

How to strengthen Japan's clinical research enterprise through large pragmatic adaptive platform trials and an efficient clinical research network: lessons from REMAP-CAP 現実主義に基づくアダプティブ・プラットフォーム試験と高効率臨床研究ネットワークにより日本の臨床試験体制を強化するために:REMAP-CAPにおける教訓



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2002年、横浜市立大学医学部卒業。循環器内科および救急診療に従事。2013年、ハーバード大学公衆衛生大学院修士課程卒業。2015年、横浜市立大学大学院博士課程卒業。2016年から現職。日本集中治療医学会の診療レジストリJIPADワーキンググループ メンバー。REMAP-CAP国際運営委員会および日本運営委員会 委員。書籍「これだけでわかる! 医療AI」(中外医学社)の一章「機械学習を取り込んで進展する次世代の医学研究」を執筆。

Graduated from Yokohama City University (YCU) School of Medicine in 2002. Engaged in clinical practice in cardiology and emergency medicine. Graduated from Harvard School of Public Health (Master of Public Health) in 2013. Graduated from YCU Graduate School of Medicine in 2015. Current position at the University of Tokyo since 2016. A member of the Japanese Society of Intensive Care Medicine JIPAD (Japanese Intensive care PATient Database) Working Group. A member of the International Trial Steering Committee and the Japan Regional Management Committee of REMAP-CAP.

REMAP-CAPは、パンデミック対策を主眼に置く国際共同アダプティブ・プラットフォーム試験 (adaptive platform trial、APT) であり、無駄を削ぎ落とした設計および実施手順に基づく現実主義的大規模試験 (large simple trial、LST) である。当初の目的に加え、すでにREMAP-CAP上で複数の試験が実施されている。国内では、約30の施設が参加しており、国内独自APTの準備も進んでいる。

APTおよびLSTは、従来答えを出せなかった臨床課題にエビデンスをもたらさう。また、国際共同研究への参加は、施設がノウハウを蓄積する機会となる。APT、LST、そして国際共同試験を臨床研究推進体制の中に適切に位置付けることが、本邦の臨床研究全体の発展につながりう。本発表では、APT、LST、および国際共同研究の特徴を述べ、この役割の広がりを紹介した上で、これを国内で活かす方策として以下を検討する：(1)大規模臨床研究ネットワーク構築の方策、(2)人材育成策、(3)法制度、研究助成、倫理審査、試験登録等のシステムの改善。

REMAP-CAP is an international adaptive platform trial (APT) with a primary goal of quickly responding to a pandemic. It is also a large simple/pragmatic trial (LST) that achieves scale by relatively simple design and minimum burden on sites. Despite its original goal, multiple clinical trials for drug approval are already running on REMAP-CAP. In Japan, approximately 30 hospitals are participating in REMAP-CAP. Some original APTs are also being developed.

APTs and LSTs may allow generation of otherwise difficult clinical evidences. Joining international clinical trials allows researchers to learn. Appropriately positioning APTs, LSTs, and international clinical trials will strengthen the entire clinical research enterprise. The following are important considerations for maximizing this opportunity: (1) Strategies for developing large clinical research networks, (2) Strategies for developing necessary human resources, and (3) Strategies for improving related regulations, funding programs, ethical review, trial registration, and other related systems.

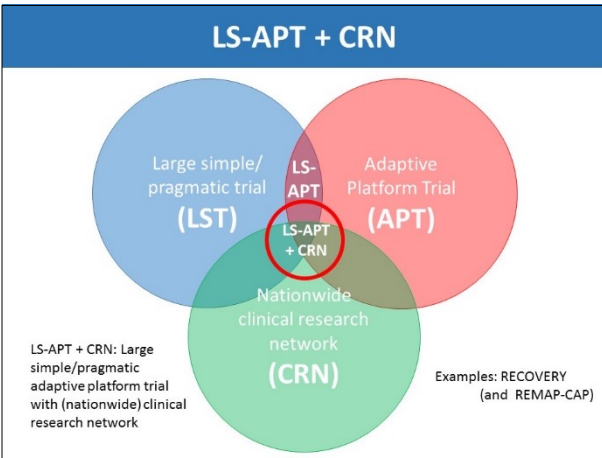
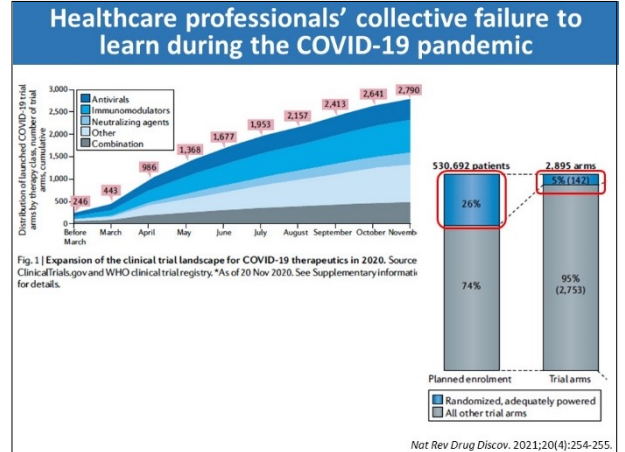



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REMAP-CAP

R: Randomised
E: Embedded
M: Multifactorial
A: Adaptive
P: Platform Trial for Community Acquired Pneumonia

- Started in 2016
- WHO endorsement as "Pandemic Special Study"
- "Pandemic appendix" pre-planned -> activated after COVID-19

Features of REMAP-CAP

Repeated analysis based on Bayesian statistics

Conventional design | Pre-determined enrolment volume

Enrolment is continued until pre-determined target volume is reached:
 (1) Potentially wasteful enrolment
 (2) Risk of failure to deliver conclusive results even with planned enrolment volume

REMAP-CAP | Repeated analysis based on Bayesian statistics

Interim analysis is conducted at a pre-specified interval, and enrolment is terminated with statistical conclusion:
 (1) No wasteful enrolment
 (2) No risk associated with pre-determined enrolment volume

Especially effective with limited preexisting knowledge, e.g., in a pandemic

Angus DC. Fusing Randomised Trials With Big Data: The Key to Self-Healing Health Care Systems? JAMA. 2018;319(15):161-166.

NIHR CRN in England as a model example of CRN

The National Institute for Health Research (NIHR) Clinical Research Network (CRN) in England, the United Kingdom

Population by country in UK

In Japan, 56M = Tokyo + Kanagawa + Osaka + Aichi + Saitama + Chiba

1. North East and North Cumbria
 2. North West Coast
 3. Yorkshire and Humber
 4. Greater Manchester
 5. East Midlands
 6. West Midlands
 7. West of England
 8. Thames Valley and Eastern
 9. Kent Surrey and Essex
 10. Kent Surrey and Essex
 11. Yorkshire
 12. South West Peninsula
 13. North Thames
 14. South London
 15. North West London
 16. North West London

17. London Health
 18. Mental Health and Endocrine
 19. Rheumatology
 20. Primary Care
 21. Public Health and Prevention
 22. Reproductive Health
 23. Respiratory Disorders
 24. Social Care
 25. Stroke
 26. Surgery
 27. Trauma and Emergency Care

28. Health Services Research
 29. Infection
 30. Kidney Disorders

<https://www.nihr.ac.uk/explore-nihr/support/clinical-research-network.htm>