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LETTER TO THE EDITOR Open Access

Why participation in an international clinical trial platform matters during a pandemic? Launching REMAP-CAP in Japan

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Abstract

REMAP-CAP, a randomized, embedded, multifactorial adaptive platform trial for community-acquired pneumonia, is an international clinical trial that is rapidly expanding its scope and scale in response to the COVID-19 pandemic. Japan is now joining REMAP-CAP with endorsement from Japanese academic societies. Commitment to REMAP-CAP can significantly contribute to population health through timely identification of optimal COVID-19 therapeutics. Additionally, it will promote the establishment of a national and global network of clinical trials to tackle future pandemics of emerging and re-emerging infectious diseases, in collaboration with multiple stakeholders, including front-line healthcare workers, governmental agencies, regulatory authorities, and academic societies.

Keywords: Randomized controlled trial, REMAP-CAP (Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia), COVID-19, Emerging infectious disease

Main text

The coronavirus disease 2019 (COVID-19) has had a formidable impact, overstretching healthcare systems locally, regionally, and globally. The COVID-19 pandemic has enlightened us on various pillars of outbreak response, such as surveillance and contact tracing, testing, case management, infection prevention and control, and logistics [1]. Learning from such experience is necessary not only to prepare for subsequent waves of COVID-19 but also to establish a system to tackle emerging and re-emerging infections in the future.

Disseminating the message that COVID-19, an emerging infection causing an unprecedented pandemic, is curable can have a significant impact on the public and global society. Off-label and compassionate use of potential therapeutics was pervasive, particularly during the initial phase of the response; such drugs were often administered without controls, making it difficult to interpret their efficacy [2]. Furthermore, even when randomized controlled trials (RCTs) were conducted, a substantial number of them carried out in early 2020 were reported to be at risk of bias [3]. This indicates an urgent need for effective and efficient infrastructures and networks that can generate high-quality clinical evidence through multicenter clinical trials worldwide.

Randomized, embedded, multifactorial adaptive platform trial for community-acquired pneumonia (REMAP-CAP) is a unique clinical trial to identify an optimal combination of therapeutic management for CAP, especially COVID-19 in the current scenario (https://www.remapcap.org/). In REMAP-CAP, participants are “randomized” to one or more categories of

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treatment, called domains, which are tested simultaneously ("multifactorial") on a single clinical trial "platform" [4]. Research implementation is to be "embedded" in everyday clinical practice, easing the research burden at participating clinical sites. Furthermore, REMAP-CAP is designed to be "adaptive," using response adaptive randomization with Bayesian statistical methods, and substituting new therapeutic categories and interventions as knowledge accumulates. In other words, information from previously enrolled patients can be fed into the system to help guide the treatment of new patients.

REMAP-CAP was originally initiated by a limited number of countries, such as Australia, New Zealand, U.S. and Canada, and is now expanding rapidly, with COVID-19 patients being enrolled at almost 300 facilities across 19 countries as of March 2021 (https://www.remapcap.org/). As COVID-19 spread globally, its preplanned pandemic protocol was activated; therapeutic candidates for COVID-19 are continually being added to this platform [4]. Findings from REMAP-CAP have led to seminal studies demonstrating the efficacy of multiple therapeutics, including corticosteroids and interleukin-6 receptor antagonists [5, 6].

Japan is now joining the REMAP-CAP community (https://www.remapcap.jp). The Japanese Society of Intensive Care Medicine and the Japanese Association for Infectious Diseases have endorsed REMAP-CAP, making efforts to reach diverse medical professionals and health facilities across the nation. To make a real impact on society, evidence generated via REMAP-CAP should effectively guide front-line providers striving for therapeutic "game-changers." This will require collaborative efforts among governmental/regulatory bodies, private sectors, academia, and policy-makers.

In this regard, REMAP-CAP will provide an opportunity to reveal the known and unknown, or perhaps "unwritten," aspects of facilitators and obstacles to carry out high-quality, influential RCTs during health emergencies. If found feasible and implemented throughout the nation, the platform can become a one-stop solution for therapeutics for COVID-19, future emerging and re-emerging infections, and respiratory infections.

Health emergencies should not be an excuse to continue practicing "compassionate care." It is time to transform clinical practice from "neither evidence-based nor evidence-generating (NEBNEG)" to "sensibly evidence-based and sustainably evidence-generating (SEBSEG) [7]." With these acronyms, we wish to propose a slogan, "avoid NEBNEG practice, foster SEBSEG practice" through REMAP-CAP as a "new normal" among medical professionals. Consequently, with the collaboration of many other countries and partners through the REMAP-CAP community, collective wisdom will prevail.

Abbreviations

COVID-19: Coronavirus disease 2019; RCT: Randomized controlled trial; REMAP-CAP: Randomized, embedded, multifactorial adaptive platform trial for community-acquired pneumonia

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Authors' contributions

Kazuhiro Kamata, Kazuaki Jindai, Nao Ichihara, and Hiroki Saito contributed equally to this manuscript. All authors participated in the development of the concept of the manuscript. Kazuhiro Kamata and Kazuaki Jindai wrote the first draft, and Nao Ichihara and Hiroki Saito provided additional feedback on the first draft. All authors have edited and finalized the manuscript. All authors read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

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