



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Trials in the COVID era

An EMA commentary on lessons learnt from 2020

ISCTM/ECNP 2021 Joint Session

Presented by Lorenzo Guizzaro on 01 October 2021

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.

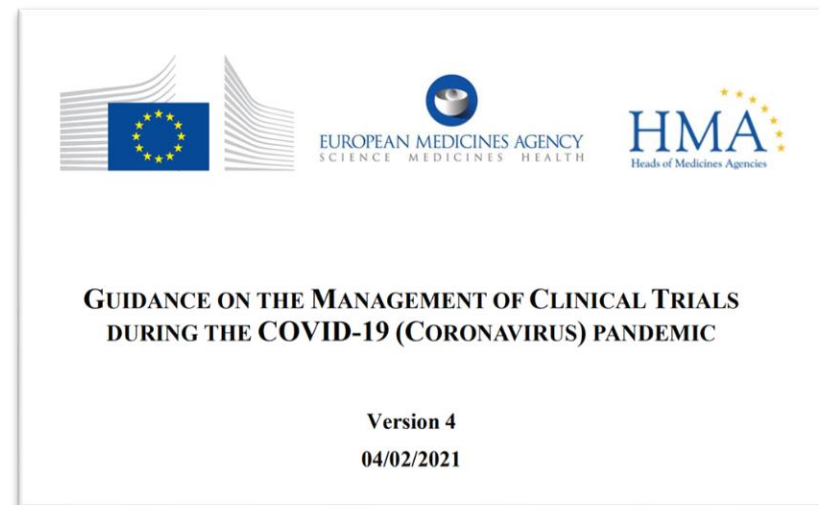


**The world around
and its changes
are important.**



What it means for trials in the COVID era

Researchers throughout the globe have displayed courage and dedication to keep trials running. Innovative solutions have been put in place. To the extent that they are robust and sustainable, those are there to stay.

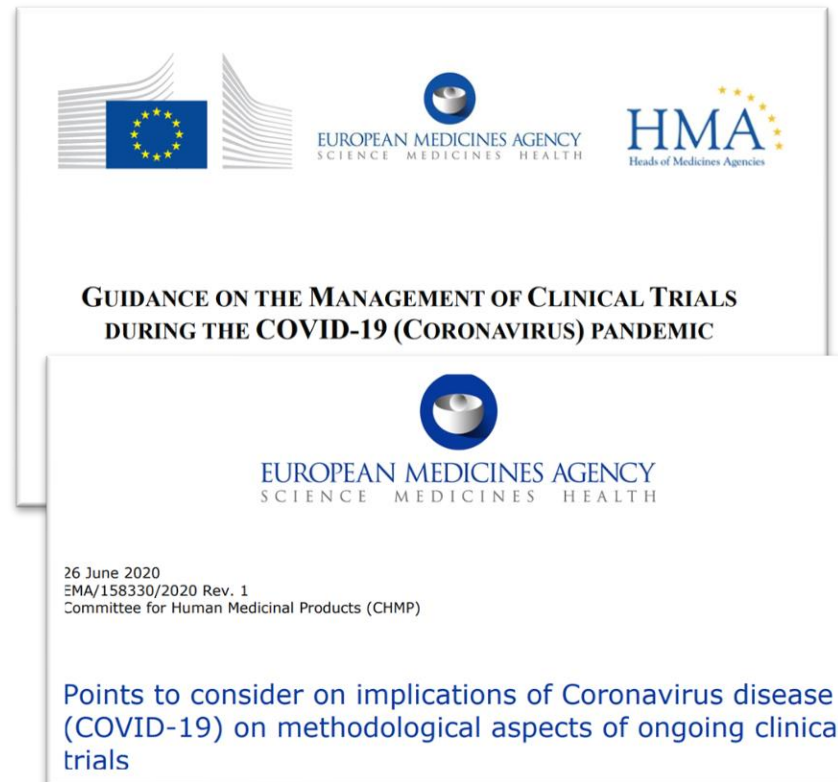




What it means for trials in the COVID era

Researchers throughout the globe have displayed courage and dedication to keep trials running. Innovative solutions have been put in place. To the extent that they are robust and sustainable, those are there to stay.

However, the interpretation of trials in the COVID era cannot ignore that a pandemic was ongoing, with important changes in daily lives of all individuals involved in the study in the affected period(s).





What it might mean for trials beyond the COVID era

- Climate extremes and extreme weather events – possibly increasing in frequency due to anthropogenic influences¹;
- Crises or other changes in the socio-economic context²;
- Seasonality (and its changes) for diseases whose course is susceptible to it^{3,4}.
- Changes in diagnostic criteria, standards of care or other healthcare practices.

1. Seneviratne et al, 2012

2. Christodoulou and Christodoulou, 2013

3. Lim et al, 2018

4. Moccia et al, 2016



**What outcome
measurement tools are really
measuring is important.**



What it means for trials in the COVID era

Changes in both the living circumstances of study participants and methods of assessment can have different impacts on the outcome measures depending not just on the disease but on what the outcome is actually measuring.

In Tourette Syndrome, it has been shown that tic severity may be increased due to stress¹ but that the global score on the YGTSS may be reduced due to less impact on social functioning².

1. Mataix-Cols et al, 2020

2. Graziola et al, 2021



What it might mean for trials beyond the COVID era

- Are scales – including those developed many years ago - still validly measuring something relevant to patients today?
- How should scales be reassessed in presence of changing living conditions, preferences, and diagnostic categories?



**The Estimand is important
(but research on Estimators
too).**



What it means for trials in the COVID era

Strategy to treat the pandemic-related events in the Estimands framework¹	Comment
Treatment-policy (as-it-is)	Analysis might still be impacted ²
Hypothetical (as it would have been without)	No universally accepted estimator ³

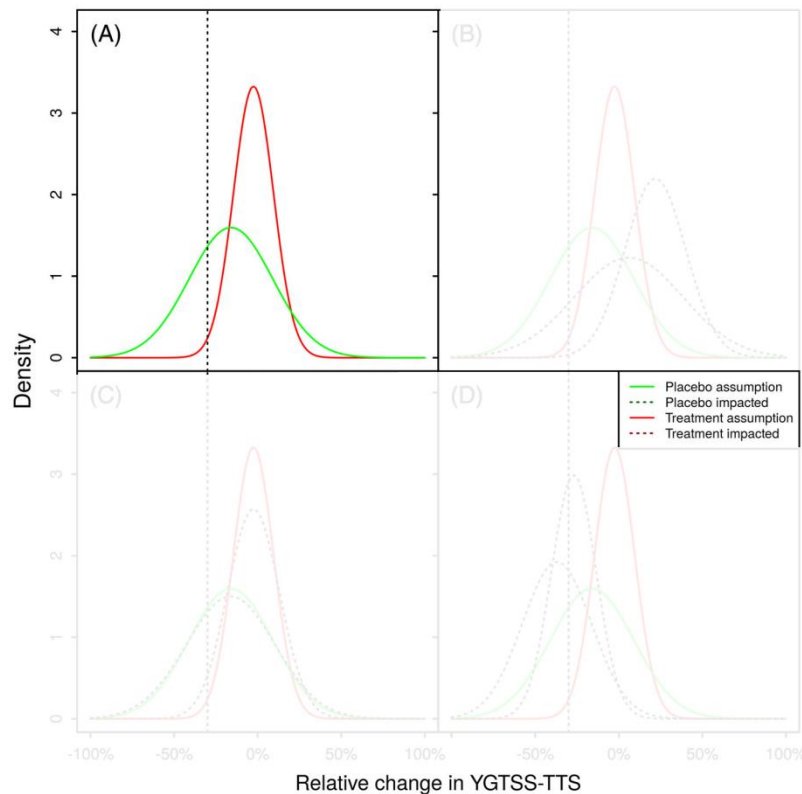
1. EMA, 2020

2. Lasch et al, 2020

3. Hemmings, 2020



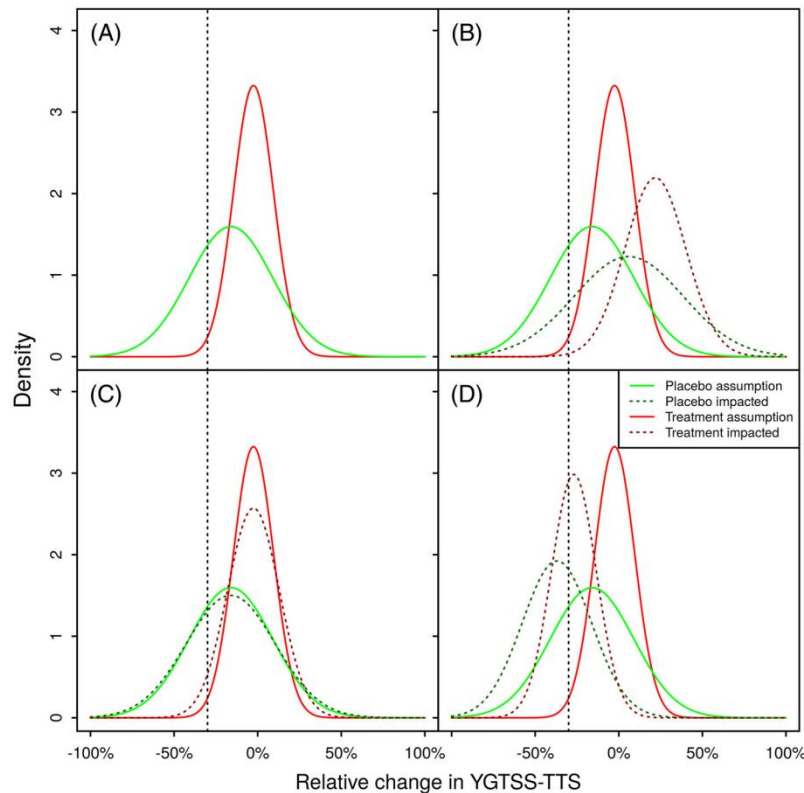
What it means for trials in the COVID era



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What it means for trials in the COVID era



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").



What it might mean for trials beyond the COVID era

- The Estimands framework offers a platform to transparently discuss and handle a multiplicity of events;
- However, even for an event whose causal structure is relatively “simple”, estimators are still an area of ongoing research.



**Most important: the
dedication shown by study
participants and
investigators. Thank you!**



Any questions?

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