

THE LANCET

Gastroenterology & Hepatology

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed.
We post it as supplied by the authors.

Supplement to: An P, Ji M, Ren H, et al. Prevention of COVID-19 in patients with inflammatory bowel disease in Wuhan, China. *Lancet Gastroenterol Hepatol* 2020; published online April 17. [https://doi.org/10.1016/S2468-1253\(20\)30121-7](https://doi.org/10.1016/S2468-1253(20)30121-7).

Appendix

Methods

No exclusion criteria were specified. Demographic information was collected on patients including age, sex, current smoking habits, profession, workplace, living location, IBD diagnosis and classification, comorbid conditions, and IBD specific treatments and medications. The study protocol was approved by the ethics committee of Renmin Hospital of Wuhan University and waiver of informed consent was obtained.

Table 1. Characteristics of 318 participants with inflammatory bowel disease.			
	Total (n=318)	CD (n=114)	UC (n=204)
Age, years (median, IQR)	39.2 (15-79)	35.5 (15-67)	43.6 (22-79)
>60	33 (10.4%)	3 (2.6%)	31 (15.2%)
40-59	171 (53.8%)	32 (28.1%)	132 (64.7%)
17-39	117 (36.8%)	76 (66.7%)	41 (20.1%)
<16	3 (0.9%)	3 (2.6%)	0
Sex			
Female	123 (38.7%)	34 (29.8%)	89 (43.6%)
Male	195 (61.3%)	80 (71.2%)	115 (56.4%)
History			
Smoking	8 (2.5%)	4 (3.5%)	4 (2.0%)
Other chronic medical conditions	49 (15.4%)	22 (19.3%)	27 (13.2%)
Hypertension	28 (8.8%)	12 (10.5%)	16 (7.8%)
Diabetes	5 (1.6%)	2 (1.8%)	3 (1.5%)
Cardiovascular disease	4 (1.3%)	1 (0.9%)	3 (1.5%)
Chronic obstructive pulmonary disease	1 (0.3%)	0	1 (0.5%)
Chronic liver disease	6 (1.9%)	4 (3.5%)	2 (1.0%)
Ankylosing spondylitis	2 (0.6%)	1 (0.9%)	1 (0.5%)
Systemic lupus erythematosus	2 (0.6%)	1 (0.9%)	1 (0.5%)
Malignancy	2 (0.6%)	0	2 (1.0%)
Pregnancy	1 (0.3%)	1 (0.9%)	0
Exposure risk or history			
High exposure risk for COVID-19	24 (7.5%)	11 (9.6%)	13 (6.4%)
Hospital healthcare workers	12 (3.8%)	10 (0.9%)	2 (1.0%)
Policemen on patrol duties	2 (0.6%)	0	2 (1.0%)
Supermarket clerks	3 (0.9%)	0	3 (1.5%)
Close contact with hospital healthcare workers	6 (1.9%)	1 (0.9%)	5 (2.5%)
Contact with confirmed or suspect COVID-19-infected patients	1 (0.3%)	0	1 (0.5%)
Montreal classification			
CD L1	-	33 (28.9%)	-
L2	-	26 (22.8%)	-
L3	-	51 (44.7%)	-
L4	-	3 (2.6%)	-
B1	-	51 (44.7%)	-
B2	-	47 (41.2%)	-
B3	-	16 (14.0%)	-

P			22 (19.3%)
UC	E1	-	28 (13.7%)
	E2	-	72 (35.3%)
	E3	-	104 (51.0%)
Disease activity*			
	Remission	190 (59.7%)	111 (54.4%)
	Active	128 (40.3%)	93 (45.6%)
Treatments before the outbreak			
	5-Amino-salicylic acid (Mesalamin, Sulfasalazine)	151 (47.5%)	140 (68.6%)
	Corticosteroid	40 (12.6%)	32 (15.7%)
	Immunosuppressive therapy (Azathioprine)	35 (11.0%)	13 (6.4%)
	Thalidomide	37 (11.6%)	12 (5.9%)
	Biologics (Infliximab)	20 (6.3%)	2 (1.0%)
	Enteral nutrition	31 (9.7%)	0
Clinical trial participants			
	stage IIb	6 (1.9%)	0
	stage IIa/IIb	3 (0.9%)	3 (1.5%)
Flare and treatment			
	Flare during the outbreak	20 (6.3%)	6 (2.9%)
	Days from consultant to treatment	1.3 (1-2)	1.2 (1-2)
	Corticosteroid	18 (5.7%)	5 (2.5%)
	Exclusive enteral nutrition	15 (4.7%)	0
Hospitalization during the outbreak			
	Surgery	5 (1.6%)	2 (1.0%)
	Surgery during the outbreak	3 (0.9%)	1 (0.5%)
	Intestine perforation	1 (0.3%)	0
	Perianal abscess	1 (0.3%)	1 (0.5%)
	Production	1 (0.3%)	0
	Surgery before the outbreak	2 (0.6%)	1 (0.5%)
COVID-19 screen			
	Positive	0	0
	Complete blood test	29 (9.1%)	12 (5.9%)
	Chest CT scan	29 (9.1%)	12 (5.9%)
	Virological test	29 (9.1%)	12 (5.9%)
	IgM, IgG	20 (6.3%)	6 (2.9%)
UC, ulcerative colitis; CD, Crohn's Disease. *According to the respective disease activity indices prior to Dec 8, 2020. All data were collected by March 30.			

Supplementary figure 1: The geographic distribution of the confirmed COVID-19-infected patients and those of our IBD registry patients living in Hubei province and Wuhan

The majority of our IBD registry patients (246 of 318 patients [77.4%]) lived in Wuhan, inside the city boundaries (226 [71.1%]), and within 30 kilometers from Huanan Seafood Market, the presumed epicenter of the COVID-19 outbreak.

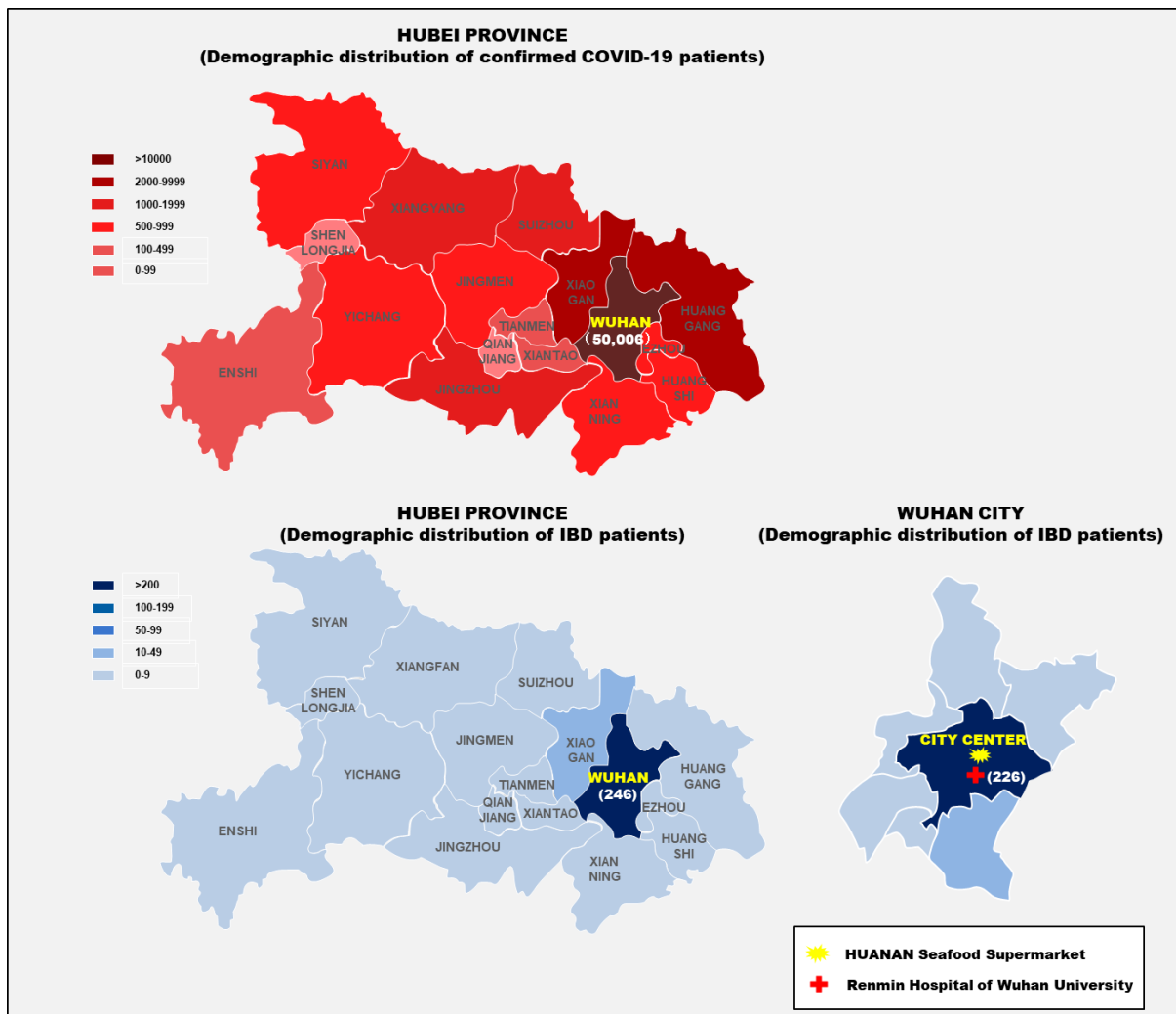
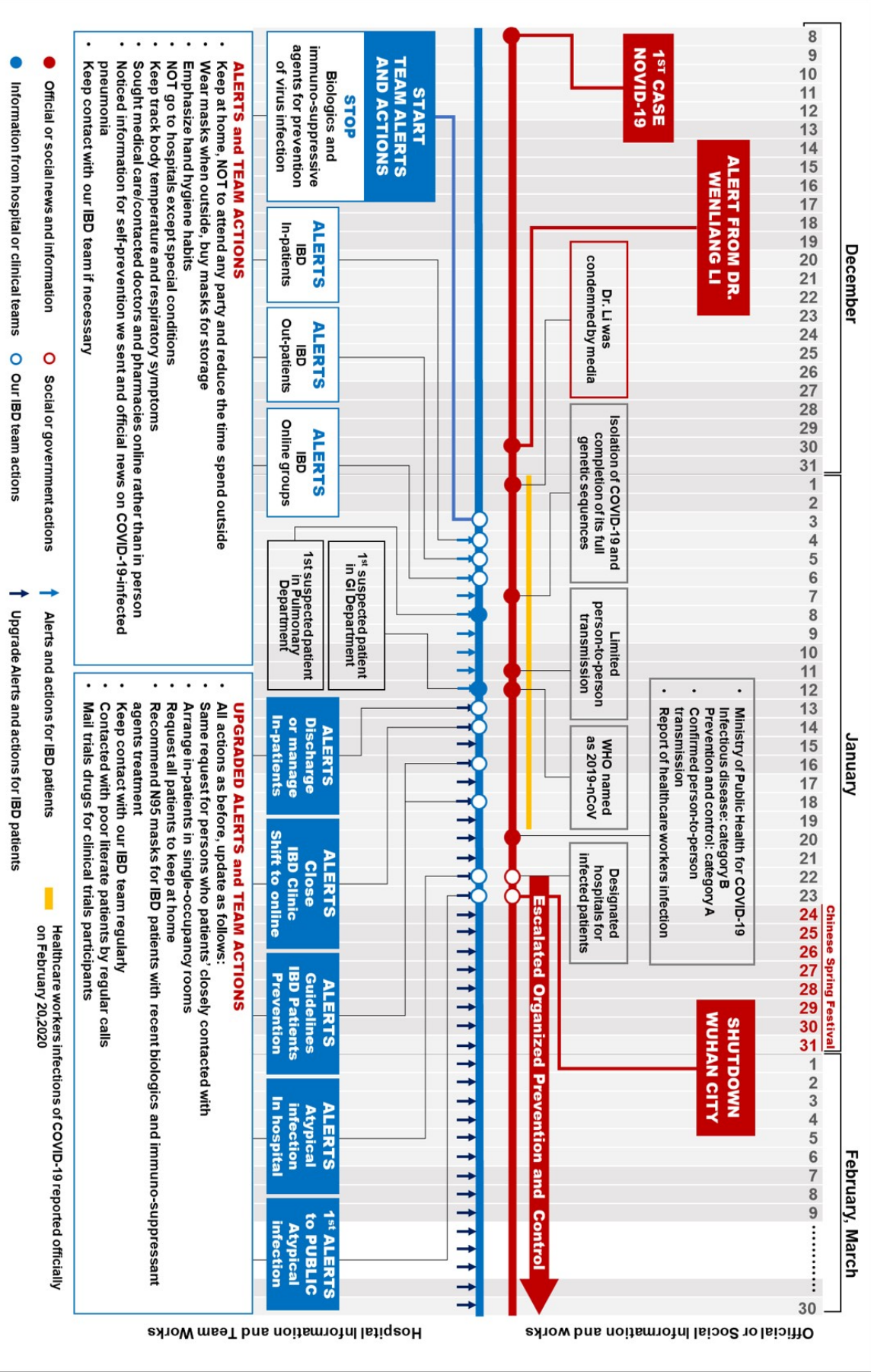


Figure 2. Timeline of official or social news and our IBD team works during the outbreak and rapid spread of COVID-19 infection.



Discussion

On December 30, 2019, Dr. Wenliang Li, a Chinese ophthalmologist in Wuhan sounded an early and stark warning that seven patients from Huanan Seafood Supermarket had been diagnosed with a SARS-like illness and quarantined in his hospital (**Fig. 2**). In total, 33 subjects (10.4%) in our IBD registry were >60 years of age, 49 (15.4%) subjects had other chronic medical illness, 35 (11.0%) patients were treated with immunosuppressive agents and 20 (6.3%) received biologics therapy (Infliximab) (**Table 1**). These were factors identified during the H1N1 influenza epidemic of 2009 as increasing the risk of infection.¹ Older age and chronic medical conditions have been shown to contribute to COVID-19-related death.^{2,3} Exposure risks of profession such as healthcare workers, poultry-workers and police officers, were assessed and close contact with healthcare workers were also identified as additional factors which increased infection risk. In our registry, 24 patients (7.5%) were at high risk for infection to COVID-19 as they were healthcare workers, policemen on patrol duties, and supermarket clerks (**Table 1**). 7 (38.7%) patients additionally reported close contact with hospital healthcare workers. Importantly, Huanan Seafood Supermarket, the suspected location from where COVID-19 emerged is located in the city center of Wuhan with over two-thirds of our IBD patients living and working within this proximity (**Fig. 1**), placing most of our patients at higher risk.

With the diagnosis of similar cases in other hospitals and suspected infections in healthcare workers, our IBD team decided to alert and guide our patients to prevent this potentially highly contagious disease. We undertook a number of steps to reduce the risk of infection in our registry patients (**Fig. 2**). We started to send mobile messages via WeChat with daily alerts on recommendations/precautions for infection prevention to our IBD patients on January 3, 2020. Subsequently, our alerts and actions for prevention focused on airborne and contact transmission. All patients were asked to stay at home and isolate, not to attend parties or outside gatherings, wear

masks if outside, maintain hand hygiene habits, and to attend regular telehealth clinics online. Daily body temperature and respiratory symptoms were also emphasized. Most patients responded to our daily alerts by (electronic medical record) messages and WeChat. Most patients decreased time spent outside (291[91.5%]), wore masks when outside (284 [89.3%]), and bought masks for storage (246 [77.3%]) (**Table 2**). Our alerts and clinical actions occurred nearly 20 days before the lockdown date of Wuhan. There was adequate provision of time for our IBD patients to prepare for this unpredictable time during lockdown.

On January 20, 2020, after official Chinese government statements confirmed person-to-person transmission and infections in healthcare workers of COVID-19, and consideration of the coming Spring Festival travel rush, we further updated alerts and actions including sending daily alerts to remind and ask all patients and persons they were closely in contact with to stay at home if possible, use N95 masks for IBD patients with recent treatment with biologics and immuno-suppressants, keep in contact with our IBD team regularly, particularly for patients at high risk for infection. By this time, all 318 of our registry patients reported adherence to our recommended infection prevention strategies (**Table 2**).

We believe that our IBD team's long-term relationships with our patients and understanding of their individual risk factors along with routine emphasis on patient education greatly contributed to their reported excellent adherence to our recommendations. As for February 13, 2020, none of our 318 IBD registry patients were diagnosed with confirmed or suspected COVID-19-infected pneumonia. It is also crucial to have a method of communication between patients and their IBD teams which allows patient's concerns including possible flare of symptoms to be addressed in a timely fashion as demonstrated by our data with a median time to response of 1 day. Within Wuhan and other areas of very high community transmission and background COVID-19 cases, we want to prevent any possible infection in our IBD cohorts. This requires more extreme social distancing measures including social isolation of themselves and their close contacts. The Chinese Society of Gastroenterology have recommended the measures of withholding

immunosuppressive therapies due to possible increased risk of infection and worsening of COVID-19 infection course.⁴ Given these unprecedented times, actions such as possibly withholding immunosuppressive medications might be indicated to prevent infections due to potential worsening infection course. However, local guidelines and isolation measures should be dictated by the background rate of COVID-19 infection in the community.

Although patients with IBD are considered to be more susceptible to infections compared to the general population owing to the immune-mediated nature of IBD as well as the immunosuppressive effects of treatment, it remains unclear if they are at a high risk for COVID-19 infection with current registry studies that are ongoing such as SECURE-IBD. Recent research has revealed that COVID-19 is a novel coronavirus that can use the same cellular receptor, angiotensin converting enzyme II (ACE2), as the SARS virus to invade host cells.^{5,6} To date, the incidence and severity of SARS infection in IBD patients have not been reported. Therefore, larger scale surveys and analysis needs to be performed. In summary, during the current outbreak of COVID-19, attention must be paid to prevent and control infection along with timely and decisive adoption and adjustment of protective measures which are key to preventing and protecting IBD patients from COVID-19. We believe our experiences provides a model of care in the setting of the advancement of COVID-19 throughout the world and in future pandemic disease response.

References

1. Naganuma M, Fujii T, Kunisaki R, et al. Incidence and characteristics of the 2009 influenza (H1N1) infections in inflammatory bowel disease patients. *J Crohns Colitis* 2013;7:308-13.
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020
3. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020
4. Wu KC, Qian JM. Management of patients with inflammatory bowel disease during epidemic of 2019 novel coronavirus pneumonia. *Chin J Dig* 2020;40: E001.

5. Hao Z, Zijian K, Haiyi G, et al. The digestive system is a potential route of 2019-nCov infection: a bioinformatics analysis based on single-cell transcriptomes. *BioRxiv*
<https://doi.org/10.1101/2020.01.30.927806>

6. Markus H, Hannah K, Nadine K, et al. The novel coronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells. *BioRxiv*
<https://doi.org/10.1101/2020.01.31.929042>