COVID-19 REGISTRY STUDY PROTOCOL

TITLE	Registry to study factors that may impact COVID-19 occurrence and severity
PROTOCOL/STUDY NO.	IQVIA_COVIDREGISTRY_2020
VERSION	4.0; 9 Mar 2021
CONDUCTED BY	IQVIA 201 Broadway Cambridge, MA 02139 USA

This protocol contains confidential information that should only be disclosed to those persons responsible for execution and organization of the study and on condition that all such persons agree not to further disseminate it.

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Documentation of Protocol Amendments

Version	Date	Summary of Revisions
Original	March 27, 2020	N/A
V2.0	April 13, 2020	Revised study title and added 3 months of longitudinal follow-up
V3.0	December 7, 2020	Revised duration of follow-up from 3 months to 12 months, removed questions on social distancing, and added questions on mental health conditions, healthcare encounters, and vaccines.
V4.0	March 9, 2021	Revised inclusion criteria to include vaccinated adults as well as participants from the UK; added questions about post-vaccination symptoms and health care encounters.

List of Abbreviations

COVID-19	coronavirus disease 2019
FDA	U.S. Food and Drug Administration
GDPR	General Data Protection Regulation
GPP	good pharmacoepidemiology practices
HIPAA	Health Insurance Portability and Accountability Act of 1996
ICF	informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	independent ethics committee
IRB	institutional review board
ISPE	International Society for Pharmacoepidemiology
NSAID	nonsteroidal anti-inflammatory drugs

Study Synopsis

Full Study Title: Registry to study factors that may impact COVID-19 occurrence and severity
Background & Rationale: The 2019 coronavirus disease (COVID-19) has presented major challenges to countries around the world. Currently there is little information about (1) symptom presentation, severity, and duration especially for cases that do not require hospitalization, (2) understanding which prescription medications, if any, influence risk, including various hypertension and anti-diabetic medications, (3) whether vitamin and mineral supplements, alone or in combination with established medications offer any degree of protection, and (4) what medical management is most effective at reducing the high toll of this infection. Initial research suggests a wide range of potential symptoms including those that would be expected with a respiratory virus (e.g., fever, cough) as well as gastrointestinal issues, dizziness, inability to concentrate, and effects on the sense of smell and taste. Additionally, there are a wide range of treatments, both prescribed and over-the-counter, that are being used to manage symptoms. Systematic data collection and analytics will contribute empirical information about benefits and risks that could have immediate public health impact. This registry will enroll participants in an observational, direct-to-participant longitudinal study to assess disease risk, progression, treatments, and vaccines.
Objectives: The objectives of this study are to: 1. Identify factors that may impact the occurrence, severity, or duration of COVID-19 infections including examining the role of underlying health conditions, prescription and over-the-counter medications, vitamins and supplements. 2. Assess post-vaccine symptoms and COVID-19 infection among participants reporting a COVID-19 vaccination

Study Design: This is an observational, direct-to-participant, web-based, longitudinal study of adults with COVID-19 or COVID-19 like illness to better understand risk factors, symptoms, and treatments for COVID-19 illness and vaccine safety and effectiveness. This study will be launched and conducted in the US and UK. Participants will be recruited through postings from partner organizations such as governments and professional associations as well as support from advertising, social media, and public relations. People with COVID-19, COVID-19 like symptoms, exposure to COVID-19, and/or COVID-19 vaccination will be asked to visit the online study portal. All study data will be reported by participants within the web-based study portal. Participants will complete an initial baseline survey reporting their demographics, relevant medical history, testing, vaccination, symptoms, use of prescription and non-prescription medications (prophylactic and curative) as well as use of supplements (e.g., vitamins, minerals, and herbals) and other factors. The study follow-up period is 12 months. During the first month of follow-up participants will be invited to complete a symptom diary weekly to gauge symptom progression and severity and to provide updates on pharmaceutical and non-pharmaceutical interventions as well as healthcare encounters. Reporting will then reduce to monthly for Month 2 through 12. Participants reporting COVID-19 vaccination (first or second dose) will be moved into weekly follow-up, if not already in weekly follow-up, for 4 weeks after vaccination to capture subsequent symptoms and healthcare encounters as well as a second vaccine dose if applicable. This survey schedule represents reminders for survey completion, noting the technology will allow for participants to enter data at any time during the follow-up window.

Study Population: The study population will include adults aged 18 and older who have COVID-19, have COVID-19 like symptoms, were exposed to COVID-19, or received a COVID-19 vaccine. Participants must have access to an internet-connected computer, smartphone or tablet to answer registry questions.

Data Management and Quality Assurance: Data will be collected using a web-based, mobile-friendly portal. Data will be collected and stored in a HIPAA-compliant manner consistent with high levels of privacy and security for storing sensitive information about participant health. Data will be encrypted during transit and at rest. Access privileges will be granular and tightly controlled with strong passwords required from administrative users. Personally identifiable information collected for registration, including personal contact information will be stored separately from other collected information and will only be accessible to staff with administrative privileges and with a specific and legitimate purpose to use that information.

Ethical and Regulatory Considerations: This observational study will be conducted in accordance with the protocol and all applicable laws and regulations including, but not limited to good pharmacoepidemiology practices (GPP), and the ethical principles that have their origins in the Declaration of Helsinki and applicable privacy laws. Data protection and privacy regulations will be strictly observed in capturing, forwarding, processing, and storing participant data. Every effort will be made to protect participant confidentiality according to the General Data Protection Regulation (GDPR) on the protection of individuals, and in compliance with EU-US Privacy Shield, and other relevant data privacy and protection regulations. An IRB/IEC must review and approve the protocol and informed consent form before any participants are enrolled. Before any protocol-directed data collection is performed, the participant must sign and date the IRB/IEC-approved informed consent form. This protocol will be posted on clinicaltrials.gov and the EU PAS Register (http://www.encepp.eu/encepp/studiesDatabase.jsp).

1. BACKGROUND AND RATIONALE

The ongoing coronavirus disease (COVID-19) pandemic has caused a worldwide crisis in terms of social, medical and financial systems. The number of cases globally has increased significantly since the first reported case in December 2019. Initially, the disease was thought to severely affect primarily older patients (60 years and above)[1] but as the virus continues to spread, it has become evident that several other patient populations are at high risk for hospitalization, complications, and even death[2].

The United States has been severely burdened by COVID-19, with over 28 million cases and 500,000 deaths reported as of 25 February 2021[3]. Additionally, there have been evolving reports of COVID-19 symptoms and progression[4,5,6,7], making it difficult for people to determine when they should seek medical attention and/or quarantine for suspected COVID-19 illness. Therefore, there is a need for systematic data collection from people who may be infected with COVID-19 but may not have access to a test to confirm their diagnosis.

Currently, there is a paucity of data describing disease risk, symptoms, and non-prescription medication use including supplements among the broader non-hospitalized community. Most publicly available data is limited to surveillance of the number of tested cases and the number of deaths, with little to no longitudinal follow-up of symptom progression, outcomes, treatments, and other related information. In addition, there is a need for long-term follow-up for people receiving COVID-19 vaccinations to continue to monitor safety and effectiveness outside of well controlled clinical trials and as COVID-19 strains evolve over time.

With recent Emergency Use Authorization of several COVID-19 vaccines, there is also a need to understand broad and long-term safety and effectiveness of the COVID-19 vaccines over time and as new strains emerge.

Systematic data collection and analytics would contribute empirical information about benefits and risks that could have immediate public health impact. This Registry will enroll participants in an observational, direct-to-participant longitudinal study to assess disease risk, progression, treatments, and vaccines.

2. OBJECTIVES

The objectives of this study are to:

1. Identify factors that may impact the occurrence or severity of COVID-19 infections including examining the role of underlying health conditions, prescription and over-the-counter medications, vitamins and supplements.
2. Assess post-vaccine symptoms and COVID-19 infection among participants reporting a COVID-19 vaccination

3. STUDY DESIGN

3.1 Study Description

This is an observational, direct-to-participant, web-based, longitudinal study of adults with potential exposure to COVID-19 to better understand risk factors, symptoms, and treatments for COVID-19 illness as well as vaccine safety and effectiveness. This study will be conducted in the US and UK. Participants will be recruited through postings from partner organizations such as governments and professional associations as well as support from advertising, social media, and public relations. People who have been vaccinated against COVID, who have COVID-like symptoms, or were exposed to COVID-19 will be asked to visit a portal landing page. All study data will be reported by participants within the web-based study portal. Upon consent and enrollment, participants will complete an initial baseline survey reporting their demographics, relevant medical history, symptoms, use of prescription and non-prescription medications (prophylactic and curative) as well as use of supplements (e.g., vitamins, minerals, herbals) and other factors. Participants are then followed for 12 months. During Month 1, participants will complete a symptom diary to record symptom progression and severity and provide updates on pharmaceutical and non-pharmaceutical interventions as well as healthcare encounters once a week. During Months 2 through 12, follow-up is reduced to twice a month to reduce patient burden and capture longer-term disease progression (now often referred to as “long COVID”) and treatment. Longer follow-up is required to assess symptoms that may linger or worsen.

No medical advice will be provided; links to credible medical resources about COVID-19 will be made available.

3.2 Study Population

There is no sample size restriction for this study. This study is designed for open enrollment of all eligible participants and can accommodate millions of respondents.

3.2.1 Inclusion Criteria

The following criteria must be met in order to be enrolled in the study:

- Adult (18 years or older)
- Currently living in the US or UK
- Have COVID-19 or COVID-19 like symptoms
- Received a COVID-19 vaccine
- Potential exposure to COVID-19

- Have regular access to a computer, smartphone or tablet and sufficient internet to support registry demands (note: this registry is designed to operate well even in regions with low bandwidth)
- Willing and able to provide informed consent
- Willing and able to follow the procedures of the study

3.2.2 Exclusion Criteria

Participants meeting ANY of the following criteria are not eligible for participation:

- Unable to provide informed consent
- Unable to perform the requested study tasks

3.2.3 Study Enrollment

The registry will engage participants through postings from partner organizations such as governments and professional associations as well as support from advertising, social media, and public relations to visit a portal landing page. Once on the landing page, the participant will answer questions to confirm eligibility, consent into the study, and then register by providing an email address and, optionally, a mobile phone number. As part of consenting into this registry, participants also agree to be contacted for future research opportunities. Participants are not required to participate in any future studies, and there is no consequence for ignoring the request or declining to participate. Participation in any future research opportunities will require a separate, study-specific consent.

At enrollment, participants will also be asked to provide an alternative contact (next of kin or close friend) who may be contacted if we are unable to reach the participant. The intent here is to minimize loss to follow-up and to allow for proxy data collection in the event of serious illness or death.

3.2.4 Participant Withdrawal

Participants may withdraw consent and discontinue participation in the study at any time. All survey data would be deleted from the central system and would not be included in any future data distributions. However, the data will not be withdrawn from past data distributions to partners or deleted from archival backup files.

3.3 Data Sources and Collection

This is a direct-to-participant registry. All data will be reported by participants through a web-enabled application. No visits or examinations, laboratory tests or procedures are mandated or required for this study. Table 1 outlines reminders for participants to complete surveys, noting the technology will allow for participants to enter data at any time during the follow-up window.

Table 1. Data Collection Schedule

	Enrollment /Baseline	Month 1 (once a week)	Month 2 through 12 (twice a month)
Informed Consent	X		
Demography	X		
Static Medical History and Risk Factors (e.g., height, weight, occupation)	X		
Medical History (e.g., diagnoses, concomitant medications, vitamins/supplements, pregnancy, seasonal flu vaccine)*	X	X*	X*
COVID-19 test, if conducted	X	X	X
COVID-19 vaccination including manufacturer, date, lot number and first shot or booster, post-vaccine symptoms, and healthcare encounters for possible reactions, if available	X	X**	X**
COVID-19 symptoms	X	X	X
COVID-19 medications, both prescription and OTC, that may be intended as prophylactic or curative treatments	X	X	X

**Participants will be asked during follow-up if they had any changes in their underlying medical history (e.g., new diagnoses, new medications). If yes, they will report changes in key medical history that may influence COVID-19 risk factors and/or recovery (e.g., new comorbidities, pregnancy, etc).*

***Participants reporting COVID-19 vaccination (first or second dose) will be moved into weekly follow-up, if not already in weekly follow-up, for 4 weeks after vaccination to capture subsequent symptoms and healthcare encounters as well as a second vaccine dose if applicable.*

3.3.1 Baseline/Enrollment

The following data are planned to be collected at baseline for all enrolled participants:

- Demographics

- geography (zip code/ postcode)
- age (date of birth)
- gender
- race/racial designation
- ethnicity
- education

- Medical History and Other Risk Factors
  - weight
  - height
  - baseline medical history including:
    - comorbidities that are thought to be potential risk factors including cardiovascular disease, lung disease, diabetes, kidney, blood disorders, and auto-immune conditions
    - history of depression, anxiety, and insomnia
    - prescription medications
  - frequency of use of certain medications of interest, including daily aspirin, Pepcid (famotidine), Tagamet HB (cimetidine), and antihistamine (cetirizine, loratadine)
  - use of supplements (vitamin D, zinc, other vitamins/minerals, herbals)
  - current smoking status
  - history of organ transplant
  - current treatment for cancer
  - pregnant
  - vaccinations, including childhood vaccinations (e.g. MMR) and seasonal flu
  - occupation, including healthcare worker or other job with heightened risk of exposure (e.g., grocery, daycare, mail/delivery)

- COVID-19
  - type of test, test results and date of test, if any
  - presence and severity (4-point scale) of symptoms including fever, cough, fatigue, dizziness, eye pain, blurry vision, shortness of breath, persistent pain or pressure in the chest, heart palpitations, new onset of confusion, inability to arouse, aches and pains, muscle twitching, rash, nasal congestion, runny nose,

sore throat, decreased sense of taste, decreased appetite, decreased sense of smell, diarrhea, vomiting, nausea, depression, anxiety, insomnia, other

- healthcare encounters, including type (telemedicine, office visit, emergency department, hospitalization), date, and whether the encounter was related to COVID-19
    - if hospitalized, duration of hospitalization
- household member has COVID-19 or flu-like symptoms
- receipt of COVID-19 vaccination, either as part of a clinical trial or standard of care once authorized by FDA or Medicines and Healthcare products Regulatory Agency (MHRA), along with date, manufacturer, and lot number if known, and whether it was the first shot or a booster shot.
    - among vaccinated:
        - symptoms following the vaccination including pain at injection site, swollen lymph nodes, fever, fatigue, headache, joint or muscle pain, nausea or vomiting, severe allergic reaction
        - impact symptoms had on ability to take care of yourself and ability to work
        - healthcare encounters, including hospitalization, following the vaccination
- medications including prescriptions (antimalarials, antivirals, antibiotics, biologics, corticosteroids, monoclonal antibody), over-the-counter (acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs]),
    - for treatments the participant reports taking, timing of treatment relative to symptom onset
- participation in clinical trials or receipt of experimental treatments

3.3.2 Follow-up

The following data are planned to be collected for all enrolled participants once a week during Month 1, twice a month during Months 2 through 12. Participants reporting a COVID-19 vaccine (first or second dose/booster) will be followed weekly for 4 weeks after their COVID-19 vaccine to capture symptoms, medical encounters and a booster, if applicable. Participants will be asked during follow-up to report any changes in their medical history (e.g., new comorbidities, prescription medications, pregnant) to reduce participant burden and allow for capture of updated medical history that may influence risk factors and disease progression.

- COVID-19
    - type of test, test results and date of test, if any

- presence and severity (4-point scale) of symptoms including fever, cough, fatigue, dizziness, eye pain, blurry vision, shortness of breath, persistent pain or pressure in the chest, heart palpitations, new onset of confusion, inability to arouse, aches and pains, muscle twitching, rash, nasal congestion, runny nose, sore throat, decreased sense of taste, decreased appetite, decreased sense of smell, diarrhea, vomiting, nausea, depression, anxiety, insomnia, other
- healthcare encounters, including type (telemedicine, office visit, emergency department, hospitalization), date, and whether the encounter was related to COVID-19
  - if hospitalized, duration of hospitalization
- household member has COVID-19 or flu-like symptoms
- receipt of COVID-19 vaccination, either as part of a clinical trial or standard of care once authorized by FDA or Medicines and Healthcare products Regulatory Agency (MHRA), along with date, manufacturer, and lot number if known
  - among vaccinated:
    - symptoms following the vaccination including pain at injection site, swollen lymph nodes, fever, fatigue, headache, joint or muscle pain, nausea or vomiting, severe allergic reaction
    - impact symptoms had on ability to take care of yourself and ability to work
    - healthcare encounters, including hospitalization, following the vaccination
- medications including prescriptions (antimalarials, antivirals, antibiotics, biologics, corticosteroids), over-the-counter (acetaminophen, NSAIDs),
  - for treatments the participant reports taking, timing of treatment relative to symptom onset
- participation in clinical trials or receipt of experimental treatments

- Medical History and Other Risk Factors (if participant reports a change in medical history since last survey)
  - comorbidities that are thought to be potential risk factors including cardiovascular disease, lung disease, diabetes, kidney, blood disorders, and auto-immune conditions
  - history of depression, anxiety, and insomnia
  - prescription medications

- frequency of use of certain medications of interest, including daily aspirin, Pepcid (famotidine), Tagamet HB (cimetidine), and antihistamine (cetirizine, loratadine)
- use of supplements (vitamin D, zinc, other vitamins/minerals, herbals)
- history of organ transplant
- current treatment for cancer
- pregnant
- flu vaccine

4. STATISTICAL METHODS

4.1 Sample Size

No formal sample size calculations were performed for this study. All interested, qualifying participants will be able to enroll without restriction.

4.2 Data Analyses

4.2.1 General Considerations

Data analysis will be designed to respond to high priority medical and public health issues, with feasibility counts and analytic plans designed in advance of conducting the analyses, as has been established in previous pandemic research on H5N1 avian influenza[8]. Computations and generation of tables, listings and data for figures will be performed using SAS® version 9.2 or higher (SAS Institute, Cary, NC, USA) and/or data visualization tools.

Descriptive analyses will be performed to gain an understanding of the qualitative and quantitative nature of the data collected and the characteristics of the respondents. Additional, in-depth analyses will be outlined in supplementary objective-specific analytic plans.

4.2.2 Limitations of Research Methods

This is a voluntary direct-to-participant study. While there are many advantages to this approach in the context of studying a pandemic, there are inherent limitations.

Participants voluntarily enroll in the study. Participants who enroll may be different from the broader population in meaningful ways. For example, they could be more aware of COVID-19 and therefore more likely to take precautions such as social distancing or be more proactive regarding their health. Participants may also include people who are more reluctant to seek medical care, despite serious symptoms. Further, the requirement of access to the internet and the ability to participate in an online study is likely to be a barrier to participation

for populations without reliable internet access, who are not literate or who are not comfortable with online or mobile technology.

Participants may misreport data or may not complete follow-up. This could result in some systematic error that will need to be addressed analytically, including various sensitivity analyses. The recruitment strategy and web-based application will be designed to minimize these risks as well as maximize high quality and complete data.

Loss-to-follow up is a limitation, particularly for participants who have become extremely sick or passed away. Efforts to engage an alternative contact (next of kin, family member or close friend) will be taken to minimize loss to follow-up.

4.3 Data Reporting

Periodic descriptive analyses will be produced at key timepoints during this study. A final study report will be generated after all data collection is complete. The final report will summarize all analyses, including a description of the complete study population, as described above and in a study-specific analysis plan. The results of this study will be made public, mostly likely in the peer-reviewed medical literature.

5. STUDY MANAGEMENT

This study will be performed by IQVIA, including development of materials, recruitment, data management and analysis.

5.1 Source Documents

There are no source documents for this registry. All data are reported by enrolled participants.

5.2 File Retention and Archiving

Key study documents will be stored in a centralized online location for the duration of the study and two years following study completion.

5.3 Quality Assurance and Monitoring

The data collection instruments will be developed to maximize data quality. This includes providing clear and appropriate response options, minimizing free text entries, and adding validation checks. Data will be reviewed on an ongoing basis to determine if alternative response options are needed to reduce missingness or ‘other’ responses, and the data collection instrument will be refined accordingly.

5.4 Data Management

Data will be collected using a secure web-based application using a computer, smartphone, or tablet. Data will be collected and stored in a manner consistent with high levels of privacy and security for storing sensitive information about participant health, and with the expectations

that the system will need to be HIPAA-compliant and subject to all relevant privacy regulations. Any personally identifiable data will be encrypted before being sent to the central database and will also be encrypted during storage. Only authorized persons will be able to access the data. Personally identifiable information (such as name and birthdate) will be stored separately from other information and will only be made available to staff with a specific need to use that information for a legitimate purpose, like re-contacting the participant for future research.

5.5 Changes to the Protocol

Changes to the protocol will be documented in written protocol amendments. Major (i.e., substantial, significant) amendments will usually require submission to the relevant IRB/IEC. In such cases, the amendment will be implemented only after approval has been obtained.

Minor (nonsubstantial) protocol amendments, including administrative changes, will be filed and submitted to the relevant IRB/IEC where required by pertinent regulations. Any amendment that could have an impact on the participant's agreement to participate in the study requires the participant's informed consent prior to continued participation in the study.

5.6 Study Governance

This study will be governed by a qualified study team consisting of epidemiologists, medical doctors, biostatisticians, technical experts and other personnel. As new analyses are proposed, appropriate governance will continue to be put in place specific to research needs.

6. SAFETY REPORTING

No product-related adverse events are being collected from participants.

7. ETHICAL AND REGULATORY CONSIDERATIONS

7.1 Guiding Principles

To ensure the quality and integrity of research, this study will be conducted under the guidelines good pharmacoepidemiology practices (GPPs) issued by the International Society for Pharmacoepidemiology (ISPE), the Declaration of Helsinki and its amendments, and any applicable national guidelines.

The study will be conducted in compliance with the US FDA Title 21 CFR Part 50 – Protection of Human Patients and/or Part 56 – Institutional Review Boards; the International Conference on Harmonisation (ICH) GCP E6(R2) guidelines (15 December 2016) as they apply to observational studies; the Declaration of Helsinki and its amendments; and the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

7.2 Participant Confidentiality

In accordance with local regulations in each of the registry countries, participants will be informed about data handling procedures and asked for their consent. Data protection and privacy regulations will be strictly observed in capturing, forwarding, processing, and storing participant data. Every effort will be made to protect participant confidentiality according to applicable data privacy laws, including the Regulation (EU) 2016/679 (General Data Protection Regulation - GDPR) on the protection of individuals. All parties will ensure protection of patient personal data and will not include patient names on any reports, publications, or in any other disclosures, except where required by law.

7.3 Participant Information and Informed Consent

An informed consent form (ICF) will be obtained from each participant through the online portal prior to participation in the study. An electronic copy of the ICF will be available for participants to download for their own records.

The ICF will be revised whenever there are changes to procedures outlined in the informed consent or when new information becomes available that may affect the willingness of the participant to participate. Separate ICFs will be used in the US and UK, according to local ethics requirements.

7.4 Independent Ethics Committee (IEC)/Institutional Review Board (IRB)

Consistent with local regulations and prior to enrollment of participants, the study protocol will be submitted together with associated documents (e.g., ICF) to the IRB/IEC for its review. Participant enrollment will not start before IQVIA has obtained written confirmation of a favorable opinion/approval from the relevant central or local IRB/IEC. The IRB/IEC will be asked to provide documentation of the date of the meeting at which the favorable opinion/approval was given that clearly identifies the study, the protocol version, and the ICF version reviewed.

Before implementation of any substantial changes to the protocol, protocol amendments will also be submitted to the relevant IRB/IEC in a manner consistent with local regulations.

Should the study be terminated early for any unanticipated reason, IQVIA will inform the IRB/IEC of the early termination.

8. REFERENCES

1. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020[J]. *China CDC Weekly*, 2020, 2(8): 113-122.
2. CDC. People Who Are Higher Risk for Severe Illness. Last updated 2 Apr 2020. Accessed 5 Apr 2020. Available at https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-higher-risk.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fspecific-groups%2Fpeople-at-higher-risk.html
3. CDC. CDC COVID Data Tracker. Accessed 25 Feb 2021. Available at: https://covid.cdc.gov/covid-data-tracker/#cases_casesinlast7days
4. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. The New England journal of medicine. 2020.
5. Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ (Clinical research ed). 2020;368:m606.
6. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* (London, England). 2020;395(10223):497-506.
7. Pan L, Mu M, Ren HG, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. *Am J Gastroenterol*. 2020;[Epub ahead of print].
8. Dreyer NA, Toovey S, Oner AF, et al. Investigating outbreaks of novel infectious disease: an international case study. Journal of Clinical Studies 2013; 5(2):52-53.