Review Psikiyatride Güncel Yaklaşımlar-Current Approaches in Psychiatry 2024; 16(4):585-594
doi: 10.18863/pgy.1407401

Just-in-Time Adaptive Interventions for Depression

Depresyonda Tam Zamanında Uyarlanabilir Müdahaleler

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ABSTRACT

Mental problems are disorders whose incidence is increasing with the effect of the global crises experienced in the world today and which significantly reduce the functionality of the individual. Depression draws attention as the most common mental problem. An average of two-thirds of individuals diagnosed with depression cannot receive treatment due to treatment cost, transportation, stigma, lack of information, low perceived need for treatment, and barriers to seeking mental health help.Internet-based interventions can offer highly effective and advantageous suggestions to overcome the disadvantages created by these barriers. As an internet-based intervention, Just-in-Time Adaptive Interventions (JITAIs) is an intervention design that aims to provide the right type and intensity of support at the right time by adapting to the changing internal and contextual situation of the individual. This intervention has emerged from the need to use mobile health in general, to address situations of vulnerability for adverse health outcomes, and to take advantage of rapid, unexpected, ecologically emerging situations of opportunity. In general, the mechanisms of JITAIs include 6 key elements: vulnerability/opportunity situation, distal outcome, proximal outcomes, decision points, intervention options, adaptation of variables and decision rules. Considering the potential rise of depression, especially in relation to new global events (e.g., pandemics and economic downturns), this application, which can be considered as a scalable, fully automated self-administered biopsychosocial transdiagnostic digital intervention, can provide widespread benefits. In this study, we focus on the working principles and advantages of JITAIs in general.
Keywords: Just-in-time adaptive interventions, depression, internet-based intervention, machine learning

ÖZ

Ruhsal sorunlar bugün, dünyada yaşanılan küresel krizlerinde etkisiyle görülme sıklığı artan ve bireyin işlevselliğini önemli ölçüde azaltan bozukluklardır. Depresyon ise en fazla görülen ruhsal sorun olarak dikkat çekmektedir. Depresyon tanılı bireylerin ortalama üçte ikisi tedavi maliyeti, ulaşım, damgalanma, bilgi eksikliği, düşük algılanan tedavi ihtiyacı ve ruhsal sağlık yardımı aramanın önündeki engeller nedeniyle tedavi edilememektedir. İnternet tabanlı müdahaleler bu engellerin yarattığı dezavantajları ortadan kaldırmak adına oldukça etkili ve avantajlı öneriler sunabilmektedir. Bir internet tabanlı müdahale olarak Tam Zamanında Uyarlanabilir Müdahaleler (TZUM) ise, bireyin değişen iç ve bağlamsal durumuna uyum sağlayarak doğru zamanda, doğru türde ve yoğunlukta destek sağlamayı amaçlayan bir müdahale tasarımıdır. Bu müdahale genel olarak mobil sağlığın kullanımı, olumsuz sağlık sonuçları için kırılganlık durumlarını ele alma ve hızlı, beklenmedik, ekolojik olarak ortaya çıkan fırsat durumlarından yararlanma ihtiyacından ortaya çıkmıştır. TZUM mekanizmaları genel olarak; kırılganlık/fırsat durumu, distal sonuç, proksimal sonuçlar, karar noktaları, müdahale seçenekleri, değişkenleri uyarlama ve karar kuralları şeklinde 6 temel unsur içermektedir. Özellikle yeni küresel olaylarla (örneğin, pandemi ve ekonomik gerileme) ilişkili olarak da depresyonun potansiyel yükselişi göz önüne alındığında, ölçeklenebilir, tam otomatik kendi kendine uygulanabilen biyopsikososyal transdiagnostik dijital müdahale olarak değerlendirilebilecek bu uygulanma, yaygın faydalar sağlayabilmektedir. Bu çalışmada da genel olarak TZUM'un çalışma prensiplerine ve avantajlarına odaklanılmaktadır.
Anahtar sözcükler: Tam zamanında uyarlanabilir müdahaleler, depresyon, internet tabanlı müdahale, makine öğrenimi

Introduction

Today, depression is a very common mental disorder in almost every society in the world (Vos et al. 2015). In 2019, the World Health Organisation reported that 280 million people worldwide, including 23 million children and adolescents, were diagnosed with depression (WHO 2022). In addition, some social events such as pandemics and earthquakes in the last few years are thought to have caused a serious increase in depression

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Received: 20.12.2023 | **Accepted:** 12.03.2024

cases. It is stated that this increase is caused by the impact of dynamics that may cause loss of usual routines such as social changes made to control the COVID-19 pandemic, long quarantine processes, reduced social interaction, insufficient information, fear of infection and financial insecurity (Brooks et al. 2020, Vindegaard and Benros 2020, Muro et al. 2021). As a matter of fact, in a study conducted after the pandemic, it was reported that the incidence of depression increased significantly in 2020 compared to 2019, almost all over the world, regardless of gender and age (Santomauro et al. 2021).

Depression is a problem that often occurs at a young age and significantly reduces the daily functionality of the individual. In fact, depression is the leading cause of disability for both men and women worldwide in terms of years lived with disability (Total Years Lived With Disability) (Wood and Johnson 2021). Depression can also lead to much more tragic consequences such as suicide in addition to disability. Studies indicate that more than 700,000 people commit suicide each year and that suicide is the fourth leading cause of death among people aged 15-29 worldwide (WHO 2023).

Despite the availability of effective treatment methods for depression, such as psychotherapy and medication, it has been found that an average of two-thirds of individuals with depression in the world remain untreated (Wood and Johnson 2021). Cost of treatment, transport, stigmatisation, lack of information and low perceived need for treatment are often cited as barriers to seeking mental health help (Andrade et al. 2014). A range of interventions may ultimately be needed to alleviate the burdens and risks of untreated mental disorders (Wang et al. 2005).

Considering all these treatment barriers, internet-based interventions are increasingly being adopted as a method to "treat the untreated" (Moritz et al. 2012). Studies have shown that Internet-based self-directed mental health interventions can alleviate some of these barriers and are effective, efficient and cost-effective in the prevention and treatment of many common mental disorders (Andrews et al. 2010, Ponzo et al. 2020, Carlozzi et al. 2022, Wang and Miller 2023, Wang et al. 2023, Bögemann et al. 2023). It is thought that mobile interventions can be used to rapidly reduce symptoms of depression while patients are on a waiting list, as an adjunctive treatment component, or as part of a stepped care model (Mason et al. 2023). The promising effects of digital interventions on depression and stress have been reported in international studies (Moritz et al. 2012, Khademian et al. 2021, Taylor et al. 2023). However, more research is needed both nationally and internationally for conclusive evidence. Internet users in Turkey account for 83.4% of the population with 71.38 million users. This rate is considerably higher than the global average. 80.7% of users use the Internet primarily for information purposes (Dijital 2023). The fact that our country has such a large mass of internet users and that this mass uses the internet within the scope of access to information in general constitutes an exemplary population in terms of internet-based interventions. As a matter of fact, according to the National Mental Health Action Plan (2020-2023) report, the number of mental health and diseases specialists per 100,000 people in our country is 3.43 and the number of child and adolescent mental health and diseases specialists is 1.63 (Saglik Bakanligi 2020). Considering the insufficiency of these numbers and the increasing need for mental support, it is thought that it is important to spread digital health applications in order to reach more populations. In this context, in this article, it is aimed to clarify the just-in-time adaptive intervention method, which is thought to be applicable to these problems encountered in depression and its treatment, and the important components related to this method.

Depression and Just-in-Time Adaptive Interventions

In today's information age, rapid developments in information and communication technologies cause radical changes in people's cultural, social, educational and health needs. These changes have created the opportunity to meet the needs anytime and anywhere without the concept of time and space, and have shown a great renewal effect on health systems on human basis (Işık and Güler 2010). In this context, mobile health methods have an important place (Cinemre et al. 2021). The rapid development and use of health-related smartphone applications offers an alternative and supportive option to reduce the symptoms of mental disorders (Durdu Akgün et al. 2019). Individuals with mental problems may prefer mobile applications more for reasons such as being easy to use, providing an environment free from stigmatisation, providing self-management opportunities and being easily accessible (Uslu and Çetinkaya 2020). In addition, it is also seen that developments in medical technology are moving towards producing personalised solutions rather than categorical evaluations, considering that diseases have different effects on each person (Bostan et al. 2022). With the spread of personalised health concepts, it is estimated that wearable devices will play a greater role in the field of health and will be better integrated into people's daily lives (Güler and Keklik 2022). In addition, recent studies indicate that there is a need to take preventive measures to improve mental health care planning (Vindegaard and Benros 2020).

Considering that the number of patients diagnosed with depressive disorder is increasing (Muro et al. 2021), it is thought that a mobile application that can be self-administered and can be accessed at any time and any place can be used as an innovative and supportive method to improve depression symptoms. Self-directed therapeutic interventions, one of the interventions offered through the Internet, are interventions designed to create positive cognitive, behavioural and emotional change. In this intervention, the content is presented in a comprehensively modularised and highly structured format. Since it targets behavioural change, it is defined as 'active' interventions in terms of programme content (Barak et al. 2009). While creating the programme content, it has been supported by evidence that individuals can learn on their own (Burns 2015, Wood and Johnson 2021) and that it is effective in reducing the severity of depression (González-Valero et al. 2019, Gautam et al. 2020, Kürümlüoğlugil and Tanrıverdi 2022, Kaplan et al. 2023), interventions such as cognitive behavioural therapy approaches and positive psychology interventions that are suitable for presentation on digital platforms can be used (Cohn et al. 2014, Aguilera et al. 2021, Economides et al. 2022, Klein et al. 2023, Lopes et al. 2023). Self-help interventions are dynamic with the delivery of online activities. The vast majority are able to provide some degree of automated feedback support via emails/SMS. According to the software and algorithms developed, the degree of personalisation of feedback can be determined (Barak et al. 2009). It is thought that self-guided personalised applications will also be beneficial in depression. When the related literature is analysed, Just-in-Time Adaptive Interventions (JITAIs) mechanisms emerge. JITAI is an intervention design that aims to provide the right type and intensity of support at the right time by adapting to the changing internal and contextual situation of the individual (Nahum-Shani et al. 2018). JITAIs aim to increase the effectiveness of the intervention and help reduce the psychological burden on the person using the intervention by providing the right type of support at the right time (Teepe et al. 2021). This design emerged from the use of mobile health, the need to address vulnerability situations for adverse health outcomes, and to take advantage of rapid, unexpected, ecologically emerging opportunity situations (Nahum-Shani et al. 2018).

In depression, as in all mental disorders, needs may change between individuals and over time. Therefore, it requires continuous, ecological monitoring of the individual's internal state and context to address these situations in a timely manner, to take advantage of them, and to determine when and how to intervene. This mechanism makes it possible to provide timely and appropriate types of support (Nahum-Shani et al. 2018). Mobile applications developed with this mechanism represent real-world conditions that give people direct access to the intervention of their choice (Klein et al. 2023). Given the potential rise of depression in relation to new global events (e.g., pandemic and economic downturn), the implementation of scalable, fully automated (highly specific, prescriptive and detailed feedback) self-administered biopsychosocial transdiagnostic digital interventions could provide widespread benefits (Klein et al. 2023).

Components of Just-in-Time Adaptive Interventions

In general, the mechanisms of JITAIs include 6 basic elements: vulnerability/opportunity status, distal outcome, proximal outcomes, decision points, intervention options, adaptation of variables, and decision rules (Nahum-Shani et al. 2018) (Figure 1).

1. States of Vulnerability and States of Opportunity: It is a component that focuses on opportunities or vulnerabilities at certain periods of an individual's life. In this component, sensitivity/sensitivity to negative health outcomes (vulnerability) or positive health behaviour changes (opportunity) is assessed. For example, problems such as fatigue, sleep difficulties, forgetting to take medication and interpersonal conflict accelerate the transition to a state of vulnerability. Frailty states can also lead to recurrence of symptoms and an increased risk of disease exacerbation. Therefore, the design of the JITAI aims to provide the right support at the right time to break the cycle that leads to the emergence of a state of frailty, symptom relapse and disease exacerbation. The intervention is also sensitive to positive health behaviours, i.e. periods of opportunity (healthy eating, adequate activity). The importance of utilising periods of opportunity is also emphasised. It is thought that identifying vulnerability and opportunity situations and providing timely support can be possible with the use of wearable, mobile devices and ecological instant assessments (Nahum-Shani et al. 2018, Teepe et al. 2021).
2. Distal Outcome: This component refers to the final goal that the intervention aims to achieve. Generally, primary clinical outcomes such as drug use, relapse duration or physical activity level constitute these components. For example; decrease in depression severity score, decrease in perceived stress level.(Teepe et al. 2021)

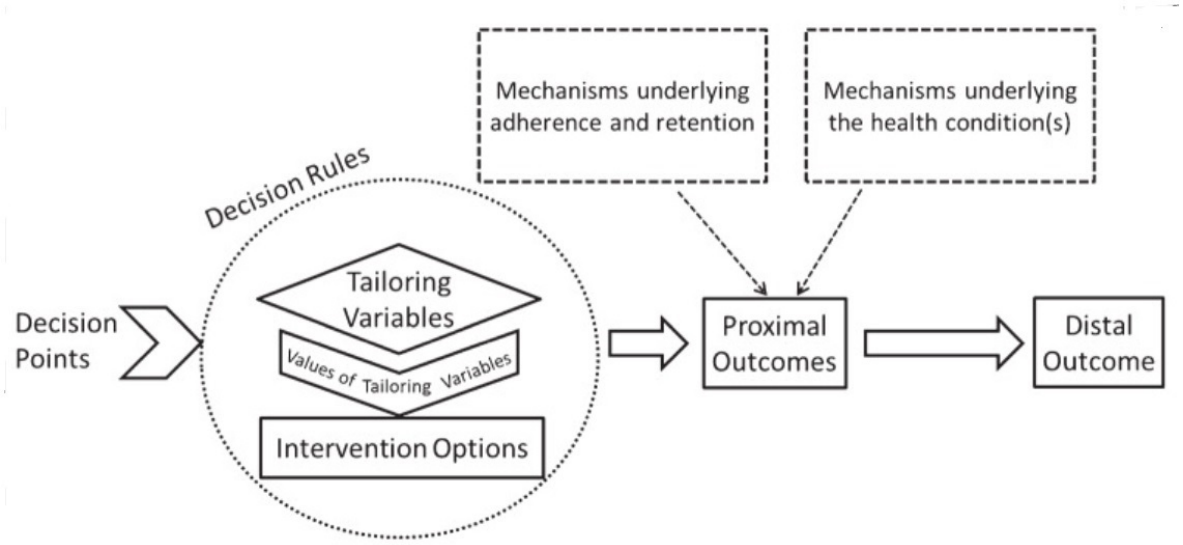

Figure 1. Conceptual model of the components of the JITAIs (Nahum-Shani et al. 2018)

3. Proximal Outcomes: Short-term goals that the intervention aims to achieve. Proximal outcomes, i.e. mediators, are important elements in the pathway that can influence the distal outcome of the intervention or can be intermediate measures of the distal outcome. It is important to consider proximal outcomes to prevent decreased adherence to JITAI, dropout and intervention fatigue (Jochems et al. 2012, Nahum-Shani et al. 2018)

   For example, psychomotor retardation is important in patient follow-up as it is associated with the severity of depression (distal outcome) and its change can be considered as an indicator of therapeutic effect (Caligiuri and Ellwanger 2000, Bennabi et al. 2013). It is thought that we can get an idea about psychomotor retardation with physical activity levels during the day (proximal outcome) (Burton et al. 2013). In this context, our proximal goal in a JITAI targeting physical activity can be '30 minutes of physical activity at least 4 days a week' (Gonul et al. 2019).

4. Decision Points: The time when an intervention decision should be made. The choice of time can change every minute, hour, day, etc. (Nahum-Shani et al. 2018). An example process for decision points is given in Table 1.

Table 1. Example processing mechanism for the decision points process

Example	Decision Rule	Decision Point (States of Vulnerability and States of Opportunity)	Tailoring Variables	Intervention Options
Physical activity intervention using passive assessments of step count.	If the total number of steps at 16:00 is low; Notification [suggest exercise] If the total number of steps is sufficient; Notification [encouraging message "You are doing very well. Keep going!" like]	A certain time of day can be determined. Around 16:00	Total number of steps	Suggest exercise or give an encouraging/motivating notification

5. Intervention Options: It is a set of possible treatments/actions that can be used at any decision point (Nahum-Shani et al. 2018). For example, as a result of the variables adapted in a JITAI targeting physical activity, two intervention options may be "Send activity recommendation" or "Do not send activity recommendation" (Coppersmith et al. 2022). Intervention options are designed to be delivered, accessed and used in a timely and ecological manner. Ecological Momentary Intervention (EMI) is used to describe intervention options that can be delivered and used quickly while people go about their daily lives. EMI can take the form of offering relaxation techniques as an intervention option at a time when a rehabilitation patient is stressed. The most basic feature of all EMI is that the treatment is provided

to people in their daily lives (i.e. in real time) and in environments (i.e. in the real world) (Heron and Smyth 2010).

6. Decision Rules: Decision rules link the intervention options, the decision point and the adapted variables in a systematic way. There is a decision rule for each decision point. An example decision rule could be as follows: If the measured stress levels are higher than a certain threshold, a relaxation intervention is sent to the user, where the change in stress level is the decision point, the relaxation intervention is the intervention option, and the measured stress level is the adaptation variable (Gonul et al. 2019).

   A simplified decision rule targeting physical exercise could take the following form:

   Total number of steps at 16:00....<ise; Then IO (Intervention Option)=Notification [recommend exercise]
   If the total number of steps...≥; then IO = notification [incentive message]

7. Tailoring Variables: It is information about the individual used to decide when (under which conditions) an intervention will be provided and which intervention will be provided (Nahum-Shani et al. 2018). Adaptation variables should be selected based on evidence (practical, clinical, theoretical or empirical) showing that a particular variable is useful for making intervention decisions (Nahum-Shani et al. 2018). The choice of adaptation variables should also be guided by proximal outcomes (Nahum-Shani et al. 2018). For the physical activity variable, decisions can be adapted in the JITAI depending on whether a person is at home/work or elsewhere, whether the person is currently walking, and whether the person currently has an outdoor space. For example, activity recommendations related to physical exercise in open space are only sent when it is not raining at the current location. Data for adapting variables can be collected actively through self-assessment reports ecological momentary assessments (EMA) and passive sensor data (location information etc.) (Coppersmith et al. 2022).

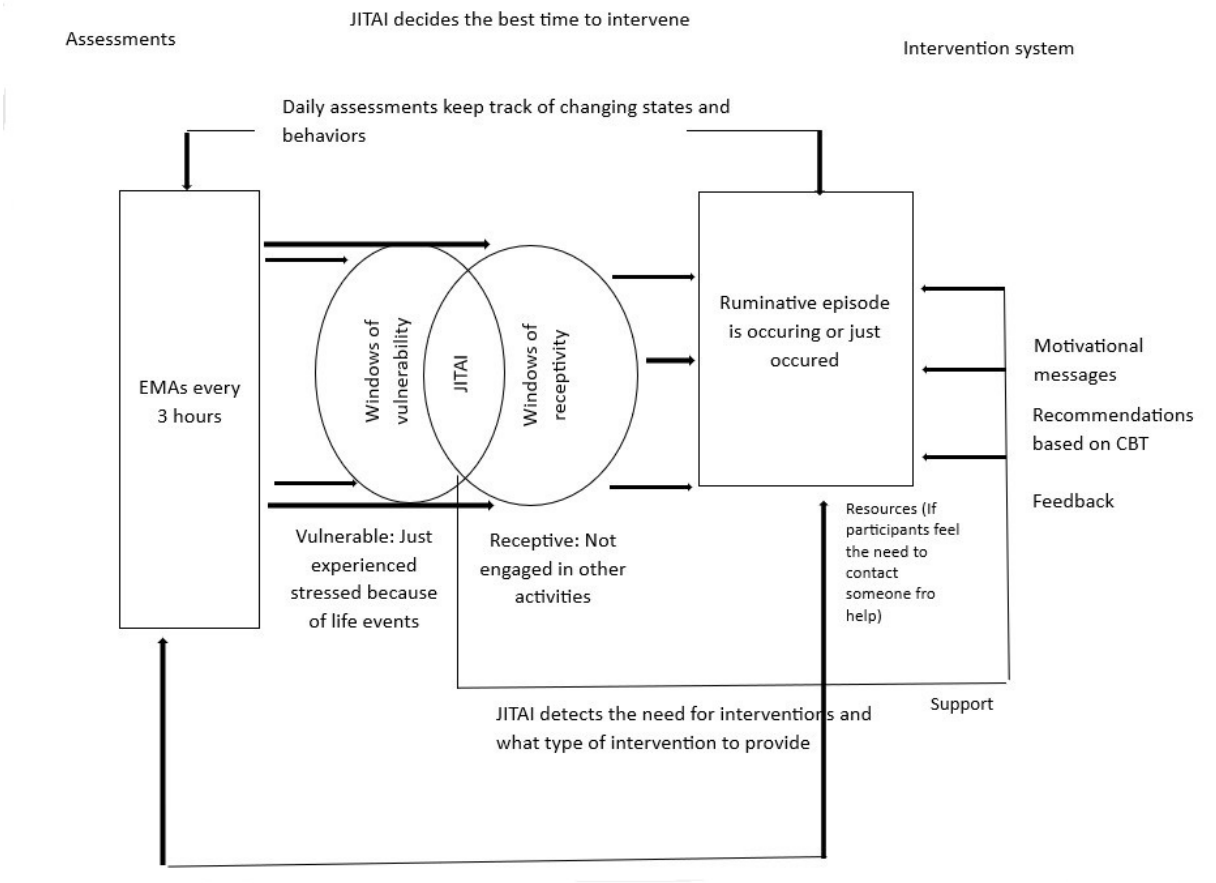

Figure 2. Just-in-time adaptive response design process (Wang and Miller 2023)

In the pilot study conducted by Wang and Miller (2023), an example of a Just-in-Time Adaptive Intervention design based on Rumination Focused Cognitive Behavioural Therapy for ruminative symptoms of individuals diagnosed with depression is shown in Figure 2. In the design, ecological momentary assessments were used as the main evaluation tool to decide which messages to deliver and when. The data obtained through EMA were obtained by asking questions about whether individuals had experienced stressful events in the last 3 hours. In addition, EMA was used to determine whether individuals were open to treatment (receptivity status) at the time they experienced a ruminative episode. If the individuals were open to treatment, that is, if they were not engaged in other activities (e.g., driving or walking), notifications created within the scope of JITAI such as problem-solving skills and motivational messages were delivered (Wang and Miller 2023).

The general working system of JITAI and the components that enable it to exist offer a personalised health plan for the needs of the individual. In particular, the fact that it provides services at the time of need and precisely in the area of need is an important dynamic that makes the mechanism new and unique. In the nature of JITAI, there are processes such as the evaluation and interpretation of many dynamics and notification to the individual with a result output. The active functioning of these processes has revealed the need to support them with some technological tools. Studies suggest evaluating the effects of mobile health interventions on mental health and methods, including machine learning, to improve personalisation (Aguilera et al. 2021).

Personalisation of JITAI and Artificial Intelligence Machine Learning

Machine learning techniques are used as a method to personalise JITAI. Machine learning makes JITAI a system that can adapt itself according to ever-changing contexts and personal variables, including both long-term (e.g. past performance, habit strength, preferences, etc.) and short-term parameters (e.g. location, time, etc.) (Gonul et al. 2019).

Machine learning involves the use of advanced statistical and probabilistic techniques to create systems capable of automatically learning from data (Shatte et al. 2019). It is thought that machine learning methods can be applied in the field of psychiatry and can produce results that support the decision-making mechanisms of experts in the field. The symptom-based diagnostic approach can be supported by existing artificial intelligence technologies and can provide benefits in the field of psychiatry in many aspects such as diagnosis, treatment, adjusting drug dosages, estimating the duration of illness or recovery, identifying individuals in the risk group, predicting diseases in advance or capturing details that the human eye can miss. In addition, these methods can be used to provide solutions to diseases with a holistic approach from a much broader perspective by evaluating the environmental, genetic and biological factors of individuals together (Emre et al. 2021).

Discussion

Diagnosis and treatment of mental disorders are largely based on clinical interviews (Lobbestael et al. 2011) and self-report of patients. However, when patients' cognitive functions are impaired and patients have serious recall difficulties when evaluating past experiences, the diagnostic process becomes complicated (Osipov 2019). Going forward, if we are interested in designing adaptive and personalised interventions to help people cope with personal challenges that arise in the moment, they are not suitable tools because they cannot capture dynamic processes. The use of contemporary mobile technologies in this field is seen as more appropriate to record the ebb and flow of symptoms and subjective experiences occurring longitudinally in individuals and to help identify immediate risk or preventive factors that can be targeted by immediate mobile interventions (Ben-Zeev et al. 2012). Therefore, artificial intelligence techniques are thought to be useful in clinical practice as a more systematic and objective approach in the treatment of psychiatric disorders by focusing on early warning signs (Osipov 2019). Such an approach will potentially allow for the continuous determination of clinical status and deterioration in patients with mental health problems and thus timely intervention (Paradiso et al. 2010).

When the literature is examined in the relevant framework, it is determined that there are quite limited number of studies. For example, in a study involving 24 students with depressive characteristics in Sweden, the Moodbuster program, a personalised program prepared with artificial intelligence support using passive sensor and EMA data of individuals, was used. Researchers found a significant decrease in depression symptoms of individuals as a result of the intervention (ICT4Depression Consortium 2013). In the study of Ponzo and colleagues (2020) with university students who used EAD and passive sensor data in the context of biofeedback, although not within the scope of JITAI, it was found that the use of BioBase, a digital therapeutic mobile application, was effective in reducing high levels of anxiety (Ponzo et al. 2020).

Wang and Miller (2023) found that the just-in-time adaptive intervention designed by Wang and Miller (2023) and created with a system supported by Rumination Focused Cognitive Behavioural Therapy provided a decrease in the rumination levels of individuals diagnosed with depression (Wang and Miller 2023). In the preliminary findings of a microrandomised study conducted by Wang et al. (2023), it was shown that just-in-time adaptive intervention applied to caregivers with chronic patients reduced depression levels (Wang et al. 2023). In addition, studies that are in the design phase in different diseases or groups within the scope of just-in-time adaptive intervention and whose results have not yet been published are seen in the literature (Carlozzi et al. 2022, Bögemann et al. 2023).

When looking at international studies, it becomes difficult to generalize the results due to the small number of participants, limited data collection time, and the use of experimental technology without taking into account long-term usability (Bardram et al. 2012, Warmerdam et al. 2012, ICT4Depression Consortium 2013). In our country, no studies have been found within the scope of JITAI for patients with depression.

Although it is stated that JITAI can overcome many difficulties of traditional treatment approaches, it should be taken into consideration that this intervention design may also bring with it some problems that need to be considered. For example, monitoring people at risk of suicide in real time may bring ethical challenges. Regarding suicide, 'at what level of suicide risk should researchers be allowed to try different interventions? It also raises questions such as 'Is human-assisted intervention necessary at a certain risk level in suicide?' (Coppersmith et al. 2022). To address some of the issues in this regard, a consensus has been published on ethical and safety practices for conducting real-time monitoring studies of individuals at risk for suicide and related behaviors (Nock et al. 2021). It is known that depression causes reluctance and loss of motivation. It is thought that this situation may cause problems with continuing to use mobile interventions (such as intervention fatigue). While designing JITAI, emphasis was placed on determining appropriate proximal outcomes to ensure adherence to the intervention, creating motivating interventions that support the autonomy of individuals while creating intervention options, and arranging the content and media presented in the intervention in a way that does not cause cognitive overload (Nahum-Shani et al. 2018). In addition, study designs and data analytics methods are needed to understand the causal effects of intervention options for studies involving JITAIs (Liao et al. 2016). In Liao et al.'s (2016) study on mobile interventions that can be implemented just in time, the basic rules that can be used in the design of a micro-randomized study are discussed.

Conclusion

It is very important for individuals diagnosed with depression to monitor themselves and notice changes in their mood early. Considering the mechanism and content of JITAI, it is envisaged that it can provide an ideal system where the individual can evaluate himself at certain periods or receive feedback about his feelings/thoughts/behaviors. As a result of this, it is thought that the probability of seeking help at a relatively earlier period will increase and therefore awareness in early diagnosis and treatment may be increased.

Considering the dynamic, heterogeneous and interactive nature of suicidal thoughts and behaviors, which are one of the most serious consequences of depression, it is thought that smartphones or wearable devices integrated with the JITAI mechanism can provide the guidance that the individual may need. The JITAI mechanism can provide this support by being internet-based, self-directed, providing a stigma-free environment and being easily accessible.

Considering the lack of mental health and disease specialists in our country and the fact that a certain proportion of depressed individuals are reached even in societies with highly developed psychiatric treatment systems, these personalized intervention practices may help close the gap between supply and need. In addition, it can be considered that these technological tools can be a preliminary step in establishing crisis intervention centers by ensuring the correct distribution of the burden in the health system. It is thought that the burden of disease can be reduced by providing early interventions by establishing crisis intervention centers and monitoring individuals in these centers.

There is a clear need to develop a more robust evidence base for the objective assessment of mental health. It is necessary to verify whether existing monitoring tools are suitable for long-term monitoring and whether they can be used in clinical populations. It is thought that such approaches may enable the creation of individual phenotypes and the determination of more objective limits that predict response to treatment, in order to better understand the complex picture of individual symptoms and provide more personalized care. These results show that JITAI applications to be developed for depression patients are important and that more studies are needed in this area.

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Authors Contributions: The author(s) have declared that they have made a significant scientific contribution to the study and have assisted in the preparation or revision of the manuscript
Peer-review: Externally peer-reviewed.
Conflict of Interest: No conflict of interest was declared.
Financial Disclosure: No financial support was declared for this study.