**ISARIC4C has produced 41 papers with an average altmetric score of 987.**

# Co-Infection with influenza virus is associated with worse outcomes in hospitalised Covid patients

[Lancet 2022](https://doi.org/10.1016/S0140-6736(22)00383-X) [SAGE minutes](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1055478/S1517_Influenza_virus_coinfection_is_associated_with_worse_COVID-19_outcomes_COCIN.pdf)

This analysis provides a clear answer to a simple question: what is the effect of co-infection with common viruses on top of Covid? We compared outcomes across people who tested positive for three different viruses (influenza (flu) virus, adenovirus, and RSV) and found that co-infection with the flu virus was associated a higher chance of critical illness and death.

This has direct implications for the NHS, suggesting that we should test patients more often for flu. It also provides another reason to vaccinate people more widely against both flu and Covid, particularly as flu is expected to make a comeback in 2022.

As with much of our work, this was discussed immediately at the UK government advisory group, SAGE, and has already influenced the thinking around policy.

Altmetric score: 3834[https://doi.org/10.1016/S0140-6736(22)00383-X]

# Sharing samples and data

ISARIC4C was designed from the outset as a foundation for the UK outbreak response, supporting researchers across the country.

The 4C consortium has:

* Responded to clinical 120 data requests, providing data to 100 collaborators
* Shipped out a total of 21,000 samples from our hub labs in Liverpool and Glasgow
* Provided sample sets to 21 different institutions (Universities, Public Health England, NIBSC, Francis Crick Inst., NIH)

Dynamic data feeds from the [data analysis platform](/ap) are provided via API to Public Health in England & Scotland & SPI-M with independent reports prepared by them for NERVTAG and SAGE.

{% include\_relative samples/samples.citemd.html %}

# Impacting Policy

ISARIC4C and CO-CIN (Tier 0) feed data dynamically to Public Health Scotland, Public Health England, SPI-M, NERVTAG and SAGE. SPI-M have been highly productive and published several analysis that informed Policy.

ISARIC4C and CO-CIN data are used to inform the NHS England Independent Advisory Group concerning the use of neutralising monoclonal antibodies and anti-viral drugs in high-risk clinical subgroups.

Other key UK policy documents citing ISARIC4C / CO-CIN data

1. COVID-19: the green book, chapter 14a.
   1. cites Docherty AB, et al. Features of 20133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study <https://doi.org/10.1136/bmj.m1985>
   2. Swann OV, et al. Clinical Characteristics of children and young people admitted to hospital with COVID-19 in United Kingdom: prospective multicentre observational cohort study <https://doi.org/10.1136/bmj.m3249>
2. Remdesivir – national prescribing guidance

# Risk prediction: the 4C Mortality Score

[BMJ 9 Mar 2020](https://doi.org/10.1136/bmj.m3339)

Using data from 57, 824 hospital admissions, we developed and validated an easy-to-use risk stratification score based on commonly available parameters at hospital presentation. The 4C Mortality Score outperformed existing scores, showed utility to directly inform clinical decision making, and can be used to stratify patients admitted to hospital with covid-19 into different management groups.

The 4C Mortality Score can be found here: [isaric4c.net/risk](/risk)

The 4C Mortality Score has been extensively validated in independent studies across the world. Validation of the 4C score showed similar discrimination in the following countries:

* [Singapore](https://doi.org/10.1093/cid/ciac087)
* [Japan](https://doi.org/10.3390/jcm11030821)
* [United States](10.2196/31549)
* [Brazil](https://doi.org/10.1016/j.ijid.2021.07.049)
* [Brazil and Spain](https://doi.org/10.1016/j.cmi.2021.03.002)
* [Belgium](https://doi.org/10.1080/23744235.2021.1896777)
* [Saudi Arabia](https://www.sjmms.net/article.asp?issn=1658-631X;year=2022;volume=10;issue=1;spage=19;epage=24;aulast=Aletreby)
* [Australia](https://search.informit.org/doi/abs/10.3316/informit.247030265377533)
* [France](https://doi.org/10.1038/s41467-020-20657-4)
* [The Netherlands](https://doi.org/10.1080/07853890.2021.1891453)
* [Italy](https://doi.org/10.1111/jgs.16956)
* [Pakistan](https://jamc.ayubmed.edu.pk/jamc/index.php/jamc/article/view/9206/3049)
* [Turkey](https://doi.org/10.1016/j.hrtlng.2021.01.006)
* [Canada, Toronto](https://doi.org/10.1503/cmaj.202795)
* [Canada, Ontario](https://doi.org/10.21203/rs.3.rs-268410/v1)
* [Romania](https://doi.org/10.3390/medicina58070848)

Using data from the second wave of the COVID-19 pandemic in the UK, a [prospective validation study](https://thorax.bmj.com/content/early/2021/11/21/thoraxjnl-2021-217629) showed that both the 4C Mortality Score and 4C Deterioration Score demonstrated consistent performance to predict clinical deterioration and mortality. Despite recent advances in the treatment and management of adults hospitalised with COVID-19, both scores can continue to inform clinical decision making.

Altmetric score: 743[https://doi.org/10.1136/bmj.m3339]

# Characterisation of hospitalised cases of COVID-19

[BMJ: 2020; 369](https://doi.org/10.1136/bmj.m1985)

Within weeks of being funded, we produced the largest study anywhere in the world of COVID-19 cases, enabling us to produce the most accurate risk prediction models for the UK population. These will continue to improve. The first one shows that obesity is an important risk factor amongst many. This finding will help to protect people at high risk of death from COVID-19. Our preprint is now online **Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol**. We have also produced an [interactive infographic](/risk/v1) to help communicate these findings.

Altmetric score: 2203[https://doi.org/10.1136/bmj.m1985]

# Genetic mechanisms of severe Covid-19

[MedRxiv September 2020; Nature online December 2020](https://doi.org/10.1038/s41586-020-03065-y)

In collaboration with the [ISARIC GenOMICC study](https://genomicc.org) we discovered multiple genes that underlie critical illness in Covid-19, including several that led directly to potential therapeutic targets.

In 2244 Covid cases, we compared severely ill patients with matched members of the population from three other studies (UK Biobank, Generation Scotland and 100,000 Genomes). We found genes involved in two molecular processes - antiviral immunity and lung inflammation - were important in determining the development of severe Covid-19. We replicated our findings in additional studies (Covid-19 HGI and 23andme). The associations with disease are robustly confirmed in these studies.

Although we know the DNA associations are real, we can’t always be sure exactly how these variants lead to disease. The most likely genes underlying each of the four new discoveries are IFNAR2, TYK2, OAS1, DPP9.

The action of some genetic variants is similar the the action of drugs - either increasing or decreasing the amount of a particular molecule or signal. We can use this to predict new treatments. This evidence has already influenced the inclusion of new therapies in the RECOVERY trial.

Altmetric score: 2827[https://doi.org/10.1038/s41586-020-03065-y]

# Clinical characterisation of Covid-19 in children

[BMJ 2020;370:m3249](https://doi.org/10.1136/bmj.m3249)

We have comprehensively characterised the burden and patterns of disease in children in the UK, demonstrating that life-threatening disease in otherwise healthy children is extremely rare. This had direct impact on public health policy in the UK and abroad.

Altmetric score: 2857[https://doi.org/10.1136/bmj.m3249]

# Characterisation of in-hospital complications associated with COVID-19

[The Lancet, 17 July 2021](https://doi.org/10.1016/S0140-6736(21)00799-6)

As well as death, severe COVID-19 disease has effects on many different organ systems. In this study, published in The Lancet, we characterised the burden of complications and organ injury in 73,197 patients admitted to hospital between January and August 2020. We found that nearly 1 in 2 people had at least one complication. Having a complication was associated with higher rates of critical care admission and mortality. When we studied predictors of complications, we identified that unlike in the case of mortality, where older, more frail people had a higher chance of death, younger people were also at risk of developing complications. This study received international media attention and coverage from the BBC, ABC, Sky news, ITV, STV and most major UK newspapers.

This work was also the subject of a system-wide [NIHR update](https://evidence.nihr.ac.uk/alert/one-in-two-people-hospitalised-with-covid-19-develop-complications-may-need-support/).

Altmetric score: 2667[https://doi.org/10.1016/S0140-6736(21)00799-6]

# Circulating histones play a central role in COVID-19-associated coagulopathy and mortality

[Haematologica Early View 8 April 2021](https://doi.org/10.3324/haematol.2021.278492)

COVID-19 has highlighted the lethal consequences of immunothrombosis; i.e. the cross-talk between coagulation, inflammation and the innate immune system. These patients have significant immune cell death, which can release pro-coagulant and cytotoxic histones. In this translational study, we showed that circulating histones play a central role in critically ill COVID-19 patients with admission histone levels significantly elevated with increasing severity of COVID-19 infection.

Altmetric score: 3[https://doi.org/10.3324/haematol.2021.278492]

# Tissue proteomic analysis identifies mechanisms and stages of immunopathology in fatal COVID-19

[American Journal of Respiratory Cell and Molecular Biology 26 October 2021](https://doi.org/10.1165/rcmb.2021-0358OC)

Peripheral blood inflammatory profiles are increasingly well characterised in Covid-19 but knowledge of the host response within inflamed tissues is lacking. Post-mortem lung and spleen whole-tissue proteomics identified differentially abundant proteins of mechanistic and translational interest (including MCP-3, TYMP, EN-RAGE and CSF-1). Lung proteomic clusters identified distinct disease stages that differed in pulmonary viral presence, inflammation severity, illness duration, and abundance of proteins of interest including IL-6 and IRAK1

Altmetric score: 7[https://doi.org/10.1165/rcmb.2021-0358OC]

# Hospital acquired COVID-19 in England during the first wave of the pandemic

[BMC Infectious Diseases June 2022](https://doi.org/10.1186/s12879-022-07490-4)

Using data from the ISARIC4C UK COVID-19 Clinical Information Network study, this study identified that 1 in 5 hospitalised patients in England during the first wave of the pandemic caught the virus while hospitalised for other causes. However, this accounted for less than 1% of all COVID-19 cases in England, both hospitalised and not.

Altmetric score: 13[https://doi.org/10.1186/s12879-022-07490-4]

# Long Covid in adults discharged from UK hospitals after Covid-19

[MedRxiv pre-prints 25 March 2021](https://doi.org/10.1101/2021.03.18.21253888)

It is emerging that long-term symptoms are often present in people who have had acute Covid-19 disease. We found that over half of patients reported not feeling fully recovered several months after onset of Covid-19 symptoms. The symptoms reported include fatigue, followed by breathlessness. These findings were present in young, previously healthy working age adults, and were most common in younger females.

Altmetric score: 852[https://doi.org/10.1101/2021.03.18.21253888]

# Treating COVID-19 patients with dexamethasone and remdesivir prevents neurological complications

[Annals of Neurology October 2022](https://doi.org/10.1002/ana.26536)

Preventing the development of neurological complications after severe COVID-19 infections remains an important aim for doctors. Data from the ISARIC4C study group showed that individuals who go on to have neurological issues after being hospitalised with COVID-19 do not recover as well and have an increased risk of death. This study showed that patients treated with dexamethasone, a commonly used steroid, or remdesivir, an antiviral drug first used in hepatitis C, were less likely to have neurological issues than those who were not treated. The use of both of these drugs together further reduced the risk of complications.

Altmetric score: 37[https://doi.org/10.1002/ana.26536]

# UK Paediatric COVID-19 cases in the first and second pandemic wave

[Pediatric Research April 2022](https://doi.org/10.1038/s41390-022-02052-5)

Data from paediatric patients in the ISARIC4C study were used to help inform SAGE for the vaccination policy in children and young people earlier in 2022. Even though there was a change in the viral variant, a relaxation of shielding, and a return to face-to-face schooling, no evidence of increased severity in paediatric COVID-19 hospital admissions was found between the second and first waves of the COVID-19 pandemic.

Altmetric score: 40[https://doi.org/10.1038/s41390-022-02052-5]

# Vitamin D insufficiency in COVID-19 and influenza A

[BMJ Open 30 Sept 2021](http://dx.doi.org/10.1136/bmjopen-2021-055435)

Vitamin D deficiency/insufficiency was present in the majority of hospitalised patients with Covid-19 (ISARIC4C study) and influenza A (MOSAIC study, 2009-10 H1N1 pandemic), correlated with severity and persisted in non-selected critical illness survivors (prior to Covid-19 pandemic) at concentrations expected to disrupt bone metabolism. These findings support early supplementation trials to determine if insufficiency is causal in progression to severe disease, and investigation of longer-term bone health outcomes.

Altmetric score: 65[http://dx.doi.org/10.1136/bmjopen-2021-055435]

# Using a double binding antigen assay to detect and measure SARS-CoV-2 antibodies

[Journal of Virological Methods, April 2022](https://doi.org/10.1016/j.jviromet.2022.114475)

Accurate and sensitive detection of antibody to SARS-CoV-2 remains an essential component of the pandemic response. Measuring antibody that predicts neutralising activity and the vaccine response is an absolute requirement for laboratory-based confirmatory and reference activity. The viral receptor binding domain (RBD) constitutes the prime target antigen for neutralising antibody. A hybrid double antigen binding assay (DABA) for anti-RBD showed a specificity of 100 % on 825 pre COVID-19 samples and a potential sensitivity of 99.6 % on 276 recovery samples, predicting quantitatively the presence of neutralising antibody determined by pseudo-type neutralization and by plaque reduction.

Altmetric score: 1[https://doi.org/10.1016/j.jviromet.2022.114475]

# Detecting SARS-CoV-2 by non-invasive means

[Journal of Infection August 2022](https://doi.org/10.1016/j.jinf.2022.05.033)

Finding non-invasive methods to detect the SARS-CoV-2 virus has been essential for rapid self-testing during the pandemic. This study compared gingival crevicular fluid (GCF), taken by swabbing the gums, to blood samples from patients in the ISARIC4C UK study. It was shown that GCF taken from the gums can detect the virus, and higher levels of SARS-CoV-2 antibodies in the GCF in the early acute phase of the illness are linked to more severe COVID-19 infections.

Altmetric score: 4[https://doi.org/10.1016/j.jinf.2022.05.033]

# Understanding the Omicron variant and how it responds to vaccination

[Cell July 2022](https://doi.org/10.1016/j.cell.2022.06.005)

The Omicron variant of the SARS-CoV-2 virus spread rapidly, even in those who had been vaccinated against it. This study examined the different DNA sequence of this viral variant to determine mutations in the virus from patient blood samples from the ISARIC4C study and the effect these mutations have on the ability for the vaccination to prevent infection or illness. Understanding these alterations can help with future vaccine strategies and prevent more rapidly spreading SARS-CoV-2 variants in the future.

Altmetric score: 1660[https://doi.org/10.1016/j.cell.2022.06.005]

# Evaluation of effectiveness of remdesivir in treating severe COVID-19

[MedRxiv pre-prints 21 June 2021](https://doi.org/10.1101/2021.06.18.21259072)

Adults with severe COVID-19 treated with remdesivir were compared with propensity-score matched control, identified from the ISARIC-CCP UK study. Remdesivir patients were matched to controls according to baseline underlying 14-day mortality risk. Remdesivir did not significantly improve mortality in this study.

Altmetric score: 22[https://doi.org/10.1101/2021.06.18.21259072]

# WHO guidelines on the use of chest imaging in COVID-19

[WHO Guidelines 2022](https://apps.who.int/iris/handle/10665/361833)

The ISARIC-CCP UK study has aided in the creation of the 2022 World Health Organisation (WHO) guidelines for the use of chest imaging in COVID-19. These guidelines state that “for patients with suspected or confirmed COVID-19, not currently hospitalized but with mild symptoms, WHO suggests using chest imaging to in addition to clinical and laboratory assessment to decide on hospital admission versus home discharge”. This guideline is based on patients first undergoing the validated risk stratification tool outlined in ISARIC-CCP.

[https://apps.who.int/iris/handle/10665/361833]

# Distinct clinical symptom patterns in patients hospitalised with COVID-19

[Scientific reports April 2022](https://doi.org/10.1038/s41598-022-08032-3)

Although the most common symptoms of COVID-19 tend to be fever, cough, and difficulty breathing, many other symptoms have been reported, including fatigue, confusion, diarrhoea, and vomiting. Using the data from 59,011 patients in the ISARI4C study. Patients presenting with gastrointestinal symptoms were more commonly female, had a longer duration of symptoms before presentation, and had lower 30-day mortality. On the other hand, patients presenting with confusion were older and had a higher unadjusted mortality. This study suggests four different groups of patients with differing symptoms, with or without the core three symptoms, that should be treated differently if hospitalised to prevent mortality.

Altmetric score: 1[https://doi.org/10.1038/s41598-022-08032-3]

# Non-steroidal anti-inflammatory drug use and outcomes of COVID-19

[The Lancet: Rheumatology May 07, 2021](https://doi.org/10.1016/S2665-9913(21)00104-1)

Early in the pandemic it was suggested that pre-existing use of non-steroidal anti-inflammatory drugs (NSAIDs) could lead to increased disease severity in patients with COVID-19. NSAIDs are an important analgesic, particularly in those with rheumatological disease, and are widely available to the general public without prescription.

Using data from 78,674 patients in ISARIC4C, we showed that NSAID use is not associated with higher mortality or increased severity of COVID-19. To our knowledge, our prospective study includes the largest number of patients admitted to hospital with COVID-19 to date, and adds to the literature on the safety of NSAIDs and in-hospital outcomes. NSAIDs do not appear to increase the risk of worse in-hospital outcomes. NSAIDs are an important analgesic modality and have a vital opioid-sparing role in pain management. Patients and clinicians should be reassured by these findings that NSAIDs are safe in the context of the pandemic.

Altmetric score: 2621[https://doi.org/10.1016/S2665-9913(21)00104-1]

# Role of blood cytokines IL-6 and GM-CSF in severe COVID-19

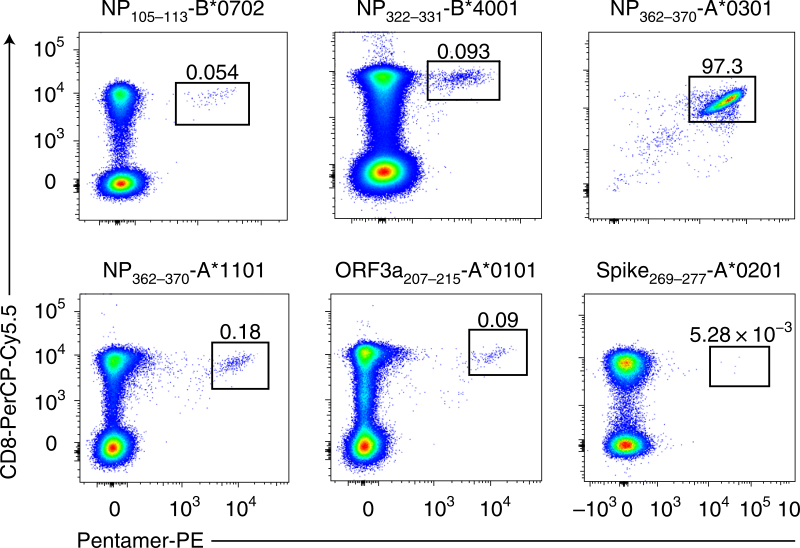
[Science Immunology 10 Mar 2021](https://doi.org/10.1126/sciimmunol.abg9873)

We have identified new biomarkers of inflammation that both reveal the severity of COVID-19 and set it apart from severe influenza. Many inflammatory cytokines were found in greater numbers in severe COVID-19 and that these levels generally indicate severe disease. We identified patterns within the data that were the most clearly linked to severe cases of COVID-19; two cytokines in particular, IL-6 (interleukin 6) and GM-CSF (granulocyte-macrophage colony stimulating factor) play central roles. With more research, we can see if GM-CSF could be used as a marker in early disease to identify those at risk of going on to develop more severe symptoms.

Altmetric score: 1363[https://doi.org/10.1126/sciimmunol.abg9873]

# T cells target many different parts of the virus

[Nature Immunology (4th September 2020)](https://doi.org/10.1038/s41590-020-0782-6))



This study by Yanchung Peng, Alex Mentzer, Tao Dong and colleagues reveals that the immune system responds to many different parts of the SARS-CoV-2 virus. This will influence vaccine design, which often focuses only on the most prominent parts of the virus. It also reveals key differences in the way immune cells fight the virus in patients who have mild disease, helping us to better understand how some people are able to fight it off without becoming very sick.

Altmetric score: 777[https://doi.org/10.1038/s41590-020-0782-6]

# Setting Serology Standards

# Setting the standard

ISARIC 4C defined the international reference standard for SARS-CoV-2 serology by providing the first samples to the [National Institute for Biological Standards and Control (NIBSC)](https://www.nibsc.org/) from COVID-19 cases. These were used to make the WHO International Standard for SARS-CoV-2 serology, which will be used all over the world to compare results from blood tests for COVID-19. 7 of the 11 patients who contributed to the standard were recruited by ISARIC 4C.

# Viral spike variants evading antibody-mediated immunity

[Cell 4 Mar 2021](https://doi.org/10.1016/j.cell.2021.01.037)

We showed that the N439K viral mutation has enhanced binding affinity to the ACE2 receptor and that this variant cause infections with similar clinical outcomes compared to the wild type. This mutation is resistant against neutralising monoclonal antibodies and from polyclonal sera from persons recovered from infection. Our findings have highlighted how this virus can mutate and the need for ongoing molecular surveillance to guide development and usage of vaccines and therapeutics.

Altmetric score: 447[https://doi.org/10.1016/j.cell.2021.01.037]

# SARS-CoV-2 surface and air contamination in a healthcare setting

[Clinical Infectious Diseases 8 Jul 2020](https://doi.org/10.1093/cid/ciaa905)

We have explored the mechanisms of viral transmission. Our findings of extensive viral RNA contamination of surfaces and air across a range of acute healthcare settings in the absence of cultured virus highlighted the potential risk from surface and air contamination in managing COVID-19, and the need for effective use of PPE, social distancing, and hand/surface hygiene.

Altmetric score: 157[https://doi.org/10.1093/cid/ciaa905]

# Impact of ethnicity

[SSRN July 2020](http://dx.doi.org/10.2139/ssrn.3618215)

We have carefully studied the effect of ethnicity on outcomes in hospitalised patients, revealing the effect of comorbidities in mediating part of the increased susceptibility in some ethic groups.

Altmetric score: 15[http://dx.doi.org/10.2139/ssrn.3618215]

# Supporting vaccine development

[The Lancet, 15 August 2020](https://doi.org/10.1016/S0140-6736(20)31604-4)

At the start of the pandemic, ISARIC4C was able to provide convalescent samples of PCR-positive hospitalised patients with COVID-19 to characterise the immunological properties of COVID-19. This was essential to the development of the viral vectored coronavirus vaccine developed by the Oxford COVID Vaccine Trial Group.

Altmetric score: 15125[https://doi.org/10.1016/S0140-6736(20)31604-4]

# ICECAP autopsy study

[American Journal of Respiratory and Critical Care Medicine 2021](https://doi.org/10.1164/rccm.202008-3265OC)

ISARIC 4C resources and consortium partners supported the COVID-19 post-mortem case series. This is one of several pieces of evidence that changes the model of COVID pathogenesis, supporting a primary role for the host immune system in causing fatal disease.

Altmetric score: 74[https://doi.org/10.1164/rccm.202008-3265OC]

# Viral RNA found in blood is not infectious

[Wellcome Open Research 29 Jul 2020](https://doi.org/10.12688/wellcomeopenres.16002.1)

Laboratory diagnosis of SARS-CoV-2 infection uses PCR to detect viral RNA (vRNA) in respiratory samples. While SARS-CoV-2 RNA has been detected in other sample types, there is very little understanding about its clinical or laboratory significance. This has implications for testing and for safe working in a laboratory setting. To answer this, we undertook a systematic review for evidence of viral RNA in blood. We also attempted viral isolation from PCR-positive blood samples. Viral RNA was detectable at very low levels, but this was not associated with infectious SARS-CoV-2. This work will help to inform biosafety precautions for handling blood from COVID-19 patients.

Altmetric score: 17[https://doi.org/10.12688/wellcomeopenres.16002.1]

# Developing methods of sequencing the virus

[Viruses 14 Oct 2020](http://doi.org/10.3390/v12101164)

Sequencing the viral genome as the outbreak progresses is important, particularly the identification of new variants and to identify whether any changes in the genome will impair clinical testing. Using the MinION/GridIONS platform, we developed a sensitive protocol to rapidly sequence the viral genome. With this study, we showed that amplicon-based detection and subsequent sequencing are feasible for identifying the SARS-CoV-2 genome or nucleic acid in samples from patients with COVID-19.

Altmetric score: 10[http://doi.org/10.3390/v12101164]

# Adverse outcomes in COVID-19 patients with underlying respiratory conditions

[Lancet Respiratory Medicine 4 March 2021](https://doi.org/10.1016/s2213-2600(21)00013-8)

Characterisation of 75 463 hospitalised COVID-19 patients from 258 participating health-care facilities showed that underlying respiratory symptoms is common and patients with asthma were more likely, and those with chronic pulmonary disease less likely, to receive critical care than patients without an underlying respiratory condition**.**

Altmetric score: 207[https://doi.org/10.1016/s2213-2600(21)00013-8]

# Pulmonary Microthrombosis and Vasculitis in Life-Threatening Respiratory Virus Diseases

[Open Forum Infectious Diseases 28 Dec 2020](http://doi.org/10.1093/ofid/ofaa640)

This study, with support and resources provided by ISARIC4C, found evidence of thrombosis present in adults with fatal influenza and SARS, with vasculitis also reported.

[http://doi.org/10.1093/ofid/ofaa640]

# Using imaging in COVID-19 – UK National COVID-19 Chest Imaging Database

[European Respiratory Journal 13 Aug 2020](http://doi.org/10.1183/13993003.01809-2020)

The National COVID-19 Chest Imaging Database (NCCID) is a repository of chest radiographs, CT and MRI images and clinical data from COVID-19 patients across the UK, to support research and development of AI technology and give insight into COVID-19 disease. To maximise efficient resource utilisation in busy hospitals during the course of the pandemic, NCCID are linking imaging data to the ISARIC4C dataset, and aim to link to the Intensive Care National Audit and Research Centre (ICNARC). ISARIC investigators are collating clinical information and biological samples for COVID-19 cases of all ages admitted to hospitals, while ICNARC collates detailed data from adults in the intensive care setting. The study has also been supported by Health Data Research UK as part of its UK response to COVID-19.

Altmetric score: 42[http://doi.org/10.1183/13993003.01809-2020]

# Outcomes of hospitalised COVID-19 patients with interstitial lung disease

[American Journal of Respiratory and Critical Care 15 Dec 2020](https://doi.org/10.1164/rccm.202007-2794oc)

We completed an international multicentre audit of patients with prior diagnosis of Interstitial Lung Diseases (ILD) admitted to hospital with COVID-19. We showed that these patients are at increased risk of death, particularly those with poor lung function and obesity. Data from this study showed that patients with ILD should follow self-isolation guidelines for vulnerable individuals and be prioritised for vaccinations.

Altmetric score: 101[https://doi.org/10.1164/rccm.202007-2794oc]

# Outcomes of COVID-19 hospitalisation among patients with HIV

[Clinical Infectious Diseases 23 Oct 2020](https://doi.org/10.1093/cid/ciaa1605)

Providing data and support to the British HIV Association, presentation characteristics and outcomes of adults with and without HIV who were hospitalized with COVID-19 at 207 centers across the UK, were compared. HIV-positive status was associated with an increased risk of day-28 mortality among patients hospitalised for COVID-19.

Altmetric score: 30[https://doi.org/10.1093/cid/ciaa1605]

# Co-Infections, Secondary Infections, and Antimicrobial Usage

[Lancet Microbe 2 June 2021](https://doi.org/10.1016/S2666-5247(21)00090-2)

We investigated the frequency and microbiological details of bacterial co-infection and secondary infection, in addition to antimicrobial usage in 48,902 patients hsopitalised with COVID-19 during the first pandemic wave. We found that Covid-19 related respiratory or bloodstream bacterial infection was rare (n=1,107); the majority (71%) were secondary infection, acquired >48 hours after admission. However, antimicrobial use is high with 37% prescribed pre-hospital antimicrobials, while 85% received one or more antimicrobials during their hospital stay.

Based on our data, we recommend a range of existing antimicrobial stewardship interventions that should be prioritised for incorporation into COVID-19 patient care to mitigate worsening of antimicrobial resistance. As well as restricting prescribing without a confirmed diagnosis, these include tailoring the choice of antimicrobials (when required) to likely pathogens and local resistance patterns, and encouraging clinicians to discontinue antimicrobials if co-infection is deemed unlikely and tests confirm that patients do not have a bacterial infection.

Altmetric score: 622[https://doi.org/10.1016/S2666-5247(21)00090-2]

# Testing the tests

[MedRxiv May 2020](https://doi.org/10.12688/wellcomeopenres.15927.1)

We proposed and established a Diagnostic Evaluation Platform at the University of Oxford (led by Dr Alex Mentzer) which is already being used to provide evidence to the UK government about the performance of new diagnostic and antibody tests. This work is essential because if tests work well they can save lives; if they don’t, they can cause enormous damage.

Altmetric score: 26[https://doi.org/10.12688/wellcomeopenres.15927.1]

# COVID-19 and Cancer

[Esmo Open 1 May 2020](http://doi.org/10.1136/esmoopen-2020-000825)

The ISARIC4C investigators collaborated with Prof Carlo Palmieri and team to characterise the first 1,797 hospitalised patients with cancer and COVID-19. From here a new study was launched to assess the impact of COVID-19 on people with cancer: The Clinical Characterisation Protocol (CCP) CANCER-UK. The project will run over 12 months and will examine questions that are important for the care of patients with cancer. With almost 7,000 patients with both confirmed cancer and COVID-19 diagnoses already enrolled, it will be one of the largest and most detailed studies in the world.

The study has received funding from UK Research and Innovation (UKRI) and the National Institute for Health Research (NIHR), with additional funding from The Clatterbridge Cancer Charity.

Altmetric score: 7[http://doi.org/10.1136/esmoopen-2020-000825]

# Detection of antibodies to determine population exposure

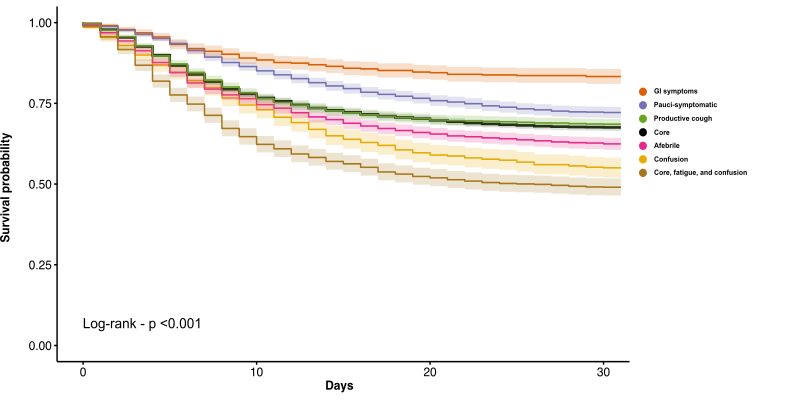
[Eurosurveillance 22 Oct 2020](https://doi.org/10.2807/1560-7917.ES.2020.25.42.2000685)

ISARIC4C provided support to this study looking at population exposure in the beginning of the outbreak showing that it is likely that SARS-CoV-2 began circulating in Scotland in late February 2020 and potentially earlier.

Altmetric score: 16[https://doi.org/10.2807/1560-7917.ES.2020.25.42.2000685]

# Symptom clusters

[MedRxiv August 16th 2020.](https://doi.org/10.1101/2020.08.14.20168088)



Different outcomes among patients presenting with different patterns of symptoms

Because of the large scale of the ISARIC-4C study, we were able to detect robust groupings of patients with different patterns of symptoms. We found four patterns that are strikingly differnet from the core symptom groups: gastro-intestinal disease, productive cough, confusion, and pauci-symptomatic presentations. Each of these has a different clinical course and a different chance of death.

These observations deepen our understanding of COVID-19 and will influence clinical diagnosis, risk prediction, and future mechanistic and clinical studies.

Altmetric score: 9[https://doi.org/10.1101/2020.08.14.20168088]

# New immune biomarkers for COVID-19

[Immunology September 2022](https://doi.org/10.1111/imm.13585)

This study looked at a specific immune process in the body, known as the complement system. This mechanism allows microbes and damaged cells to be removed from the body, attacks pathogens, and promotes inflammation. This system is more active in patients with COVID-19 and blocking the system has been considered as a potential treatment. Blood samples from 682 hospitalised patients, including those from the ISARIC4C study, were compared to healthy individuals and multiple components of the complement system were shown to be altered. The levels of some of these markers, known as Ba, iC3b, and properdin, were shown to be associated with disease severity and death. Identifying these new biomarkers helps us to understand how the body responds to COVID-19 and allows new targets for treatment strategies.

Altmetric score: 77[https://doi.org/10.1111/imm.13585]

# Vulnerability of Down’s syndrome (DS) patients to severe COVID-19

[EClinical Medicine 22 Feb 2021](https://doi.org/10.1016/j.eclinm.2021.100769))

Providing data and support to the Trisomy 21 Society, a study was conducted to determine if health conditions, immune dysfunction, and premature aging associated with trisomy 21 (Down syndrome, DS) may impact the clinical course of COVID-19. Whilst signs/symptoms of COVID-19 and risk factors for severe disease course are similar to the general population, individuals with DS present significantly higher rates of medical complications and mortality, especially from age 40.

Altmetric score: 623[https://doi.org/10.1016/j.eclinm.2021.100769]

# Modelling the association of tiered restrictions with COVID-19 deaths and hospital admissions

[Lancet Infectious Diseases 23 Dec 2020](https://doi.org/10.1016/s1473-3099(20)30984-1)

To look at the impact of tiered restrictions, the team fitted a mathematical model of transmission to data on hospital admissions. Results showed that lockdown measures outperformed less stringent restrictions in reducing cumulative deaths.

Altmetric score: 247[https://doi.org/10.1016/s1473-3099(20)30984-1]

# ISARIC4C within the global ISARIC-network

An alternate weekly data share is made with global ISARIC CCP partners in 42 countries and a summary report is posted on medRxiv, the global health network (TGHN.org) and WHO. CO-CIN has contributed 82% of global data reported.

Selected publications include:

* COVID-19 symptoms at hospital admission vary with age and sex: ISARIC multinational study <https://doi.org/10.1101/2020.10.26.20219519>
* [ISARIC Global Clinical Data Report(https://doi.org/10.1101/2020.07.17.20155218)

# Multi-model forecasts to inform the response to COVID-19 in the UK

[MedRxiv pre-print 4 Dec 2020](https://doi.org/10.1101/2020.11.11.20220962)

Groups of multi-model forecasts can inform the policy response to the Covid-19 pandemic by assessing future resource needs and expected population impact of morbidity and mortality.

Altmetric score: 28[https://doi.org/10.1101/2020.11.11.20220962]

# Remdesivir Statistical Analysis Plan

The [Remdesivir Statistical Analysis Plan](/files/StatisticalAnalysisPlanv1.0.pdf) was approved on 16 December 2020.