Cognitive-behavioural therapy and personalized treatment

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published in
Behaviour Research and Therapy
2020

DOI (link to publisher)
10.1016/j.brat.2020.103595

document version
Publisher's PDF, also known as Version of record

document license
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Behaviour Research and Therapy 129 (2020) 103595

Contents lists available at ScienceDirect

Behaviour Research and Therapy

journal homepage: www.elsevier.com/locate/brat

Editorial

Cognitive-behavioural therapy and personalized treatment: An introduction to the special issue

In 1967 Gordon Paul famously stated that the question towards which all outcome research should ultimately be directed is what treatment, by whom, is most effective for this individual with that specific problem, and under which set of circumstances? Half a century later this question still remains largely unanswered, although there is a renewed research interest to determine what works for whom. Knowledge about moderator variables that can help to predict whether a patient will benefit more from one treatment relative to another is still limited.

In medicine the term 'precision medicine' is a relatively new term referring to identifying which approaches will be effective for which patients based on genetic, environmental, and lifestyle factors. Personalized medicine is an older term with a similar meaning but could be misunderstood as implying that interventions are being developed uniquely for each single individual. Given the current state of affairs it seems somewhat pretentious to speak of precision psychological treatment. So, when we use the term personalized treatment one has to realize that the goal is to generate personalized predictions to select the right treatment for a given subgroup of patient and not for a unique patient. The long-term benefits of research progress in personalized treatment not only include an improved ability to predict which treatments will work best for specific patient groups, but also improved approaches to preventing, diagnosing and treating a wide range of mental disorders as well as a better understanding of determinants and course of mental disorders (Cohen & DeRubeis, 2018).

Personalized psychological treatment is a rapidly evolving field and many competing and complementary methodological/statistical approaches can be identified (Kessler, 2018). The aim of this special issue of Behaviour Research and Therapy is to provide an introduction to this innovative approach that already has been proven to be efficacious and efficient in medicine and may also have a great impact on future developments in mental health care.

In the opening piece, *Robert DeRubeis* gives a historical overview of the development during the past 50 years of clinical judgements about what works for whom to increasingly more sophisticated actuarial methods to identify person characteristics that can predict treatment response. Research on individual moderators, variables that interact statistically with treatment type, has shifted to research involving multivariable machine-learning-based algorithms. Individual moderators have rarely proved powerful enough to inform treatment decisions resulting in the development of approaches in which multiple variables are combined in making treatment recommendations. Promises and pitfalls are discussed (DeRubeis, 2019).

In the second paper of this special issue, *Ronald Kessler and colleagues*, point at the problem that randomized trials can only contribute to the identification of relevant predictors of outcome and composite precision rules, because of small sample sizes. The authors make a plea to work with large observational data from routine practice to develop composite precision rules and test these in subsequent randomized trials. The authors indicate that this approach is not without problems, but it is clearly one of the most promising approaches to develop precision treatments in mental health. This paper gives a clear, convincing overview of this fascinating and innovative approach (Kessler, Bossarte, Luedtke, Zaslavsky, & Zubizarreta, 2019).

The remaining papers in the special issue are empirical in nature and describe the most important methodological/statistical approaches to personalized treatment. As the field is rapidly evolving, there is room for complementary, competing and sometimes antagonistic approaches (Petkova et al., 2017). Consequently, there is no historical or logical order in which these diverse approaches to personalized treatment are presented.

Marleen ter Avest and colleagues describe their use of so-called QUalitativeINteraction Trees (QUINT) in order to determine for which patients Mindfulness-Based Cognitive Therapy for depression had additional value compared to treatment as usual. If some subgroup of patients may display a better outcome with treatment A than with B, whereas for another subgroup, the reverse may be true, a qualitative (i.e., disordinal) treatment–subgroup interaction is present. QUINT is a nonparametric tree-based subgroup identification method, appropriate for data from randomized controlled trials involving two experimental conditions. The aim of QUINT is to induce subgroups of patients, defined in terms of baseline characteristics that are involved in qualitative treatment-subgroup interactions. The result of an analysis with QUINT is a binary tree from which treatment assignment criteria can be derived. Study results suggested that MBCT might be more beneficial for patients with earlier onset of depression, higher levels of rumination and a lower quality of life (Ter Avest et al., 2019).

Lynn Boschloo and colleagues show the potential of network estimation techniques for personalized treatment. Based on a network model of depression specifically focusing on individual symptoms and the associations between them, the authors showed that the internet-based intervention Deprexis was related to larger improvements in particular symptoms, indicating that these larger improvements were independent of changes in other symptoms. They assumed that participants primarily suffering from symptoms that were directly targeted by the internet-based intervention would benefit more from the intervention than other participants. Using a severity measure based on the weighted sum of all depression symptoms, in which the weighting was

https://doi.org/10.1016/j.brat.2020.103595

Available online 24 February 2020

based on the direct effects of the intervention on individual symptoms, they were able to show that the intervention was more effective in improving overall depression severity for participants with higher scores on those symptoms that were directly affected by the intervention. This approach suggests that estimating a network with direct and indirect connections between treatment condition and changes in all individual symptoms may have potential in deriving individualized treatment recommendations (Boschloo et al., 2019).

Wolfgang Lutz and colleagues describe their use of a computer-based feedback, decision and clinical problem-solving system, the Trier Treatment Navigator (TTN), based on modern statistical machine learning techniques. TTN not only yields personalized pre-treatment recommendations for drop-out risk and optimal early treatment strategy selection, but also personalized adaptive recommendations during treatment. Moreover, an expected trajectory of recovery for individual patients based on pre-treatment characteristics is estimated, actual treatment progress is compared to the expected course of treatment and warning signals are provided to therapists if a patient's progress falls below a predefined failure boundary. Next, clinical problem-solving tools (CPST) build on these warning signals are provided to these so-called "not-on-track" (NOT) or signal cases. Using the TTN, drop-out risk and optimal early treatment strategies could be determined. Moreover, NOT cases could be reliably identified and subsequently offering CPST in risk areas improved treatment outcome. This approach shows that technologically advanced systems like the TTN can easily be implemented in routine care to personalize treatment during treatment by using outcome monitoring and feedback tools (Lutz, Rubel, Schwartz, Schilling, & Deisenhofer, 2019).

Aaron Fisher and Hannah Bosley tested a novel person-specific method for identifying discrete mood profiles on the basis of time-series data and examined the degree to which these profiles could be predicted by time-based variables. Data were collected four times daily over the course of a month and latent classes representing discrete mood profiles were prepared for each participant. Elastic net regularization was then used to identify time-bound predictors of each mood profile and logistic regression used to model the timing of latent class expression. The presence/absence of each mood profile could be predicted from temporal variables alone (Fisher & Bosley, 2020).

Saunders and colleagues describe a person-centered approach that makes use of clinical profiles of patients to personalize medicine as an alternative to more traditional variance-centered approaches. Latent variable mixture modeling is applied to recovery, deterioration, and attrition patterns from over 20,000 patients to determine eight distinct profiles that were consistent over time and that predicted differential response to CBT vs Counselling. The authors provide an alternative to more widely used approaches that might be superior in some respects to the latest cutting edge technology in this emerging domain (Saunders, Buckman & Pilling, 2020).

The study from *Jessica Hartmann and colleagues* focuses on persons with an Ultra-High Risk (UHR) for psychosis and is aimed at identifying subclasses of these individuals based on trajectories of symptomatic and functional change over time. They followed 304 individuals for 40 months and found that all trajectories showed parallel slopes with improving symptoms over time and were primarily distinct in severity of symptoms at baseline. Although this study did not manage to identify divergent trajectories, it does show that baseline severity is strongly associated with outcome at the longer term (Hartmann et al., 2020).

Rayner, Eley, Breen and colleagues explore the role of genetic influences on four lifetime treatment-related behaviors (seeking, receiving, self-help, and self-medication). The majority of those with common mental disorders (anxiety and depression) do not receive treatment. Treatment seeking behaviors were only modestly heritable but overlap was found between lifetime treatment-related phenotypes and psychiatric disorders and behavioral traits. The article demonstrates how the UK Biobank can be used to explore the contribution of genetic influences on behaviors of interest with respect to psychopathology and treatment (Rayner et al., 2019).

Davies and colleagues describe the Genetic Links to Anxiety and Depression (GLAD) study that seeks to recruit individuals with common mental disorders (depression or anxiety) into the NIHR Mental Health BioResource. Participants are recruited on-line with tens of thousands of individuals already having signed up with very high rates of recurrent depression and severe anxiety both separately and together (comorbid). The approach can generate large numbers of high risk and afflicted participants at minimal cost with the sample skewing toward young adults who are female and more educated (Davies et al., 2019).

Taken together, we still have much to learn before we will be able to answer the famous question about personalized treatment as posed by Gordon Paul in 1967. We hope that the innovative and novel research approaches featured in this special issue will stimulate more critical, creative and meaningful clinical science focused on personalized recommendations for the most optimal treatment for a particular patient. Bringing together the most promising methodological and statistical approaches may help to approach the ultimate aim of deriving evidence-based personalized predictions in order to increase the efficiency and effectiveness of mental health systems.

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