



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Estimands in CNS trials

A review of strategies accepted by EMA to handle intercurrent events

ISCTM 20th Annual Scientific Meeting

Presented by Lorenzo Guizzaro
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An agency of the European Union





About the speaker



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10 years at the European Medicines Agency

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Research interests: estimands, estimation methods aligned with estimands, and ethics and methods of medicines' regulation

This presentation does not represent the position of EMA or of its Committees or Working Parties, but solely the personal opinion of the speaker



Outline

Background

Methods

Results

Discussion



Background

- The Estimands framework provides a tool to transparently and precisely define treatment effects of interest;
- There is still limited knowledge on which estimands* are of interest for regulatory purposes.



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Strategy for data collection

- Scientific Advice given between January 2018 and December 2022 for commonly researched CNS conditions, and with keywords suggesting that Estimands were discussed;
- For the intercurrent events, specific wordings were grouped into categories;
- Strategies classified as per the Addendum.



Intercurrent event categories

Treatment discontinuation	Permanent discontinuation of the assigned treatment, for any cause
Changes in additional therapies	Change in therapies compatible with the one assigned to (sometime referred to as “background”)
Use of alternative therapies	Use of treatments that are not co-administered with the treatment assigned
Death	Death (for any cause)
Dose interruption	Skipping doses of the assigned treatment, without permanent discontinuation
Pandemic-related disruption	Any IE attributed to the pandemic
Other IEs	Any other IE



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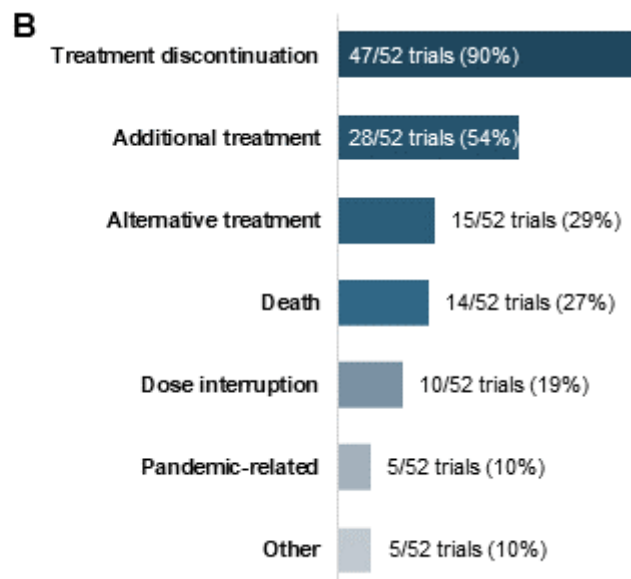
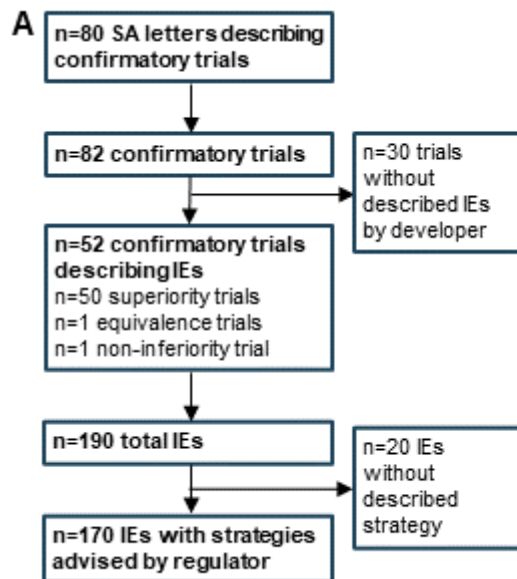
Methods

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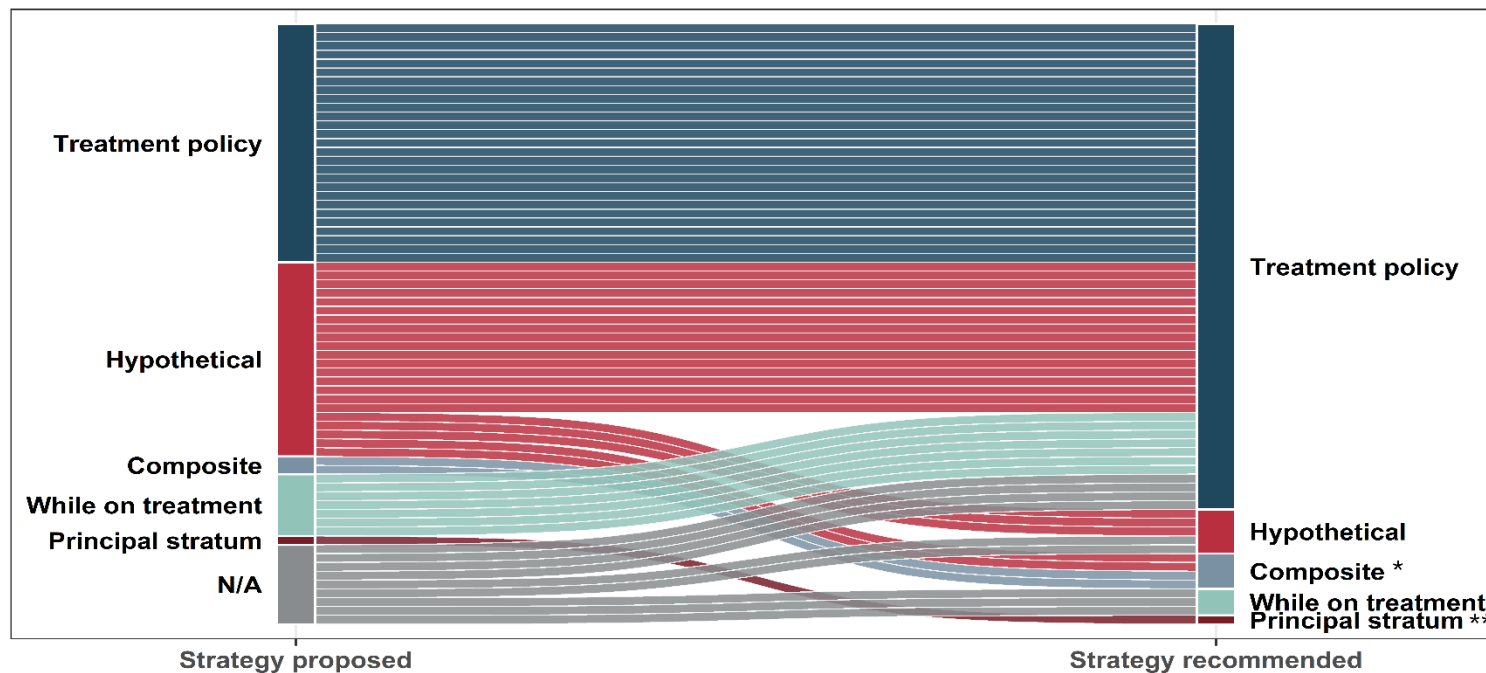


Demographics



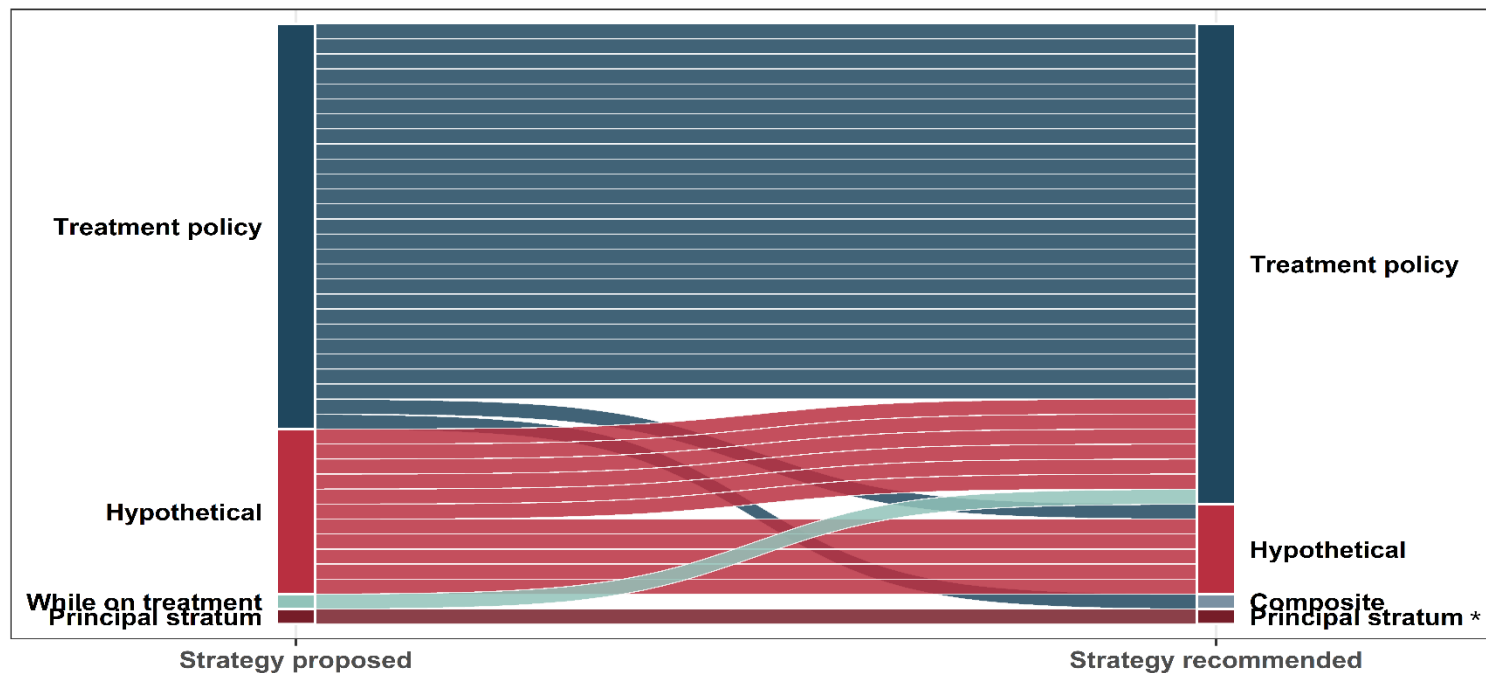


Treatment Discontinuation



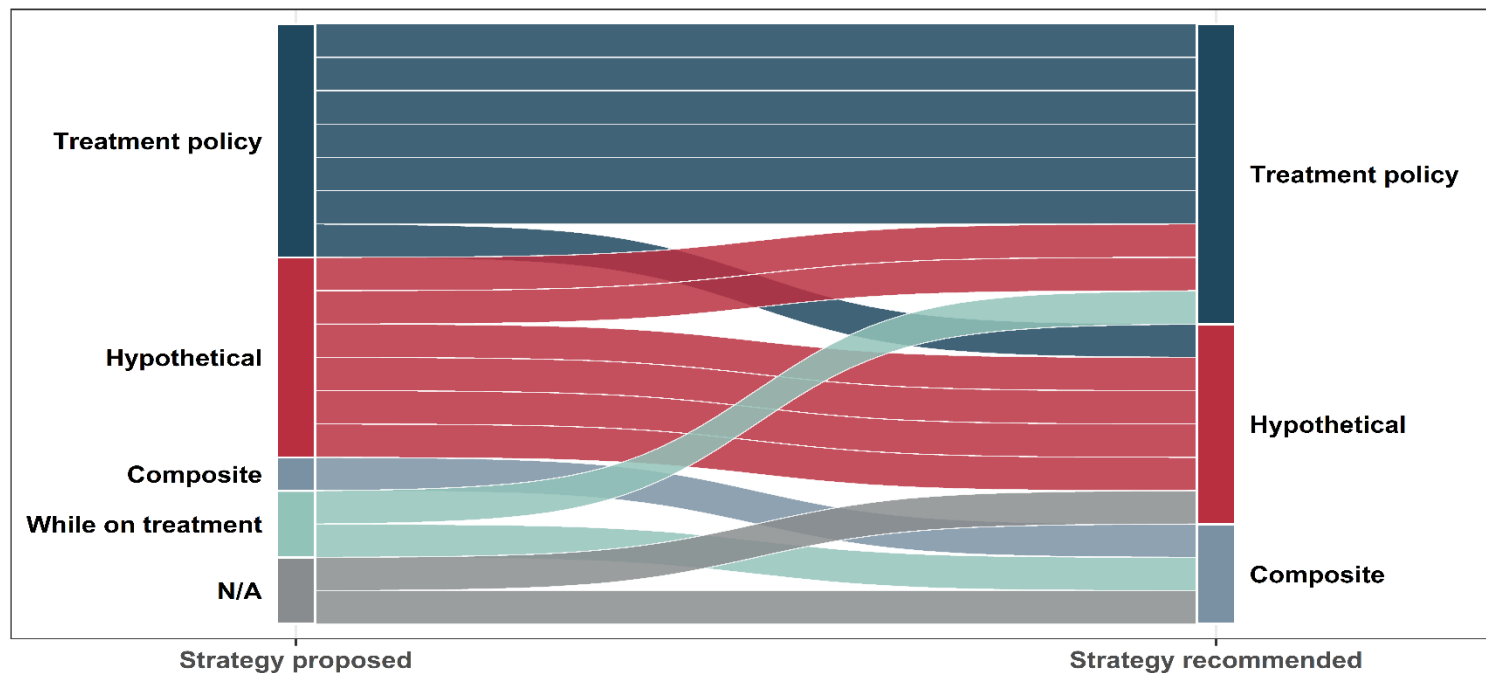


Change in additional treatments



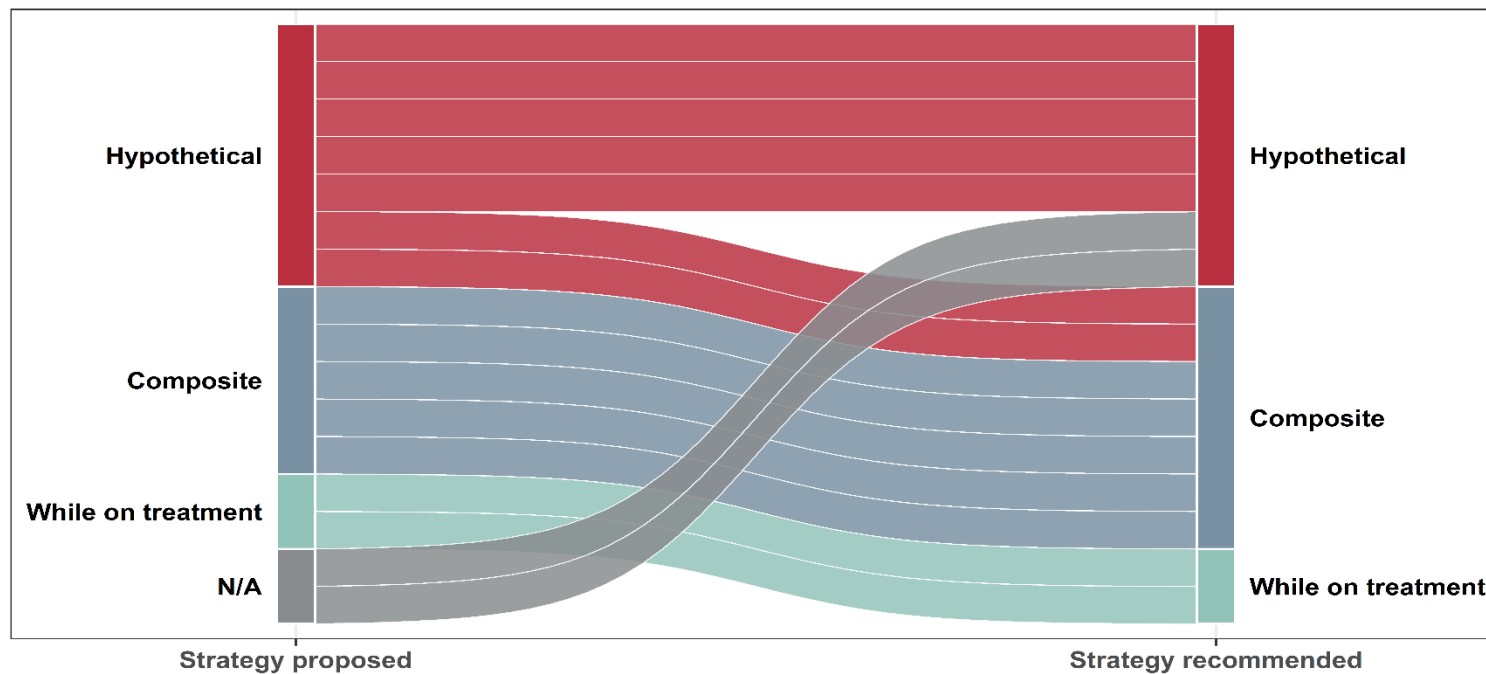


Change in alternative treatments



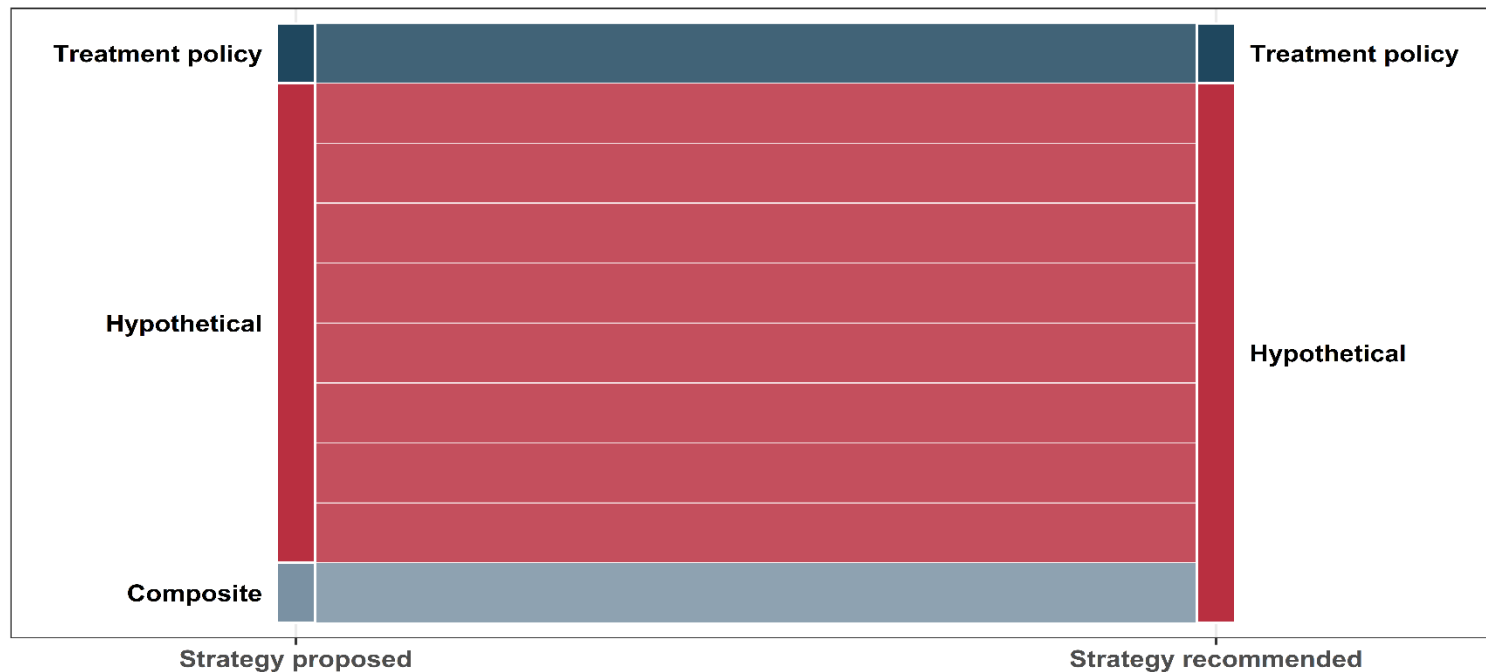


Death





Pandemic-related IEs





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First impression of the results

- No 1-to-1 correspondence between IE and strategy: the choice is a multi-dimensional problem
- Oversimplistic beliefs about regulators' preferences for any particular strategy appear incompatible with our results.



The way forward

- Well described and justified proposals enable the most detailed responses;
- Regulators will continue to increase the amount of guidance provided (e.g. in guidelines on specific conditions)



Acknowledgment and disclaimer

Thanks to the co-authors of the study, **Lisa Meszaros**, **Florian Lasch** and **Bruno Delafont**

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