StopCOVID cohort: An observational study of 3,480 patients admitted to the Sechenov University hospital network in Moscow city for suspected COVID-19 infection

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Summary

Age, male sex, and chronic comorbidities are associated with higher in-hospital mortality. The combination of clinical features may be sufficient to diagnose COVID-19 infection indicating that laboratory testing is not critical in real-life clinical practice.

ABSTRACT

Background: The epidemiology, clinical course, and outcomes of COVID-19 patients in the Russian population are unknown. Information on the differences between laboratory-confirmed and clinically-diagnosed COVID-19 in real-life settings is lacking.

Methods: We extracted data from the medical records of adult patients who were consecutively admitted for suspected COVID-19 infection in Moscow, between April 8 and May 28, 2020.

Results: Of the 4261 patients hospitalised for suspected COVID-19, outcomes were available for 3480 patients (median age 56 years (interquartile range 45-66). The commonest comorbidities were hypertension, obesity, chronic cardiac disease and diabetes.

Half of the patients (n=1728) had a positive RT-PCR while 1748 were negative on RT-PCR but had clinical symptoms and characteristic CT signs suggestive of COVID-19 infection.

No significant differences in frequency of symptoms, laboratory test results and risk factors for in-hospital mortality were found between those exclusively clinically diagnosed or with positive SARS-CoV-2 RT-PCR.

In a multivariable logistic regression model the following were associated with in-hospital mortality; older age (per 1 year increase) odds ratio [OR] 1.05 (95% confidence interval (CI) 1.03 - 1.06); male sex (OR 1.71, 1.24 - 2.37); chronic kidney disease (OR 2.99, 1.89 – 4.64); diabetes (OR 2.1, 1.46 - 2.99); chronic cardiac disease (OR 1.78, 1.24 - 2.57) and dementia (OR 2.73, 1.34 – 5.47).

Conclusions: Age, male sex, and chronic comorbidities were risk factors for in-hospital mortality. The combination of clinical features were sufficient to diagnoseCOVID-19 infection indicating that laboratory testing is not critical in real-life clinical practice.

INTRODUCTION

In Russia, the first confirmed cases of coronavirus disease 2019 (COVID-19) were reported by the state authorities in early March 2020 [1]. Since then the Russian Federation climbed into the top three nations in the world affected by COVID-19 surpassing 400 000 cases by the end of May 2020.

The rate of infections in Moscow and Moscow Metropolitan area, with its high population density and number of inhabitants (20 million), has exceeded 180 000 confirmed cases, accounting for half of all the COVID-19 cases in Russia [2].

The clinical characteristics of COVID-19 have been described in studies from China [3], Italy [4], United States [5-7] and United Kingdom [8]. At present no information on the clinical epidemiology, including clinical course, and outcomes of COVID-19 patients in the Russian population are available. A recent editorial in the Lancet highlighted a surprisingly low mortality rate (around one percent) in Russia [9]. With no academic data, perspectives on the COVID-19 pandemic in Russia are mainly based on media reports and briefs from Russian officials.

This study aimed to present demographic characteristics, symptoms, comorbidities, clinical test results, outcomes and risk factors associated with mortality in a cohort of consecutively admitted patients with COVID-19 at the Sechenov University hospital network in Moscow. Secondarily, we aimed to test whether patients presenting with symptoms and radiological findings consistent with COVID-19 but without laboratory confirmation of SARS-CoV-2 have similar outcomes to those with positive RT-PCR.

METHODS

Study design and ethics

StopCOVID is an observational cohort study which took place at four large adult tertiary university hospitals in Moscow, Russia. All people aged ≥18 years admitted to any of four Sechenov University hospital network hospitals between 8th April and 28th May 2020 with suspected COVID-19 infection (**Supplementary Box 1**) were included in the study. Reverse transcriptase-polymerase chain reaction (RT-PCR) to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was the recommended mode of testing by the Russian ministry of health and was used throughout the study period in all the hospitals. We enrolled all patients with confirmed or suspected COVID-19 infection, due to concerns of a high false-negative rate from RT-PCR results [10].

This study was approved by the Sechenov University institutional review board on the 22nd of April 2020 (protocol number 08-20).

Data collection process

The data were collected between 22nd April and 6th June 2020. We reviewed electronic medical records for signs and symptoms on admission, baseline comorbidities, computer tomography (CT) imaging and laboratory results for all admitted patients. Weight and height were self-reported by the patients to the clinical staff.

The data extraction was performed by a group of 40 medical students and resident doctors who went through personal protocol explanation webinars and data entry training prior to the beginning of the study. The team was supervised by senior academic staff members. The baseline characteristics were collected using the case report form (CRF) that was developed by the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) and World Health Organisation (WHO) for use in outbreak investigations [11]. REDCap (Research Electronic Data Capture, Vanderbilt University, US, hosted at Sechenov University) was used for data collection, storage and management [12, 13].

Study definitions

Patients were defined as confirmed COVID-19 if the diagnosis was confirmed by laboratory testing (at least one SARS-CoV-2 RT-PCR positive result).

Patients were defined as 'clinically diagnosed COVID-19' if laboratory confirmation was inconclusive or not available. Details of COVID-19 case definitions, criteria for hospitalisation, grading of severity and recommended treatment approaches are presented in **Supplementary Box 1**.

We reviewed radiology reports of chest CT imaging during hospitalisation. The data on the presence/absence of ground-glass opacities, consolidation, and degree of radiologic changes severity were retrieved. Incomplete reports containing no information on severity were excluded from the analysis. The severity of changes was graded by radiologists as per national COVID-19 guidelines using the modified visual assessment scale by Inui et al [14]. (**Supplementary Table 1**).

The primary outcome in this study was in-hospital mortality.

Statistics

Descriptive statistics were calculated for baseline characteristics. Continuous variables were summarised as median (interquartile range) and categorical variables as frequency (percentage). The chi-squared test or Fisher's exact test was used for testing differences in proportions between individuals. The Wilcoxon rank-sum test was used to test for differences in laboratory test results between the groups.

We first ran univariate analysis to investigate associations between demographic characteristics and comorbidities with mortality. Then we performed multivariable logistic regression model, which included all statistically significant (at P=0.001) potential predictors from the univariate analysis.

A Bonferroni correction was used to adjust for multiple comparisons, such that p values ≤0.001 were considered statistically significant for the analysis of symptoms and comorbidities and p values <0.001 were considered statistically significant for laboratory markers. All routine clinical laboratory measurements were used in the analysis, unless the sample size in the group who died was less than ten individuals.

Statistical analysis was performed using R version 3.5.1.

RESULTS

A total of 4261 adults with suspected COVID-19 infection were admitted to the hospitals. Primary outcome data were available for 3535 patients who were discharged, died or transferred to another hospital. The study primary end point was available for all but 55 individuals transferred to other hospitals, thus 3480 (82%) individuals were included in the statistical analysis.

Half of the patients (n=1728) had positive results of RT-PCR while the second half (n=1748) were negative on RT-PCR but had clinical symptoms and CT signs suggestive of COVID-19. No differences were noted in the baseline demographic, clinical characteristics, laboratory and radiologic findings of those with RT-PCR-confirmed vs clinically diagnosed COVID-19 (**Table 4 and supplementary tables 2, 4, 5, 6, 7**).

Baseline characteristics

Table 1 and Supplementary Table 2 presents an overview of baseline characteristics, stratified by the primary outcome. The median age of all patients at admission was 56 years (interquartile range [IQR] 45-66, range 18-100). Similar numbers of men (50.5%, n=1758) and women (49.5%, n=1722) were admitted to the hospitals (p=0.55). Median age of patients who died in the hospital was higher, 72 years (61.5-81) than 55 years (44-65) in survivors. Time from hospitalisation to discharge/death was 14.5 (11.8-17.7) days, with shorter hospital stay in patients who died. Severity at admission was recorded as mild in 632 (18.2%), moderate in 2634 (75.7%), severe in 204 (5.9%) and critical in 7 (0.2%) of patients, respectively.

Only 218 (6.3%) patients required admission and/or transfer to the ICU, with some patients requiring non-invasive ventilation and/or invasive mechanical ventilation 80 (2.3%) and 171 (5.0%), respectively. Although the proportion discharged alive from the ICU facilities was 42.5%, among all patients who received care in the ICU during the hospital stay 57 (26.1%) were discharged from the hospital alive. Eight (4.7%) patients who received invasive mechanical ventilation during the hospital stay were discharged alive.

Data on symptoms and comorbidities at the time of hospital admission were available in 3382 (97%) patients. The most common symptoms in the medical records were fever (3157, 93.3%), fatigue/malaise (2684, 79.4%), cough (2476, 73.2%) and shortness of breath (2013, 59.5%). We also found a significant overlap between the top three most common symptoms, with 1912 (56.5%) patients having all three (**Figure 1**). Shortness of breath, altered consciousness and inability to walk were present significantly more often in patients who died, while anosmia, sore throat, fever and muscle pain were found more frequently in those discharged alive (**Supplementary Table 3**). Symptoms at admission did not differ significantly between the patients with laboratory-confirmed and clinically diagnosed COVID-19 (**Supplementary Table 4**).

Detailed information on comorbidities in our cohort is presented in **Table 2, Supplementary Table 5** and **Figure 1**. The most common comorbidities were hypertension (1539, 45.5%), obesity (1129, 33.4%), chronic cardiac disease (621, 18.4%) and diabetes (predominantly type 2) (459, 13.6%). One in ten patients reported current (139, 4.1%) or former (235, 6.9%) smoking. There was little overlap between top three most common comorbidities, with only 145 (4%) patients having all three, while 965 (28.5%) did not report any comorbidities.

Clinical investigations

Most patients (71.6%) had significant changes on chest CT, equivalent to CT-2 - CT-3 severity grade. Ground-glass opacity was found in over 95% of the patients and 77.95% had lung consolidation in accordance with the radiologist reports .

We reviewed routine clinical test measurements at admission and found abnormal changes to the coagulation profile, greater median levels of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), aspartate aminotransferase (AST) and lactate dehydrogenase, and decreased iron levels. Those patients who died in the hospital had more abnormal changes to their coagulation profile (D-dimer, international normalised ratio, prothrombin time, ferritin, fibrinogen), lymphocytopenia, neutrophilia, much higher levels of CRP and ESR, high blood urea nitrogen, AST, gamma-glutamyltransferase when compared with survivors (**Table 3**). Platelet to lymphocyte ratio was associated with higher in-hospital mortality odds ratio 1.003 (95% confidence interval 1.002 to 1.004) adjusted for age and sex.

Results of the laboratory tests routinely performed in the clinical setting did not differ significantly between confirmed and clinically diagnosed COVID-19 patients for 48 out of 51 parameters (**Table 4**). Platelets, leukocytes, and neutrophil count were significantly lower in confirmed COVID-19 patients, but the differences were unlikely to be relevant, being within the normal reference ranges for both groups.

Patient outcomes and risk factors

Among the 3480 patients who were discharged or died during hospitalisation, the overall mortality was 5.5% with a total number of 191 people dying.

In a univariate analysis chronic cardiac disease, hypertension, chronic pulmonary disease, chronic kidney disease, chronic neurological disorder, malignant neoplasm, diabetes and dementia significantly differed between survivors and patients who died(**Table 2**). In multivariable analysis, older age was a predictor of in-hospital mortality with an odds ratio (per 1-year increase) of 1.05 (95% confidence interval 1.03 to 1.06). Other predictors associated with in-hospital mortality were male sex (1.71, 1.24 to 2.37), chronic kidney disease (2.99, 1.89 to 4.64), diabetes (2.1, 1.46 to 2.99), chronic cardiac disease (1.78, 1.24 to 2.57) and dementia (2.73, 1.34 to 5.47) (**Figure 2**). The same risk factors were significantly associated with the admission/transfer to the ICU with dementia only not reaching statistical significance (**Supplementary Figure 1**).

When including COVID-19 laboratory confirmed/suspected status as a covariate in the multivariable logistic regression model we found no evidence that is was associated with mortality (odds ratio 1.22, 0.89 to 1.69) and it did not have major impact on the effect size and significance of other predictors (**Supplementary Figure 2**).

We did not find any statistically significant association of CT severity grade with in-hospital mortality, adjusting for age and sex (**Supplementary Table 6**). With respect to CT imaging, no evidence of differences was found between the patients with confirmed and clinically diagnosed COVID-19 (**Supplementary Table 7**).

Treatment

Hydroxychloroquine was the most frequently used (84%) medication, followed by antibiotics (azithromycin (77.7%) and ceftriaxone (30.3%)), heparin 56.4%, paracetamol (34.4%), mucolytics (25.4%), lopinavir/ritonavir (16.2%) and systemic corticosteroids (10.4%), respectively (**Supplementary Table 8**). There was a significant overlap between top three most commonly used medications, with hydroxychloroquine, azithromycin and heparin used in 1322 patients (**Supplementary Figure 3**).

DISCUSSION

To our knowledge, StopCOVID cohort is the first large scale study of consecutively hospitalised patients with COVID-19 in Russia assessing clinical characteristics and risk factors for in-hospital mortality. This is also the first large cohort, including both RT-PCR confirmed COVID-19 cases and patients, diagnosed with COVID-19 based on clinical and radiological presentation in the absence of the SARS-CoV-2 RT-PCR confirmation. We found that older age and male sex as well as existing comorbidities were associated with in-hospital mortality. We found no significant difference between patients with clinical COVID-19 and laboratory-confirmed COVID-19, either in clinical presentation, or in clinical measurements and risk factors of in-hospital mortality. We feel it is entirely appropriate to treat patients with clinical and radiological signs of COVID-19 who do not have an alternative diagnosis to explain their symptoms equivalently to PCR-confirmed cases. Sequential RT-PCR testing can identify patients with COVID-19 whose initial result was a false-negative [15]. In settings where repeat testing is not performed, it can also be appropriate to include patients with clinical and radiological COVID-19 alongside those with laboratory-confirmed disease.

Patients in our study were of a very similar age to the New York cohort [6] and of a much lower median age than similar cohorts in Italy [4] and UK [8]. This may be partly explained by a lack of a clear message from the authorities to the public with regards to whom should present to hospital. Healthcare-seeking behavior may further explain a younger age at admission which differs between the countries. Russian people are known for active specialist-seeking behavior [16], particularly in the presence of distrust of media sources [17] and easy access to free healthcare. It is however more likely to be a reflection of varying approaches from health services in different countries.

Patients in Moscow typically presented with fever, fatigue, cough and shortness of breath, which is in agreement with the previously reported symptom patterns in other countries [5, 8, 18]. Among symptoms, anosmia was associated with a more favourable outcome, which is similar with the data from Hopkins and co-authors [19] showing rapid improvement in COVID-19 patients presenting with a loss of smell.

Similar to other cohorts, cardiological conditions, hypertension, obesity and diabetes were common problems in the hospitalised population. Lower median age of the patients in our cohort may explain lower comorbidity rate when compared to some other studies [6, 8]. We recorded a much lower number of patients with chronic pulmonary diseases, which is in agreement with data from Richardson et al [7] but in contrast to other US [6] and particularly UK [8] cohorts. We also found low rates of asthma in our cohort not exceeding the prevalence in the general population which has been reported previously [20].

Patient age, male sex and major comorbidities were all predictors of in-hospital mortality. These findings are in line with other international cohorts [6, 21], including a UK ISARIC study using a similar data collection protocol [8]. We also found common changes to the coagulation profile [6] and previously reported clinical patterns, such as lymphocytopenia, neutrophilia and very high levels of CRP and ESR in patients who subsequently died from COVID-19. Platelet to lymphocyte ratio has been previously reported to be associated with higher severity and mortality in COVID-19 patients [22]. Our findings agree with previous research but require further validation.

The proportion of patients admitted to ICU in our cohort study was much lower than in the similar cohorts from the UK (17%) [8] and US (14.2%) [7], but similar to published data from China [18]. Decision for ICU admission within the Sechenov University hospitals network is normally based on a joint opinion of a multidisciplinary team of respiratory physicians and intensivists. Due to good access to high-flow oxygen and non-invasive ventilation within the COVID-19 wards , only critical patients were transferred into ICU, which may explain a lower need for ICU admission in our cohort. Active use of non-invasive ventilation on the wards may explain low in-hospital mortality in this group of patients. As only the most severely unwell patients were admitted for invasive mechanical ventilation, this may explain the high mortality recorded in ICU patients. Overall mortality rate in our cohort was similar to the average worldwide estimate [23] but much lower than in other international cohorts of hospitalised individuals, which may be a direct reflection of their much younger age and moderate state of disease at the time of admission in most of the patients.

Half of the patients admitted to the Sechenov University hospital network did not have positive RT-PCR test result, despite having clinical features of COVID-19 infection. Our findings are similar to the US data, with 42 [5] to 51.8 [6] % of individuals having negative RT-PCR test result. The false-negative rate of the RT-PCR tests, varies between 20 and 66%, depending on the day since symptom onset [10] meaning that results must be cautiously interpreted [24] and represent a major concern by compromising control of the pandemic [25]. Previous research suggests that negative RT- PCR test result does not exclude the possibility of COVID- 19. Repeated testing and sampling was shown to improve the sensitivity of RT-PCR [15]. To our knowledge, previous studies of COVID-19 patients excluded those with suspected COVID-19 infection in the absence of the positive test result [3-8]. However, this approach differs from pragmatic clinical practice, in which, in the absence of an alternative diagnosis, patients with a clinical diagnosis of COVID-19 are treated equally to laboratory-confirmed cases. When evaluating radiological findings in COVID-19, it must be born in mind that some patients may present with clinical symptoms or extrapulmonary manifestations such as hepatic, cardiac or kidney injury but initially will

have normal CT findings [26]. In our study we did not solely rely on CT findings for clinical diagnosis of COVID-19. However, new approaches to minimize the exclusion of patients with false-negative RT-PCR should be sought, as highlighted in a recent report suggesting real-time lung ultrasound as an auxiliary method to rule-in COVID-19 during screening [27].

Limitations

This cohort study has some limitations. First, the study population only included patients within Moscow. Second, the data were collected retrospectively from the electronic medical records with no access to additional information which could be potentially retrieved from the medical notes. Third, half of the patients in our cohort did not have RT-PCR confirmed COVID-19 infection, although this is unlikely to affect the outcomes as we failed to find any significant differences between clinically diagnosed and laboratory confirmed cases. Fourth, endpoint outcome data were available for 83% of admitted patients. Patients admitted and/or transferred to ICU and receiving invasive mechanical ventilation can spend a significant amount of time attached to the machine [7, 8]. The absence of data on patients (18%) who remained in the hospital at the time of data analysis completion may lead to bias and may influence overall mortality calculations. Fifth, morbidity related to invasive procedures or sequelae in clinically suspected and/or laboratory confirmed cases has not been recorded. Sixth, definition of "clinically diagnosed COVID-19" implies changes on chest CT and nonspecific signs and symptoms, which may be present in other respiratory viral illnesses. The scoring system used for radiological signs, is able to differentiate between symptomatic and asymptomatic cases of COVID-19 but is not fully able to differentiate between COVID-19 from other similar conditions.

Conclusions

The clinical features, chest CT, and blood test results did not differ between test confirmed and clinically diagnosed patients. Furthermore, clinical outcomes were also identical. Our study results suggest that in order to assess the full impact of this pandemic on populations, all clinically diagnosed patients should be included. Comorbidities associated with death were similar to other published studies on COVID-19. Mortality in our cohort was low, which may have been due to the mean age of patients being lower than in some other published studies. Anosmia was associated with milder disease while asthma did not appear to pose an increased risk of adverse outcome. As with other studies manifestations of non-respiratory problems including coagulopathy, immune deficiency, hyper-inflammation and renal deficits were associated with higher risks of death. The data collection within StopCOVID cohort is continuing and further analysis focused on predictive models of adverse outcomes for routine clinical practice is in progress.

Author roles (CRediT)

DM, NAN, PB, DB, PG contributed equally to this manuscript.

Term	Definition	Authors
Conceptualisation	Ideas; formulation or evolution of overarching research goals and aims	Daniel Munblit, Denis Butnaru, Oleg Blyuss, Nikita Nekliudov, Polina Bugaeva
Methodology	Development or design of methodology; creation of models	Daniel Munblit, Denis Butnaru, Oleg Blyuss, Nikita Nekliudov, Polina Bugaeva, Emmanuelle A. Dankwa, Christiana Kartsonaki, Mark Pritchard
Software	Programming, software development; designing computer programs; implementation of the computer code and supporting algorithms; testing of existing code components	Oleg Blyuss
Validation	Verification, whether as a part of the activity or separate, of the overall replication/ reproducibility of results/experiments and other research outputs	Daniel Munblit, Oleg Blyuss
Formal analysis	Application of statistical, mathematical, computational, or other formal techniques to analyze or synthesize study data	Oleg Blyuss, Daniel Munblit, Nikita Nekliudov, Maria Kislova
Investigation	Conducting a research and investigation process, specifically performing the experiments, or data/evidence collection	The StopCOVID Research Team, Nikita Nekliudov, Polina Bugaeva, Maria Kislova, Ekaterina Listovskaia, Aysylu Gamirova, Anastasia Shikhaleva, Sergey Avdeev, Andrey Yavorovsky
Resources	Provision of study materials, reagents, materials, patients, laboratory samples, animals, instrumentation, computing resources, or other analysis tools	Vladimir Belyaev, Daniel Munblit, Denis Butnaru, Petr Timashev
Data Curation	Management activities to annotate (produce metadata), scrub data and maintain research data (including software code, where it is necessary for interpreting the data itself) for initial use and later reuse	Nikita Nekliudov, Polina Bugaeva, Maria Kislova, Daniel Munblit, Oleg Blyuss
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Writing - Review & Editing	Preparation, creation and/or presentation of the published work by those from the original research group, specifically critical review, commentary or revision – including pre-or postpublication stages	All authors
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Potential Conflicts of Interest

J.W. reports grants and personal fees from Danone/Nutricia and Airsonnet, non-financial support from Anaphylaxis Campaign, and lecture fees from Friesland Campina, outside the submitted work. All other authors have no potential conflicts to disclose.

REFERENCES

1. Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing. About confirmed case of the novel coronavirus infection COVID-2019 in Russia. Available at: https://www.rospotrebnadzor.ru/about/info/news/news_details.php?ELEMENT_ID=13870. Accessed 9-th of June.
2. The government of Russian Federation. Stopcoronavirus.rf - Official information about covid-19 in Russia. Available at: https://xn--80aesfpebagmfblc0a.xn--p1ai/. Accessed 10-th of June.
3. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet **2020**; 395(10229): 1054-62.
4. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA **2020**.
5. Argenziano MG, Bruce SL, Slater CL, et al. Characterization and clinical course of 1000 Patients with COVID-19 in New York: retrospective case series. medRxiv **2020**.
6. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. BMJ **2020**; 369: m1966.
7. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA **2020**.
8. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ **2020**; 369: m1985.
9. The L. Salient lessons from Russia's COVID-19 outbreak. Lancet **2020**; 395(10239): 1739.
10. Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J. Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction-Based SARS-CoV-2 Tests by Time Since Exposure. Ann Intern Med **2020**.
11. International Severe Acute Respiratory and Emerging Infection Consortium and World Health Organisation. Clinical Data Collection – The COVID-19 Case Report Forms (CRFs). Available at: https://isaric.tghn.org/COVID-19-CRF/. Accessed 22-nd of June.
12. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform **2009**; 42(2): 377-81.
13. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform **2019**; 95: 103208.
14. Inui S, Fujikawa A, Jitsu M, et al. Chest CT Findings in Cases from the Cruise Ship "Diamond Princess" with Coronavirus Disease 2019 (COVID-19). Radiology: Cardiothoracic Imaging **2020**; 2(2): e200110.
15. Zhang JJ, Cao YY, Dong X, et al. Distinct characteristics of COVID-19 patients with initial rRT-PCR-positive and rRT-PCR-negative results for SARS-CoV-2. Allergy **2020**.
16. IPSOS. Global Views on Healthcare in 2018. Available at: https://www.ipsos.com/sites/default/files/ct/news/documents/2018-07/Global%20Views%20on%20Healthcare%202018%20Graphic%20Report.pdf. Accessed 17-th of June.
17. Benisovich SV, King AC. Meaning and knowledge of health among older adult immigrants from Russia: a phenomenological study. Health Educ Res **2003**; 18(2): 135-44.
18. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med **2020**; 382(18): 1708-20.
19. Hopkins C, Surda P, Whitehead E, Kumar BN. Early recovery following new onset anosmia during the COVID-19 pandemic - an observational cohort study. J Otolaryngol Head Neck Surg **2020**; 49(1): 26.

20. Avdeev S, Moiseev S, Brovko M, et al. Low prevalence of bronchial asthma and chronic obstructive lung disease among intensive care unit patients with COVID-19. Allergy **2020**.
21. Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet **2020**; 395(10239): 1763-70.
22. Chan AS, Rout A. Use of Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios in COVID-19. J Clin Med Res **2020**; 12(7): 448-53.
23. World Health Organisation. Coronavirus disease 2019 (COVID-19) Situation Report – 46. Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200306-sitrep-46-covid-19.pdf?sfvrsn=96b04adf_4. Accessed 22-nd of June.
24. Tahamtan A, Ardebili A. Real-time RT-PCR in COVID-19 detection: issues affecting the results. Expert Rev Mol Diagn **2020**; 20(5): 453-4.
25. Woloshin S, Patel N, Kesselheim AS. False Negative Tests for SARS-CoV-2 Infection - Challenges and Implications. N Engl J Med **2020**.
26. Harmon SA, Sanford TH, Xu S, et al. Artificial intelligence for the detection of COVID-19 pneumonia on chest CT using multinational datasets. Nat Commun **2020**; 11(1): 4080.
27. Smallwood N, Walden A, Parulekar P, Dachsel M. Should point-of-care ultrasound become part of healthcare worker testing for COVID? Clin Med (Lond) **2020**; 20(5): 486-7.

Figure legends

Figure 1. Stacked bar charts presenting (a) top ten most common symptoms and (b) most common comorbidities. Venn plots presenting coexistence of (c) top three symptoms and (d) top three comorbidities at the time of hospital admission.

Figure 2. Odds ratios and 95% confidence intervals for in-hospital mortality from multivariable logistic regression model.

Table 1. Baseline characteristics of patients admitted to Sechenov University hospitals, stratified by outcome. *Proportion of patients in each subgroup is calculated from the total number of patients receiving a particular type of care (ICU, non-invasive ventilation and invasive mechanical ventilation). Calculations were performed for each type of care, regardless of whether patients were discharged/died within the ICU facilities or were transferred to the ward and were discharged/died there.

Variable	Total (n=3480)	Discharged alive (n=3289)	Died (n=191)
Age at admission, years			
Median, (interquartile range)	56 (45-66)	55 (44-65)	72 (61.5-81)
Age groups			
18-39	574 (16.5)	570 (17.3)	4 (2.1)
40-49	621 (17.8)	614 (18.7)	7 (3.7)
50-59	865 (24.9)	837 (25.4)	28 (14.7)
60-69	728 (20.9)	687 (20.9)	41 (21.5)
70-79	402 (11.6)	349 (10.6)	53 (27.7)
>=80	290 (8.3)	232 (7.1)	58 (30.4)
Male sex, n (%)	1758 (50.5)	1653 (50.3)	105 (55)
Temperature at admission, median (IQR), °C	37.4 (37-38)	37.5 (37-38)	37.7 (37-38)
ICU care during hospital stay, n (%)*	218 (6.3)	57 (26.1)	161 (73.9)
Invasive mechanical ventilation during hospital stay, n (%)*	171 (5.0)	8 (4.7)	163 (95.3)
Non-invasive ventilation during hospital stay, n (%)*	80 (2.3)	31 (38.8)	49 (61.2)
Time from hospitalisation to discharge/death, median (IQR), days	14.5 (11.8-17.7)	14.6 (12-17.7)	9.5 (5.4-15.5)
Number of RT-PCR covid positive patients, n (%)	1728 (49.7)	1618 (49.2)	110 (57.6)

Table 2. Patient-reported comorbidities at the time of hospital admission and chest computed tomography (CT) imaging stratified by outcome. Statistically significant results at p value ≤0.001 are presented in bold. *Obesity defined as BMI based on electronic medical records data and if data on height and weight was missing, records were screened for obesity definition by clinical staff.

Characteristics	Total (n=3382)	Discharged alive (n=3191)	Died (n=191)	p-value
Chronic cardiac disease	621 (18.4)	518 (16.2)	103 (53.9)	**<0.001**
Hypertension	1539 (45.5)	1388 (43.5)	151 (79.1)	**<0.001**
Peripheral and/or coronary artery revascularisation	108 (3.2)	101 (3.2)	7 (3.7)	0.67
Chronic pulmonary disease**	249 (7.4)	220 (6.9)	29 (15.2)	**<0.001**
Asthma (physician diagnosed)	127 (3.8)	120 (3.8)	7 (3.7)	1.0
Chronic kidney disease	164 (4.8)	121 (3.8)	43 (22.5)	**<0.001**
Obesity*	1129 (33.4)	1062 (33.3)	67 (35.1)	0.67
Moderate or severe liver disease	21 (0.6)	19 (0.6)	2 (1)	0.33
Mild liver disease	71 (2.1)	66 (2.1)	5 (2.6)	0.60
Asplenia	11 (0.3)	10 (0.3)	1 (0.5)	0.47
Chronic neurological disorder	170 (5)	139 (4.4)	31 (16.2)	**<0.001**
Malignant neoplasm	135 (4)	114 (3.6)	21 (11)	**<0.001**
Chronic hematologic disease	27 (0.8)	21 (0.7)	6 (3.1)	0.003
AIDS / HIV				
Yes – on ART	5 (0.1)	5 (0.2)	0 (0)	1.0
Yes – not on ART	7 (0.2)	7 (0.2)	0 (0)	1.0
Diabetes				
Yes – Type 1	9 (0.3)	8 (0.3)	1 (0.5)	0.41
Yes – Type 2	450 (13.3)	389 (12.2)	61 (31.9)	**<0.001**
Rheumatological disorder	102 (3)	100 (3.1)	2 (1)	0.13
Dementia	53 (1.6)	33 (1)	20 (10.5)	**<0.001**
Tuberculosis	5 (0.1)	5 (0.2)	0 (0)	1
Malnutrition	19 (0.6)	15 (0.5)	4 (2.1)	0.02
Smoking				
Yes	139 (4.1)	128 (4)	11 (5.8)	0.32
Former smoker	235 (6.9)	227 (7.1)	8 (4.2)	0.14

CT-grade (n=3187)				
CT-0	93 (2.9)	87 (2.9)	6 (3.6)	0.85
CT-1	608 (19.1)	575 (19.1)	33 (19.5)	
CT-2	1245 (39.1)	1176 (39)	69 (40.8)	
CT-3	1034 (32.4)	981 (32.5)	53 (31.4)	
CT-4	207 (6.5)	199 (6.6)	8 (4.7)	
Ground-glass opacity (n=3165)				1.0
Yes	3020 (95.4)	2864 (95.5)	156 (94.5)	
No	145 (4.6)	136 (4.5)	9 (5.5)	
Consolidation (n=2813)				0.45
Yes	2194 (77.9)	2076 (77.8)	118 (80.8)	
No	621 (22.1)	593 (22.2)	28 (19.2)	

Table 3. Laboratory test results (median, interquartile range), stratified by outcome. Statistically significant results at p value <0.001 and parameters with levels higher/lower than the reference range are presented in bold. Number of patients is presented for each variable.

Test	Marker Name	Reference range	Unit	Total	Discharged	Died	P-value
Coagulation Profile	% PT (Quick)	70-130	%	78 (71-86), n=1207	78 (71-86), n=1131	70 (61.75-81.25), n=76	**<0.001**
Coagulation Profile	Activated patrial thromboplastin time (APTT)	0.75-1.25	Ratio	1.04 (0.97-1.12), n=938	1.04 (0.97-1.12), n=869	1.05 (0.91-1.13), n=69	0.668
Coagulation Profile	D-dimer, Quantitative	0-0.5	µg/mL	0.58 (0.36-1.04), n=288	**0.525 (0.33-0.928), n=246**	**1.075 (0.575-2.125), n=42**	**<0.001**
Coagulation Profile	International normalised ratio (INR)	0.9-1.16	–	**1.17 (1.12-1.27), n=1207**	**1.17 (1.11-1.26), n=1131**	**1.25 (1.157-1.38), n=76**	**<0.001**
Coagulation Profile	Prothrombin time	9.4-12.5	s	**12.8 (12.2-13.8), n=1207**	**12.8 (12.1-13.7), n=1131**	**13.6 (12.6-15), n=76**	**<0.001**
Coagulation Profile	Ferritin	7-200	µg/L	**252.8 (155.4-482.1), n=213**	**249.5 (150.933-483.525), n=194**	**290.55 (217.55-360.65), n=19**	0.619
Coagulation Profile	Fibrinogen	1.8-4	g/L	**5.45 (4.4-6.93), n=1570**	**5.45 (4.4-6.93), n=1488**	**5.645 (4.602-7.572), n=82**	0.187
Complete Blood Count	Haemoglobin (HGB)	117-180	g/L	137 (126-147), n=2392	137 (127-147), n=2255	131 (120-142), n=137	**<0.001**
Complete Blood Count	Mean corpuscular haemoglobin (MCH)	27-38	pg	29.2 (28.1-30.3), n=2392	29.2 (28.1-30.3), n=2255	29.2 (28.3-30.4), n=137	0.512
Complete Blood Count	Mean platelet volume (MPV)	8.7-9.6	fL	9.3 (8.9-9.8), n=340	9.3 (8.9-9.8), n=313	9.3 (8.9-10.35), n=27	0.454
Complete Blood Count	Plateletcrit (PCT)	0.14-0.28	%	0.16 (0.13-0.2), n=339	0.16 (0.14-0.2), n=312	0.15 (0.105-0.19), n=27	0.017
Complete Blood Count	Platelets (PLT)	150-450	*10^9/L	188 (151-237), n=2392	188 (152-238), n=2255	171 (134-228), n=137	0.005
Complete Blood Count	Red blood cells (RBC)	3.8-6.1	*10^12/L	4.7 (4.35-5.05), n=2392	4.72 (4.37-5.06), n=2255	4.45 (4.14-4.76), n=137	**<0.001**
Complete Blood Count	Red cell distribution width (RDW)	10.5-18	%	13.6 (13.1-14.3), n=2392	13.6 (13-14.3), n=2255	14.2 (13.8-15), n=137	**<0.001**
Complete Blood Count	White blood cells (WBC)	4-11	*10^9/L	5.175 (4.038-6.7), n=2392	5.1 (4.015-6.6), n=2255	6 (4.15-8.6), n=137	**<0.001**

Complete Blood Count	Basophils #	0-0.1	*10^9/L	0.02 (0.01-0.04), n=904	0.02 (0.01-0.04), n=846	0.015 (0.01-0.03), n=58	0.093
Complete Blood Count	Lymphocytes #	1-3.7	*10^9/L	1.2 (0.895-1.51), n=2391	1.2 (0.9-1.58), n=2254	**0.8 (0.59-1.08), n=137**	**<0.001**
Complete Blood Count	Monocytes #	0-0.7	*10^9/L	0.4 (0.29-0.5), n=2387	0.4 (0.3-0.5), n=2250	0.3 (0.2-0.42), n=137	**<0.001**
Complete Blood Count	Neutrophils #	1.5-7	*10^9/L	3.3 (2.3-4.7), n=2391	3.3 (2.3-4.6), n=2254	4.7 (2.98-7.3), n=137	**<0.001**
Complete Blood Count	Eosinophils #	0-0.4	*10^9/L	0.05 (0.01-0.1), n=1184	0.05 (0.01-0.1), n=1122	0.02 (0.01-0.075), n=62	**<0.001**
Complete Blood Count	Haematocrit (HCT)	35-52	%	41.55 (38.7-44.6), n=2394	41.6 (38.8-44.7), n=2256	40.5 (37.2-43.475), n=138	0.001
Complete Blood Count	Mean corpuscular haemoglobin concentration (MCHC)	300-380	g/dL	323 (310-331), n=2392	323 (310-331), n=2255	315 (301-329), n=137	0.006
Complete Blood Count	Mean cellular volume (MCV)	80-99	fL	88.7 (85.4-91.7), n=1982	88.65 (85.4-91.6), n=1884	90 (86.2-94.175), n=98	0.002
Complete Blood Count	Erythrocyte sedimentation rate (ESR)	–	mm/h	**32 (21-40), n=2337**	**32 (21-40), n=2203**	**36 (23-45), n=134**	0.014
Complete Blood Count	Colour index	0.8-1.05	–	0.88 (0.84-0.91), n=2392	0.88 (0.84-0.91), n=2255	0.87 (0.85-0.91), n=137	0.492
Complete Blood Count	Eosinophils %	0-5	%	0.4 (0.2-0.9), n=2363	0.4 (0.2-1), n=2230	0.3 (0.1-0.5), n=133	**<0.001**
Complete Blood Count	Basophils %	0-2	%	0.4 (0.2-0.5), n=2390	0.4 (0.2-0.5), n=2253	0.3 (0.2-0.4), n=137	**<0.001**
Complete Blood Count	Lymphocytes %	18-44	%	23.3 (16.6-31.4), n=2391	24 (17.225-31.875), n=2254	**13.8 (7.7-21.1), n=137**	**<0.001**
Complete Blood Count	Monocytes %	2-12	%	7 (5.2-9.2), n=2391	7.2 (5.4-9.4), n=2254	4.9 (3.3-6.3), n=137	**<0.001**
Complete Blood Count	Neutrophils %	45-72	%	65.8 (56.05-74.7), n=2391	65 (55.3-73.7), n=2254	**78.6 (71-86.6), n=137**	**<0.001**
Metabolic Panel	C-reactive protein	0-5	mg/L	**42 (15.135-87), n=2424**	**39 (14-81), n=2293**	**107 (64-160.5), n=131**	**<0.001**
Metabolic Panel	Urea nitrogen	3.2-8.2	mmol/L	5.3 (4.25-6.9), n=1543	5.2 (4.2-6.7), n=1445	**8.75 (5.75-12.575), n=98**	**<0.001**
Metabolic Panel	Alanine Aminotransferase (ALT)	10-49	U/L	32 (22-49), n=2299	32 (22-48), n=2175	35 (23-54.25), n=124	0.202
Metabolic Panel	Aspartate Aminotransferase (AST)	0-34	U/L	**36 (27-51), n=2322**	**36 (27-50), n=2194**	**50 (38-75), n=128**	**<0.001**
Metabol	Total protein	57-82	g/L	71.1 (67.4-	71.2 (67.6-	68.6 (64.05-	**<0**

ic Panel				74.6), n=1879	74.7), n=1772	72.65), n=107	**.001**
Metabolic Panel	Total bilirubin	3-21	µmol/L	10.1 (7.5-13.2), n=2027	10 (7.6-13.1), n=1912	10.3 (7-14.2), n=115	0.94
Metabolic Panel	Direct bilirubin	0-5	µmol/L	3.1 (2.3-4.1), n=981	3 (2.3-4), n=927	3.8 (2.375-4.675), n=54	0.017
Metabolic Panel	Gamma-glutamyltransferase (GGT)	0-73	U/L	46 (26-79), n=338	45 (26-73), n=315	**93 (34.5-143), n=23**	0.023
Metabolic Panel	Potassium	3.5-5.5	mmol/L	4.5 (4.1-4.9), n=2113	4.5 (4.1-4.9), n=1996	4.4 (4-5), n=117	0.736
Metabolic Panel	Calcium	2.08-2.65	mmol/L	2.105 (2-2.203), n=156	2.11 (2.012-2.21), n=138	**2.055 (1.88-2.18), n=18**	0.114
Metabolic Panel	Creatinine	44-115	µmol/L	94.805 (82.797-108.305), n=2368	94.4 (82.523-107.362), n=2240	106.565 (88.785-133.765), n=128	**<0.001**
Metabolic Panel	Creatine kinase (CK)	0-190	U/L	127 (71-233), n=608	122 (70-222), n=561	**207 (117.5-350), n=47**	0.003
Metabolic Panel	Lactate Dehydrogenase (LDH)	240-480	U/L	**484 (376-616), n=1543**	**481 (378-609.75), n=1446**	**575 (1.591-764), n=97**	0.044
Metabolic Panel	Uric acid	145-415	µmol/L	310 (246.75-395), n=752	307 (244-388), n=691	343 (284-442), n=61	0.008
Metabolic Panel	Sodium	132-150	mmol/L	141 (138-144), n=2046	141 (138-144), n=1933	141 (138-145), n=113	0.679
Metabolic Panel	Chloride	99-109	mmol/L	102 (97-105.5), n=243	102 (98-105), n=217	101.5 (95.25-105.5), n=26	0.799
Metabolic Panel	Cholesterol	3.2-5.6	mmol/L	4.03 (3.38-4.69), n=701	4.055 (3.413-4.72), n=654	3.67 (3.015-4.32), n=47	0.006
Metabolic Panel	Albumin	32-48	mmol/L	40.3 (37.8-42.925), n=1776	40.5 (38.1-43.1), n=1673	37.2 (35-39.7), n=103	**<0.001**
Metabolic Panel	Amylase	30-118	U/L	46.9 (35-60), n=427	47 (35-59.4), n=397	40.55 (27.1-70.975), n=30	0.473
Metabolic Panel	Glucose	4.1-5.9	mmol/L	5.4 (4.8-6.3), n=2296	5.4 (4.8-6.2), n=2170	**6.25 (5.4-8.325), n=126**	**<0.001**
Other	Iron	9-30.4	µmol/L	**4 (2.2-6.9), n=385**	**4.1 (2.375-7.2), n=356**	**1.9 (1.8-4.8), n=29**	0.001

Table 4. Laboratory test results (median, interquartile range) in patients with clinically diagnosed COVID-19 infection (RT-PCR negative) and patients with RT-PCR confirmed COVID-19 infection. Statistically significant results at p-value <0.001 are presented in bold. Number of patients is presented for each parameter.

Marker Name (Covid)	Reference range	Unit	Confirmed COVID-19	Clinically diagnosed COVID-19	P-value
% PT (Quick)	70-130	%	79 (71-86), n=606	78 (70-85), n=600	0.246
Activated patrial thromboplastin time (APTT)	0.75-1.25	Ratio	1.05 (0.97-1.12), n=482	1.03 (0.96-1.115), n=455	0.333
D-dimer, Quantitative	0-0.5	µg/mL	0.57 (0.33-1.015), n=151	0.59 (0.39-1.08), n=137	0.114
International normalised ratio (INR)	0.9-1.16	–	1.17 (1.11-1.26), n=606	1.17 (1.12-1.27), n=600	0.307
Prothrombin time	9.4-12.5	s	12.8 (12.1-13.7), n=606	12.9 (12.2-13.8), n=600	0.304
Ferritin	7-200	µg/L	253.7 (150.875-464.35), n=108	252.8 (159.13-510), n=105	0.318
Fibrinogen	1.8-4	g/L	5.33 (4.32-6.84), n=776	5.59 (4.51-7), n=793	0.016
Haemoglobin (HGB)	117-180	g/L	137 (126-148), n=1201	137 (127-146), n=1188	0.902
Mean corpuscular haemoglobin (MCH)	27-38	pg	29.2 (28.1-30.3), n=1201	29.2 (28-30.2), n=1188	0.854
Mean platelet volume (MPV)	8.7-9.6	fL	9.3 (8.925-9.775), n=170	9.3 (8.9-9.8), n=170	0.782
Plateletcrit (PCT)	0.14-0.28	%	0.16 (0.13-0.198), n=170	0.17 (0.13-0.21), n=169	0.182
Platelets (PLT)	150-450	*10^9/L	181 (146-228), n=1201	195 (156.75-246), n=1188	**<0.001**
Red blood cells (RBC)	3.8-6.1	*10^12/L	4.71 (4.34-5.07), n=1201	4.69 (4.37-5.03), n=1188	0.963
Red cell distribution width (RDW)	10.5-18	%	13.6 (13.1-14.3), n=1201	13.6 (13-14.3), n=1188	0.304
White blood cells (WBC)	4-11	*10^9/L	4.97 (3.9-6.3), n=1201	5.4 (4.2-7), n=1188	**<0.001**
Basophils #	0-0.1	*10^9/L	0.02 (0.01-0.03), n=427	0.02 (0.01-0.04), n=476	0.868
Lymphocytes #	1-3.7	*10^9/L	1.1 (0.8-1.5), n=1200	1.2 (0.9-1.6), n=1188	0.003
Monocytes #	0-0.7	*10^9/L	0.4 (0.25-0.5), n=1197	0.4 (0.3-0.5), n=1187	0.026
Neutrophils #	1.5-7	*10^9/L	3.2 (2.2-4.5), n=1200	3.5 (2.4-4.9), n=1188	**<0.001**
Eosinophils #	0-0.4	*10^9/L	0.04 (0.01-0.1), n=545	0.06 (0.01-0.1), n=637	0.053
Haematocrit (HCT)	35-52	%	41.6 (38.525-44.8), n=1202	41.5 (38.8-44.4), n=1189	0.65
Mean corpuscular haemoglobin concentration (MCHC)	300-380	g/dL	323 (311-331), n=1201	322 (307.75-331), n=1188	0.106
Mean cellular volume (MCV)	80-99	fL	88.8 (85.5-92.1), n=993	88.7 (85.325-91.5), n=986	0.31
Erythrocyte sedimentation	–	mm/	32 (21-40),	32 (22-41), n=1161	0.49

rate (ESR)		h	n=1173		9
Colour index	0.8-1.05	–	0.88 (0.84-0.91), n=1201	0.88 (0.84-0.91), n=1188	0.79
Eosinophils %	0-5	%	0.4 (0.2-0.8), n=1183	0.4 (0.2-1), n=1177	0.416
Basophils %	0-2	%	0.4 (0.2-0.5), n=1200	0.4 (0.2-0.5), n=1187	0.343
Lymphocytes %	18-44	%	23.4 (16.5-32), n=1200	23.2 (16.6-31.125), n=1188	0.513
Monocytes %	2-12	%	7.1 (5.2-9.4), n=1200	6.9 (5.2-9.1), n=1188	0.357
Neutrophils %	45-72	%	65.8 (55.375-74.8), n=1200	65.8 (56.5-74.625), n=1188	0.402
C-reactive protein	0-5	mg/L	40 (14-84), n=1213	44 (17-87.25), n=1208	0.175
Urea nitrogen	3.2-8.2	mmol/L	5.3 (4.3-7), n=803	5.2 (4.2-6.9), n=737	0.503
Alanine Aminotransferase (ALT)	10-49	U/L	32 (22-47), n=1162	33 (22-50), n=1134	0.486
Aspartate Aminotransferase (AST)	0-34	U/L	36 (28-50), n=1171	37 (27-52), n=1148	0.569
Total protein	57-82	g/L	71.25 (67.4-74.8), n=952	70.9 (67.475-74.4), n=924	0.647
Total bilirubin	3-21	µmol/L	9.5 (7.4-12.725), n=1020	10.4 (7.7-13.4), n=1005	0.002
Direct bilirubin	0-5	µmol/L	3 (2.2-4), n=534	3.2 (2.3-4.2), n=445	0.186
Gamma-glutamyltransferase (GGT)	0-73	U/L	43 (26-72.25), n=172	48 (26-88), n=165	0.443
Potassium	3.5-5.5	mmol/L	4.4 (4.1-4.9), n=1080	4.5 (4.1-4.8), n=1030	0.891
Calcium	2.08-2.65	mmol/L	2.12 (2.05-2.21), n=91	2.07 (1.95-2.18), n=65	0.122
Creatinine	44-115	µmol/L	95.4 (83.7-109.5), n=1195	94.1 (81.57-106.968), n=1170	0.044
Creatine kinase (CK)	0-190	U/L	134 (75-252), n=294	117 (70-206), n=314	0.081
Lactate Dehydrogenase (LDH)	240-480	U/L	476 (372-609), n=745	492.5 (382.75-623), n=796	0.113
Uric acid	145-415	µmol/L	313 (247-396), n=405	306 (247-388), n=347	0.676
Sodium	132-150	mmol/L	141 (138-144), n=1053	141 (138.25-145), n=990	0.09
Chloride	99-109	mmol/L	102 (98-106), n=141	102 (97-105), n=102	0.335
Cholesterol	3.2-5.6	mmol/L	4.01 (3.36-4.66), n=367	4.08 (3.47-4.81), n=333	0.342
Albumin	32-48	mmol/L	40.4 (37.6-43.2), n=924	40.2 (37.9-42.6), n=849	0.185
Amylase	30-118	U/L	46.9 (34.8-58.35), n=231	47 (35-65.5), n=195	0.41
Glucose	4.1-5.9	mmol/L	5.4 (4.9-6.3), n=1159	5.4 (4.8-6.2), n=1134	0.194
Iron	9-30.4	µmol/L	3.8 (2.1-6.4), n=218	4.1 (2.5-7.8), n=165	0.207

Figure 1

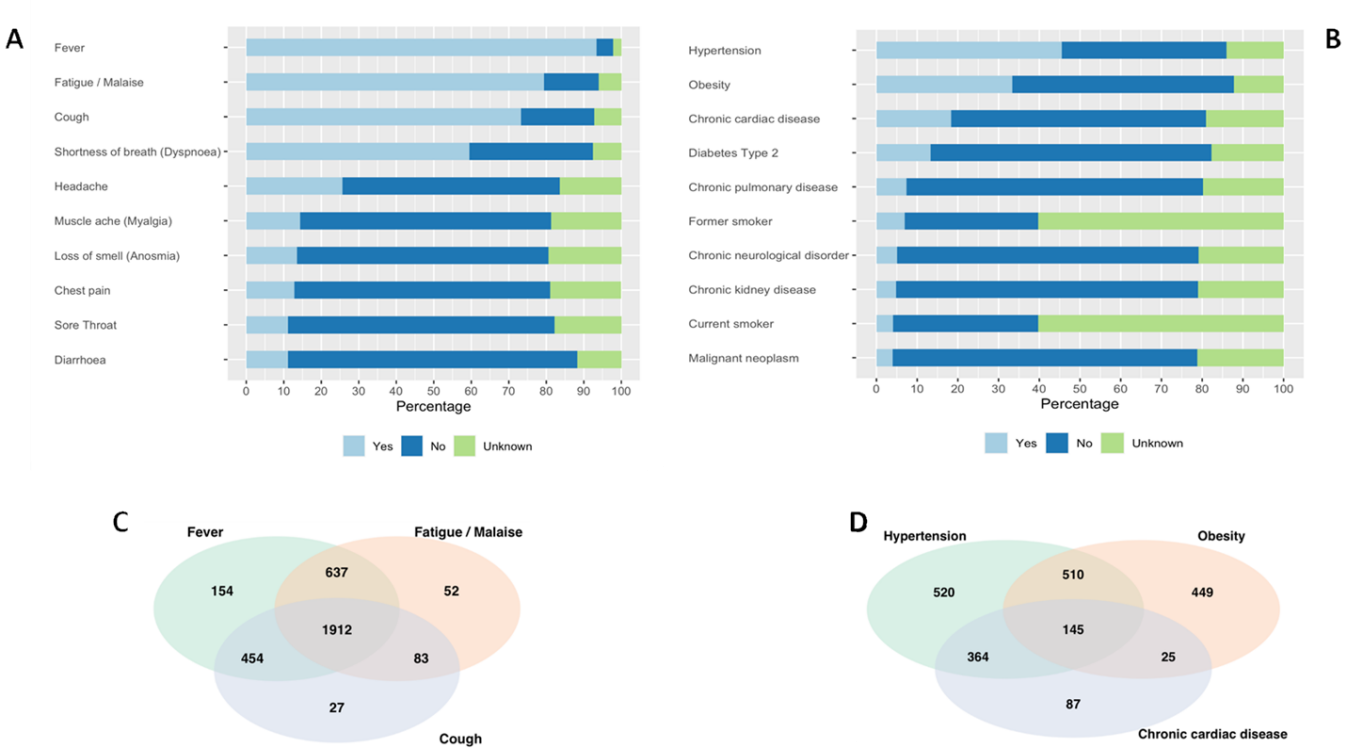

Figure 2