04	-	-
Cardiovascular disease ^F	0.00 (0.00-5.91)	1	0.00 (0.00-32.66)	1	-	-
Chronic kidney disease ^F	0.00 (0.00-180.21)	1	0.00 (0.00-497.12)	1	-	-
Chronic liver disease ^F	1.39 (0.03-10.35)	0.54	4.49 (0.08-61.09)	0.26	0.00 (0.00-39.27)	1