The healthcare and pharmaceutical vulnerability emerging from the new Coronavirus outbreak

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With a constantly increasing number of infected people world-wide,¹ the COVID-19 (2019-nCoV) outbreak risks becoming a pandemic emergency, and for this reason, on 28 February 2020 the WHO upgraded the global risk of the coronavirus outbreak to 'very high'.² As many studies have shown, in the first phase of the onset of 2019-nCoV there is an exponential curve of infection with a reproduction number (R_0) ranging from 2 to 5,³ an indication that the spread of the virus cannot spontaneously decrease. A significant reduction in these R_0 values can possibly be achieved by implementing specific containment actions, according to the results of a study of the evolution of the infections detected in China.⁴ The spread of the virus is favoured by its ability to be transmitted by asymptomatic patients,⁵ a particularly grave consideration, given that the currently estimated incubation period extends from 2 to 12 days.⁶ Furthermore, the easiest screening methods based on the execution of a nasopharyngeal swab displayed false negative results in both asymptomatic and symptomatic patients,⁷ making it more complex to intercept possible infected subjects, especially before a clinical manifestation of the infection.

Since its onset in Europe, the 2019-nCoV emergency has been addressed by implementing social containment measures. This is particularly true in Italy, the first European country struck by an important 2019-nCoV outbreak. On 4 March 2020 the national government approved a series of important social limitation measures including the closure of schools and universities, and the quarantine of exposed persons; it also urges residents to avoid crowded events, and has set in motion contact tracing efforts. Considering that containment of the spread of the virus seems very unlikely, the

restriction measures adopted by Italy seem more focused on dilution of the epidemic peak over a wider timeframe. As reported in a scientific paper,⁸ the first outcomes of these measures would be to buy time for preparations in the healthcare system, to avoid overwhelming the healthcare system, and to enable better management of 2019-nCoV infected patients.

This seems essential for the Italian health system, as, since 2009, more than €37 billion have been cut in healthcare costs and hospital beds have been reduced to 3.2 per 1000 inhabitants, compared with a European average of 5 per 1000 inhabitants.⁹ The number of hospital beds, in particular, seems to be a crucial issue in management of the 2019-nCoV emergency, which is characterised by the need for hospitalisation in intensive care units for >15% of infected patients.¹⁰ For this reason, the Italian government has set up a 50% increase in the number of beds in these critical hospital areas and a patient distribution agreement between healthcare institutions aimed at avoiding the collapse of some hospitals affected by a greater influx of infected patients.¹¹

Delaying the peak of the epidemic could also be useful for a subsequent introduction of some pharmacological interventions. At present, there is no defined therapeutic protocol to be used on patients with 2019-nCoV, and the drugs that have shown significant efficacy in some studies,^{12–13} such as remdesivir, lopinavir/ritonavir, and hydroxychloroquine, are currently undergoing phase 3 clinical trials (ClinicalTrials.gov register). Another aid that could take place later is the possible availability of an effective vaccine capable of blocking the virus spread. Currently >15 vaccines are in the pipeline¹² but none are foreseen to be available before the third quarter of 2020.¹⁴

Another important aspect of the global emergency is certainly linked to its social impact. Our life dynamics are deeply influenced by the containment measures, and for the first time in the 21st century we are facing a health emergency on a global scale. However, while solutions

such as remote smart working, video calls and e-commerce allow us to carry on with our lifestyle to some degree, other aspects of our society such as our global and connected economy and crucial import supply chains could be deeply affected.

The supply of medicines is a crucial issue when facing a global health emergency. We have become used to hearing news about shortages of hand sanitiser and facemasks dictated by so-called 'panic-buying', but a much more serious threat is the potential shortage of drugs. Locally, shortages can be linked to increased demand and difficulties in transport in the areas most affected by the emergency. Globally, there could be a remarkable reduction in the production capability of pharmaceutical manufacturing facilities where active pharmaceutical ingredients (API) are produced, as work is interrupted to update sanitisation procedures for the infrastructure and production rooms, or as scientists, managers and line workers fall ill with the virus. Moreover, it is well known that drug makers rely heavily on ingredients made in Chinese factories. According to the CEO of Sanofi, 60% of the world's API is made in China¹⁵ and this could cause supply problems as the virus' disruption of the Chinese economy continues. In fact, a drug was recently added to the US Food and Drug Administration's (FDA's) Drug Shortages List specifically because of the effects of the coronavirus. The manufacturer notified the FDA that the shortage is due to problems with the production of an active pharmaceutical ingredient at a site affected by coronavirus.¹⁶ However, this news is only the tip of the iceberg, as according to some sources¹⁷ the monitoring of the risk of shortage related to the 2019-nCoV would concern "About 150 prescription drugs—including antibiotics, generics and some branded drugs without alternatives".

Unfortunately, not only drug supplies may risk shortfalls: the production of medical devices may falter as well. Indeed, as reported by the FDA, "The agency reached out to 63 companies with a total of 72 facilities in China that make essential medical devices". FDA Commissioner Dr Stephen Hahn said that "several of these facilities in China are adversely affected" by the epidemic and that their workforces have taken a hit from the outbreak, including employees being quarantined.¹⁶

These worrying developments provide an opportunity to discuss economic realities that create vulnerability in our healthcare sector. It is becoming clear that production backup sites are needed to ensure adequate supplies, even in the most

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complex situations. Also, the fact that, before this crisis, our healthcare system had not developed a strategy to deal with potential epidemics, could provide an opportunity to reflect on where to act to be prepared in the event of similar or even more serious health threats.

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