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Special report

COVID-19: ensuring our medical equipment can meet the challenge

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Abstract

To predict the spread of coronavirus disease globally and consequently prepare the hospital facilities with the required technology is a challenge. The availability of essential medical equipment to support patients affected by Covid-19 is globally limited.

Areas covered: This perspective gives a technical view of the pandemic focusing on the main actions taken by regulatory agencies to cope with the shortage of devices. The risk/benefit assessment and the main infection control policies in the clinical practices are also looked at.

Expert opinion: Regulatory agencies have amended their medical devices directives to address the pandemic, but each in a different way. In this exceptional situation scientist and technology experts in collaboration with medical specialists should work together to re-assess the risk analysis on medical equipment management and their use and re-use in this context with the aim to improve global healthcare. Every effort must be made to provide the necessary devices at least with the minimum acceptable performances for Covid-19 patients while maintaining a high standard of safety for users. The aim of the present manuscript is to highlight the technical challenges in order to prevent, through targeted actions, operating standards from falling below the standards of care due to a lack of medical devices

Keywords

Covid-19, medical devices, equipments, regulatory, healthcare,

Article highlights:

- Predict the global spread of coronavirus disease and consequently prepare the hospital facilities with the required technology is a challenge
- Covid-19 patients require a fully equipped ICU facilities with mechanical ventilation devices and accessories, monitoring systems, infusion pumps for nutrition and drugs/fluids delivery. Less severe patients mainly requires high flow nasal cannula, Continuous Positive Airway Pressure ventilation/ non invasive ventilation and monitoring.
- Local resources and constraints will impact how the provision of the above equipments can best be implemented
- The availability of essential medical equipments to support patients affected by Covid-19 is globally limited and the regulatory agencies have acted differently
- Scientist and technology experts in collaboration with medical specialists should work together to re-assess the risks analysis on medical equipment management in order to facilitate the local health care institutions

Introduction

To predict the global spread of coronavirus disease and consequently prepare the hospital facilities with the required technology is a challenge motivated by many cultural, socio-economic and political grounds. Forecasts are currently mainly based on observed trends in China, South Korea and Italy where different levels of restrictions have been taken.

Moreover, the average age in China is of 8 years lower than in Italy (37 vs 45.9 years) (similar situation in other European countries) and the over 65 are 10 % less (respectively 12.6% vs 22.8%). The higher number of comorbidities and the fragility of elderly patients may have a relevant impact on the proportion of patients who need healthcare support and on mortality [1]. It could, almost in part, explain the higher proportion of patients admitted in intensive Care Unit (ICU) in Italy, >10% [2] comparing to China, 5%. The planning of new facilities for the coronavirus disease (Covid-19) patients in Europe and other countries should carefully consider the data that are emerging from Italy and particularly on the different spreads observed in three lockdowned regions. The Italian trend observed at a regional level can be an interesting model that highlights the difficulties of predicting the extent of the disease and, above all, the number of hospitalized patients. The National healthcare system in Italy transfer to a regional level a significant autonomy in determining the macro structure of their health organization. We briefly analysed the trend of the available data regarding the hospitals and intensive care units (ICUs) admission and the proportion of patients who needed an intensive care support in these regions. Clinical indications and medical equipments required to treat these patients are reported focusing on technical and safety notes. Actions taken by regulatory agencies to address the emergency and the main challenges to be faced have discussed based on our experience. The aim of the present is to highlight the technical challenges, that will be widely addressed to policy makers and healthcare institutions, in order to prevent, through targeted actions, operating standards from falling below normal standards of care [3].

Healthcare and Intensive Care Units load

As describe by Grasselli [4] a positive patient was firstly found on February the 20th in Codogno, Lombardia Region (LR) (10 million inhabitants), Italy: a cluster of unknown magnitude was present and additional spread was likely based on the assumption that secondary transmission was already occurring, a containment was provided in the area. Similarly, in the Veneto Region (VR) (5 million inhabitants) where the same were imposed Severe measures of containment were progressively expanded due to further cluster identified also in Emilia Romagna, enforcing social distancing for the entire population, isolation of all positive cases, forcing quarantines of entire households close to anyone with positive swab, and closing all schools and universities. Further containment measures have been issued up to a decree to lock down the whole country on March the 10th. The up mentioned regions are bordering, notwithstanding they have implemented the same containment policies, at the same time, they have a completely different virus spread and hospitalized patients as featured by figure1 [5]. So far any attempt to justify a such a discrepancy turned out to be unfounded and any model that tried to fit both trends (mainly Veneto and Emilia vs Lombardia), has failed. With the current knowledge of the disease, a model that can be universally validated seems to be unavailable. It should be at least, but not only, adjusted considering the initial spread (outbreaks), the containment policy, the containment strategy (e.g. laboratory tests per thousand inhabitant), the protective measures, the population demographic and probably also the density of inhabitants per square meter (magnitude of the metropolitan area). Moreover the expected efficacy of other mitigation efforts taken to slowdown the virus spread are noticeable in ICU several days after their implementation [1]. There's currently no standard of care for these patients, several clinical trials are ongoing, healthcare resources are limited and ICU length of stay may differ considerably. Nevertheless, the proportion of hospitalized patients who have required an intensive care unit (ICU) support on the above regions is relatively stable (Average-Maximum: LR:13%-18%, ER:12%-13.5% and VR:22.5%-25%, Figure 2). Modelling the number of hospitalized patients can be a reliable strategy to predict the real load on hospital facilities. The data monitoring from our group in Padova (<https://r-ubesp.dctv.unipd.it/shiny/covid19italy/>) showed several signs that the overall efforts of the Veneto Region are actually proving their effectiveness in slowing down the outbreak, with a significant number of

inpatients and people in intensive care avoided during the first week of the epidemic. From the above reported data on the magnitude on ICU admissions, some facilities will face with an enormous demand of medical devices to meet the patient care needs. In Europe the sub-regions of Italy, France, the Netherlands and Spain have already reported healthcare system saturation due to very high patient loads requiring intensive care [6].

Patient care, medical equipments

The Clinical management of severe acute respiratory infection for coronavirus patients published by the World Health Organization (WHO) [7] give some technical address alongside clinical ones: for patients admitted to hospital with severe acute respiratory infection (SARI) and respiratory distress, hypoxaemia or shock and target SpO₂ > 94%, it is recommended to provide supplemental oxygen therapy immediately; “all areas where patients with SARI are cared for should be equipped with pulse oximeters, functioning oxygen systems and disposable, single-use, oxygen-delivering interfaces (nasal cannula, nasal prongs, simple face mask, and mask with reservoir bag)”. In the most severe cases, COVID-19 can be complicated by acute respiratory disease syndrome (ARDS), sepsis and septic shock, multiorgan failure, including acute kidney injury (AKI) and cardiac injury [7]. These patients require a fully equipped ICU facilities with mechanical ventilation devices and accessories, monitoring systems, infusion pumps for nutrition and drugs/fluids delivery. A comprehensive list of medical devices for Covid-19 and related standards is available on the WHO disease commodity package [8]. Furthermore Renal Replacement Therapy (RRT) system to treat AKI and Fluid Overload (FO) [9] and Extracorporeal membrane oxygenation (ECMO) are also devices to consider [10]. In a retrospective study [11] 59% of the cases developed SEPSI, 15% AKI, and 5% were treated with RRT. Studies specifically focused on CRRT as supportive therapies for the Covid-19- septic patients are currently lack but treatments and devices aimed to reduce the cytokine storm associated with the Covid-19 [12] have been extensively reported [13]. For less severe patients high flow nasal cannula, Continuous Positive Airway Pressure / non invasive ventilation (CPAP/NIV), monitors and dedicate equipment are also necessary and should be provided to the respiratory, infectious disease or COVID-19 dedicated units.

Regulatory actions and risk/benefit assessment

Local resources and constraints will impact how the provision of the above equipments can best be implemented, always fulfilling with the care standards. Medical devices regulatory, the CE Mark in the European Union (EU), the Food and Drug Administration FDA-approval in the United States (US), the Australian Regulatory Guidelines for Medical Devices (ARGMD) and other similar procedures for other countries, essentially performs the same functions assessing the safety and efficacy of devices. The “general safety and performance requirements” of the European Medical Device Regulation (MDR) [14] (postponed to May 2021), defined on Annex I, is extremely clear and can be used as reference: devices “shall be safe and effective and shall not compromise the clinical condition or the safety of patients, or the safety and health of users...” and “...any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient...” this in the context of “the generally acknowledged state of the art”. To provide these evidences the benefit-risk determination is required. It is based on the determination of “all assessments of benefit and risk of possible relevance for the use of the device...” where risk is defined in MDR-Article 2 as the “combination of the probability of occurrence of harm and the severity of that harm”. All the above-mentioned regulatory programs are risk-based and are normally evaluated in routine patient care. The current demand for medical facilities, particularly for those related to the ICUs, exceeds the local availability with potential serious

consequence on patients care. Benefits, which includes the impact on patient health, quality of life and on survival, and the risks (no further available therapies) are assessed differently in such context. In this perspective, the regulatory agencies have acted differently. The Food and Drug Administration (FDA) allow medical device makers to more easily make changes to existing products, such as changes to suppliers or materials[15]. Furthermore, to permit for the emergency use in health care settings of certain ventilators, anesthesia gas machines modified for use as ventilators, and positive pressure breathing devices, FDA issued an Emergency Use Authorization (EUA) [16]. In particular the use of a ventilator for multiple patients simultaneously, has been made possible utilizing dedicated ventilator tubing connectors.. A guideline on how to utilize anesthesia ventilators, normally not labelled for long term ventilatory support, has been provided by American Society of Anesthesiologists and Anesthesia Patient safety foundation [17]. Health Canada also look to approvals granted by others regulatory authorities in deciding whether to approve an application for the importation or sale of COVID-19-related medical devices. Intended use of existing devices, not originally COVID-19-related, could also be expanded under this Interim Order. The United Kingdom (UK) Medicines and Healthcare products Regulatory Agency MHRA authorise industries to supply a non-CE marked device in the interest of the protection of health [18] establishing a fast-track approval of medical devices during COVID-19 outbreak. Furthermore, specification for ventilators to be used in UK hospitals during the coronavirus (COVID-19) outbreak has been issued [19], promoting and boosting the manufacturers on further developments. The European commission provide a guideline on Medical Device requirements [20]. An interest Annex on the standards to comply with, under various jurisdictions of the International Medical Device Regulators Forum, highlight how a global harmonization is hard. The common effect of these initiatives is to increase the availability of the devices in the respective countries, but without a coordination between them. The creation of regional and international networks allows the timely distribution of devices where they are more needed. Moreover, hospitals and stockholders must be prepared to utilize anesthesia units for ICU ventilation, within the required sources and supplies. Actions aimed at facilitating and standardizing device management and resources optimization at the hospital level, as WHO has done for patients[7], has not yet been widely implemented. The involvement of repurposed hospital staff to manage and support ICU physicians may strongly take advantage on a such documentation. Some exceptions on actions aimed to support the workload during a crisis are those done by FDA in attempt to minimize the risk of exposure to coronavirus, reconsidering the benefit/risk for the remote controls systems (non-invasive, vital sign-measuring devices). Extending, temporary, their use so that health care providers can use them to monitor patients remotely [21], the need for hospital visits are reduced and the risk of exposure to coronavirus minimized. With the aim to highlight the challenge healthcare institutions and hospitals face with, when evaluating the infection control policies and practices related to the medical equipment use, we summarize the most common issues. Firstly, an adequate training to personnel and appropriate protocols are mandatory to prevent hospitals became the main Covid-19 carriers [3]. A strategy for selecting the devices for covid-19 patients, especially for ventilators (intensive care, transportable, anesthesia) has to be implemented, including the training for the new ones. To mitigate the high demand for ventilators, one strategy that hospitals can use, is to split the ventilator to serve two patients. We have several concerns about this technique, but it is allowed in some countries and goes beyond the purposes of our analysis. To reduce the risk of spreading the disease, filters on the exhalation limb of ventilator circuits can be placed, but devices performance must be often evaluated. A decrease on efficiency can in fact occur. Breathing circuits, and any other devices that are exposed to the patient's oral secretions are also potential sources of contaminations. When a ventilator is used in a hazardous environment, it is recommended that gas delivered to the patient comes from either a pressurized medical-grade oxygen source and/or filtered ambient air passed through the Fresh Gas/Emergency Air Intake (or through the Fresh Gas Air inlet using an appropriate filter). A reduction in the

workload for the management of the device is mandatory. RRT can be performed utilizing regional citrate anticoagulation: circuit life span is higher and technical downtimes due to central venous catheter malfunction or circuit/filter coagulation are avoided[22]. The more easier and effective protocol for device disinfection should be adopted. The reutilization of a device, even not envisaged by the manufacturer, can be considered re-evaluating the benefit/risk ratio. According to the degree of risk of infection associated with the use of the device they are categorized in three classes by the FDA. In Europe, the MDR defines a new reusable/reprocessed class I device (Ir) where safety and efficacy of the cleaning, disinfection and sterilization processes have to be supported by the manufacturer. An extreme example is the case of helmets for non-invasive ventilation that may delay or prevent the need of an endotracheal intubation [23] in the context of limited availability of devices. Manufacturers, under particular circumstance, may try to provide actions aimed to mitigate (not eliminate) the risk of cross-contamination when reutilized. Hospital institutions, involving the risk prevention unit, may also evaluate their re-use. Generalizing, when the destination use and the utilization, differs from those provided by the manufacturer, a minimally acceptable performance must be guaranteed in order to ensure an adequate clinical benefit and prevent increased harms. In this exceptional situation scientists and technology experts in collaboration with medical specialists should work together to re-assess the risks analysis [24] on medical equipment management and to search for the most appropriate solutions globally. Demand to local institutions these responsibilities may impact on patient safety as the case of extension tubing applied to extracorporeal treatments[25]. Procedure and adequate training to all the healthcare workers should be provided in order to prevent cross-contaminations and safety. Figure 3 summarizes the information flows.

Conclusions

The availability of essential medical equipments to support patients affected by Covid-19 is globally limited. Our data on the ICUs load confirms the enormous pressure they will be under. Our review on the measures taken by countries to address this criticality, highlights the limited availability of dedicated actions. Furthermore, there is no link between them, discouraging a wide action. A globally harmonised regulation for the most useful medical devices for coronavirus patients can standardise their production and thus ensure compliance with all national legislation. Furthermore, a guideline on how to handle medical equipments under the Covid-19 emergency, as done by WHO for the management of patients, is of utmost necessity, leaving room for dangerous actions. In this exceptional situation scientists and technology experts in collaboration with medical specialists should work together to re-assess the risks analysis [24] on medical equipment management and their use (and re-use) in a biohazard context with the aim to improve the global healthcare. Every effort must be made to provide the necessary devices at least with the minimum acceptable performances for Covid-19 patients while maintaining a high standard of safety for users. Predicting when and where exactly to allocate these resources with the current knowledge of the disease is a challenge. Demand mitigation can currently only occur when early and appropriate virus containment measures are provided, followed by a rapid and effective response in handling positive cases.

Expert Opinion:

Clinical management of Covid-19 patients has been promptly updated by WHO following the most recent evidences. Medical devices, in absence of a dedicated medical therapy, are in the forefront of supporting critically ill patients. Healthcare institutions would benefit from guidance on how to make the best use of hospital technology and resources.

Several efforts by national healthcare institutions are providing actions and guidance on possible solutions to meet the increased demand of medical equipment. A coordination may improve global knowledge optimising strategic resources. Regulatory agencies should also try to define a shared documentation on the minimum standard of performance and essential requirements to treat patients with Covid-19 facilitating and stimulating manufactures in investments and new production. Standard procedure based on a revisited risk/benefit analysis contextualized to the current crisis may also be appreciated by several healthcare institution who daily face with these multidisciplinary activities.

In five years, the complex world of medical devices will harmonize the different approaches in the evaluation of the existing and new technologies. The new European Directive on MDR medical devices will further coordinate the efforts of national manufacturers and health institutions in the regulatory process, which is strongly focused on producing clinical evidence. From the other side, hospitals and clinicians should be ready to give adequate support with the common aim to improve global health. In this context, the lessons from national health institutions in the management of medical equipment in the Covid-19 crisis must be exploited and further strengthened by establishing a network of national health institutions.

List of abbreviations

AKI Acute Kidney Injury

ARGMD Australian Regulatory Guidelines for Medical Devices

Covid-19 Coronavirus disease

FDA Food and Drug Administration

ECMO Extracorporeal Membrane Oxygenation

EU European Union

ICU Intensive Care Unit

WHO World Health Organization

MHRA Medicines and Healthcare products Regulatory Agency

MDR Medical Device Regulation

SARI Severe Acute Respiratory Infection

Availability of data and materials

Data on Covid-19 are available here: <https://r-ubesp.dctv.unipd.it/shiny/covid19ita/>

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Authors' contributions

Paper conception: F Garzotto; providing intellectual content: F Garzotto, E Ceresola, G Meneghesso, G Opocher; data analysis: D Gregori, C Lanera, S Panagiotakopoulou, E Ceresola, F Menotto, M Casarotto; paper final approval: MG Bonavina, G Meneghesso, G Opocher; Paper draft: F Garzotto, E Ceresola, M Benozzi, C Lanera; revising paper: S Panagiotakopoulou, G Spina, MG Bonavina; literature investigation: S Panagiotakopoulou, M Benozzi, F Menotto, M Casarotto; Supervision: MG Bonavina, G Spina, D Gregori.

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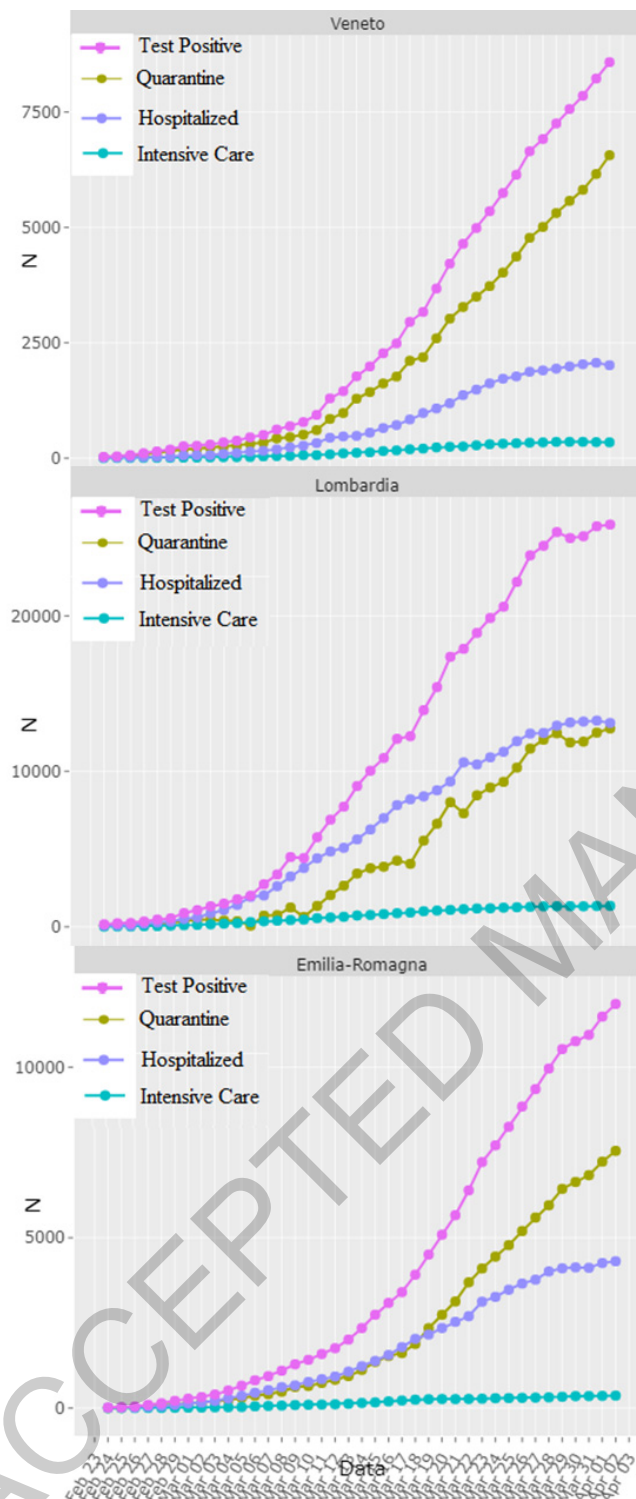


figure 1

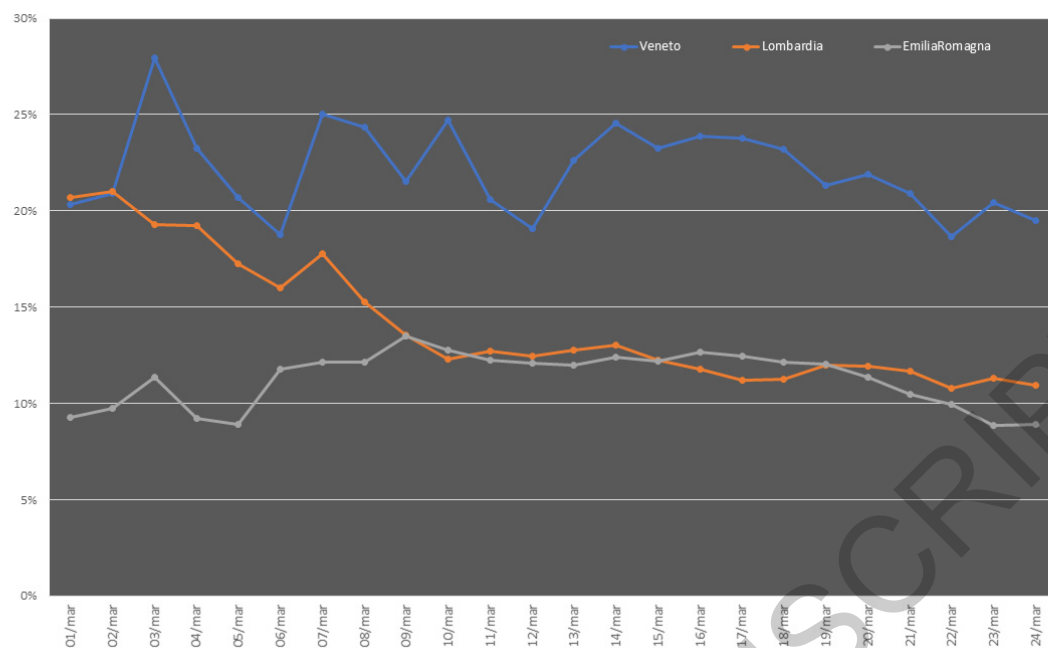


Figure 2

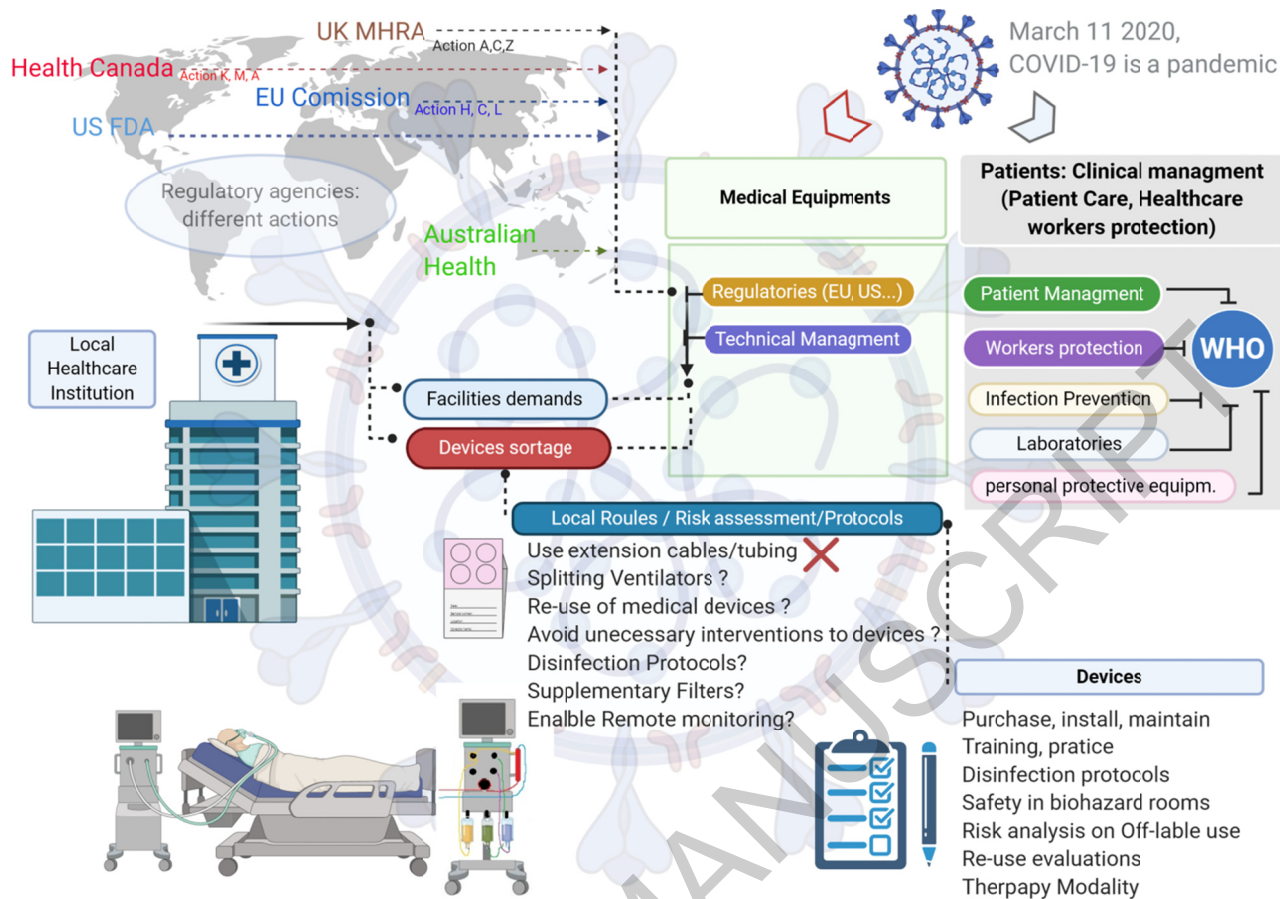


Figure 3