DCT, the new kid on the block
Here to stay?

Anja Schiel; PhD; Lead Methodologist in Regulatory and Pharmacoeconomic Statistics, NoMA

Norwegian
Medicines Agency

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The regulators/SAWP/ITF perspective

- At SAWP we have not yet seen a submission for advice on a full DCT
- This does not mean that there might not be plans to come to CHMP with a submission (SA is no prerequisite)
- We have discussed proposals at the ITF
- We do see all kind of variations of submissions with elements of decentralisation, mainly driven by COVID 19
- Some of the proposals are more acceptable than others…..

The archetypes

- Limited changes, often in the direction of remote actions
  - Switch from F2F to remote interview, remote monitoring or remote assessments
  - Exchange of assessment method(s)
  - Minor adjustments to ongoing studies (case by case)
  - Potential changes to the statistical analysis plan (case by case)

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➢ Elements of remote trial designs are tested due to necessity (not a bad thing)

➢ Exchange of estimation; this is all about Sensitivity/Specificity

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➢ Goes further than just replacement of the ‘how we measure’. The estimator is changed (MRI vs CT; investigator reported vs caregiver/patient; 6 MWT vs 24 hr activity)

➢ Are we answering the same question or not?

➢ What is the impact on the interpretation?

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➢ Be aware of the danger of ‘minor’.

➢ Changes in any of the 5 elements of the Estimand can lead to changes in the actual Estimand and must be properly understood

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➢ They answer a different question, have the potential to allow new views on trial protocols (decluttering), are potentially more patient focused (after all the patient isn't just the until of observation anymore) and reflect the real world …..

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➢ But this does not automatically guarantee better generalisability!

Is the kid to stay?

- Yes, the 7 most expensive words in business are: ‘We have always done it that way’
- COVID has taught us that ‘when we have to we have’ to and it still works
- But using element of decentralisation isn’t where we really want to go.
- So what is the place of the DCT?

Is the kid to stay?

- A full DCT can potentially provide a link between RCT's and RWD.
- It can help to understand the properties of both types of data and build the bridge between both worlds helping to cross the gap between optimized investigation of treatment effects and the relative effectiveness in a more real-world setting.
- How close the DCT can come to the real world is to be seen and will also depend on the chosen design.

What's in it for me?

- This is an important question, many assumptions are made but nothing is ever only 'better' for everyone
- DCT element's but for sure full DCT trials need to be carefully assessed in terms of new challenges for the interpretation of results (investigators, sponsors, regulators and HTA's need to be able to interpret the data)
- We need to understand the potential incentives, advantages but also disadvantages to trial participants. Are we changing our patient population by new selection mechanisms?

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➢ We all need to learn, but so we did have to when we invented the RCT.

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