Testing the identification effectiveness of an unknown outbreak of the Infectious Diseases Seeker (IDS) using and comparing the novel coronavirus disease (COVID-19) outbreak with the past SARS and MERS epidemics

Federico Baldassi [a],[*], Orlando Cenciarelli [b], Andrea Malizia [c], Pasquale Gaudio [a]

[a] Department of Industrial Engineering, University of Rome "Tor Vergata", Italy
[b] International CBRNe Master Courses, University of Rome "Tor Vergata", Italy
[c] Department of Biomedicine and Prevention, University of Rome "Tor Vergata", Italy

A B S T R A C T

Background: The aim of this research is to assess the predictive accuracy of the Infectious Diseases Seeker (IDS) – an innovative tool for prompt identification of the causative agent of infectious diseases during outbreaks – when field epidemiological data collected from a novel outbreak of unknown origin are analysed by the tool. For this reason, it has been taken into account the novel coronavirus disease (COVID-19) outbreak, which began in China at the end of December 2019, has rapidly spread around the globe, and it has led to a public health emergency of international concern (PHEIC), declared to the 30th of January 2020 by the World Health Organization (WHO).
Methods: The IDS takes advantage of an off-line database, built before the COVID-19 pandemic, which represents a pivotal characteristic for working without an internet connection. The software has been tested using the epidemiological data available in different and progressive stages of the COVID-19 outbreak. As a comparison, the results of the tests performed using the epidemiological data from the Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) epidemic in 2002 and Middle East Respiratory Syndrome coronavirus (MERS-CoV) epidemic in 2012, are shown.
Results: The overall outcomes provided by the software are comforting, as a matter of the fact that IDS has identified with a good accuracy the SARS and MERS epidemics (over 90%), while, as expected, it has not provided erroneous and equivocal readings after the elaboration COVID-19 epidemic data.
Conclusions: Even though IDS has not recognized the COVID-19 epidemic, it has not given to the end user a false result and wrong interpretation, as expected by the developers. For this reason, IDS reveals itself as useful software to identify a possible epidemic or outbreak. Thus, the intention of developers is to plan, once the software will be released, dedicated updates and upgrades of the database (e.g., SARS-CoV-2) in order to keep this tool increasingly useful and applicable to reality.

Introduction

An outbreak of pneumonia of unknown aetiology in Wuhan since December 2019 has been drawing great attention around the world reminds how urgent and critical is to assure a strong global and domestic preparedness capacity, including an appropriate surveillance. On 11 February 2020, the World Health Organization (WHO) announced "Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)" as the name of the new virus and "COVID-19" as the name of this disease it cause.

Coronaviruses (CoVs) are a large family of viruses that are known to cause illness ranging from the common cold to more severe dis-

eases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). They can infect respiratory, gastrointestinal, hepatic, and central nervous system of human, livestock, birds, bat, mouse, and many other wild animals [1–4]. The outbreaks of SARS in 2002/2003 and MERS in 2012 have demonstrated the possibility of animal-to-human and human-to-human transmission of newly emerging CoVs [4–6].

A respectable surveillance of this kind of infectious disease aims to rapidly detecting changes in the incidence rate and in promptly recognizing and characterizing syndrome caused by an agent. It is a systematic and ongoing collection, collation, and analysis of health-related information that is communicated in a timely manner to decision makers in order to direct and organize the countermeasures. In fact, the goal of an appropriate infectious disease surveillance is to help in reducing the incidence and prevalence of infectious diseases by providing relevant public health information and knowledge to public health professionals, health care professionals, and decision makers, to promote actions that can result in the timely prevention and control of infectious diseases [7].

To control COVID-19 outbreak, at national level, the Chinese government and researchers took swift measures and conduct the etiological studies. For example, the causative agent of unknown pneumonia has been identified as a novel coronavirus (nCoV) by sequencing its viral genome and etiological investigations by at least five independent laboratories from China.

Instead of in the United States (US), a few weeks before the first confirmed case of COVID-19 was reported, the US Centers for Disease Control and Prevention (CDC) enhanced its prevention and control system using multiple surveillance systems run in collaboration with state, local, territorial, and academic partners to monitor COVID-19 disease in the US. COVID-19 surveillance in the US draws from a combination of data sources from existing influenza and viral respiratory disease surveillance, syndromic surveillance, case reporting, commercial lab reporting, the healthcare safety system, ongoing research platforms, and other new systems designed to answer specific questions. These systems, combined, create an updated picture of SARS-CoV-2 spread and its effects in the US and provide data used to inform the US national public health response to COVID-19 [8].

At the international level, WHO declared that an early epidemiologic and clinical investigations are critical to contrast this outbreak. WHO provided guidance to Member States for the implementation of global surveillance of COVID-19. The objectives of this global surveillance are: to monitor trends of the disease where human to human transmission occurs; rapidly detect new cases in countries where the virus is not circulating; provide epidemiological information to conduct risk assessments at the national, regional and global level; and provide epidemiological information to guide preparedness and response measures [9].

The current national, regional and global system for contrasting upcoming outbreaks needs to be improved and helped with innovative systems of surveillance, prevention and management [9].

In this context, this study has the intention to test the performance of a new software package, called the Infectious Disease Seeker (IDS), to the COVID-19 data. The IDS version applied in this study has been developed before COVID-19 emerged and hence provides a great opportunity for the authors to develop an understanding of IDS behaviour with a novel agent, such as SARS-CoV-2, before further software revisions and future updates. As a comparison, the results of the tests performed using the epidemiological data from the severe acute respiratory syndrome coronavirus (SARS-CoV) epidemic in 2002 and Middle East respiratory syndrome coronavirus (MERS-CoV) epidemic in 2012, are shown.

Table 1

Example of a database string and the related agent parameters. *A 95% Confidence Interval (95% CI) for all of detailed numeric parameters has been considered (CFR, Transmission rate, Incubation rate, Recovery rate, Infectious mortality rate). **SEIR mathematical model describes how individuals move through each compartment (Susceptible, Exposed, Infected, Recovery) in the model.

Agent parameters	Value
Agent name	SARS-associated coronavirus (SARS-CoV)
Agent type	Virus
Disease	Severe acute respiratory syndrome (SARS)
Mortality	Medium
Duration of illness	Long
Geographical distribution	Eastern Asia, Southeast Asia, Northern America, Southern America, Europe
Signs & symptoms	Fever, headache, an overall feeling of discomfort, body aches, mild respiratory symptoms at the outset, diarrhoea, dry cough, pneumonia
Age group	Adult, senior
Gender	Male, female
Transmission route	Person-to-person, aerosol, faecal-oral
Reservoir/host/source	Human
Vector/Other	None
Transmission	Person to person. Predominantly spread in droplets that are shed from the respiratory secretions of infected persons. Faecal or airborne transmission seem to be less frequent.
Prevention and control	The best way to prevent infections include avoiding close contact with affected individuals. Using good hand washing with soap and water is important. Encourage people with viral respiratory infections to cover their mouth when coughing or sneezing.
Treatment	There's currently no cure for SARS, but research to find a vaccine is ongoing. A person suspected of having SARS should be admitted to hospital immediately and kept in isolation under close observation. Treatment is mainly supportive, and may include: assisting with breathing using a ventilator to deliver oxygen.
CFR (decimals)	0,15*
Transmission rate (day^{-1})	0,25*
Incubation rate (day^{-1})	0,15*
Recovery rate (day^{-1})	0,04*
Infectious mortality rate (day^{-1})	0,015*
Compartmental model	Susceptible-Exposed-Infected-Recovery (SEIR)**

Methods

Database implementation

The key point of this first software prototype to be useful and workable in practice is the quality and reliability of the database on which the predictions are based. As recommended in previous studies [10,11], the database has been extended and populated with data from 60 pathogens and the infectious diseases they cause. The list of pathogens has been built up selecting different categories of agents (viruses, bacteria and parasites) in order to cover a wide range of infectious diseases.

In addition, since the first prototype [10,11], the agent parameters (epidemiological parameters, other important disease features and relevant information) have been improved in order to define unequivocally with refined factors each pathogen, and consequently to help the software in its searching, prediction and analysis process.

Table 1 shows an example of a database string. Principally, this table contains the epidemiological parameters and other significant data of an agent (e.g., SARS-CoV) and its related disease (e.g., SARS) that has been considered. In particular, it is possible to consult:

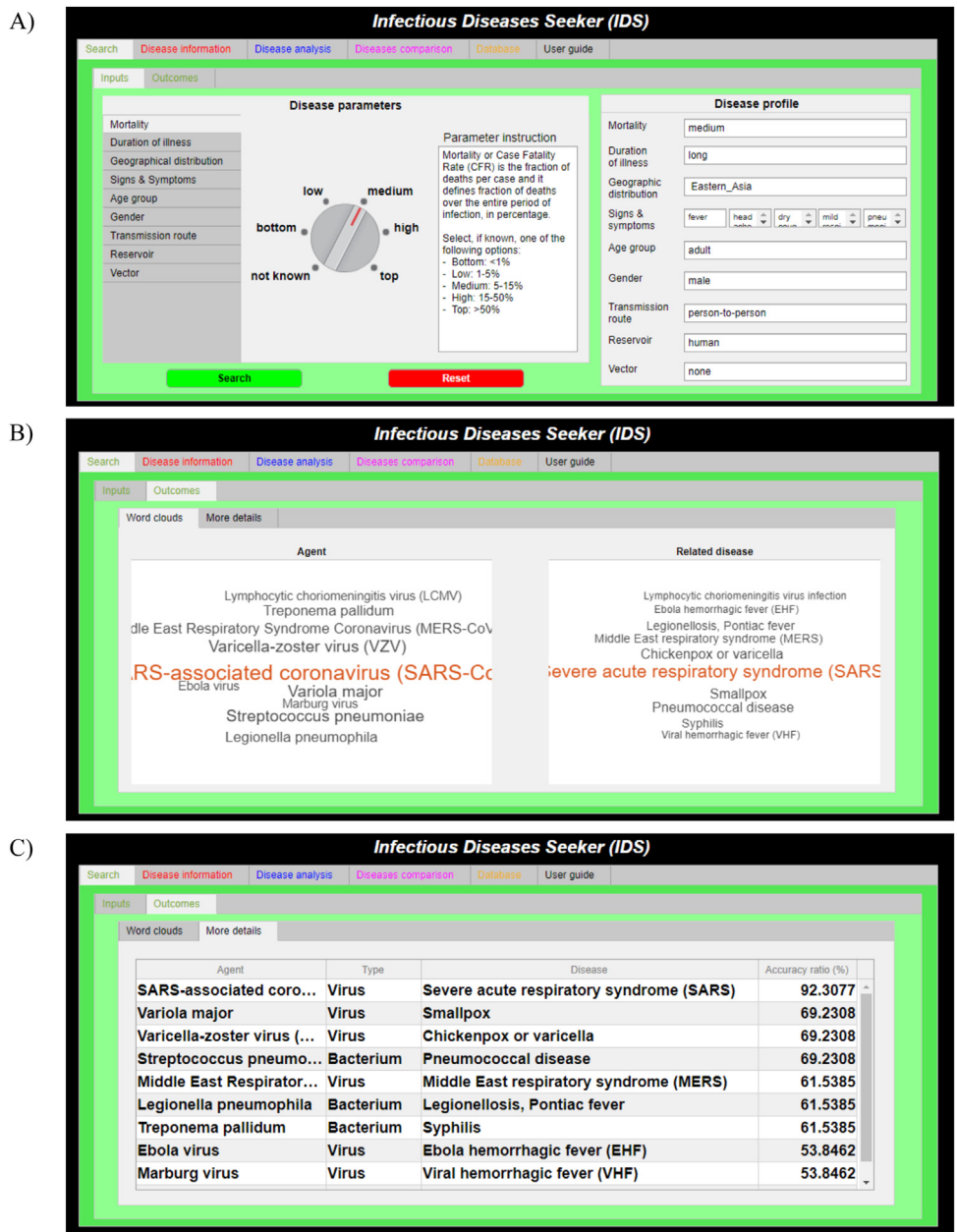- the agent name, agent type and related disease;

Fig. 1. IDS screenshots of "Search" tab or green tab. (A) "Inputs" subtab, (B) "Outcomes" subtab – "Word clouds" section, and (C) "Outcomes" subtab – "More details" section. The example showed refers to SARS epidemic identification.

- the mortality or Case Fatality Rate (CFR), which is the fraction of deaths per case and it defines the fraction of deaths over the entire period of infection, typically in percentage;
- the duration of illness, which is the period in which sick people start to be sick and the signs and symptoms of illness begin to decline;
- the geographical distribution;
- the signs and symptoms, which are respectively any objective and subjective evidence of a disease;
- the age group, which is defined as the age susceptibility for a specific agent and the related disease;
- the gender, male or female, that is more susceptible for a specific disease;
- the transmission route, which is the pathway of causative agents from a source to infection of a susceptible host;

- the reservoir, which is a living host inside of which a pathogen survives, often (though not always) without causing disease for the reservoir itself;
- the vector, which is any carrier able to transmit a pathogen into a living organism; most carriers regarded as vectors are living organisms, but they could be inanimate media of infection such as dust particles;
- the transmission, which is a short description of how the disease spreads to people and they can get infected;
- the prevention and control, which is a short description of how people can prevent and control the spreading of disease;
- treatment, which is a short description of how people can manage and combat disease;
- CFR (see above), that in this case is indicate in decimals;
- the transmission rate, which is the rate at which infectious cases cause secondary or new cases in a population with susceptible

Table 2
The diseases data loaded in IDS "Disease Profile" section. (A) Early COVID-19; (B) Latest COVID-19; (C) SARS; (D) MERS.

		Parameters	Value	Ref.
(A)	Initial COVID-19 data	Mortality	Low	
		Duration of illness	Long	
		Geographical distribution	Eastern Asia (China)	
		Signs & Symptoms	Fever, cough, dyspnoea, fatigue	
		Age group	Adult	[12–14]
		Gender	Male	
		Transmission routes	Zoonosis	
		Reservoir	Infected animal	
		Vector	//	
(B)	Latest COVID-19 data	Mortality	Low	
		Duration of illness	Long	
		Geographical distribution	Eastern Asia (China)	
		Signs & Symptoms	Fever, cough, sore throat, shortness of breath, fatigue	[12,14,15]
		Age group	Adult	
		Gender	Male	
		Transmission routes	Person-to-person	
		Reservoir	Human	
		Vector	Human	
(C)	SARS data (2002–2003)	Mortality	Medium (5–15%)	
		Duration of illness	Long	
		Geographical distribution	Eastern Asia (China)	
		Signs & Symptoms	Fever, headache, dry cough, mild respiratory symptoms, pneumonia	[12,15–17]
		Age group	Adult and senior	
		Gender	Male or female	
		Transmission routes	Person-to-person	
		Reservoir	Human	
		Vector	//	
(D)	MERS data (2012)	Mortality	High (>15%)	
		Duration of illness	Long	
		Geographical distribution	Western Asia	
		Signs & Symptoms	Fever, cough, shortness of breath, pneumonia, diarrhoea	[12,15,18]
		Age group	Adult and senior	
		Gender	Male or female	
		Transmission routes	Zoonosis or person-to-person	
		Reservoir	Camel	
		Vector	//	

individuals; it is a constant rate and it has units of inverse time (days^{-1});

- the incubation rate, which is the time elapsed between exposure to a pathogenic organism, and when symptoms and signs appear; it is given in units of inverse time (days^{-1});
- the recovery rate, which is the rate of individuals who recover or die, leave the infected class (recover or die) at constant per capita probability per unit of time (days^{-1});
- the infectious mortality rate, which represents the rate at which infected people die per unit of time (days^{-1}); it is not to be confused with the CFR;
- the compartmental model, which is the mathematical model allows for understanding how a disease can spread in populations.

Software

The software has been named Infectious Disease Seeker (IDS) and it has been developed in the MATLAB^{TM} environment. This software has been designed for working standalone (outside the MATLAB$^{®}$ environmental), without an internet connection. This is possible because IDS is loaded with a database that includes 60 (sixty) different pathogens and related infectious diseases (Table 1). Thus, the tool can be useful and applicable in many different situations, in the field and remote areas where an internet connection and other kinds of communication systems are not always available.

At this stage of development, IDS is structured as a single user-friendly layout with six tabs, characterized by a specific color. Given that the aim of this study has been to test the predictive accuracy of the IDS, this paper is focused only on the "Search" tab capabilities (Fig. 1). Only a short description of other tabs is reported here.

Search tab

The search tab or green tab (Fig. 1) is the core of the tool where the identification of an agent and the related disease reporting some indispensable parameters is run. It has been selected nine essential parameters ("Inputs" subtab) for the reason that they have been considered the most important factors that even a non-health worker can identify and recognize (Fig. 1A). The end user is able to load these parameters in the "Disease parameters" section as free text values, using a drop down menu or switchers, following the instructions reported in the "Parameter instruction" frame of each parameter sheet. The inputs that the user loads in this tab are summarized in the "Disease profile" section (Fig. 1A). The MATLAB$^{®}$ code developed for regressive analysis (logistic regression analysis) determines if data loaded by the user in the "Disease profile" section are in the database datasets and then recognizes the associated correspondences and the related accuracy ratio [10,11]. Once the "Search" button, the results of the calculation can be consulted in the "Outcomes" subtab. The closest 10 matched results can be visualized in two different types of representation, as:

- word cloud plots for agents and related diseases in the "Word clouds" section (Fig. 1B);
- a detailed table in the "More details" section (Fig. 1C).

The example showed in Fig. 1 refers to SARS epidemic identification.

Fig. 2. IDS outcomes screenshots of "Related disease" word clouds ("Search" tab->"Outcomes" subtab->"Word clouds" section – "Related disease" word clouds). Each word cloud plot is a visual representation of the IDS outcomes and the size and colour of each disease identified indicating its relative accuracy ratio. (A) "Related disease" word cloud for the initial COVID-19 data; (B) "Related disease" word cloud for the latest COVID-19 data; (C) "Related disease" word cloud for SARS epidemic data (China, 2002–2003); and (D) "Related disease" word cloud for MERS epidemic data (Middle East, 2012).

Other tabs

Listed below are briefly described the others IDS tabs:

- The disease information tab or red tab, which is the section where users can consult relevant information for controlling, preventing and contrasting the agents and related disease identified.
- The disease analysis tab or blue tab, which is the section in which expert users can simulate the spreading of a disease in a population using a specific compartmental models, either the Susceptible-Infected-Recovered (SIR) or Susceptible-Exposed-Infected-Recovered (SEIR) models.
- The disease comparison tab or pink tab, which is the section in which expert users can analyse and compare other specific epidemiological parameters (CFR, transmission rate, incubation rate, recovery rate, infectious mortality rate) of two or more diseases.
- The database tab or orange tab, which is the section in which the entire database has been loaded and users can directly consult it in the tool.
- The user guide tab or black tab, which is the section containing the user manual.

Diseases data for simulation

The diseases data (inputs) that have been loaded into the IDS to fill in the "Disease profile" section are reported in Table 2. These data have been organized, respectively, as follows:

- initial COVID-19: the data in Table 2A has been collected consulting the first reports and scientific papers published at the beginning of the COVID-19 outbreak;
- latest COVID-19: the data in Table 2B has been collected consulting the latest COVID-19 outbreak reports and related scientific papers at the time of writing this article;
- SARS epidemic: the data in Table 2C has been collected consulting scientific papers that refer to the SARS outbreak occurred in China in 2002–2003;
- MERS epidemic: the data in Table 2D has been collected consulting scientific papers that refer to the MERS outbreak occurred in Middle East in 2012.

Results

As already described in *2.2.1 Search tab* paragraph, the data summarized in Table 2 has been loaded in the IDS and, once the calculation, the software outcomes for each simulation ("Search" tab -> Outcomes" subtab -> Word clouds" section – "Related disease" word clouds) are represented in word cloud plots for an easy first look (Fig. 2). Each word cloud plot is a visual representation of the IDS outcomes and the size and colour of each disease identified indicating its relative accuracy ratio. As illustrated in Fig. 2, the first two word clouds, referring to the initial COVID-19 epidemic and the latest COVID-19 epidemic respectively, do not show clear results (Fig. 2A and 2B) as compared with the two word clouds related to SARS and MERS epidemics, where the outcomes are clear (Fig. 2C and 2D).
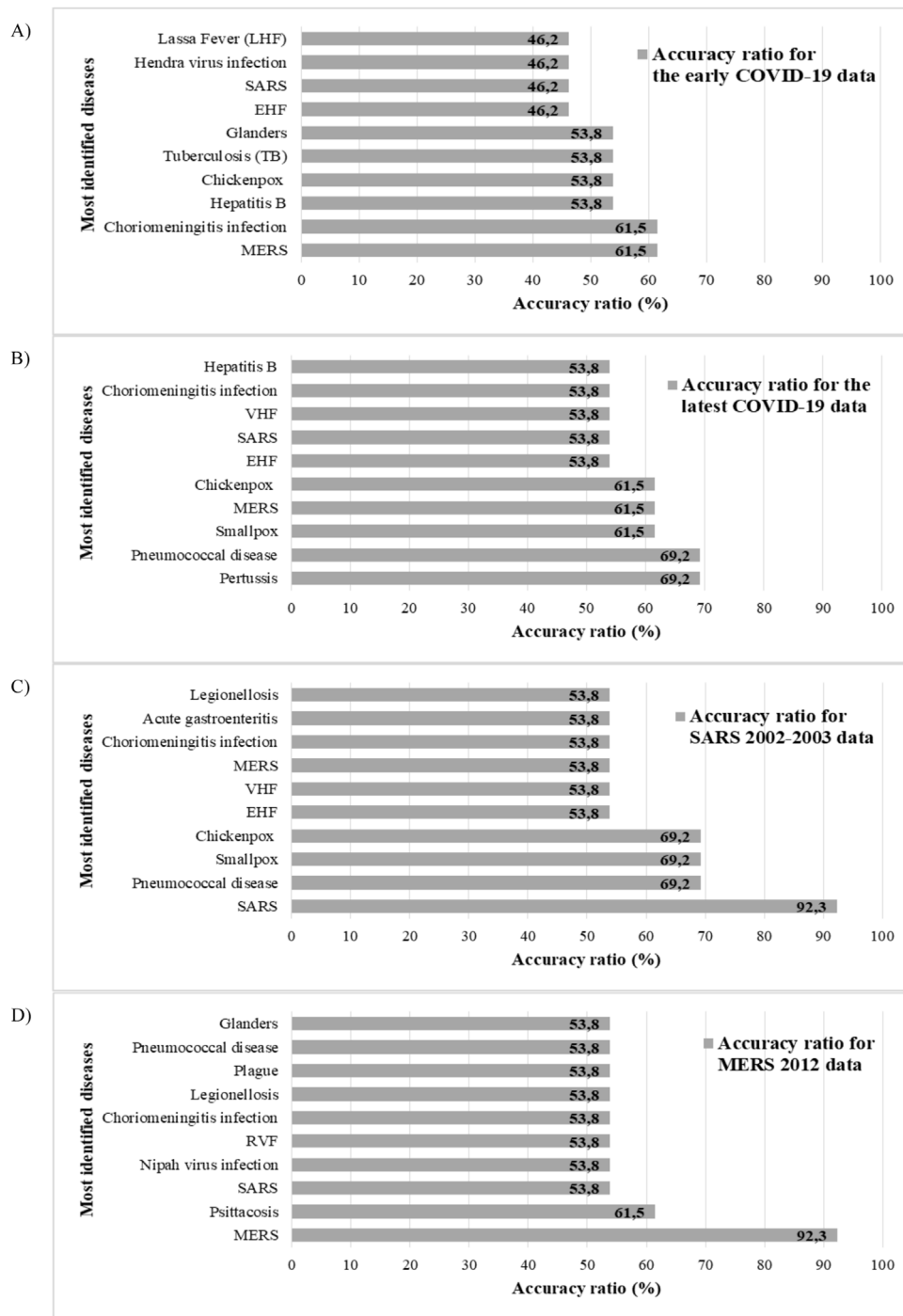
Fig. 3. Bar plots that show the most 10 matched diseases and related accuracy ratio for each disease that has been taken into account: (A) initial COVID-19; (B) latest COVID-19; (C) SARS epidemic (China, 2002–2003); and (D) MERS epidemic (Middle East, 2012).

The detailed data about the identification and the related accuracy ratio for each disease that has been taken into account are showed in Fig. 3. The accuracy ratio is expressed in percentage and it is calculated as a summary quantitative measure of matched values between data available and the database.

As evident to the outcomes shown in Figs. 2 and 3, IDS has identified with high accuracy the SARS and MERS epidemics (over 90%) and it has not provided any precise result for the COVID-19 epidemic, either using initial or more recent epidemic data. The percentage of accuracy of SARS and MERS shows a significant difference between the first disease recognized and the rest of the diseases identified (>23% and >38% respectively). This percentage of accuracy is not so clear for COVID-19 outcomes. The 10 diseases most recognized show similar accuracy and they are in a small range of ~15% (red double arrow in Fig. 4). In addition, it is important to note that in both COVID-19 outcomes SARS and MERS diseases are present, even if with different levels of confidence, as showed in Fig. 4. Specifically, in the initial COVID-19 simulation MERS is in first place (61,5%) and SARS in third place (46,2%), while in the case of the latest COVID-19 simulation MERS is in second place (61,5%) and SARS in third place (53,8%).
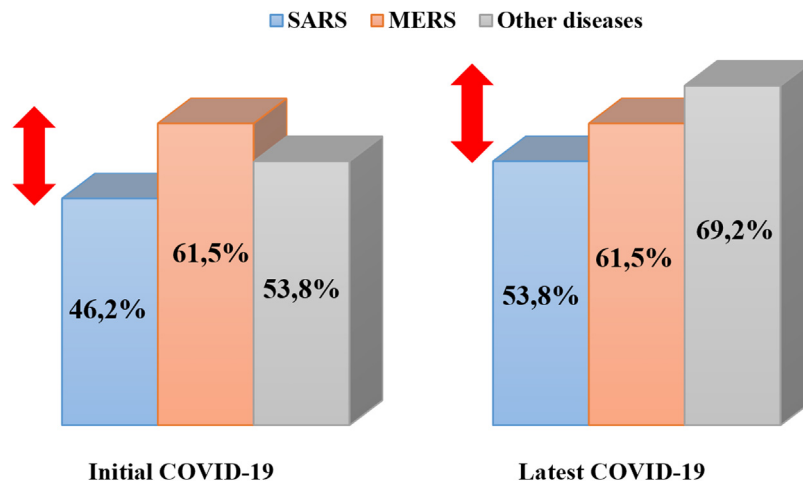
Fig. 4. SARS and MERS outcomes comparison in cases of initial and latest COVID-19 simulations. In grey, the accuracy of other diseases. The two double red arrows represent the small range of ~15% accuracy ratio.

Discussion

The overall outcomes provided by the software are comforting and IDS reveals itself as useful software to identify a possible epidemic or outbreak. In fact, as previously anticipated, the aim of this research is to assess the predictive accuracy of IDS when field epidemiological data collected from a novel outbreak of unknown origin, like COVID-19, are analysed by the tool. Even though in both COVID-19 simulations the search function (green tab) of IDS does not provide clear outcomes to the user unlike SARS and MERS analysis, it also has not showed false result and wrong interpretation. This is expected due to the early level of development of IDS and its correlated database. The fact that IDS has provided outcomes in a small range of ~15%, and that MERS and SARS, both part of the Coronaviruses family, have been included in the first ten diseases recognized (Fig. 4), is however a valuable feedback for software developers. In fact, these outcomes bring out at least two different aspects, both important and that do not exclude each other. The first aspect is that IDS in case of COVID-19 simulations does not recognized this disease but it provides in the results with high accuracy ratio the related Coronaviruses family members: SARS and MERS. Thus, also at this level of development, IDS would provide to a potential end user some useful information on the nature of this unknown disease. The second aspect, directly linked to the first one, even if IDS provides in the outcomes of COVID-19 simulations SARS (46,2% in the initial COVID-19 and 53,8% in the latest COVID-19) and MERS (61,5% in both COVID-19 simulations), these results do not reflect properly the phylogenetic analysis among SARS-CoV-1, MERS-CoV and SARSCoV-2. The molecular analyses revealed that SARS-CoV-1 and SARS-CoV-2 are closely related to each other. More than 90% genetic sequence are matching between these two viruses. If MERS-CoV and SARS-CoV-2 genes are compared, only 68% genetic similarity is observed among them [19].

These aspects and others have to be take into account by the software developers in order to set up a software that should be useful and applicable in many different situations, in the field and remote areas where an internet connection and other kinds of communication systems are not always available. Nowadays the diseases due to emerging and re-emerging viral pathogens are common. In fact, in addition to SARS virus, MERS virus, COVID-19 virus, in nature there are innumerable viruses as Ebola, Influenza type A (swine flu and bird flu), Dengue, Chikungunya, West Nile virus, and so on that cause huge morbidity and mortality in humans. Most of these viruses have the ability to spread rapidly and can cause severe epidemic and pandemics among human population within a short

span of time covering broader geographical area [19]. Moreover, in the current scenario, these viruses not only affect human health but also devastate several country's economy. For instance, during the current outbreak of COVID-19, China, American, South Korean, Indian and other developed countries stock markets were severely affected [20].

For these reasons, having a system of surveillance enriched and improved by this kind of original and innovative tool is essential. IDS reveals in part itself as suitable software to identify a possible epidemic or outbreak. To do this, IDS takes advantage of an off-line database that represents a pivotal characteristic for working without an internet connection. Therefore, the intention of the developers is to plan a dedicated and focused update and upgrade of the database to keep this tool increasingly useful and applicable to reality.

Conclusions

At this stage of development of IDS, this study had the intention to test this tool using the epidemiological data available in different and progressive stages of the COVID-19 outbreak. The aim of the tests have been to assess the predictive accuracy of the IDS when field epidemiological data collected from an outbreak of unknown origin are analysed by the tool. As a comparison, the results of the tests performed using the epidemiological data from the SARS epidemic in 2002 and MERS epidemic in 2012, have been shown.

The analytical results show that this version of IDS software is a good starting point for further developments. The future steps for this software regard as first point the development of the tool as a useful and standalone predictive platform increasingly appropriate for first responders, health care workers, and public health decision makers to help them in predicting, assessing and contrasting outbreaks. Once a standalone desktop app will be able to run without passing or retrieving any arguments to or from MATLAB®, the intention of the developers is initially to update the database in order to cover at least the COVID-19 data lack and finally to consider specific tool upgrades with the aim of improving the others IDS capabilities as, for instance, the diseases analysis section.

Authors' contribution

The authors contributed equally to the article and all authors have approved the final article.

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