

(Dis)continuation of antipsychotic medication

September 28 – October 1 2020 Lorentz Center@Oort/Online

Scientific

Description and aims

Antipsychotic medication is effective for symptomatic treatment in schizophrenia-spectrum disorders. After remission, continuation of antipsychotics is associated with lower relapse rates and lower symptom severity compared to dose reduction/discontinuation. Most international guidelines recommend continuation with antipsychotic medication for at least one year. In clinical practice, patients often have a strong wish to stop earlier due to side-effects that affect their everyday social functioning. Recently, the guidelines have been questioned as the Dutch MESIFOS study showed that more patients achieved long-term (social) functional remission after early discontinuation of antipsychotic medication. Yet, the sample size was relatively small and their finding was not replicated in another recently published study. Psychiatrists, patients and family are unsure which medication regime to follow: to continue or not to continue?

To address this issue of uncertainty, we started the HAMLETT (Handling Antipsychotic Medication: Long Term Evaluation of Targeted Treatment) study in September 2017 (granted by ZonMw; www.hamlett.nl). In this large multicenter single-blind randomized controlled trial, we compare maintenance treatment versus discontinuation/dose reduction of antipsychotic medication in 512 patients remitted from first-episode psychosis. We now work together with 23 mental health care organizations across the Netherlands to reach potential participants. Worldwide, three other (dis)continuation studies are currently being conducted: TAILOR (Denmark), RADAR (United Kingdom) and REDUCE (Australia).

We invited junior and senior researchers, as well as clinicians and individuals with lived experience, with various backgrounds (psychology, psychiatry, linguists, data managers) from different countries, with the aim of exchanging experiences and knowledge and to better streamline our joint efforts on this important research topic. All (dis)continuation studies are currently in the first or second year of their implementation, so this was the ideal time to organize a joint meeting.

Tangible outcome

The encounters between our international colleagues at conferences have been very limited till now. This workshop at the Lorentz Center provided the unique opportunity to create an international community within this field of research. Ultimately, the main goal of this workshop was to enable a closer cooperation between scientists at both a national and international level by facilitating face to face in-depth discussions. Three tangible outcomes:

- 1) A summary describing the most important hurdles and difficulties encountered in the international studies, together with the (joint) decisions that were made to overcome these issues and identify common limitations of these kind of studies. These can be incorporated in the discussion section, when researchers will be writing up the results in the final research articles.
- 2) An overview will be made of the overlap between study variables between the international studies. Syntaxes will be prepared based on preliminary data in preparation of final data analyses, which are streamlined between the international studies as much as possible.
- 3) Joint research article(s) will be initiated, summarizing the first preliminary findings. Article(s) will be further prepared for publication after the workshop. An author group will be registered on PubMed.

Scientific breakthrough

The plenary lectures as well as the separate breakout sessions led to several new ideas. For example, improvement of the inclusion rate by involving psychiatrists and nurses in training on a national level instead of only via the institutions as currently the case. We have also discussed the extra measurements/work packages that will be added to the HAMLETT protocol before the end of 2020. The clinicians that attended the workshop provided important input on the selection bias that is inevitably created when recruiting for research. Together with the international investigators in this field of research that attended the workshop on Thursday October 1 2020 (Denmark, UK, Australia), we decided to form a large research group. This way, we can join forces by organizing similar meetings on a regular basis. The next meeting is already planned for April 2021, during the Schizophrenia International Research Society meeting for which we will send in a symposium on the topic of

antipsychotic discontinuation. During the workshop, seven working groups have been formed. During the coming year(s), they will come together to work on specific research questions (see below).

- Guideline for tapering medication: Iris Sommer
- Ethical consideration on discontinuing antipsychotics: Eóin Killackey
- Selection bias and baseline characteristics: Wim Veling
- Position paper + common definitions: Sanne Schuite-Koops
- Alternative study designs and analyses: Helene Speyer
- Tapering trajectories: Jim van Os
- Attitude of clinicians towards discontinuing: Martijn Kikkert & Joanna Moncrieff
- Harmonizing data (future plan, also legally sharing data): To be decided

“Aha” moments

It was very informative and inspiring to have all our researchers together and talk about the different areas of expertise that they bring to our study on antipsychotic medication use in first-episode psychosis (HAMLETT/OPHELIA study). The study team was also present, who actually perform study visits, as well as our experience expert and a representative from the family organization Ypsilon. This way, we could not only reflect on scientific relevance but also on what patients gain from study examinations and scientific output. Finally, it was truly exciting to have the international investigators in this field of research together in the same (digital) room for the first time, which was the starting point for several collaborative plans.

Organization

Format of the workshop

Given the COVID-19 circumstances, we had to change the format from live to blended. We ended up with inviting 20 participants to Leiden, the other researchers joined digitally using MS Teams. Also, in the original plan, we invited international researchers for the full four days. As it is quite tiring to digitally participate for four days, we chose to invite the international participants for Thursday October 1, 2020.

Other comments

The blended form worked well for us: the digital participants also felt involved. MS Teams has excellent features, in having a plenary “room” as well as separate break-out rooms to have multiple parallel sessions with a smaller number of participants. However, it proved difficult for some participants to attend as there were some additional safety features by Leiden University. Some researchers also used MS Teams with a different account than was registered for the Lorentz Center meeting, which resulted in no access. Moreover, the sound was sometimes difficult for digital participants, which made that strict use of the microphone and/or walking to the front of the room was necessary. Although we had to improvise throughout the week, we felt tremendously lucky that we were able to organize this blended workshop given the circumstances. The Lorentz Center team also had a lot of extra work improvising but provided us with as much support as possible.

Dr. Marieke Begemann (Groningen, the Netherlands)

Prof. Dr. Iris Sommer (Groningen, the Netherlands)

Prof. Dr. Wim Veling (Groningen, the Netherlands)

Dr. Helene Speyer (Kopenhagen, Denmark)

Zoë Haime (London, UK)