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Cohort profile:

Actionable Register of Geneva Outpatients with SARS-CoV-2 (ARGOS)

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Abstract:

Purpose

The Actionable Register of Geneva Outpatients with SARS-CoV-2 (ARGOS) is an ongoing prospective cohort created by the Geneva Directorate of Health (GDH). It consists of an operational database compiling all SARS-CoV-2 test results conducted in the Geneva area since late February 2020. While the disease evolution of patients hospitalized with SARS-CoV-2 are now relatively numerous, the same cannot be said for outpatients. This article aims at presenting a comprehensive outpatient cohort in light of the varying public health measures in Geneva, Switzerland, since March 2020.

Participants

As of July 28, 2020, the database included 58'226 patients, among which 6848 had at least one positive test result for SARS-CoV-2. Among all positive patients, 66.8% were contacted once, and 21% of participants had 3 or more follow-up calls. Participation rate is 96.9%. Data collection is ongoing.

Findings to date

ARGOS data illustrates the magnitude of COVID-19 pandemic in Geneva, Switzerland, and details a variety of population factors and outcomes. The content of the cohort includes demographic data, comorbidities and risk factors for poor clinical outcome, COVID-19 symptoms, environmental and socio-economic factors, contact tracing data, hospitalizations and deaths.

Future plans:

The data of this large real-world registry provides a valuable resource for various types of research, such as epidemiological research or policy assessment as it illustrates the impact of public health policies and overall disease burden of COVID-19.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ARGOS' main strength consists of its large number of cases, representative of all diagnosed cases on a regional level with the primary aim of assessing all cases.
- ARGOS involves every tested individual and is not limited to hospitalized patients, thus providing a valuable resource to assess the impact of public health policies and overall disease burden of COVID-19 in a geographically defined population.
- To mitigate confounding effects and improve data analysis and interpretation, we present the data according to four policy periods.
- This cohort is multicentric as it includes all tests performed in Geneva's hospitals (both public and private), private practices and medical centers.
- Due to operational needs, symptoms and comorbidities are self-reported, which may lead to measurement error or misclassification.

Text word count: 2670 words

Introduction

In December 2019, an increasing number of cases of pneumonia caused by a novel coronavirus, SARS-CoV-2[1], was observed in Wuhan, China. On March 11, 2020, the World Health Organization (WHO) declared the coronavirus disease 2019 (COVID-19) outbreak a global pandemic(1,2). As of July 29, 2020, the virus spread to 188 countries, infected close to 17 million people and caused 662 000 deaths(3,4). In Switzerland, the cumulative incidence of laboratory confirmed COVID-19[2] cases is one of the highest in Europe, with about 400 confirmed cases per 100'000 population at the end of July 2020(4,5) In the Geneva area, the first COVID-19[2] patient was diagnosed on February 26, 2020(6). Possibly due to the city's geographical proximity to Northern Italy(7), the epidemic curve showed a steep upward trend. The first wave of the epidemic peaked in Geneva on April 2nd with 233 cases in 24 hours in an area with a population of 500'000. Geneva's cumulative incidence of confirmed cases is almost 3 times that of Switzerland(5), with more than 1'000 cases per 100'000 population(6), while the seroprevalence was estimated to be close to 10 times that of the confirmed cases as 9.7% of the population had antibodies three weeks after the height of the epidemic(8,9).

A database was created in early March in order to contact new cases and keep track of their follow-up. The Actionable Register of Geneva Outpatients with SARS-CoV-2[1] (ARGOS) includes all SARS-CoV-2[1] test results conducted in the Geneva area since late February 2020, as well as those from Geneva residents being tested in other Swiss cantons. The primary aim of this article is to present this comprehensive cohort, its

[1] Severe acute respiratory syndrome coronavirus 2
[2] coronavirus disease 2019

characteristics and the content of the data collected. The secondary aim is to interpret the data according to the public health measures implemented over time since the cohort profile was influenced by the varying policies enacted by the Swiss government and the Geneva State.

COHORT DESCRIPTION

The ARGOS database

ARGOS is an ongoing prospective cohort created by the Geneva Directorate of Health (GDH) and consists of an operational database compiling all SARS-CoV-2 test results conducted in the Geneva area. Data are collected and managed using the REDCap electronic data capture tools(10,11) allowing the GDH to contact positive cases in order to promote public health measures and coordinate medical follow-up. It is set up as a collaborative tool between different institutions and medical entities, including the GDH, Geneva University Hospitals (HUG), and Geneva's main private medical centers. The latter have restricted access to data regarding their own patients only. The GDH and HUG are the only users to implement follow-up data in the electronic register. The data is hosted on HUG's secure servers. The register is administered by a committee of co-Principal Investigators belonging to the GDH and HUG, with the agreement of the cantonal ethic committee (CCER protocol 2020-01273). Participants in the database had the opportunity to refuse to participate in the registry, and those who did are excluded from the analyses presented here. The participation rate was 96.9%. Deidentified ARGOS data can be available upon reasonable request, including a research protocol, using the form.

Data collection

All Geneva laboratories performing SARS-CoV-2 testing are required to send the results to the GDH. Swabs are collected from the upper respiratory tract in medical centers, private practice or during home visits by trained healthcare professionals(12). Between January 24 and July 28, 2020, 68577 tests for SARS-CoV-2 were performed by real-time reverse transcriptase–polymerase chain reaction assays and recorded in the ARGOS database. The majority were performed in the Geneva area and a small number consisted of tests conducted on Geneva residents in other Swiss Cantons, and declared to the GDH by the Federal Office of Public Health. Furthermore, hospitals and the Geneva Cantonal Population Office are required to declare COVID-19 related hospitalizations and deaths respectively, which are also recorded in ARGOS. Importantly, patients reporting COVID-19 symptoms between March 13 and March 29, 2020, did not get tested due to shortage of testing materials, unless they were healthcare workers, considered at-risk or hospitalized. However, symptomatic patients who visited the HUG COVID-19 testing center without fulfilling testing criteria were entered in the database as “suspected cases”. Some of these patients later received a test as policy evolved on March 30, 2020.

Patient and Public involvement

Patients or the public were not involved in research.

What is being measured?

An overview of collected data is provided in Table 1. The surveys were created by the GDH and HUG medical task forces. Within the first 48h of testing, patients with a positive test result for COVID-19 receive a call by a professional nurse with support from a medical doctor if needed. During this call, demographic data are collected(13), as well as symptoms(14–17), clinical and environmental risk factors, and clinical red flags. A special attention is paid to psychosocial and cultural factors, and resources are provided when needed. The clinical evaluation is used to identify patients who need immediate emergency care, or to address them for syw-up care by their general practitioner, by one of Geneva's medical centers, or by the GDH-HUG team via telemedicine. These follow-up calls are performed either by a professional nurse or by a medical student with supervision from a medical doctor. Patients' symptoms are recorded in subsequent surveys on the database. Patients' estimated compliance to isolation measures are also assessed. Depending on the patients' health condition, follow-up calls continue every one to two days until recovery. Some patients from the cohort are also called back at 1-month and 3-months to monitor the persistence of symptoms. All SARS-CoV-2 positive patients in Geneva who require hospitalization are admitted at HUG. At the time of discharge from the hospital, they receive follow-up calls by the HUG team as long as required by their health condition. COVID-19 positive patients identified as nursing home residents or who are hospitalized at the time of diagnosis are not systematically called since they already receive medical attention and isolation measures are enforced by the medical staff. As of April 27, 2020, close contacts of index cases are individually contacted and followed up until the end of the quarantine period (10 days). The type of contact they had with the index case, the

presence of COVID-19 symptoms and their compliance to quarantine measures are also recorded.

Findings to date

On July 28, 2020, of all 58'226 patients recorded in the ARGOS database, 6848 had at least one positive test result, 51'378 had one or more negative test results and no positive one, and 236 were suspected COVID-19 cases without a positive test to confirm the disease. Therefore, the positivity rate of recorded patients from February 26 to July 28 was 11.5%. Among these patients, 791 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 6635. 66.8% of participants have a first contact only, 8.3% and 3.9% have one and two follow-up call respectively. 21% of participants have three or more follow-up calls. From the end of February until the end of April, nearly all positive patients had symptoms. The cohort shows a slight female predominance, with women representing 51.3% to 57.1% of all patients depending on the defined period (Table 2). Eighty to 90 percent of all recorded patients have no risk factor for a poor clinical outcome(18). Significant differences are observed for age, comorbidities and presence of acute symptoms upon testing depending on the phases of the epidemic and of public health measures, highlighting the impact of changes in testing policies over time in Geneva. To mitigate confounding effects and improve data analysis and interpretation, we present the data according to four policy periods.

February 26 to March 13, 2020 (first phase)

Unlike many countries which implemented near-complete lockdowns(19) and despite a high burden of confirmed cases, Switzerland decided to adopt less severe measures. On February 26, 2020, gatherings of more than 1000 people were prohibited in the country. The first two and a half weeks of the epidemic were characterized by a majority of positive tests among people aged 20 to 64 years-old (82.2%). Five percent of cases were above 80 years old, and all cases were experiencing acute symptoms. The main risk factors among infected patients were advanced age, with 15.4% being older than 65, followed by chronic respiratory disease, cardio-vascular disease and diabetes (5%, 4.6%, 2.9% respectively). During this period, the positivity rate was 9.5%.

March 14 to March 30, 2020 (second phase)

On the evening of March 13, 2020, the Swiss government and local authorities placed the country under partial lockdown. Border crossings were restricted to essential workers, schools were closed, workers were asked to work from home and only essential services remained open(20). Public and private gatherings of more than 100 people and more than 5 people were banned on March 13, and March 20, 2020, respectively. From March 13 to March 29, 2020, SARS-CoV-2 reverse transcriptase–polymerase chain reaction testing was temporarily restricted to hospitalized and at-risk patients (>64 years old, presence of at least one risk factor for severe COVID-19, healthcare workers) due to shortage of testing materials. As patients receiving a test were selected based on their medical history and clinical course, we observed a first shift in the age of positive cases: the proportion of individuals 65 years and older, who are considered at risk for poor outcome, was higher (23.9%), and so was the presence of risk factors (chronic respiratory disease (11%), cardio-vascular disease (7.6%),

diabetes (5.3%) and immunosuppression (3.9%)). Individuals aged 20 to 39 years old were less represented during this period (28.5%). Healthcare workers were tested independently of their personal risk factors, and represented 12.2% of the positive patients. Limited testing modified the shape of the epidemic curve. It was concomitant with a sudden decrease of daily cases, mainly for younger people (Figure 1) and we witnessed a higher positivity rate (30.9%).

March 31 to April 27, 2020 (third phase)

During this period, political measures remained identical but testing policy evolved. As of March 30, 2020, all patients visiting Geneva's hospitals and medical centers and presenting symptoms consistent with COVID-19 were tested regardless of their age or comorbidities. The number of daily cases reached its peak shortly after this policy came into effect and the positivity rate decreased to 18.4%. The proportion of individuals 65 years and older was 23.7% during this period. Nursing home residents were significantly more impacted by COVID-19, reaching 8.5% of all positive cases. 10.5% of positive patients were identified as living in an at-risk environment (collective house resident, homeless people)(21). The proportion of healthcare workers decreased significantly as of April 2020, reaching 4.2% of cases.

April 28 to July 28, 2020 (fourth phase)

On April 27, 2020, the Swiss authorities started to lift some of the lockdown measures following the decreasing incidence of new cases and hospitalizations. During the first step of containment release, non-urgent medical and surgical care, do-it-yourself stores and basic services like hairdressers could reopen. Primary schools opened under some

regulations as well. The second step started on May 11, 2020 with the reopening of all shops, restaurants, and museums. Finally, on June 6, 2020, gatherings of less than 300 people were allowed, and nightclubs, cinemas, theaters and most schools reopened. The end of the lockdown measures was accompanied by the regulation of test prices in order to facilitate the access to free testing of symptomatic patients in Geneva. During this fourth phase, the cumulative number of cases reached a plateau. The proportion of patients with acute symptoms decreased significantly, reaching 86.5%. We observed a second shift in the age of positive cases, with 56.6% aged from 0 to 39 years, and only 10.8% older than 65 years old. 90.6% had no risk factor for severe disease. The positivity rate was 2.1%.

One month after the beginning of the third step of containment release, we observed a new increase in daily cases, mainly affecting people from 20 to 39 years old, and leading to implementation of new public health policies. This ongoing phase of the epidemic will not be discussed in this article.

Discussion

COVID-19 represents a major challenge to each country's healthcare system. Collaboration between healthcare providers and public health authorities is particularly important in order to improve both our understanding of the disease and our response(22–24). The publication of the ARGOS cohort underscores our willingness to share data for research purposes and for optimizing public health measures.

Furthermore, analysis from the ARGOS database illustrates the impact of various testing policies on the proportion of risk factors or age groups identified among

confirmed cases. The partition of data analysis and interpretation according to policy period confirms the variations within each group depending on the period of interest and could thus guide public health decisions.

STRENGTHS AND LIMITATIONS

The state of Geneva accounts for half a million residents and the local Directorate of Health ordered the recording of all COVID-19 positive cases since the beginning of the epidemic, according to recommendations from the Federal Office of Public Health. Due to this policy, the database's main strength consists of its large number of cases, representative of all diagnosed cases on a regional level primarily serving operational needs and not scientific purposes, with one main objective: assessing all cases. This cohort is also multicentric as it includes all tests performed in Geneva's hospitals (both public and private), private practices and medical centers. The fact that a very large proportion of all cases are assessed reduces the risk of biased data. Also, as data is recorded on the day of the call to the patient, recall bias is very low. Finally, the ARGOS[3] database is characterized by a high number of follow-ups.

Despite these strengths, ARGOS has been influenced by the testing policy and the results must be seen in light of these influences. First, individuals without risk factors for COVID-19 and those younger than 65 years old are underrepresented in the database during the testing restriction period. The shapes of the graphics in Figure 1 and 2 confirm the impact of this policy as there is a sudden decrease in number of cases after March 20, 2020, when restriction started. Other factors could have amplified this phenomenon such as less symptomatic forms of disease in younger people and

children. Reasons to get tested have also evolved over the first months of the epidemic. For example, anosmia or ageusia became a testing criteria only in late April. Patients who presented with these isolated symptoms within the first two months of the epidemic could thus have been undertested. Seroprevalence study results confirm the underrepresentation of certain groups and the undertesting of the overall population (8).

Nevertheless, ARGOS has several limitations. First, measurement error due to lack of detail of some variables can be observed, since efficiency was prioritized over detail-oriented data collection. For instance, individuals' level of education is not recorded. Secondly, misclassification also certainly occurs as symptoms and risk factors are self-reported. Moreover, recording of information in ARGOS is performed by a large and evolving team of professionals, including healthcare workers with various backgrounds, medical students, or police recruits as of May 2020. Due to the crisis situation, training contents delivered to the GDH team often evolved, leading to a certain level of heterogeneity of phone interviews and a greater risk for misclassification of medical information. Thirdly, the patient information gathered is tailored to operational needs and growing scientific knowledge. For example, anosmia and ageusia were initially classified as general ENT symptoms, and were later detailed separately as they were recognized as frequent and specific manifestations of COVID-19 (25).

In conclusion, ARGOS is a large, real-world registry of individuals tested for SARS-Cov2[1]. Unlike many other registries, it involves every tested individual and is not limited to hospitalized patients, thus providing a precious resource to assess the impact of public health policies and overall disease burden of COVID-19.

COLLABORATION

The publication of the ARGOS cohort underscores our willingness to share data for research purposes and for optimizing public health measures. Deidentified ARGOS data can be available upon reasonable request, including a research protocol, using the following form.

DATA SHARING STATEMENT

The deindentified data underlying this article will be shared on reasonable request to the corresponding author, using the form (https://edc.hcuge.ch/surveys/?s=TLT9EHE93C)

ETHICS APPROVAL

Research received the agreement of the Cantonal Ethic Committee of Geneva (CCER protocol 2020-01273).

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CONFLICTS OF INTERESTS

The authors declare no conflict of interest.

AUTHORS CONTRIBUTION

Each author contributed to this article, based on the criteria of the International Committee for Medical Journal Editors. Camille Genecand and Flora Koegler conceptualized and designed the article format, analyzed and interpreted the data, and conducted the literature review. Dan Lebowitz participated to the article design and reviewed it. Delphine Courvoisier designed the study's analytic strategy, reviewed the article, and revisited it critically. Denis Mongin conducted the data analysis and participated in its formulation in the text. Simon Regard, Pierre Chopard, Marwène Grira, Elisabeth Delaporte, Mayssam Nehme, Olivia Braillard, Dominique Joubert, Idris Guessous, Jerome Stirnemann and Aglaé Tardin helped acquisition of data and reviewed the article's content critically.

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Test result	– Positive – Negative – COVID-19 suspected, no test performed – COVID-19 suspected, negative test result
Reason for testing	– Acute symptoms consistent with COVID-19 – Screening, no symptoms – Patient transfer between hospitals
Demographics	– Date of birth – Gender – Basic professional information – Personal and professional addresses
Medical risk factors for COVID-19 negative outcome	– Cardiovascular disease – Hypertension – Chronic respiratory disease – Cancer – Immunosuppression – Diabetes
Environmental risk factors	– Homelessness – Nursing home resident

	– Asylum seeker or other migrant living in a collective housing – Living in another type of collective housing
Symptoms	– Cough – Presence of sputum – Dyspnea – Fever (> 38C) – Headache – Fatigue – Arthralgia and/or myalgia – ENT complaints (sore throat, rhinorrhea, anosmia or ageusia) – Gastrointestinal symptoms
Factors likely to adversely influence the course of disease	– High anxiety level – Feeling of isolation – Difficulties in daily management
Red Flags	– New-onset or worsening dyspnea – Fever for more than 5 days, or worsening fever non responding to treatment

	– Deterioration of the general status – Worsening cough – Hemoptysis – Confusion – Gastrointestinal symptoms with dehydration – Moderate to severe chest pain
Positive patients' compliance to recommended isolation measures	– Full compliance – Partial compliance – Insufficient compliance
Timeline	– Date of symptom onset – Date of testing – Initial date of (self-)isolation

Hospitalizations	– Date of hospitalization
	– Date of release
	– Hospitalization ward:
	  – Visit at the emergency department only
	  – Stay in non-intensive care units
	  – Stay in intensive care unit

Deaths	– Site (at home, nursing home, hospital)

	– Date

Contact tracing	– Number of close contacts per index case
	– Type of contact between index case and close contact:
	  – Living in the same household
	  – Intimate contact
	  – Professional
	  – Healthcare environnement
	  – Social interaction
	  – Recreational
	  – Schooling
	– Presence of symptoms at first call and follow-up calls
	– Compliance to quarantine measures at first call and follow-up calls

Table 1, Actionable Register of Geneva Outpatients with SARS-CoV-2 (ARGOS) collected data

	2020-02-26 ->2020-03-13	2020-03-14 ->2020-03-30	2020-03-31 ->2020-04-27	2020-04-28 ->2020-07-28	p	Total
Number of positive patients						
n	241	2793	2785	816		6635
Number of follow-up per patient recorded in ARGOS					<0.001	
First contact only	83 (65.9)	1662 (75.5)	1757 (71.7)	223 (28.1)		3725 (66.8)
1 Follow-up call	9 (7.1)	196 (8.9)	150 (6.1)	105 (13.2)		460 (8.3)
2 follow-up calls	11 (8.7)	75 (3.4)	71 (2.9)	63 (7.9)		220 (3.9)
3 or more follow-up calls	23 (18.3)	269 (12.2)	473 (19.3)	404 (50.8)		1169 (21.0)
Patients addressed to their general practitioner for clinical follow up						
	5 (2.1)	496 (18.5)	1057 (44.1)	190 (51.9)	<0.001	1748 (30.8)

Patients addressed to a medical center (not HUG[5]) for clinical follow up						
	1 (0.4)	41 (1.5)	246 (8.8)	16 (2.0)	<0.001	304 (4.6)
Age					<0.001	
0-19	6 (2.5)	65 (2.3)	109 (3.9)	74 (9.1)		254 (3.8)
20-39	93 (38.6)	795 (28.5)	797 (28.6)	385 (47.5)		2070 (31.2)
40-64	105 (43.6)	1264 (45.3)	1219 (43.8)	263 (32.5)		2851 (43.0)
65-80	25 (10.4)	380 (13.6)	279 (10.0)	44 (5.4)		728 (11.0)
>80	12 (5.0)	289 (10.3)	381 (13.7)	44 (5.4)		726 (11.0)
Gender					0.004	
Male	114 (47.3)	1242 (44.5)	1196 (42.9)	395 (48.5)		2947 (44.4)
Female	127 (52.7)	1551 (55.5)	1589 (57.1)	418 (51.3)		3685 (55.5)
Non binary	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)		2 (0.0)
Comorbidities						
Cardiovascular disease	11 (4.6)	213 (7.6)	183 (6.6)	31 (3.8)	0.001	438 (6.6)
Hypertension	10 (4.1)	339 (12.1)	258 (9.3)	49 (6.0)	<0.001	656 (9.9)
Chronic respiratory illness	12 (5.0)	306 (11.0)	207 (7.4)	21 (2.6)	<0.001	546 (8.2)
Cancer	1 (0.4)	36 (1.3)	37 (1.3)	9 (1.1)	0.742	83 (1.3)
Immunosupression	3 (1.2)	108 (3.9)	91 (3.3)	17 (2.1)	0.021	219 (3.3)

Diabetes	7 (2.9)	149 (5.3)	121 (4.3)	22 (2.7)	0.006	299 (4.5)
No risk factor	215 (89.2)	2241 (80.2)	2343 (84.1)	739 (90.6)	<0.001	5538 (83.5)
Age 65 and older	37 (15.4)	669 (24.0)	660 (23.7)	88 (10.9)	<0.001	1454 (21.9)
Profession						
health care professional	27 (11.2)	340 (12.2)	320 (11.5)	34 (4.2)	<0.001	721 (10.9)
Environmental risk factor						
Homelessness	0 (0.0)	5 (0.2)	10 (0.4)	0 (0.0)	0.274	15 (0.2)
Nursing home resident	0 (0.0)	75 (2.7)	238 (8.5)	23 (2.8)	<0.001	336 (5.1)
Asylum seeker or other migrant living in a collective home	0 (0.0)	6 (0.2)	19 (0.7)	0 (0.0)	0.007	25 (0.4)
Collective home resident (other than migrant)	0 (0.0)	2 (0.1)	26 (0.9)	9 (1.1)	<0.001	37 (0.6)
Reason for testing						
Acute symptoms	241 (100.0)	2793 (100.0)	2784 (100.0)	678 (86.5)	<0.001	6496 (98.4)

Testing						
Total number of tests perfromed	2603	9522	16053	39044		67222
Positivity rate (patient)	9.5 %	30.9%	18.4%	2.1%	<0.001	10.2%

Table 2, ARGOS baseline characteristics of positive patients, Geneva, February 26 ,2020 – July 28, 2020. Policy periods are presented by grouping together before any measures, limited testing and confinement, increased testing and confinement, end of confinement. Comparison between subgroups is performed with Fisher's exact test, with p values computed by Monte Carlo simulation.

FIGURE LEGENDS

Figure 1, Number of cases per age category, Geneva, February 26 ,2020 – July 28, 2020. Vertical bars represent the daily cases, solid line represent the weekly moving average.

Figure 2, Epidemic Curve of the Confirmed Cases of Coronavirus Disease 2019 (COVID-19) in Geneva state, February 26 ,2020 – July 28, 2020, with policies timeline as described in the text. Vertical bars represent the daily cases (based on the date of the test result), solid blue line represents the weekly moving average and the solid black line the cumulative cases.

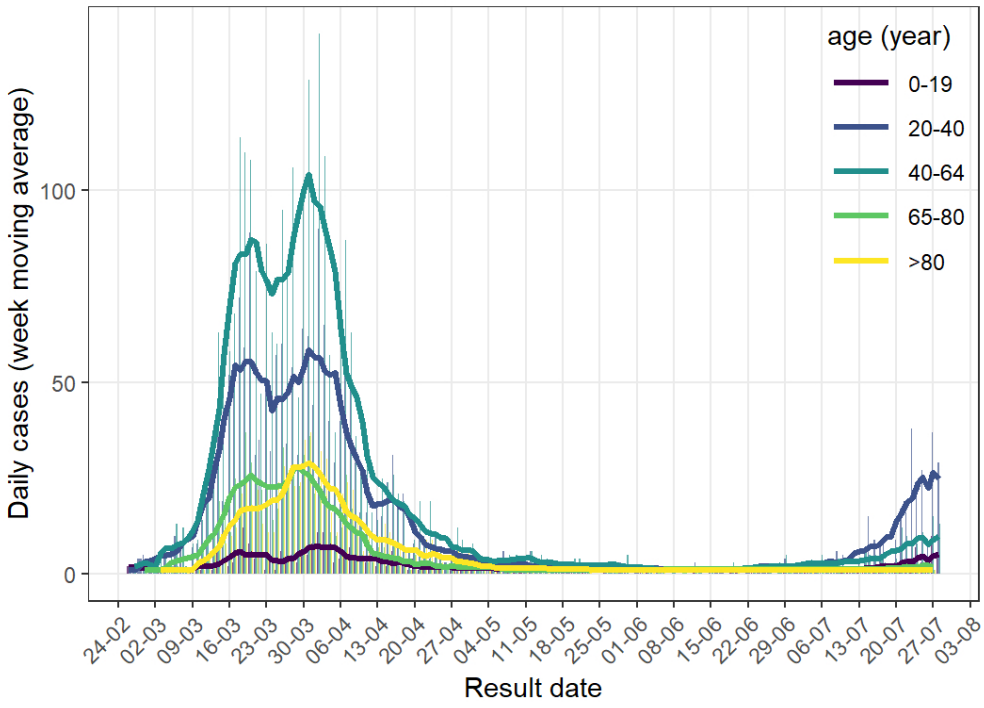

Figure 1, Number of cases per age category, Geneva, February 26 ,2020 – July 28, 2020. Vertical bars represent the daily cases, solid line represent the weekly moving average.

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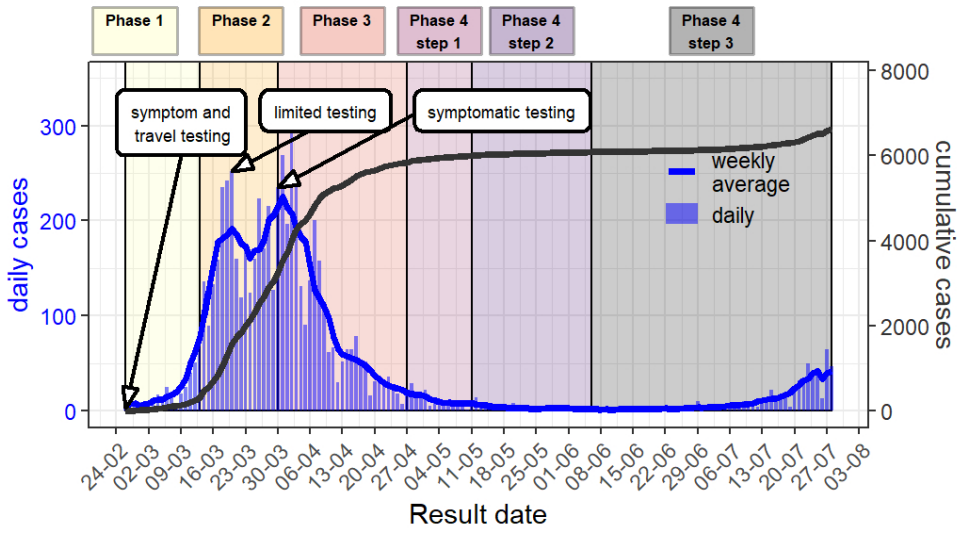

Figure 2, Epidemic Curve of the Confirmed Cases of Coronavirus Disease 2019 (COVID-19) in Geneva state, February 26 ,2020 – July 28, 2020, with policies timeline as described in the text. Vertical bars represent the daily cases (based on the date of the test result), solid blue line represents the weekly moving average and the solid black line the cumulative cases.

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Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohortreporting guidelines, and cite them as:

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		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	#3	State specific objectives, including any prespecified hypotheses	5-6
Methods			
Study design	#4	Present key elements of study design early in the paper	6-7
Setting	#5	Describe the setting, locations, and relevant dates, including periods of	7-8

		recruitment, exposure, follow-up, and data collection	
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	7-8
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8, table 1
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	7-9
Bias	#9	Describe any efforts to address potential sources of bias	13-14
Study size	#10	Explain how the study size was arrived at	9
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	n/a
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	table 2, legend
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	n/a
Statistical methods	#12c	Explain how missing data were addressed	13
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	n/a
Statistical methods	#12e	Describe any sensitivity analyses	n/a
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	6, 9

Participants	#13b	Give reasons for non-participation at each stage	9, table 2
Participants	#13c	Consider use of a flow diagram	n/a
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	9-12, table 2, figure 2
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	9
Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)	9-12, figure 1
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	9-12
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-12, table 2
Main results	#16b	Report category boundaries when continuous variables were categorized	n/a
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	#18	Summarise key results with reference to study objectives	12
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	13-14
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	14

Generalisability	#21	Discuss the generalisability (external validity) of the study results	14
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

Notes:

- 7: 7-8, table 1
- 12a: table 2, legend
- 14a: 9-12, table 2, figure 2
- 14c: 9-12, figure 1
- 16a: 9-12, table 2 This checklist was completed on 08. November 2020 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

BMJ Open

Cohort profile: Actionable Register of Geneva Out- and inpatients with SARS-CoV-2

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Keywords:	COVID-19, Public health < INFECTIOUS DISEASES, Epidemiology < INFECTIOUS DISEASES

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Cohort profile:

Actionable Register of Geneva Out- and inpatients with SARS-CoV-2 (ARGOS)

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Abstract:

Purpose

The Actionable Register of Geneva Out- and inpatients with SARS-CoV-2 (ARGOS) is an ongoing prospective cohort created by the Geneva Directorate of Health (GDH). It consists of an operational database compiling all SARS-CoV-2 test results conducted in the Geneva area since late February 2020. This article aims at presenting this comprehensive cohort, in light of some of the varying public health measures in Geneva, Switzerland, since March 2020.

Participants

As of June 1st, 2021, the database included 356'868 patients, among which 65'475 had at least one positive test result for SARS-CoV-2. Among all positive patients, 37.6% were contacted only once, 10.6 % had one follow-up call, 8.5% had two, and 27.7% had 3 or more follow-up calls. Participation rate among positive patients is 94%. Data collection is ongoing.

Findings to date

ARGOS data illustrates the magnitude of COVID-19 pandemic in Geneva, Switzerland, and details a variety of population factors and outcomes. The content of the cohort includes demographic data, comorbidities and risk factors for poor clinical outcome, self-reported COVID-19 symptoms, environmental and socio-economic factors, prospective and retrospective contact tracing data, travel quarantine data, and deaths. The registry

has already been used in several publications focusing on symptoms and long COVID, infection fatality rate, and re-infection.

Future plans:

The data of this large real-world registry provides a valuable resource for various types of research, such as clinical research, epidemiological research or policy assessment as it illustrates the impact of public health policies and overall disease burden of COVID-19.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ARGOS' main strength consists of its large number of cases, representative of all diagnosed cases on a regional level with the primary aim of assessing all cases.
- ARGOS involves every individual who performed a SARS-CoV-2 test (PCR or antigenic) and is not limited to hospitalized patients, thus providing a valuable resource to assess the overall disease burden of COVID-19 in a geographically defined population.
- To mitigate confounding effects and improve data analysis and interpretation, we present the data according to four policy periods.
- This cohort is multicentric as it includes all tests performed in Geneva's hospitals (both public and private), private practices and medical centers.
- Due to operational needs, symptoms and comorbidities are self-reported, which may lead to measurement error or misclassification.

Text word count: 3140 words

Introduction

In December 2019, an increasing number of cases of pneumonia caused by a novel coronavirus, SARS-CoV-2[1], was observed in Wuhan, China. On March 11, 2020, the World Health Organization (WHO) declared the coronavirus disease 2019 (COVID-19) outbreak a global pandemic(1,2). As of June 1st, 2021, the virus spread to 207 countries, infected close to 171 million people and caused 3.68 million deaths(3,4). In Switzerland, the cumulative incidence of laboratory confirmed COVID-19[2] cases during the first wave was in the top five countries in Europe, with about 400 confirmed cases per 100'000 population at the end of July 2020(4,5). In the Geneva area, the first COVID-19[2] patient was diagnosed on February 26, 2020(6). Possibly due to the city's geographical proximity to Northern Italy(7), the epidemic curve showed a steep upward trend. The first wave of the epidemic peaked in Geneva on April 2nd with 233 cases in 24 hours in an area with a population of 500'000. Geneva's cumulative incidence of confirmed cases is almost 3 times that of Switzerland(5), with more than 1'000 cases per 100'000 population(6), while the seroprevalence was estimated to be close to 10 times that of the confirmed cases as 9.7% of the population had antibodies three weeks after the height of the epidemic(8,9).

A database was created in early March in order to contact new cases and keep track of their follow-up. The Actionable Register of Geneva Out- and inpatients with SARS-CoV-

[1] Severe acute respiratory syndrome coronavirus 2
[2] coronavirus disease 2019

2[1] (ARGOS) includes all SARS-CoV-2[1] test results conducted in the Geneva area since late February 2020, as well as those from Geneva residents being tested in other Swiss cantons. After more than a year of pandemic and guided by operational needs, ARGOS has been enriched by various data, including contact tracing information. The primary aim of this article is to present this comprehensive cohort, its characteristics and the content of the data collected. The secondary aim is to interpret the data according to the public health measures implemented over time since the cohort profile was influenced by the varying policies enacted by the Swiss government and the Geneva State.

Cohort description

The ARGOS database

ARGOS is an ongoing prospective cohort created by the Geneva Directorate of Health (GDH) and consists of an operational database compiling all SARS-CoV-2 test results conducted in the Geneva canton. Data are collected and managed using the REDCap electronic data capture tools(10,11) allowing the GDH to contact positive cases in order to promote public health measures and coordinate medical follow-up. It is set up as a collaborative tool between different institutions and medical entities, including the GDH, Geneva University Hospitals (HUG), and Geneva's main private medical centers. The latter have restricted access to data regarding their own patients only. The GDH and HUG are the only users to implement follow-up data in the electronic register. The data is hosted on HUG's secure servers. The register is administered by a committee of co-Principal Investigators belonging to the GDH and HUG, with the agreement of the cantonal ethic committee (CCER protocol 2020-01273). Participants in the database had

the opportunity to refuse to participate in the registry, and those who did are excluded from the analyses presented here and any data sharing. 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). As recommended by the World Health Organization, deidentified ARGOS data are made available upon reasonable request, including a research protocol, using the form https://edc.hcuge.ch/surveys/?s=TLT9EHE93C.

Data collection

All Geneva laboratories performing SARS-CoV-2 testing are required to send the results to the GDH. Swabs are collected from the upper respiratory tract in medical centers, private practice or during home visits by trained healthcare professionals(12). Between January 24, 2020 and June 1st, 2021, 655'464 tests for SARS-CoV-2 recorded in the ARGOS database, 584'512 were performed by real-time reverse transcriptase–polymerase chain reaction assays and 70'952 by rapid antigen tests. The majority were performed in the Geneva area and a small number consisted of tests conducted on Geneva residents in other Swiss Cantons, and declared to the GDH by the Federal Office of Public Health (FOPH). Importantly, patients reporting COVID-19 symptoms between March 13 and March 29, 2020, did not get tested due to shortage of testing materials, unless they were healthcare workers, considered at-risk or hospitalized. However, symptomatic patients who visited the HUG COVID-19 testing center without fulfilling testing criteria were entered in the database as "suspected cases". Some of these patients later received a test as policy evolved on March 30, 2020. For each positive or suspect case, a series of surveys is filled using REDCap platform.

Depending on the needs, follow-up calls are performed either by a professional nurse, a medical student or a contact tracer with supervision from a medical doctor. Findings are documented in the database. 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. All SARS-CoV-2 positive patients in Geneva who require hospitalization at HUG received follow-up calls by the HUG team at the time of discharge from the hospital. COVID-19 positive patients identified as nursing home residents or who are hospitalized at the time of diagnosis are not systematically called since they already receive medical attention and isolation measures are enforced by the medical staff. During the second wave, which started in late September 2020, the incidence of SARS-CoV-2 positive patients became so high that the GDH team could not contact everyone in time. A semi-automatic process was put in place. Positive patients and their declared contacts received an invitation to an online survey where they filled basic information. Only then and when the workload allowed it, they received a phone call from the GDH team to complete the data already provided. At the peak of the second wave, not all SARS-CoV-2 positive patients could be contacted. Follow-up calls as well as calls to close contacts were also temporarily abandoned. Finally, the Geneva Cantonal Population Office are required to declare COVID-19 related deaths, which are also recorded in ARGOS. Patients or the public were not involved in research.

What is being measured?

An overview of collected data is provided in Table 1. The surveys were created by the GDH and HUG medical task forces. Within the first 48h of testing, patients with a

positive test result for COVID-19 receive a call by a professional nurse or a trained contact tracer with support from a medical doctor if needed. During this call, demographic data are collected (13), as well as symptoms (14–17), clinical and environmental risk factors, and clinical red flags. A special attention is paid to psychosocial and cultural factors, and resources are provided when needed. The clinical evaluation is used to identify patients who need immediate emergency care, or to address them for follow-up care by their general practitioner, by one of Geneva's medical centers, or by the GDH-HUG team via telemedicine, which is recorded in the database as well. Patients' declared symptoms are recorded in subsequent surveys. Patients' self-reported compliance to isolation measures are also recorded. As of April 27, 2020, close contacts of index cases are individually contacted and basic information is recorded. Demographics, the type of contact they had with the index case, vaccine information, the presence of COVID-19 symptoms and their compliance to quarantine measures are also recorded at first call and during follow-up calls. Since July 6, 2020, the FOPH has established an evolving red list of countries where incidence rate is considered high or with variant of concern. Travelers who stayed in one of these countries have to quarantine for 10 days at their arrival in Switzerland. People staying in Geneva must self-declare upon arrival and fill an online survey containing basic information which data is also part of ARGOS. Depending of the work load, travelers are called by contact tracers during their quarantine period. Self-reported compliance to quarantine measures and the presence of symptoms are recorded during these calls.

Findings to date

On June 1st, 2021, of all 360'525 patients recorded in the ARGOS database, 65'475 had at least one positive test result, 294'723 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. During the same period, 655527 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%. 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. Of these patients, 37.6% have only a first contact, 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). The cohort shows a slight female predominance, with women representing 50.2% to 55.9% of all patients depending on the defined period (Table 2). More than 60 percent of all recorded patients have no risk factor for a poor clinical outcome(18). The context of infection recorded for COVID19 positive patients since June 2020 indicates that infection mostly occurs at home, at work or via the educational system. Around 23.2% of the patient reported having no idea of their contamination context. Information about 114'690 close contacts of positive patients has been registered, and 639'153 days of quarantine have been notified. 9'551 close contacts of a positive COVID19 case had a positive test result during their quarantine. Given that the standard duration of a quarantine is 10 days, we can estimate that around 15% of the persons in quarantine after being in contact with a

positive COVID19 case received a positive test result during their quarantine (see table 2).

273'189 days of quarantine concerning 27920 persons were ordered for persons coming back from a country at risk. These country were in order of importance Spain (19.4%), France (14.8%), Kosovo (7.6%), United States (7.0%), United Kingdom (7.0%), Portugal (6.2%) and Brazil (4.2%). 96 persons received a positive test result during their quarantine, among which 26 came back from Kosovo, 11 from France and 10 from Spain, the total of these infection occurring in 0.35% of the quarantines.

To mitigate confounding effects and improve data analysis and interpretation, we present the data according to four periods (see Figure 1).

February 26 to April 27, 2020 (first phase)

The first phase starts on February 26, 2020, when the first case was tested positive for SARS-CoV-2 in the Geneva area. The Swiss authorities implemented lockdown measures which remained moderate in comparison with many other countries (19). This first phase ends on April 27, 2020, when some of the measures started to be lifted following the decreasing incidence of new cases and hospitalizations. During this first wave, contact tracing was not implemented. Between March 13 and March 29, 2020, symptomatic individuals did not get tested due to shortage of testing materials, unless they were healthcare workers, considered at-risk or hospitalized. The percentage of healthcare professionals among positive cases was significantly higher during this phase (15.6%) and the percentage of patients declaring no risk factors was smaller

(32.4%) when compared to the other phases. The positivity (i.e. the ratio between positive tests results and the total amount of test performed) was of 23%.

April 28 to September 24, 2020 (second phase)

Between May and the end of September, 2020, incidence of SARS-CoV-2 positive cases remained low. Nearly all restrictions were lifted at the end of June. Nightclubs were closed again at the end of July after a surge of incidence mostly amongst Geneva youth, as can be seen by the relative higher incidence of the 20-39 year age category compared to the others during this period (Figure 2). 14.1% of the positive tests during this period were stemming from screening campaigns and more than 70% of cases reported no risk factor. The positivity was only 4.6% during this period.

September 24, 2020 to February 28, 2021 (third phase)

A second wave of SARS-CoV-2 positive cases hit Geneva in late September, 2020, at the same time as in the neighboring countries. New restrictions were imposed mid-October but no real lockdown was enacted. The peak lasted about 8 weeks. Due to political and economic pressure, some restrictions measures were lifted long before incidence reached low level. The number of SARS-CoV-2 positive cases in Geneva area remained significant during several months. During February 2021, the B.1.1.7 variant completely replaced SARS-CoV-2 wild type . At the same time, federal and local policies evolved and testing among symptomatic children over 5 years old was newly encouraged. Concurrently with these changes, the incidence of the 0-19 year age population almost doubled to reach those of the older age categories (19–21). The positivity during this period was 15.9%.

As of February 8th, 2021, quarantine measures for close contacts were lifted after 7 days if the person tested negative for SARS-CoV-2. Concurrently, the percentage of close contacts tested positive increased (see table 2). Considering vaccination program, the first dose of vaccine in Geneva was given to an elderly patient the 28th December 2020. At first, only residents over 74 years old and patients with risk factors received vaccination. The decline of the incidence for people of the corresponding age category compared to the others can be observed since February 2021 in figure 2.

March 1st to 1st June, 2021 (fourth phase)

On March 1st, access to vaccination continued to broaden. Resident over 65 years were allowed to be vaccinated since March 17, 2021, followed by the 45-65 year old residents starting at April 12, 2021. By 19 May, 2021, all Geneva residents over 15 years old were eligible to get vaccinated. The incidence COVID among the 65-79 year old population started to decline by end of March (figure 2), followed by a rapid decline of the incidence overall by mid-May. The amount of screening tests increased, as 21% of the positive tests were performed during a screening campaign. The positivity decreased to 5.2% during this period.

Discussion

COVID-19 represents a major challenge to each country's healthcare system. Collaboration between healthcare providers and public health authorities is particularly important in order to improve both our understanding of the disease and our response(22–24). The publication of the ARGOS cohort underscores our willingness to share data for research purposes. Indeed, data from this registry has already been used

to investigate symptoms and long COVID (25), infection fatality rate (9), and re-infection rates (26), as well as viral load kinetics (27). Several projects using these data to develop more accurate mathematical models to estimate transmission chains are also ongoing.

Furthermore, analysis from the ARGOS database illustrates the impact of various testing policies on the proportion of risk factors or age groups identified among confirmed cases. The partition of data analysis and interpretation according to policy period confirms the variations within each group depending on the period of interest and could thus guide public health decisions.

Strength and limitations

The state of Geneva accounts for half a million residents and the local Directorate of Health ordered the recording of all COVID-19 positive cases since the beginning of the epidemic, according to recommendations from the Federal Office of Public Health. Due to this policy, the database's main strength consists of its large number of cases, representative of all diagnosed cases on a regional level primarily serving operational needs and not scientific purposes, with one main objective: assessing all cases. This cohort is also multicentric as it includes all tests performed in Geneva's hospitals (both public and private), private practices and medical centers. The fact that a very large proportion of all cases are assessed reduces the risk of biased data. Also, as data is recorded on the day of the call to the patient, recall bias is very low. Finally, the ARGOS[3] database is characterized by a high number of follow-ups.

Despite these strengths, ARGOS has been influenced by the testing policy and the results must be seen in light of these influences. First, individuals without risk factors for COVID-19 and those younger than 65 years old are underrepresented in the database during the testing restriction period. The shapes of the graphics in Figure 1 and 2 confirm the impact of this policy as there is a sudden decrease in number of cases after March 20, 2020, when restriction started. Other factors could have amplified this phenomenon such as less symptomatic forms of disease in younger people and children. Reasons to get tested have also evolved over the first months of the epidemic. For example, anosmia or ageusia became a testing criteria only in late April. Patients who presented with these isolated symptoms within the first two months of the epidemic could thus have been undertested. Seroprevalence study results confirm the underrepresentation of certain groups and the undertesting of the overall population (8).

Nevertheless, ARGOS has several limitations. First, measurement error due to lack of detail of some variables can be observed, since efficiency was prioritized over detail-oriented data collection. For instance, individuals' level of education is not recorded. Secondly, misclassification also certainly occurs as symptoms and risk factors are self-reported. Moreover, recording of information in ARGOS is performed by a large and evolving team of professionals, including healthcare workers with various backgrounds, medical students, police recruits, or contact tracers with no particular medical and health knowledge. Due to the crisis situation, training contents delivered to the GDH team often evolved, leading to a certain level of heterogeneity of phone interviews and a greater risk for misclassification of medical information. Thirdly, the patient information gathered is tailored to operational needs and growing scientific knowledge. For

example, anosmia and ageusia were initially classified as general ENT symptoms, and were later detailed separately as they were recognized as frequent and specific manifestations of COVID-19 (28). Finally, during some periods of the pandemic, the GDH team was overworked and could not call not verify self-reported information for all positive cases. This resulted in missing and incomplete data.

In conclusion, ARGOS is a large, real-world registry of individuals tested for SARS-Cov2[1]. Unlike many other registries, it involves every tested individual and is not limited to hospitalized patients, thus providing a precious resource to assess the impact of public health policies and overall disease burden of COVID-19.

Collaboration

The publication of the ARGOS cohort underscores our willingness to share data for research purposes and for optimizing public health measures. Deidentified ARGOS data are available upon reasonable request, including a research protocol, using the following form: https://edc.hcuge.ch/surveys/?s=TLT9EHE93C .

Further details

Data sharing statement

The deidentified data underlying this article will be shared on reasonable request using the form (https://edc.hcuge.ch/surveys/?s=TLT9EHE93C)

Ethics approval

Research received the agreement of the Cantonal Ethic Committee of Geneva (CCER protocol 2020-01273).

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Conflicts of interest

The authors declare no conflict of interest.

Authors contribution

Each author contributed to this article, based on the criteria of the International Committee for Medical Journal Editors. Camille Genecand conceptualized, designed the article format, interpreted the data, and conducted the literature review. Denis Mongin conducted the data analysis and participated in its formulation and its interpretation in the text. Flora Koegler conceptualized and designed the article format, interpreted the data, and conducted the literature review. Dan Lebowitz participated to the article design and reviewed it. Delphine Courvoisier designed the study's analytic strategy, reviewed the article, and revisited it critically. Simon Regard, Pierre Chopard, Marwène Grira, Elisabeth

Delaporte, Mayssam Nehme, Olivia Braillard, Dominique Joubert, Idris Guessous, Jerome Stirnemann and Aglaé Tardin helped acquisition of data and reviewed the article's content critically.

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Test result	– Positive – Negative – COVID-19 suspected, no test performed – COVID-19 suspected, negative test result
Test type	– RT-PCR – Rapid antigen test
Reason for testing	– Acute symptoms consistent with COVID-19 – Screening, no symptoms – Screening in the workplace (no symptoms) – Screening based on Swisscovid notification (no symptoms) – Patient transfer between hospitals
Demographics	– Date of birth – Gender – Basic professional information – Personal and professional addresses – School information : o School address o Name of class and professor
Medical risk factors for COVID-19 negative outcome	– Cardiovascular disease – Hypertension – Obesity (based of calculated BMI) – Chronic respiratory disease – Chronic kidney disease – Cancer – Immunosuppression – Diabetes – Pregnancy – Smoking habits
Vaccination	– Number of doses – Dates of doses
Environmental risk factors	– Homelessness – Nursing home resident – Asylum seeker or other migrant living in a collective housing – Living in another type of collective housing – Economic insecurity

Possible context of infection	– In the family or living in the same household – In the workplace – At school – As a healthcare professional – During a public event – At a private party – In a night club – In a bar/ restaurant – During a spontaneous gathering (including between friends) – No idea
Symptoms	– Cough – Presence of sputum – Dyspnea – Fever (> 38C) – Chills – Headache – Fatigue – Arthralgia and/or myalgia – Sore throat – Rhinorrhea, nasal congestion – Anosmia or ageusia – Gastrointestinal symptoms – Skin rash – None
Factors likely to adversely influence the course of disease	– High anxiety level – Feeling of isolation – Difficulties in daily management
Red Flags	– New-onset or worsening dyspnea – Fever for more than 5 days, or worsening fever non responding to treatment – Deterioration of the general status – Worsening cough – Hemoptysis – Confusion – Gastrointestinal symptoms with dehydration – Moderate to severe chest pain
Positive patients' self-reported compliance to	– Full compliance – Partial compliance – Insufficient compliance

recommended isolation measures	
Timeline	– Date of symptom onset – Date of testing
Death	– Site (at home, nursing home, hospital) – Date

Contact tracing	– Number of close contacts per index case
	– Type of contact between index case and close contact:
	  – Living in the same household
	  – Intimate contact
	  – Professional
	  – Healthcare environnement
	  – Social interaction
	  – Recreational
	  – Schooling
	– Date of last contact between index case and close contact

Close contact information	– Demographics:
	  ○ Date of birth
	  ○ Gender
	  ○ Personnal and professional addresses
	– Vaccination information (number of doses, dates)
	– Environmental risk factors
	  ○ Homelessness
	  ○ Nursing home resident
	  ○ Asylum seeker or other migrant living in a collective housing
	  ○ Living in another type of collective housing
	  ○ Economic insecurity
	  ○ Healthcare professional
	– Presence of symptoms at first call and follow-up calls
	– Compliance to quarantine measures at first call and follow-up call
	– Quarantine period (dates of onset and end)
	– Tested positive during quarantine

Quarantine after travelling in a red list country	– Number of people in quarantine
	– Demographics:
	  ○ Date of birth
	  ○ Gender
	  ○ Personal address in Geneva / during stay

	– Red list country
	  ○ Name
	  ○ Date of departure
	– Vaccination (number of doses, dates)
	– Quarantine period (dates of onset and end)
	– Presence of symptoms at first call and follow-up calls
	– Compliance to quarantine measures at first call and follow-up call
	– Tested positive during quarantine

Table 1, Actionable Register of Geneva Out- and inpatients with SARS-CoV-2 (ARGOS) collected data

	Overall	2020-02-25 -> 2020-04-27	2020-04-27 -> 2020-09-24	2020-09-24 -> 2021-02-14	2021-02-14 ->2021-06-02
Number of positive patients					
n	60788	5782	3274	40882	10824
Living in Geneva	53344 (88.2)	4793 (84.4)	2827 (86.5)	35936 (88.3)	9775 (90.4)
Number of follow-up per patient recorded in ARGOS					
Not called	9514 (15.7)	1135 (19.6)	108 (3.3)	8128 (19.9)	131 (1.2)
First contact only	22847 (37.6)	3402 (58.8)	578 (17.7)	17541 (42.9)	1316 (12.2)
1 Follow-up call	6427 (10.6)	346 (6.0)	735 (22.4)	4387 (10.7)	959 (8.9)
2 follow-up calls	5178 (8.5)	152 (2.6)	683 (20.9)	2362 (5.8)	1977 (18.3)
3 or more follow-up calls	16822 (27.7)	747 (12.9)	1170 (35.7)	8464 (20.7)	6441 (59.5)
Age					
0-19	6997 (11.5)	175 (3.0)	364 (11.1)	4052 (9.9)	2406 (22.2)
20-39	21080 (34.7)	1690 (29.2)	1558 (47.7)	14356 (35.1)	3473 (32.1)
40-64	23879 (39.3)	2567 (44.4)	1101 (33.7)	16007 (39.2)	4202 (38.8)
65-80	5046 (8.3)	676 (11.7)	138 (4.2)	3693 (9.0)	539 (5.0)
>80	3750 (6.2)	674 (11.7)	108 (3.3)	2769 (6.8)	199 (1.8)
Gender					

Male	28314 (46.6)	2549 (44.1)	1628 (49.8)	18890 (46.2)	5238 (48.4)
Female	32433 (53.4)	3233 (55.9)	1643 (50.2)	21972 (53.8)	5574 (51.5)
Non binary	22 (0.0)	0 (0.0)	1 (0.0)	8 (0.0)	12 (0.1)
Comorbidities and risk factors					
Cardiovascular disease	1835 (3.0)	396 (6.8)	95 (2.9)	1103 (2.7)	241 (2.2)
Hypertension	4469 (7.4)	600 (10.4)	196 (6.0)	2968 (7.3)	705 (6.5)
Diabetes	1975 (3.2)	273 (4.7)	95 (2.9)	1295 (3.2)	312 (2.9)
Chronic respiratory illness	2170 (3.6)	512 (8.9)	83 (2.5)	1269 (3.1)	306 (2.8)
kidney	229 (0.4)	N/A	N/A	186 (0.5)	43 (0.4)
Cancer	545 (0.9)	73 (1.3)	28 (0.9)	349 (0.9)	95 (0.9)
Immunosupression	600 (1.0)	192 (3.3)	30 (0.9)	301 (0.7)	77 (0.7)
obesity	1081 (1.8)	N/A	N/A	778 (1.9)	303 (2.8)
Age 65 and older	8796 (14.5)	1350 (23.3)	246 (7.5)	6462 (15.8)	738 (6.8)
No risk factor	36905 (60.8)	1868 (32.4)	2523 (77.1)	24093 (59.0)	8419 (77.8)
Missing information	8698 (14.3)	1854 (32.1)	209 (6.4)	6221 (15.2)	411 (3.8)
Other potential risks					
Chronic disease	787 (1.3)	56 (1.0)	28 (0.9)	550 (1.3)	152 (1.4)
smoking	4659 (7.7)	N/A	N/A	3345 (8.2)	1313 (12.1)
pregnancy	533 (0.9)	41 (0.7)	24 (0.7)	352 (0.9)	116 (1.1)
Other risk	4284 (7.0)	107 (1.9)	364 (11.1)	2741 (6.7)	1072 (9.9)
Self reported symptoms					
Missing information	12735 (21.0)	2632 (45.5)	264 (8.1)	9217 (23.3)	604 (5.0)
no symptoms ever declared	3893 (6.4)	254 (4.4)	416 (12.7)	1807 (4.6)	1413 (11.6)
At least one symptom	44159 (72.6)	2896 (50.1)	2594 (79.2)	28516 (72.1)	10148 (83.4)
Possible context of infection					
family	17266 (28.4)	N/A	511 (15.6)	11861 (29.0)	4889 (45.2)
work	8535 (14.0)	N/A	304 (9.3)	6588 (16.1)	1639 (15.1)
school	3302 (5.4)	N/A	0 (0.0)	2200 (5.4)	1101 (10.2)
Health care worker	894 (1.5)	N/A	17 (0.5)	808 (2.0)	67 (0.6)
Public event	204 (0.3)	N/A	22 (0.7)	138 (0.3)	44 (0.4)
private_party	1372 (2.3)	N/A	184 (5.6)	933 (2.3)	255 (2.4)
club	70 (0.1)	N/A	24 (0.7)	41 (0.1)	5 (0.0)
restaurant	1346 (2.2)	N/A	161 (4.9)	1125 (2.8)	60 (0.6)

Spontaneous gathering	2527 (4.2)	N/A	81 (2.5)	1718 (4.2)	728 (6.7)
No idea	14090 (23.2)	N/A	410 (12.5)	10451 (25.6)	3222 (29.8)
Other	4921 (8.1)	N/A	488 (14.9)	3574 (8.7)	858 (7.9)
Missing information	16520 (27.2)	5775 (100)	1356 (41.4)	8885 (21.7)	486 (4.5)
Profession					
health care professional	4503 (7.4)	902 (15.6)	175 (5.3)	2973 (7.3)	452 (4.2)
Environmental risk factor					
Homelessness	135 (0.2)	15 (0.3)	6 (0.2)	102 (0.2)	12 (0.1)
Nursing home resident	1895 (3.1)	377 (6.5)	63 (1.9)	1403 (3.4)	49 (0.5)
Asylum seeker or other migrant living in a collective home	267 (0.4)	25 (0.4)	2 (0.1)	172 (0.4)	68 (0.6)
Collective home resident (other than migrant)	627 (1.0)	34 (0.6)	31 (0.9)	431 (1.1)	131 (1.2)
Reason for testing					
Acute symptoms	45321 (88.0)	5633 (99.9)	2693 (85.9)	28785 (89.2)	8204 (78.8)
Testing					
Total number of tests performed	655527	28931	80342	291510	254744
PCR	584573 (89.2)	28879 (99.8)	80339 (100.0)	263182 (90.3)	212173 (83.3)
Number of patient tested	360525	25853	71269	210598	169164
Positivity rate	9.4	21.0	4.1	14.3	4.3
deaths					
Deaths number	747	280	20	421	22
Age	87.1 [80.2, 91.5]	86.3 [79.4, 91.3]	89.2 [85.8, 93.3]	87.7 [81.4, 91.8]	83.6 [70.5, 90.3]
Gender	354 (47.4)	130 (46.4)	10 (50.0)	200 (47.7)	11 (45.8)
Contact tracing					
Number total of contact	114690	118	12420	77990	24162
Number of contact per index patient	3 [1, 6]	0 [0, 0]	7 [4, 11]	3 [1, 6]	3 [2, 5]
Quarantine after contact with positive					

Number of days	639153	N/A	31615	445468	162003
Number of infection during quarantine	9551	N/A	333	6009	3209
Pourcentage of quarantine leading to infection	14.94	N/A	10.53	13.49	19.81
Quarantine after traveling					
Number of days	273189	N/A	85490	121202	66429
Number of infection during quarantine	96	N/A	29	42	25
Pourcentage of quarantine leading to infection	0.35	N/A	0.34	0.35	0.38

Table 2, ARGOS baseline characteristics of positive patients, Geneva, February 26 ,2020 – June 1st, 2021. Periods are presented by grouping together the first wave of cases, the period between the two waves, the second wave and the following period of sustained epidemic activity, and finally the more recent period following the start of the vaccination campaign.

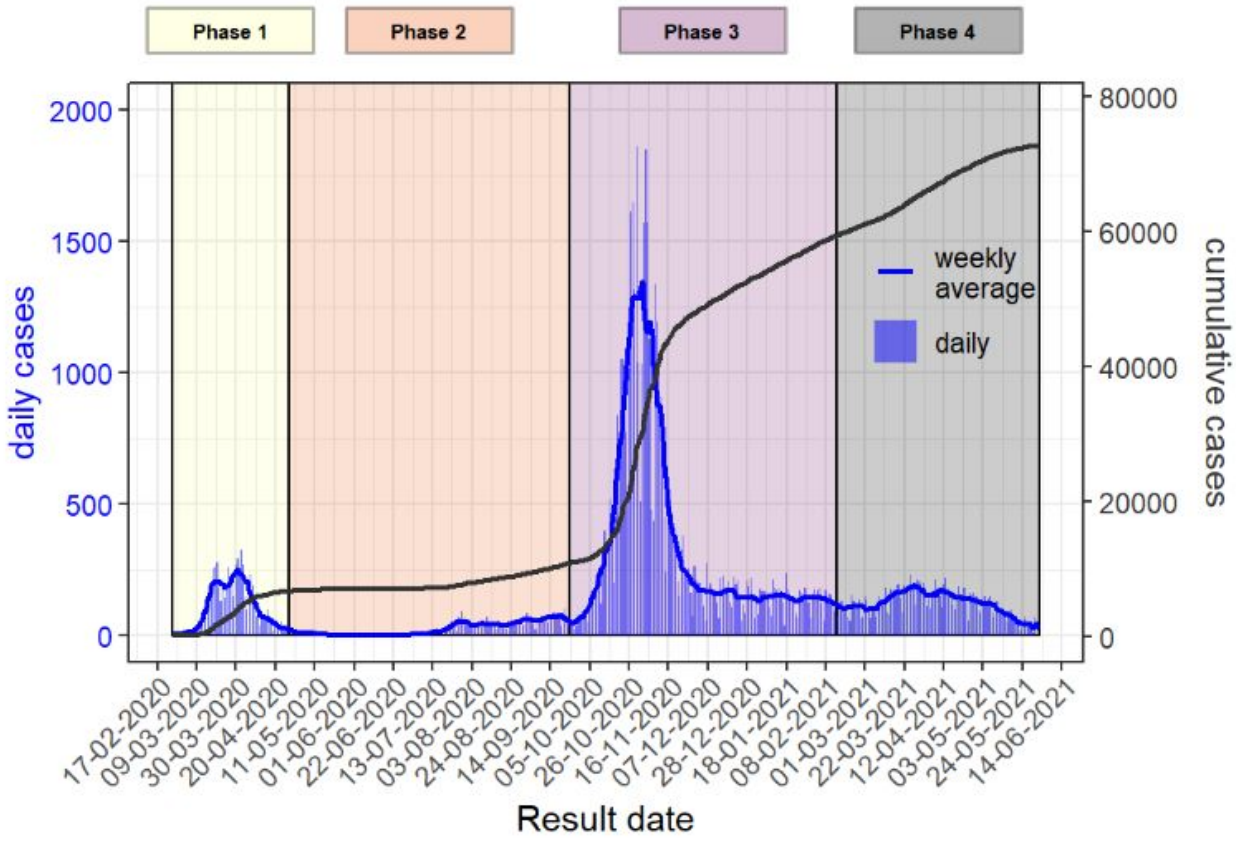


Figure 1, Epidemic Curve of the cases of Coronavirus Disease 2019 (COVID-19) in Geneva state, February 26 ,2020 – June 1st, 2021. Vertical bars represent the daily cases (based on the date of the test result), solid blue line represents the weekly moving average and the solid black line the cumulative cases.

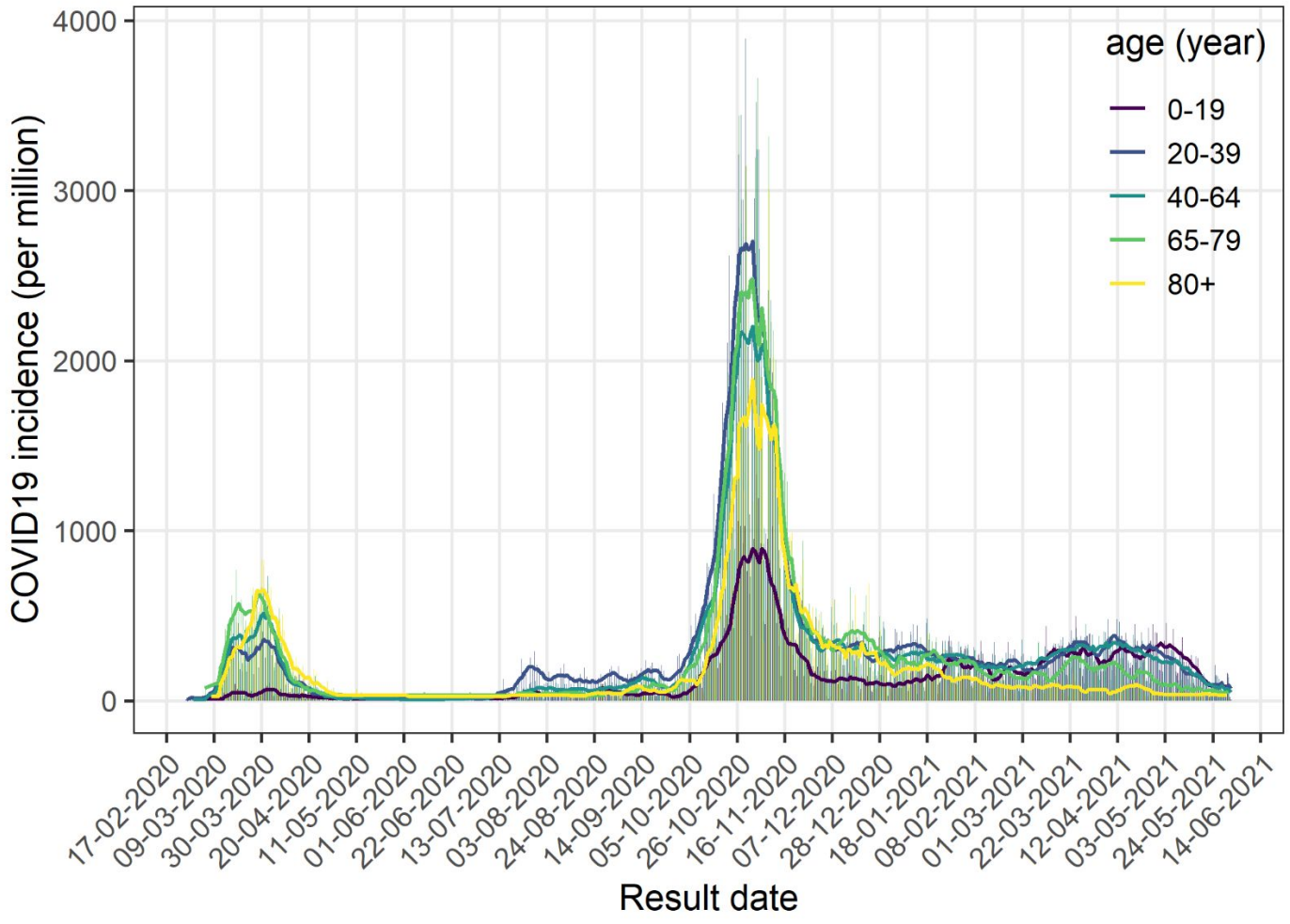
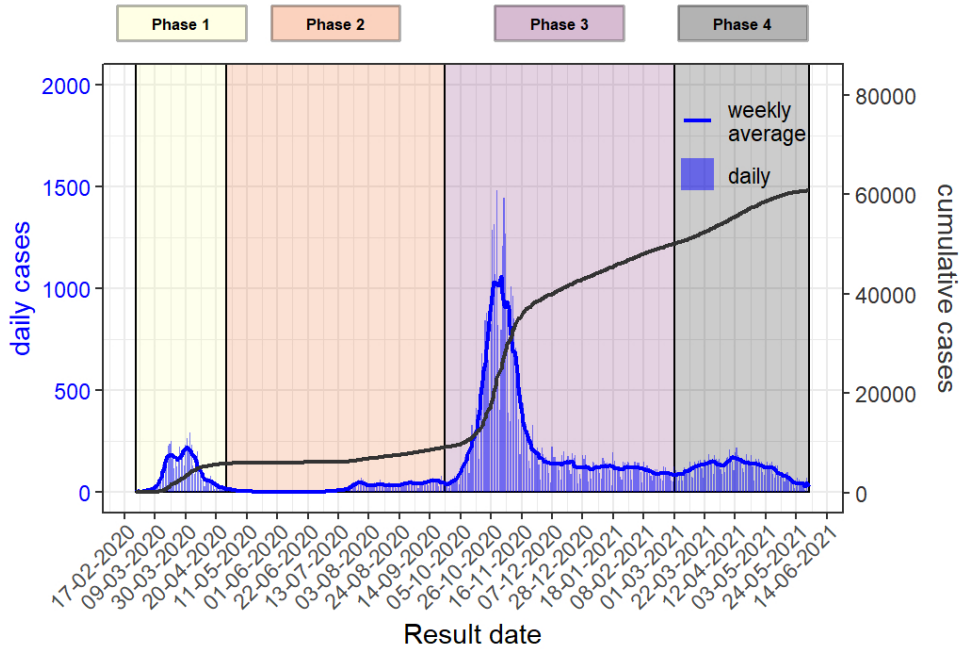


Figure 2, Incidence per age category, Geneva, February 26 ,2020 – June 1st, 2021. Vertical bars represent the daily incidence, solid line represent the weekly moving average.



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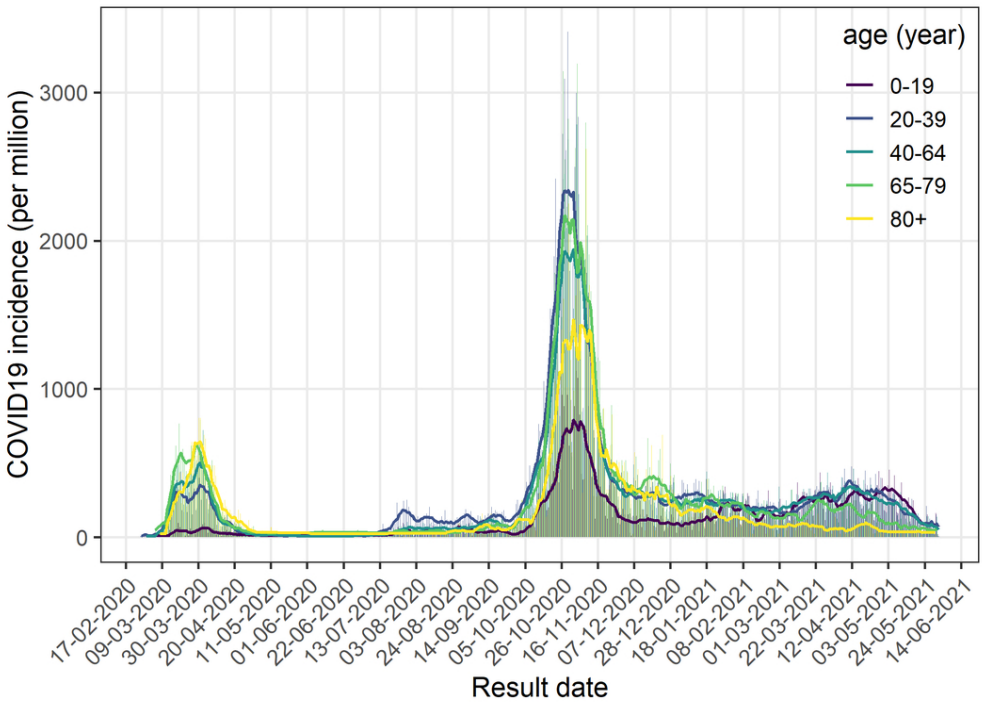
89x64mm (300 x 300 DPI)



Incidence per age category, Geneva, February 26 ,2020 – June 1st, 2021. Vertical bars represent the daily incidence, solid line represent the weekly moving average.

89x64mm (300 x 300 DPI)

Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the STROBE cohortreporting guidelines, and cite them as:

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		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	#3	State specific objectives, including any prespecified hypotheses	5-6
Methods			

Study design	#4	Present key elements of study design early in the paper	6
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	7-8
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-9, table 1
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	7-9
Bias	#9	Describe any efforts to address potential sources of bias	14-16
Study size	#10	Explain how the study size was arrived at	9-10
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	n/a
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	Along text
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	n/a
Statistical methods	#12c	Explain how missing data were addressed	15
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	n/a
Statistical methods	#12e	Describe any sensitivity analyses	n/a

Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	9
Participants	#13b	Give reasons for non-participation at each stage	9, table 2
Participants	#13c	Consider use of a flow diagram	n/a
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	9-13, table 2, figure 2
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	Table 2
Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)	9-13, figure 1
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	9-13
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-13, table 2
Main results	#16b	Report category boundaries when continuous variables were categorized	n/a
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	#18	Summarise key results with reference to study objectives	13-14

Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	14-15
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	15-16
Generalisability	#21	Discuss the generalisability (external validity) of the study results	15-16
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

Notes:

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BMJ Open

Cohort profile: Actionable Register of Geneva Out- and inpatients with SARS-CoV-2 (ARGOS)

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Cohort profile:

Actionable Register of Geneva Out- and inpatients with SARS-CoV-2 (ARGOS)

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Abstract:

Purpose

The Actionable Register of Geneva Out- and inpatients with SARS-CoV-2 (ARGOS) is an ongoing prospective cohort created by the Geneva Directorate of Health (GDH). It consists of an operational database compiling all SARS-CoV-2 test results conducted in the Geneva area since late February 2020. This article aims at presenting this comprehensive cohort, in light of some of the varying public health measures in Geneva, Switzerland, since March 2020.

Participants

As of June 1st, 2021, the database included 356'868 patients, among which 65'475 had at least one positive test result for SARS-CoV-2. Among all positive patients, 37.6% were contacted only once, 10.6 % had one follow-up call, 8.5% had two, and 27.7% had 3 or more follow-up calls. Participation rate among positive patients is 94%. Data collection is ongoing.

Findings to date

ARGOS data illustrates the magnitude of COVID-19 pandemic in Geneva, Switzerland, and details a variety of population factors and outcomes. The content of the cohort includes demographic data, comorbidities and risk factors for poor clinical outcome, self-reported COVID-19 symptoms, environmental and socio-economic factors, prospective and retrospective contact tracing data, travel quarantine data, and deaths. The registry

has already been used in several publications focusing on symptoms and long COVID, infection fatality rate, and re-infection.

Future plans:

The data of this large real-world registry provides a valuable resource for various types of research, such as clinical research, epidemiological research or policy assessment as it illustrates the impact of public health policies and overall disease burden of COVID-19.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ARGOS' main strength consists of its large number of cases, representative of all diagnosed cases on a regional level with the primary aim of assessing all cases.
- ARGOS involves every individual who performed a SARS-CoV-2 test (PCR or antigenic) and is not limited to hospitalized patients, thus providing a valuable resource to assess the overall disease burden of COVID-19 in a geographically defined population.
- To mitigate confounding effects and improve data analysis and interpretation, we present the data according to four policy periods.
- This cohort is multicentric as it includes all tests performed in Geneva's hospitals (both public and private), private practices and medical centers.
- Due to operational needs, symptoms and comorbidities are self-reported, which may lead to measurement error or misclassification.

Text word count: 3140 words

Introduction

In December 2019, an increasing number of cases of pneumonia caused by a novel coronavirus, SARS-CoV-2[1], was observed in Wuhan, China. On March 11, 2020, the World Health Organization (WHO) declared the coronavirus disease 2019 (COVID-19) outbreak a global pandemic(1,2). As of June 1st, 2021, the virus spread to 207 countries, infected close to 171 million people and caused 3.68 million deaths(3,4). In Switzerland, the cumulative incidence of laboratory confirmed COVID-19[2] cases during the first wave was in the top five countries in Europe, with about 400 confirmed cases per 100'000 population at the end of July 2020(4,5). In the Geneva area, the first COVID-19[2] patient was diagnosed on February 26, 2020(6). Possibly due to the city's geographical proximity to Northern Italy(7), the epidemic curve showed a steep upward trend. The first wave of the epidemic peaked in Geneva on April 2nd with 233 cases in 24 hours in an area with a population of 500'000. Geneva's cumulative incidence of confirmed cases is almost 3 times that of Switzerland(5), with more than 1'000 cases per 100'000 population(6), while the seroprevalence was estimated to be close to 10 times that of the confirmed cases as 9.7% of the population had antibodies three weeks after the height of the epidemic(8,9).

A database was created in early March in order to contact new cases and keep track of their follow-up. The Actionable Register of Geneva Out- and inpatients with SARS-CoV-

[1] Severe acute respiratory syndrome coronavirus 2
[2] coronavirus disease 2019

2[1] (ARGOS) includes all SARS-CoV-2[1] test results conducted in the Geneva area since late February 2020, as well as those from Geneva residents being tested in other Swiss cantons. After more than a year of pandemic and guided by operational needs, ARGOS has been enriched by various data, including contact tracing information. The primary aim of this article is to present this comprehensive cohort, its characteristics and the content of the data collected. The secondary aim is to interpret the data according to the public health measures implemented over time since the cohort profile was influenced by the varying policies enacted by the Swiss government and the Geneva State.

Cohort description

The ARGOS database

ARGOS is an ongoing prospective cohort created by the Geneva Directorate of Health (GDH) and consists of an operational database compiling all SARS-CoV-2 test results conducted in the Geneva canton. Data are collected and managed using the REDCap electronic data capture tools(10,11) allowing the GDH to contact positive cases in order to promote public health measures and coordinate medical follow-up. It is set up as a collaborative tool between different institutions and medical entities, including the GDH, Geneva University Hospitals (HUG), and Geneva's main private medical centers. The latter have restricted access to data regarding their own patients only. The GDH and HUG are the only users to implement follow-up data in the electronic register. The data is hosted on HUG's secure servers. The register is administered by a committee of co-Principal Investigators belonging to the GDH and HUG, with the agreement of the cantonal ethic committee (CCER protocol 2020-01273). Participants in the database had

the opportunity to refuse to participate in the registry, and those who did are excluded from the analyses presented here and any data sharing. 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). As recommended by the World Health Organization, deidentified ARGOS data are made available upon reasonable request, including a research protocol, using the form https://edc.hcuge.ch/surveys/?s=TLT9EHE93C.

Data collection

All Geneva laboratories performing SARS-CoV-2 testing are required to send the results to the GDH. Swabs are collected from the upper respiratory tract in medical centers, private practice or during home visits by trained healthcare professionals(12). Between January 24, 2020 and June 1st, 2021, 655'464 tests for SARS-CoV-2 recorded in the ARGOS database, 584'512 were performed by real-time reverse transcriptase–polymerase chain reaction assays and 70'952 by rapid antigen tests. The majority were performed in the Geneva area and a small number consisted of tests conducted on Geneva residents in other Swiss Cantons, and declared to the GDH by the Federal Office of Public Health (FOPH). Importantly, patients reporting COVID-19 symptoms between March 13 and March 29, 2020, did not get tested due to shortage of testing materials, unless they were healthcare workers, considered at-risk or hospitalized. However, symptomatic patients who visited the HUG COVID-19 testing center without fulfilling testing criteria were entered in the database as "suspected cases". Some of these patients later received a test as policy evolved on March 30, 2020. For each positive or suspect case, a series of surveys is filled using REDCap platform.

Depending on the needs, follow-up calls are performed either by a professional nurse, a medical student or a contact tracer with supervision from a medical doctor. Findings are documented in the database. 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. All SARS-CoV-2 positive patients in Geneva who require hospitalization at HUG received follow-up calls by the HUG team at the time of discharge from the hospital. COVID-19 positive patients identified as nursing home residents or who are hospitalized at the time of diagnosis are not systematically called since they already receive medical attention and isolation measures are enforced by the medical staff. During the second wave, which started in late September 2020, the incidence of SARS-CoV-2 positive patients became so high that the GDH team could not contact everyone in time. A semi-automatic process was put in place. Positive patients and their declared contacts received an invitation to an online survey where they filled basic information. Only then and when the workload allowed it, they received a phone call from the GDH team to complete the data already provided. At the peak of the second wave, not all SARS-CoV-2 positive patients could be contacted. Follow-up calls as well as calls to close contacts were also temporarily abandoned. Finally, the Geneva Cantonal Population Office are required to declare COVID-19 related deaths, which are also recorded in ARGOS. Patients or the public were not involved in research.

What is being measured?

An overview of collected data is provided in Table 1. The surveys were created by the GDH and HUG medical task forces. Within the first 48h of testing, patients with a

positive test result for COVID-19 receive a call by a professional nurse or a trained contact tracer with support from a medical doctor if needed. During this call, demographic data are collected (13), as well as symptoms (14–17), clinical and environmental risk factors, and clinical red flags. A special attention is paid to psychosocial and cultural factors, and resources are provided when needed. The clinical evaluation is used to identify patients who need immediate emergency care, or to address them for follow-up care by their general practitioner, by one of Geneva's medical centers, or by the GDH-HUG team via telemedicine, which is recorded in the database as well. Patients' declared symptoms are recorded in subsequent surveys. Patients' self-reported compliance to isolation measures are also recorded. As of April 27, 2020, close contacts of index cases are individually contacted and basic information is recorded. Demographics, the type of contact they had with the index case, vaccine information, the presence of COVID-19 symptoms and their compliance to quarantine measures are also recorded at first call and during follow-up calls. Since July 6, 2020, the FOPH has established an evolving red list of countries where incidence rate is considered high or with variant of concern. Travelers who stayed in one of these countries have to quarantine for 10 days at their arrival in Switzerland. People staying in Geneva must self-declare upon arrival and fill an online survey containing basic information which data is also part of ARGOS. Depending of the work load, travelers are called by contact tracers during their quarantine period. Self-reported compliance to quarantine measures and the presence of symptoms are recorded during these calls.

Findings to date

On June 1st, 2021, of all 360'525 patients recorded in the ARGOS database, 65'475 had at least one positive test result, 294'723 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. During the same period, 655527 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%. 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. Of these patients, 37.6% have only a first contact, 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). The cohort shows a slight female predominance, with women representing 50.2% to 55.9% of all patients depending on the defined period (Table 2). More than 60 percent of all recorded patients have no risk factor for a poor clinical outcome(18). The context of infection recorded for COVID19 positive patients since June 2020 indicates that infection mostly occurs at home, at work or via the educational system. Around 23.2% of the patient reported having no idea of their contamination context. Information about 114'690 close contacts of positive patients has been registered, and 639'153 days of quarantine have been notified. 9'551 close contacts of a positive COVID19 case had a positive test result during their quarantine. Given that the standard duration of a quarantine is 10 days, we can estimate that around 15% of the persons in quarantine after being in contact with a

positive COVID19 case received a positive test result during their quarantine (see table 2).

273'189 days of quarantine concerning 27920 persons were ordered for persons coming back from a country at risk. These country were in order of importance Spain (19.4%), France (14.8%), Kosovo (7.6%), United States (7.0%), United Kingdom (7.0%), Portugal (6.2%) and Brazil (4.2%). 96 persons received a positive test result during their quarantine, among which 26 came back from Kosovo, 11 from France and 10 from Spain, the total of these infection occurring in 0.35% of the quarantines.

To mitigate confounding effects and improve data analysis and interpretation, we present the data according to four periods (see Figure 1).

February 26 to April 27, 2020 (first phase)

The first phase starts on February 26, 2020, when the first case was tested positive for SARS-CoV-2 in the Geneva area. The Swiss authorities implemented lockdown measures which remained moderate in comparison with many other countries (19). This first phase ends on April 27, 2020, when some of the measures started to be lifted following the decreasing incidence of new cases and hospitalizations. During this first wave, contact tracing was not implemented. Between March 13 and March 29, 2020, symptomatic individuals did not get tested due to shortage of testing materials, unless they were healthcare workers, considered at-risk or hospitalized. The percentage of healthcare professionals among positive cases was significantly higher during this phase (15.6%) and the percentage of patients declaring no risk factors was smaller

(32.4%) when compared to the other phases. The positivity (i.e. the ratio between positive tests results and the total amount of test performed) was of 23%.

April 28 to September 24, 2020 (second phase)

Between May and the end of September, 2020, incidence of SARS-CoV-2 positive cases remained low. Nearly all restrictions were lifted at the end of June. Nightclubs were closed again at the end of July after a surge of incidence mostly amongst Geneva youth, as can be seen by the relative higher incidence of the 20-39 year age category compared to the others during this period (Figure 2). 14.1% of the positive tests during this period were stemming from screening campaigns and more than 70% of cases reported no risk factor. The positivity was only 4.6% during this period.

September 24, 2020 to February 28, 2021 (third phase)

A second wave of SARS-CoV-2 positive cases hit Geneva in late September, 2020, at the same time as in the neighboring countries. New restrictions were imposed mid-October but no real lockdown was enacted. The peak lasted about 8 weeks. Due to political and economic pressure, some restrictions measures were lifted long before incidence reached low level. The number of SARS-CoV-2 positive cases in Geneva area remained significant during several months. During February 2021, the B.1.1.7 variant completely replaced SARS-CoV-2 wild type . At the same time, federal and local policies evolved and testing among symptomatic children over 5 years old was newly encouraged. Concurrently with these changes, the incidence of the 0-19 year age population almost doubled to reach those of the older age categories (19–21). The positivity during this period was 15.9%.

As of February 8th, 2021, quarantine measures for close contacts were lifted after 7 days if the person tested negative for SARS-CoV-2. Concurrently, the percentage of close contacts tested positive increased (see table 2). Considering vaccination program, the first dose of vaccine in Geneva was given to an elderly patient the 28th December 2020. At first, only residents over 74 years old and patients with risk factors received vaccination. The decline of the incidence for people of the corresponding age category compared to the others can be observed since February 2021 in figure 2.

March 1st to 1st June, 2021 (fourth phase)

On March 1st, access to vaccination continued to broaden. Resident over 65 years were allowed to be vaccinated since March 17, 2021, followed by the 45-65 year old residents starting at April 12, 2021. By 19 May, 2021, all Geneva residents over 15 years old were eligible to get vaccinated. The incidence COVID among the 65-79 year old population started to decline by end of March (figure 2), followed by a rapid decline of the incidence overall by mid-May. The amount of screening tests increased, as 21% of the positive tests were performed during a screening campaign. The positivity decreased to 5.2% during this period.

Discussion

COVID-19 represents a major challenge to each country's healthcare system. Collaboration between healthcare providers and public health authorities is particularly important in order to improve both our understanding of the disease and our response(22–24). The publication of the ARGOS cohort underscores our willingness to share data for research purposes. Indeed, data from this registry has already been used

to investigate symptoms and long COVID (25), infection fatality rate (9), and re-infection rates (26), as well as viral load kinetics (27). Several projects using these data to develop more accurate mathematical models to estimate transmission chains are also ongoing.

Furthermore, analysis from the ARGOS database illustrates the impact of various testing policies on the proportion of risk factors or age groups identified among confirmed cases. The partition of data analysis and interpretation according to policy period confirms the variations within each group depending on the period of interest and could thus guide public health decisions.

Strength and limitations

The state of Geneva accounts for half a million residents and the local Directorate of Health ordered the recording of all COVID-19 positive cases since the beginning of the epidemic, according to recommendations from the Federal Office of Public Health. Due to this policy, the database's main strength consists of its large number of cases, representative of all diagnosed cases on a regional level primarily serving operational needs and not scientific purposes, with one main objective: assessing all cases. This cohort is also multicentric as it includes all tests performed in Geneva's hospitals (both public and private), private practices and medical centers. The fact that a very large proportion of all cases are assessed reduces the risk of biased data. Also, as data is recorded on the day of the call to the patient, recall bias is very low. Finally, the ARGOS[3] database is characterized by a high number of follow-ups.

Despite these strengths, ARGOS has been influenced by the testing policy and the results must be seen in light of these influences. First, individuals without risk factors for COVID-19 and those younger than 65 years old are underrepresented in the database during the testing restriction period. The shapes of the graphics in Figure 1 and 2 confirm the impact of this policy as there is a sudden decrease in number of cases after March 20, 2020, when restriction started. Other factors could have amplified this phenomenon such as less symptomatic forms of disease in younger people and children. Reasons to get tested have also evolved over the first months of the epidemic. For example, anosmia or ageusia became a testing criteria only in late April. Patients who presented with these isolated symptoms within the first two months of the epidemic could thus have been undertested. Seroprevalence study results confirm the underrepresentation of certain groups and the undertesting of the overall population (8).

Nevertheless, ARGOS has several limitations. First, measurement error due to lack of detail of some variables can be observed, since efficiency is prioritized over detail-oriented data collection. For instance, individuals' level of education is not recorded. Furthermore, fear of sanction could lead to underreporting of compliance to isolation and quarantine measures. However, compliance is assessed by asking the patient whether he is able to comply to measures and by offering solutions (e.g. online grocery shopping, or dog-walking by a third-party) if not. Secondly, misclassification also certainly occurs as symptoms and risk factors are self-reported. Moreover, recording of information in ARGOS is performed by a large and evolving team of professionals, including healthcare workers with various backgrounds, medical students, police recruits, or contact tracers with no particular medical and health knowledge. Due to the

crisis situation, training contents delivered to the GDH team often evolved, leading to a certain level of heterogeneity of phone interviews and a greater risk for misclassification of medical information. Thirdly, the patient information gathered is tailored to operational needs and growing scientific knowledge. For example, anosmia and ageusia were initially classified as general ENT symptoms, and were later detailed separately as they were recognized as frequent and specific manifestations of COVID-19 (28). Finally, during some periods of the pandemic, the GDH team was overworked and could not call not verify self-reported information for all positive cases. This resulted in missing and incomplete data.

In conclusion, ARGOS is a large, real-world registry of individuals tested for SARS-Cov2[1]. Unlike many other registries, it involves every tested individual and is not limited to hospitalized patients, thus providing a precious resource to assess the impact of public health policies and overall disease burden of COVID-19.

Collaboration

The publication of the ARGOS cohort underscores our willingness to share data for research purposes and for optimizing public health measures. Deidentified ARGOS data are available upon reasonable request, including a research protocol, using the following form: https://edc.hcuge.ch/surveys/?s=TLT9EHE93C .

Further details

Data sharing statement

The deidentified data underlying this article will be shared on reasonable request using the form (https://edc.hcuge.ch/surveys/?s=TLT9EHE93C)

Ethics approval

Research received the agreement of the Cantonal Ethic Committee of Geneva (CCER protocol 2020-01273).

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Conflicts of interest

The authors declare no conflict of interest.

Authors contribution

Each author contributed to this article, based on the criteria of the International Committee for Medical Journal Editors. Camille Genecand conceptualized, designed the article format, interpreted the data, and conducted the literature review. Denis Mongin conducted the data analysis and participated in its formulation and its interpretation in the text. Flora Koegler conceptualized and designed the article format, interpreted the data, and conducted the literature review. Dan Lebowitz participated to the article design and

reviewed it. Delphine Courvoisier designed the study's analytic strategy, reviewed the article, and revisited it critically. Simon Regard, Pierre Chopard, Marwène Grira, Elisabeth Delaporte, Mayssam Nehme, Olivia Braillard, Dominique Joubert, Idris Guessous, Jerome Stirnemann and Aglaé Tardin helped acquisition of data and reviewed the article's content critically.

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Test result	– Positive – Negative – COVID-19 suspected, no test performed – COVID-19 suspected, negative test result
Test type	– RT-PCR – Rapid antigen test
Reason for testing	– Acute symptoms consistent with COVID-19 – Screening, no symptoms – Screening in the workplace (no symptoms) – Screening based on Swisscovid notification (no symptoms) – Patient transfer between hospitals
Demographics	– Date of birth – Gender – Basic professional information – Personal and professional addresses – School information : o School address o Name of class and professor
Medical risk factors for COVID-19 negative outcome	– Cardiovascular disease – Hypertension – Obesity (based of calculated BMI) – Chronic respiratory disease – Chronic kidney disease – Cancer – Immunosuppression – Diabetes – Pregnancy – Smoking habits
Vaccination	– Number of doses – Dates of doses

Environmental risk factors	– Homelessness – Nursing home resident – Asylum seeker or other migrant living in a collective housing – Living in another type of collective housing – Economic insecurity
Possible context of infection	– In the family or living in the same household – In the workplace – At school – As a healthcare professional – During a public event – At a private party – In a night club – In a bar/ restaurant – During a spontaneous gathering (including between friends) – No idea
Symptoms	– Cough – Presence of sputum – Dyspnea – Fever (> 38C) – Chills – Headache – Fatigue – Arthralgia and/or myalgia – Sore throat – Rhinorrhea, nasal congestion – Anosmia or ageusia – Gastrointestinal symptoms – Skin rash – None
Factors likely to adversely influence the course of disease	– High anxiety level – Feeling of isolation – Difficulties in daily management
Red Flags	– New-onset or worsening dyspnea – Fever for more than 5 days, or worsening fever non responding to treatment – Deterioration of the general status – Worsening cough – Hemoptysis – Confusion

	– Gastrointestinal symptoms with dehydration – Moderate to severe chest pain
Positive patients' self-reported compliance to recommended isolation measures	– Full compliance – Partial compliance – Insufficient compliance
Timeline	– Date of symptom onset – Date of testing
Death	– Site (at home, nursing home, hospital) – Date

Contact tracing	– Number of close contacts per index case
	– Type of contact between index case and close contact:
	  – Living in the same household
	  – Intimate contact
	  – Professional
	  – Healthcare environnement
	  – Social interaction
	  – Recreational
	  – Schooling
	– Date of last contact between index case and close contact

Close contact information	– Demographics:
	  ○ Date of birth
	  ○ Gender
	  ○ Personnal and professional addresses
	– Vaccination information (number of doses, dates)
	– Environmental risk factors
	  ○ Homelessness
	  ○ Nursing home resident
	  ○ Asylum seeker or other migrant living in a collective housing
	  ○ Living in another type of collective housing
	  ○ Economic insecurity
	  ○ Healthcare professional
	– Presence of symptoms at first call and follow-up calls
	– Compliance to quarantine measures at first call and follow-up call
	– Quarantine period (dates of onset and end)
	– Tested positive during quarantine

Quarantine after travelling in a red list country	– Number of people in quarantine
	– Demographics:
	  ○ Date of birth
	  ○ Gender
	  ○ Personal address in Geneva / during stay
	– Red list country
	  ○ Name
	  ○ Date of departure
	– Vaccination (number of doses, dates)
	– Quarantine period (dates of onset and end)
	– Presence of symptoms at first call and follow-up calls
	– Compliance to quarantine measures at first call and follow-up call
	– Tested positive during quarantine

Table 1, Actionable Register of Geneva Out- and inpatients with SARS-CoV-2 (ARGOS) collected data

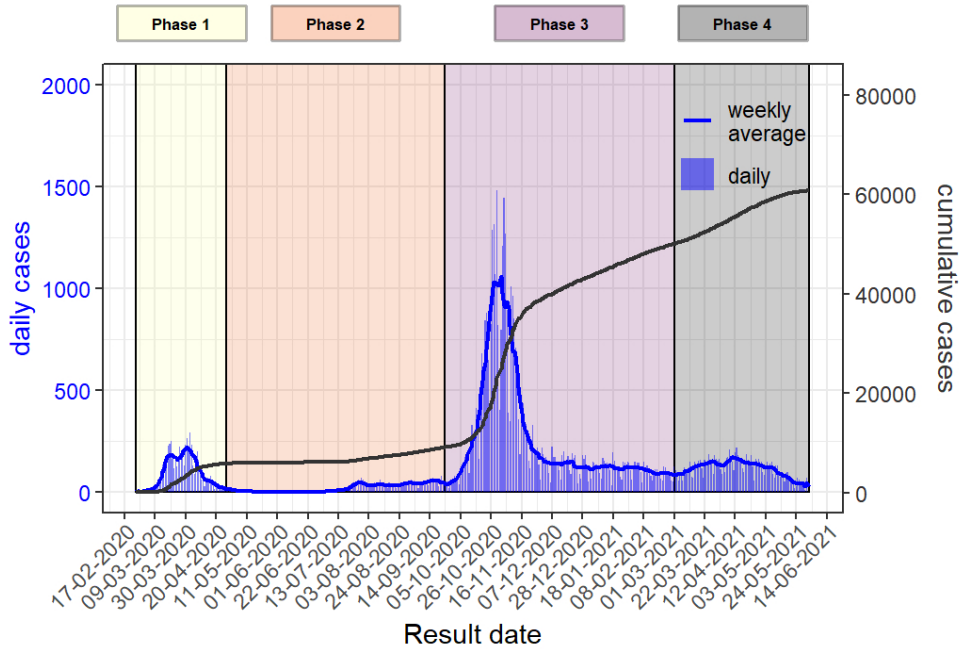
	Overall	2020-02-25 -> 2020-04-27	2020-04-27 -> 2020-09-24	2020-09-24 -> 2021-02-14	2021-02-14 ->2021-06-02
Number of positive patients					
n	60788	5782	3274	40882	10824
Living in Geneva	53344 (88.2)	4793 (84.4)	2827 (86.5)	35936 (88.3)	9775 (90.4)
Number of follow-up per patient recorded in ARGOS					
Not called	9514 (15.7)	1135 (19.6)	108 (3.3)	8128 (19.9)	131 (1.2)
First contact only	22847 (37.6)	3402 (58.8)	578 (17.7)	17541 (42.9)	1316 (12.2)
1 Follow-up call	6427 (10.6)	346 (6.0)	735 (22.4)	4387 (10.7)	959 (8.9)
2 follow-up calls	5178 (8.5)	152 (2.6)	683 (20.9)	2362 (5.8)	1977 (18.3)
3 or more follow-up calls	16822 (27.7)	747 (12.9)	1170 (35.7)	8464 (20.7)	6441 (59.5)
Age					
0-19	6997 (11.5)	175 (3.0)	364 (11.1)	4052 (9.9)	2406 (22.2)
20-39	21080 (34.7)	1690 (29.2)	1558 (47.7)	14356 (35.1)	3473 (32.1)

40-64	23879 (39.3)	2567 (44.4)	1101 (33.7)	16007 (39.2)	4202 (38.8)
65-80	5046 (8.3)	676 (11.7)	138 (4.2)	3693 (9.0)	539 (5.0)
>80	3750 (6.2)	674 (11.7)	108 (3.3)	2769 (6.8)	199 (1.8)
Gender					
Male	28314 (46.6)	2549 (44.1)	1628 (49.8)	18890 (46.2)	5238 (48.4)
Female	32433 (53.4)	3233 (55.9)	1643 (50.2)	21972 (53.8)	5574 (51.5)
Non binary	22 (0.0)	0 (0.0)	1 (0.0)	8 (0.0)	12 (0.1)
Comorbidities and risk factors					
Cardiovascular disease	1835 (3.0)	396 (6.8)	95 (2.9)	1103 (2.7)	241 (2.2)
Hypertension	4469 (7.4)	600 (10.4)	196 (6.0)	2968 (7.3)	705 (6.5)
Diabetes	1975 (3.2)	273 (4.7)	95 (2.9)	1295 (3.2)	312 (2.9)
Chronic respiratory illness	2170 (3.6)	512 (8.9)	83 (2.5)	1269 (3.1)	306 (2.8)
kidney	229 (0.4)	N/A	N/A	186 (0.5)	43 (0.4)
Cancer	545 (0.9)	73 (1.3)	28 (0.9)	349 (0.9)	95 (0.9)
Immunosupression	600 (1.0)	192 (3.3)	30 (0.9)	301 (0.7)	77 (0.7)
obesity	1081 (1.8)	N/A	N/A	778 (1.9)	303 (2.8)
Age 65 and older	8796 (14.5)	1350 (23.3)	246 (7.5)	6462 (15.8)	738 (6.8)
No risk factor	36905 (60.8)	1868 (32.4)	2523 (77.1)	24093 (59.0)	8419 (77.8)
Missing information	8698 (14.3)	1854 (32.1)	209 (6.4)	6221 (15.2)	411 (3.8)
Other potential risks					
Chronic disease	787 (1.3)	56 (1.0)	28 (0.9)	550 (1.3)	152 (1.4)
smoking	4659 (7.7)	N/A	N/A	3345 (8.2)	1313 (12.1)
pregnancy	533 (0.9)	41 (0.7)	24 (0.7)	352 (0.9)	116 (1.1)
Other risk	4284 (7.0)	107 (1.9)	364 (11.1)	2741 (6.7)	1072 (9.9)
Self reported symptoms					
Missing information	12735 (21.0)	2632 (45.5)	264 (8.1)	9217 (23.3)	604 (5.0)
no symptoms ever declared	3893 (6.4)	254 (4.4)	416 (12.7)	1807 (4.6)	1413 (11.6)
At least one symptom	44159 (72.6)	2896 (50.1)	2594 (79.2)	28516 (72.1)	10148 (83.4)
Possible context of infection					
family	17266 (28.4)	N/A	511 (15.6)	11861 (29.0)	4889 (45.2)
work	8535 (14.0)	N/A	304 (9.3)	6588 (16.1)	1639 (15.1)
school	3302 (5.4)	N/A	0 (0.0)	2200 (5.4)	1101 (10.2)
Health care worker	894 (1.5)	N/A	17 (0.5)	808 (2.0)	67 (0.6)

Public event	204 (0.3)	N/A	22 (0.7)	138 (0.3)	44 (0.4)
private_party	1372 (2.3)	N/A	184 (5.6)	933 (2.3)	255 (2.4)
club	70 (0.1)	N/A	24 (0.7)	41 (0.1)	5 (0.0)
restaurant	1346 (2.2)	N/A	161 (4.9)	1125 (2.8)	60 (0.6)
Spontaneous gathering	2527 (4.2)	N/A	81 (2.5)	1718 (4.2)	728 (6.7)
No idea	14090 (23.2)	N/A	410 (12.5)	10451 (25.6)	3222 (29.8)
Other	4921 (8.1)	N/A	488 (14.9)	3574 (8.7)	858 (7.9)
Missing information	16520 (27.2)	5775 (100)	1356 (41.4)	8885 (21.7)	486 (4.5)
Profession					
health care professional	4503 (7.4)	902 (15.6)	175 (5.3)	2973 (7.3)	452 (4.2)
Environmental risk factor					
Homelessness	135 (0.2)	15 (0.3)	6 (0.2)	102 (0.2)	12 (0.1)
Nursing home resident	1895 (3.1)	377 (6.5)	63 (1.9)	1403 (3.4)	49 (0.5)
Asylum seeker or other migrant living in a collective home	267 (0.4)	25 (0.4)	2 (0.1)	172 (0.4)	68 (0.6)
Collective home resident (other than migrant)	627 (1.0)	34 (0.6)	31 (0.9)	431 (1.1)	131 (1.2)
Reason for testing					
Acute symptoms	45321 (88.0)	5633 (99.9)	2693 (85.9)	28785 (89.2)	8204 (78.8)
Testing					
Total number of tests performed	655527	28931	80342	291510	254744
PCR	584573 (89.2)	28879 (99.8)	80339 (100.0)	263182 (90.3)	212173 (83.3)
Number of patient tested	360525	25853	71269	210598	169164
Positivity rate	9.4	21.0	4.1	14.3	4.3
deaths					
Deaths number	747	280	20	421	22
Age	87.1 [80.2, 91.5]	86.3 [79.4, 91.3]	89.2 [85.8, 93.3]	87.7 [81.4, 91.8]	83.6 [70.5, 90.3]
Gender	354 (47.4)	130 (46.4)	10 (50.0)	200 (47.7)	11 (45.8)
Contact tracing					

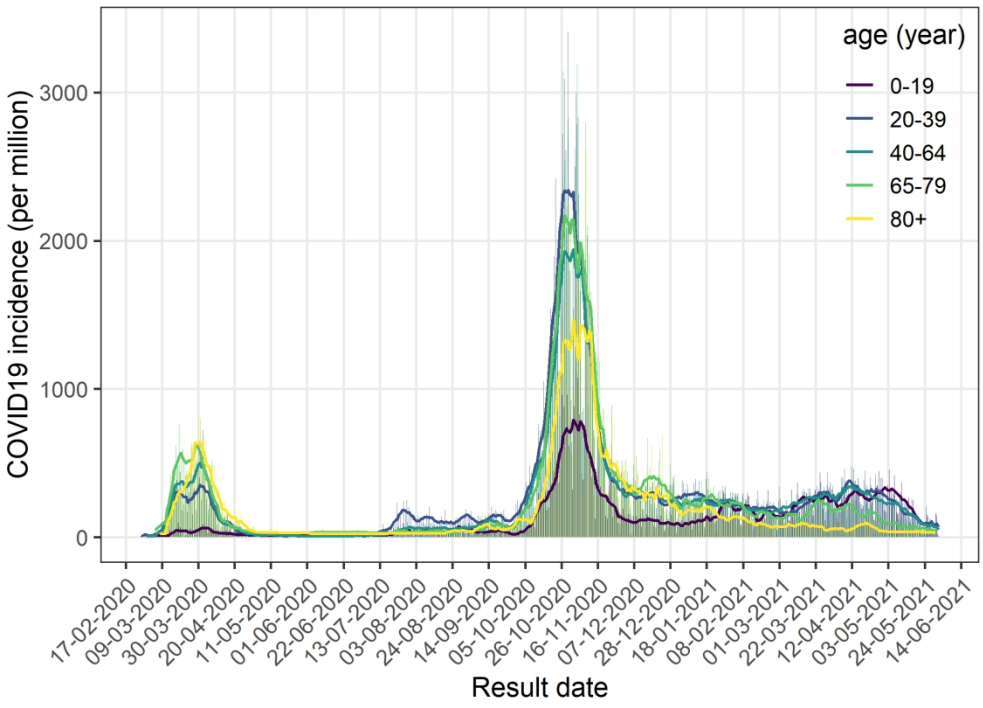
Number total of contact	114690	118	12420	77990	24162
Number of contact per index patient	3 [1, 6]	0 [0, 0]	7 [4, 11]	3 [1, 6]	3 [2, 5]
Quarantine after contact with positive					
Number of days	639153	N/A	31615	445468	162003
Number of infection during quarantine	9551	N/A	333	6009	3209
Pourcentage of quarantine leading to infection	14.94	N/A	10.53	13.49	19.81
Quarantine after traveling					
Number of days	273189	N/A	85490	121202	66429
Number of infection during quarantine	96	N/A	29	42	25
Pourcentage of quarantine leading to infection	0.35	N/A	0.34	0.35	0.38

Table 2, ARGOS baseline characteristics of positive patients, Geneva, February 26 ,2020 – June 1st, 2021. Periods are presented by grouping together the first wave of cases, the period between the two waves, the second wave and the following period of sustained epidemic activity, and finally the more recent period following the start of the vaccination campaign.



Epidemic Curve of the cases of Coronavirus Disease 2019 (COVID-19) in Geneva state, February 26 ,2020 – June 1st, 2021. Vertical bars represent the daily cases (based on the date of the test result), solid blue line represents the weekly moving average and the solid black line the cumulative cases.

89x64mm (300 x 300 DPI)



Incidence per age category, Geneva, February 26 ,2020 – June 1st, 2021. Vertical bars represent the daily incidence, solid line represent the weekly moving average.

89x64mm (600 x 600 DPI)

Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cohortreporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	#3	State specific objectives, including any prespecified hypotheses	5-6
Methods			

Study design	#4	Present key elements of study design early in the paper	6
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	7-8
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-9, table 1
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	7-9
Bias	#9	Describe any efforts to address potential sources of bias	14-16
Study size	#10	Explain how the study size was arrived at	9-10
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	n/a
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	Along text
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	n/a
Statistical methods	#12c	Explain how missing data were addressed	15
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	n/a
Statistical methods	#12e	Describe any sensitivity analyses	n/a

Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	9
Participants	#13b	Give reasons for non-participation at each stage	9, table 2
Participants	#13c	Consider use of a flow diagram	n/a
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	9-13, table 2, figure 2
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	Table 2
Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)	9-13, figure 1
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	9-13
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-13, table 2
Main results	#16b	Report category boundaries when continuous variables were categorized	n/a
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	#18	Summarise key results with reference to study objectives	13-14

Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	14-15
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	15-16
Generalisability	#21	Discuss the generalisability (external validity) of the study results	15-16
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

Notes:

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