

**Therapies for mental health difficulties: finding the sweet spot between standardization
and personalization**

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Short title: Standardization and personalization of therapies

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Short Summary:

There are strong arguments for standardizing therapies for mental health difficulties in young people and for the development of digital therapies. At the same time, the importance of personalized treatments is also increasingly apparent. In this editorial we discuss challenges and the continued need to find the sweet spot between standardization and personalization when it comes to therapies for mental health difficulties. We illustrate our discussion with reference to insomnia in adolescents/ young adults as well as the chronic health condition type 1 diabetes (T1D).

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There are strong arguments for standardizing therapies for mental health difficulties in young people – ensuring the consistent delivery of empirically supported treatment (Scott, 2016). Perhaps in line with this, there has been a recent interest in digital therapy aimed at the widescale dissemination of empirically based treatments (Hollis et al., 2017). Digital therapy offers additional advantages of increasing access to therapy, increasing convenience (they can be delivered in homes), and avoiding stigma (therapies be accessed without consulting a health care professional). These therapies are also cost-effective. What is more, research focusing on transdiagnostic approaches highlights that in some cases, treatment principles do not need to be tailored for specific disorders (Dalglish et al., 2020). Instead, they can focus on the shared features among different disorders and are therefore useful for a wide range of conditions.

At the same time, the importance of personalized treatments is also increasingly apparent (Ng and Weisz, 2016). In medicine, this is perhaps best illustrated by research into biomarkers informing treatments for cancer (Sporikova et al., 2018) and cardiovascular disease (Ho et al., 2018). While less-well established, personalization also applies to mental health difficulties (Scott, 2016), whereby therapies are personalized based on various factors including the specific symptoms reported as well as the acceptability of treatments to the young person and their parents/ guardians. In this editorial we discuss challenges and the continued need to find the sweet spot between standardization and personalization when it comes to therapies for mental health difficulties. We illustrate our discussion with reference to insomnia in adolescents/ young adults as well as the chronic health condition type 1 diabetes (T1D).

The perceived aetiology of a disorder has sometimes impacted treatment decisions. Indeed, historically, insomnia was considered a ‘secondary disorder’(Harvey, 2001). When it occurred, it was often considered to be a symptom of other mental health difficulties such as

anxiety or depression. Treatment for insomnia reflected this thinking and those with insomnia might be treated primarily for their comorbid condition, whether it was anxiety, depression or a chronic health condition.

Over time, data from various sources converged against the idea of insomnia being a 'secondary diagnosis' and perception shifted. Insomnia is now considered a diagnosis in its own right. Chronic cases are best treated by CBT-I which can be used with both adult populations and young people (Baglioni et al., 2020) although behavioural interventions are sometimes preferable and are more typically used with infants and children. CBT-I has been demonstrated to be effective despite comorbid conditions including anxiety and depression. What is more, therapies for sleep difficulties may have implications beyond improving sleep quality and have been found to result in better mental health in both adults (Scott et al., 2021) and adolescents (de Zambotti et al., 2018).

The effectiveness of CBT-I and other treatments for sleep difficulties, combined with access challenges, have led to digital therapies (Williamson, 2021). These are plentiful, and include in pediatric samples, Sleep Ninja (Werner-Seidler et al., 2019; Werner-Seidler et al., 2022), Doze (Carmona et al., 2021) as well as another online CBT-I therapy (de Bruin et al., 2015). These applications appear promising in supporting sleep in young people. While programs of this type are standardized to some extent, it is possible to include algorithms in digital therapies which can result in a degree of adaptation or personalization, with therapy focusing on the specific symptoms flagged by the user for example. Modular therapy, involving a 'menu' from which treatment components can be 'ordered' depending on specific characteristics of an individual (based on research evidence as well as patient preferences)

provides another example of personalization (e.g. TranS-C, (Harvey and Buysse, 2017). This exciting option could be key for the further personalization of therapies.

Arguments for personalization of therapies focus on the finding that some people do not respond to even the best available treatments. This suggests that further understanding of the risk factors associated with treatment resistance is required so that therapies can be adapted (or personalized) for those who are not improving despite access to the best available methods. One potential risk factor for treatment resistance is comorbidity. CBT-I has been widely established to be effective in treating insomnia regardless of comorbidities. However, certain disorders appear to create unique challenges for treatment. Those with these conditions may benefit from modifications to their standardized therapy (including the addition of comorbidity-specific treatment components). Recently, we wrote an article on type 1 diabetes (T1D) as a prototypical condition challenging some of what we know about sleep (Gregory et al., 2022). T1D occurs when the pancreas fails to produce enough insulin meaning that blood glucose can become dangerously high. This condition is treated with life-saving insulin, but that can result in low blood glucose – severe cases of which can result in coma and death.

When it comes to knowledge about sleep, T1D challenges the dogma in many ways. For example, blood glucose in those with T1D needs to stay within a safe range day and night, meaning that despite the many advantages of undisturbed sleep, in some cases, nighttime monitoring may prove essential. Second, gold-standard treatments for monitoring and treating T1D may, in themselves, disturb sleep: state-of-the-art technology moves into the bedroom in the form of insulin pumps, glucose monitors and phones, with associated alarms. Conversely, in its standardized format, the gold-standard treatments for sleep disturbances may create challenges for those with T1D. For example, therapies can involve sleep restriction designed to ensure more

consolidated sleep (from which waking from alarms could prove more difficult); diet and exercise recommendations may need to be altered depending on blood glucose levels; and the removal of technology from the bedroom is not always possible. Research should further examine the extent to which such factors need to be addressed and whether modifications of standard CBT-I is required. As one example, adding a module with psychoeducation focused on the role of technology in the bedroom could prove valuable when considering sleep in young people living with T1D.

The example of T1D can further highlight the possible need for personalization for other aspects of treatment for mental health difficulties. Young people living with T1D may have comorbid mental health difficulties, including anxiety, depression and neurocognitive difficulties including issues with attention (Delamater et al., 2018). Explanations for these symptoms are sometimes directly related to T1D, with evidence that impairment in neurocognitive performance is associated with blood glucose in a U-shaped manner for example (Delamater et al., 2018).

It might make sense that recommendations for addressing attention difficulties which appear to stem from blood glucose extremes, should focus on these same factors (i.e. attempting to avoid extreme blood glucose levels) as a first line approach. But given that blood glucose levels can be difficult to control in those living with T1D, other approaches can be useful to address remaining symptoms. Similarly, it would make sense to adapt standardized treatment for comorbid anxiety, particularly given that those living with T1D who have a real and constant risk of serious medical sequelae. Conversely, some of the techniques that are useful for those with T1D (i.e. techniques specific to this condition) might be irrelevant to those without. Treatment aims might also differ in those living with T1D – for whom an inappropriately *low* level of anxiety could prove maladaptive (resulting in reduced blood glucose monitoring for example).

Clinicians already personalize therapies depending on medical and psychological histories and factors such as intellectual ability – but further research into determining when to use standardized treatment and when to adapt or modify a treatment is required. We suggest a research agenda including: 1) consideration of challenges stemming from standardized treatments in relation to specific comorbidities and health inequalities such as ethnicity and deprivation which could reduce the efficacy, safety or acceptability of treatments (e.g. from trial evidence and bringing together experts from fields such as T1D and sleep treatment research); 2) establishing which comorbidities require therapy adaptation (and which do not) and consider how best to approach the issue of multiple comorbidities; 3) greater patient and public involvement (PPI) in research at each stage to highlight current issues and understand patient preferences; 4) where indicated adapt/ modify standardized treatments based on comorbidities and health inequalities; 5) pilot adapted/ modified programmes; 6) conduct thorough RCTs to compare the effectiveness of adapted/ modified programmes against best available standardized treatments in specific patient groups.

If greater personalization proves valuable and cost-effective, then a further challenge will be to access suitably trained therapists. Lack of expertise in mental health in the setting of specific comorbidities creates unique challenges. Adapting and personalizing within standardized (and possibly digital) treatments could prove valuable and the inclusion of modules for different comorbidities within standardized treatments may provide one key way of doing this. If therapy adaptation for a specific comorbidity is required then it is key to have a 360-degree understanding of these comorbidities and health inequalities. This will be the starting point for carefully designed studies which will ultimately be the only way to truly optimise treatment and mental health outcomes for all young people despite their situation.

Conflicts of Interests

AMG was an advisor for a project initially sponsored by Johnson's Baby. She is a consultant for Perrigo (2021+). She receives royalties for two books: *Nodding Off* (Bloomsbury Sigma, 2018) and *The Sleepy Pebble* (Flying Eye, 2019). She has another contract with Lawrence King Publishers (publication due 2023). She was previously a director of Sleep Universal LTD (2022); She is a regular contributor to BBC Focus and has contributed to other outlets (such as The Guardian). She occasionally receives sample products related to sleep (e.g. blue light blocking glasses) and has given a paid talk to a business (Investec). She is a specialist subject editor at JCPP (sleep) for which she receives a small honorarium. She has contributed a paid article to *Neurodiem*. Over the past 3 years, Dr. Buysse has served as a paid or unpaid consultant to National Cancer Institute, Pear Therapeutics, Sleep Number, Idorsia, Eisai, and Weight Watchers International. All consulting agreements have been for a total of less than \$5000 per year from any single entity. Dr. Buysse is an author of the Pittsburgh Sleep Quality Index, Pittsburgh Sleep Quality Index Addendum for PTSD (PSQI-A), Brief Pittsburgh Sleep Quality Index (B-PSQI), Daytime Insomnia Symptoms Scale, Pittsburgh Sleep Diary, Insomnia Symptom Questionnaire, and RU_SATED (copyrights held by University of Pittsburgh). These instruments have been licensed to commercial entities for fees. He is also co-author of the Consensus Sleep Diary (copyright held by Ryerson University), which is licensed to commercial entities for a fee. He has received grant support from US federal agencies including NIH, PCORI, AHRQ, and the VA. All other authors have declared that they have no competing or potential conflicts of interest.

Author contributions

All authors contributed to the critical writing of this editorial.

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