Just-in-time adaptive interventions for long COVID related symptom cluster: A scoping review and a checklist for decision rules

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Abstract

Background: Long COVID, a persistent condition arising after acute COVID-19, is currently researched in different ways. Just-in-time adaptive interventions (JITAIs) offer a potential self-management or treatment strategy via technological devices, though their scholarly examination lacks comprehensive review, particularly in the context of long COVID.

Objective: This thesis aimed to examine the research status on JITAIs for selected long COVID symptoms, such as *fatigue with bodily pain*, *cognitive problems*, *respiratory problems*, and psychological problems (depression, anxiety, insomnia). The core elements of JITAI's *tailoring variable, decision-making, context sensing, and monitoring* and *intervention options* were examined. As a follow-up, the decision-making process should be elaborated and a checklist for JITAI development created.

Method: A scoping review according to PRISMA guidelines was performed. The PubMed, Scopus, and PsycINFO databases were searched using a search string and predefined criteria such as language, date of publication, and availability in full text. A total of 288 studies were extracted into the software *Rayyan* and then screened. 51 full texts where screened. Eventually, 11 studies were included, evaluated according to the research questions, and tabulated.

Results: Findings show that JITAIs are promising for managing long COVID symptoms like fatigue and psychological problems but lack coverage for cognitive and respiratory problems. The reviewed studies also vary widely in research methodology as well as methods used in their JITAIs. To address these gaps and differences, we propose a checklist to guide future JITAI development, aiming to improve both rigor and standardization.

Conclusion: While JITAIs have shown promise as a new technology, it is not possible to say conclusively whether this form of intervention is suitable for long COVID. So far, the study situation appears to be insufficient, and further research is needed to address the current challenges. These include improving data collection mechanisms such as self-reporting, careful documentation of decision-making processes, and methodological uniformity. To determine the extent to which respiratory and cognitive problems can be improved through the use of JITAIs, interventions need to be created and reviewed for this purpose.

Keywords: just-in-time adaptive intervention, JITAI, long COVID, symptom management, scoping review, decision-making

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Introduction

In the health and medical sector, efforts should always be made to ensure that patients receive appropriate treatment. Evidently, this can only be ensured if the healthcare system is not strained beyond its capacity. The COVID-19 pandemic has put our healthcare infrastructure, which is designed to provide adequate treatments, to the test. More than 770 million infections with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have currently been confirmed as part of the pandemic (World Health Organization, 2023). Of these, approximately 6.95 million people have died as a result of COVID. According to recent studies, 10% of infected individuals suffer from long COVID, a multisystemic disease that can follow infection with SARS-CoV-2 (Davis et al., 2023). Patients with asymptomatic, mild, and severe infections may develop long COVID symptoms (Crook et al., 2021). In total, more than 200 different symptoms associated with different organ systems have been reported to date (Davis et al., 2023). In particular, fatigue, respiratory problems, cognitive dysfunction, cardiovascular difficulties, and psychological problems have been reported (Global Burden of Disease Long COVID Collaborators, 2022; Raveendran et al. 2021).

The immense burden placed on individuals and the healthcare systems by the COVID-19 pandemic and the resulting long-term consequences, such as Long COVID, underscore the need to find innovative solutions to provide patients with appropriate and effective treatment options. In this context, eHealth approaches that use mobile technologies to complement psychological and medical interventions are becoming increasingly important. A relatively new branch of research is investigating what are known as just-in-time adaptive intervention (JITAIs). They are a type of technology-based intervention that leverages real-time data to deliver tailored support to individuals when and where they need it most. It is designed to be used in conjunction with other forms of therapy and might help enhance the effectiveness of existing treatments by providing personalized support in real-time. JITAIs can be delivered remotely and require different resources than traditional face-to-face therapy sessions. This makes them a promising tool for improving access to mental health care and supporting individuals in managing chronic health conditions. Despite the promising potential of JITAIs as a technology-based intervention, there is currently a lack of literature on this topic (Wang & Miller, 2020). While there has been an increasing interest in JITAIs in recent years, the research available is often inconsistent regarding the design and implementation of JITAIs, making it challenging to draw clear conclusions about their efficacy (Coppersmith et al., 2022). This hinders our understanding of how they can best be utilized to support individuals in managing their mental and physical health. Thus, there is an urgent need to investigate the possible use cases as well as key factors for their effectiveness.

The objective of this part of the thesis was to conduct a comprehensive literature review on JITAIs, with a special focus on exploring how their structural and functional elements could potentially apply to long COVID symptom clusters. This review aimed to identify tailoring variables, decision-making strategies, technical devices used for context sensing, intervention options, methods for measuring effectiveness, and reported barriers or challenges within the JITAI framework that might inform future research on long COVID, frequently occurring long COVID symptoms were selected to represent a diverse clinical picture which could be grouped into a symptom cluster. The research employed a scoping review methodology, which involves systematically identifying and analyzing existing literature on JITAIs for long COVID symptom cluster. By doing so, this research could help to inform the development of more targeted and effective JITAIs that can support individuals in managing the diverse array of symptoms associated with long COVID.

The introduction is followed by a presentation of important terms and basic principles that serve to provide a better understanding and derivation of the research questions. Then, the methodological approach was described in more detail, which is based on the guidelines for a scoping review according to Tricco et al. (2018). In the next chapter, the results were presented, after which they were discussed. In the second part of the thesis, the planning of JITAIs was examined in more detail. The objective was to identify possible guidelines for the use of algorithms and machine learning approaches from the literature as well as other steps in the JITAI development and to compile them into a checklist.

Background

Long COVID

Multiple definitions of long COVID stem from its unexplored nature. This article adopts NICE's definition, encompassing three phases: Acute COVID-19, persistent symptomatic COVID-19, and post-COVID-19 syndrome (NICE, 2021). The latter phase involves fluctuating symptom clusters across body systems, even before 12 weeks, while exploring alternative causes. The term "long COVID" encompasses both persistent symptomatic COVID-19 and post-COVID-19 syndrome. Other scholars suggest symptoms persisting two or more weeks after COVID-19 onset, not reverting to baseline, may indicate long-term effects (Lopez-Leon et al., 2021). This article employs "long COVID" while recognizing distinct phases.

Long COVID entails symptoms across diverse systems, including neurological, respiratory, gastrointestinal, cardiac, endocrine, dermatological, hepatic, and renal systems (López-León et al., 2021). Castanares-Zapatero et al. (2022) offer a comprehensive analysis, suggesting viral-induced changes, neural tissue affinity, autonomic nervous system dysfunction, and immune imbalances as mechanisms causing complications like autoimmunity, coagulation, fibrosis, and metabolic disturbances. Common symptoms include fatigue (58%), headache (44%), attention disorders (27%), hair loss (25%), and dyspnea (24%). Mental health concerns encompass anxiety (13%), depression (12%), and insomnia (11%). Other symptoms relate to lung, cardiovascular, neurological, and nonspecific issues (Lopez-Leon et al., 2021). Gender disparities emerge, with women experiencing weariness and alopecia more. Bai et al. (2022) find a 3.3 times higher risk of long COVID among women; age and active smoking elevate risk, while the severity of COVID infection lacks impact. Consequently, the symptoms and their occurrence in the population are subject to a relatively large dispersion. The variance between individual patient groups speaks for an individualization of possible interventions. This is where JITAIs come into consideration, whose characteristics include individualization. In order to keep the variety of symptoms manageable, it is useful to examine only a sample of the symptoms, which are grouped into symptom clusters in the following.

Symptom Cluster

Grouping similar symptoms into clusters is common practice in health research for improved classification and literature exploration. The Global Burden of Disease Long COVID Collaborators (2022) proposed three symptom clusters: persistent fatigue with bodily pain or mood swings, cognitive problems (e.g., brain fog), and ongoing respiratory issues. Raveendran et al. (2021) identified distinct symptom patterns, with Pattern 1 encompassing fatigue, headache, and respiratory issues, and Pattern 2 involving multi-system complaints. Castanares-Zapatero et al. (2022) highlighted potential factors contributing to long COVID, including viral-induced cellular changes, neural tissue affinity, autonomic nervous system dysfunction, and imbalanced immune responses leading to complications. Since there are different categorizations with different justifications here, a hybrid is used in this work. Although, for example, mood swings are associated with fatigue (Global Burden of Disease Long COVID Collaborators (2022), these were rather assigned to cognitive problems here. These subdivisions, which will consequently be briefly explained, were also made with a view to locating potential studies for the scoping review.

Fatigue with bodily pain

Consequently, symptom clusters were formed for physical and psychological symptoms. Fatigue is prevalent in long COVID (Global Burden of Disease Long COVID Collaborators, 2022), affecting daily functioning (Van Herck et al., 2021). It resembles chronic fatigue syndrome (CFS) and encompasses physical and mental aspects (Lewko et al., 2009; Wostyn, 2021). This study groups physical fatigue with bodily pain and mental fatigue with cognitive issues. Therapies include taking pain medication, physical therapy and also cognitive behavioral therapy.

Cognitive problems

Cognitive problems are debilitating in long COVID (Nalbandian et al., 2021), including memory lapses, concentration difficulties, and brain fog (Almeria et al., 2020; Dyrbye, 2019). Inflammation, vascular damage, virus effects, and stress contribute (Nalbandian et al., 2021; Santabárbara et al., 2020). Tailored approaches, such as cognitive rehabilitation, can be effective (Kesler et al., 2013).

Respiratory problems

Respiratory problems are common in long COVID (Global Burden of Disease Long COVID Collaborators, 2022), impacting daily life and mobility. Shortness of breath, cough, and chest discomfort are prevalent (Global Burden of Disease Long COVID Collaborators, 2022). Further, pulmonary fibrosis and inflammation biomarkers as well as lung vascular disorders have been identified in patients with long COVID (Castanares-Zapatero et al., 2022). Due to a lack of high-quality evidence, feasible pulmonary rehabilitation is recommended (Soril et al., 2022).

Depression, anxiety, and insomnia

Depression, anxiety, and insomnia often co-occur (Kyzar et al., 2021). Virus-related stress contributes to these symptoms (Rogers et al., 2020), impacting brain function (Kyzar et al., 2021). Psychotherapy, counseling, medication, and lifestyle modifications are effective treatments (Shaukat, Ali, & Razzak, 2020). Ongoing support is crucial due to potential long-term mental health repercussions (Sher, 2020).

JITAI's origin and structure

Technologically advanced interventions, including JITAIs, address the self-management imperative for chronic conditions like long COVID (Gonul et al., 2019). JITAIs are distinct from related concepts like dynamic or tailored interventions, demonstrating enhanced technological sophistication and real-time adaptability (Collins et al., 2004; Krebs et al., 2010; Lustria et al., 2013). They parallel Ecological Momentary Interventions (EMI), building on Ecological Momentary Assessment (EMA), and provide real-time feedback for behavioral change (Heron & Smyth, 2010).

JITAIs outshine EMI and other dynamic interventions through heightened technological interactivity and advanced adaptation capabilities. They can predict and respond to user behaviors more effectively (Wang & Miller, 2020). Accordingly, JITAIs outperform interventions that are less dynamic (Krebs et al., 2010) and warrant differential assessment. Despite EMI's similarities, JITAIs demonstrate greater technological development. Analyzing JITAIs' characteristics and their contribution to efficacy becomes essential (Wang & Miller, 2020).

JITAIs are designed for real-time, individualized adaptation, shaped by the user's context, goals, and theoretical framework. Wearable sensors, smart devices, and omnipresent computing enable continuous data collection, identifying opportune moments for behavioral change (Nahum-Shani et al., 2015). Interventions are tailored to individual needs, with adaptable decision points, intervention options, and rules (Coppersmith et al., 2022; Wang & Miller, 2020). JITAIs provide personalized, timely support, vital in addressing long COVID's symptom clusters. The forthcoming sections delve into key aspects of JITAIs: tailoring variables, decision-making, context sensing, monitoring, and intervention options, drawing from Coppersmith et al. (2022), Nahum-Shani (2018) and Wang and Miller (2020).

Tailoring variable

Tailoring variables encompass contextual cues for appropriate intervention decisions. For example, in a physical activity JITAI, location, current activity, and availability can function as tailoring variables (Coppersmith et al., 2022). The role of interactivity in capturing patient data and delivering interventions is key, as it improves the tailoring of intervention content. Accordingly, user interaction with intervention platforms is critical to identifying tailoring variables and using them as optimal moment for intervention content (Wang & Miller, 2020). These variables can be collected flexibly, allowing interventions to be timely and responsive to rapidly changing conditions. Data for these tailoring variables can come from active assessments like self-reports, which require user engagement, or passive assessments that are automatically gathered with minimal user involvement.

Decision-making algorithms

Wang and Miller (2020) could show that decision-making in JITAIs benefits from the combination of automatic and human algorithms. This underscores the synergy of AI and human agents for diagnostic and treatment decisions. Their focus on tailoring's impact on outcomes deems it the primary assessment goal for JITAIs. Gonul et al. (2019) propose an adaptive intervention framework, refining personalized delivery strategies for chronic conditions. Some systems, like Gustafson et al.'s (2019) static modules, lack systematic adaptability, while dynamic models employ feedback loops for personalized engagement and adherence (Gonul et al., 2019).

Computational approaches amplify intervention adaptivity by capturing long-term changes. Chih et al. (2019) employ agent-based models for food choice and obesity prediction, Goldstein et al. (2019) predict dietary lapses through machine learning. Mobile technology and machine learning amalgamate for intervention timing optimization. Reinforcement learning and context sensing devices refine real-time intervention delivery (Chih et al., 2019; Goldstein et al., 2019). The diverse learning algorithms employed offer personalized adaptability, tapping into a contextual dataset.

Context sensing and monitoring

JITAIs employ passive wearable and smart device data alongside active EMAs to gather vital contextual cues, customizing interventions (Klasnja et al., 2023). Wearables like smartwatches and fitness bands provide physiological insights such as heart rate and sleep patterns, aiding condition inference and intervention tailoring (Klasnja et al., 2023). Smartphones with sensors like GPS and accelerometer offer location, movement, and environmental data (Klasnja et al., 2023). Self-reported mood, cravings, and pain levels, though user-dependent, enhance context understanding (Klasnja et al., 2023). Consent-based online activity monitoring informs interventions; search history or app usage guide tailored support (Klasnja et al., 2023). Integration with Electronic Health Records adapts interventions based on diagnoses or medication changes (Klasnja et al., 2023). Smart home devices or environmental sensors, exemplified by asthma management (Anan et al., 2021), further enrich contextual awareness in JITAIs.

Intervention Options

JITAI content, encompassing feedback, messages, and materials, draws from behavior-specific theories (Nahum-Shani et al., 2016). *Intervention options* denote adaptable strategies targeting specific situations, shaped by tailoring variables reflecting the individual's present state (Coppersmith et al., 2022). Suicide prevention exemplifies such options, spanning evidence-based interventions like social support promotion, cognitive-behavioral skills, safety planning, and means restriction (Coppersmith et al., 2022). Individual risk factors and states inform the choice of intervention, enabling personalized selection, such as promoting social support or enhancing distress tolerance based on individual needs (Coppersmith et al., 2022).

Effectiveness

Wang and Miller (2020) claimed notable improvements in health outcomes when comparing JITAIs to alternative interventions. Such findings align with previous JITAI component efficacy studies (Krebs et al., 2010). Although many studies are pilot-sized, a common limitation in emerging fields, these results suggest JITAI effectiveness. Notably, age, treatment length, and primary outcomes generally lack significance as moderators in JITAI effectiveness studies. This indicates the potential generalizability of the JITAI concept to different populations (Wang & Miller, 2020). While scoping through the literature there appears to be a positive basic tone for the utilization of JITAIs. This may arise from the many studies that have already sufficiently investigated methodical predecessors of JITAIs as for example EMA or EMI. The question remains to what extent the effectiveness of other adaptive interventions is maintained for this intervention form. In addition, Xu and Smit (2023) asserted in their meta-analysis that there is some evidence for the effectiveness of JITAIs on behaviour change (g = 0.77), although they could not find proof of the moderating effects of theory-based interventions or the form of assessment. They suggested that more randomized trials are necessary to further evaluate the effectiveness of JITAIs.

Research Questions

JITAIs uniquely combine mechanisms from related methods such as EMI in more advanced ways. The individual design elements of JITAIs have been postulated (Coppersmith et al., 2022; Nahum-Shani et al., 2015; Wang & Miller, 2020). In some domains, such as addiction recovery and physical activity, there is a strong case for the effectiveness of JITAIs and their underlying design elements. The extent to which this is transferable to long COVID symptom clusters and the extent to which research on this is already underway needs to be explored.

1. Tailoring variables: Which tailoring variables can be found?
2. Decision-making: Which decision-making strategies were used?
3. Context sensing: Which technical devices were used for sensing and monitoring?
4. Intervention Options: Which intervention options were applied?
5. Effectiveness: How was the effectiveness measured and with what outcome?
6. Barriers: Which potential barriers or challenges have been reported by the researchers?

Method

To comprehensively review research on JITAIs for long COVID symptoms, a scoping review approach was employed. This method enables efficient identification and dissemination of findings, particularly suited for complex topics and research gaps (Peterson et al., 2017). Following Arksey and O'Malley's (2005) framework for scoping reviews with modifications proposed by Levac et al. (2010), the process involved: (1) identifying relevant literature, (2) selecting suitable studies, (3) organizing data, and (4) summarizing outcomes. The final step aligned with the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist (Tricco et al., 2018).

Identifying relevant literature.

The initial scoping review phase encompassed literature identification, a pivotal step to ensure comprehensiveness. To achieve this, electronic databases including PubMed, Scopus, and PsycINFO were queried. A preliminary search utilized terms such as "JITAIs" and "just-in-time adaptive interventions" combined with respective symptom clusters for baseline availability assessment. Subsequently, refined search terms were used, employing Boolean operators AND and OR. The search string encompassed: ("JITAI" OR "Just-in-time adaptive intervention" OR "just-in-time" OR "adaptive intervention" OR "dynamic intervention") AND ("long COVID" OR "fatigue" OR "chronic fatigue syndrome" OR "bodily pain" OR "pain" OR "myalgia" OR "cognitive problems" OR "attention disorder" OR "memory impairment" OR "respiratory problems" OR "lung disease" OR "depression" OR "anxiety" OR "insomnia"). Additionally, reference list snowballing and gray literature exploration were performed to ensure inclusiveness, encompassing unpublished research (Tricco et al., 2018).

Study selection

To refine search outcomes, criteria for inclusion and exclusion were defined. Inclusion entailed studies in English or German, exploring JITAIs, and addressing long COVID symptom clusters: fatigue with bodily pain, cognitive problems, respiratory problems, depression, anxiety, and insomnia, with full-text availability. Studies were required to have been published (or in preliminary form) between January 1, 2015, and April 15, 2023, striking a balance between timeliness and consideration of recent developments. Exclusions encompassed non-definable studies and conference proceedings. Given the scoping review's nature, all study designs except from review studies were included, ensuring broad yet informative inclusion. After exporting studies to Mendeley and Rayyan, duplicates and irrelevant papers were eliminated. Abstracts and titles were then screened for appropriateness against the criteria, followed by full-text evaluation for relevance.

Charting the data.

The third phase of the scoping review involved data charting. A categorization aligned with the research question was developed to extract pertinent details such as study design, long COVID cluster, tailoring variables, decision-making, context sensing mechanisms, intervention type, outcome measures, and barriers. Data were structured into tables providing a summary of key findings and enabling pattern recognition and gap identification. Adherence to the PRISMA-ScR checklist assured the process's comprehensiveness, transparency, and reproducibility.

Collating and summarizing the results.

The last phase of the scoping review entailed summarizing findings from the included studies. This step aimed to offer a comprehensive understanding of JITAIs for long COVID symptom clusters, highlighting significant attributes and effectiveness factors. Data were categorized thematically, aligning with the hypotheses, covering areas like tailoring variables, decision-making, context sensing, intervention options, effectiveness, and potential barriers. The results were subsequently reported to convey the research outcomes.

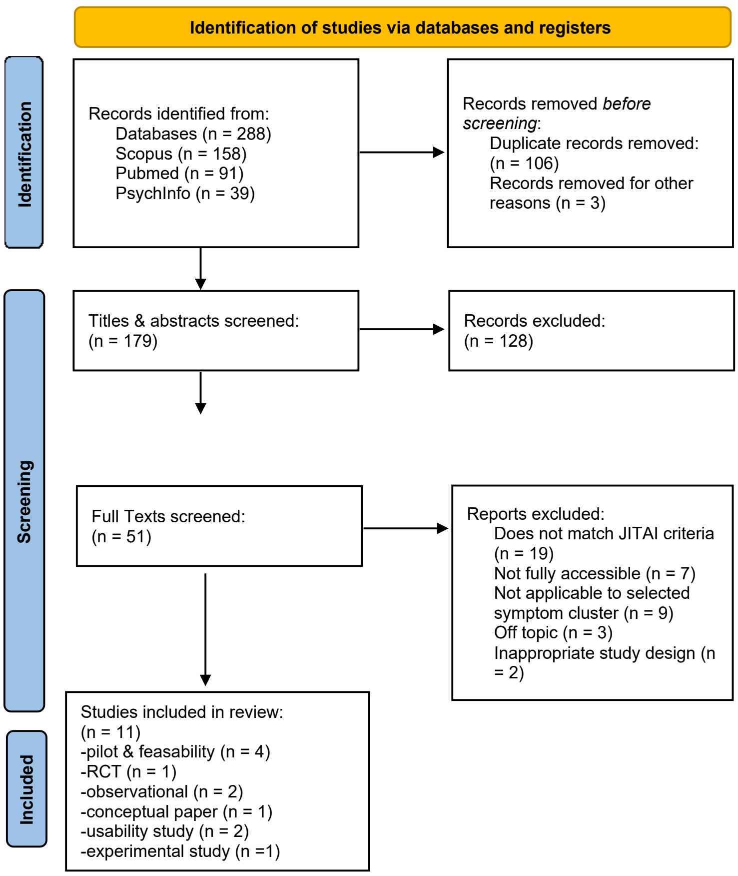
Results

Description of the studies

The initial search identified 288 records from various databases (Figure 1): 158 from Scopus, 91 from PubMed, and 39 from PsycINFO. After removing 106 duplicate records and three records flagged as unusable on the part of the software, 179 records remained for title and abstract screening. The three records mentioned were reports that could not be clearly classified. Out of these 179 records, 128 were excluded for not meeting the inclusion criteria. This left 51 full-text articles to be screened. Out of these, 18 did not match the JITAI criteria, seven were not yet fully accessible, nine were not applicable to the selected symptom cluster, three were off-topic, and two had an inappropriate study design (review studies). Eventually, 11 studies were included in the review. These consisted of four pilot & feasibility studies, one randomized controlled trial (RCT), two observational studies, one conceptual paper, two usability studies, and one experimental study.

Figure 1

Prisma flow chart for a scoping review



The 11 studies encompassed diverse research designs, including pilot and feasibility studies exploring viability, RCTs offering rigorous experimental evidence, observational studies providing real-world insights, a conceptual paper establishing a theoretical framework, 2 usability studies gauging acceptability, and an experimental study employing innovative methodologies. This diverse array of study types facilitated a comprehensive exploration of the JITAI approach. However, some studies exhibited information gaps in light of the research questions. Notably, two studies didn't explicitly address all aspects of the research questions (Carlozzi et al., 2021; Schneider et al., 2023). In addition, two symptom clusters—cognitive problems and respiratory problems—were not represented in any of the selected studies. Moreover, Jacobson & Chung (2020), Nirmal et al. (2022) and Ren et. al., (2022) developed predictive models rather than actual JITAIs, but still offered valuable insights for the decision-making process in JITAIs, as state prediction could be utilized there. Details of study characteristics are provided in Appendix A.

Tailoring variables

In the examined studies, a multifaceted, data-driven approach was a consistent theme for personalizing interventions. These studies didn't rely on just one data source; they integrated multiple contextual cues to enhance intervention effectiveness. For example, Beltzer et al. (2022) identified critical variables for anxiety patients, refining interventions through motivation and prompt timing. Carlozzi et al. (2022) used health-related quality of life, physical activity, and sleep data from Fitbit devices to tailor interventions for depression and insomnia. For fatigue and bodily pain, Hiremath et al. (2019) recognized the potential of contextual cues like baseline physical activity levels for individualized interventions. Jacobson & Chung (2020) combined passive sensor data with self-reported emotions to predict future depressed moods. Similarly, Nirmal et al. (2022) harnessed a variety of passive sensing data, like physiology, movement, location, light, and phone calls, to anticipate mood shifts. Various other studies, from Pulantara et al. (2018, 2018b) to Wang & Miller (2023), incorporated both passive and active data streams, from patient-reported data to rumination timing patterns. This common thread across the studies underscores the value of a comprehensive, multifaceted approach, especially when addressing complex psychological symptoms such as depression, anxiety, and insomnia. Utilizing diverse data sources can potentially refine intervention predictions and outcomes. Yet, these insights don't guarantee their direct applicability for long COVID without more rigorous validation. For example, it would be interesting to see how well individual variables are also at predicting appropriate interventions. In addition, as noted above, not all symptom groups were consistently considered, indicating a gap in research.

Decision-making

The reviewed studies employ diverse decision-making algorithms, primarily machine learning models, to decide when to provide an intervention option. Decision-making processes vary across studies, tailored to specific objectives. Beltzer et al. (2022) used contextual bandits, considering motivation and prompt timing for anxiety intervention. Carlozzi et al. (2022) employed participant data for personalized push notifications. Hiremath et al. (2019) used decision tree algorithms for patients' physical activity responses, trying to improve fatigue symptoms. Machine learning was central in Jacobson & Chung (2020), Nirmal et al. (2022), and Ren et al. (2022), predicting mood states from sensor data. Pulantara et al. (2018a) iteratively adjusted recommendations based on patient data. Schneider et al. (2023) used Computerized Adaptive Testing and Classification Testing, while Wang & Miller (2023) applied network analysis and GIMME models. Wahle et al. (2016) trained machine learning models to classify subjects by PHQ-9 scores. Importantly, the use of machine learning and other complex algorithms enables the interventions to be highly adaptive and responsive to real-time or near-real-time data. This means that interventions can be adjusted on-the-fly, allowing for highly personalized treatment that is continuously optimized for the patient's current condition. Given the complex and often fluctuating nature of long COVID symptoms, this adaptability could be crucial. However, it's important to note that while these methods have shown promise, the reviewed studies didn't universally cover all the symptom clusters associated with long COVID. Symptoms of depression, anxiety, insomnia and fatigue are treated with adaptive interventions, for cognitive and respiratory problems no JITAIs and decision-making processes were found. This suggests that additional research is needed to validate the applicability and effectiveness of these data-driven algorithms specifically for long COVID symptom management.

Context sensing and monitoring mechanisms

JITAIs rely on essential context sensing and monitoring mechanisms, employing diverse tools for data collection. Beltzer et al. (2022), Jacobson & Chung (2020), Nirmal et al. (2022), and Ren et al. (2022) used mobile apps and passive sensing like GPS on smartphones to collect real-time data on activities and behaviors. Wearable devices, exemplified by Carlozzi et al. (2022) and Pulantara et al. (2018), utilized sensors like accelerometers and heart rate monitors for monitoring physical activity and sleep patterns. Hiremath et al. (2019) combined smartphones, smartwatches, and a wheel speed sensor. These devices could monitor real-time data related to physical activity and pain levels, thereby allowing for the personalization of interventions such as tailored exercise regimens or pain management strategies. Pulantara et al. (2018b) used Fitbit devices in conjunction with a mobile app. Jacobson & Chung (2020) extended data collection to include Google places, weather, and phone logs. Wahle et al. (2016) employed a system, Wang & Miller (2023) utilized SMS reminders, and Schneider et al. (2023) used computerized adaptive testing. Beltzer et al. (2022) and Jacobson & Chung (2020) employed these technologies to collect data related to anxiety and depressed mood.

Such data collection methods might make it possible to identify patterns that may trigger these symptoms. For example, Jacobson and Chung (2020) harnessed passively collected sensor data from smartphones and wearables to predict hourly depressed mood fluctuations within a day. By analyzing this data on an hourly basis over a week and applying a combination of generalized and individual-specific machine learning models, they achieved a notable prediction accuracy, with a correlation of 0.587 between predicted and observed moods. The models' effectiveness was consistent across 97% of the sample, suggesting the potential for real-time interventions tailored to mood shifts in daily life. These results show the value of passive data in understanding and potentially intervening in depression dynamics. Further, the use of Fitbit devices and similar wearables for monitoring sleep patterns, as in Pulantara et al. (2018), could also provide actionable insights for dealing with insomnia. Thus, physical conditions such as heart rhythm or even measured environmental variables such as loudness could be used to look at potential causes of insomnia in that individual. Moreover, the diverse types of data collected, such as weather and location data by Jacobson & Chung (2020), offer the potential to understand how various external factors could influence long COVID symptoms. Consequently, on the one hand, measuring the context can be seen as helping to identify the appropriate time for an intervention. On the other hand, there is the possibility of obtaining more detailed information about the patients' symptoms via the measurements.

Intervention options

The research landscape on intervention options for long COVID-related symptoms, particularly within the realm of JITAIs, is diverse and innovative. For example, Hiremath et al. (2019) aimed to enhance physical activity for fatigue and pain by setting personalized goals using real-time data, a strategy that may be especially effective for long COVID patients with these symptoms. Pulantara et al. (2018a, 2018b) provided individualized sleep interventions via an app and compared them to traditional face-to-face sleep interventions. Based on the measured sleep data from wearables, they provided indiviualized sleep recommendations with regard to stimulus control. Beltzer et al. (2022) presented a context-aware, bandit algorithm. This approach was designed to manage anxiety and uses emotion regulation (ER) strategies provided via an app. Based on contextual data (e.g., GPS) or randomization, individuals were suggested different ER strategies. The best strategy was the algorithm that suggested the best 10 individual ER strategies based on contextual data. Similarly, Carlozzi et al. (2022) provided personalized interventions through an app for depression symptoms, using e.g., Fitbit data for tailoring. Based on this, they used push notifications to suggest alternative behaviors for depressive or anxious symptoms. Although the suggestions were based on collected data, they were random. Jacobson & Chung (2020) and Nirmal et al. (2022) predicted future depressed mood using passive sensing data and machine learning algorithms. Consequently, we can refer here to predictive models rather than full interventions. Ren et al. (2022) employed predictive modeling for elevated negative affect in adolescents. Even if they did not make an intervention in the classical sense, the prediction of critical states can be seen as part of a JITAI and be the starting point for an intervention. Wahle et al. (2016) utilized mobile sensing and support for context-sensitive interventions for depressive symptoms. The study included an app that provided evidence-based interventions from cognitive behavioral therapy, such as social, relaxation, mindfulness, and activity exercises. Contextual sensor data from the smartphone were collected, including accelerometer, Wi-Fi, and GPS. These data were used to tailor interventions to each subject's preferences for time, location, and personal preferences. Wang & Miller (2023) implemented personalized rumination-focused cognitive behavioral therapy using SMS reminders. These studies suggest that JITAIs could effectively address psychological symptoms through personalized, real-time monitoring and intervention. It is noticeable that predictive models were designed and tested in 3 studies. It is possible that an important part of JITAIs is to predict states in order to proactively provide just-in-time support.

Effectiveness & outcome measures

The studies within this scoping review used a variety of outcome measures to gauge the effectiveness of interventions. Beltzer et al. (2022) employed subjective evaluation to gauge perceived effectiveness. Carlozzi et al. (2022) utilized quality of life measures, daily steps, sleep patterns, and surveys. Jacobson & Chung (2020) and Nirmal et al. (2022) focused on the success of predictive models in forecasting mood changes. Wahle et al. (2016) used the Patient Health Questionnaire-9 to track improvements. Ren et al. (2022) evaluated the ability of predictive models to anticipate various emotional states. Wang & Miller (2023) measured reductions in rumination episode counts and duration. Pulantara et al. (2018) relied on self-report measures. Hiremath et al. (2019) assessed energy expenditure and intensity, while Schneider et al. (2023) compared adaptive and fixed-length

EMAs focusing on the methodological improvement of JITAIs. These diverse measurements highlight the comprehensive approach researchers are taking to understand long COVID symptom clusters.

The diverse outcome measures used in these studies reflect a comprehensive approach to understanding and evaluating interventions for long COVID symptom clusters. However, the effectiveness of an intervention is best determined through standardized, validated, and widely accepted measures. While many of the studies employed recognized tools, such as the Patient Health Questionnaire-9, the use of subjective evaluations or less common metrics could introduce variability in interpretation. It's essential to consider the methodological rigor, consistency in measurement tools, and the validation of newer or less common metrics to ensure that the effectiveness reported is both reliable and comparable across studies.

Potential barriers reported in the literature

Sample size and representativeness, e.g., through self selection bias are recurring issues, as noted by Beltzer et al. (2022) and Carlozzi et al. (2022). These limitations could be particularly relevant when targeting long COVID symptom clusters, as small and biased samples may not capture the complexity and heterogeneity of these symptoms. This makes it difficult to determine how well these interventions would work on a broader scale. Similarly, the barrier of significant individual differences in the strength of the effect across persons highlighted by Nirmal et al. (2022) could be especially salient when considering long COVID, which presents a diverse range of symptoms among patients. Personalizing interventions to account for these individual differences is crucial but also challenging. Practical barriers, like travel distance and scheduling conflicts noted by Pulantara et al. (2018a), underscore the need for remote or digital solutions, which are more urgent given the fatigue and physical limitations often associated with long COVID. Technical issues and data specificity, pointed out by Hiremath et al. (2019) and Schneider et al. (2023), may also hamper the development of JITAIs that are robust and specific enough to manage complex long COVID symptoms. Building systems that can accurately capture and respond to the nuances of these symptoms is vital but currently a challenge. Although these characteristics are at the core of JITAIs, incomplete studies to date do not clearly identify where the causes lie. Ethical and privacy issues are less mentioned but cannot be neglected, especially considering that JITAIs for long COVID will collect sensitive health data. The example provided by Wang & Miller (2023) about review board approval and addressing patient concerns indicates a growing awareness of this crucial dimension.

Discussion

Summary of study results

The primary objective of this thesis was to conduct an exhaustive literature review focusing on JITAIs and their potential applicability in managing long COVID symptom clusters. There are several key findings and important nuances that emerged from this research. First, existing JITAIs have not yet been applied to all of the symptom groups of long COVID mentioned here, particularly cognitive and respiratory problems. Many of the examined studies have specialized in tailoring interventions for emotional and psychological symptoms like anxiety, depression, and insomnia, often relying on health-related quality of life metrics and wearables for data collection. However, this leaves a gap in adequately dealing with other prominent symptoms of long COVID, especially those related to cognitive and respiratory issues.

Second, while current JITAIs show promise in managing emotional and physical symptoms, such as fatigue and bodily pain, they require further development for more complex symptomology. Studies such as that by Hiremath et al. (2019) suggest that employing contextual cues, like previous physical activity levels, can enhance the effectiveness of interventions. This approach could be particularly valuable for managing interconnected symptoms like fatigue and bodily pain, which can vary greatly among individuals. However, these methodologies haven't been rigorously validated for long COVID, a condition with complex and often fluctuating symptoms.

Third, the existing JITAI research largely leans on machine learning and algorithmic approaches for real-time adaptation, yet further validation is necessary for long COVID management. The studies reviewed employ a range of decision-making algorithms, from contextual bandits to decision tree algorithms and network analysis, to optimize interventions. While these algorithms allow JITAIs to be highly adaptive, their applicability and effectiveness for long COVID symptom management remain largely untested.

Fourth, context sensing and monitoring mechanisms are essential to JITAI efficacy and have shown promise in other symptom domains. Mobile apps, wearables like Fitbit devices, and even smartwatches are employed to collect a myriad of data, from physical activity to sleep patterns. The capability for real-time or near-real-time data collection allows JITAIs to be incredibly responsive, a feature that could be essential given the fluctuating nature of long COVID symptoms. However, such approaches have not been universally examined across all long COVID symptom clusters.

Lastly, the landscape of intervention options within JITAIs is diverse and innovative, employing various types of personalized, real-time monitoring and intervention strategies, such as personalized exercise regimens or sleep restriction strategies. However, there is a lack of direct research examining these intervention options specifically for long COVID-related symptoms, indicating a need for studies targeting this specific patient population.

Linking findings to previous research

The results of this thesis are consistent with previous work suggesting the efficacy of JITAIs in managing chronic conditions (Wang & Miller, 2020; Nahum-Shani et al., 2015). However, whereas past researchers have primarily focused on less complex symptom clusters (Carlozzi et al., 2021; Schneider et al., 2023), the present study emphasizes the urgent need for targeted JITAI interventions to manage more debilitating symptoms like cognitive and respiratory issues in long COVID (Lopez-Leon et al., 2021). Additionally, as Xu and Smit (2023) have previously noted, the effectiveness of JITAIs has not been conclusively established. Although JITAIs have been better researched in other areas, such as physical activity, incomplete reports or inconsistent methodological approaches or inadequate theoretical underpinnings have been reported there as well (Oikonomidi et.al., 2022; Wunsch et. al., 2022). Consequently, it cannot be argued that a research gap exists only in the area of long COVID, but presumably across the spectrum of this form of intervention.

Discussing research results

Nevertheless, our findings highlight the significant gaps in current JITAI research concerning long COVID. While they show promise in addressing particular symptom clusters, they seem to falter when confronted with the multifaceted, ever-changing tapestry of long COVID symptoms. In my opinion, one compelling reason for this inadequacy lies in the relatively nascent stage of long COVID research itself. This initial phase of the investigation has resulted in a lack of JITAIs specifically designed to address the complexity of the long COVID.

There are a couple of other aspects of the current research landscape that are particularly noteworthy. Firstly, the employment of varied technologies—like wearable devices and mobile apps—in JITAIs is indeed commendable for its potential for real-time data collection. This kind of instantaneous monitoring is especially vital in managing long COVID, a condition marked by its fluctuating symptoms. However, the question remains: Are these technologies being deployed effectively enough to capture the diversity of long

COVID symptoms? Simply collecting data is one thing; making meaningful interventions based on this data is another challenge altogether.

Further, I find the diversity in outcome measures quite revealing. On one hand, this range—from subjective evaluations like health-related quality of life measures to more concrete metrics like sleep pattern tracking—provides a rich tapestry of perspectives for evaluating the effectiveness of JITAIs. Yet, this multiplicity also raises concerns. It hints at a lack of a unified methodological approach to evaluating these interventions. When we are dealing with something as complex as long COVID, the need for a standardized, universally accepted set of outcome measures becomes obvious. A cohesive evaluation system could facilitate more definitive conclusions and comparisons across various studies, something that is keenly needed to advance the field (Pulantara et al., 2018).

Lastly, the ethical considerations surrounding data privacy were not exhaustively dealt with in the existing literature. Especially in the case of automated processing of personal data, it must be clear that an ethical discussion must take place. JITAIs could have the potential to become a widely used tool. Therefore, ethical and data security aspects, in a time of data overload, should definitely be considered. Presumably, this has fallen into the background so far, as it is still an insufficiently researched area.

Study strengths & limitations

The strength of this review lies primarily in the clean execution. Scoping reviews, by their very nature, allow for a broad overview without occasionally providing a detailed look at specifics. This not only provided good descriptive answers to the research questions, but also identified gaps. Furthermore, this was an exploration into an area that is obviously under-researched. On the one hand, this circumstance makes it difficult to clearly separate the researched constructs, since there are no precise specifications, but on the other hand, it offers a valuable insight into an exciting form of intervention. The ambition of the research is also worth mentioning, as it seems important to search for efficient and effective forms of intervention for patients with long COVID.

There are limitations concerning the results of this scoping review. A potential limitation is the heterogeneity of long COVID symptoms, which might make JITAI applications more complex. Cognitive and respiratory problems lack robust study coverage, possibly due to limited interest, funding, or perceived incompatibility with JITAIs. The novelty of JITAIs might also explain their selective application. These gaps could skew results and highlight unmet research needs. Notably, two studies (Carlozzi et al., 2021; Schneider et al., 2023) incompletely address research questions, affecting scoping review comprehensiveness. Ethical considerations around data privacy also warrant more attention, as JITAIs for long COVID would necessarily involve the collection of sensitive health data (Wang & Miller, 2023). Although the present research cannot rule out these limitations, they could be addressed in future research. 4

Additional considerations

The present study represents a first attempt to thoroughly investigate the role of JITAIs in managing long COVID. In line with the adopted NICE definition of long COVID, future research should differentiate among its various phases while designing JITAIs. Given the extensive symptom range, selecting symptoms for research should consider both frequency and the feasibility of JITAIs. Technologically advanced interventions like JITAIs present a unique opportunity for self-management of chronic conditions like long COVID, as they offer real-time adaptability (Gonul et al., 2019). Further studies are essential for building on these preliminary insights and for developing a more comprehensive JITAI approach to long COVID.

While our initial investigation emphasized the potential of JITAIs in managing the multifaceted nature of long COVID, as defined by NICE, it is crucial to delve deeper into the technological underpinnings that make these interventions adaptable and effective. Specifically, understanding the algorithms and machine-learning methods that drive real-time adaptability is an essential component of optimizing JITAIs for long COVID symptom management and JITAIs in general. The present study lays the foundation by raising questions about the existing guidelines for the use of such algorithms.

A framework for decision rules in JITAIs

The decision process is particularly interesting because it offers the possibility of using real-time data for adaptive interventions. Accordingly, the goal of this section was to create a comprehensive checklist that not only captures the diversity of decision algorithms, but also highlights the challenges of practical implementation. To meet this objective, the question was asked whether published guidelines exist for the use of algorithms and machine learning methods in decision-making processes that could be applied in the development of JITAIs. The focus was not only on interventions for long COVID, to avoid an overly narrow view ignoring the complexity of decision-making. Further, the data collection and evaluation processes related to the decision-making have been examined. By extrapolating from the existing literature, we aspired to support future researchers and practitioners.

Decoding decision-making

To comprehend the landscape of decision-making in JITAIs it is essential to categorize and explore the diverse array of algorithms employed. A general taxonomy exists that classifies algorithms into three primary categories: rule-based, machine learning, and hybrid approaches. Rule-based algorithms operate on predefined heuristics and guidelines, while machine learning algorithms utilize historical data to make predictions. Hybrid algorithms amalgamate both rule-based and machine learning components to enhance adaptability (Menictas et al. 2019).

Rule-based algorithms operate on a set of predefined rules and decision-making guidelines (Gustafson et al., 2019). These rules are often established by domain experts or clinicians and are designed to guide intervention adjustments based on specific user responses or contextual cues. For example, Schneider et al. (2023) evaluated the concept of a subset of JITAIs using different forms of rule-based algorithms. These rules determine when to end an assessment. The rule-based algorithms employed in the Schneider et al. (2023) study offer the advantage of standardized and efficient assessments. However, they lack the adaptability and learning potential that could make them more responsive to the unique and evolving needs of individual patients. Rule-based algorithms are particularly suitable for scenarios where explicit decision logic can be articulated, making them valuable for interventions targeting straightforward and well-understood trigger-response relationships. This category includes algorithms such as decision trees, expert systems, and logic-based rule engines (Nahum-Shani et al., 2018).

Machine learning algorithms have gained significant prominence in JITAI interventions due to their capacity to learn patterns from historical data and make predictions based on complex relationships. These algorithms leverage a diverse array of techniques, including regression, classification, clustering, and deep learning, to model user behavior and to tailor interventions. For example, Hiremath et al. (2019) utilized a decision tree machine-learning algorithm. Their JITAI responded automatically based on monitored Physical Activity levels. Machine learning algorithms are adept at capturing intricate nuances and non-linear associations within the data, allowing them to provide personalized recommendations and adapt interventions dynamically. On the contrary, these models can be like 'black boxes,' making it difficult to understand how decisions are made. Besides, machine learning algorithms typically require a large amount of data to train effectively. Common examples encompass support vector machines, random forests, neural networks, and k-means clustering (Goodfellow et al., 2016).

Hybrid algorithms combine the strengths of rule-based and machine learning approaches to create more flexible and adaptable decision-making frameworks. These algorithms merge predefined rules with learning capabilities, allowing them to refine their decision strategies over time. Ren et al. (2022) employed decision tree-based algorithms like random forest and multiple kernel learning algorithms like support vector machines. The study combined different algorithms for predicting states of elevated negative affect. Hybrid algorithms offer a balanced approach, leveraging explicit guidelines where available and learning from data where complexity demands it. This fusion of techniques enhances the precision of interventions while retaining a degree of interpretability. Although, the combination of methods can make it even more difficult to understand how decisions are made. Ensemble methods, reinforcement learning, and adaptive heuristics are illustrative of hybrid algorithms employed in JITAIs.

Existing guidelines

In the development and optimization of JITAIs, a structured framework is essential, often guided by the seminal work of Nahum-Shani et al. (2018). This framework delineates key components such as distal outcomes, proximal outcomes, tailoring variables, decision points, decision rules, and intervention options. Among these, decision rules serve as the central mechanism for determining the timing and nature of interventions. These rules are generally grounded in theoretical models and often utilize conditional statements to manage a variety of tailoring variables. To address the challenge of managing these variables, machine learning has been introduced as a statistical methodology, as discussed by

Menictas et al. (2019). It utilizes historical data to forecast proximal outcomes and assists in variable selection.

The decision-making points in JITAIs are intricately tied to user responses to EMA prompts. Algorithmic predictions for subsequent assessments employ new data and assess risk probabilities, which are calibrated based on factors like app prototyping stages and desired alert frequency (Heron & Smyth, 2010). This leads to an ongoing optimization process that includes pilot testing to refine algorithms based on their performance and user feedback. The implementation of machine learning in JITAIs brings several challenges; these range from handling missing data and model selection to integrating machine learning models into JITAI applications. Recommendations for the successful application of machine learning in JITAIs include its employment in scenarios where empirical evidence is insufficient for formulating effective decision rules and emphasize the necessity of interdisciplinary collaboration (Wang et al., 2021).

In JITAIs a dual-phase approach might be applied which begins with data collection and offline analysis to construct a preliminary decision rule and conduct Micro-Randomized Trials (MRTs). Techniques such as Q-learning are used to refine decision rules, which are subsequently personalized during the online learning phase. This online strategy incorporates an adaptive balance between exploitation and exploration, continually adjusting to user behavior over time. The significance of user feedback as an input for ongoing refinements highlights an active area of research.

Besides, the iterative nature of JITAIs supports a comprehensive feedback loop that encompasses user data collection, algorithmic decision-making, intervention delivery, and user response (Gonul et al., 2019). Despite challenges such as data availability, the potential for JITAIs integrated with Artificial Intelligence to offer personalized, evidence-based, and cost-effective healthcare solutions is promising. Furthermore, according to Suilaman et al. (2022), JITAIs synthesize personalized health interventions, robust technological infrastructure, and user feedback to foster an integrated approach to enhancing healthy behaviour in indivuduals. It is important that features like robustness, security, and privacy are prioritized.

Data collection

MRTs play a crucial role in JITAIs by guiding decision-making, collecting data, and enabling the customization of interventions in real-time. Furthermore, MRTs are vital for continually improving JITAIs by offering insights into participant behavior and supporting the adaptability of interventions. In the context of the paper from Seewald et al. (2019) the MRT assumes a pivotal role as a component of the decision-making process in JITAIs. MRTs can guide data collection, thereby informing researchers' key decisions about the effectiveness of each intervention component within the JITAI paradigm. MRTs facilitate treatment allocation decisions at discrete decision points, where participants are sequentially randomized to various treatment options, including abstaining from treatment altogether. This allocation process aligns seamlessly with the principle of JITAIs embodying the principle of tailoring interventions to real-time conditions. Employing adaptive decision rules, the MRT supports the selection of optimal treatment choices grounded in participant states and contexts. Consequently, the MRT functions as an essential conduit for the acquisition of empirical data that underpins decision-making (Seewald et al., 2019). By examining the effects of different interventions on proximal outcomes, such as the number of steps, researchers can make reasonable decisions about integrating intervention components into the final JITAI framework. Furthermore, the MRT enables the evaluation of the causal effects of interventions on proximal outcomes, encompassing the temporal evolution of these effects and their moderation by contextual variables (Seewald et. al., 2019). In this context, the MRT emerges as a significant method within the decision-making process, navigating treatment allocation, discerning intervention efficacy, and orchestrating adaptive intervention tailoring within the dynamic milieu of JITAIs (Leong & Chakraborty, 2022).

Beyond its important role in shaping real-time interventions, the MRT also serves as a foundational structure for iterative improvement in JITAIs (Seewald et al., 2019). It enables researchers and clinicians to effectively evaluate the limitations and strengths of existing algorithms and intervention components. Data gathered through MRTs often reveal insights into participant behavior and response, enriching the machine learning models and rule-based algorithms that power the JITAI. This continuous cycle of data collection and analysis ensures that JITAIs can adapt to emerging trends in user behavior or unexpected challenges, such as handling missing data or resolving inconsistencies in user feedback. MRTs also align well with the broader goals of JITAIs to provide individualized, context-aware healthcare solutions, emphasizing the real-time adaptability and individual-centric nature of these systems. Notably, the inherent flexibility of the MRT design accommodates an array of intervention components and tailoring variables, making it a versatile tool for developing more effective and patient centered JITAIs. Therefore, the MRT is not just a component but rather a vital mechanism that amplifies the efficacy, adaptability, and individualization of JITAIs, ensuring they are rooted in empirical evidence while remaining agile in a rapidly evolving healthcare landscape.

Proposing a checklist for decision-making

Developing JITAIs is an intricate endeavor, requiring careful planning, robust algorithmic decision-making, comprehensive data collection, and ongoing optimization. As JITAIs increasingly become part of the healthcare landscape, it is crucial to establish best practices for research and implementation. The checklist that follows serves as a comprehensive guide designed to assist future researchers and clinicians while creating their JITAIs, with a focus on decision-making but also considering general ideas.

Planning and Conceptualization

1. **Define Objective**: Clearly outline the purpose and desired outcomes of the JITAI.
    - *Suggestion:* For instance, the objective could be to provide real-time, adaptive interventions to manage and reduce fatigue symptoms in individuals experiencing long COVID. This could include sending timely reminders or suggestions for rest, activity pacing, or medication adjustments based on continuous health monitoring by wearables, smartphones, or other smart devices.
2. **Review Existing Guidelines**: Familiarize yourself with seminal works and frameworks in JITAI, such as Nahum-Shani et al. (2018).
    - *Suggestion:* Assess the methodologies in existing literature to inform your own JITAI.

Decision Algorithm Selection

1. **Choose Algorithm Type**:
    - *Rule-based algorithms* for well-defined scenarios.
    - *Machine learning algorithms* for complex, data-rich environments.
    - *Hybrid algorithms* for nuanced decision-making.
    - *Suggestion:* Use hybrid algorithms when you seek to combine automatic and human decision-making, as indicated by Wang and Miller (2020).
2. **Consider Existing Taxonomies**: Be aware of how algorithms can be classified to better understand their advantages and limitations.
    - *Suggestion:* Referring to Gonul et al. (2019), you might consider whether an algorithm is better suited for static modules or dynamic models with feedback loops.

Algorithm Design and Development

1. **Consult Domain Experts**: Engage clinicians or domain experts for rule-based algorithms.
    - *Suggestion*: Involve medical experts or data scientists when developing algorithms related to healthcare interventions.
2. **Data Requirements**:
    - *Evaluate the data volume* needed for machine learning models.
    - *Ensure data quality and relevance*.
3. **Algorithm Transparency**:
    - *Aim for interpretability* in machine learning or hybrid models.
    - *Clearly document rule-based decision logic.*

Data Collection

1. **Micro-randomized Trial (MRT):**
    - *Plan and conduct MRTs* for empirical validation.
    - *Utilize MRT data for iterative refinement.*
    - *Suggestion:* Use MRTs to validate your reinforcement learning models, as in the data-driven behavioral simulator paper.
2. **User Feedback**: Integrate real-time user feedback for ongoing adaptability.
    - *Suggestion:* Use mHealth apps to collect user feedback for real-time adaptivity.
3. **Handling Missing Data**: Develop strategies to cope with data gaps.
    - *Suggestion:* When missing data, consider data imputation methods or sensitivity analyses.

Ethical Considerations

1. **Data Security**: Implement robust security measures to protect user data.
2. **Privacy**: Maintain user anonymity and consent.
3. **Ethical Frameworks**: Ensure the intervention aligns with ethical guidelines (e.g., Jones & Moffitt, 2016)

Implementation and Optimization

1. **Pilot Testing**: Conduct preliminary tests to evaluate the JITAI's performance.
    - *Suggestion:* Conduct a small-scale pilot study before deploying your JITAI on a larger scale.
2. **Interdisciplinary Collaboration**: Engage with specialists from relevant fields for a more robust JITAI.
    - *Suggestion:* Involve experts in Artificial Intelligence, Behavioral Sciences, and Clinical Medicine for a holistic approach.
3. **Ongoing Refinement**:
    - *Use Q-learning or other techniques* for online strategy adjustments.
    - *Continually update the algorithm* based on performance metrics and user feedback.

Evaluation and Feedback Loop

1. **Performance Metrics**: Establish criteria to evaluate the JITAI's effectiveness and efficiency.
    - *Suggestion:* Consider using "tailoring's impact on outcomes" as a key metric, following the findings from Wang and Miller (2020).
2. **Observation**: Monitor how well the JITAI adapts to individual user behaviors and needs.
    - *Suggestion:* Use machine learning algorithms like those employed by Chih et al. (2019) for capturing long-term changes.
3. **Iterative Improvement**: Utilize feedback and data for continuous improvement.
    - *Suggestion:* Implement feedback loops as shown in dynamic models by Gonul et al. (2019) for personalized engagement and adherence.

The checklist delineated in this chapter serves a dual purpose: to act as a roadmap for the systematic development and optimization of JITAIs and to advance the rigor and reproducibility in this emerging interdisciplinary domain. Structured around key developmental stages—planning and conceptualization, decision algorithm selection, design and development, data management, ethical considerations, implementation, and evaluation—this checklist provides targeted suggestions and contextual examples. It is intended to guide both researchers and clinicians by integrating existing scientific findings, such as those by Wang and Miller (2020) on algorithmic decision-making and Gonul et al.

(2019) on adaptive frameworks, to fortify the JITAI's empirical basis. This checklist contributes to the cumulative scientific knowledge essential for the practical advancement of JITAIs in healthcare.

Conclusion

Drawing together the multiple strands of research and inquiry examined throughout this thesis, it is clear that JITAIs offer considerable promise in the realm of personalized long COVID symptom management. However, this potential is tempered by a host of challenges that span technical, methodological, and ethical considerations. Our investigation unequivocally revealed that current JITAIs exhibit certain limitations, particularly in addressing specific symptom clusters like cognitive and respiratory issues. It appears that researchers are prefering certain symptoms, such as emotional and psychological conditions, leaving cognitive and respiratory problems underserved. Given the intricate and fluctuating nature of long COVID, we are confronted with an urgent need for more exhaustive research. Specifically, this should focus on expanding the existing JITAI frameworks to include rigorous clinical trials, improving data collection mechanisms, and robustly addressing ethical considerations around data privacy and security.

Regarding limitations, we recognize the issues around the heterogeneity of long COVID symptoms and the ethical quagmires surrounding data privacy. Additionally, our scoping review's comprehensiveness was affected by some studies incompletely addressing research questions. Future research can plug these gaps, offering a more complete picture of the JITAI landscape as it relates to long COVID.

The checklist introduced in this study serves a dual purpose: it provides a methodological guide for JITAI development and enhances scientific rigor in this evolving field. By following this evidence-based roadmap, both clinicians and researchers can more effectively navigate the complexities of JITAIs, from algorithms to ethics.

In conclusion, while JITAIs represent a promising frontier in healthcare, particularly in managing the diverse world of long COVID symptoms, a considerable amount of work lies ahead. The issues range from the technical—improving data collection and algorithms—to the methodological, such as the need for standardized outcome measures and larger sample sizes, and even to the ethical, including data privacy concerns. However, the introduction of the comprehensive checklist and the potential for collaboration across disciplines paint an optimistic picture for the future. By tackling these multifaceted challenges head-on, we can drive significant advancements, resulting in more effective, ethical, and comprehensive JITAIs. This would not only contribute to improved long COVID symptom management but also to broader progress in healthcare technology and individualized treatment paradigms.

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Appendix

Appendix A: Review table

Study	Study Design	Study Objective	Long COVID Cluster (or symptom)	Tailoring Variables	Decision-Making	Context Sensing	Intervention options	Effectiveness & Outcome Measures	Potential Barriers
Beltzer et al. (2022)	experimental study	developing and evaluating a contextual bandit algorithm to predcit effectiveness	depression, *anxiety,* insomnia	algorithm identified 2 important variables; current motivation to change their thoughts, well perceived timing of the prompt	contextual bandits to predict the effectiveness of the strategy, learned from historical data, estimated counterfactual outcomes, and compared its performance with other policies	mobile App (MetricWIre), passive sensoring (GPS)	ER strategies: either based on meta-analysis or the 10 most frequent strategies	perceived effectiveness and post-ER affect	limited sample, individual differences, modelling decisions
Carlozzi et al. (2022)	RCT	determine the feasibility and acceptability of an intensive app-based intervention in three distinct care partner groups	*depression,* anxiety, *insomnia*	Health-related quality of life (HRQOL) measures, physical activity, and sleep data from Fitbit	not explicitly mentioned (push notifications are delivered randomly, but personalized based on participant' data)	Fitbit Inspire 2 (for physical activity, i.e., steps, distance, calories, and sleep)	personalized "pushes" delivered via the CareQOL app, based on Behavioral Activation (BA) theory; pushes include data feedback, facts, tips, or support	focuses on feasability not effectiveness, HRQOL measures, daily steps, daily sleep, daily HRQOL surveys, monthly surveys, adherence and acceptibility	limited sample size (60-90), results not generalizable; lack of control group with personalized feedback; self selection bias due to voluntary participation; short duration of intervention, limited assessment of care recipient outcomes; lack of

Study	Study Design	Study Objective	Long COVID Cluster (or symptom)	Tailoring Variables	Decision-Making	Context Sensing	Intervention options	Effectiveness & Outcome Measures	Potential Barriers
									detailed information on decision making algorithms
Hiremath et al. (2019)	pilot & feasability study	mobile health-based physical activity measurement system to track physical activity levels of individuals with spinal cord injury and provide a behavior-sensitive, JITAI to improve their physical activity levels	fatigue with bodily pain (via physical activity)	personalized daily goals and feedback were provided based on their moderate-intensity PA of theS previous days	decision tree machine-learning algorithm, JITAI responds automatically based on monitored PA levels	Android-based smartphone (Nexus 5 or 5X), Wrist-worn smartwatch (LG-Urbane), Bluetooth-based wheel rotation monitor (PanoBike)	prompting individuals to perform physical activity (PA)	PA levels were measured in energy expenditure in kilocalories, Minutes of light- and moderate- or vigorous-intensity PA were also measured	small sample size, non-randomization, limited statistical analyses, wireless sensors led to partial data loss; recommendations: implement trial study to assess long-term effects of the JITAI
Jacobson & Chung (2020)	observational study	investigate the feasibility of using smartphone-based passive sensing data to predict future	*depression, anxiety, insomnia*	passive sensor data (GPS, google places, weather information, light level, heart rate, outgoing phone calls), self reported	machine learning algorithms, extreme gradient boosting algorithm, random forest models to predict	GPS, location speed sensor, location accuracy sensor, location-based information source sensor, google places, local weather information, heart	prediction of depressed mood rather than an actual intervention	effectiveness of model by comparing predicting measured values with predictions (r = 0.587)	not generalizable sample, depression severity was exclusively based on self reports, did not explore the full range of depressive mood constructs, digital phenotyping should be

Study	Study Design	Study Objective	Long COVID Cluster (or symptom)	Tailoring Variables	Decision-Making	Context Sensing	Intervention options	Effectiveness & Outcome Measures	Potential Barriers
		depressed mood levels		sadness and loneliness	depressed mood based on sensor data	rate sensor, outgoing phone calls			tested in different settings
Nirmal et al. (2022)	usability study	explore the use of mobile health and sensor monitoring as supplements to clinical care for individuals with Spinal Cord Injury	*depression*, anxiety, insomnia	passive sensing data including physiology, movement, location, light, and phone calls to predict future changes in depressed mood	machine learning models to make predictions with ARIMA (autoregressive Integrated Moving Average) based on the collected data; employs parallel predictive modeling techniques to analyze the correlated survey and sensor data	passive sensor data from mobile devices to collect sensor data on physiology, movement, location, light, and phone calls	focused on predicting depressed mood using passive data	ability to predict depressed mood across time	significant differences in the strength of the effect across persons, suggesting that individual differences could be a potential barrier to the generalizability
Pulantara et al. (2018a)	pilot & feasability study	explore the potential effectiveness of delivering sleep interventions through the iREST (interactive Resilience Enhancing Sleep Tactics) platform compared to	depression, anxiety, *insomnia*	patient-reported data to personalize interventions, adjusting recommendations based on changes in behaviors and improvements in sleep quality	system iteratively reassesses what behavioral changes may be required based on patient-reported data, and with clinician's approval, sends an adjustment in the	records sleep data with wearable devices	personalized recommendations for the implementation of sleep restriction and stimulus control, delivered through the iREST app	self-report measures were used, including the Insomnia Severity Index (ISI), the Pittsburgh Sleep Quality Index (PSQI), and the PSQI Addendum for	traditional in-person treatment formats often create barriers to receiving or adhering to treatment visit schedules due to travel distance, conflict with work and family

Study	Study Design	Study Objective	Long COVID Cluster (or symptom)	Tailoring Variables	Decision-Making	Context Sensing	Intervention options	Effectiveness & Outcome Measures	Potential Barriers
		traditional in-person delivery methods			personalized recommendations.			Posttraumatic Stress Disorder	
Pulantara et al. (2018b)	usability study	develop and assess the usability of a JITAI application platform iREST	depression, anxiety, *insomnia*	iREST system uses self-administered measurements	human based decision-making through clinicians which can prescribe sleep tips	iREST system uses mobile app for recording sleep data, uses Fitbit devices to measure sleep patterns.	sleep education, personalized sleep tips, and secure messaging between clinicians and users	effectiveness of the iREST system was measured through usability evaluation, of adherence to treatment regimens, and comparison of sleep diary and Fitbit-reported sleep data	need for improvements in the architecture to increase the sensitivity of Fitbit's measuring sleep parameters, the need for the iREST app to support background services, and the need for further investigation of clinician usability
Ren et al. (2022)	observational study	investigate the potential of using smartphone sensors to predict states of elevated negative affect (specifically anger, sadness, and anxiety) in adolescents	*depression, anxiety,* insomnia	activity level, percentage of time spent at home, sleep onset and duration, phone usage	employs decision tree-based algorithms like random forest and multiple kernel learning algorithms like support vector machines; combines different algorithms and compares the ensemble ML with conventional statistical prediction of	smartphone accelerometer, location, and device state data to derive fourteen discrete estimates of behavior, including activity level, percentage of time spent at home, sleep onset	predictive models could be used to trigger brief “just-in-time” interventions via smartphone notifications or mental health apps	ability to predict states of elevated anger, anxiety, and sadness with acceptable discrimination ability (area under the curve (AUC) = 74% for anger, 71% for anxiety, and 66% for sadness)	limited set of smartphone-derived variables, relatively poor estimates of sleep (wristbands would be more precise), small sample size, sparse EMA sampling strategy

Study	Study Design	Study Objective	Long COVID Cluster (or symptom)	Tailoring Variables	Decision-Making	Context Sensing	Intervention options	Effectiveness & Outcome Measures	Potential Barriers
					high negative affect	and duration, and phone usage			
Schneider et al. (2023)	conceptual paper	evaluate the concept of just-in-time adaptive to Ecological Momentary Assessment as a strategy to improve the measurement of tailoring variables in JITAIs	fatigue with bodily pain	momentary states of fatigue, study uses a uniform cutoff for classifying momentary fatigue states	computerized Adaptive Testing (CAT, these rules determine when end an assessment and record the final theta value) and Computerized Classification Testing (CCT, dynamically tailoring the classification cutoffs)	not explicitly mentioned	not explicitly mentioned	measurement error led to inaccurate classification of individual states, fixed length EMA resulted in false classification, adaptive length improved accuracy while reducing the number of items needed by 54%	data specificity, compliance influence, generalizability

Study	Study Design	Study Objective	Long COVID Cluster (or symptom)	Tailoring Variables	Decision-Making	Context Sensing	Intervention options	Effectiveness & Outcome Measures	Potential Barriers
Wahle et al. (2016)	pilot & feasability study	explore the use of smartphone sensors to detect behavioral patterns that could indicate depressive symptoms; also aimed to investigate the potential of delivering context-sensitive interventions through smartphones to provide in-situ support for individuals with depressive symptoms	*depression,* anxiety, insomnia	mobile Sensing and Support (MOSS), collected context-sensitive sensor information to tailor interventions based on each subject's preferences regarding time, location, and personal preference	supervised, nonlinear machine learning models trained on multiple features calculated from collected sensor data to distinguish between subjects above and below a clinically relevant Patient Health Questionnaire-9 (PHQ-9) score	smartphone's sensors, including accelerometer, Wi-Fi, and GPS	app provided evidence-based interventions derived from cognitive-behavioral therapy (CBT), including social, relaxation, thoughtfulness, and physical activity exercises. A set of eighty interventions were designed and implemented	tracking change in self-reported symptom severity using the PHQ-9 survey. Participants with clinical depression (PHQ-9 ≥ 11) and adherence to the app for at least 8 weeks showed significant drop in PHQ-9 scores. Binary classification models achieved accuracies of 60.1% and 59.1% for predicting PHQ-9 levels	non-randomized and uncontrolled study design, lack of direct causal link between symptom improvement and app use, need to quantify the efficacy of the recommendation algorithm

Study	Study Design	Study Objective	Long COVID Cluster (or symptom)	Tailoring Variables	Decision-Making	Context Sensing	Intervention options	Effectiveness & Outcome Measures	Potential Barriers
Wang & Miller (2023)	RCT	this study aimed to pilot-test a fully automated JITAI leveraging RFCBT and ways to identify and block cascading depressive rumination	*depression,* anxiety, insomnia	leveraged rumination timing patterns to personalize the mobile RFCBT (MRFCBT) intervention, JITAI-MRFCBT condition was personalized	algorithms were used in the study to perform network analysis, estimate GIMME models, evaluate the effects of the intervention, and visualize network connections among variables; these techniques allowed for the examination of within-person dynamics and the personalized effects of the JITAI intervention on rumination episodes	smartphones, participants received SMS text message reminders on their smartphones to self-report their rumination-related symptoms	rumination-focused cognitive behavioral therapy (RFCBT) called mobile RFCBT (MRFCBT)	effectiveness was measured by comparing the JITAI-MRFCBT condition with a no-treatment control condition; Effect Size for Reduction in Rumination Episode Counts: Cohen's d: 2.5 Effect Size for Reduction in Average Time Spent in Rumination: Cohen's d: 1.84	self-reported nature of participants' depression diagnoses, small sample size, limited generalizability on patients not in therapy or with other forms of depression, inability to evaluate potential mediators