



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Regulatory considerations on integrated therapeutics

Design features and other regulatory considerations

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An agency of the European Union





Disclaimer

The views expressed in this presentation are the personal opinion of the author and should not be understood as being made on behalf of or reflecting the position of the EMA or one of its committees or working parties.



Table of content

- Possible regulatory frameworks
- Other design considerations
- Conclusion



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Hypothesis

The medicine works in combination with **a specific talking therapy** modality

The medicine works in combination with **any talking therapy**



Hypothesis	Known Framework
The medicine works in combination with a specific talking therapy modality	Fixed-dose combination of medicinal products
The medicine works in combination with any talking therapy	Medicine to be administered in add-on to any other of a class



Hypothesis	Known Framework	Development/ deployment burden
The medicine works in combination with a specific talking therapy modality	Fixed-dose combination of medicinal products	The approval will be specific for the use in combination with a specific therapy modality
The medicine works in combination with any talking therapy	Medicine to be administered in add-on to any other of a class	The clinical trials will need to show evidence of effect across associated modalities



The good thing of putting new wine into old bottles

- Developers can already engage with regulators on a known basis;
- While specific methodological literature (methodological publications, guidelines and case studies) is produced there is no substantial delay to developments;
- Lessons learnt from the two known contexts can be applied here.

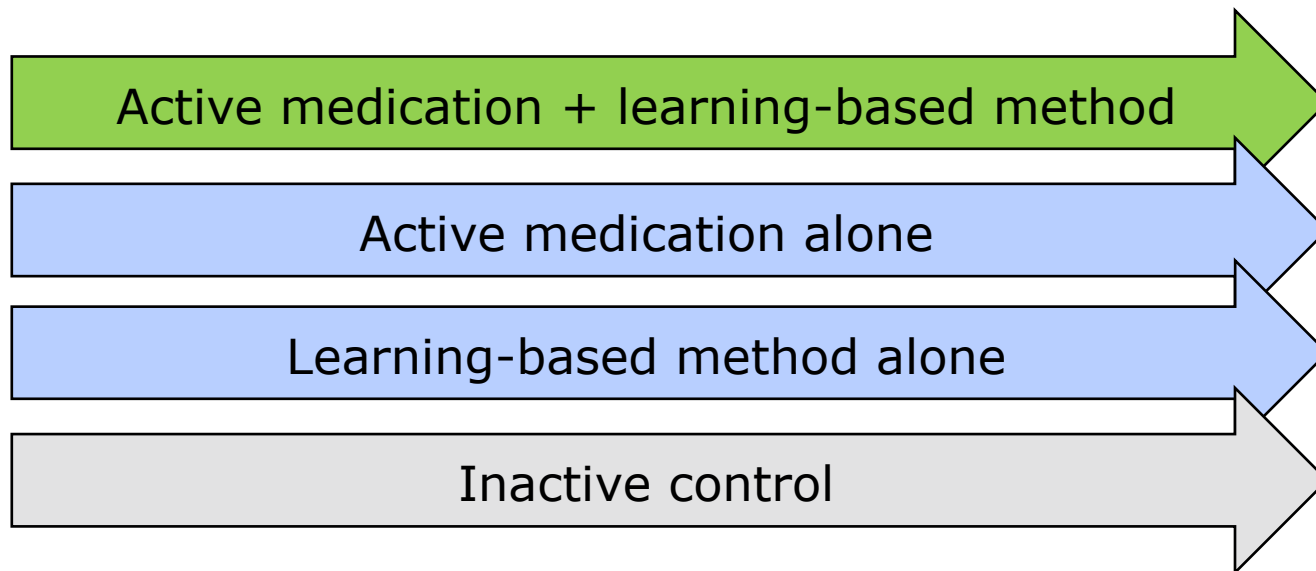


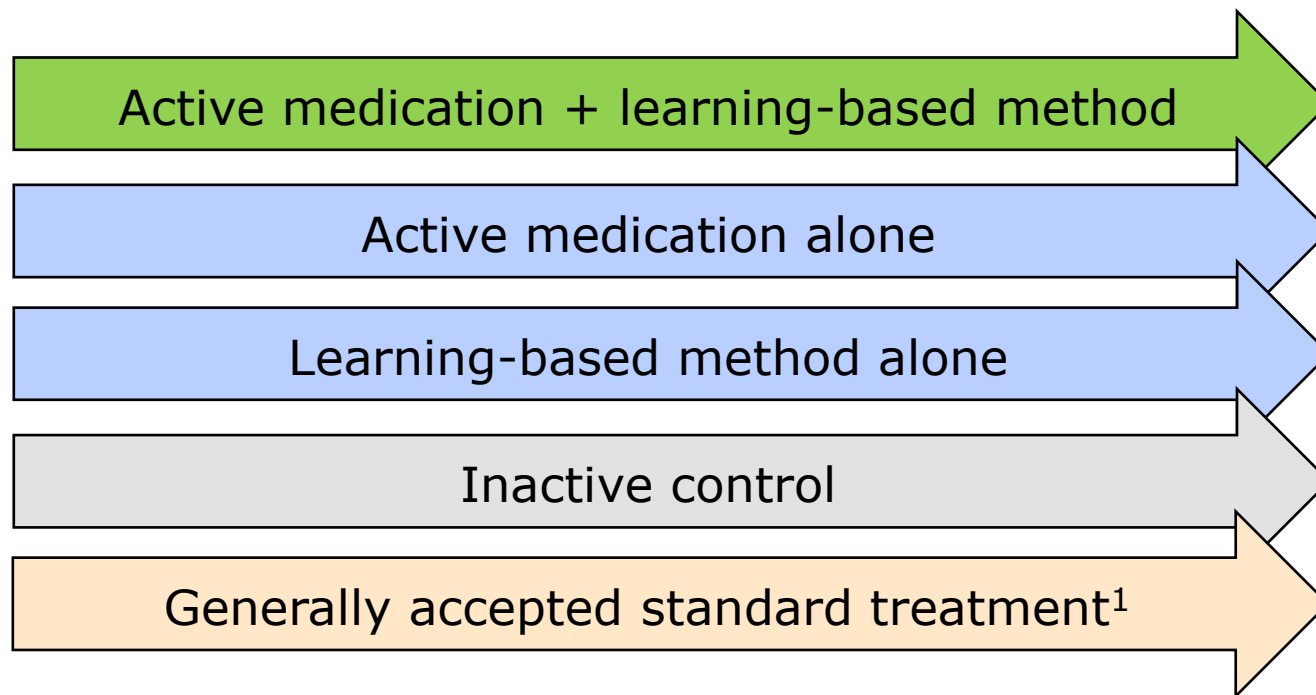
Table of content

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- Other design considerations
- Conclusion

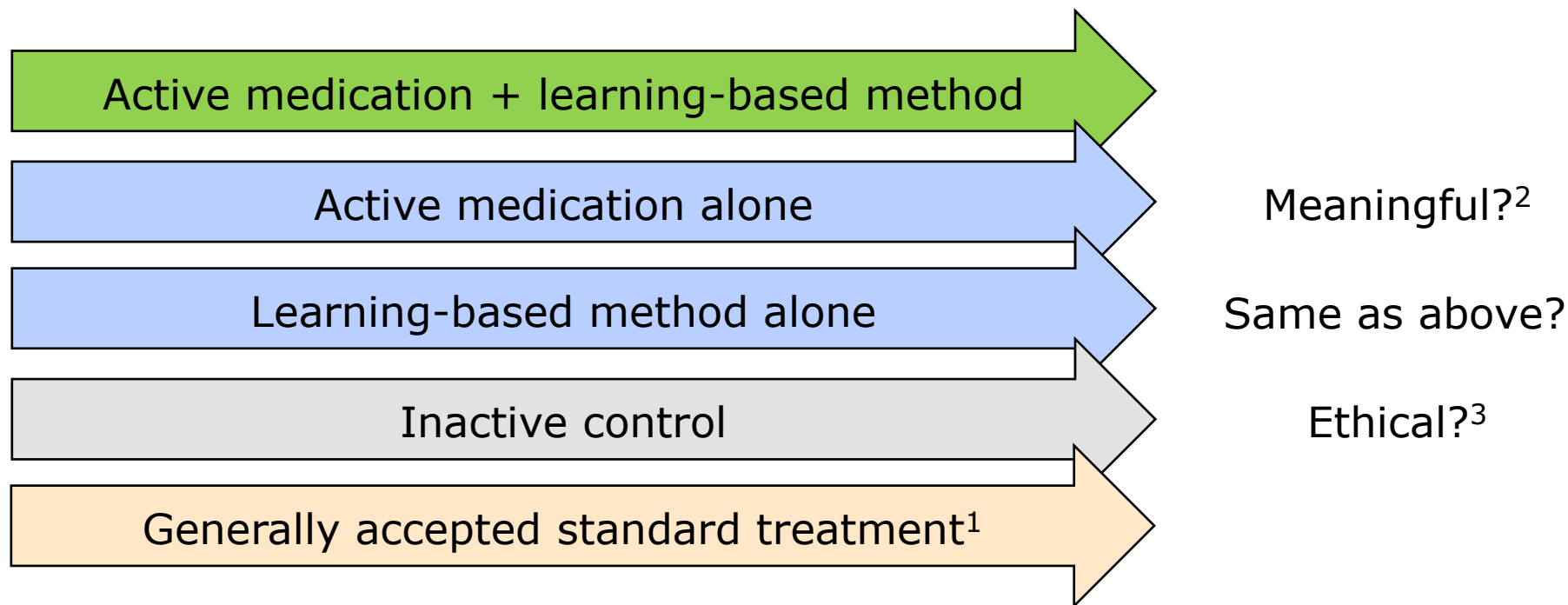


Active medication + learning-based method





¹ EMA. 2013. Guideline on clinical investigation of medicinal products in the treatment of depression.



¹ EMA. 2013. Guideline on clinical investigation of medicinal products in the treatment of depression.

² By analogy with PK enhancers in EMA 2017. Guideline on clinical development of fixed combination medicinal products.

³ ICH. 2001. E10. Choice of Control Group in Clinical trials.



Blinding

- Feasibility and ethical issues are acknowledged¹, and blinding is not all or nothing¹: even if patients and therapists cannot be blinded, others can;
- Active placebos might be considered² but add a layer of complexity, both ethical and for interpretation (does the active placebo positively or negatively affect the outcome?);
- The risks exist but can be mitigated by appropriate controls and robust outcome assessment.

¹ ICH. 1998. E9. Statistical principles for clinical trials.

² Jensen, J.S., et al. 2017 J Clin Epidemiol., 87, pp.35-46.



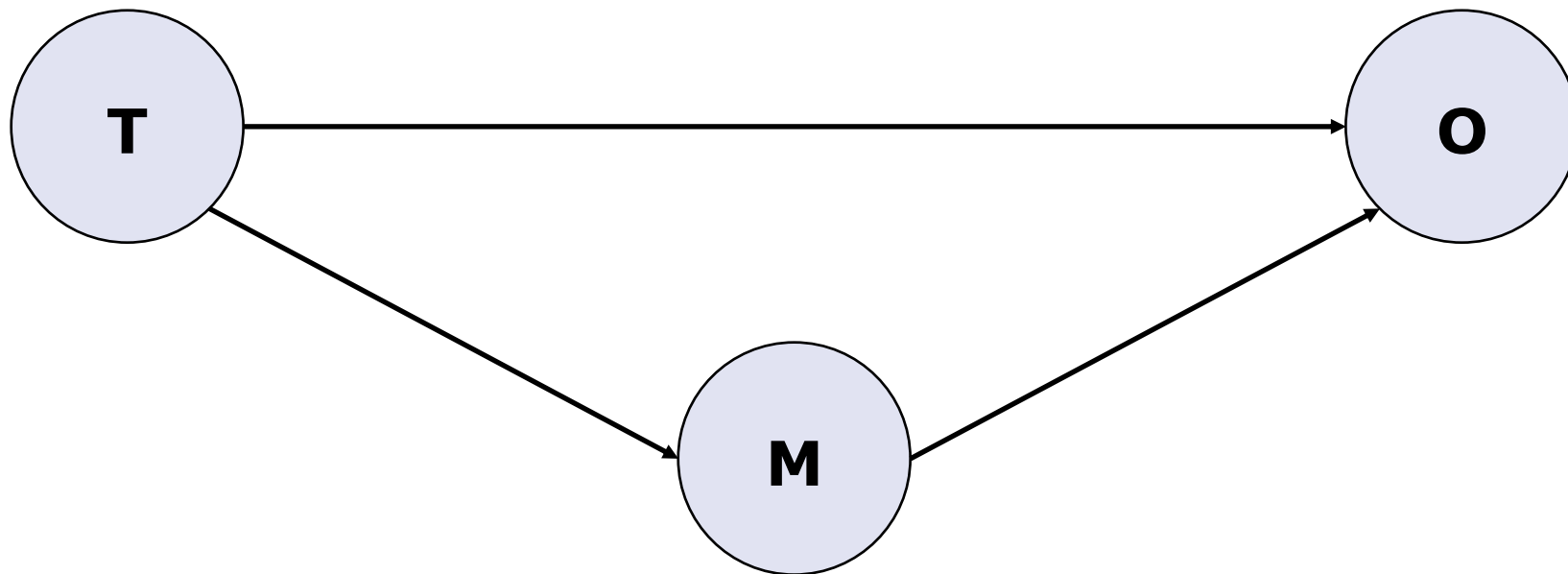
Additional trial objectives

Study of mediators

The estimand framework with appropriate estimation methods can be used to study whether e.g. a certain qualitative subjective experience is a necessary mediator.



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Long term efficacy

Studying long-term efficacy might be more or less difficult depending on the hypothesis being tested.



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"It is not only the medicine that maintains well-being. Once we function competently, the world may pitch in" ²

"It's the relationship that heals, the relationship that heals, the relationship that heals" ³

¹ For a discussion on non-debunking explanations see Radcliffe Richards, J., 2000. Human Nature After Darwin, pp. 177-180.

² Kramer, P.D., 2016. Ordinarily Well, The Case for Antidepressants D

³ Yalom, I.D., 1989. Love's Executioner & Other Tales of Psychotherapy



Any questions?

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