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Frequency of nasopharyngeal swab collection and positivity for SARS-CoV-2 infection in the population of the Italian province of Udine with and without chronic conditions

Francesca Valent*, Giada Mazzilis, Anna Doimo, Corrado Pipan

Institute of Hygiene and Clinical Epidemiology, University Hospital of Udine, Italy

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ABSTRACT

Severity of SARS-CoV-2 infection is associated with comorbidities. However, no information is available on the frequency of nasopharyngeal swab collection and positivity depending on comorbidities. Using a cross-sectional design, we assessed the prevalence of SARS-CoV-2 tests and of positivity in the general population of the 530,000-inhabitant Italian province of Udine and in subgroups affected by chronic conditions in the first weeks of SARS-CoV-2 epidemic.

Anonymous health databases were used as source of information to identify persons with 14 chronic conditions. From laboratory records we assessed the likelihood of real-time reverse-transcriptase polymerase chain reaction for SARS-CoV-2 and the frequency of positivity from February 29 to April 19, 2020, i.e., 7 weeks from the first case detected in the study area. Sex and age-stratified proportions were calculated in comorbidity subgroups. Multivariate regression was used to adjust for confounders. In the province, 236,623 persons had ≥1 chronic condition; 869 had positive tests. Persons with comorbidities were tested more than the others. However, most chronic conditions were not significantly associated with the prevalence of positivity, except psychiatric and neurological diseases and diabetes. In conclusion, despite more frequent testing, patients with most chronic diseases where equally likely to be diagnosed with SARS-CoV-2 as the general population. Chronic patients should adhere to general recommendations for preventing SARS-CoV-2 infection, but ad hoc restrictions do not seem necessary.

1. INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is a pandemic disease caused by a novel Coronavirus (SARS-CoV-2). The infection started in China where a pneumonia of unknown cause was first reported in Wuhan to the World Health Organization (WHO) Country Office in China on 31 December 2019 [1] and as of 27 April, according to official estimates, almost three million people were infected and 200,000 had died worldwide [2].

In Italy, 60 million inhabitants, the first autochthonous case was detected on 21 February in the Lombardy Region and since then almost 200,000 persons were reported to be infected and more than 25,000 had died in the entire 60-million inhabitant county [3]. Nurchis et al [4] estimated that on 28 April 2020 the burden of disease due to COVID-19 in Italy was 121,449 Disability Adjusted Life years (DALYs), i.e., 2.01 DALYs per 1000 inhabitants, with a rate increasing with age. However, the infection did not spread uniformly across the Italian area [3]. In the 530,000 North-Eastern province of Udine, the first cases were reported on 29 February. Since then, the Hospital of Udine has implemented real-time reverse-transcriptase polymerase chain reaction (RT-PCR) analyses on upper and lower respiratory specimen for the detection of SARS-CoV-2 infection. RT-PCR on specimen collected through nasopharyngeal or oropharyngeal swabs or through bronchoalveolar lavage is recommended by the WHO for COVID-19 clinical management and outbreak control purposes [5].

From the end of February, Italy was progressively put into a strict lockdown with the closure of all schools and most commercial activities and the restrictions of inter-regional mobility. A so-called "phase 2" of the COVID-19 emergency with partial reopenings was enforced from 18 May to June 3. In the province of Udine, of all the 916 COVID-19 cases diagnosed in those months, more than 90% were detected before mid-April. Only less than 2% were diagnosed during phase 2. In those months, 34 persons living in the province died in hospital from COVID-19.

* Corresponding author at: SOC Istituto di Igiene ed Epidemiologia Clinica, Azienda Sanitaria Universitaria Friuli Centrale, Via Colugna 50, 33100 Udine, Italy.
E-mail address: francesca.valent@asufc.sanita.fvg.it (F. Valent).

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Various studies have described the frequency of comorbidities among patients hospitalized for COVID-19 in China [6,7]. It has been shown that various comorbidities, i.e., hypertension, diabetes, chronic obstructive pulmonary disease (COPD), cardiovascular disease, and cerebrovascular disease increase the risk of severe COVID-19 disease, whereas no association was found with liver disease, malignancy, or renal disease [8]. In Italy, an analysis of the medical charts of the first 3032 persons who died from COVID-19 showed a significantly higher prevalence of heart diseases, diabetes mellitus, and renal failure than in the general Italian population [9]. We do not know, however, whether persons with those comorbidities are more represented among fatal COVID-19 cases because pre-existing conditions are associated with SARS-CoV-2 likelihood of infection or because, once a person is infected, the outcome is worse. In particular, whether the prevalence of SARS-CoV-2 infection in groups of persons with comorbidities is analogous to that of the general population is not known.

In addition, no information is available on the frequency of laboratory testing in persons with comorbidities. WHO recommended laboratory testing for the clinical management of COVID-19 patients, for cluster investigation, and for public health surveillance [10]; thus, the guiding principles of testing should be both clinical and epidemiological. In the earliest weeks of epidemic in Italy, the Ministry of Health issued some recommendations for the management of patients with selected severe comorbidities, e.g. cancer [11], however, they were cautious because only limited evidence was available at that time. Persons with comorbidities might experience different symptom severity or have a different frequency of close contacts with probable or confirmed cases as compared with the general population, possibly determining a different need of diagnostic tests.

The objective of this study was to estimate the likelihood of being tested for SARS-CoV-2 and that of testing positive in the general population of the Italian province of Udine and in subgroups of the population with chronic diseases, during the first weeks of spread of the virus.

2. MATERIALS AND METHODS

This is a cross-sectional study using the anonymous administrative health databases of the Local Health Agency of Central Friuli (ASUFC) of Udine as the source of information. The databases are included in a datawarehouse and can be deterministically linked with each other at the individual patient level though an anonymous stochastic key which is univocal for each patient in all databases. In particular, we linked the following databases: the laboratory database, including information on type of laboratory test, data of the test, and result; the hospital discharge database, including information on dates of admission and discharge, main diagnosis and secondary diagnoses for all hospitalizations at public or private accredited hospitals in the region; the ambulatory care database, including information on type and date of the access for all outpatient visits and exams at public or private accredited hospitals and health centers; the drug prescription database, including type of drug and date of prescription for all medications prescribed by physicians working within the regional health system; the database of exemptions from medical discharges, including information on patients who are entitled to receive completely free care because of chronic or rare diseases listed by the Italian Ministry of Health [12,13].

Hospital discharge data, ambulatory care data, drug prescription data, and data on exemptions from medical charges, which are virtually complete for all the inhabitants of the province of Udine, regarding calendar year 2019 were used to identify persons affected by one or more comorbidities according to algorithms by the Italian Local Health Authority of Brescia [14]. The comorbidities included in the analysis are 14 chronic conditions (patient with transplanted organ, psychiatric disease, rare disease, disease of lipid metabolism, endocrine disease, autoimmune disease, neurologic disease, gastroenteric disease, bronchopulmonary disease, cardiovascular disease, diabetes mellitus, cancer, HIV, chronic kidney failure) corresponding to the macro-groups of conditions defined by Local Health Authority of Brescia [14]. The algorithms for identifying patients with comorbidities have been used in Brescia for many years; we used them in our study because all the definitions and methods are clearly described [14,15], allowing us to produce comparable estimates In fact, the algorithms developed in Brescia are applicable in our setting since the required databases are available and the same coding systems are used in the province of Udine (i.e., the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) for hospital discharge diagnoses; the Anatomical Therapeutic Chemical classification system (ATC) for drug prescriptions; and the national exemption codes for exemption from medical charges).

Data on patients with chronic conditions were linked with the laboratory database to assess the number, dates, and results of RT-PCR for the detection do SARS-CoV-2 infection from upper or lower respiratory specimen collected through nasopharyngeal or oropharyngeal swabs or through bronchoalveolar lavage [4], in the first seven weeks of COVID-19 outbreak in the province of Udine (from the first case detected on February 29 to April 19, 2020), accounting for 95% of all COVID-19 cases detected up to the end of COVID-19 emergency phase 2. We decided not to include in the study population the few subjects who were diagnosed later to minimize the possibility that our results could be affected by changes in patient management associated with the reduction of SARS-CoV-2 circulation in the study area.

The proportion of persons who were tested at least once in the seven-week period and the proportion of those with at least one positive test result (i.e., COVID-19 confirmed cases) were calculated among persons affected by each of the 14 chronic conditions, stratified by sex and age category (0-14, 15-44, 45-64, 65-74, 75-89, $\geq$90 years). Age categories up to age 74 are among those listed in the in the WHO Global Health Observatory metadata [16] and are consistent with other reports [17,18]; the last two categories were modified because of the relatively large proportion of very elderly population in our region [19]. 95% Confidence Intervals (95%CI) were calculated according to the exact method.

Multivariate logistic regression analyses were conducted on the entire population of the province to evaluate the association of the likelihood of being tested and that of having a positive test with the presence/absence of each of the 14 comorbidities, sex and age category (treated as categorical variable using the same categories described above), adjusting for the potential mutual confounding of each variable on the others. The associations were described through the odds ratios (OR) and 95% confidence intervals (95%CI).

All the analyses were conducted using SAS v9.4 (SAS Institute Inc., Cary, NC, USA).

3. RESULTS

In the province of Udine, almost half inhabitants (N = 236,623) were affected by at least one of the 14 chronic conditions considered in the study. The most common comorbidities were cardiovascular diseases (30.0%), diseases of lipid metabolism (12.2%), gastroenteric diseases (13.5%), cancers (10.0%), diabetes mellitus (6.5%). Among persons with comorbidities, 56.7% had more than one.

In the whole province population, 12,959 persons were tested for SARS-CoV-2 infection in the first seven weeks of the outbreak,

from a minimum of one to a maximum of eight times (in total, 20,006 tests were conducted), and 869 had ≥1 positive result.

The numbers and proportions of tested and positive persons overall and by chronic condition are shown in Table 1. In most chronic disease subgroups the proportion of persons tested for SARS-CoV-2 infection was greater than in the general population, However, the prevalence of persons testing positive was similar to that of the general population.

Proportions of persons tested and positive stratified by sex, age category, and type of comorbidity (if any) are shown in Supplementary Table 1. In most strata, the proportion of patients who were tested for SARS-CoV-2 was analogous to the general population, with only few population groups (e.g., diabetes mellitus in the age group 15-44 years or rare diseases in the age group 45-64 years) being tested more than the general population.

Table 2 illustrates the associations between the likelihood of being tested for SARS-CoV-2 and the likelihood of having a positive test and comorbidities, sex, and age category. According to multivariate analyses also adjusting for the simultaneous presence of more than one comorbidity, females and the very elderly were more likely to be tested, as were patients with comorbidities. The likelihood of having a SARS-CoV-2 infection confirmed by RT-PCR was also increased among females and the elderly ≥75 years as compared with young adults; patients with psychiatric and neurological comorbidities (and those with diabetes mellitus with a borderline significance) had increased likelihood of having the infection; those with diseases of the lipid metabolism had decreased risk of having the infection. The other chronic conditions were not significantly associated with the likelihood of infection.

4. DISCUSSION

Our results show that, especially in the young and adult ages, persons with some chronic conditions were tested more than the general population of the same age group. From multivariate analyses, almost all comorbidities were associated with increased likelihood of being tested. There are a number of possible explanations for this finding.

First, chronic patients may be more often symptomatic or have increased disease severity. Then, patients with chronic conditions may have an overall risk of SARS-CoV-2 infection (of any severity) different from the general population, either because some chronic conditions might themselves increase the risk of being infected after a contact with a COVID-19 case, or because of the medications used to treat the disease [20,21]. Then, patients with a chronic condition may be exposed to sources of infection differently from the general population: they may be less exposed if they are more prone to remain at home or more exposed if they need to attend hospitals where the virus may spread easily. Further, they may have increased likelihood of experiencing nonspecific symptoms, common to their underlying condition and to COVID-19, that justify testing. Finally, they may have easier access to screening testing because of well established relationships with clinicians and periodical access to the hospital for treatment or monitoring of their underlying conditions.

The role of corticosteroids in chronic patients for their underlying disease (e.g, transplanted organs, autoimmune diseases) is controversial: recent evidence suggests that systemic corticosteroids reduce 28-day all-cause mortality in patients with severe COVID-19 [22], however, the effectiveness of systemic corticosteroid use in the early phases of the disease on preventing symptoms or on reducing access to hospital has not been established. Similarly, there is no evidence on either benefits or harms of inhaled steroids in COVID-19 patients with asthma or COPD [23].

In the province of Udine, however, the proportion of persons who actually had a positive RT-PCR test were not substantially different from those of the general population of the same age and sex groups. This was reflected by the generally lower proportions of tested persons who had a positive test in chronic disease groups compared with the general population, with only few exceptions, e.g., young adults with diabetes mellitus, adults with rare diseases, adult and elderly patients with endocrine diseases, elderly with chronic kidney diseases. This suggests that in many cases patients with comorbidities might have been tested as a precaution, or for screening before accessing hospitals, without really being at increased risk of infection. Multivariate analyses, adjusting for sex, age category, and the simultaneous presence of multiple comorbidities confirmed that patients with chronic conditions had no significantly increased prevalence of infection. Actually, persons with diseases of lipid metabolism appeared to have a reduced prevalence.

This study analyzed data from the very first weeks of COVID-19 outbreak in the province. In those weeks, official indications recommended testing patients with symptoms compatible with COVID-19 (such as fever, cough, sore throat, general weakness, fatigue, muscular pain, anosmia, ageusia and, in the most severe cases, pneumonia, acute respiratory distress syndrome, sepsis and septic shock) [24], close contacts of confirmed cases, or high-risk categories such as health workers. Virtually all testing was provided at the University Hospital of Udine and in the whole study period testing availability and capability of the local health system to provide care were not an issue.

This study has a number of advantages. First, it was based on administrative data which were available with very little delay, allowing a prompt assessment of the risk in the population with chronic diseases. The use of administrative data avoided recall bias and minimized selection bias, since the databases include the entire population of the province and completeness is not an issue. The number of patients and of COVID-19 cases included in the analyses was large, allowing for a presentation of risks stratified by sex and age categories. Also, the databases are completely anonymous, so the privacy of patients was preserved by default. In addition, the possibility to link various databases allowed for a relatively easy identification of patients with many chronic conditions and to assess whether they underwent a SARS-CoV-2 test, in a way that can be replicated in the future allowing for periodic re-assessments.

One limitation of this study is that, at this moment, the information on clinical outcomes is not yet available in our administrative health databases, since hospital discharge records are available with a delay of up to three or four months and mortality data including the cause of death may have a delay of nine months or even more. When such information is available, an analysis of disease severity, measured through hospitalization, intensive care unit stay, in-hospital procedures and mortality will have to be conducted on each cohort of chronic disease patients, also taking into account the role of each different comorbidity on the final outcome.

Another limitation is that the algorithms for detecting comorbidities are based on hospital discharge records, ambulatory care records, and drugs prescription data. Thus, our ability to identify comorbidities depends on the quality of recording and coding such information. In addition, comorbidities were identified from 2019 data, so patients who developed chronic conditions in the first months of 2020 were not identified.

Finally, our results may be affected by residual confounding since most clinical information are not available in the administrative databases we used as the source of information. Similarly, we could not assess personal concern with the disease or willingness of the patient to request care, which may actually differ in patients with different comorbidities.

Table 1
Number and proportion of persons who were tested and who resulted positive for SARS-CoV-2 infection in the general population of the Italian province of Udine and in subgroups affected by chronic conditions, February 29 to April 19, 2020.

	Population	N tested	% tested	N positive	% positive in the population	% positive among persons tested
General population	528791	12959	2.5%	869	0.16%	6.7%
Transplanted organ	790	68	8.6%	0	0	0
Psychiatric disease	2592	149	5.7%	10	0.39%	6.7%
Rare disease	3809	119	3.1%	7	0.18%	5.9%
Lipid metabolism disease	64697	1707	2.6%	108	0.17%	6.3%
Endocrine disease	36805	1199	3.3%	74	0.20%	6.2%
Autoimmune disease	16695	611	3.7%	37	0.22%	6.1%
Neurological disease	20347	850	4.2%	62	0.30%	7.3%
Gastroenteric disease	71725	2504	3.5%	158	0.22%	6.3%
COPD	14023	574	4.1%	18	0.13%	3.1%
Cardiovascular disease	159282	4595	2.9%	349	0.22%	7.6%
Diabetes mellitus	34418	1161	3.4%	80	0.23%	6.9%
Cancer	53163	2134	4.0%	111	0.21%	5.2%
HIV	541	20	3.7%	0	0	0
Chronic kidney disease	6230	487	7.8%	13	0.21%	2.7%

Table 2
Association between the likelihood of being tested for SARS-CoV-2 and the likelihood of having a positive test and comorbidities, sex, and age category in the Italian province of Udine, February 29 to April 19, 2020.

	Likelihood of being tested				Likelihood of a positive result			
Independent variable	OR[a]	95%CI	OR[b]	95%CI	OR[a]	95%CI	OR[b]	95%CI
Female (vs male)			1.40	1.35-1.45			1.20	1.05-1.38
Age 0-14 (vs 15-44)			0.17	0.15-0.21			0.16	0.09-0.28
Age 45-64 (vs 15-44)			1.09	1.04-1.14			1.24	1.03-1.49
Age 65-74 (vs 15-44)			0.61	0.55-0.64			1.20	0.93-1.54
Age 75-89 (vs 15-44)			0.86	0.80-0.92			1.69	1.31-2.18
Age ≥90 (vs 15-44)			2.12	1.93-2.34			5.66	4.19-7.66
Transplanted organ (yes vs no)	4.84	4.09-5.74	1.65	1.26-2.15	0.82	0.12-5.86	<0.01	<0.01->99
Psychiatric disease (yes vs no)	2.77	2.48-3.08	2.15	1.81-2.56	2.40	1.32-4.36	2.02	1.07-3.81
Rare disease (yes vs no)	1.35	1.22-1.51	1.09	0.90-1.31	1.24	0.62-2.49	1.11	0.53-2.34
Lipid metabolism disease (yes vs no)	1.06	1.03-1.10	0.82	0.77-0.87	0.73	0.59-0.90	0.68	0.54-0.85
Endocrine disease (yes vs no)	1.19	1.14-1.23	1.00	0.94-1.07	0.99	0.78-1.26	0.93	0.72-1.20
Autoimmune disease (yes vs no)	1.25	1.18-1.32	1.25	1.14-1.37	1.23	0.88-1.71	1.30	0.91-1.84
Neurological disease (yes vs no)	1.82	1.74-1.90	1.58	1.46-1.70	1.58	1.22-2.04	1.54	1.18-2.02
Gastroenteric disease (yes vs no)	1.54	1.49-1.59	1.26	1.19-1.32	1.04	0.87-1.24	1.05	0.86-1.27
COPD (yes vs no)	1.87	1.77-1.98	1.73	1.58-1.89	0.86	0.55-1.35	0.78	0.49-1.25
Cardiovascular disease (yes vs no)	1.34	1.30-1.38	1.06	1.01-1.12	1.08	0.91-1.28	1.11	0.92-1.34
Diabetes mellitus (yes vs no)	1.46	1.40-1.52	1.32	1.23-1.41	1.23	0.98-1.55	1.27	0.99-1.63
Cancer (yes vs no)	1.79	1.74-1.85	1.71	1.62-1.80	1.15	0.95-1.41	1.10	0.89-1.34
HIV (yes vs no)	2.05	1.57-2.67	1.41	0.90-2.22	<0.01	<0.01->99	<0.01	<0.01->99
Chronic kidney disease (yes vs no)	3.43	3.20-3.67	3.13	2.82-3.47	1.29	0.78-2.12	1.15	0.66-2.02

[a] Odds Ratios are adjusted only for sex and age category.
[b] Odds Ratios are adjuested for all the variables shown in the Table.

5. CONCLUSION

This analysis showed that, during the first seven weeks of COVID-19 outbreak in the province of Udine, despite more frequent testing, patients with chronic diseases, with the exception of psychiatric, neurological, and diabetic patients, where equally likely to be diagnosed with SARS-CoV-2 as those without chronic diseases. These findings are important because they help defining the impact of the epidemic on the groups of population with chronic diseases and guiding general practitioners and specialists in the management of patients. Since prevalence of SARS-CoV-2 infection in persons with most chronic conditions did not appear higher than in the general population, our results do not support particular restrictions among these patients, who should however strictly adhere to the general recommendations for self-protection from COVID-19. Patients with psychiatric and neurological diseases and those with diabetes mellitus should be further monitored to verify the finding of higher prevalence of positive tests. Future analyses should aim at assessing the associations of comorbidities with COVID-19 severity and outcomes.

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7. Prior presentations

None.

8. Ethics approval and consent to participate

The authors assert that all of the procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and the Helsinki Declaration of 1975 as revised in 2008. This article does not contain any studies with human or animal subjects performed by any of the authors. Since this analysis was based on anonymous administrative data, patient informed consent and Ethical Committee approval were not required in Italy.

9. Contributors

None.

Declaration of Competing Interest

The authors have no conflicts of interest.

References

[1] World Health Organization. Rolling updates on coronavirus disease (COVID-19). https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen [accessed 31.08.20].
[2] World Health Organization. Coronavirus disease 2019 (COVID-19). Situation Report – 98 https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200427-sitrep-98-covid-19.pdf?sfvrsn=90323472_4 [accessed 31.08.20].
[3] Ministero della Salute. Covid-19, i casi in Italia il 27 aprile ore 18. http://www.salute.gov.it/imgs/C_17_notizie_4623_0_file.pdf [accessed 28.04.20].
[4] Nurchis MC, Pascucci D, Sapienza M, Villani L, D'Ambrosio F, Castrini F, Specchia ML, Laurenti P, Damiani G. Impact of the Burden of COVID-19 in Italy: Results of Disability-Adjusted Life Years (DALYs) and Productivity Loss. Int J Environ Res Public Health 2020;17:4233.
[5] World Health Organization. Laboratory testing for coronavirus disease (COVID-19) in suspected human cases. Available at https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117 [accessed 25.03.20].
[6] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.
[7] Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507–13.
[8] Wang B, Li R, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. Aging (Albany NY) 2020;12:6049–57.
[9] Istituto Superiore di Sanità. EpiCentro. Il ruolo delle patologie croniche pregresse nella prognosi dei pazienti COVID-19. Available at https://www.epicentro.iss.it/coronavirus/sars-cov-2-flussi-dati-confronto-patologie-croniche-pregresse [accessed 02.11.2020].
[10] World Health Organization, Interim guidance. 11 September Diagnostic testing for SARS-CoV-2; 2020.
[11] Ministero della Salute. Raccomandazioni per la gestione dei pazienti oncologici e onco-ematologici in corso di emergenza da COVID-19; 2020. March 10, Available at https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2020&codLeg=73635&parte=1%20&serie=null [accessed 02.11.2020].
[12] Ministero della Salute. Elenco malattie e condizioni croniche e invalidanti. Allegato 8 DPCM 12 gennaio 2017. http://www.trovanorme.salute.gov.it/norme/renderPdf.spring?seriegu=SG&datagu=18/03/2017&redaz=17A02015&artp=13&art=1&subart=1&subart1=10&vers=1&prog=001 [accessed 31.08.20].
[13] Ministero della Salute. Elenco malattie rare esentate dalla partecipazione al costo. Allegato 7 DPCM 12 gennaio 2017.http://www.trovanorme.salute.gov.it/norme/renderPdf.spring?seriegu=SG&datagu=18/03/2017&redaz=17A02015&artp=12&art=1&subart=1&subart1=10&vers=1&prog=001[accessed 31.08.20].
[14] ASL di Brescia in «La presa in carico dei malati cronici nell'ASL di Brescia: monitoraggio BDA 2013». https://www.ats-brescia.it/media/documenti/cure_primarie/anno%202013/Medici%20Cure%20Primarie/Strumenti%20Professionali/Malati%20cronici%20e%20PDT%20-%20monitoraggio/BDA2012_Finale_esteso.pdf [accessed 31.08.20].
[15] Lonati F, Scarcella C, Indelicato A, et al. La Banca dati assistito dell'ASL di Brescia: una metodologia basata su dati correnti per il monitoraggio delle patologie croniche e per la gestione delle risorse [Brescia Local Health Autority Population Database: a method based on current data for monitoring chronic diseases and management]. Epidemiol Prev 2008;32:137–44.
[16] World Health Organization. Global Health Observatory metadata. Age group codelist. https://apps.who.int/gho/data/node.metadata.AGEGROUP?lang=en [accessed 15.12.20].
[17] Government of Canada. Office of the Superintendent of Financial Institutions. Mortality Projections for Social Security Programs in Canada. https://www.osfi-bsif.gc.ca/Eng/oca-bac/as-ea/Pages/mpsspc.aspx#TOC-IVb [accessed 15.12.20].
[18] EUROMOMO. Graphs and maps. Available at: https://www.euromomo.eu/graphs-and-maps/ [accessed 15.12.20].
[19] Istat. Demografia in cifre. http://www.demo.istat.it/popres/index.php?anno=2020&lingua=ita [accessed 15.12.20].
[20] Jani M, Barton A, Hyrich K. Prediction of infection risk in rheumatoid arthritis patients treated with biologics: are we any closer to risk stratification? Curr Opin Rheumatol 2019;31:285–92.
[21] Quartuccio L, Zabotti A, Del Zotto S, Zanier L, De Vita S, Valent F. Risk of serious infection among patients receiving biologics for chronic inflammatory diseases: Usefulness of administrative data. J Adv Res 2018;15:87–93.
[22] WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, Sterne JAC, Murthy S, Diaz JV, Slutsky AS, Villar J, Angus DC, Annane D, Azevedo LCP, Berwanger O, Cavalcanti AB, Dequin PF, Du B, Emberson J, Fisher D, Giraudeau B, Gordon AC, Granholm A, Green C, Haynes R, Heming N, Higgins JPT, Horby P, Jüni P, Landray MJ, Le Gouge A, Leclerc M, Lim WS, Machado FR, McArthur C, Meziani F, Møller MH, Perner A, Petersen MW, Savovic J, Tomazini B, Veiga VC, Webb S, Marshall JC. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis. JAMA 2020, http://dx.doi.org/10.1001/jama.2020.17023.
[23] Halpin DMG, Singh D, Hadfield RM. Inhaled corticosteroids and COVID-19: a systematic review and clinical perspective. Eur Respir J 2020;55:2001009, http://dx.doi.org/10.1183/13993003.01009-2020.
[24] European Centre for Disease Prevention and Control. Q & A on COVID-19. Medical information. Available at: https://www.ecdc.europa.eu/en/covid-19/questions-answers. [accessed 20.07.20].