Accessing unproven interventions in the COVID-19 pandemic: discussion on the ethics of ‘compassionate therapies’ in times of catastrophic pandemics

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ABSTRACT
Since the onset of the SARS-CoV-2 pandemic, an array of off-label interventions has been used to treat patients, either provided as compassionate care or tested in clinical trials. There is a challenge in determining the justification for conducting randomised controlled trials over providing compassionate use in an emergency setting. A rapid and more accurate evaluation tool is needed to assess the effect of these treatments. Given the similarity to the Ebola Virus Disease (EVD) pandemic in Africa in 2014, we suggest using a tool designed by the WHO committee in the aftermath of the EVD pandemic: Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI). Considering the uncertainty around SARS-CoV-2, we propose using an improved MEURI including the Plan–Do–Study–Act tool. This combined tool may facilitate dynamic monitoring, analysing, re-evaluating and re-authorising emergency use of unproven treatments and repeat it in cycles. It will enable adjustment and application of outcomes to clinical practice according to changing circumstances and increase the production of valuable data to promote the best standard of care and high-quality research—even during a pandemic.

INTRODUCTION
Research on COVID-19 evolved as quickly and intensively as the disease itself. The first patient with COVID-19 in the USA was confirmed on 20 January 2020.1 In terms of treatment, the use of an antimalarial drug as a potential therapy (unapproved by the Food and Drug Administration (FDA)) began in China in February–March, 2020.2,3 Initially, the drug appeared beneficial. However, the FDA very quickly issued a Drug Safety Communication regarding known side effects of hydroxychloroquine and chloroquine, including serious and potentially life-threatening heart rhythm complications.2,4 A week later, on 1 May 2020, the FDA issued an Emergency Use Authorization (EUA) for remdesivir in the treatment of COVID-19, stating that the potential benefits of the drug outweigh the risks. EUAs offer a lower regulatory bar than full FDA approval. Remdesivir, like chloroquine, is a repurposed drug previously used to treat Ebola Virus Disease (EVD) and other viruses. Authorisation of the medication followed a clinical trial, which demonstrated encouraging results as we will discuss later. Nonetheless, although some drugs have been shown to have some effect (ie, dexamethasone and monoclonal antibodies), there is yet no proven effective treatment as of the time of writing this paper to reliably prevent severe complications from COVID-19. In fact, the most effective preventive intervention so far is massive worldwide vaccination.

The FDA communication on antimalarial drugs and its subsequent EUA regarding remdesivir exemplify the process of approval for off-label drugs used in the treatment of patients with COVID-19. The term ‘off-label’ has various definitions.4 For the purpose of this article, we will use the WHO definition, which is the most appropriate in a pandemic setting: ‘A repurposed, unregistered, experimental, unproven, untested (in humans/animals) or a trial investigational drug’.5 In routine clinical practice, the use of repurposed medications is widely used in disciplines such as critical care medicine,6 paediatrics7 and oncology.8 In general, the main requirements for using repurposed medications are ensuring quality, safety, efficacy, evidence for novel use and affordability.9 In the past decade, ethicists across the globe have advocated for more deliberate conduct and strict regulation for off-label prescribing and use.10–12 At the same time, the need to identify, report and research repurposed drugs for off-label use has been discussed,13 including the definition of the requirements for expanded access to investigational therapies.14

In the USA, in order to balance speed and safety, access and data collection, and short-term and long-term goals, the FDA provided an ‘expanded access’ pathway. The main goal of the expanded access pathway is to allow seriously ill patients access to interventions when they do not qualify for trials. Notably, the requirement to ensure that expanded access does not interfere with ongoing research is a constraint on expanded access aimed to protect public health interests.15 In 2018, the ‘Right to Try’ Act was enacted in the USA to allow terminally ill patients to access investigational drugs. Unlike expanded access, this pathway requires limited FDA involvement in implementation of the Right to Try Act. The FDA role in this pathway is largely focused on those obligations outlined in the law, specifically the receipt and posting of certain information submitted regarding Right to Try use.16 This track thereby bypasses the standard FDA review procedures,17 a pathway criticised by researchers.18 In response to the uncertainty regarding the use of unproven interventions, in this paper, we examine when and how unproven therapies should be used in public health emergencies. For that purpose, we focus on research conducted during the Ebola virus epidemic of 2014 as a key example. We then suggest following the protocol designed by the WHO committee for public health emergencies:
Monitored Emergency use of Unregistered and Investigational Interventions (MEURI). In addition, given the uncertainty around SARS-CoV-2 and the dynamic nature of research into effective therapies, we suggest dynamically monitoring, analysing, re-evaluating and re-authorising emergency use by applying the Plan–Do–Study–Act (PDSA) tool. The combined use of MEURI protocol and PDSA tool we argue, will enable swift adjustment and application of outcomes to clinical practice in changing circumstances and increase the production of valuable data.

LESSONS FROM EBOLA: THE CHALLENGE IN DETERMINING THE JUSTIFICATION FOR CONDUCTING RCTS OVER PROVIDING COMPASSIONATE USE IN AN EMERGENCY

International and national guidelines emphasise the need for ethical conduct and evidence-based research even during disasters and emergencies. One important challenge faced by researchers in this regard is the question of primacy of randomised controlled trials (RCTs) over compassionate use of unproven drugs during public health emergencies.

Generally, the more widespread and severe the disease, the more compelling it is to allow earlier access to experimental treatments. During the 2014 EVD epidemic in West Africa, no proven intervention was available accompanied by a scarcity of unproven medications and a high mortality rate. Consequently, the justification for compassionate use as opposed to RCTs was debated among researchers. One of the notable opponents of RCTs during the harsh EVD epidemic was Adebamowo. In response, Rid and Emanuel emphasised the importance of strengthening health systems and basic infrastructure rather than focusing on experimental treatments. On the other hand, Shaw and Cox et al argued that experimental Ebola treatments or vaccines should only be deployed in clinical trials meeting the ethical principles of research.

The U.S. Bioethics Commission being more permissive, argued that ‘no one clinical trial design is ethically required in the context of the current Ebola epidemic or research conducted during a public health emergency more generally. Rather, the full range of trial designs that protect and promote the welfare of participants and are capable of yielding credible and reliable results should be considered.”

In practice, RCTs for EVD therapies were conducted by the National Institute of Health (NIH) and other entities, but many were unable to produce results as the pandemic was gradually contained with public health measures. In contrast to the current COVID-19 pandemic, only one trial with an unusual design involving a ring vaccination strategy (randomisation to earlier or delayed vaccination among different groups of people that has come into contact with an infected individual) was able to produce results that demonstrated high efficacy.

Six years after the EVD outbreak, COVID-19 emerged, refuelling the debate over compassionate use versus clinical trials and making guidance in emergency contexts essential. It is important to note that there is a difference in context between EVD and COVID-19. In particular, the fact that COVID-19 is characterised by a lower mortality rate, specifically among young people, increases its contagiousness, thereby causing more cumulative harm than Ebola. As we argue in the next section, given those factors, MEURI was the appropriate mechanism to implement at the early stages of the pandemic.

OFF-LABEL USE OF INTERVENTIONS IN THE COVID-19 PANDEMIC

The COVID-19 pandemic of 2020, undoubtedly one of the major public health challenges of the past century, brings the question of off-label use dramatically back to the table. The virulence, high mortality among the elderly and those with underlying conditions, and the fact that patients may be infectious in the pre-symptomatic period have put pressure on governments, researchers and pharmaceutical companies to find therapies or a vaccine as soon as possible. While currently (September 2021) vaccines are available in most western countries, from its onset, coping with the unexpected and overwhelming public health challenge of the COVID-19 pandemic has encouraged the use of unproven medications. These include antiviral agents such as remdesivir, lopinavir/ritonavir, favipiravir, baricitinib, hydroxychloroquine and chloroquine, plasma from convalescent patients, and anti-cytokine treatments such as tocilizumab.

RCTs in various forms were conducted as early as January 2020 in China. According to Kalil, the type of RCTs to be prioritised in an outbreak is one with an adaptive design. These are able to rapidly accept or reject multiple experimental therapies throughout the trial while being adequately powered for meaningful clinical outcomes. Two examples of RCTs were the WHO’s SOLIDARITY trial and the UK’s RECOVERY trial.

In just 6 months, SOLIDARITY, the world’s largest trial on COVID-19 therapies, indicated that remdesivir, hydroxychloroquine, lopinavir/ritonavir and interferon regimens have no effect on 28-day mortality. In RECOVERY, a controlled, open-label trial comparing a range of possible treatments in patients with COVID-19, corticosteroid therapy, such as dexamethasone, increased 28-day survival in patients that had developed acute respiratory distress syndrome.

At the same time, the conduct of clinical trials in a public health emergency may be challenging for several reasons. To begin with, in some cases, widespread compassionate use made it very difficult to conduct RCTs and determine whether interventions such as convalescent plasma actually worked as patients had no incentive to join RCTs when they could access therapies outside of the trial. In addition, given time constraints, recruitment of participants is time consuming and it is difficult to identify the best option of the many possible treatments and determine what may be effective. If patient recovery requires orchestration of complex stage-dependent therapies, designing simple RCTs aiming to isolate the impact of specific agent may be impossible or even lead to the incorrect conclusions due to irrelevant design. For example, in the current pandemic, most of the RCTs that were conducted in order to appreciate the effect of anti-interleukin 6 receptor antibodies have excluded patients on dexamethasone, which is now considered the main anti-inflammatory therapy. The fact that the placebo group did not receive steroids is not enough to exclude the possibility that...
these agents may prove efficacious in the context of a broader anti-inflammatory therapy just as antibiotic medication by itself may fail in septic shock patients if it is given without concomitant fluids. The case of COVID-19 is especially unique since this disease is complex and multistaged and has an extremely high mortality rate among ventilated patients. Those are only some of the obstacles in generating high-quality data in the midst of a pandemic.45,46

Alas, a more significant barrier in carrying out well conducted RCTs is the need for large sample sizes. Moreover, when trials do not provide clear evidence of an effect, the results are ‘erroneously’ interpreted as ‘evidence’ of no effect.47 The Danish trial of face masks for COVID-19 prevention47 is a good example of that practice. The researchers based their sample size calculation on the assumption that a simple recommendation to use masks for protection outdoors would halve the risk of infection. They based their sample size calculations on observational evidence on other ‘non-SARS’ respiratory viruses that supported the efficacy of face masks in healthcare environments but eventually the study was underpowered, rendering the trial results of limited value for decision makers. We believe that a prior pilot study would have helped in understanding the real effect of face masks in patients with COVID-19 and allowed for a more realistic power calculation.

Thus, it seems mandatory to base our rational of new intervention on structured observations that may indicate benefit with minimal harm to patients. Moreover, as some authors suggested, it may be considered unethical to recruit participants to a study that is unlikely to yield conclusive results.48 Finally, when patients are asked to join an RCT, the rational needs to be clarified to them.

To summarise, in our view, compassionate therapies and treatments are a strong tool that can provide preliminary data for RCT designers not only for power calculations but also for better decisions regarding inclusion and exclusion criteria. In such circumstances, it is possible to design proper RCTs with the number of patients needed to be recruited based on more realistic assumptions. By using data from compassionate care, clinicians could avoid underpowered studies that may miss a potential beneficial effect.

In the absence of relevant animal models or observational studies, the experience gained from ongoing compassionate therapies may provide the only knowledge on adverse effects and potential efficacy.

TREATMENT OF PATIENTS WITH COVID-19 IN ISRAEL

In Israel, the SARS-CoV-2 outbreak began in mid-March 2020. The Ministry of Health defined virus-specific hospital wards where patients were admitted and treated regardless of the severity of their illness. There were no national recommendations at the time for a standard of care. Consequently, physicians treated patients individually according to their own perception and experience. From our own experience, intensive care physicians focused on the immediate improvement of patients’ prognosis under their care as the following two studies indicate.

Amir et al50 published a nation-based registry study of critically ill patients with COVID-19 that were admitted to Intensive Care Units (ICUs) in Israel during the first wave. The overall mortality rate was 56%, which was considered much lower than the mortality worldwide. The authors recommended a prospective evaluation of the role of antimicrobial therapy in critically ill patients and suggested that their findings highlight the importance of novel therapies, antibiotics use and the availability of resources such as ICU beds and ventilator support in the treatment of patients with COVID-19.

Lev et al50 reported a very low mortality rate when using a cytokine-based decision support algorithm intended to individually modify steroid dose and duration. In this report coming from Israel, the ICU mortality rate was less than 10% with a 60-day mortality rate of 25%. We claim that these kind of pilot studies of combination of compassionate care therapies are a promising way to pave the way for larger broad scale studies. Moreover, luckily the medical system in Israel was not overburdened by the first wave in terms of patient load, thus not compromising the standard of care.

In terms of regulation, in September 2020, the Ministry of Health issued recommendations for monitoring and treating patients with COVID-19 in Israeli hospitals.51 The guidelines include definitions of illness severity and provide recommendation for care according to severity. These guidelines represent the current expert consensus regarding standard of care. However, while there is no national registry or database for treatments and results let alone a database of clinical trials within Israel (other than the voluntary internal databases of several hospitals), there is a U.S. National Library of Medicine resource that provides an international registry database of privately and publicly funded clinical studies conducted around the world in 50 states and 220 countries.52 Following the EVD epidemic, the WHO designed a tool to specifically respond to this challenge. We will discuss this tool, MEURI in the next section.

UNPROVEN INTERVENTIONS IN PUBLIC HEALTH EMERGENCY USING MEURI

During the EVD epidemic, the WHO Ethics Working Group39 coined the term MEURI. MEURI is based on the ethical principles of respect for patient autonomy and beneficence. It requires that countries not authorise MEURI unless it has first been recommended by an appropriately qualified scientific advisory committee especially established for this purpose. MEURI enables an exceptional decision-making process for individuals. However, it is not a substitute for properly designed trials. This model attempts to reconcile the conflict of interests between the individual and those of the public during catastrophic events.

In 2016, the WHO issued a Guidance Document for Managing Ethical Issues in Infectious Disease Outbreaks.53 Guideline 9 of the document discusses emergency use of unproven interventions outside of research in the context of an outbreak characterised by high mortality and recommends the following conditions for approving such interventions:

1. No proven effective treatment exists.
2. It is not possible to initiate clinical studies immediately.
3. Data providing preliminary support of the intervention’s efficacy and safety are available at least from laboratory or animal studies, and use of the intervention outside of clinical trials has been suggested by an appropriately qualified scientific advisory committee on the basis of a favourable risk–benefit analysis.
4. The relevant country authorities as well as an appropriately qualified ethics committees have approved such use either nationally or in certain situations, such as an Institutional Review Board.
5. Adequate resources are available to ensure that risks can be minimised.
6. The patient’s informed consent is obtained.

7. The emergency use of the intervention is monitored, and the results are documented and shared in a timely manner with the wider medical and scientific community.

In early 2020, the WHO reported many ongoing clinical trials testing various potential antivirals. It was emphasised that doctors should use investigational anti-COVID-19 therapeutics only under ethically approved, randomised and controlled trials. If conducting an RCT is not possible or until it is conducted, the WHO suggested the use of investigational therapeutics in the structure of an MEURI.

In late 2020, the Pan American Health Organization and the WHO published a document shedding light on the use of MEURI during the COVID-19 pandemic. The document discusses the development of the MEURI protocol. It states:

At minimum, protocol must include the following: (a) background; (b) scientific justification on the basis of the recommendations of a scientific committee; (c) objectives; (d) population to be offered the intervention; (e) risks and potential benefits; (f) scientific data to be collected to provide information on the intervention’s safety and efficacy; (g) plan to offer the intervention to patients; (h) informed consent documents and details about the process; (i) data sharing plan; and (j) measures to protect confidentiality. The protocol must also include the planned time frame for offering the intervention under MEURI and presenting it to be evaluated as part of a research protocol (ideally a randomized clinical trial).55

Although MEURI is a warranted and valuable tool, it has several limitations. The first limitation is the difficulty in implementing MEURI successfully across a large country or in a decentralised healthcare system such as the USA, including the challenge of coordinating the responses of individual clinicians. The second limitation, related to the first one, is that MEURI lacks a dynamic parameter in its framework that would allow for a repeated reevaluation of the protocol in order to produce high quality data—similar to data gathered through RCTs. To address those limitations, we suggest using the PDSA cycle to complement the MEURI model as we discuss in the following section.

DYNAMIC MEURI USING PDSA TOOL FOR RE-EVALUATION OF INTERVENTIONS AT A PUBLIC HEALTH EMERGENCY

Since the onset of the pandemic, researchers and clinicians have argued that the circumstances justify fast track institutional ethical review of repurposed drugs such as chloroquine, either by adhering to the MEURI framework or after ethical approval as a trial, as stated by the WHO. At the same time, others have challenged the use of MEURI without well-established guidelines/protocols: ‘...there may be a role for MEURI in COVID-19, but unconstrained, unevaluated use of therapeutics under the guise of compassionate use or panicked rhetoric about right-to-try must be aggressively discouraged in order for scientists to learn what regimens or vaccines actually work.’ (p. 3)55

In line with these concerns, we agree that the MEURI protocol by itself does not sufficiently resolve the need for fast and continuous data gathering and re-evaluation of the treatment protocols at the early stages of pandemic response. We therefore propose, before trials can be launched or in sites that cannot conduct clinical trials because they lack the infrastructure, applying the PDSA cycle as a complementary tool to MEURI for facilitating dynamic continuous re-evaluation, enabling data collection and planning of the effect size. The combination of MEURI and PDSA, we argue, will allow dynamic monitoring, analysing, re-evaluating and re-authorising emergency use in cycles and increase the production of valuable data.

PDSA was initially introduced as Plan–Do–Check–Act by Shewhart and was subsequently modified by Deming in the 1980s as a model of organisational development and leadership. The cycle includes four phases:

1. Identify the problem and plan a change to be tested or implemented (Plan).
2. Execute your plan, carry out your test or change (Do).
3. Implement, examine and study your actions based on the measurable outcomes agreed before starting out, collect data before and after the change and reflect on the impact of the change and what was learnt (Check/Study).
4. Act towards the next planning phase based on your previous actions, then plan the next change cycle or full implementation (Act).

PDSA became a widespread methodology used in many industries, encouraging continuous improvement at work processes as well as in patient safety and quality improvement programmes.56 It was first applied to healthcare by Langley in the 1990s. According to the Institute of Healthcare Improvement, the benefit of PDSA in healthcare is the ability to assess the process of a project relatively fast after

![Figure 1](https://example.com/figure1.png)

**Figure 1** The various stages of the dynamic MEURI protocol using PDSA cycles are described and performed repeatedly, and reevaluation is conducted at the end of each cycle. The various stages are differentiated by the colors. Red for the major planning stage, including understanding the background, provision of scientific justification on the basis of the recommendations of a scientific committee, description of objectives of the protocol, determination of a population to be offered the intervention, consideration of risks and potential benefits of the intervention and tailoring a plan to offer the intervention to patients. Purple for the doing stage including collection of scientific data aimed to provide information on the interventions’ safety and efficacy, obtaining informed consent following the provision of details about the intervention, its monitoring and reevaluation, sharing data and reassuring measures to protect confidentiality. Black for the studying stage, in which the intervention is evaluated as part of a research protocol, ideally a randomised clinical trial. MEURI, Monitored Emergency Use of Unregistered and Investigational Interventions; PDSA, plan–do–study–act; RCT, randomised controlled trial.
its implementation and, based on this assessment, determine further actions. The NHS ACT Academy\(^6^2\) states that using PDSA cycles enables you to test out changes on a small scale, building on the learning from these test cycles in a structured way before wholesale implementation. This way, the process of change is safer and less disruptive for patients and staff. PDSA is a tool used to investigate and improve medical care programmes in an organised and systematic process. It also helps medical managers and leading clinicians recognise problems and methodically fix them. Its iterative approach to test interventions allows for rapid assessment and provides flexibility to adapt the change according to feedback, thereby ensuring fit-for-purpose solutions.\(^6^3\) This is exactly the method the COVID-19 pandemic circumstances required, at least in the early stages before vaccination was initiated. Figure 1 illustrates how we propose to use the modified MEURI PDSA protocol: the various stages of the protocol are described and performed in a cycle, with reevaluation conducted at the end of each cycle.

Furthermore, in March 2020, this tool was already used in Hubei province in China to manage severe patients with COVID-19 for more than 50 days.\(^6^4\) According to Li and his colleagues, in the Hubei case, the intensive care medical staff from Heilongjiang province moved to Wuhan Union hospital to support the local staff. They faced numerous obstacles: unfamiliar working environment and workflow, non-independent elderly patients speaking in unfamiliar local accents, limited understanding of the disease, dealing with isolated patients, long working hours and team stress. Consequently, the support team decided to establish a new emergency management strategy by applying the PDSA cycle to dynamically summarise, analyse, modify and re-execute. In addition to applying PDSA cycles, the team took steps to strengthen the implementation of core medical care, increase the ratio of medical staff to bed, centralise management of intensive medical equipment, reasonably arrange working time to improve efficiency, use WeChat platform for communication and integrate psychological counselling.

Indeed, although in terms of effective treatment, interventions and protocols for patients with COVID-19, healthcare professionals still face uncertainty, the situation as of time of writing of this paper is dramatically different from the Hubei case in March 2020 both in terms of understanding the diseases and patient profiles and in the experience of medical staff treating patients with COVID-19. In addition, vaccination of the public and healthcare workers is now in full swing in many countries. However, in the initial stages of a pandemic or in sites that cannot conduct clinical trials because they lack the infrastructure, we agree with Meagher\(^6^5\) and her colleagues that ‘there is a compelling need to provide an evidence base that informs improved standards of care, develops novel interventions, and guides management... RCTs are often considered the ideal for grounding causal inference although, importantly, RCTs also exhibit epistemic limits for addressing population health. Adaptive and pragmatic clinical trial designs are often preferred as alternatives, but these designs also present challenging trade-offs between the type of knowledge produced and the prioritisation of direct benefits provided to participants.’ (p. 1120).\(^6^6\) Given those limitations of RCTs and its alternatives we recommend combining MEURI with the PDSA tool as illustrated. This approach takes into account changing circumstances and may be implemented locally even in large countries, such as China, or where healthcare is spread out. We believe this strategy may help the clinical research community guide interventions and treatment in an organised, meaningful and safe manner.

CONCLUSION

In cases of rapid, highly infectious and severe epidemics such as EVD and COVID-19, compassionate use of unproven drugs is considered ethically acceptable by international and national guidelines as well as by practicing clinicians and public health professionals. However, the guidelines for clinical trials of unproven interventions in such situations, in particular if the disease has high infection and mortality rates, are unclear with the adequate designs for its conduct controversial. In the current COVID-19 pandemic, urgent clinical trials in various forms have been performed since the early stages of the outbreak first in Wuhan China and later on worldwide.\(^6^7\) Designing trials is time and resource consuming given the extensive array of possible drugs to choose from. For example, 200 clinical trials for COVID-19 drugs have started in the first 18 months since the onset of the pandemic, many of which are not yet completed. Though understandable, this situation is ethically questionable.

As an alternative, at the initial stages of the pandemic response when the infrastructure for RCT is lacking or if a new vaccine resistant viral variant were to develop and spread rapidly, we propose using the MEURI tool and protocol as recommended by the WHO for public health emergencies.\(^6^8\) We further recommend improving it with the PDSA for monitoring, analysing, re-evaluating and re-authorising emergency use in cycles and planning effect size. PDSA has been applied to healthcare\(^6^9\)\(^7^0\) and was recently used successfully in China for managing severe patients with COVID-19 by ICU staff.\(^7^1\)

Dynamic MEURI using the PDSA cycle tool can facilitate adjustment and application of outcomes to clinical practice and may thus increase the production of valuable data even in a fragmented healthcare system and in the midst of a public health emergencies. We believe that this suggested approach would not only give patients the chance to try potentially beneficial therapies, but also would facilitate the production of vital knowledge and data that will help propagate more robust study designs.

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**REFERENCES**

19 Zuckerman S, Crit Care 2020;24(1).


