Global Research Trends on Digital therapeutics in Early 21st Century: A Data-driven Bibliometric Analysis

Fanyu Meng, Ruiying Ruiying Quan, Zhiying Cui, Xin Tian, Zheng Li, Jiuyue Wang, Zhongqing Wang, Zhongqing Peng

Submitted to: JMIR Mental Health
on: August 24, 2025

Table of Contents

Global Research Trends on Digital therapeutics in Early 21st Century: A Data-driven Bibliometric Analysis

Fanyu Meng[1]; Ruiying Ruiying Quan[2]; Zhiying Cui[1]; Xin Tian[1]; Zheng Li[1]; Jiuyue Wang[1]; Zhongqing Wang[1]; Zhongqing Peng[3]

[1] the First Hospital of China Medical University Shenyang CN
[2] The Queen's University of Belfast Joint College Shenyang CN
[3] Fourth Affiliated Hospital of China Medical University Shenyang CN

Corresponding Author:
Zhongqing Peng

Fourth Affiliated Hospital of China Medical University
102 Nanqi Road
Shenyang
CN

Abstract

As an emerging therapeutics plan, digital therapeutics has attracted increasing attention in recent years, with numerous research hotspots continually emerging. This study aims to explore the evolving trends in digital therapeutics publications since the beginning of the 21st century. A total of 660 publications that met the requirements were included. The United States of America was the top contributing country. Harvard University and Journal of Medical Internet Research were the institution and journal with the largest number of publications, respectively. Marsch, Lisa A and Maricich, Yuri A. were the top two contributing authors. Research hotspots of digital therapeutics were divided into four clusters based on the co-occurrence analysis of keywords: (1) Application of Digital Therapeutics in Chronic Disease; (2) Applications of Digital Therapeutics in the Intervention of Mental Disorders; (3) Applications of Digital Therapeutics in Addiction Treatment; (4) Applications of Digital Therapeutics in Cognitive Behavioral Recovery.

(JMIR Preprints 24/08/2025:82911)
DOI: https://doi.org/10.2196/preprints.82911

Original Manuscript

Global Research Trends on Digital therapeutics in Early 21st Century: A Data-driven Bibliometric Analysis

Title Page

Fanyu Meng[1,2], BSc; Ruiying Quan[3], BSc; Zhiying Cui[1,2], BSc; Xin Tian[1,2], BSc; Zheng li[1,2], BSc; Jiuyue Wang[1], BSc; Zhongqing Wang[1,*], Ph. D; Cheng Peng[4,*], Ph. D

1 Department of Information Center, the First Hospital of China Medical University, Shenyang, China

2 School of Health Management, China Medical University, Shenyang, China

3 The Queen's University of Belfast Joint College, China Medical University, Shenyang, China

4 Department of Ophthalmology, Fourth Affiliated Hospital of China Medical University, Shenyang, China

* Corresponding Authors:

Zhongqing Wang, Ph. D,
Department of Information Center, the First Hospital of China Medical University, 155 Nanjingbei Street, Shenyang, 110001, China (wangzhongqing@cmu.edu.cn).

Cheng Peng, Ph. D,
Department of Ophthalmology, Fourth Affiliated Hospital of China Medical University, 102 Nanqi Road, Shenyang, 110005, China (pengcheng@cmu.edu.cn).

Abstract

As an emerging therapeutics plan, digital therapeutics has attracted increasing attention in recent years, with numerous research hotspots continually emerging. This study aims to explore the evolving trends in digital therapeutics publications since the beginning of the 21st century. A total of 660 publications that met the requirements were included. The United States of America was the top contributing country. Harvard University and Journal of Medical Internet Research were the institution and journal with the largest number of publications, respectively. Marsch, Lisa A and Maricich, Yuri A. were the top two contributing authors. Research hotspots of digital therapeutics were divided into four clusters based on the co-occurrence analysis of keywords: (1) Application of

Digital Therapeutics in Chronic Disease; (2) Applications of Digital Therapeutics in the Intervention of Mental Disorders; (3) Applications of Digital Therapeutics in Addiction Treatment; (4) Applications of Digital Therapeutics in Cognitive Behavioral Recovery.

Keywords

Digital Therapeutics; Bibliometrix Analysis; VOSviewer; WOS

1. Introduction

Digital therapeutics is a treatment plan that uses digital or online health technologies to treat medical or mental conditions, aiming to enhance the accessibility and effectiveness of healthcare by preventing, monitoring, managing and treating symptoms and diseases or optimizing treatment [1–3].

Compared with traditional diagnostic and therapeutic approaches, a distinctive feature of digital therapeutics lies in its ability to optimize individualized treatment strategies and offer diverse forms of intervention. It may take the form of smartphone applications that promote dietary or physical activity changes, or apps that enhance medication adherence to support effective disease management, thereby embodying the principles of personalized medicine [3,4].

Over the past decade, digital therapeutics has emerged as a novel form of therapeutic intervention. A variety of digital therapeutics-based products have received approval from relevant regulatory agencies in several countries, while many others are currently undergoing clinical trials. The market share of digital therapeutics is also steadily expanding. According to a January 2020 report by the U.S.-based market research firm Allied Market Research, the global digital therapeutics (DTx) market was valued at 2.88 billion in 2019. The market is projected to grow at a compound annual growth rate (CAGR) of 20.5%, with total revenue expected to reach 13.8 billion by 2027[5]. In 2021, the US Food and Drug Administration (FDA) also launched the Digital Health Precertification Program to facilitate the development and regulatory oversight of digital therapeutics

products[6]. These digital therapeutic products can be further categorized based on their delivery modalities, such as virtual reality[7,8],artificial intelligence[9],web applications[10] and mobile games [11]. Currently, digital therapeutics can provide treatment interventions for a range of conditions, including but not limited to depression[12],hypertension[13] and rheumatic diseases[14]. During the COVID-19 pandemic, multiple digital therapeutic products received emergency use authorization and demonstrated beneficial effects, particularly when patients' locations, socioeconomic factors, or global health conditions were constrained[6,11]. Furthermore, studies have highlighted that the momentum generated by the COVID-19 pandemic has substantially accelerated advancements in digital therapeutics and facilitated their widespread implementation[15].

Bibliometrics is a popular and rigorous quantitative method for exploring and analyzing literature-based textual data. It can reveal the performance of articles and journals, uncover collaboration patterns among groups from different perspectives, identify emerging hotspots in a specific research field, and explore the knowledge structure within existing literature in a particular domain [16–19]. Because of its capability to analyze large volumes of textual data and quantitatively organize knowledge structures, bibliometrics has seen widespread development and application in recent years[20–22]. Currently, scholars from various fields, including but not limited to medicine[23],finance[24],environmental science[25],agriculture[26] and medical informatics[27],have utilized bibliometrics to retrospectively analyze the research progress within their respective domains.

Despite breakthrough progress in digital therapeutics research in recent years, the field remains in its early stages. Moreover, previous studies have not conducted retrospective analyses using bibliometric methods. This study aims to apply bibliometric analysis to examine the publication output and collaboration patterns of countries/regions, institutions, and authors within, as well as to identify highly cited publications. Additionally, we performed keywords co-occurrence analysis to reveal research hotspots and reasonably predict future directions, providing valuable insights for practitioners and researchers.

2. Method

2.1 Search Methodology and Process

The Web of Science is a comprehensive and specialized citation database that offers extensive bibliometric data. Therefore, it was selected as the data source for this study. The search process and steps were illustrated in Figure 1. In this study, an advanced search was conducted in the Science Citation Index Expanded (SCI-EXPANDED) and the Social Science Citation Index (SSCI) of Web of Science Core Collection (WOSCC). The search query used was TS = ("Digital Therap*"), with the publication time span limited to January 1, 2000, to February 19, 2025, resulting in a total of 968 original publications retrieved. After excluding non-article/review publications and non-English language records, a total of 660 publications were retained for subsequent bibliometric analysis. It is important to note that, to avoid potential inconsistencies caused by database updates, all 660 publications data were downloaded on February 19, 2025. Additionally, the dataset is publicly available from an open data source, involves no ethical concerns, and does not require patient consent, as it is considered non-human subject research.

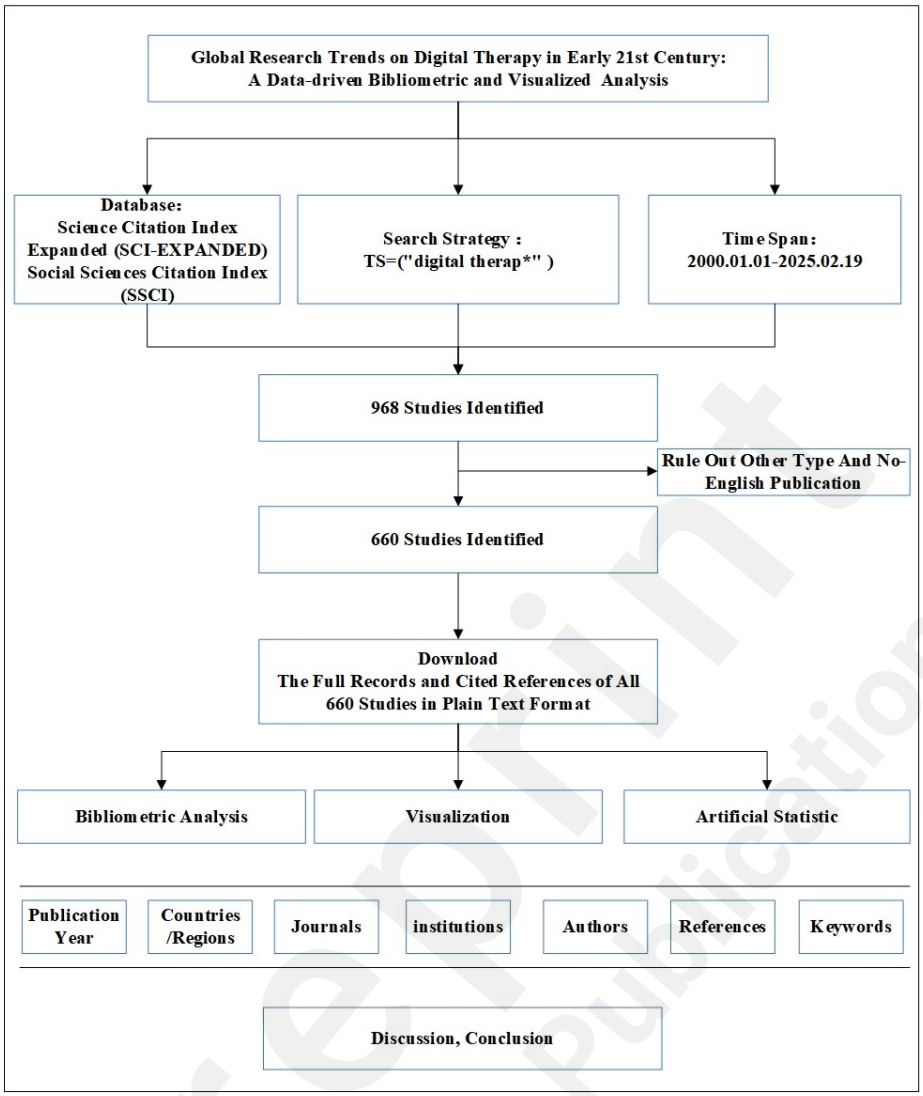

Figure 1 The search process and steps for retrieving publications in digital therapeutics.

2.2 Analysis Methods and tools

The analysis of relevant bibliometric indicators in this study was primarily conducted using VOSviewer (version 1.1.18), a specialized tool for constructing and visualizing bibliometric networks. VOSviewer is a free computer program developed in 2009 by Van Eck and Waltman from the Centre for Science and Technology Studies (CWTS) at Leiden University in the Netherlands. It is designed for constructing and visualizing bibliometric maps. VOSviewer is capable of performing two of the most common types of bibliometric analysis: co-authorship analysis and co-occurrence analysis. This study employed co-authorship analysis to reveal collaboration patterns among countries/regions, authors, and institutions. Additionally, key bibliometric indicators such as publication volume, average citation, and average publication year were summarized for the most productive countries/regions, authors, and institutions. This study utilized co-occurrence analysis, which determines the strength of association between keywords based on their frequency of appearing together within the same publication. This enabled keywords clusters analysis and overlay visualization based on average publication year, thereby assisting researchers in identifying research hotspots and emerging trends in digital therapeutics. Additionally, this study identified highly cited publications within in digital therapeutics and conducted a summary analysis of their relevant bibliometric indicators.

3.Result

3.1 Number of global publications

The temporal trend in publication volume can serves as an indicator of the popularity and evolution of a given research domain. Since the beginning of the 21st century, the annual publication volume in digital therapeutics has shown an overall increasing trend, as illustrated in Figure 1 (data for 2025 are partial and therefore not displayed). As shown in the figure 2, following the publication of the first article in digital therapeutics in 2015, the annual number of publications surpassed 10 for the first time in 2018, and has exhibited a clear year-by-year increase. In 2022, the annual number of publications exceeded 100, reaching 190 in 2024. Moreover, publications from 2023 to 2025 accounted for more than half of the total publications, indicating a growing attention to digital therapeutics in recent years.

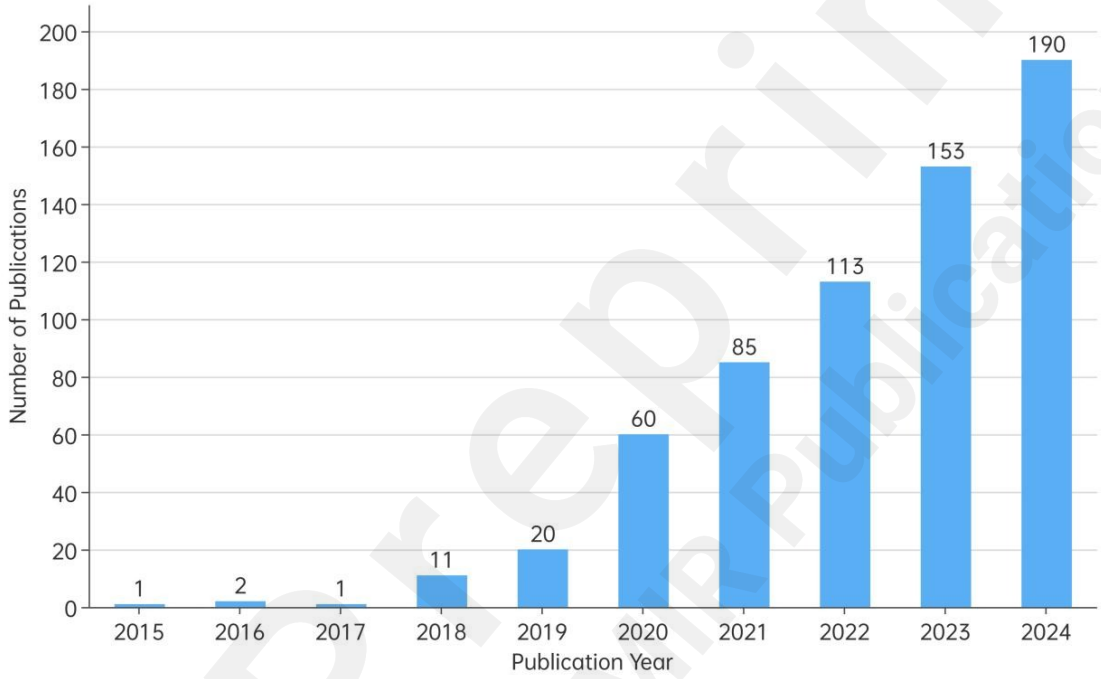

Figure 2 The annual number of publications in digital therapeutics.

3.2 Contributions of countries/regions

A total of 54 countries/regions have contributed publications to digital therapeutics. A world distribution map of these 54 countries/regions, based on the number of publications, was presented in Figure 3. As shown in the Figure 3, countries/regions with more than 50 publications were highlighted in red, those with 10 to 50 publications in yellow, and those with fewer than 10 publications in blue. Only a few of countries—primarily located in Asia, Europe, and North America—have contributed publications to digital therapeutics. Among them, the United States ranked first in publication output with 278 articles, followed by South Korea with 88 and the United Kingdom with 81.

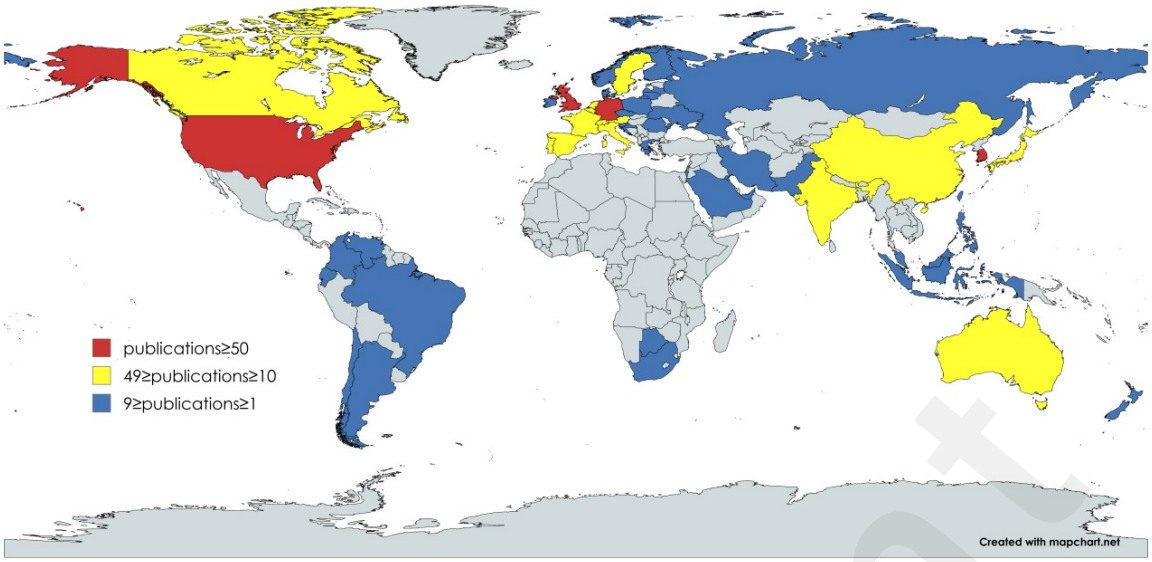

Figure 3 Global publication distribution map in digital therapeutics.

Table 1 summarized key bibliometric indicators for the top 10 countries/regions in terms of publication volume in digital therapeutics. As shown in Table 1, the United States leaded by a wide margin with 278 publications, accounting for 42.1% of the total, significantly surpassing all other countries/regions. Because of its high publication volume, the United States also demonstrated strong performance in total citation count, with 3,987 citations. With respect to average citation, the United Kingdom (19.26), Switzerland (18.50) and Australia (18.25) rank highest, suggesting that publications from these countries were of comparatively high quality and have received broad scholarly recognition. Regarding the average publication year, the majority of countries/regions had an average publication year between 2022 and 2023. The United States had the earliest average publication year, at 2022.08.

Table 1 The top 10 productive countries/regions in digital therapeutics.

Rank	Country/Region	Publications	Citations	Avg.Citations	Avg.Pub.Year
1	United States of America	278	3987	14.34	2022.08
2	South Korea	88	537	6.10	2023.19
3	United Kingdom	81	1560	19.26	2022.16
4	Germany	68	768	11.29	2023.00
5	China	43	174	4.05	2023.44
6	Italy	40	649	16.23	2023.23
7	Canada	31	512	16.52	2022.71
8	Australia	28	511	18.25	2022.57
9	Switzerland	28	518	18.50	2022.57
10	Japan	26	429	16.50	2022.35

3.3 Contributions of institutions

A total of 1,364 institutions have contributed publications to digital therapeutics. When applying a publication threshold of five or more articles, 74 institutions met the criteria. A co-authorship network of 63 institutions which existing collaborative relationships was illustrated in Figure 4. As shown in the figure 4, six distinct clusters were identified, represented by the colors red, yellow, blue, green, cyan, and purple. Among the six clusters, the red cluster—comprising 25 institutions—had the highest publications volume, with a total of 240 publications, accounting for 36.4% of the total publications. Collaboration among institutions appeared relatively limited, with several institutions serving as key nodes linking different co-authorship clusters—for example, the University of California, Los Angeles; the University of California, San Francisco.

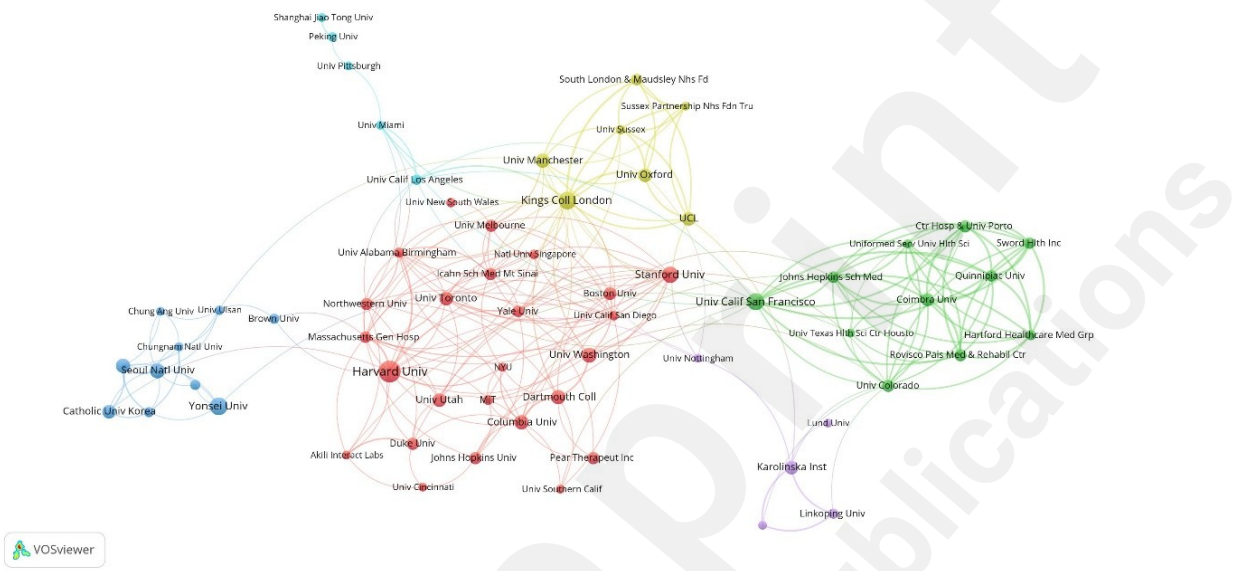

Figure 4 The co-authorship network map of productive research institutions in digital therapeutics.

Table 2 summarized key bibliometric indicators for the top 10 institutions in terms of publication volume in digital therapeutics. Of the top ten most productive institutions, nine appeared in the institutional co-authorship network depicted in Figure 4, with CureApp Inc. (ranked ninth) being the only exception. Harvard University leaded other institutions with a notable publication volume of 29 publications. In terms of average citation per publication, the top three institutions are King's College London (27.60), Stanford University (25.50), and Harvard University (15.90), indicating a higher average quality of their publications. Dartmouth College had the earliest average publication year, suggesting that it has been engaged in digital therapeutics research slightly earlier than other institutions.

Table 2 The top 10 productive institutions in digital therapeutics.

Rank	Institution	Publications	Citations	Avg.Citations	Avg.Pub.Year
1	Harvard University	29	461	15.90	2022.00
2	King's College London	20	552	27.60	2021.90
3	Yonsei University	19	122	6.42	2023.32
4	University of California, San Francisco	18	338	18.78	2021.67
5	Stanford University	16	408	25.50	2021.81
6	Seoul National University	14	85	6.07	2022.86
7	University of Washington	14	114	8.14	2022.14

8	Columbia University in the City of New York	13	157	12.08	2021.77
9	Cureapp Inc	13	309	23.77	2021.62
10	Dartmouth College	13	159	12.23	2020.92

3.4 Contributions of authors

A total of 3521 authors had contributed publications to digital therapeutics. When applying a publication threshold of two or more articles, 391 authors met the criteria. A co-authorship network of 47 institutions which existing collaborative relationships were illustrated in Figure 5. Since most authors were not appear in the co-authorship network, this indicated that collaboration among researchers worldwide was relatively limited, highlighting the need to strengthen international cooperation. As shown in Figure 5, seven clusters were identified, with only the red and green clusters containing more than 10 nodes each. The remaining five clusters relied on specific authors to establish co-authorship links with other clusters.

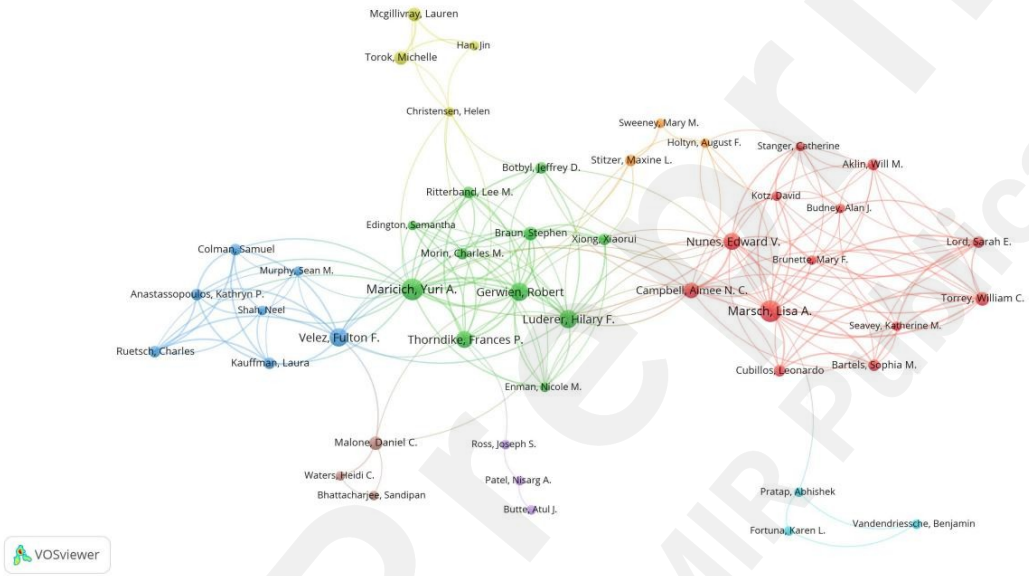

Figure 5 The co-authorship network map of productive authors in digital therapeutics.

Table 3 summarized key bibliometric indicators for the top 10 authors in terms of publication volume in digital therapeutics. All ten of the top authors appeared in the co-authorship network illustrated in Figure 5, with eight of them clustered within the red and green groups. The top three most productive authors were Marsch, Lisa A. (n = 10), Maricich, Yuri A. (n = 10) and Gerwien, Robert (n = 7). Most of the authors had an average citation exceeding 10, with the exception of Thorndike, Frances P. (5.67) and Malone, Daniel C. (2.00). In terms of average publication year, the earliest and latest authors are Marsch, Lisa A. (2020.90) and Malone, Daniel C. (2022.75), respectively.

Table 3 The top 10 productive authors in digital therapeutics.

Rank	Author	Publications	Citations	Avg.Citations	Avg.Pub.Year
1	Marsch, Lisa A.	10	121	12.10	2020.90

2	Maricich, Yuri A.	10	118	11.80	2022.00
3	Gerwien, Robert	7	70	10.00	2022.14
4	Luderer, Hilary F.	7	103	14.71	2021.71
5	Velez, Fulton F.	7	92	13.14	2021.57
6	Nunes, Edward V.	6	92	15.33	2021.00
7	Thorndike, Frances P.	6	34	5.67	2022.50
8	Campbell, Aimee N. C.	5	66	13.20	2021.60
9	Braun, Stephen1	4	65	16.25	2021.75
10	Malone, Daniel C.	4	8	2.00	2022.75

3.5 Contributions of journals

A total of 307 journals had contributed publications to digital therapeutics. Table 4 presented the top ten journals ranked by the number of publications in digital therapeutics. Journal of Medical Internet Research leaded by a significant margin, with 69 publications—far surpassing all other journals. Despite not being among the top journals by publication volume, NPJ Digital Medicine leads in average citations per article (33.60), suggesting that its publications are of high impact and that the journal has made a sustained contribution to the advancement of digital therapeutics.

Rank	Journal	Publications	Citations	Avg.Citations	Avg.Pub.Year
1	Journal of Medical Internet Research	69	860	12.46	2022.23
2	Digital Health	25	80	3.20	2023.72
3	JMIR Mental Health	23	403	17.52	2021.09
4	Frontiers in Psychiatry	21	117	5.57	2022.67
5	JMIR Mhealth and Uhealth	16	237	14.81	2021.88
6	BMJ Open	11	55	5.00	2022.64
7	NPJ Digital Medicine	10	336	33.60	2021.20
8	Healthcare	9	16	1.78	2023.44
9	Applied Sciences-Basel	8	12	1.50	2023.50
10	Hypertension Research	8	76	9.50	2023.38

3.6 The top 10 highly-cited Publications.

A total of 660 publications were included in this study. The ten most-cited publications were summarized in Table 4. The most highly cited publication was a research article by McIntyre, Roger S., titled “Treatment-resistant depression: definition, prevalence, detection, management, and investigational interventions,” published in 2023. This article highlighted the potential role of digital therapeutics in managing treatment-resistant depression (TRD). Despite its recent publication, it has already received a substantial number of citations, indicating its significant impact and contribution to digital therapeutics. Notably, most of the other publications listed in Table 5 have each been cited more than 100 times.

Table 4 The top 10 highly-cited publications in digital therapeutics.

Rank	Title	First Author	Journal	Citations	Y
1	Treatment-resistant depression: definition, prevalence, detection, management, and investigational interventions	Mcintyre, Roger S.	World Psychiatry	178	2
2	A novel digital intervention for actively reducing severity of paediatric adhd (stars-adhd): a randomised controlled trial	Kollins, Scott H.	Lancet Digital Health	172	2
3	Digital health for optimal supportive care in oncology: benefits, limits, and future perspectives	Aapro, M.	Supportive Care in Cancer	167	2
4	Convolutional recurrent neural networks for glucose prediction	Li, Kezhi	Ieee Journal of Biomedical and Health Informatics	151	2
5	Artificial intelligence: the future for diabetes care	Ellahham, Samer	American Journal of Medicine	137	2
6	Long-term outcomes of a web-based diabetes prevention program: 2-year results of a single-arm longitudinal study	Sepah, S. Cameron	Journal of Medical Internet Research	136	2
7	Psychiatric diagnosis and treatment in the 21st century: paradigm shifts versus incremental integration	Stein, Dan J.	World Psychiatry	108	2
8	Efficacy of a digital therapeutics system in the management of essential hypertension: the herb-dh1 pivotal trial	Kario, Kazuomi	European Heart Journal	102	2
9	Digital health technologies: opportunities and challenges in rheumatology	Solomon, Daniel H.	Nature Reviews Rheumatology	102	2
10	Digital therapeutics: an integral component of digital innovation in drug development	Sverdlov, Oleksandr	Clinical Pharmacology & Therapeutics	86	2

3.7 Analysis of keywords

As the keywords of publications encapsulate core knowledge, concepts, and scientific ideas, keywords co-occurrence analysis is an effective method in bibliometric research to identify research hotspots within a scientific domain. After cleaning the keywords data, a total of 2,521 unique keywords were included in this study. By applying a minimum occurrence threshold of five, 223 keywords met the inclusion criteria. A co-occurrence network of these 223 keywords was generated and was shown in Figure 6. Four keywords' clusters were identified through this analysis.

The first cluster (red cluster) primarily included keywords related to the use of digital therapeutics as treatment modalities, such as "digital therapy" and "telemedicine," as well as terms associated with

chronic diseases, including “hypertension,” “stroke,” and “diabetes”. This cluster was presumed to represent the research theme of applying digital therapeutics in chronic disease management.

The second cluster (green cluster) was primarily composed of keywords related to the use of digital therapeutics in the intervention of mental disorders, such as “psychotherapy,” along with keywords referring to mental health conditions or diseases including “depression,” “anxiety,” and “disorder.” This cluster likely reflected the research theme of applying digital therapeutics in mental health interventions.

The third cluster (blue cluster) was mainly composed of keywords related to the use of digital therapeutics in addiction treatment, such as “digital intervention” and “prescription digital therapeutic,” along with keywords referring to addictive behaviors or triggers, including “addiction,” “alcoholism,” and “dependence.” This cluster was presumed to represent the research theme of applying digital therapeutics in the treatment of addiction.

The fourth cluster (yellow cluster) primarily included keywords related to the use of digital therapeutics in cognitive and behavioral rehabilitation, such as “cognitive behavioral therapy,” “virtual reality,” and “communication,” along with keywords describing manifestations of cognitive or behavioral impairments, including “attention deficit disorder with hyperactivity” and “impairment.” This cluster was likely associated with the research theme of applying digital therapeutics in cognitive and behavioral rehabilitation.

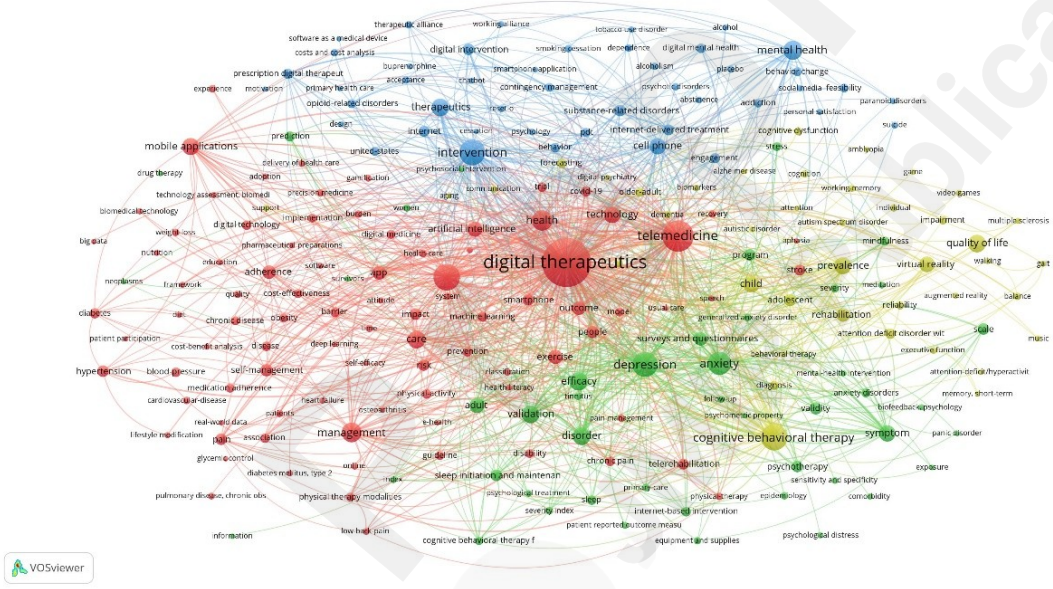

Figure 6 The co-occurrence network keywords map of keywords in digital therapeutics.

An overlay visualization of the average publication year (AAY) for the 223 keywords included in Figure 6 was generated and was presented in Figure 7. To evaluate the novelty of keywords in the overlay visualization map, VOSviewer defines the AAY as an indicator. The color gradient represents the range of AAY values, with keywords shaded closer to red indicating more recent emergence. As shown in the Figure 7, most of the keywords related to digital therapeutics appeared after 2021, suggesting that digital therapeutics was a relatively recent treatment approach or has only recently gained broader attention. Keywords with relatively late AAY values and high cumulative frequencies included “virtual reality” (AAY = 2023.22), “digital health” (AAY = 2022.64), and “digital therapeutics” (AAY = 2022.61).

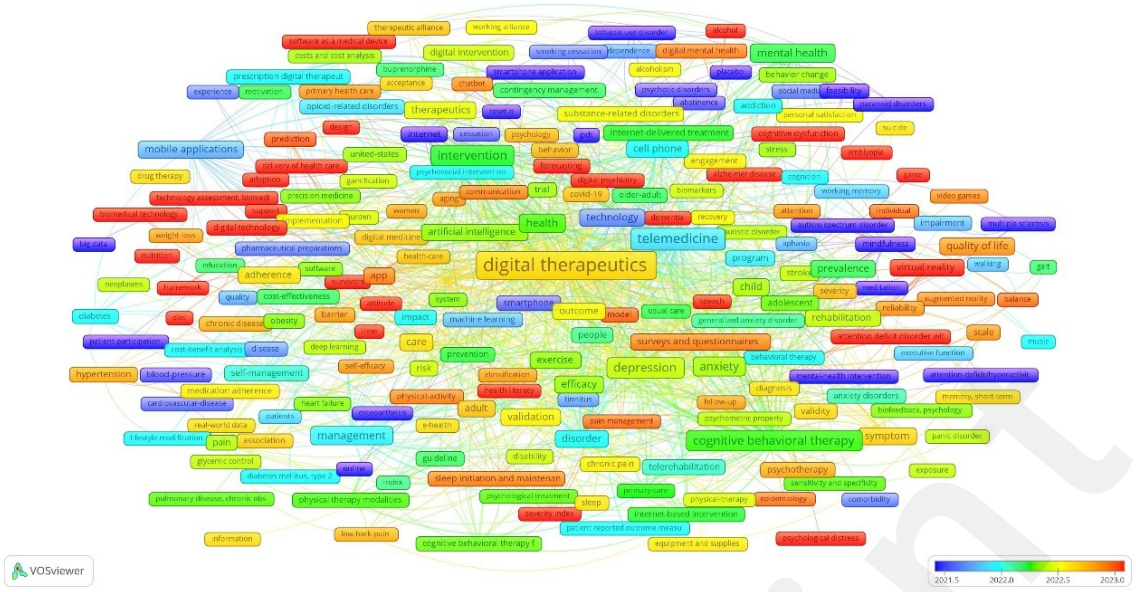

Figure 7 The overlay visualization map of keywords in digital therapeutics.

4.Discussion

Basic knowledge

The number of scientific publications in a given domain often reflects the progress and depth of research. The volume of publications has surged significantly since 2019 in digital therapeutics. Notably, more than 50% of the total publications have been produced within the past three years, indicating a growing level of interest and attention toward digital therapeutics. This trend may be closely associated with several underlying factors.

First of all, 2019 was precisely the time point when the COVID-19 pandemic broke out globally. Due to the limitation of space, the traditional medical model has been greatly impacted, and the demand for digital therapy, a treatment method that can provide telemedicine, home health management and digital health solutions, has gradually intensified [28].

Secondly, the gradual improvement of policies and regulatory systems for digital therapeutics have also been an important contributing factor. For example, in the United States, the Food and Drug Administration (FDA) issued several temporary guidance documents in 2020 concerning digital therapeutics and telemedicine products, which relaxed certain approval requirements and promoted the clinical research and implementation of digital therapeutic products[6]. Moreover, the European Union, including Germany, as well as several Asian countries such as South Korea, Japan, and China, had also gradually introduced policies to regulate emerging sectors and digital therapeutics[29].

Finally, the mature application of technologies such as artificial intelligence, big data and mobile health has provided a solid technical foundation for the implementation of digital therapeutic products, enabling remote data collection, data analysis and the development of personalized treatment approaches[30–34].

In the analysis of countries'/regions' contributions, as shown in Table 1, the United States leaded significantly with 278 publications, accounting for 42.1% of the total publications. This is approximately three times the number of publications from the second-ranked country. This may be related to the relaxation of certain approval requirements by the USA Food and Drug Administration (FDA) for digital therapeutics and related products. Moreover, diseases commonly targeted by digital therapeutics, such as obesity, diabetes, and depression, have relatively high prevalence rates in the

United States of America, which has generated a substantial amount of real-world research and subsequently driven the advancement of digital therapeutics[35–37].

In the analysis of institutional contributions, not all institutions meeting the publication threshold appeared in the co-authorship network, indicating relatively weak collaboration among institutions conducting research in digital therapeutics. Therefore, enhancing communication and cooperation between institutions are needed. CureApp Inc., ranked ninth in terms of publication count in digital therapeutics, was a digital health startup founded in 2014 and headquartered in Tokyo. The company mainly focuses on developing medical device programs that utilize advanced software technologies and clinical evidence for disease treatment. Although CureApp Inc. has limited collaboration with other institutions and did not appear in the co-authorship network under the set publication threshold, it demonstrated a strong publication output due to its research focus being highly aligned with the research direction of digital therapeutics.

In the analysis of authors' contributions, less than one-fifth of authors appeared in the co-authorship network after applying the minimum publication threshold, and most of the top ten authors by publication count were clustered within large groups. This indicated relatively weak collaboration among authors in digital therapeutics, highlighting the need to strengthen international communication and cooperation. The average publication years of productive authors in digital therapeutics were all prior to 2023, indicating that these researchers started their work relatively early and likely accumulated foundational studies that contributed to advancements in the field.

In the analysis of journals' contribution, *Journal of Medical Internet Research* has contributed 69 publications to digital therapeutics, significantly outperforming other journals. Its thematic focus is highly aligned with the scope of digital therapeutics research. Moreover, in terms of average citation counts, journals such as *NPJ Digital Medicine*, *JMIR Mental Health*, and *JMIR Mhealth and Uhealth* all rank in the Q1 quartile of the Journal Citation Reports (JCR). This indicated that these journals have consistently contributed high-quality publications to digital therapeutics and have maintained strong scholarly impact through frequent citations.

Hotspots of digital therapeutics

Keyword co-occurrence analysis is a commonly used bibliometric method for predicting research hotspots. As illustrated in Figure 6, by distinguishing different clusters based on the color-coded appearance of keywords, four thematic clusters related to digital therapeutics were identified.

Cluster 1 (Red Cluster): Application of Digital Therapeutics in Chronic Disease Management

Chronic diseases have a high incidence rate and require personalized health management, early warning and prevention[38]. According to statistics from the World Health Organization, nearly three-quarters of deaths worldwide are related to chronic diseases, making them a major public health issue that significantly reduced quality of life[39]. Due to the increasing prevalence of chronic diseases and rising healthcare costs, more and more startups are entering the field of digital therapeutics and related products. As a result, products based on digital therapeutics are gradually being introduced to the market. These products can take the form of mobile devices, computers, video games, applications, sensors, and virtual reality, providing evidence-based therapeutic interventions driven by the internet or software for the management of chronic diseases[40]. In particular, the home-based application environment of digital therapeutics aligns well with the reality that most patients with chronic diseases require at-home care. In the red cluster of the keyword co-occurrence map (Figure 6), we identified numerous nodes representing chronic diseases, such as "hypertension," "stroke," "diabetes," "chronic pain," and "obesity." These keywords, along with their frequencies, were summarized in Supplementary Table 1. This indicated that digital therapeutics have already been applied in the intervention and management of various chronic conditions.

In the application of digital therapeutics for chronic disease management, diabetes care has seen particularly widespread adoption and notable progress. Several digital therapeutic products have

already been implemented in clinical practice, including but not limited to iSageRx, Go Dose, Go Dose Pro, and the BlueStar® Rx System (BlueStar). In addition, several other products are currently under development and are expected to be deployed in the near future[41]. The application of digital therapeutics in diabetes management has been implemented through various forms, including web platforms[42], mobile applications[43], artificial intelligence systems[44] and even automated telephone inquiries designed for patient convenience[45]. Compared with traditional approaches, digital therapeutics-based diabetes management has enabled patients to monitor blood glucose levels in real time, allowing healthcare providers to adjust treatment plans accordingly based on dynamic data[46].

Cluster 2 (Green Cluster): Applications of Digital Therapeutics in the Intervention of Mental Disorders

According to statistics, as of 2019, the global cumulative cases of depression and anxiety disorders have exceeded 970 million[47]. According to the latest report statistics, more than 13% of teenagers worldwide suffer from mental disorders. Mental health problems caused by mental disorders not only weaken people but are even risk factors for fatal outcomes such as suicide and all-cause mortality[48,49]. Because of their advantages of high accessibility, convenience, low cost, and freedom from time and space constraints in intervening in mental disorders, digital therapeutic products/programs have attracted considerable research attention in recent years, with several such products/programs being implemented in practice[50]. Currently, digital therapeutic products/programs are capable of intervening in or monitoring the mental states of patients with psychiatric disorders such as depression[51], anxiety disorders[52], schizophrenia[53], attention-deficit/hyperactivity disorder (ADHD) [54] and post-traumatic stress disorder (PTSD)[55]. Currently, some unresolved issues remain in the applications available on the market for intervening in mental disorders. For example, many programs lack adequate security, putting the privacy of millions at risk[56] and potentially exposing vulnerabilities exploitable by malicious actors. Moreover, increasing evidence indicated that developers of digital therapeutic programs generally lack sufficient expertise, resulting in insufficiently detailed security guidelines, tight budgets and deadlines, and inadequate security testing[57].

Cluster 3 (Blue Cluster): Applications of Digital Therapeutics in Addiction Treatment

Addiction encompasses both substance and non-substance forms. Substance addiction, including drug dependence, is characterized by the repeated use of a substance despite awareness of its potentially severe consequences. Non-substance addiction, also referred to as behavioral addiction, includes conditions such as food addiction, internet addiction, and smartphone addiction[58]. Addiction can lead to immeasurable social consequences and losses. Given the home-based and user-targeted nature of digital therapeutics, they hold significant potential in supporting individuals to alleviate or overcome addictive behaviors. Digital therapeutics for addiction intervention can take various forms, including mobile applications [59], internet-delivered interventions[60], chatbots[61], , prescription digital therapeutics [62] and virtual reality technologies[63]. Digital therapeutics can be applied to a wide range of addiction types. In Supplementary Table 2, we summarized the addiction-related keywords that appeared in the co-occurrence map (Figure 6), along with their corresponding frequencies and related metrics. As shown in the table, digital therapeutics can be applied to both substance addictions—such as "alcohol"—and behavioral (non-substance) addictions, such as "cell phone" and "social media."

However, the evidence supporting the use of digital therapeutics for addiction treatment outcomes assessment and case management remains limited and is still in its early stages of development[64]. The main existing challenges include insufficient data-driven innovation to support addiction treatment, the persistence of data gaps and the issue of stigma [65]. Nevertheless, for patients who

have access to online digital interventions for addiction treatment, these approaches have demonstrated promising outcomes[66–69]. With increasing financial investment and the advancement of real-world technologies, more digital therapeutic products are expected to be applied in the treatment of addiction in the future[41].

Cluster 4 (Yellow Cluster): Applications of Digital Therapeutics in Cognitive Behavioral Recovery

Mild cognitive impairment (MCI) is an increasingly prominent public health issue in the context of global aging. A meta-analysis revealed that the prevalence of MCI among individuals aged 50 and above worldwide was 15.56%, with a significant increase observed as age advances[70]. In certain multiethnic populations, such as among the Indian community in Singapore, this proportion approaches nearly one-quarter (24.6%)[71]. Cognitive and behavioral impairments not only diminish quality of life but may also lead to limitations in daily functioning and increased caregiving burdens on families and society. Without timely intervention, these impairments can progress to Alzheimer or other forms of dementia[72]. Although traditional cognitive behavioral therapy (CBT) had demonstrated efficacy in improving executive function, verbal learning and working memory, its effects on enhancing patients' attention were comparatively modest. Furthermore, inconsistent follow-up durations have limited the evaluation of its long-term effects. Studies have shown that digital therapeutics yield significant benefits as a treatment approach for cognitive behavioral recovery. Personalized module designs can enhance therapeutic outcomes and improve service precision for different patient groups, with particularly better effects observed in younger and tech-savvy individuals[73].

5.Conclusion

In this study, we conducted a bibliometric analysis of publications on digital therapeutics in early 21st century, aiming to reveal the research progress and future trends in this domain. We identified the productive countries/regions, institutions, authors and journals and identified significant high-cited articles in digital therapeutics. Additionally, we analyzed co-authorship networks among institutions and authors, as well as the co-occurrence networks of keywords. The results showed that countries/regions and institutions respectively have a lackluster cooperative relationship and need to enhance the frequency and depth of cooperation. In addition, research hotspots suggested by keywords co-occurrence clusters: (1) Application of Digital Therapeutics in Chronic Disease; (2) Applications of Digital Therapeutics in the Intervention of Mental Disorders; (3) Applications of Digital Therapeutics in Addiction Treatment; (4) Applications of Digital Therapeutics in Cognitive Behavioral Recovery, reflected the frontier hotspots in digital therapeutics. We hope these findings can provide references for practitioners and reasonably predict the research directions in digital therapeutics

Data Availability

All data is available upon reasonable request to the corresponding author.

Reference

1. Aapro M, Bossi P, Dasari A, Fallowfield L, Gascon P, Geller M, Jordan K, Kim J, Martin K, Porzig S. Digital health for optimal supportive care in oncology: Benefits, limits, and future perspectives. Support Care Cancer New York: Springer; 2020 Oct;28(10):4589–4612. doi: 10.1007/s00520-020-05539-1

2. Sepah SC, Jiang L, Peters AL. Long-term outcomes of a web-based diabetes prevention program: 2-year results of a single-arm longitudinal study. J Med Internet Res Toronto: Jmir Publications, Inc; 2015 Apr;17(4):e92. doi: 10.2196/jmir.4052

3. Sverdlov O, van Dam J, Hannesdottir K, Thornton-Wells T. Digital therapeutics: An integral component of digital innovation in drug development. Clin Pharmacol Ther Hoboken: Wiley; 2018 July;104(1):72–80. doi: 10.1002/cpt.1036

4. Kvedar JC, Fogel AL, Elenko E, Zohar D. Digital medicine's march on chronic disease. Nat Biotechnol New York: Nature Publishing Group; 2016 Mar;34(3):239–246. doi: 10.1038/nbt.3495

5. Hong JS, Wasden C, Han DH. Introduction of digital therapeutics. Comput Meth Programs Biomed Clare: Elsevier Ireland Ltd; 2021 Sept;209:106319. doi: 10.1016/j.cmpb.2021.106319

6. Phan P, Mitragotri S, Zhao Z. Digital therapeutics in the clinic. Bioeng Transl Med Hoboken: Wiley; 2023 July;8(4). doi: 10.1002/btm2.10536

7. Solca M, Ronchi R, Bello-Ruiz J, Schmidlin T, Herbelin B, Luthi F, Konzelmann M, Beaulieu J-Y, Delaquaize F, Schnider A, Guggisberg AG, Serino A, Blanke O. Heartbeat-enhanced immersive virtual reality to treat complex regional pain syndrome. Neurology Philadelphia: Lippincott Williams & Wilkins; 2018 July 31;91(5):E479–E489. doi: 10.1212/WNL.0000000000005905

8. Gold JI, SooHoo M, Laikin AM, Lane AS, Klein MJ. Effect of an immersive virtual reality intervention on pain and anxiety associated with peripheral intravenous catheter placement in the pediatric setting a randomized clinical trial. JAMA Netw Open Chicago: Amer Medical Assoc; 2021 Aug 25;4(8):e2122569. doi: 10.1001/jamanetworkopen.2021.22569

9. Gupta A, Scott K, Dukewich M. Innovative technology using virtual reality in the treatment of pain: Does it reduce pain via distraction, or is there more to it? Pain Med Oxford: Oxford Univ Press; 2018 Jan;19(1):151–159. doi: 10.1093/pm/pnx109

10. Khan K, Hollis C, Hall CL, Murray E, Davies EB, Andren P, Mataix-Cols D, Murphy T, Glazebrook C. Fidelity of delivery and contextual factors influencing children's level of engagement: Process evaluation of the online remote behavioral intervention for tics trial. J Med Internet Res Toronto: Jmir Publications, Inc; 2021 June 21;23(6):e25470. doi: 10.2196/25470

11. Penev Y, Dunlap K, Husic A, Hou C, Washington P, Leblanc E, Kline A, Kent J, Ng-Thow-Hing A, Liu B, Harjadi C, Tsou M, Desai M, Wall DP. A mobile game platform for improving social communication in children with autism: A feasibility study. Appl Clin Inf Stuttgart: Georg Thieme Verlag Kg; 2021 Oct;12(5):1030–1040. doi: 10.1055/s-0041-1736626

12. Mcintyre RS, Alsuwaidan M, Baune BT, Berk M, Demyttenaere K, Goldberg JF, Gorwood P, Ho R, Kasper S, Kennedy SH, Ly-Uson J, Mansur RB, McAllister-Williams RH, Murrough JW, Nemeroff CB, Nierenberg AA, Rosenblat JD, Sanacora G, Schatzberg AF, Shelton R, Stahl SM, Trivedi MH, Vieta E, Vinberg M, Williams N, Young AH, Maj M. Treatment-resistant depression: Definition, prevalence, detection, management, and investigational interventions. World Psychiatry Hoboken: Wiley; 2023 Oct;22(3):394–412. doi: 10.1002/wps.21120

13. Kario K, Nomura A, Harada N, Okura A, Nakagawa K, Tanigawa T, Hida E. Efficacy of a digital therapeutics system in the management of essential hypertension: The HERB-DH1 pivotal trial. Eur Heart J Oxford: Oxford Univ Press; 2021 Oct 21;42(40):4111–4122. doi: 10.1093/eurheartj/ehab559

14. Solomon DH, Rudin RS. Digital health technologies: Opportunities and challenges in rheumatology. Nat Rev Rheumatol Berlin: Nature Research; 2020 Sept;16(9):525–535. doi: 10.1038/s41584-020-0461-x

15. Kario K, Harada N, Okura A. Digital therapeutics in hypertension: Evidence and perspectives. Hypertension Philadelphia: Lippincott Williams & Wilkins; 2022 Oct;79(10):2148–2158. doi: 10.1161/HYPERTENSIONAHA.122.19414

16. Donthu N, Kumar S, Mukherjee D, Pandey N, Lim WM. How to conduct a bibliometric analysis: An overview and guidelines. J Bus Res New York: Elsevier Science Inc; 2021 Sept;133:285–296. doi: 10.1016/j.jbusres.2021.04.070

17. Donthu N, Kumar S, Pandey N, Lim WM. Research constituents, intellectual structure, and collaboration patterns in journal of international marketing: An analytical retrospective. J Int Mark Thousand Oaks: SAGE Publications Inc; 2021 June;29(2):1–21. doi: 10.1177/1069031X211004234

18. Verma S, Gustafsson A. Investigating the emerging COVID-19 research trends in the field of business and management: A bibliometric analysis approach. J Bus Res New York: Elsevier Science Inc; 2020 Sept;118:253–261. doi: 10.1016/j.jbusres.2020.06.057

19. Donthu N, Kumar S, Pandey N. A retrospective evaluation of marketing intelligence and planning: 1983-2019. Mark Intell Plan Bingley: Emerald Group Publishing Ltd; 2021 Feb 1;39(1):48–73. doi: 10.1108/MIP-02-2020-0066

20. Pereira V, Bamel U, Temouri Y, Budhwar P, Del Giudice M. Mapping the evolution, current state of affairs and future research direction of managing cross-border knowledge for innovation. Int Bus Rev Amsterdam: Elsevier; 2023 Apr;32(2):101834. doi: 10.1016/j.ibusrev.2021.101834

21. Li T, Cui L, Song X, Cui X, Wei Y, Tang L, Mu Y, Xu Z. Wood decay fungi: An analysis of worldwide research. J Soils Sediments Heidelberg: Springer Heidelberg; 2022 June;22(6):1688–1702. doi: 10.1007/s11368-022-03225-9

22. Pereira V, Bamel U. Charting the managerial and theoretical evolutionary path of AHP using thematic and systematic review: A decadal (2012-2021) study. Ann Oper Res Dordrecht: Springer; 2023 July;326(2):635–651. doi: 10.1007/s10479-022-04540-7

23. Ma C, Su H, Li H. Global research trends on prostate diseases and erectile dysfunction: A

bibliometric and visualized study. Front Oncol 2021 Feb 12;10:627891. doi: 10.3389/fonc.2020.627891

24. Goodell JW, Kumar S, Lim WM, Pattnaik D. Artificial intelligence and machine learning in finance: Identifying foundations, themes, and research clusters from bibliometric analysis. J Behav Exp Finance Amsterdam: Elsevier; 2021 Dec;32:100577. doi: 10.1016/j.jbef.2021.100577

25. Yue T, Liu H, Long R, Chen H, Gan X, Liu J. Research trends and hotspots related to global carbon footprint based on bibliometric analysis: 2007-2018. Environ Sci Pollut Res Heidelberg: Springer Heidelberg; 2020 May;27(15):17671–17691. doi: 10.1007/s11356-020-08158-9

26. Duque-Acevedo M, Belmonte-Urena LJ, Joaquin Cortes-Garcia F, Camacho-Ferre F. Agricultural waste: Review of the evolution, approaches and perspectives on alternative uses. Global Ecol Conserv Amsterdam: Elsevier; 2020 June;22:e00902. doi: 10.1016/j.gecco.2020.e00902

27. He X, Peng C, Xu Y, Zhang Y, Wang Z. Global scientific research landscape on medical informatics from 2011 to 2020: Bibliometric analysis. JMIR Med Inf Toronto: Jmir Publications, Inc; 2022 Apr;10(4):47–59. doi: 10.2196/33842

28. Ellis TD, Earhart GM. Digital therapeutics in parkinson's disease: Practical applications and future potential. J Parkinsons Dis Amsterdam: Ios Press; 2021;11:S95–S101. doi: 10.3233/JPD-202407

29. Hong JS, Wasden C, Han DH. Introduction of digital therapeutics. Comput Methods Programs Biomed Clare: Elsevier Ireland Ltd; 2021 Sept;209:106319. doi: 10.1016/j.cmpb.2021.106319

30. Washington P, Park N, Srivastava P, Voss C, Kline A, Varma M, Tariq Q, Kalantarian H, Schwartz J, Patnaik R, Chrisman B, Stockham N, Paskov K, Haber N, Wall DP. Data-driven diagnostics and the potential of mobile artificial intelligence for digital therapeutic phenotyping in computational psychiatry. Biol Psychiatry: Cognit Neurosci Neuroimaging Amsterdam: Elsevier; 2020 Aug;5(8):759–769. doi: 10.1016/j.bpsc.2019.11.015

31. Dahlhausen F, Zinner M, Bieske L, Ehlers JP, Boehme P, Fehring L. There's an app for that, but nobody's using it: Insights on improving patient access and adherence to digital therapeutics in germany. DIGITAL HEALTH London: SAGE Publications Ltd; 2022 July;8:20552076221104672. doi: 10.1177/20552076221104672

32. Yoo JH, Jeong H, Chung T-M. Cutting-edge technologies for digital therapeutics: A review and architecture proposals for future directions. Appl Sci-Basel Basel: MDPI; 2023 June;13(12):6929. doi: 10.3390/app13126929

33. Na J, Kim SJ, Lim Y. Designing digital therapeutic content using chronic disease data: A focus on improving urinary dysfunction. Int Neurourol J Yeongotong-Gu: Korean Continence Soc; 2023 Nov;27:S51–S63. doi: 10.5213/inj.2346290.145

34. Lee H, Youm S. Developing a digital therapeutic for obesity management through 3D human body reconstruction. Expert Syst Hoboken: Wiley; 2025 Feb;42(2). doi: 10.1111/exsy.13678

35. Hales CM. Prevalence of obesity and severe obesity among adults: United states, 2017–2018.

2020;(360).

36. Weinberger AH, Gbedemah M, Martinez AM, Nash D, Galea S, Goodwin RD. Trends in depression prevalence in the USA from 2005 to 2015: Widening disparities in vulnerable groups. Psychol Med New York: Cambridge Univ Press; 2018 June;48(8):1308–1315. doi: 10.1017/S0033291717002781

37. Saelee R, Hora IA, Pavkov ME, Imperatore G, Chen Y, Benoit SR, Holliday CS, Bullard KM. Diabetes prevalence and incidence inequality trends among US adults, 2008-2021. Am J Prev Med New York: Elsevier Science Inc; 2023 Dec;65(6):973–982. doi: 10.1016/j.amepre.2023.07.009

38. Kamei T, Kanamori T, Yamamoto Y, Edirippulige S. The use of wearable devices in chronic disease management to enhance adherence and improve telehealth outcomes: A systematic review and meta-analysis. J Telemed Telecare London: SAGE Publications Ltd; 2022 June;28(5):342–359. doi: 10.1177/1357633X20937573

39. Zhu C, Huang X, Ying F. Research on disease management of chronic disease patients based on digital therapeutics: A scoping review. Digit Health London: SAGE Publications Ltd; 2024;10:20552076241297064. doi: 10.1177/20552076241297064

40. Manchanda N, Aggarwal A, Setya S, Talegaonkar S. Digital intervention for the management of alzheimer's disease. Curr Alzheimer Res Sharjah: Bentham Science Publ Ltd; 2022;19(14):909–932. doi: 10.2174/1567205020666230206124155

41. Phan P, Mitragotri S, Zhao Z. Digital therapeutics in the clinic. Bioeng Transl Med Hoboken: Wiley; 2023 July;8(4). doi: 10.1002/btm2.10536

42. Krishnakumar A, Verma R, Chawla R, Sosale A, Saboo B, Joshi S, Shaikh M, Shah A, Kolwankar S, Mattoo V. Evaluating glycemic control in patients of south asian origin with type 2 diabetes using a digital therapeutic platform: Analysis of real-world data. J Med Internet Res Toronto: Jmir Publications, Inc; 2021 Mar 25;23(3):e17908. doi: 10.2196/17908

43. Lee SE, Park S-K, Park Y-S, Kim K-A, Choi HS, Oh SW. Effects of short-term mobile application use on weight reduction for patients with type 2 diabetes. J Obes Metab Syndr 2021 Dec;30(4):345–353. doi: 10.7570/jomes21047

44. Sheng B, Pushpanathan K, Guan Z, Lim QH, Lim ZW, Yew SME, Goh JHL, Bee YM, Sabanayagam C, Sevdalis N, Lim CC, Lim CT, Shaw J, Jia W, Ekinci EI, Simo R, Lim L-L, Li H, Tham Y-C. Artificial intelligence for diabetes care: Current and future prospects. Lancet Diabetes Endocrinol New York: Elsevier Science Inc; 2024 Aug;12(8):569–595. doi: 10.1016/S2213-8587(24)00154-2

45. Block G, Azar KMJ, Romanelli RJ, Block TJ, Hopkins D, Carpenter HA, Dolginsky MS, Hudes ML, Palaniappan LP, Block CH. Diabetes prevention and weight loss with a fully automated behavioral intervention by email, web, and mobile phone: A randomized controlled trial among persons with prediabetes. J Med Internet Res Toronto: Jmir Publications, Inc; 2015 Oct;17(10):e240. doi: 10.2196/jmir.4897

46. Whaley CM, Bollyky JB, Lu W, Painter S, Schneider J, Zhao Z, He X, Johnson J, Meadows ES. Reduced medical spending associated with increased use of a remote diabetes management

program and lower mean blood glucose values. J Med Econ Abingdon: Taylor & Francis Ltd; 2019;22(9):869–877. doi: 10.1080/13696998.2019.1609483

47. Murray CJL, Aravkin AY, Zheng P, Abbafati C, Abbas KM, Abbasi-Kangevari M, Abd-Allah F, Abdelalim A, Abdollahi M, Abdollahpour I, Abegaz KH, Abolhassani H, Aboyans V, Abreu LG, Abrigo MRM, Abualhasan A, Abu-Raddad LJ, Abushouk AI, Adabi M, Adekanmbi V, Adeoye AM, Adetokunboh OO, Adham D, Advani SM, Agarwal G, Aghamir SMK, Agrawal A, Ahmad T, Ahmadi K, Ahmadi M, Ahmadieh H, Ahmed MB, Akalu TY, Akinyemi RO, Akinyemiju T, Akombi B, Akunna CJ, Alahdab F, Al-Aly Z, Alam K, Alam S, Alam T, Alanezi FM, Alanzi TM, Alemu BW, Alhabib KF, Ali M, Ali S, Alicandro G, Alinia C, Alipour V, Alizade H, Aljunid SM, Alla F, Allebeck P, Almasi-Hashiani A, Al-Mekhlafi HM, Alonso J, Altirkawi KA, Amini-Rarani M, Amiri F, Amugsi DA, Ancuceanu R, Anderlini D, Anderson JA, Andrei CL, Andrei T, Angus C, Anjomshoa M, Ansari F, Ansari-Moghaddam A, Antonazzo IC, Antonio CAT, Antony CM, Antriyandarti E, Anvari D, Anwer R, Appiah SCY, Arabloo J, Arab-Zozani M, Ariani F, Armoon B, Arnlov J, Arzani A, Asadi-Aliabadi M, Asadi-Pooya AA, Ashbaugh C, Assmus M, Atafar Z, Atnafu DD, Atout MMW, Ausloos F, Ausloos M, Quintanilla BPA, Ayano G, Ayanore MA, Azari S, Azarian G, Azene ZN, Badawi A, Badiye AD, Bahrami MA, Bakhshaei MH, Bakhtiari A, Bakkannavar SM, Baldasseroni A, Ball K, Ballew SH, Balzi D, Banach M, Banerjee SK, Bante AB, Baraki AG, Barker-Collo SL, Barnighausen TW, Barrero LH, Barthelemy CM, Barua L, Basu S, Baune BT, Bayati M, Becker JS, Bedi N, Beghi E, Bejot Y, Bell ML, Bennitt FB, Bensenor IM, Berhe K, Berman AE, Bhagavathula AS, Bhageerathy R, Bhala N, Bhandari D, Bhattacharyya K, Bhutta ZA, Bijani A, Bikbov B, Bin Sayeed MS, Biondi A, Birihane BM, Bisignano C, Biswas RK, Bitew H, Bohlouli S, Bohluli M, Boon-Dooley AS, Borges G, Borzi AM, Borzouei S, Bosetti C, Boufous S, Braithwaite D, Breitborde NJK, Breitner S, Brenner H, Briant PS, Briko AN, Briko NI, Britton GB, Bryazka D, Bumgarner BR, Burkart K, Burnett RT, Nagaraja SB, Butt ZA, Caetano dos Santos FL, Cahill LE, Camera LA, Campos-Nonato IR, Cardenas R, Carreras G, Carrero JJ, Carvalho F, Castaldelli-Maia JM, Castaneda-Orjuela CA, Castelpietra G, Castro F, Causey K, Cederroth CR, Cercy KM, Cerin E, Chandan JS, Chang K-L, Charlson FJ, Chattu VK, Chaturvedi S, Cherbuin N, Chimed-Ochir O, Cho DY, Choi J-YJ, Christensen H, Chu D-T, Chung MT, Chung S-C, Cicuttini FM, Ciobanu LG, Cirillo M, Classen TKD, Cohen AJ, Compton K, Cooper OR, Costa VM, Cousin E, Cowden RG, Cross DH, Cruz JA, Dahlawi SMA, Damasceno AAM, Damiani G, Dandona L, Dandona R, Dangel WJ, Danielsson A-K, Dargan PI, Darwesh AM, Daryani A, Das JK, Das Gupta R, Das Neves J, Davila-Cervantes CA, Davitoiu DV, De Leo D, Degenhardt L, DeLang M, Dellavalle RP, Demeke FM, Demoz GT, Demsie DG, Denova-Gutierrez E, Dervenis N, Dhungana GP, Dianatinasab M, da Silva DD, Diaz D, Forooshani ZSD, Djalalinia S, Do HT, Dokova K, Dorostkar F, Doshmangir L, Driscoll TR, Duncan BB, Duraes AR, Eagan AW, Edvardsson D, El Nahas N, El Sayed I, El Tantawi M, Elbarazi I, Elgendy IY, El-Jaafary SI, Elyazar IRF, Emmons-Bell S, Erskine HE, Eskandarieh S, Esmaeilnejad S, Esteghamati A, Estep K, Etemadi A, Etisso AE, Fanzo J, Farahmand M, Fareed M, Faridnia R, Farioli A, Faro A, Faruque M, Farzadfar F, Fattahi N, Fazlzadeh M, Feigin VL, Feldman R, Fereshtehnejad S-M, Fernandes E, Ferrara G, Ferrari AJ, Ferreira ML, Filip I, Fischer F, Fisher JL, Flor LS, Foigt NA, Folayan MO, Fomenkov AA, Force LM, Foroutan M, Franklin RC, Freitas M, Fu W, Fukumoto T, Furtado JM, Gad MM, Gakidou E, Gallus S, Garcia-Basteiro AL, Gardner WM, Geberemariyam BS, Gebreslassie AAAA, Geremew A, Hayoon AG, Gething PW, Ghadimi M, Ghadiri K, Ghaffarifar F, Ghafourifard M, Ghamari F, Ghashghaee A, Ghiasvand H, Ghith N, Gholamian A, Ghosh R, Gill PS, Ginindza TG, Giussani G, Gnedovskaya EV, Goharinezhad S, Gopalani SV, Gorini G, Goudarzi H, Goulart AC, Greaves F, Grivna M, Grosso G, Gubari MIM, Gugnani HC, Guimaraes RA, Guled RA, Guo G, Guo Y, Gupta R, Gupta T, Haddock B, Hafezi-Nejad N, Hafiz A, Haj-Mirzaian A, Haj-Mirzaian

A, Hall BJ, Halvaei I, Hamadeh RR, Hamidi S, Hammer MS, Hankey GJ, Haririan H, Haro JM, Hasaballah AI, Hasan MM, Hasanpoor E, Hashi A, Hassanipour S, Hassankhani H, Havmoeller RJ, Hay SI, Hayat K, Heidari G, Heidari-Soureshjani R, Henrikson HJ, Herbert ME, Herteliu C, Heydarpour F, Hird TR, Hoek HW, Holla R, Hoogar P, Hosgood HD, Hossain N, Hosseini M, Hosseinzadeh M, Hostiuc M, Hostiuc S, Househ M, Hsairi M, Hsieh VC-R, Hu G, Hu K, Huda TM, Humayun A, Huynh CK, Hwang B-F, Iannucci VC, Ibitoye SE, Ikeda N, Ikuta KS, Ilesanmi OS, Ilic IM, Ilic MD, Inbaraj LR, Ippolito H, Iqbal U, Irvani SSN, Irvine CMS, Islam MM, Islam SMS, Iso H, Ivers RQ, Iwu CCD, Iwu CJ, Iyamu IO, Jaafari J, Jacobsen KH, Jafari H, Jafarinia M, Jahani MA, Jakovljevic M, Jalilian F, James SL, Janjani H, Javaheri T, Javidnia J, Jeemon P, Jenabi E, Jha RP, Jha V, Ji JS, Johansson L, John O, John-Akinola YO, Johnson CO, Jonas JB, Joukar F, Jozwiak JJ, Jurisson M, Kabir A, Kabir Z, Kalani H, Kalani R, Kalankesh LR, Kalhor R, Kanchan T, Kapoor N, Matin BK, Karch A, Karim MA, Kassa GM, Katikireddi SV, Kayode GA, Karyani AK, Keiyoro PN, Keller C, Kemmer L, Kendrick PJ, Khalid N, Khammarnia M, Khan EA, Khan M, Khatab K, Khater MM, Khatib MN, Khayamzadeh M, Khazaei S, Kieling C, Kim YJ, Kimokoti RW, Kisa A, Kisa S, Kivimaki M, Knibbs LD, Knudsen AKS, Kocarnik JM, Kochhar S, Kopec JA, Korshunov VA, Koul PA, Koyanagi A, Kraemer MUG, Krishan K, Krohn KJ, Kromhout H, Defo BK, Kumar GA, Kumar V, Kurmi OP, Kusuma D, La Vecchia C, Ben L, Lal DK, Lalloo R, Lallukka T, Lami FH, Landires I, Lang JJ, Langan SM, Larsson AO, Lasrado S, Lauriola P, Lazarus JV, Lee PH, Lee SWH, LeGrand KE, Leigh J, Leonardi M, Lescinsky H, Leung J, Levi M, Li S, Lim L-L, Linn S, Liu S, Liu S, Liu Y, Lo J, Lopez AD, Lopez JCF, Lopukhov PD, Lorkowski S, Lotufo PA, Lu A, Lugo A, Maddison ER, Mahasha PW, Mahdavi MM, Mahmoudi M, Majeed A, Maleki A, Maleki S, Malekzadeh R, Malta DC, Mamun AA, Manda AL, Manguerra H, Mansour-Ghanaei F, Mansouri B, Mansournia MA, Herrera AMM, Maravilla JC, Marks A, Martin RV, Martini S, Martins-Melo FR, Masaka A, Masoumi SZ, Mathur MR, Matsushita K, Maulik PK, McAlinden C, McGrath JJ, Mckee M, Mehndiratta MM, Mehri F, Mehta KM, Memish ZA, Mendoza W, Menezes RG, Mengesha EW, Mereke A, Mereta ST, Meretoja A, Meretoja TJ, Mestrovic T, Miazgowski B, Miazgowski T, Michalek IM, Miller TR, Mills EJ, Mini GK, Miri M, Mirica A, Mirrakhimov EM, Mirzaei H, Mirzaei M, Mirzaei R, Mirzaei-Alavijeh M, Misganaw AT, Mithra P, Moazen B, Mohammad DK, Mohammad Y, Mezerji NMG, Mohammadian-Hafshejani A, Mohammadifard N, Mohammadpourhodki R, Mohammed AS, Mohammed H, Mohammed JA, Mohammed S, Mokdad AH, Molokhia M, Monasta L, Mooney MD, Moradi G, Moradi M, Moradi-Lakeh M, Moradzadeh R, Moraga P, Morawska L, Morgado-da-Costa J, Morrison SD, Mosapour A, Mosser JF, Mouodi S, Mousavi SM, Khaneghah AM, Mueller UO, Mukhopadhyay S, Mullany EC, Musa KI, Muthupandian S, Nabhan AF, Naderi M, Nagarajan AJ, Nagel G, Naghavi M, Naghshtabrizi B, Naimzada MD, Najafi F, Nangia V, Nansseu JR, Naserbakht M, Nayak VC, Negoi I, Ngunjiri JW, Nguyen CT, Nguyen HLT, Nguyen M, Nigatu YT, Nikbakhsh R, Nixon MR, Nnaji CA, Nomura S, Norrving B, Noubiap JJ, Nowak C, Nunez-Samudio V, Oiu AO, Oancea B, Odell CM, Ogbo FA, Oh I-H, Okunga EW, Oladnabi M, Olagunju AT, Olusanya BO, Olusanya JO, Omer MO, Ong KL, Onwujekwe OE, Orpana HM, Ortiz A, Osarenotor O, Osei FB, Ostroff SM, Otstavnov N, Otstavnov SS, Overland S, Owolabi MO, Section MPA, Padubidri JR, Palladino R, Panda-Jonas S, Pandey A, Parry CDH, Pasovic M, Pasupula DK, Patel SK, Pathak M, Patten SB, Patton GC, Toroudi HP, Peden AE, Pennini A, Pepito VCF, Peprah EK, Pereira DM, Pesudovs K, Pham HQ, Phillips MR, Piccinelli C, Pilz TM, Piradov MA, Pirsaheb M, Plass D, Polinder S, Polkinghorne KR, Pond CD, Postma MJ, Pourjafar H, Pourmalek F, Poznanska A, Prada SI, Prakash V, Pribadi DRA, Pupillo E, Quazi Syed Z, Rabiee M, Rabiee N, Radfar A, Rafiee A, Raggi A, Rahman MA, Rajabpour-Sanati A, Rajati F, Rakovac I, Ram P, Ramezanzadeh K, Ranabhat CL, Rao PC, Rao SJ, Rashedi V, Rathi P, Rawaf DL, Rawaf S, Rawal L, Rawassizadeh R, Rawat R, Razo C, Boston S, Reiner RC, Reitsma MB, Remuzzi G, Renjith V, Renzaho AMN, Resnikoff S, Rezaei N, Rezaei N,

Rezapour A, Rhinehart P-A, Riahi SM, Ribeiro DC, Ribeiro D, Rickard J, Rivera JA, Roberts NLS, Rodriguez-Ramirez S, Roever L, Ronfani L, Room R, Roshandel G, Roth GA, Rothenbacher D, Rubagotti E, Rwegerera GM, Sabour S, Sachdev PS, Saddik B, Sadeghi E, Sadeghi M, Saeedi R, Moghaddam SS, Safari Y, Safi S, Safiri S, Sagar R, Sahebkar A, Sajadi SM, Salam N, Salamati P, Salem H, Salem MR, Salimzadeh H, Salman OM, Salomon JA, Samad Z, Kafil HS, Sambala EZ, Samy AM, Sanabria J, Sanchez-Pimienta TG, Santomauro DF, Santos IS, Santos JV, Santric-Milicevic MM, Saraswathy SYI, Sarmiento-Suarez R, Sarrafzadegan N, Sartorius B, Sarveazad A, Sathian B, Sathish T, Sattin D, Saxena S, Schaeffer LE, Schiavolin S, Schlaich MP, Schmidt MI, Schutte AE, Schwebel DC, Schwendicke F, Senbeta AM, Senthilkumaran S, Sepanlou SG, Serdar B, Serre ML, Shadid J, Shafaat O, Shahabi S, Shaheen AA, Shaikh MA, Shalash AS, Shams-Beyranvand M, Shamsizadeh M, Sharafi K, Sheikh A, Sheikhtaheri A, Shibuya K, Shield KD, Shigematsu M, Shin JI, Shin M-J, Shiri R, Shirkoohi R, Shuval K, Siabani S, Sierpinski R, Sigfusdottir ID, Sigurvinsdottir R, Silva JP, Simpson KE, Singh JA, Singh P, Skiadaresi E, Skou ST, Skryabin VY, Smith EUR, Soheili A, Soltani S, Soofi M, Sorensen RJD, Soriano JB, Sorrie MB, Soshnikov S, Soyiri IN, Spencer CN, Spotin A, Sreeramareddy CT, Srinivasan V, Stanaway JD, Stein C, Stein DJ, Steiner C, Stockfelt L, Stokes MA, Straif K, Stubbs JL, Sufiyan MB, Suleria HAR, Abdulkader RS, Sulo G, Sultan I, Szumowski L, Tabares-Seisdedos R, Tabb KM, Tabuchi T, Taherkhani A, Tajdini M, Takahashi K, Takala JS, Tamiru AT, Taveira N, Tehrani-Banihashemi A, Temsah M-H, Tesema GA, Tessema ZT, Thurston GD, Titova MV, Tohidinik HR, Tonelli M, Topor-Madry R, Topouzis F, Torre AE, Touvier M, Tovani-Palone MR, Tran BX, Travillian R, Tsatsakis A, Car LT, Tyrovolas S, Uddin R, Umeokonkwo CD, Unnikrishnan B, Upadhyay E, Vacante M, Valdez PR, Van Donkelaar A, Vasankari TJ, Vasseghian Y, Veisani Y, Venketasubramanian N, Violante FS, Vlassov V, Vollset SE, Vos T, Vukovic R, Waheed Y, Wallin MT, Wang Y, Wang Y-P, Watson A, Wei J, Wei MYW, Weintraub RG, Weiss J, Werdecker A, Westerman R, Whisnant JL, Whiteford HA, Wiens KE, Wolfe CDA, Wozniak SS, Wu A-M, Wu J, Hanson SW, Xu G, Xu R, Yadgir S, Jabbari SHY, Yamagishi K, Yaminfirooz M, Yano Y, Yaya S, Yazdi-Feyzabadi V, Yeheyis TY, Yilgwan CS, Yilma MT, Yip P, Yonemoto N, Younis MZ, Younker TP, Yousefi B, Yousefi Z, Yousefinezhadi T, Yousuf AY, Yu C, Yusefzadeh H, Moghadam TZ, Zamani M, Zamanian M, Zandian H, Zastrozhin MS, Zhang Y, Zhang Z-J, Zhao JT, Zhao X-JG, Zhao Y, Zhou M, Ziapour A, Zimsen SRM, Brauer M, Afshin A, Lim SS. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: A systematic analysis for the global burden of disease study 2019. Lancet New York: Elsevier Science Inc; 2020 Oct 17;396(10258):1223–1249. doi: 10.1016/S0140-6736(20)30752-2

48. Moitra M, Santomauro D, Degenhardt L, Collins PY, Whiteford H, Vos T, Ferrari A. Estimating the risk of suicide associated with mental disorders: A systematic review and meta-regression analysis. J Psychiatr Res Oxford: Pergamon-Elsevier Science Ltd; 2021 May;137:242–249. doi: 10.1016/j.jpsychires.2021.02.053

49. Moitra M, Owens S, Hailemariam M, Wilson KS, Mensa-Kwao A, Gonese G, Kamamia CK, White B, Young DM, Collins PY. Global mental health: Where we are and where we are going. Curr Psychiatry Rep New York: Springer; 2023 July;25(7):301–311. doi: 10.1007/s11920-023-01426-8

50. Kwon H, Choi IY, Kim D-J, Yoo JH. A review of current digital mental health care applications for anxiety symptoms and future prospects. Psychiatry Investig Seoul: Korean Neuropsychiatric Assoc; 2024 June;21(6):551–560. doi: 10.30773/pi.2023.0339

51. Orsolini L, Longo G, Volpe U. Practical application of digital therapeutics in people with mood

disorders. Curr Opin Psychiatr Philadelphia: Lippincott Williams & Wilkins; 2024 Jan;37(1):9–17. doi: 10.1097/YCO.0000000000000906

52. Roy A, Hoge EA, Abrante P, Druker S, Liu T, Brewer JA. Clinical efficacy and psychological mechanisms of an app-based digital therapeutic for generalized anxiety disorder: Randomized controlled trial. J Med Internet Res Toronto: Jmir Publications, Inc; 2021 Dec 2;23(12):e26987. doi: 10.2196/26987

53. Fulford D, Marsch LA, Pratap A. Prescription digital therapeutics: An emerging treatment option for negative symptoms in schizophrenia. Biol Psychiatry New York: Elsevier Science Inc; 2024 Oct 15;96(8):659–665. doi: 10.1016/j.biopsych.2024.06.026

54. He F, Qi Y, Zhou Y, Cao A, Yue X, Fang S, Zheng Y. Meta-analysis of the efficacy of digital therapies in children with attention-deficit hyperactivity disorder. Front Psychiatry Lausanne: Frontiers Media Sa; 2023 May 16;14:1054831. doi: 10.3389/fpsyt.2023.1054831

55. Ostacher MJ, Fischer E, Bowen ER, Lyu J, Robbins DJ, Suppes T. Investigation of a capnometry guided respiratory intervention in the treatment of posttraumatic stress disorder. Appl Psychophysiol Biofeedback New York: Springer/Plenum Publishers; 2021 Dec;46(4):367–376. doi: 10.1007/s10484-021-09521-3

56. Papageorgiou A, Strigkos M, Politou E, Alepis E, Solanas A, Patsakis C. Security and privacy analysis of mobile health applications: The alarming state of practice. IEEE Access Piscataway: Ieee-Inst Electrical Electronics Engineers Inc; 2018;6:9390–9403. doi: 10.1109/ACCESS.2018.2799522

57. Iwaya LH, Babar MA, Rashid A, Wijayarathna C. On the privacy of mental health apps an empirical investigation and its implications for app development. Empir Softw Eng Dordrecht: Springer; 2023 Feb;28(1):2. doi: 10.1007/s10664-022-10236-0

58. Zou Z, Wang H, Uquillas F d'Oleire, Wang X, Ding J, Chen H. Definition of substance and non-substance addiction. In: Zhang X, Shi J, Tao R, editors. SUBSTANCE AND NON-SUBSTANCE ADDICTION Singapore: Springer-Verlag Singapore Pte Ltd; 2017. p. 21–41. doi: 10.1007/978-981-10-5562-1_2ISBN:978-981-10-5562-1

59. Webb J, Lin Y-T, Ang A, Michero D, Majeed A, Eisingerich A, Glasner S. Feasibility and preliminary outcomes of a mobile intervention combining cognitive behavioral therapy, virtual coaching, and nicotine replacement therapy for nicotine vaping cessation. Telemed Rep 2023;4(1):48–52. doi: 10.1089/tmr.2023.0009

60. Xiong X, Braun S, Stitzer M, Luderer H, Shafai G, Hare B, Stevenson M, Maricich Y. Evaluation of real-world outcomes associated with use of a prescription digital therapeutic to treat substance use disorders. Am J Addict Hoboken: Wiley; 2023 Jan;32(1):24–31. doi: 10.1111/ajad.13346

61. Prochaska JJ, Vogel EA, Chieng A, Kendra M, Baiocchi M, Pajarito S, Robinson A. A therapeutic relational agent for reducing problematic substance use (woebot): Development and usability study. J Med Internet Res Toronto: Jmir Publications, Inc; 2021 Mar 23;23(3):e24850. doi: 10.2196/24850

62. Palazzo L, Dorsey CN, Mogk J, Beatty T, King D, Stefanik-Guizlo K, Key D, Matson TE, Shea

M, Caldeiro RM, McWethy AG, Wong ES, Idu AE, Glass JE. Formative evaluation of the implementation of digital therapeutics for opioids and other substance use disorders in primary care (DIGITS trial). Implement Res Pract 2024;5:26334895241301670. doi: 10.1177/26334895241301670

63. Taubin D, Berger A, Greenwald D, Greenwald H, Burke C, Gongora DS, Wilens T. A systematic review of virtual reality therapies for substance use disorders: Impact on secondary treatment outcomes. Am J Addict Hoboken: Wiley; 2023 Jan;32(1):13–23. doi: 10.1111/ajad.13342

64. Hamideh D, Nebeker C. The digital health landscape in addiction and substance use research: Will digital health exacerbate or mitigate health inequities in vulnerable populations? Curr Addict Rep London: Springernature; 2020 Sept;7(3):317–332. doi: 10.1007/s40429-020-00325-9

65. Kosonen J, Shorter GW, Kuusisto K. Navigating challenges and opportunities: Perspectives on digital service development in substance use disorder treatment. Subst/ Abus Treatment Prev Pol London: BMC; 2024 Aug 1;19(1):36. doi: 10.1186/s13011-024-00618-6

66. Johansson M, Berman AH, Sinadinovic K, Lindner P, Hermansson U, Andreasson S. Effects of internet-based cognitive behavioral therapy for harmful alcohol use and alcohol dependence as self-help or with therapist guidance: Three-armed randomized trial. J Med Internet Res Toronto: Jmir Publications, Inc; 2021 Nov 1;23(11):e29666. doi: 10.2196/29666

67. Riper H, Hoogendoorn A, Cuijpers P, Karyotaki E, Boumparis N, Mira A, Andersson G, Berman AH, Bertholet N, Bischof G, Blankers M, Boon B, Boss L, Brendryen H, Cunningham J, Ebert D, Hansen A, Hester R, Khadjesari Z, Kramer J, Murray E, Postel M, Schulz D, Sinadinovic K, Suffoletto B, Sundstrom C, de Vries H, Wallace P, Wiers RW, Smit JH. Effectiveness and treatment moderators of internet interventions for adult problem drinking: An individual patient data meta-analysis of 19 randomised controlled trials. PLos Med San Francisco: Public Library Science; 2018 Dec;15(12):e1002714. doi: 10.1371/journal.pmed.1002714

68. Johansson M, Sinadinovic K, Hammarberg A, Sundstrom C, Hermansson U, Andreasson S, Berman AH. Web-based self-help for problematic alcohol use: A large naturalistic study. Int J Behav Med New York: Springer; 2017 Oct;24(5):749–759. doi: 10.1007/s12529-016-9618-z

69. Johansson M, Sinadinovic K, Gajecki M, Lindner P, Berman AH, Hermansson U, Andreasson S. Internet-based therapy versus face-to-face therapy for alcohol use disorder, a randomized controlled non-inferiority trial. Addiction Hoboken: Wiley; 2021 May;116(5):1088–1100. doi: 10.1111/add.15270

70. Bai W, Chen P, Cai H, Zhang Q, Su Z, Cheung T, Jackson T, Sha S, Xiang Y-T. Worldwide prevalence of mild cognitive impairment among community dwellers aged 50 years and older: A meta-analysis and systematic review of epidemiology studies. Age Ageing Oxford: Oxford Univ Press; 2022 Aug 2;51(8):afac173. doi: 10.1093/ageing/afac173

71. Wong MYZ, Tan CS, Venketasubramanian N, Chen C, Ikram MK, Cheng C-Y, Hilal S. Prevalence and risk factors for cognitive impairment and dementia in Indians: A multiethnic perspective from a singaporean study. J Alzheimers Dis Amsterdam: Ios Press; 2019;71(1):341–351. doi: 10.3233/JAD-190610

72. Mitchell AJ, Shiri-Feshki M. Rate of progression of mild cognitive impairment to dementia - meta-analysis of 41 robust inception cohort studies. Acta Psychiatr Scand Hoboken: Wiley; 2009 Apr;119(4):252–265. doi: 10.1111/j.1600-0447.2008.01326.x

73. Gkintoni E, Vassilopoulos SP, Nikolaou G. Next-generation cognitive-behavioral therapy for depression: Integrating digital tools, teletherapy, and personalization for enhanced mental health outcomes. Med Lith Basel: MDPI; 2025 Feb 28;61(3):431. doi: 10.3390/medicina61030431