



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# Commentary on the session on impact of World Events

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Estimands, power and general considerations

2022 ISCTM Autumn conference

Presented by Lorenzo Guizzaro on 9 September 2022

An agency of the European Union





## Disclaimer

The views expressed in this presentation and in the following panel discussion 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.

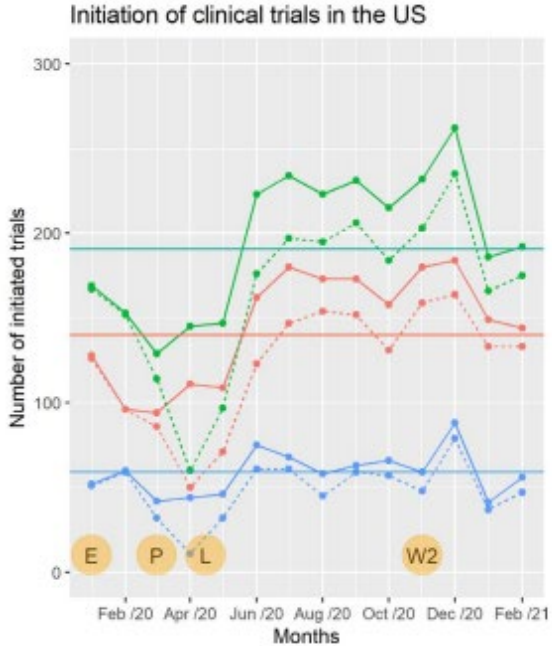
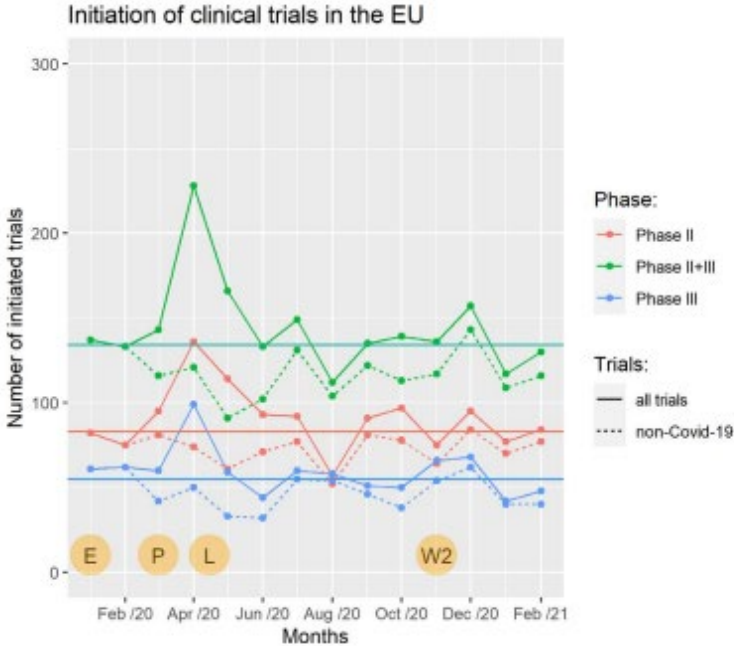


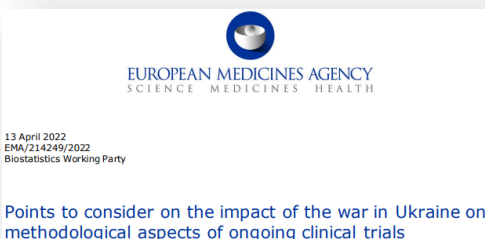
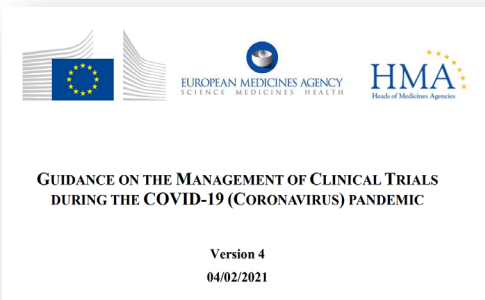


**Primum non nocere  
(and try to do good)**



# The resilience of the clinical trials ecosystem





- Trial participants' safety is the first priority;
- Collection of affected and unaffected data "strongly encouraged";
- Where applicable, Estimands framework to handle the impact of the events.



## World events as intercurrent events

(“events precluding the observation of the variable or affecting its interpretation”)

<b>Strategy as per the Estimands framework<sup>1</sup></b>	<b>Comment</b>
Treatment-policy (as-it-happened)	Analysis might still be impacted <sup>2</sup>
Hypothetical (as it would have been without)	No universally accepted estimator <sup>3,4</sup>

1. EMA, 2020

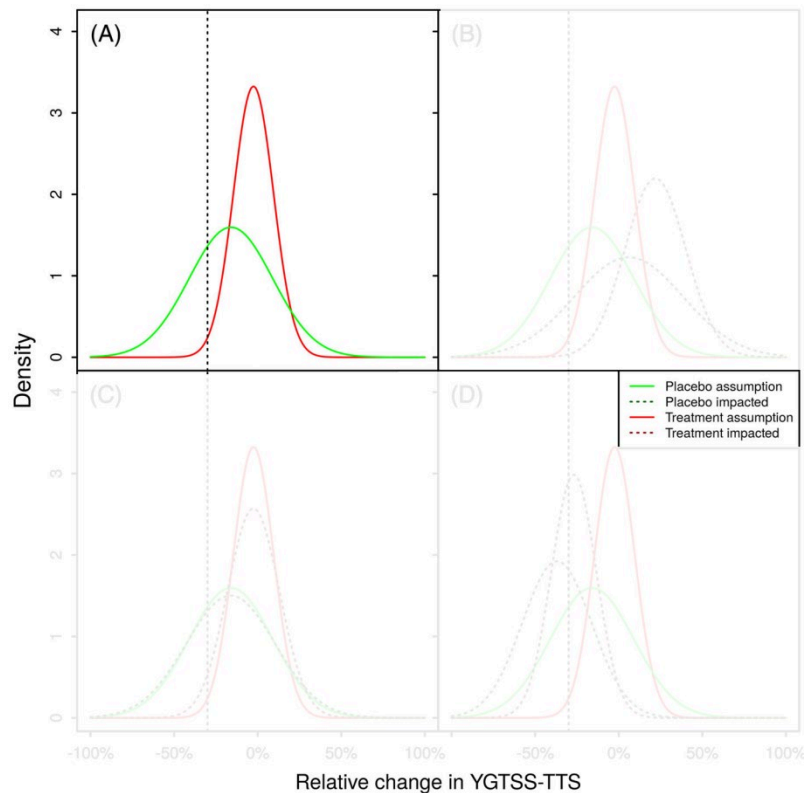
2. Lasch et al, 2020

3. Hemmings, 2020

4. Lasch and Guizzaro, 2022



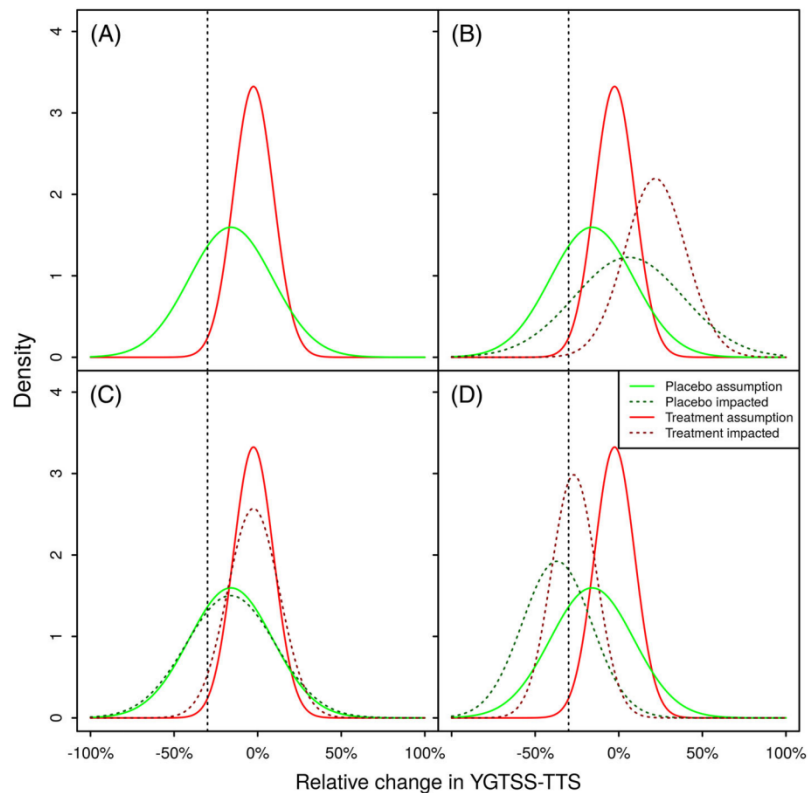
# The pandemic and trials in Tourette: treatment policy strategy



Trials are planned with certain assumptions regarding the course of the disease and the response to treatment.



# The pandemic and trials in Tourette: treatment policy strategy

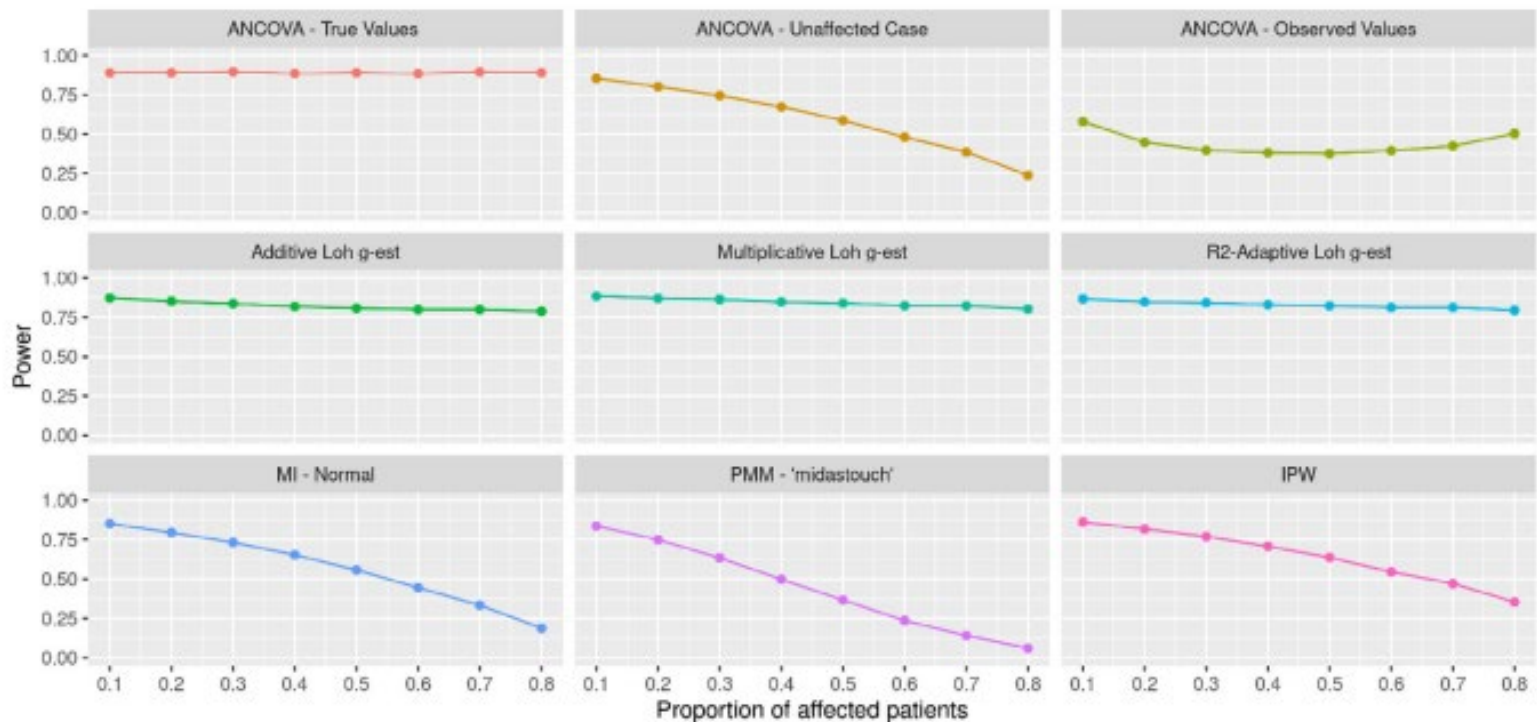


Trials are planned with certain assumptions regarding the course of the disease and the response to treatment.

The pandemic might lead to violation of such assumptions (that can sometimes be inferred from published observational studies) that can result in a reduction of the study's ability to detect an effect ("power").

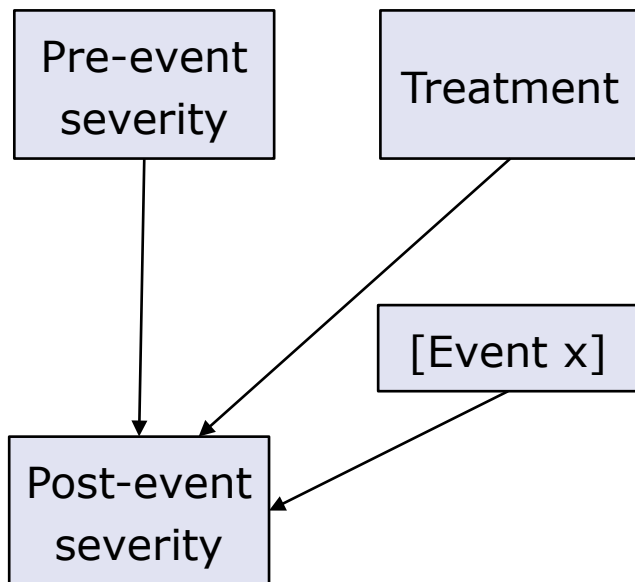


# The pandemic and trials in Tourette: hypothetical strategy





## Granularity in the information on events and mechanisms



- What does exactly happen to each patient?
- When does it exactly happen?
- Does it happen entirely due to the external circumstances or for a mix of circumstances and health status of that particular patient?



**The learnings from conducting trials in difficult circumstances can make trial methodology better (meaningfulness of scales across times? Different ways of collecting outcomes...)**

**Most importantly, many thanks to all trial participants and investigators who continue working to make medicine better in difficult circumstances!**



# Any questions?

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