



Digital Therapeutics in Pain Treatment

- **Marta Čeko, PhD**, Institute of Cognitive Science, University of Colorado, Boulder, CO, USA.
- **David Hohenschurz-Schmidt, MSc**, Pain Research, Department of Surgery & Cancer, Faculty of Medicine, Imperial College London, United Kingdom; Research Centre, University College of Osteopathy, London, United Kingdom.
- **Serge Marchand, PhD**, Department of Surgery, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Sherbrooke, Québec, Canada; Centre de Recherche du Centre Hospitalier Universitaire de Sherbrooke (CRCHUS), Sherbrooke, Québec, Canada.

Definitions and Status Quo

Digital therapeutics (DTx), ('software as medical device',^[1]) are defined by the Digital Therapeutics Alliance (DTA) as "evidence-based therapeutic interventions that are driven by high-quality software programs to treat, manage, or prevent a disease or disorder. They are used independently or in concert with medications, devices, or other therapies to optimize patient care and health outcomes"^[24]. For pain, DTx typically use software to record pain perception and physiological signals (e.g., heart rate or blood oxygenation) or to manage pain-related health issues such as sleep or mood^[14]. Smartphone or online applications can provide treatment-specific content, including education or psychologically informed programs, or interaction with chatbots^[2,20]. Wearables can be used to guide different lifestyle parameters related to pain reduction, such as exercise and stress^[8,20,21]. An increasingly popular type of DTx showing great promise for the treatment of pain is immersive virtual reality (VR), pioneered by Hoffman and colleagues for acute pain control during wound care in burn patients^[9]. Since then, VR applications have shown robust efficacy for the management of acute pain and as adjunct treatment for burn pain and other painful medical procedures^[6,12,22,23]. More recently, VR has emerged as a stand-alone treatment with the potential to achieve long-lasting relief in chronic pain, such as low back pain^[4] or endometriosis^[15]. The promise of VR and other DTx to provide viable adjuncts or alternatives to side-effect-prone pharmacological options is reflected in the FDA's recent first-time approval of a VR device for the treatment of chronic pain^[3,4,16].

Potential Benefits for Integrative Health

As articulated by Keefe and colleagues a decade ago^[13], DTx might improve clinical pain outcomes in several ways^[6,12,22,23]. These include distraction-based methods, with greater treatment effects observed for high-tech immersive DTx utilizing multiple sensory inputs (haptic, audio, visual); by acting on pain-related movement patterns (e.g., in chronic pain disorders with pronounced kinesiophobia); and by simulating movement of avoided or missing body parts (e.g., CRPS or phantom limb pain) in safe (virtual) environments. Additionally, DTx can have direct neuromodulatory effects^[6,22] as well as indirect effects on pain by improving mood outcomes^[12,23]. Using the opportunities of DTx to promote treatment adherence and individualization^[20], DTx can be integrated with evidence-based behavioral interventions to provide a more immersive and experiential pain intervention. This approach has the potential to enhance the efficacy and long-term benefits of such interventions^[13], and to reduce cost and enhance access to care^[17].

To date, DTx are mainly used as stand-alone interventions, often sought out by patients themselves, and the line to wellness applications is often blurred. Practitioners may on occasion recommend individual DTx or use them to provide digital exercise sheets or educational content. The use of telehealth, another digital approach to pain management, was accelerated by the COVID-19 pandemic^[10], and continues to be used as a replacement for in-person care^[16]. For integrative models of pain care, however, DTx and other digital tools have the potential to be used as integrated treatment components alongside in-person care, as platforms where patients can

interact with providers or experience peer support, to monitor patient progress, and to support self-management once in-person therapy has been completed. Further, electronic health records are important to harmonize care across providers, especially in interdisciplinary settings. As technology develops, DTx are beginning to influence clinical care, research, and healthcare policy^[1].

Potential Issues and Future Needs

In the US and in Europe, DTx are becoming increasingly regulated, with the first pain-related applications already approved for prescribing and reimbursement^[11]. Regulation has also ushered in higher standards for the scientific evaluation of DTx through clinical trials^[25], with the goal of improving the evidence base for DTx.

For research, data collection through smartphone applications and wearables holds the promise of large-scale high-density data from the real world. Not only can this make large clinical trials more feasible^[19], but the analysis of such datasets may also improve scientific understanding of individual differences in pain and interventions. App developers and clinicians will then strive to use this information to personalize care to individuals. Drug companies are also highly active in the DTx space, for example, by exploring options to increase medication adherence^[7]. Whether these endeavors will also promote integration with non-pharmacological care remains to be seen.

Despite rapid and promising developments, there are challenges for the widespread use of technological solutions in healthcare, including the allocation of resources, ethical issues (including privacy and data security), governance, the development of eSkills and a technology-friendly culture^[5].

In pain management, as in other chronic disease areas, the potential for personalization, improved accessibility, and better care is significant. For DTx and other digital solutions to be effectively integrated with in-person care, however, joint efforts continue to be necessary from developers, healthcare providers, research, and policy-makers.

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