

ICU EVIDENCE • RESEARCH METHODS

Adaptive Bayesian Platform trials in critical care

Benefits, challenges and a REMAP-CAP worked examples

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24-9-24

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ICU EVIDENCE • RESEARCH METHODS

Trials in critical care



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Why the conventional trial struggles in ICU

Patients deteriorate before a study can enrol them
Consent, eligibility and treatment windows are compressed.

Clinical practice changes while recruitment continues
Pathogen waves, co-interventions and site pressures can alter the comparison.



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What is a Platform?



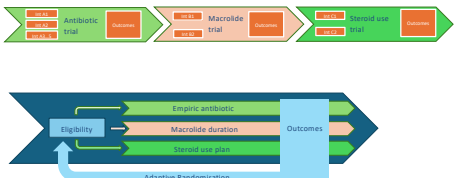
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A platform can address several questions

One master protocol supports multiple treatment domains
An eligible patient may enter one or more randomised comparisons.

Traditional RCTs – serial testing of single hypotheses



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One master protocol supports multiple treatment domains
An eligible patient may enter one or more randomised comparisons.

Arms can enter, graduate or stop as evidence accumulates
The trial infrastructure stays active between questions and outbreaks.

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The Bayesian decision loop

- Specify priors, outcomes and decision rules in advance**
Simulate the design to assess operating characteristics.
- Update probabilities at planned analyses**
Estimate benefit, futility or equivalence against prespecified thresholds.
- Apply independent monitoring and interpret the clinical effect**
A probability of superiority.

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Potential benefits and their conditions

- More answers from shared recruitment infrastructure**
Several questions can be studied within a standing ICU network.
- Earlier decisions about promising or futile interventions**
Benefit depends on recruitment rate, outcome delay and decision thresholds.
- Evidence across patient states and treatment combinations**
Interpret interactions cautiously when some combinations recruit few patients.

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The hard (ish) parts happen at the bedside

- Rapid eligibility and consent for critically ill patients**
Include patient and public partners when explaining randomisation and outcomes.
- Delivering several interventions without burdening the team**
Site training, pharmacy workflows and data capture need continual support.
- Preserving valid comparisons as care changes**
Concurrent controls, time adjustment and transparent reporting matter.

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Worked example: REMAP-CAP

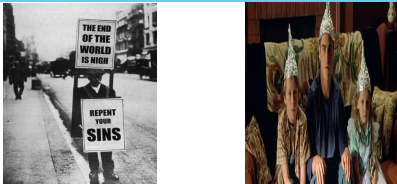
Randomized Embded Multifactorial Adpative Platform-
Community Acquired Pneumonia

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REMAP-CAP Trial

There is always one



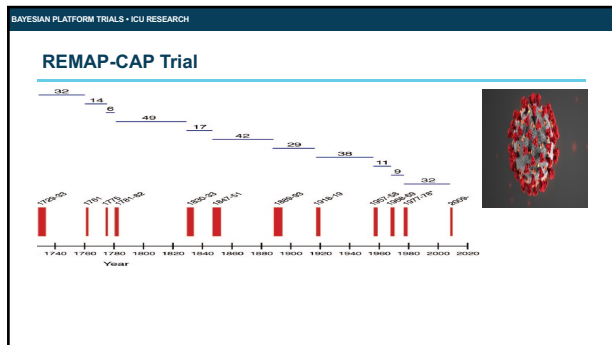
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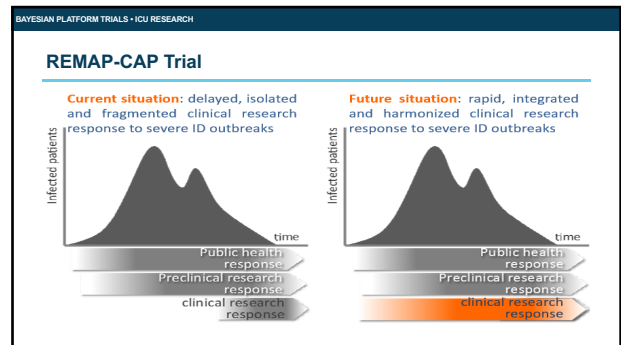
REMAP-CAP Trial



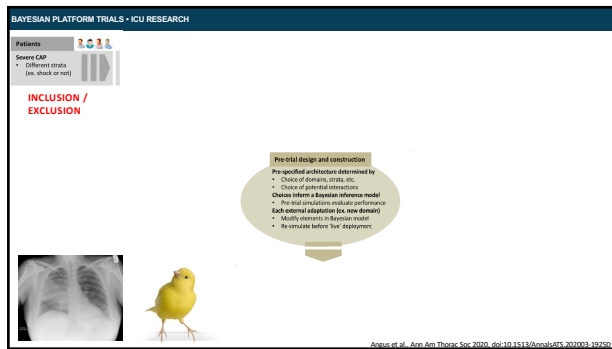
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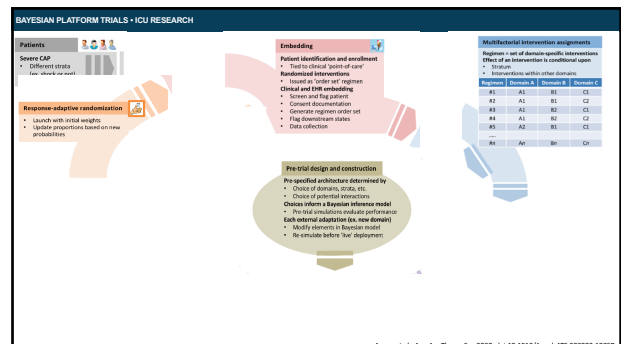
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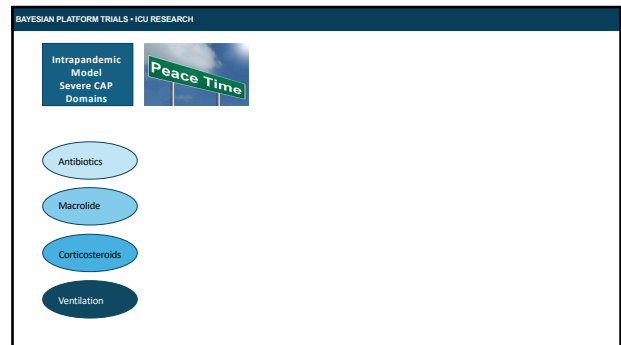
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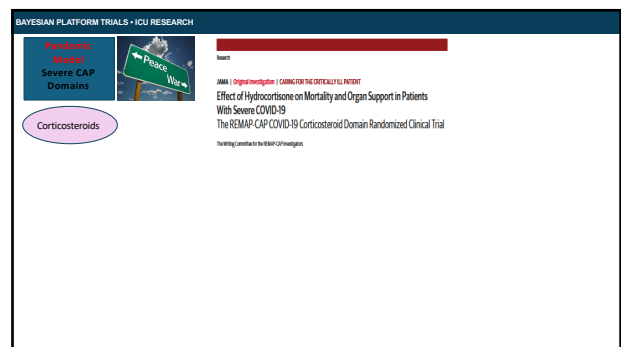
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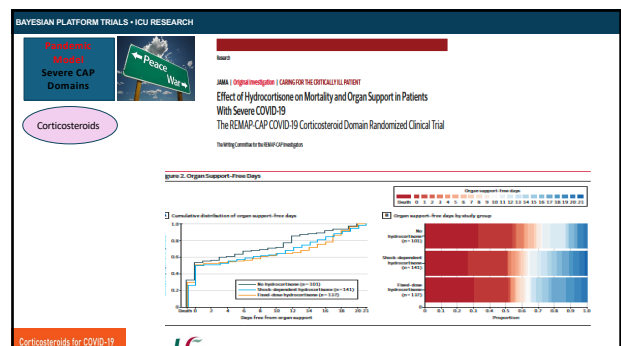
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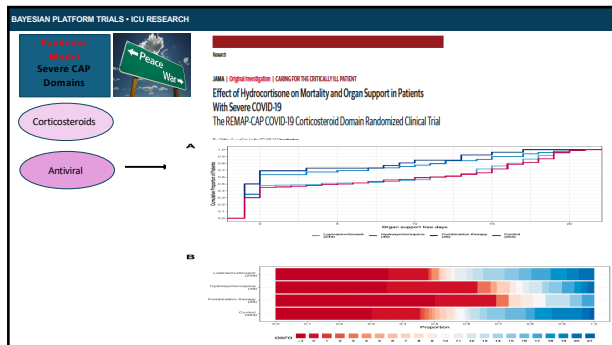
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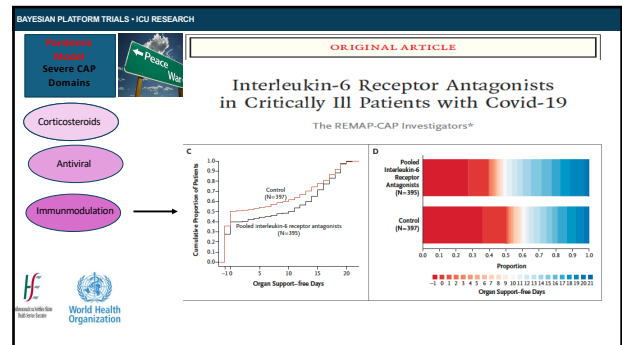
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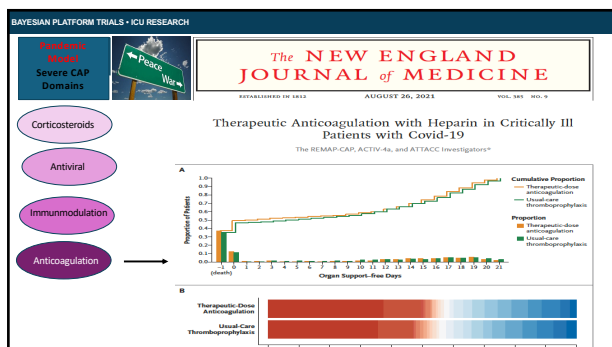
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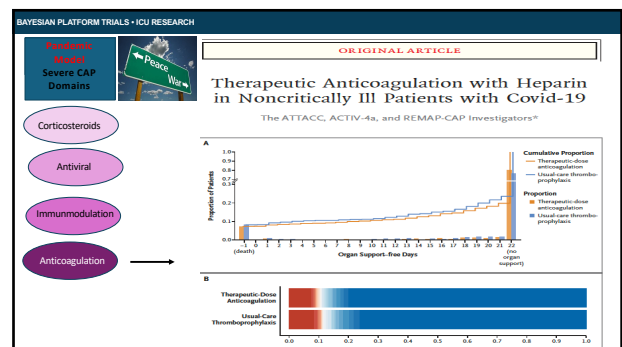
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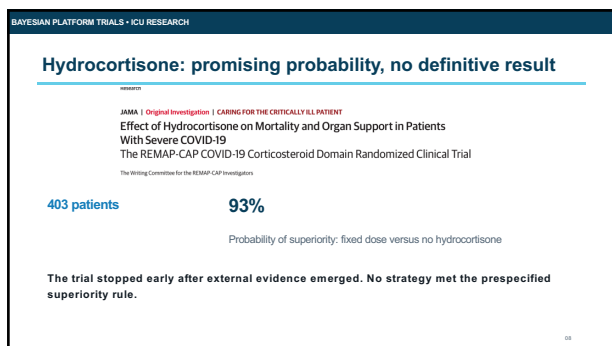
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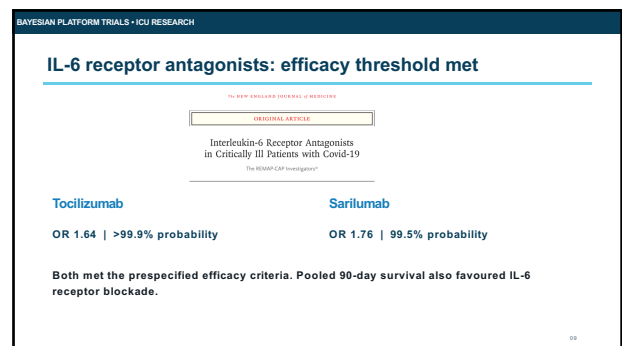
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ICU EVIDENCE • SELECTED PRIMARY PUBLICATIONS

More results from the standing platform

JAMA 2022	Antiplatelet therapy and organ support-free days
JAMA 2022	180-day outcomes following COVID-19 critical illness
NEJM 2022	Simvastatin in critically ill COVID-19
THORAX 2022	Tocilizumab, sarilumab and anakinra: final domain results
JAMA 2021	Convalescent plasma and organ support-free days

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Take-home messages

A platform is a durable clinical research system
Its value depends on preplanned analysis and a network ready to recruit.

Bayesian probabilities need their prespecified context
Distinguish a promising signal from a result that meets a decision rule.

Full REMAP-CAP publications: remapcap.org/publications

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ICU EVIDENCE • IMPLEMENTATION

Funding and regulation shape what platforms can test

Sustained core funding A platform needs staff, data systems, pharmacy and statistical capacity between individual treatment questions.	Repeated approvals New domains and arms can require ethics and regulatory amendments in several jurisdictions.
Design scrutiny Reviewers need prespecified simulations, stopping rules and a credible plan for changing standard care.	International alignment Nonconcurrent controls, multiplicity and differing consent requirements require early regulator dialogue.

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ICU EVIDENCE • FUTURE PLATFORMS

The next wave: PRACTICAL and PANTHER

PRACTICAL A global Bayesian adaptive platform evaluating interventions for acute hypoxemic respiratory failure.	PANTHER A precision medicine platform in hypoxaemic respiratory failure that tests therapies across biologically defined ARDS subphenotypes.
Future direction: embed trials in care, test treatment heterogeneity, align data and collaborate across platforms.	

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Thanks

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