

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Cohort profile: Actionable Register of Geneva Out- and inpatients with SARS-CoV-2 (ARGOS)
AUTHORS	Genecand, Camille; Mongin, Denis; Koegler, Flora; Lebowitz, Dan; Regard, Simon; Falcone, Jean-Luc; Nehme, Mayssam; Braillard, Olivia; Grira, Marwene; Joubert, Dominique; Chopard, Pierre; Delaporte, Elisabeth; Stirnemann, Jerome; Guessous, Idris; Tardin, Aglaé; Courvoisier, Delphine

VERSION 1 – REVIEW

REVIEWER	Fortunato, Francesca Universita degli Studi di Foggia, Department of Medical and Surgical Sciences
REVIEW RETURNED	09-Mar-2021

GENERAL COMMENTS	<p>Comments to the Authors</p> <p>This article aims at presenting a comprehensive outpatient cohort in light of the varying public health measures in Geneva, Switzerland, since March 2020. The manuscript was enough well written and partially in line with the objectives. The methods are not sufficiently described and the discussion is incomplete.</p> <p>Title The title refers to outpatients with SARS-CoV-2 but ARGOS involves every tested individual included hospitalized patients.</p> <p>Material and Methods Authors should consider including in the material and methods the statistical analysis.</p> <p>Page 8, line 50: What is the formula for calculating the participation rate? Please specify Page 10, line 3: The description of data collection should be reported in the materials and methods, e.g. questionnaires, tests, etc.) Page 10, line 33: I would suggest indicating the number of patients called back at 1-month and 3-months to monitor the persistence of symptoms</p> <p>Results Page 11, lines 12-30: this presentation of the results is not clear enough. Authors are suggested to better organize the results. For</p>
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	<p>example, what is the formula for calculating the positivity rate? Please, specify numerator and denominator</p> <p>Page 11, lines 31-33: Please, describe the symptoms and the clinical presentation (e.g. mild, severe, critical)</p> <p>Page 11, lines 49: I would recommend shifting this section in the methods</p> <p>Page 12, line 22: What is the formula for calculating the positivity rate? Please specify</p> <p>Discussion</p> <p>The discussion should report the interpretation of obtained data in relation to the literature.</p> <p>Table 2</p> <p>Comparison between subgroups is performed with Fisher's exact test. This analysis is not clear enough and the variables are not comparable.</p>
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REVIEWER	Cohen, Pieter Cambridge Health Alliance
REVIEW RETURNED	12-Apr-2021

GENERAL COMMENTS	<p>The authors have created an invaluable database for future research investigations – a comprehensive database of patients with the COVID in the Geneva area. The manuscript gives many details about who is included in the database and reviews the regional changes in testing and public health changes over the time period covered by the registry. This will be valuable background resource for researchers in the future who plan to use to the Geneva registry to study COVID. However, the current manuscript does not contain new, generalizable data that would merit publication as a research paper. I would recommend submitting to a specialty journal so that this information can be available to future researchers.</p>
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REVIEWER	Telle, Kjetil Norwegian Institute of Public Health
REVIEW RETURNED	30-Apr-2021

GENERAL COMMENTS	<p>Review report on bmjopen-2021-048946: Cohort profile: Actionable Register of Geneva Outpatients with SARS-CoV-2</p> <p>I'm not familiar with the article format cohort profile, and when reading I keep wanting more results (but I understand that this is outside of the format). Thus I like the information about positivity rates associated with testing availability, which I guess fits with the article format since it tells a lot about possible selection biases. But I still keep wanting some more "result-like" information, for example about hospitalization rates and deaths since we believe (in Geneva too, I presume) that most infections will go largely unregistered (in absence of abundant testing), while hospitalization and death will not. Hospitalization rates may thus be a better indicator of actual new infections (with a lag of 1-2 weeks) than positive PCR-tests, illustrating further the point from</p>
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positivity rates varying with testing. This may further enrich the discussion in STRENGTHS AND LIMITATIONS?

Much of the data are self-reported, which can be important for interpretation, and you should rephrase with “self-reported” instead of “Patients estimated compliance” (p. 8), “their compliance” (p.9), etc. Especially when interpreting compliance (with isolation/quarantine measures), more information would be useful: For example, would the patients fear – correctly or not – any sanctions if they report to have violated such measures?

In Table 1 I missed number of tested individuals (in addition to number of positive patients and number of tests). It would also be very interesting to see number of close contacts (if available), and, as mentioned, number of hospitalized and dead.

It should be stated much earlier in the manuscript (maybe even in abstract) what is meant by “tested individuals”, i.e. PCR-test.

The name of the registry emphasizes outpatients so much that I believed too long that inpatients were not included. I suggest you make this completely clear several places in the text, including in the abstract.

Is some text or link missing after/in last sentence under COLLABORATION?

I wish the authors the best with the important ongoing work with the registry,

Kjetil Telle
Director of Health Services Research
Norwegian Institute of Public Health

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Francesca Fortunato, Università degli Studi di Foggia

This article aims at presenting a comprehensive outpatient cohort in light of the varying public health measures in Geneva, Switzerland, since March 2020. The manuscript was enough well written and partially in line with the objectives. The methods are not sufficiently described and the discussion is incomplete.

Title

The title refers to outpatients with SARS-CoV-2 but ARGOS involves every tested individual included hospitalized patients.

R: We modified the title to include inpatients, and also specified more precisely the scope of the cohort in the text

Material and Methods

Authors should consider including in the material and methods the statistical analysis.

R: Given that there is no real statistical analysis in this cohort description, and that “material and methods” is not a section of the “cohort profile” article type (see <https://bmjopen.bmj.com/pages/authors/#Cohort>), we tried to provide precision on the few calculations along the text.

Page 8, line 50: What is the formula for calculating the participation rate? Please specify

R : participation rate, and in particular definition of numerator and denominator, was clarified in the text:

The participation rate for positive patients is 93.9% (calculated as the ratio between the number of patients who gave their consent for the reuse of their data and the total number of patients)

Page 10, line 3: The description of data collection should be reported in the materials and methods, e.g. questionnaires, tests, etc.)

R : The author tried to follow the structure given by the journal for the “cohort profile” format. It specifies to “Describe methods of data collection and follow-up, and any external data sources used.” In the “Cohort description” paragraph. We tried to improve paragraph delimitation, and added a “Data collection” subparagraph to the “Cohort description” paragraph.

Page 10, line 33: I would suggest indicating the number of patients called back at 1-month and 3-months to monitor the persistence of symptoms

R: We added in the Data collection subparagraph of the cohort description:

669 patients from the cohort were also called back at 6 week and 7 months to monitor the persistence of symptoms, of which 510 and 410 answered respectively.

Results

Page 11, lines 12-30: this presentation of the results is not clear enough. Authors are suggested to better organize the results. For example, what is the formula for calculating the positivity rate? Please, specify numerator and denominator

R : We tried to improve the organization of the findings. The paragraph now reads:

On June 1st, 2021, of all 356'868 patients recorded in the ARGOS database, 65'475 had at least one positive test result, 295'753 had one or more negative test results and no positive one, and 327 were suspected COVID-19 cases without a positive test to confirm the disease. Therefore, the share of positive patients (number of positive patients divided by the total amount of patients) from February 26 of 2020 to June 1st 20221 was 18.1%.

Among the positive patients, 4'687 persons did not allow their data to be used for research and were excluded from analyses. The remaining number of positive cases available for analysis is 60'788. 37.6% of participants have a first contact only, 10.6% and 8.5% have one and two follow-up call respectively, and 27.7% of participants have three or more follow-up calls. 15.7% of the patients were not contacted, mainly during the periods of active pandemic activity when the GDH team was overworked (see Table 2).

Page 11, lines 31-33: Please, describe the symptoms and the clinical presentation (e.g. mild, severe, critical)

R : In this cohort of outpatients, initially detected by tests, the symptoms are self-reported. We can thus describe the frequency of symptoms, but the clinical presentation would have to be estimated by a clinical exam, which is not available in this cohort. We added in table 2 the frequency of symptoms. We also clarified that participants' medical visits are not available in this cohort:

Patients' declared symptoms are recorded in subsequent surveys

Page 11, lines 49: I would recommend shifting this section in the methods

R : The section "Findings to date" is an independent section in the structure of the "cohort profile" article type. This article type does not provide a method section.

Page 12, line 22: What is the formula for calculating the positivity rate? Please specify

R : Following the definition of CDC, the positivity rate is calculated as the ratio between positive test results and the total number of tests performed.

We amended the text as follow:

During the same period, 655,527 tests were performed, among which 89.2% were PCR. The positivity, i.e. the ratio between the positive tests and the total amount of tests, was of 10.7%.

Discussion

The discussion should report the interpretation of obtained data in relation to the literature.

R : since this article is the presentation of a cohort (see "cohort profile" type of article), it does not address a specific research question, but present the data acquired within our cohort (instruction for authors explicitly states: "Papers addressing a specific research question using cohort data should be submitted as a Research paper."). Thus, we do not interpret data in relation to the literature

Table 2

Comparison between subgroups is performed with Fisher's exact test. This analysis is not clear enough and the variables are not comparable.

R : We agree with the reviewer. In order to avoid misleading the readers with superfluous information, we decided to remove p values from the table2.

Reviewer: 2

Dr. Pieter Cohen, Cambridge Health Alliance

Comments to the Author:

The authors have created an invaluable database for future research investigations – a comprehensive database of patients with the COVID in the Geneva area. The manuscript gives many details about who is included in the database and reviews the regional changes in testing and public health changes over the time period covered by the registry. This will be valuable background resource for researchers in the future who plan to use to the Geneva registry to study COVID. However, the current manuscript does not contain new, generalizable data that would merit publication as a research paper. I would recommend submitting to a specialty journal so that this information can be available to future researchers.

R : While we fully agree with the assessment that the information here is valuable background resource for researchers who plan to use this registry, we respectfully disagree with the reviewer on the usefulness of publishing this information. Our article is not a research paper, and has been submitted under the “cohort profile” type proposed by BMJ. This type of article allows the extended description of a cohort without aiming at addressing a specific research question (see <https://bmjopen.bmj.com/pages/authors/#Cohort> and <https://blogs.bmj.com/bmjopen/2014/08/22/bmj-open-now-publishes-cohort-profiles/>).

It is our sincere hope that many researchers will be interested in obtaining these data, and that it will provide opportunity for valuable insights. For instance, it has already been used to estimate a more accurate infection fatality rate [1], reinfection estimates [2], and several studies are ongoing using these cohort data.

We added in the text the reference to several already published study using the presented cohort:

VERSION 2 – REVIEW

REVIEWER	Fortunato, Francesca Universita degli Studi di Foggia, Department of Medical and Surgical Sciences
REVIEW RETURNED	27-Jul-2021

GENERAL COMMENTS	I suggest statistical review
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REVIEWER	Telle, Kjetil Norwegian Institute of Public Health
REVIEW RETURNED	30-Jun-2021

GENERAL COMMENTS	<p>I am generally pleased with the revision, and recommend the Cohort Profile is accepted.</p> <p>I do think, however, that the authors could have undertaken some efforts in providing some very brief background on how patients' response to questions about compliance (with isolation/quarantine measures) may be affected by patients fear – correctly or not – of sanctions if they report to have violated such measures. This will be important for future users of these data, since I presume inaccurate or misreporting may occur if patients have reason to fear sanctions.</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Dr. Francesca Fortunato, Universita degli Studi di Foggia Comments to the Author:

I suggest statistical review

R: Analyses were conducted and verified by experienced statisticians, of which the last author. We also limited inferential analyses as they are out of scope of this descriptive presentation of a new registry.

Reviewer: 3

Dr. Kjetil Telle, Norwegian Institute of Public Health Comments to the Author:

I am generally pleased with the revision, and recommend the Cohort Profile is accepted.

I do think, however, that the authors could have undertaken some efforts in providing some very brief background on how patients' response to questions about compliance (with isolation/quarantine measures) may be affected by patients fear – correctly or not – of sanctions if they report to have violated such measures. This will be important for future users of these data, since I presume inaccurate or misreporting may occur if patients have reason to fear sanctions.

R : we added some explanations in the limitations paragraph :

patients

Reviewer: 1

Competing interests of Reviewer: None

Reviewer: 3

Competing interests of Reviewer: None