



# Systematic Review Could Avatar Therapy Enhance Mental Health in Chronic Patients? A Systematic Review

Marta Franco<sup>1,2</sup>, Carlos Monfort<sup>1,2</sup>, Antonio Piñas-Mesa<sup>3</sup> and Esther Rincon<sup>1,2,\*</sup>

- <sup>1</sup> School of Medicine, Universidad San Pablo-CEU, CEU Universities, 28925 Madrid, Spain; marta.francoparro@usp.ceu.es (M.F.); carlos.monfortvinuesa@ceu.es (C.M.)
- <sup>2</sup> Department of Psychology and Pedagogy, Universidad San Pablo-CEU, CEU Universities, Campus de Monteprincipe, Urbanizacion Monteprincipe, Pabellón MED, Despacho 00.22, 28925 Alcorcon, Spain
- <sup>3</sup> Department of Humanities, Universidad San Pablo-CEU, CEU Universities, Paseo Juan XXIII, 6-8, 28040 Madrid, Spain; anpime@ceu.es
- \* Correspondence: maria.rinconfernande@ceu.es; Fax: +34-913-724-700 (ext. 15076)

**Abstract:** The use of avatars in the psychological treatment of some chronic diseases is in their infancy, and it represents a growing field of research with many possibilities for innovation. However, there is a lack of studies seeking to determine if avatar-based therapies could improve mental health in chronic care settings. In fact, to the best of our knowledge, this is the first systematic review addressing this research topic. The objectives of this study were to review the scientific literature on those studies involving avatar-based therapies for chronic patients, as well as different ways to develop them and their efficacy on mental health outcomes. Two main questions were addressed: (1) Are avatar-based strategies useful to improve mental health in chronic patients? (2) Which is the best way to develop avatar-based strategies regarding chronic diseases? A systematic review of the peer-reviewed literature was conducted in March 2021. The results were, not only useful for establishing suitable ways to develop avatar-based strategies to improve mental health in chronic care, but also for providing an ad hoc taxonomy regarding this research topic. Five modalities were effective (61.1%) in enhancing mental health in chronic care.

Keywords: avatar; chronic disease; chronic illness; mental health; patient care; quality of life

## 1. Introduction

Addressing chronic illnesses is one of the greatest international challenges for public health in the 21st century in terms of both the continuous suffering experienced by the patient, and the large-scale socio-economic consequences; particularly in the poorest and most vulnerable countries with average or low incomes [1].

The intervention strategies undertaken to tackle chronic illnesses are eminently preventative and focus on the self-management of symptoms [2,3]. These techniques include, for example, educational meetings to improve knowledge of the illness and a sense of responsibility [4]; lifestyle changes, including daily physical exercise, a balanced diet, weight control and reducing stress levels [5]; and the implementation of actions geared towards increasing perceived self-efficiency in health [3]. As such, we seek to improve the prognosis of chronic illness [2] and obtain relevant benefits in terms of the physical and psychological health of patients, which will increase their quality of life [5].

In order to improve patient chronic care, several digital health tools have recently been used, including avatar-based therapies. Avatars are digital animations or self-representations that allow users to interact in a virtual environment [3,6,7]. Furthermore, they can be personalized so that they are more realistic and are as similar as possible to the patient using them, which helps patients to better identify with them [8]. Avatars have been used in many different fields, including in healthcare and educational settings.



Citation: Franco, M.; Monfort, C.; Piñas-Mesa, A.; Rincon, E. Could Avatar Therapy Enhance Mental Health in Chronic Patients? A Systematic Review. *Electronics* 2021, 10, 2212. https://doi.org/10.3390/ electronics10182212

Academic Editor: Srinivas Sampalli

Received: 31 July 2021 Accepted: 3 September 2021 Published: 9 September 2021

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**Copyright:** © 2021 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). For example, they have been developed with obesity patients [9–11] and to treat mental health diseases such as depressive disorders [12], eating disorders [13,14], addictive disorders [15,16], social anxiety disorders [17–19] and agoraphobia [20]. They have also been developed as educational tools in order to enhance healthcare staff performance [21–25]. Facial emotion recognition is another area of study in which virtual reality has been used. The results found in the scientific literature suggest that immersive virtual reality, through the use of avatars, can be used as a tool for training patients in recognizing emotions [26]. This finding is particularly useful for people with schizophrenia, as they find it difficult to recognize facial emotions, causing alterations in their interpersonal relationships [27,28]. Its usefulness has also been established for people with autism, given their deficiency in social cognition and communication [29], and for major depressive disorders in which patients have a negative response bias towards sadness, tending to assess positive, neutral, and ambiguous facial expressions as being sadder [30]. The use of avatars for autism spectrum disorders (ASD) is of particular interest. It has been found that an improvement in the social behavior of minors diagnosed with ASD can be achieved when using a humanoid robot or avatar as opposed to a human [31]. Furthermore, in patients with autism, other benefits have also been shown, such as being able to imitate the movements of the avatar [32]; improving the ability to recognize and express basic emotions [33]; and increasing the capability for social interactions, by practicing verbal and non-verbal behavior in virtual reality environments [34].

Virtual reality is also booming in the context of video games, where tools have been developed and are becoming increasingly more accessible to users. These include the virtual reality devices head-mounted display (HMD), Oculus Go©, HTC Vive©, and Playstation©'s connected virtual reality platform. Despite the growth in virtual reality technology, therapies based on virtual reality in the clinical setting have not experienced the massive accessibility that recreational activities have seen, with mental health professionals still having relatively low access to such devices [35].

Avatars may be used in many different ways. They have been used through twodimensional electronic devices (e.g., with an app on a mobile telephone or tablet, in which the avatar provides an extensive range of information according to the purpose of use; as well as via an online platform on which users can access a two-dimensional virtual environment and interact with other users via their avatars); through three-dimensional virtual reality, using a technology known as augmented reality, via which three-dimensional digital images can be incorporated and interacted with in a real-life physical environment [36]; and through mixed reality, which combines augmented and virtual reality, combining the physical and virtual worlds, and allowing the immersive interaction of the subject with this mixed reality [37]. However, there are still many questions regarding the best way to use avatars to improve the care of chronic patients, such as: What kind of patient would benefit the most from this treatment? What psychological variables could be improved with the use of this kind of technology (e.g., anxiety and depressive symptoms, quality of life, coping and symptom self-management strategies)? Therefore, a greater number of studies that review the use of this kind of technology in the field of psychology are required. Through these, the patients that could most highly benefit from its use, and the variables that could be most improved by it, may be determined. Similarly, factors that could indicate its unsuitability for certain groups of patients could also be determined.

Recent systematic reviews have indicated the different uses of avatar-based therapies for chronic patients in the area of mental health [7,38]. Despite the fact that avatars are used in different ways and with patients suffering from diverse conditions, no standard description exists of the different ways an avatar can be used with chronic patients. Such a description would make it easier for researchers and/or systemized clinics to use and test the methods' effectiveness. There is also no categorization of the psychological variables that could benefit from using this kind of technology with chronic patients.

Therefore, the objectives of this study are as follows: (1) to determine the specific chronic pathologies in which avatars have been used; (2) to categorize different kinds of

avatars according to how they have been used in order to tackle psychological variables in patients diagnosed with a chronic illness; (3) to establish the kind of psychological variables that have been studied, including the standardized instruments used for their evaluation; (4) to specify whether or not said psychological variables have benefited from the use of avatars (effectiveness); (5) to specify the level of patient satisfaction with the use of avatars.

Following the review of the scientific literature on the use of avatars in mental illness treatment, and having established the objectives of this paper, the methodology used in the systematic review and the estimated risk of methodological bias are discussed in the following sections.

## 2. Materials and Methods

#### 2.1. General Description

A systematic search strategy was implemented in March 2021 to find all the relevant studies that involved the use of avatars to treat chronic illnesses. The systematic research protocol is registered in PROSPERO (CRD42021248171).

## 2.2. Scientific Literature Review

Selection criterion: The study papers considered relevant were those in which a psychological intervention was undertaken, including the use of an avatar, with the aim of improving any psychological variable of an adult patient (over 18 years old) diagnosed with a chronic condition.

Papers that did not include adult patients (under 18 s) and that were not published in English were excluded, as were manuscripts that did not study any psychological variables (focusing on medical concepts or technological aspects), protocols with unpublished results, studies geared towards educating or teaching, and those that did not include a psychological intervention.

The search strategy was guided by the standards of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 Statement. Studies were searched for in EBSCO (PsycINFO and MEDLINE), PubMed, Scopus, Ovid, and The Cochrane Library in March 2021. When conducting the search, we sought keywords in the field "Abstract" in EBSCO and Ovid, in "Title/Abstract" in PubMed, in "Title/Abstract/Keywords" in Scopus and in "Keywords" in The Cochrane Library. Results with the following keywords were extracted: "avatar + review", "avatar + chronic illness", "avatar + chronic disease", "avatar + patient care", "avatar + anxiety", "avatar + depression", "avatar + quality of life" and "avatar + mental health". Two of the authors of this study (MF and ER) independently reviewed the titles and abstracts of all the search results in order to identify eligible papers. If, after reading the titles and the abstracts, a reviewer considered that a reference was relevant, the full text of the paper was extracted. Duplicated studies were eliminated.

Data extraction: All references were downloaded and inserted into a Microsoft Excel spreadsheet, and duplicates were removed. A total of 2 independent investigators conducted the screening for inclusion and exclusion criteria in 3 phases: first, the titles of the records were assessed; then their abstracts; finally, the full-text papers. After this, Cohen kappa scores were calculated to measure the inter-rater agreement between the two investigators (MF and ER). The interpretation of the Cohen kappa coefficient was calculated using SPSS version 27 (IBM Corp) based on the categories developed by Douglas Altman [39]: 0.00–0.20 (poor), 0.21–0.40 (fair), 0.41–0.60 (moderate), 0.61–0.80 (good), and 0.81–1.00 (very good) [39,40]. The two raters consulted a third investigator (CM) in case of disagreements.

## 2.3. Data

The following data were extracted from the papers selected: (1) year of publication, (2) country of study, (3) type of study, (4) objective of study, (5) number of participants, (6) average age, (7) chronic pathology diagnosed, (8) type of avatar used, (9) user identification with the avatar, (10) device with which the avatar was created, (11) variables

evaluated and evaluation instrument, (12) additional information, (13) results obtained, (14) statistical method, (15) effectiveness of the intervention, and (16) participant satisfaction. Disagreements were resolved by consensus. The reporting of this systematic review was guided by the standards of PRISMA 2020 Statement (the details are provided in Supplementary File S2).

## 2.4. Risk of Methodological Bias

As the research designs of the papers included were extremely varied, it was decided, for the purpose of analyzing the transparency of the studies and the quality of the corresponding evidence, to assess the risk of bias via the Consolidated Standards of Reporting Trials (CONSORT) verification list [41]. The tool used comprises 25 items and a score of 0 or 1 was assigned for each RCT included, indicating whether or not the study satisfactorily met the criteria. Studies different from RCTs were also analyzed through the CONSORT checklist to unify the risk of bias assessment. The overall scores with the highest values indicated a lower methodological risk of bias (the details are provided in Supplementary File S3).

#### 3. Results

## 3.1. Study Selection and Inclusion

Through the electronic database search, 960 results were obtained. These were reduced to 505 after the elimination of duplicates, which were evaluated based on the title and abstract. Of the 505, 463 were ruled out for not complying with the inclusion criteria, and 42 papers were selected for a full text reading. Of the 42 studies, 24 were finally ruled out on the following grounds: 11 studies were excluded for not providing published results; six papers had the objective of teaching or educating healthcare professionals or students through the use of an avatar, but did not undertake a psychological intervention; three papers did not have the objective of treating a chronic illness; two manuscripts did not relate to the study of any psychological variable; one paper included subjects under the age of 18, and one paper was a conference summary.

Finally, a total of 18 publications were included in the review. The Cohen kappa showed a substantial level of agreement, and it was categorized as "good" ( $\kappa = 0.69$ ) (range 0.61–0.80) based on the categories developed by Altman [39]. A PRISMA flow diagram is provided in Figure 1.

## 3.2. Characteristics of the Studies Included

For points 1 (year of publication), 2 (country of the study) and 3 (type of study), the following results were extracted (Table 1): the 18 selected studies were published between 2010 and 2020 (38.9%). Many of them (n = 7) were published in 2020 [3,42–47]). The majority of the studies were conducted in the United States (n = 6) [6,25,43–45,48], Australia (n = 4) [3,49–51] and the United Kingdom (n = 4) [42,46,52,53]. The remaining papers were published in Canada [54], China [47], Ireland [55] and Italy [56].

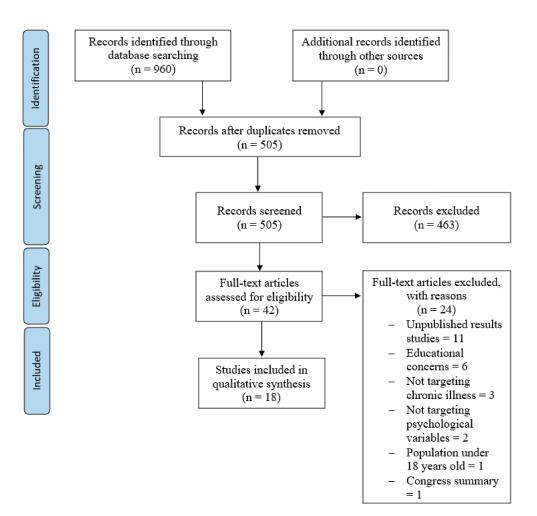


Figure 1. Systematic review of the literature flowchart.

**Table 1.** Characteristics of included papers.

Study	<b>Publication Year</b>	Country	Type of Study
Aali et al. [42]	2020	England	Review
Andrade et al. [6]	2015	ŬSA	RCT <sup>1</sup>
Cho et al. [43]	2020	USA	RCT
Clarke et al. [55]	2019	Ireland	Review
Dang et al. [44]	2020	USA	Feasibility study
du Sert et al. [54]	2018	Canada	RCT
Falconer et al. [52]	2017	England	Feasibility study
Leff et al. [53]	2013	England	RCT
Pinto et al. [48]	2013	USA	Pilot testing
Robinson-Whelen et al. [45]	2020	USA	RCT
Rus-Calafell et al. [46]	2020	England	RCT
Stewart et al. [25]	2010	USA	Narrative review
Thomas et al. [49]	2019	Australia	Narrative review
Tong et al. [47]	2020	China	Case series
Tongpeth et al. [50]	2018	Australia	Feasibility pilot testing
Triberti et al. [56]	2019	Italy	Pilot testing
Wonggom et al. [51]	2019	Australia	Review
Wonggom et al. [3]	2020	Australia	RCT

<sup>1</sup> RCT: randomized controlled trial.

The most common studies were randomized controlled trials (RCTs) (n = 7) [3,6,43,45,46,53,54], used in 38.9% of the studies, followed by reviews (n = 3) [42,51,55], accounting for 16.7% of the papers. Other types of studies used included feasibility

studies (n = 2) [44,52], narrative reviews (n = 2) [25,49] and pilot testing (n = 2) [48,56], each corresponding to 11.1%. The least common were feasibility pilot tests (n = 1) [50] and case series (n = 1) [47], each accounting for 5.6% of the total (Table 1).

For points 4 (objective of the study), 5 (number of participants), 6 (average age) and 7 (chronic pathology diagnosed), the following results were extracted:

The objectives of the studies were extremely varied. In 22.2% of the studies (n = 4), the effectiveness was examined in terms of educating patients using avatar-based technology regarding the knowledge and the self-care behavior of patients with chronic conditions [3,48,50,51], as well as the effect of the therapy [6,42,54,55]. In 16.7% of the papers (n = 3) [45,49,52] the viability and acceptability of the use of an avatar was studied. In the remaining studies, the adherence of patients to, and the acceptability of, the intervention were evaluated (n = 1) [44]; the benefits of the intervention were explained (n = 1) [25]; the long-term effects of the interventions based on virtual reality were examined (n = 1) [47]; the opinions of consumers regarding the avatar-based application were studied (n = 1) [43]; the effect of the feeling of presence afforded by having a voice connected to an avatar with regard to the reduction of anxiety was explored (n = 1) [46]; a computerized system that allowed patients to speak to the avatar was developed (n = 1) [53]; the relationship between the personalized avatar and the symptoms of anxiety and depression was explored (n = 1) [56].

The number of participants ranged from 5, in the paper with the lowest number of subjects [47], to 1535, in a review that compiled information from several studies [55]. In total, 44.4% of the papers (n = 8) [44,45,48,50,52–54,56] included between 10 and 30 participants (Table 2).

Study	Participant Number	Mean Age	Target Population
Aali et al. [42]	195	Not provided	Schizophrenia or related disorders
Andrade et al. [6]	41	61	Overactive bladder
Cho et al. [43]	39	55	HIV with HANA conditions
Clarke et al. [55]	1535	Not provided	Psychosis
Dang et al. [44]	11	Not provided	Cancer
du Sert et al. [54]	19	42.9	Schizophrenia
Falconer et al. [52]	11	31.2	Borderline personality disorder
Leff et al. [53]	26	Not provided	Schizophrenia
Pinto et al. [48]	28	Not provided	Depression
Robinson-Whelen et al. [45]	21	Not provided	Spinal cord injury
Rus-Calafell et al. [46]	39	43.87	Schizophrenia
			People with disabilities (physical, psychological,
Stewart et al. [25]	Not provided	Not provided	cognitive rehabilitation, chronically ill, convalescing or homebound)
Thomas et al. [49]	Not provided	Not provided	Schizophrenia
Tong et al. [47]	5	50.2	Phantom limb pain (brachial plexus avulsion injury and amputees' outpatients)
Tongpeth et al. [50]	10	52.2	Acute coronary syndrome
Triberti et al. [56]	22	49.4	Cancer
Wonggom et al. [51]	752	Not provided	Chronic disease (cardiovascular and chronic respiratory disease, diabetes, cancer)
Wonggom et al. [3]	36	67.5	Heart failure

Table 2. Characteristics of included	papers	(part 2).
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The average age of patients was 50.36 years (SD = 10.59). However, nine papers did not disclose the ages of the participants [25,42,44,45,48,49,51,53,55] (Table 2).

A wide variety of diagnosed chronic pathologies for which avatars were used were found, the most common being schizophrenia/psychosis (n = 6) [42,46,49,53–55], accounting for 33.3% of cases; cardiovascular disease (n = 2) [3,50] and cancer (n = 2) [44,56]; overactive bladder (n = 1) [6]; HIV (n = 1) [43]; borderline personality disorder (n = 1) [52]; depression (n = 1) [48]; spinal cord injury (n = 1) [45] and phantom limb pain (n = 1) [47].

Two systematic reviews included several pathologies, one of which (n = 1) referred to multiple chronic illnesses (cardiovascular disease and chronic respiratory disease, diabetes, and cancer) [51], and the other (n = 1) to a disability (physical, psychological, or cognitive rehabilitation) or subjects that are either suffering from a chronic illness, are convalescing, or are housebound [25] (Table 2).

In relation to points 8 (type of avatar used), 9 (user identification with the avatar) and 10 (device with which the avatar was created), the following results were extracted (Table 3): five different modalities were categorized during use of an avatar (Figure 2), along with the corresponding percentages of frequency of appearance in the papers (Figure 3). The five different modalities consisted of the following:

- Modality 1 (Graphic representation)—The avatar as a "virtual twin" without interaction with the patient. The simplest modality, from a technological point of view, this involved a two-dimensional graphic representation produced on a mobile or tablet screen, with the avatar representing the user. In the study in which this modality was used (*n* = 1) [56], the patients with breast cancer experienced a higher degree of identification with the avatar, given that they were able to personalize it to have a greater level of physical similarity to them.
- Modality 2 (Virtual representation: F2F with symptoms)—The avatar as "another virtual patient that interacts only with the patient". This was a two-dimensional virtual representation of an avatar that embodied the symptoms of the user and with which they could communicate face to face. It was the second most used modality (n = 4) [42,46,53,55], and the objective of the studies that applied this kind of avatar was to make subjects confront their own auditory hallucinations in a face-to-face conversation, so that, with help from the therapist, who also guided the avatar, they could gradually take control of these hallucinations.
- Modality 3 (Virtual environment)—The avatar as a "virtual twin that interacts with the avatars of other patients". This modality involved a digital self-representation in a non-immersive, two-dimensional virtual environment (*n* = 3) [25,45,52]. Here, the users could interact with other people, also represented by avatars, on a screen through a written and/or audio messaging platform. The fact that it was not immersive meant that the virtual environment was two-dimensional rather than three-dimensional and users did not receive sensory stimuli, which does occur in immersive experiences. Two of the studies that used this modality [25,45] used the Second Life© platform (SL), and, while one [25] allowed users to personalize the avatar, the other [45] did not specify whether the users adapted the avatars to resemble themselves. The other study [52] used the ProReal© platform, and the degree of identification with the avatar was low, as the representations consisted of colorless silhouettes with neither facial nor bodily elements.
- Modality 4 (Embodiment)—The avatar as a "virtual incarnation that interacts with the avatars of other patients". This modality entailed the incarnation of an avatar from a first-person perspective using a virtual reality device called a head-mounted display (HMD) (*n* = 2), which creates a three-dimensional, non-immersive virtual environment that reduced the users' feeling of pain [47] or improved their verbal communication via the movements and gestures involved in operating the avatar [44];
- Modality 5 (Graphic representation: virtual health coach)—The avatar as "coach" that only interacts with the patient. The graphic representation here could also comprise an avatar that represented a person other than the user. This was the modality most frequently used (*n* = 5), [3,6,43,48,50]. Here, the avatar was used as a virtual health coach that guided and instructed the user in managing their illness. In one study using this modality [6], two types of avatars were used: one with a high degree of physical resemblance to the patient, a self-avatar "peer" mentor (SAP) that produced an increased sense of identification; and another that had no physical resemblance to the user, a generic avatar coach (GAC), the sense of identification with which was consequentially lower.

As regards the three remaining papers, in two [49,51], information was compiled from several studies employing different avatar modalities, and in the other [54], a combination of virtual representation (F2F with symptoms) and embodiment was used. Here, the users confronted their symptoms by talking to an avatar which embodied them (Modality 2), while also having a three-dimensional immersive experience through the virtual reality device (Modality 4).

The devices most commonly used to generate the avatar, accounting for 16.7%, were mobile apps (n = 3) [3,50,56], computer systems (n = 3) [42,53,55], online platforms (n = 3) [6,25,45] and headset devices (n = 3) [44,47,54]. The least used were screen-based devices (n = 1) [48] and virtual reality software (n = 1) [52], at 5.6%. Lastly, four papers (n = 4) did not provide information on the type of device used [43,46,49,51].

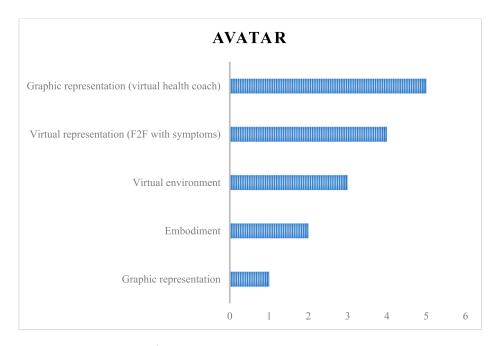


Figure 2. Categorization of avatars.

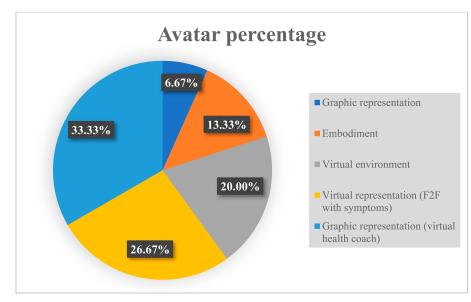


Figure 3. Avatar percentage.

Study	Avatar	Identification	Device
Aali et al. [42]	F2F with symptoms	No	Computerized system
Andrade et al. [6]	Virtual health coach	Both	Online platform
Cho et al. [43]	Virtual health coach	Yes	Not applicable
Clarke et al. [55]	F2F with symptoms	No	Computerized system
Dang et al. [44]	Embodiment	Yes	Headset
du Sert et al. [54]	Embodiment and F2F with symptoms	Both	Headset
Falconer et al. [52]	Virtual environment	No	VR software
Leff et al. [53]	F2F with symptoms	No	Computerized system
Pinto et al. [48]	Virtual health coach	No	Screen-based
Robinson-Whelen et al. [45]	Virtual environment	Not applicable	Online platform
Rus-Calafell et al. [46]	F2F with symptoms	No	Not applicable
Stewart et al. [25]	Virtual environment	Not applicable	Online platform
Thomas et al. [49]	Several types of avatars	Not applicable	Not applicable
Tong et al. [47]	Embodiment	Yes	Headset
Tongpeth et al. [50]	Virtual health coach	No	Арр
Triberti et al. [56]	Graphic representation	Yes	Арр
Wonggom et al. [51]	Several types of avatars	Not applicable	Not applicable
Wonggom et al. [3]	Virtual health coach	No	App

Table 3. Types of avatars, users' identification with the avatars, and device.

As regards points 11 (variables evaluated and evaluation instrument), 12 (additional information), 13 (results obtained) and 14 (statistical method), the following results were extracted: the variables most studied were quality of life (n = 5) [6,42,44,51,54], psychotic symptoms (n = 5) [46,49,53–55] and symptoms of depression (n = 5) [45,47,53,54,56], found in 27.8% of the studies, followed by symptoms of anxiety (n = 4) [46,47,54,56], which appeared in 22.2% of the studies. Self-care behavior (n = 3) [3,45,51], knowledge of the illness (n = 3) [3,50,51], self-efficiency [6,45,51] and beliefs regarding the voices [46,53,54] appeared in 16.7% of the studies. The rest of the variables appeared only in one or two studies.

The instruments used were extremely varied. Those used with greater frequency, appearing in 22.2% of the studies, were PSYRATS [57] (n = 4) [42,53–55] and BAVQ-R [58] (n = 4) [42,46,53,54], while PHQ-9 [59] which was used in 11.1% (n = 2) of the studies [45,56]. The other instruments are set out in the multimedia Supplementary File S1.

Additionally, it was found that in 38.9% of the studies (n = 7) [3,43,44,46,48,53,54], a follow-up was undertaken after the intervention; 22.2% performed a literature review (n = 4) [25,42,49,55], one of which [55] reviewed 21 papers while another [42] reviewed three trials; in 22.2% of the studies (n = 4), an outcome measure was undertaken prior to applying the intervention, and another after it (pre-post) [6,47,50,51]; in two studies (n = 2) [45,56], the measure was only undertaken after the treatment (post), which, in one of the studies, was done via telephone [45]; lastly, in another study (n = 1) [52] group sessions were carried out at weekly intervals.

In 16.7% of the studies (n = 3), the avatar-based technology geared towards educating patients were shown to have a positive effect on the knowledge and self-care behaviors that foster health in patients with chronic illnesses, compared with normal care [3,45,51], as well as the corresponding self-efficiency [51]; in 11.1% of the studies (n = 2) [47,48], an improvement in symptoms of anxiety and depression was observed, as well as a significant improvement in the pain rating [47], and two studies (n = 2) [53,54] found significant improvements in terms of psychotic symptoms. In the other studies, an increase was observed in the score relating to knowledge, as well as in patient satisfaction after using

the application (n = 1) [50]; an inverse relationship was found between positive attitudes (kindness, intensity, and appeal) towards the avatars that realistically represented the patient and symptoms of anxiety and depression (n = 1) [56]; significant improvements in quality of life were found (n = 1) [6]. Finally, one study (n = 1) [42] found a lack of clear evidence for or against the use of avatar therapy as a treatment for people suffering from serious mental illnesses, while another study (n = 1) [55] added that the avatar-based therapies seem promising.

Extensive heterogeneity was found in the statistical methods used in the studies (see multimedia Supplementary File S1), with diversity in the presentation of the results obtained. A single meta-analysis was found (n = 1) [55].

Lastly, as regards points 15 (effectiveness of the intervention) and 16 (participant satisfaction), the following results were extracted (see Table 4): 61.1% of the studies (n = 11) [3,6,43,45–48,50,51,53,54] found that the avatar-based intervention was effective, while other authors (n = 4) concluded that there was a lack of effectiveness [42,44,52,55] or that the information was simply not provided (n = 3) [25,49,56]. Patient satisfaction was high in 44.4% of the studies (n = 8) [3,25,43–45,50–52].

Table 4. Effectiveness and patient satisfaction.

Study	Effectiveness	Patient Satisfaction Measured
Aali et al. [42]	No	Unknown
Andrade et al. [6]	Yes	Unknown
Cho et al. [43]	Yes	Yes
Clarke et al. [55]	No	Unknown
Dang et al. [44]	No	Yes
du Sert et al. [54]	Yes	Unknown
Falconer et al. [52]	No	Yes
Leff et al. [53]	Yes	Unknown
Pinto et al. [48]	Yes	Unknown
Robinson-Whelen et al. [45]	Yes	Yes
Rus-Calafell et al. [46]	Yes	Unknown
Stewart et al. [25]	Unknown	Yes
Thomas et al. [49]	Unknown	Unknown
Tong et al. [47]	Yes	Unknown
Tongpeth et al. [50]	Yes	Yes
Triberti et al. [56]	Unknown	Unknown
Wonggom et al. [51]	Yes	Yes
Wonggom et al. [3]	Yes	Yes

#### 4. Discussion

The use of avatars in treating illnesses has advanced in recent years, offering many possibilities in terms of the pathologies they are geared towards. Although not all the benefits of this kind of intervention are currently known, good results have been obtained in the treatment of anxiety in disorders such as agoraphobia [20] and social phobia [17–19], as well as in treating eating disorders [13,14], addictions [15,16], weight control [9–11], facial pattern recognition [26–30], and ASD [31–33]. Education is another area in which they have been used. As such, many have tried to improve the skills of healthcare professionals through role-play exercises in specifically designed virtual environments [21–25]. The objective of this paper was to review the scientific literature on studies that have used avatars to treat patients with chronic conditions in order to discover the most suitable intervention strategies and determine whether such interventions improve the mental health of said patients.

After reviewing the 18 papers included in this systematic review, five modalities were established according to technological complexity and avatar presentation. These were: Modality 1—"Graphic representation", only used in one study [56], in which patients diagnosed with cancer described a high degree of identification with the avatar as they

were allowed to personalize it so that it bore a resemblance to them. The authors did not provide information on either the effectiveness of the avatar intervention (created in a mobile app) or patient satisfaction. However, they did confirm that anxiety and depression seem to be inversely related to the attitude of the patient towards the avatar representing them. Modality 2---"Virtual representation: F2F with symptoms", the second most commonly used modality [42,46,53,55]. Patients affirmed that the hallucinations described by the avatars resembled their own, but they did not report any sense of identification with them [42,46,53,55]. The condition for which this modality was used was schizophrenia or psychotic disorders, and the results show that this intervention was effective in two of the five studies [46,53], finding that the frequency and intensity of the hallucinations, as well as the perception of omnipotence and wickedness in the voices [53], paranoiac effects, and levels of self-reported anxiety [46], were all significantly reduced. The avatar therapy produced fear and stress via the invoking of hallucinations, but in a safe space and under conditions controlled by the therapist. This allowed them to incorporate new information and change their relationship with the voices, thus achieving a reduction in anxiety during the sessions. In this regard, recent research [60] has revealed that empathic listening—attempting to reconcile with the avatar representing their auditory hallucinations and taking control of the experience—seems to improve the relationship between the patients and their hallucinated voices. As such, the interaction between the strong sense of presence of the hallucinations and the decrease in anxiety was key in reducing the frequency of the hallucinations, although the level of patient satisfaction was unknown, as the authors did not provide this information. In the avatar modality that entailed a digital self-representation in a non-immersive, two-dimensional virtual environment (Type 3) [25,45,52], the users could interact with other people (also represented by avatars) via a screen, through written and/or audio messaging. In this modality, the avatar could be personalized to make it more realistic, and it could be made to resemble the patients as much as possible, which increased their identification with it. They could also incorporate differences in order to maintain anonymity or address intentions and aspirations that were currently unrealistic for them due to the limitations of their condition. This was the case for patients with some kind of disability (physical, psychological, cognitive rehabilitation, chronic illnesses, convalescing or housebound) [25], who, through the avatar, were able to walk, perform a job they had always wanted, and interact with other users, giving them a greater feeling of empowerment and of being more socially connected than in their normal daily environment. All participants rated SL as enjoyable, with the majority describing it as more enjoyable and more convenient than meeting face-to-face. The use of avatars did not hinder the development of support among group members. In fact, several participants explicitly expressed satisfaction with the anonymity of SL [45]. One of the three studies that used this modality [45] was effective. It found that patients with a spinal cord injury noticed an improvement in two behaviors that foster health (spiritual growth and interpersonal relations), and in these three studies [25,45,52], the satisfaction of users was high. In the study of patients diagnosed with borderline personality disorder [52], the authors found that the combination of avatars and mentalization-based therapy (MBT) was useful in providing patients with perspective, group participation, expression, aloofness, and the general experience, but added that more research was required with controlled trials to assess the effectiveness of this type of intervention. Modality 4—"Embodiment", a term for virtual reality that provides a much greater sense of presence than other modalities. Patients with whom this modality was used had been diagnosed with cancer [44], had phantom limb pain after an amputation, or had a brachial plexus avulsion injury [47]. In addition to helping users experience real-world sensations via identification with the avatar, this modality allowed a greater degree of identification between the user and the avatar. That was due to the use of the HMD device, via which the subject personified the avatar in an immersive virtual environment. In one of the studies that used this modality [47], this was found to be effective in reducing the pain felt by patients, and in improving the levels of anxiety and depression. However, it was not possible to determine whether or not the level

of patient satisfaction was high. The majority of the studies used Modality 5—"Graphic representation (virtual health coach)", in which the avatar represented a virtual health coach guiding the user in managing their illness. All the interventions undertaken with this avatar modality [3,6,43,48,50] were effective; specifically, in 40% of the studies, the patients had heart disease [3,50], and the use of an avatar application improved specific knowledge of the condition [3,50] as well as self-care behavior [3]. In the study with patients diagnosed with an overactive bladder [6], two types of avatars were used: one with a high degree of physical resemblance to the patient (a self-avatar "peer" mentor (SAP)), which produced an increased sense of identification, and one that had no physical resemblance to the user (a generic avatar coach (GAC)), with which the sense of identification was consequentially lower. It was concluded that the benefits felt by the patients increased when there was a higher degree of identification (physical resemblance) with the avatar, achieving an improvement in quality of life and in the symptoms reported by the patients. The patients with HIV with HANA conditions [43] showed improvements in general health, as well as their management of symptoms. Furthermore, those with depression showed significant reductions in depressive symptoms during the three-month period of the study. In 50% of the studies included in this modality [3,43,50], patient satisfaction was high.

Personalizing avatars to bear a resemblance to users increases the probability that patients adopt healthier behaviors [10], as suggested by Andrade et al., [6] who stated that patients with an avatar that looked like them obtained better results than those who had no such avatar. It should be mentioned that, despite these preliminary results, the majority of studies do not allow users to design the appearance of the avatar. The fact that patients can use avatars with a greater resemblance to them, with the aim of addressing different chronic pathologies, may provide benefits, as using an avatar that is physically similar establishes a psychological or emotional bond, giving rise to a greater degree of identification. Recent data confirms that avatars with a greater physical resemblance to users, affording greater identification, are more persuasive than those that are less physically similar [61]. Therefore, designing avatars to look like users may further increase their persuasiveness [62,63]. In comparison with non-avatar computer programs, an avatar that talks establishes a relationship that is not only more appealing, but that is also more persuasive and longer lasting [64,65]. Importantly, a higher degree of identification with the avatar may give rise to positive consequences for users, such as in pursuing personal desires or needs, that the user is not able to fulfil themselves. However, negative consequences may also arise; for example, for those that use avatars to play in virtual environments, greater identification may increase the likelihood of developing a gaming addiction [66]. As such, a lower degree of identification with the avatar is a variable that may be beneficial for some patients, but not others. Future research in this regard is required in order to specify the extent to which, and the kinds of patients for whom, greater physical resemblance (identification) between the user and the avatar is advisable.

The most commonly used instruments were PSYRATS [57] and BAVQ-R [58] for assessing psychotic symptoms and PHQ-9 [59] for assessing the health and mood of patients. All three of these are deemed reliable and valid in assessing different constructs. PSYRATS [57] is a structured and hetero-applied scale that helps assess the seriousness of psychotic symptoms. It comprises 17 items with Likert-type responses of 0–4 and an administration time of 10–30 min; it is applicable to an adult population (over 18 s) and groups the items into two scales for the assessment of auditory hallucinations and the assessment of delirium, respectively, which have suitable reliability and validity. BAVQ-R [58] is a self-reporting tool that measures the beliefs of people regarding their hallucinations, as well as the behaviors and emotions related to them. It comprises 35 items that are rated through a four-point Likert scale, grouped into five subscales: wickedness, benevolence, omnipotence, tolerance, and commitment. The mean Cronbach coefficient alpha used is 0.86 (range 0.74–0.88). Therefore, it is considered a highly reliable scale. PHQ-9 [59] is a structured and self-applied questionnaire that aims to assess the health of patients over the age of 18, comprising nine items with Likert-type responses of 0–3.

The administration time is under 10 min, and it is considered a reliable scale with a Cronbach's alpha of 0.89. As such, the instruments most commonly used were PSYRATS [57], BAVQ-R [58] and PHQ-9 [59]. However, none of the papers incorporated a scale specifically designed to evaluate treatments of chronic patients including avatars.

The results reveal that over half of the studies (61.1%) were effective [3,6,43,45–48,50,51,53,54], achieving reductions in the anxiety [46,47,54,56] and depression symptoms [45,47,53,54,56] of patients and improving variables such as quality of life [6,42,44,51,54], knowledge of the condition [3,50,51] and self-care behavior [3,45,51].

As other authors have mentioned [51], there are several different definitions of avatarbased patient educational programs, as well as of the avatar-based technologies developed for use with chronic patients. As a result, a taxonomy is required to design power RCTs that can test the most suitable approach for each chronic patient.

Therapies based on virtual reality are very promising, due to their potential use during the lockdowns brought about by the pandemic, as can be seen in several recently published studies [67–70]. The events that have unfolded over the last year as a result of the pandemic have driven important growth in virtual reality technology in order to provide online care. However, the 18 studies included in the systematic review were not conducted during lockdowns, and the patients received outpatient care. Therefore, taking into account the most recent studies conducted during the pandemic, it seems that patients can benefit from both outpatient care and remote care through virtual reality.

## 5. Conclusions

In accordance with the objectives proposed and the results obtained in this systematic review, the following conclusions may be reached: (1) An extensive range of chronic pathologies was found, for which avatars-with extensive heterogeneity between themhave been used, some displaying greater clinical complexity than others. Therefore, although the most frequent diagnosis in the 18 studies analyzed was schizophrenia (33.3%), various other pathologies were also included, such as cardiovascular disease, cancer, overactive bladder, HIV, borderline personality disorders, depression, spinal cord injury and phantom limb pain, highlighting the great heterogeneity in the diagnoses for which avatars have been used. (2) Taking into account the different types of avatar proposed in the studies included in the review, five modalities were established, according to technological complexity and avatar presentation. (3) The psychological variables most studied were quality of life, psychotic symptoms, depressive symptoms, anxiety symptoms, knowledge of the disease, self-care behavior, and self-efficacy, with PSYRATS, BAVQ-R and PHQ-9 being the most commonly used standardized instruments. (4) The results reveal that 61.1% of the studies were effective at improving patients' mental health. (5) The level of patient satisfaction was high in 44.4% of the studies. Ultimately, most avatar-based treatments were found to be effective.

Future randomized controlled trials are needed to determine the following remaining questions: Does the effectiveness of the avatar-based strategies depend on the type of avatar modality used? Are there specific modalities of avatar that allow for a greater degree of identification (physical resemblance) between avatar and user, producing a greater psychological benefit for patients? Are there modalities of avatar that produce a greater level of patient satisfaction? Do some chronic illnesses benefit more from the use of avatars than others? Do some psychological variables benefit more from the use of avatars than others?

Taking into account the benefits that the avatar-based interventions can have in terms of improving the mental health of chronic patients, as well as in improving quality of life, there is still a long way to go in developing treatment programs with augmented and mixed reality technology. This approach is still not common in the field of psychology but represents a great step forward in the treatment of mental illnesses.

#### 5.1. Clinical and Researcher Implications

Further, larger randomized controlled trials are needed to determine the best way to develop avatar-based treatments that can enhance mental healthcare in chronic patients. As such, further research is needed to establish scientific protocols for answering the remaining questions.

## 5.2. Limitations

The main limitations of this study include the great methodological heterogeneity of the 18 studies included, as well as the great diversity in the chronic diagnoses of the patients who were treated with avatar-based therapies. This hinders the uniformity of the results, as well as their generalizability, although it also highlights one of the main advantages of the use of avatars in the clinical setting: the great versatility of their use in different pathologies and under different methodological designs. However, in order to produce meta-analyses that provide conclusive results on the effectiveness of this approach, greater homogeneity in the corresponding diagnoses as well as in the methodology used would be desirable.

Likewise, the technology of the devices used for virtual reality-based therapy is undergoing significant and rapid advancement. As such, the devices included in future studies could improve upon the quality of those featured in this systematic review. This necessitates future updates through systematic reviews and meta-analyses.

**Supplementary Materials:** The following are available online at https://www.mdpi.com/article/ 10.3390/electronics10182212/s1, Multimedia Supplementary File S1: Complete list of characteristics of the included studies. Multimedia Supplementary File S2: PRISMA 2020 Checklist. Multimedia Supplementary File S3: Risk-of-bias assessment.

**Author Contributions:** M.F. and E.R. were responsible for the study design and search strategy. M.F., E.R. and C.M. were responsible for the screening and data extraction. M.F., E.R. and C.M. were responsible for the data analysis. M.F., E.R., C.M. and A.P.-M. were responsible for the first draft. All authors have read and agreed to the published version of the manuscript.

**Funding:** This work was supported by grant from Fundación Universitaria San Pablo-CEU, CEU Universities, (Madrid, Spain), Grant number MPFI20AP.

Data Availability Statement: The data presented in this study are available in Supplementary File S1.

Conflicts of Interest: The authors declare no conflict of interest.

## References

- 1. World Health Organization. *Global Status Report on Noncommunicable Diseases 2014;* World Health Organization: Geneva, Switzerland, 2015.
- 2. Kang, E.; Kim, S.; Rhee, Y.E.; Lee, J.; Yun, Y.H. Self-management strategies and comorbidities in chronic disease patients: Associations with quality of life and depression. *Psychol. Health Med.* **2021**, *26*, 1031–1043. [CrossRef] [PubMed]
- Wonggom, P.; Nolan, P.; Clark, R.A.; Barry, T.; Burdeniuk, C.; Nesbitt, K.; O'Toole, K.; Du, H. Effectiveness of an avatar educational application for improving heart failure patients' knowledge and self-care behaviors: A pragmatic randomized controlled trial. *J. Adv. Nurs.* 2020, 76, 2401–2415. [CrossRef]
- Fehily, C.; Hodder, R.; Bartlem, K.; Wiggers, J.; Wolfenden, L.; Dray, J.; Bailey, J.; Wilczynska, M.; Stockings, E.; Clinton-McHarg, T.; et al. The effectiveness of interventions to increase preventive care provision for chronic disease risk behaviours in mental health settings: A systematic review and meta-analysis. *Prev. Med. Rep.* 2020, 19, 101–108. [CrossRef] [PubMed]
- Golubić, M.; Schneeberger, D.; Kirkpatrick, K.; Bar, J.; Bernstein, A.; Weems, F.; Ehrman, J.; Perko, J.; Doyle, J.; Roizen, M. Comprehensive Lifestyle Modification Intervention to Improve Chronic Disease Risk Factors and Quality of Life in Cancer Survivors. J. Altern. Complement. Med. 2018, 24, 1085–1091. [CrossRef] [PubMed]
- 6. Andrade, A.D.; Anam, R.; Karanam, C.; Downey, P.; Ruiz, J.G. An Overactive Bladder Online Self-management Program with Embedded Avatars: A Randomized Controlled Trial of Efficacy. *Urology* **2015**, *85*, 561–567. [CrossRef]
- Rehm, I.C.; Foenander, E.; Wallace, K.; Abbott, J.-A.M.; Kyrios, M.; Thomas, N. What Role Can Avatars Play in e-Mental Health Interventions? Exploring New Models of Client–Therapist Interaction. *Front. Psychiatry* 2016, 7, 186. [CrossRef] [PubMed]
- 8. Liu, Y.; Liu, Y.; Xu, S.; Cheng, K.; Masuko, S.; Tanaka, J. Comparing VR- and AR-Based Try-On Systems Using Personalized Avatars. *Electronics* **2020**, *9*, 1814. [CrossRef]

- Knoblock-Hahn, A.L.; Wray, R.; LeRouge, C.M. Perceptions of adolescents with overweight and obesity for the development of user-centered design self-management tools within the context of the chronic care model: A qualitative study. *J. Acad. Nutr. Diet.* 2016, 116, 957–967. [CrossRef] [PubMed]
- 10. Rheu, M.; Jang, Y.; Peng, W. Enhancing Healthy Behaviors through Virtual Self: A Systematic Review of Health Interventions Using Avatars. *Games Health J.* **2020**, *9*, 85–94. [CrossRef] [PubMed]
- 11. Yoshida-Montezuma, Y.; Ahmed, M.; Ezezika, O. Does gamification improve fruit and vegetable intake in adolescents? A systematic review. *Nutr. Health* **2020**, *26*, 347–366. [CrossRef] [PubMed]
- Burton, C.; Tatar, A.S.; McKinstry, B.; Matheson, C.; Matu, S.; Moldovan, R.; Macnab, M.; Farrow, E.; David, D.; Pagliari, C.; et al. Pilot randomised controlled trial of Help4Mood, an embodied virtual agent-based system to support treatment of depression. *J. Telemed. Telecare* 2016, 22, 348–355. [CrossRef]
- Porras-Garcia, B.; Serrano-Troncoso, E.; Carulla-Roig, M.; Soto-Usera, P.; Ferrer-Garcia, M.; Figueras-Puigderrajols, N.; Yilmaz, L.; Sen, Y.O.; Shojaeian, N.; Gutiérrez-Maldonado, J. Virtual Reality Body Exposure Therapy for Anorexia Nervosa. A Case Report with Follow-Up Results. *Front. Psychol.* 2020, 11, 956. [CrossRef]
- 14. Ralph-Nearman, C.; Arevian, A.C.; Moseman, S.; Sinik, M.; Chappelle, S.; Feusner, J.D.; Khalsa, S.S. Visual mapping of body image disturbance in anorexia nervosa reveals objective markers of illness severity. *Sci. Rep.* **2021**, *11*, 1–12. [CrossRef] [PubMed]
- 15. Hone-Blanchet, A.; Wensing, T.; Fecteau, S. The Use of Virtual Reality in Craving Assessment and Cue-Exposure Therapy in Substance Use Disorders. *Front. Hum. Neurosci.* **2014**, *8*, 844. [CrossRef] [PubMed]
- Skeva, R.; Gregg, L.; Jay, C.; Pettifer, S. Views of Practitioners and Researchers on the Use of Virtual Reality in Treatments for Substance Use Disorders. *Front. Psychol.* 2021, 12, 1852. [CrossRef] [PubMed]
- 17. Hartanto, D.W.; Kang, N.; Brinkman, W.-P.; Kampmann, I.L.; Morina, N.; Emmelkamp, P.G.M.; Neerincx, M.A. Automatic mechanisms for measuring subjective unit of discomfort. *Stud. Health Technol. Inform.* **2012**, *181*, 192–196. [PubMed]
- Holmberg, T.T.; Eriksen, T.L.; Petersen, R.; Frederiksen, N.N.; Damgaard-Sørensen, U.; Lichtenstein, M.B. Social Anxiety Can Be Triggered by 360-Degree Videos in Virtual Reality: A Pilot Study Exploring Fear of Shopping. *Cyberpsychol. Behav. Soc. Netw.* 2020, 23, 495–499. [CrossRef] [PubMed]
- 19. James, L.K.; Lin, C.-Y.; Steed, A.; Swapp, D.; Slater, M. Social Anxiety in Virtual Environments: Results of a Pilot Study. *Cyberpsychol. Behav.* **2003**, *6*, 237–243. [CrossRef]
- 20. Peñate, W.; Pitti, C.T.; Bethencourt, J.M.; de la Fuente, J.; Gracia, R. The effects of a treatment based on the use of virtual reality exposure and cognitive-behavioral therapy applied to patients with agoraphobia. *Int. J. Clin. Health Psychol.* **2008**, *8*, 5–22.
- 21. Foronda, C.; Gattamorta, K.; Snowden, K.; Bauman, E.B. Use of virtual clinical simulation to improve communication skills of baccalaureate nursing students: A pilot study. *Nurse Educ. Today* **2014**, *34*, e53–e57. [CrossRef] [PubMed]
- 22. Hay, L.; Pymm, B. Real learning in a virtual world: A case study of the school of information studies' learning centre in Second Life. *Educ. Inf.* **2011**, *28*, 187–202. [CrossRef]
- 23. Lange, E.J. Teachlive: A Qualitative Study on Pre-Services Teachers' Perspectives. Ph.D. Thesis, Lamar University, Beaumont, TX, USA, 2019.
- 24. Lowell, V.L.; Alshammari, A. Experiential learning experiences in an online 3D virtual environment for mental health interviewing and diagnosis role-playing: A comparison of perceived learning across learning activities. *Educ. Technol. Res. Dev.* 2019, 67, 825–854. [CrossRef]
- 25. Stewart, S.; Pope, D.; Duncan, D. Using Second Life to enhance ACCEL an online accelerated nursing BSN program. In *Connecting Health and Humans*; IOS Press: Amsterdam, The Netherlands, 2009; Volume 146, pp. 636–640. [CrossRef]
- del Aguila, J.; González-Gualda, L.M.; Játiva, M.A.; Fernández-Sotos, P.; Fernández-Caballero, A.; García, A.S. How interpersonal distance between avatar and human influences facial affect recognition in immersive virtual reality. *Front. Psychol.* 2021, 12, 675515. [CrossRef] [PubMed]
- Fernández-Sotos, P.; García, A.S.; Vicente-Querol, M.A.; Lahera, G.; Rodriguez-Jimenez, R.; Fernández-Caballero, A. Validation of dynamic virtual faces for facial affect recognition. *PLoS ONE* 2021, *16*, e0246001. [CrossRef] [PubMed]
- Muros, N.; García, A.; Forner, C.; López-Arcas, P.; Lahera, G.; Rodriguez-Jimenez, R.; Nieto, K.; Latorre, J.; Fernández-Caballero, A.; Fernández-Sotos, P. Facial Affect Recognition by Patients with Schizophrenia Using Human Avatars. J. Clin. Med. 2021, 10, 1904. [CrossRef] [PubMed]
- 29. Hirosawa, T.; Kontani, K.; Fukai, M.; Kameya, M.; Soma, D.; Hino, S.; Kitamura, T.; Hasegawa, C.; An, K.-M.; Takahashi, T.; et al. Different associations between intelligence and social cognition in children with and without autism spectrum disorders. *PLoS ONE* **2020**, *15*, e0235380. [CrossRef]
- Bourke, C.; Douglas, K.; Porter, R. Processing of Facial Emotion Expression in Major Depression: A Review. Aust. N. Z. J. Psychiatry 2010, 44, 681–696. [CrossRef] [PubMed]
- Kumazaki, H.; Warren, Z.; Swanson, A.; Yoshikawa, Y.; Matsumoto, Y.; Yoshimura, Y.; Shimaya, J.; Ishiguro, H.; Sarkar, N.; Wade, J.; et al. Brief report: Evaluating the utility of varied technological agents to elicit social attention from children with autism spectrum disorders. J. Autism Dev. Disord. 2019, 49, 1700–1708. [CrossRef]
- Forbes, P.A.G.; Pan, X.; Hamilton, A.F.D.C. Reduced Mimicry to Virtual Reality Avatars in Autism Spectrum Disorder. J. Autism Dev. Disord. 2016, 46, 3788–3797. [CrossRef] [PubMed]

- Lecciso, F.; Levante, A.; Fabio, R.A.; Caprì, T.; Leo, M.; Carcagnì, P.; Distante, C.; Mazzeo, P.L.; Spagnolo, P.; Petrocchi, S. Emotional Expression in Children With ASD: A Pre-Study on a Two-Group Pre-Post-Test Design Comparing Robot-Based and Computer-Based Training. *Front. Psychol.* 2021, 12, 678052. [CrossRef] [PubMed]
- 34. Wang, X.; Xing, W.; Laffey, J.M. Autistic youth in 3D game-based collaborative virtual learning: Associating avatar interaction patterns with embodied social presence. *Br. J. Educ. Technol.* **2018**, *49*, 742–760. [CrossRef]
- 35. Lindner, P. Better, Virtually: The Past, Present, and Future of Virtual Reality Cognitive Behavior Therapy. *Int. J. Cogn. Ther.* 2020, 14, 23–46. [CrossRef]
- 36. Boboc, R.G.; Chiriac, R.-L.; Antonya, C. How Augmented Reality Could Improve the Student's Attraction to Learn Mechanisms. *Electronics* **2021**, *10*, 175. [CrossRef]
- Andrews, C.; Southworth, M.K.; Silva, J.N.A.; Silva, J.R. Extended Reality in Medical Practice. *Curr. Treat. Opt. Cardiovasc. Med.* 2019, 21, 18. [CrossRef]
- Bérubé, C.; Schachner, T.; Keller, R.; Fleisch, E.; Wangenheim, F.V.; Barata, F.; Kowatsch, T. Voice-Based Conversational Agents for the Prevention and Management of Chronic and Mental Health Conditions: Systematic Literature Review. *J. Med. Internet Res.* 2021, 23, e25933. [CrossRef] [PubMed]
- 39. Altman, D.G. Practical Statistics for Medical Research; Chapman and Hall: London, UK, 1990; pp. 1–624.
- 40. Cohen, J. A Coefficient of Agreement for Nominal Scales. Educ. Psychol. Meas. 1960, 20, 37–46. [CrossRef]
- 41. Schulz, K.F.; Altman, D.G.; Moher, D.; CONSORT Group. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. *PLoS Med.* **2010**, *7*, e1000251. [CrossRef] [PubMed]
- 42. Aali, G.; Kariotis, T.; Shokraneh, F. Avatar Therapy for people with schizophrenia or related disorders. *Cochrane Database Syst. Rev.* **2020**, *5*, CD011898. [CrossRef] [PubMed]
- 43. Kato-Lin, Y.-C.; Strotbaum, V.; Cho, H.; Porras, T.; Flynn, G.; Schnall, R. Usability of a Consumer Health Informatics Tool Following Completion of a Clinical Trial: Focus Group Study. *J. Med. Internet Res.* **2020**, *22*, e17708. [CrossRef]
- 44. Dang, M.; Noreika, D.; Ryu, S.; Sima, A.; Ashton, H.; Ondris, B.; Coley, F.; Nestler, J.; del Fabbro, E. Feasibility of delivering an avatar-facilitated life review intervention for patients with cancer. *J. Palliat. Med.* **2021**, *24*, 520–526. [CrossRef]
- 45. Robinson-Whelen, S.; Hughes, R.B.; Taylor, H.B.; Markley, R.; Vega, J.C.; Nosek, T.M.; Nosek, M.A. Promoting psychological health in women with SCI: Development of an online self-esteem intervention. *Disabil. Health J.* **2020**, *13*, 100867. [CrossRef]
- Calafell, M.D.M.R.; Ward, T.; Zhang, X.C.; Edwards, C.J.; Garety, P.; Craig, T. The Role of Sense of Voice Presence and Anxiety Reduction in AVATAR Therapy. J. Clin. Med. 2020, 9, 2748. [CrossRef] [PubMed]
- Tong, X.; Wang, X.; Cai, Y.; Gromala, D.; Williamson, O.; Fan, B.; Wei, K. "I Dreamed of My Hands and Arms Moving Again": A Case Series Investigating the Effect of Immersive Virtual Reality on Phantom Limb Pain Alleviation. *Front. Neurol.* 2020, 11, 876. [CrossRef] [PubMed]
- 48. Pinto, M.D.; Hickman, R.L.; Clochesy, J.; Buchner, M. Avatar-based depression self-management technology: Promising approach to improve depressive symptoms among young adults. *Appl. Nurs. Res.* **2013**, *26*, 45–48. [CrossRef] [PubMed]
- Thomas, N.; Bless, J.J.; Alderson-Day, B.; Bell, I.H.; Cella, M.; Craig, T.; Delespaul, P.; Hugdahl, K.; Laloyaux, J.; Larøi, F.; et al. Potential Applications of Digital Technology in Assessment, Treatment, and Self-help for Hallucinations. *Schizophr. Bull.* 2019, 45, S32–S42. [CrossRef] [PubMed]
- 50. Tongpeth, J.; Du, H.Y.; Clark, R.A. Development and feasibility testing of an avatar-based education application for patients with acute coronary syndrome. *J. Clin. Nurs.* **2018**, *27*, 3561–3571. [CrossRef] [PubMed]
- Wonggom, P.; Kourbelis, C.; Newman, P.; Du, H.; Clark, R.A. Effectiveness of avatar-based technology in patient education for improving chronic disease knowledge and self-care behavior: A systematic review. *JBI Evid. Synth.* 2019, 17, 1101–1129. [CrossRef] [PubMed]
- 52. Falconer, C.J.; Cutting, P.; Bethan-Davies, E.; Hollis, C.; Stallard, P.; Moran, P. Adjunctive avatar therapy for mentalization-based treatment of borderline personality disorder: A mixed-methods feasibility study. *Evid.-Based Ment. Health* **2017**, *20*, 123–127. [CrossRef] [PubMed]
- 53. Leff, J.; Williams, G.; Huckvale, M.A.; Arbuthnot, M.; Leff, A.P. Computer-assisted therapy for medication-resistant auditory hallucinations: Proof-of-concept study. *Br. J. Psychiatry* **2013**, *202*, 428–433. [CrossRef]
- 54. du Sert, O.P.; Potvin, S.; Lipp, O.; Dellazizzo, L.; Laurelli, M.; Breton, R.; Lalonde, P.; Phraxayavong, K.; O'Connor, K.; Pelletier, J.-F.; et al. A virtual reality therapy for refractory auditory verbal hallucinations in schizophrenia: A pilot clinical trial. *Schizophr. Res.* 2018, 197, 176–181. [CrossRef]
- 55. Clarke, S.; Hanna, D.; Mulholland, C.; Shannon, C.; Urquhart, C. A systematic review and meta-analysis of digital health technologies effects on psychotic symptoms in adults with psychosis. *Psychosis* **2019**, *11*, 362–373. [CrossRef]
- Triberti, S.; Gorini, A.; Savioni, L.; Sebri, V.; Pravettoni, G. Avatars and the Disease: Digital Customization as a Resource for Self-Perception Assessment in Breast Cancer Patients. *Cyberpsychol. Behav. Soc. Netw.* 2019, 22, 558–564. [CrossRef]
- Haddock, G.; McCarron, J.; Tarrier, N.; Faragher, E.B. Scales to measure dimensions of hallucinations and delusions: The psychotic symptom rating scales (PSYRATS). *Psychol. Med.* 1999, 29, 879–889. [CrossRef]
- 58. Chadwick, P.; Lees, S.; Birchwood, M. The revised Beliefs about Voices Questionnaire (BAVQ–R). *Br. J. Psychiatry* **2000**, 177, 229–232. [CrossRef] [PubMed]
- 59. Kroenke, K.; Spitzer, R.L.; Williams, J.B. The PHQ-9: Validity of a brief depression severity measure. *J. Gen. Intern. Med.* 2001, 16, 606–613. [CrossRef]

- 60. Beaudoin, M.; Potvin, S.; Machalani, A.; Dellazizzo, L.; Bourguignon, L.; Phraxayavong, K.; Dumais, A. The therapeutic processes of avatar therapy: A content analysis of the dialogue between treatment-resistant patients with schizophrenia and their avatar. *Clin. Psychol. Psychother.* **2021**, *28*, 500–518. [CrossRef] [PubMed]
- Green, R.; Delfabbro, P.H.; King, D.L. Avatar identification and problematic gaming: The role of self-concept clarity. *Addict. Behav.* 2021, 113, 106694. [CrossRef]
- 62. Grogan, S.; Flett, K.; Clark-Carter, D.; Conner, M.; Davey, R.; Richardson, D.; Rajaratnam, G. A randomized controlled trial of an appearance-related smoking intervention. *Health Psychol.* 2011, *30*, 805–809. [CrossRef] [PubMed]
- 63. Fox, J.; Bailenson, J.N. Virtual Self-Modeling: The Effects of Vicarious Reinforcement and Identification on Exercise Behaviors. *Media Psychol.* 2009, 12, 1–25. [CrossRef]
- 64. Baylor, A.L.; Ryu, J. The Effects of Image and Animation in Enhancing Pedagogical Agent Persona. J. Educ. Comput. Res. 2003, 28, 373–394. [CrossRef]
- 65. Rosenberg-Kima, R.B.; Baylor, A.L.; Plant, E.A.; Doerr, C.E. The importance of interface agent visual presence: Voice alone is less effective in impacting young women's attitudes toward engineering. In *International Conference on Persuasive Technology*; Springer: Heidelberg, Germany, 2007; pp. 214–222. [CrossRef]
- 66. T'ng, S.T.; Pau, K. Identification of Avatar Mediates the Associations between Motivations of Gaming and Internet Gaming Disorder among the Malaysian Youth. *Int. J. Ment. Health Addict.* **2020**, *19*, 1346–1361. [CrossRef]
- 67. Ye, J. Pediatric Mental and Behavioral Health in the Period of Quarantine and Social Distancing with COVID-19. *JMIR Pediatr. Parent.* **2020**, *3*, e19867. [CrossRef] [PubMed]
- Alevizopoulos, A.; Kritikos, J.; Alevizopoulos, G. Intelligent machines and mental health in the era of COVID-19. *Psychiatriki* 2021, 32, 99–102. [CrossRef] [PubMed]
- 69. Stasolla, F.; Matamala-Gomez, M.; Bernini, S.; Caffò, A.O.; Bottiroli, S. Virtual Reality as a Technological-Aided Solution to Support Communication in Persons with Neurodegenerative Diseases and Acquired Brain Injury during COVID-19 Pandemic. *Front. Public Health* **2021**, *8*, 635426. [CrossRef] [PubMed]
- Sampaio, M.; Haro, M.V.N.; De Sousa, B.; Melo, W.V.; Hoffman, H.G. Therapists Make the Switch to Telepsychology to Safely Continue Treating Their Patients During the COVID-19 Pandemic. Virtual Reality Telepsychology May Be Next. *Front. Virtual Real.* 2021, 1. [CrossRef] [PubMed]