

Learning from the Italian experience during COVID-19 pandemic waves: be prepared and mind some crucial aspects

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Abstract. COVID-19 pandemic has rapidly spread worldwide causing a serious challenge to the global medical community. Italy was struck hard during the first wave earlier this year and several weaknesses as well as general unpreparedness of the national healthcare system were acknowledged. Learning essential lessons from the past, we realized how implementing contingency response measures, human resources and social dynamics could have changed the outcome if promptly adopted. This review translates the previous experience into strategic actions that has to be considered when developing appropriate national and regional operational plans to respond to a pandemic.

Key words: COVID-19, hospital response, emergency planning, drug supply, lung ultrasound, telemedicine, drug shortage.

Introduction

After the Spanish Flu in 1918 COVID-19 pandemic can be declared the widest viral infection.

It started at the end of 2019 in Wuhan, China. SARS-CoV-2 rapidly spread worldwide affecting more than 83 million people and led to death of over 1,8 million according to the WHO data (1).

In 2020 COVID-19 caused more deaths than AIDS (near 700.000) and malaria (near 400.000), reaching almost 1.5 million deaths of tuberculosis. However, when compared to Spanish Flu COVID-19 pandemic appears far less fatal than the former which caused almost 50 million deaths (2).

The temporal distribution of Spanish Flu is similar to COVID-19: a "first wave" followed by a "second wave" with higher peak occurred in both pandemics.

Infection with SARS-CoV-2 (or COVID-19) can be classified into three stages: the early infection or viral response phase followed by the pulmonary one

and finally the hyperinflammatory condition related to the cytokine storm in conjunction with microvascular pulmonary thrombosis (3,4).

The majority of the patients with SARS-CoV-2 do not develop interstitial pneumonia and remain asymptomatic but still require the measure of quarantine. Only 4-5% of the affected population develop respiratory symptoms and the most severe cases require ICU admission (5).

Currently, Europe as well as many other countries are facing the second pandemic wave of COVID-19.

A range of potential treatments have been suggested for COVID-19 but it's still unclear whether any of them will turn out to be more effective than the usual standard of care. In this regard, many clinical trials are still ongoing, but so far social distance remains the only proven effective strategy (6).

Besides the hospital settings, many social and practical aspects have to be taken into account in preparation of the second wave, since contribution of

family medicine, out of hospital services and an appropriate resources allocation can contribute to avoid overwhelming the healthcare system again.

In this scoping review we highlight the strengths and weaknesses of the Italian healthcare response during the COVID-19 outbreak earlier this year. Being aware of previous mistakes and right decisions could help national healthcare systems to reassess their strategies and be prepared to tackle the second and probably the third waves of the pandemic.

Prevention of SARS-CoV2 infection: the only proven effective strategy

SARS-CoV-2 is a highly contagious virus which diffuses rapidly among humans by aerosol droplets transmission (7). As a result, the only strategy to limit the spread is limiting contacts between people. When

necessary, close contacts should take place with all precautions including face masks and frequent hand hygiene (8).

When the COVID-19 infection rate peaked, the Italian Govern imposed the national lock down, forcing everyone to stay home and self isolate if they had positive result to nasal swabs even in absence of symptoms. Only key workers were allowed to travel (9).

As demonstrated by figure 1, following the restrictions, the reproduction number R , meaning expected number of secondary cases arising from a primary case infected at time t , diminished and after 12 days the rate of new infected cases started to decrease (10).

Similar findings are supported by a recent study conducted by Li and al. that analyzed non-pharmaceutical interventions in more than 130 countries all around the world (11).

Notably, the encouraging outcomes from strict restrictions took up to three weeks before being

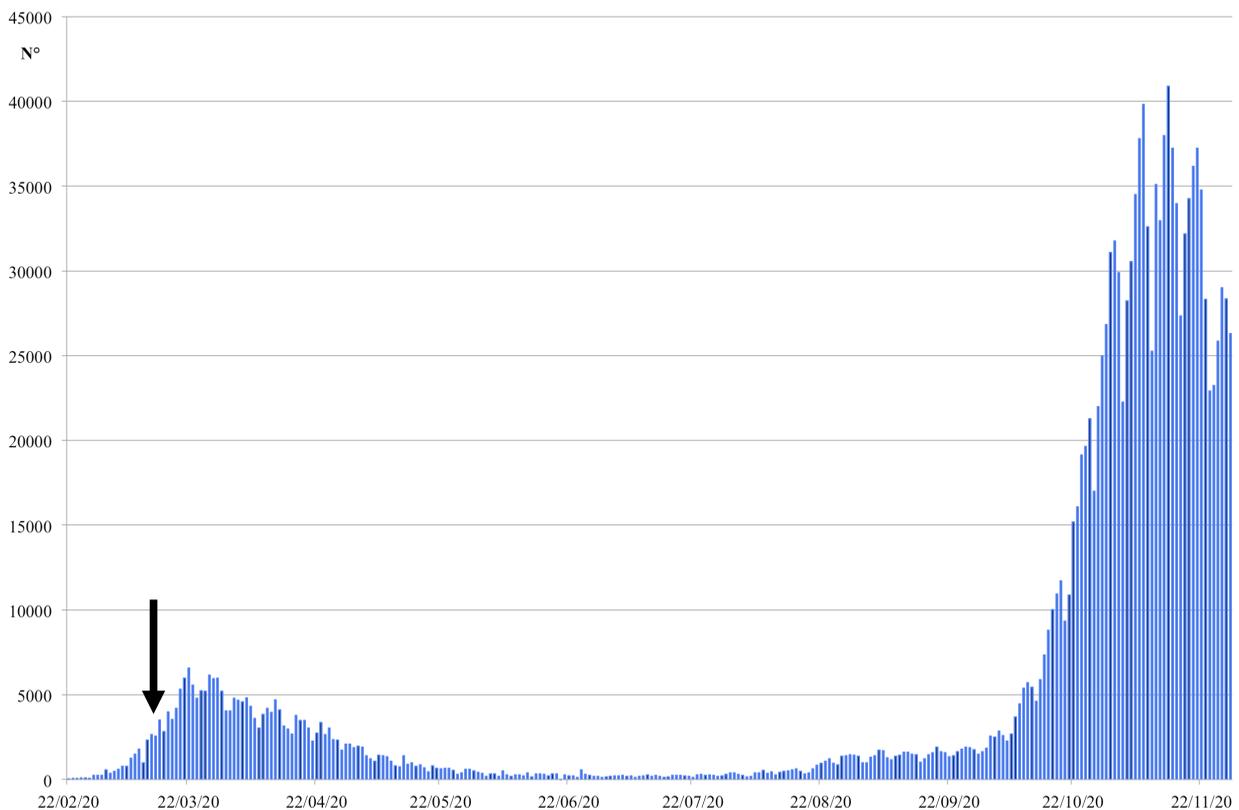


Figure 1. Effect of lockdown on new contagions.

noticed. This aspect has to be considered anytime restrictions are enforced, in order to anticipate infection trends and act in advance.

The black arrow represents the day when lockdown was announced in Italy. After almost 14 days the number of new infected people dropped, as a demonstration that non-pharmaceutical interventions are effective in reducing the viral spread.

The role of family medicine during the pandemic

The need for hospitalization is unpredictable and the ability to assess the patient's severity prior to admission to hospital is crucial. Data shows variability in the pandemic distribution: Northern Italy was struck hard by COVID-19, with significantly higher incidence and related casualties during the first wave, whereas other regions experienced a higher demand for hospital admission and intensive care beds during the current and latest wave (12).

In Italy, the healthcare system has been led by district authorities since 1992 and each region has developed different protocols according to its local needs (13).

Patients suspected or at high risk for COVID-19 infection, unless with moderate disease, should be screened and treated home initially. Special local units with family medicine doctors need to be able to perform a screening test at home (nasal swab), limiting the viral spread (14).

With a positive swab and reported symptoms, the patient is categorized as follows: asymptomatic, mild, moderate and severely ill (Figure 2). Six minutes walking test (6MWT), positive when $SpO_2 < 90\%$, and lung ultrasound (LUS) are relatively simple but crucial investigations that can be performed at home by medical staff (15).

The role of family medicine is essential as prevents patients from presenting to the emergency departments, avoids the overwhelming of healthcare facilities and expedites admission of those patients that are likely to deteriorate due to comorbidities and illness evolution.

Following infection, the patient is perceived as a 'bomb' that could potentially blow up if the process

is not interrupted. Patients asymptomatic or mildly symptomatic could be diagnosed with nasal swabs and treated safely at home. Examinations such as a 6 minutes walking test and LUS help clinician to decide the patient's management when at home and monitored or when attending ED. Criteria for admission are need of oxygen supply and worsening despite the therapy. In these circumstances the further investigation with Ct scan is indicated. If mechanical ventilation is required the patient is admitted to ICU. Some of the most critically ill patients have a cytokines storm leading to a terminal multiorgan failure.

Lung ultrasound: a new era for bedside sonography

During the current pandemic, lung ultrasound (LU) is being used extensively to diagnose and monitor viral lung damage in infected patients (16). Sensibility of sonography is very high in detecting lung involvement ("light beam" is the typical sign of COVID-19 pneumonia), however specificity remains poor as sonographic patterns described in COVID-19 patients are similar to those reported in interstitial disease (17).

A lung ultrasound score (LUS) is currently adopted in clinical routine to assess and follow up the severity of lung manifestations (18).

The standard scanning technique has been suggested before by Vetrugno and Colleagues(19). Each hemithorax is divided into 3 regions: anterior (ventral to the anterior axillary line), middle (between the anterior and posterior axillary lines) and posterior (dorsal to the posterior axillary line); each region is further divided into an upper and lower zone by a transverse plane passing through the xiphoid process. The worst scan from each zone is the one representative of the zone and is scored as follows: A lines or < 3 separate B lines (normal or A-pattern, plus lung sliding), 0 points; well-spaced B lines (B-pattern, plus lung sliding), 1 point; ≥ 3 coalescent B-lines, plus sliding, 2 points; lung consolidation, including multiple small subpleural consolidations, 3 points. The score ranges from 0 to 36 with increasing severity of the disease at higher scores. A LUS score lower or equal to 12 may be reassuring, while higher scores should be considered as a warning sign.

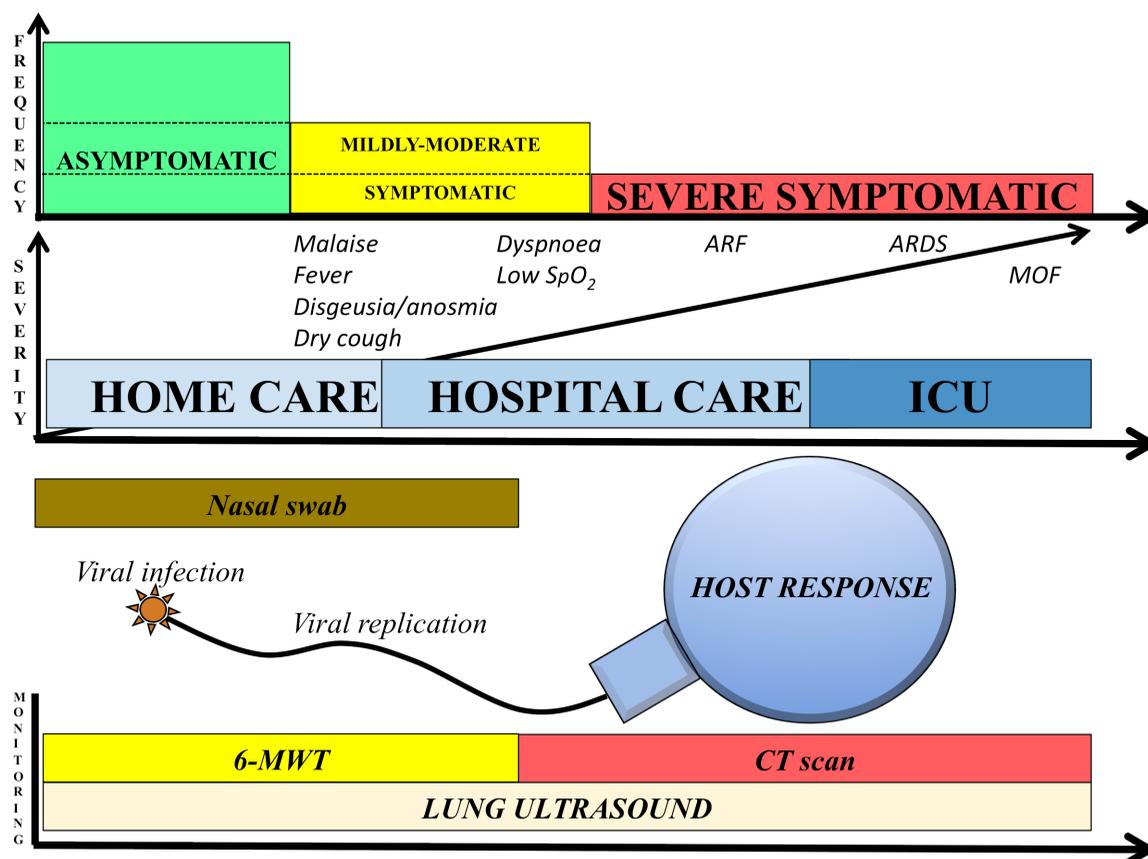


Figure 2. Clinical and management aspects for COVID-19 patients.

Several patient's worsening predictive scores have been implemented to support clinical decisions, mostly based on lab tests and standard radiological examinations (20).

A new score relying on LUS findings has been developed as a rapid bedside tool. The so-called COVID-19 Worsening Score accurately identifies patients who unlikely need intensive care unit (ICU) admission (21).

Teaching specific sonographic patterns on LUS is feasible and achievable with a short training course (22). As a result, focused ultrasound COVID-19 projects are currently ongoing recruiting clinicians and assistant practitioners with minimal sonographic experience in order to provide an extensive ultrasound service starting from the hospital triage to the community (figure 3).

The use of LUS for the pandemic has been implemented worldwide in different medical scenarios, including the ED triage, medical departments, ICUs

and out of hospital rehabilitation clinics. Hand held devices allowed medical staff to perform examinations and share sonographic findings real-time with colleagues throughout Telemedicine support. (Image courtesy of Serena Rovida, M.D.)

Hospitals reorganization when facing a pandemic

During the first wave, Italian hospitals faced an unprecedented massive inflow in a short period of time. This unexpected event translated into one of the greatest challenges for the national healthcare system. Entire buildings were transformed into COVID-19 units (23). Doctors and nurses were retrieved from other departments and ambulatory as well as elective surgery activities were withheld. For several months only urgent interventions were allowed and a few healthcare facilities were able to provide service for



Figure 3. Lung Ultrasound for COVID-19 patients.

non COVID-19 patients, resulting in delays and postponement treatments for patients affected by chronic disorders (24).

Learning from our past experience we recommend hospitals to ‘behave like armonions: to widen during the wave and shrink after the storm’ (figure 4).

The following steps have to be taken as soon as possible when facing a pandemic:

- specific distinct pathways for COVID-19 and non COVID-19 patients should be defined at the earliest to ensure safety for those vulnerable patients that still need access to their usual treatment and follow up (25)
- scheduled ambulatory activities which are not essential should be temporarily suspended and those areas converted in COVID-19 dedicated hubs to allow expansion of sub intensive departments that can provide non invasive ventilation (NIV) treatments (26).
- healthcare staff and more generally human resources from non critical care wards should be deployed to COVID-19 departments and familiarize with NIV methods including

Venturi Mask, High Flow Nasal Cannula and C-PAP devices.

- droplets dispersion up to one meter distance during NIV increases the risk of infection of the healthcare providers, therefore adequate aeration systems and spaces big enough to reduce cross contamination risk have to be set up properly (27).
- rapid and structured increase of ICU beds should happen before overwhelming the system. The main concern with ICU is that the reorganization is limited not only by machine and monitoring supply, but mostly by human resources (28). Preparing a team for patient’s care in ICU can be very challenging without any critical care background. Access to ICU and availability of ICU beds have been recently demonstrated to be potentially related to COVID-19 patients’ mortality (29) rehabilitation after hospitalization for COVID-19 pneumonia also matters. Increasing evidence emphasizes the need to establish multidisciplinary post-COVID-19 care pathways considering the raising rate of post intensive care syndrome (PICS) (30,31).

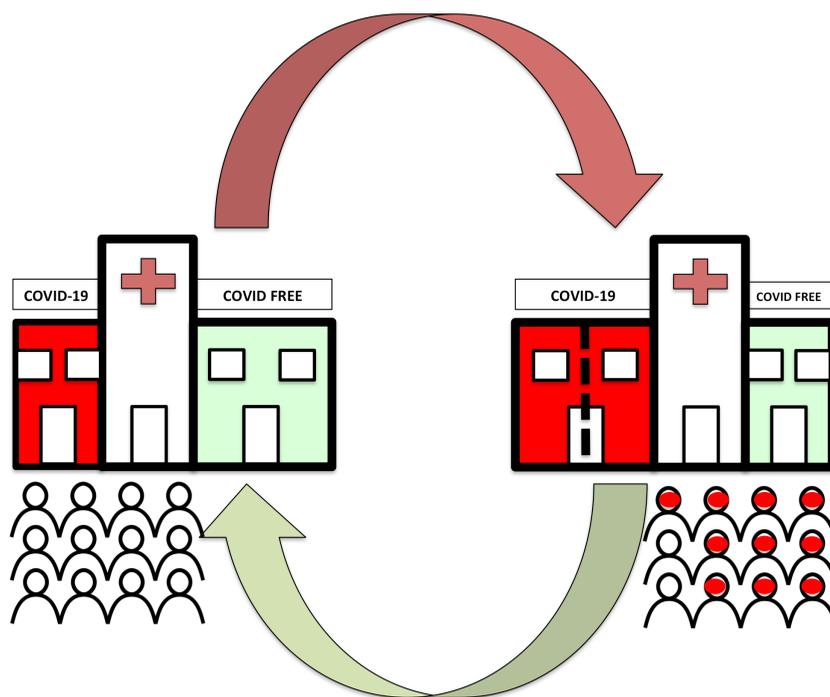


Figure 4. Hospital reorganization during the pandemic and afterwards

Since the emergence of the first cases the pressure caused by the epidemic revealed the need for a profound reorganization of the hospitals in a very short time. Spaces, human resources, technology were diverted from standard departments (green zone in the figure) to those dedicated to COVID19 patients (red one). Once the situation returned under control, the original disposition was restored, making hospitals acting like accordions and ready to adapt the system in case of further waves.

Anticipating the drug supply shortage.

Since the beginning of the pandemic the shortage of medications due to the high demand and low chain supply was a serious issue (figure 5). Every medication with a supposed role against the virus, such as Hydroxychloroquine, was initially delivered largely to the population. As a result, many drugs became unavailable for treatment of other conditions rather than COVID-19 (32).

Besides the erroneous mass consumption of non yet scientifically proven drugs, WHO listed the scarcity

of medications mostly endorsed in the ICU settings: Propofol, paralytics and intravenous opioids. Scientific authorities as well as hospital pharmacies encouraged medical staff to use certain drugs only if strictly needed and rather select others with similar effects. At that time, hospital pharmacists covered a strategic function between monitoring prescriptions and holding a solid link with manufacturers (33).

Here some recommendations from our experience:

- since the majority of the drugs are produced in India or China and imported, possible limitations imposed by trading restrictions have to be considered in advance. The Drug National Agencies should retrieve drugs needed and if necessary export manufacturers to increase production.
- if no other options are available, pharmaceutical factories should convert their usual production chain to cover the acute deficit

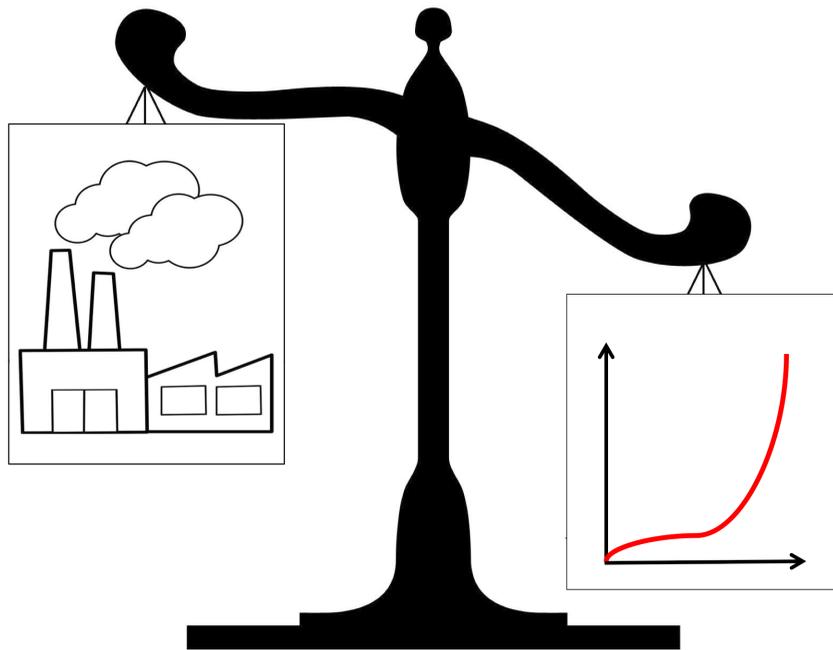


Figure 5. Lack of drug supply.

- hospital facing major surge of patients should be prioritized with drug stockpiles
- an international collaboration should be promoted in support to the most affected countries

A rapid increase in drug consumption, especially antiviral and critical care drugs, was not followed initially by an adequate supply. Some of the usual ICU medications needed to be replaced by others with analogous pharmacological action (propofol with midazolam, rocuronium with cisatracurium or vice versa). In light of this problem, hospital pharmacies should plan ahead together with regional and national health authorities and drug companies.

The potential role of telemedicine during a pandemic

The usefulness of telemedicine in disasters and health emergencies has been previously described (34). The availability of a telehealth service providing

patient's virtual appointments with doctors has been very useful under the pandemic restrictions. It greatly limited risk exposure, saved time and resources for travel to hospital and costs. Blood tests and the majority of the radiological investigations could be carried out in a delocalized center rather than in hospital and uploaded remotely on a common platform, enabling the doctor to see and validate the findings.

In the family medicine scenario, telemedicine allowed general practitioners to monitor the majority of COVID-19 patients that did not require hospitalization. Nursing staff during home visits were instructed by doctors to perform 6MWT with real time patient's plan adjustments.

In the Emergency Departments, those patients attending with minor accidents and not requiring immediate treatment were quickly discharged home with a virtual appointment within 24 hours with results communication and further medical therapy discussion.

Finally, after discharge from ICU, COVID-19 patients required a long period of rehabilitation which was challenging due to the lack of healthcare providers (figure 6). Reorganizing the service with nurses at

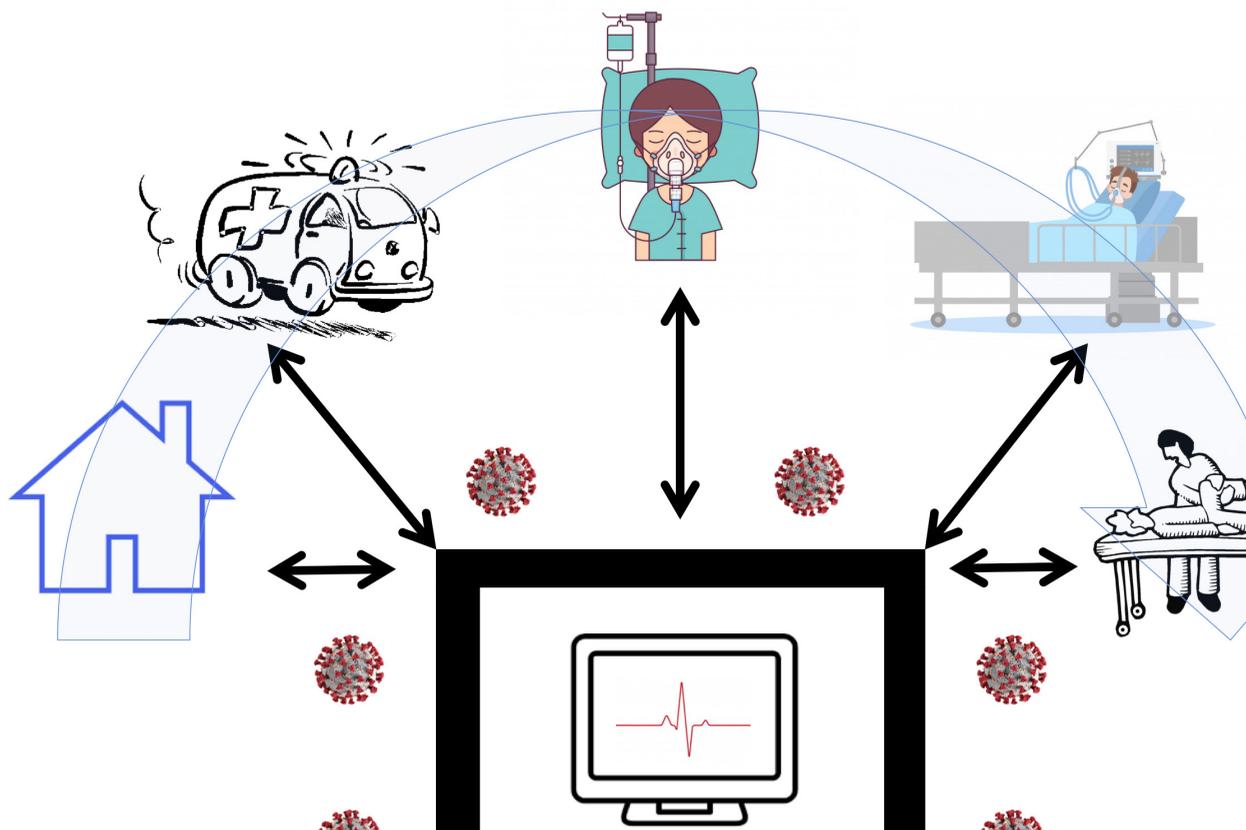


Figure 6. Telemedicine.

patient's bedside and doctor interacting with them via web call was a safe alternative to treat patients in a familiar environment (35).

Despite the clear benefit of telemedicine, there are still several barriers that prevent its implementation including availability of robust IT infrastructure, licensing and regulatory services, equipment costs, efficient training for both physicians and nursing staff.

Conclusions

COVID-19 outbreak emphasized the importance of a multidisciplinary approach including reorganization of the entire national healthcare system from hospital to family medicine, implementation of new

reliable investigation tools overcoming usual standard imaging as well as social habits change.

A tight control of the trend of infections led by main international health organizations is also necessary to guide prompt response and correct resources allocation.

The impact of Telemedicine during pandemic has been striking. It allowed continuous care to distinct categories of COVID19 patients: those home requiring minimal medical care, those needing escalation of treatment and admission to hospital and those discharged in the community undergoing assisted rehabilitation programs.

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