Evaluación clínica y económica de la Terapia deAceptación y Compromiso y de la Terapia deActivación Conductual en pacientes con dolorlumbar crónico y síntomas de depresión

Juan P. Sanabria-Mazo

TESIS DOCTORAL

Evaluación clínica y económica de la Terapia de Aceptación y Compromiso y de la Terapia de Activación Conductual en pacientes con dolor lumbar crónico y síntomas de depresión

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Evaluación clínica y económica de la Terapia de Aceptación y Compromiso y de la Terapia de Activación Conductual en pacientes con dolor lumbar crónico y síntomas de depresión

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El **Dr. Juan Vicente Luciano Devis**, investigador del Departament de Psicologia Clínica i de la Salut de la Universitat Autònoma de Barcelona y de la Unitat de Docència, Recerca i Innovació del Parc Sanitari Sant Joan de Déu, así como el **Dr. Antoni Sanz Ruiz** y la **Dra. Sílvia Edo Izquierdo**, investigador e investigadora del Departament de Psicologia Bàsica, Evolutiva i de l'Educació de la Universitat Autònoma de Barcelona, certificamos que el doctorando Juan Pablo Sanabria Mazo realizó la tesis doctoral titulada *"Evaluación clínica y económica de la Terapia de Aceptación y Compromiso y de la Terapia de Activación Conductual en pacientes con dolor lumbar crónico y síntomas de depresión"* bajo nuestra dirección y tutorización, con el fin de obtener el título de Doctor en Psicología.

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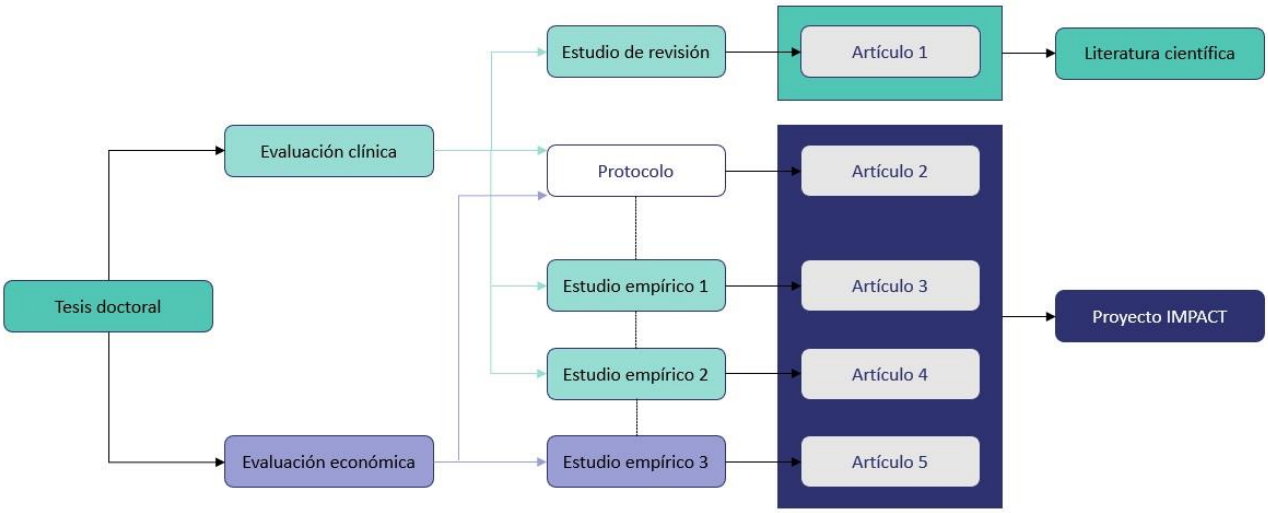
Preámbulo

En esta tesis doctoral se expone parte del trabajo desarrollado por Juan Pablo Sanabria Mazo como investigador predoctoral en la Unitat de Docència, Recerca i Innovació del Parc Sanitari Sant Joan de Déu (Barcelona). Esta tesis, enmarcada dentro del Proyecto IMPACT y desarrollada durante el período comprendido entre enero de 2021 y enero de 2024, se presenta mediante la modalidad de compendio de publicaciones.

Este trabajo está compuesto por 4 estudios, representados en 5 artículos. Como se observa en la siguiente figura, en esta tesis doctoral se reporta un estudio de revisión de la literatura científica (**Artículo 1**) y 3 estudios empíricos asociados a un ensayo clínico controlado y aleatorizado (**Artículos 3, 4** y **5**), que comparten como preámbulo común un protocolo (**Artículo 2**).



Los **Artículos 1, 2, 3, 4 y 5** -enumerados según la secuencia argumental de este trabajo- están disponibles en acceso abierto en revistas indexadas en *Journal of Citation Reports* (JCR) y en *Scimago Journal & Country Rank* (SJR). En la siguiente tabla se presenta una descripción de las métricas de las revistas en las que se publicaron o se aceptaron para publicación los artículos directamente vinculados a esta tesis doctoral.

Artículo	Autores (año)	Revista	JCR*	SJR*
1	Sanabria-Mazo et al. (2023a)	Frontiers in Psychology	Q1	Q2
2	Sanabria-Mazo et al. (2020)	BMJ Open	Q2	Q1
3	Sanabria-Mazo et al. (2023b)	The Journal of Pain	Q2	Q1
4	Sanabria-Mazo et al. (2023c)	Disability and Rehabilitation	Q2	Q1
5	Sanabria-Mazo et al. (2024)	The Journal of Pain	Q2	Q1

* Según las métricas más recientes (2022).

Compendio de publicaciones

Artículo 1

Sanabria-Mazo, J. P., Colomer-Carbonell, A., Fernández-Vázquez, Ó., Noboa-Rocamora, G., Cardona-Ros, R., McCracken, L. M., Montes-Pérez, A., Castaño-Asins, J. R., Edo, S., Borràs, X., Sanz, A., Feliu-Soler, A. y Luciano, J. V. (2023). A systematic review of psychological therapies for comorbid chronic pain and clinically relevant psychological distress. *Frontiers in Psychology, 14*, 1-18. https://doi.org/10.3389/fpsyg.2023.1200685

Artículo 2

Sanabria-Mazo, J. P., Forero, C. G., Cristóbal-Narváez, P., Suso-Ribera, C., García-Palacios, A., Colomer-Carbonell, A., Pérez-Aranda, A., Andrés-Rodríguez, L., McCracken, L. M., D'Amico, F., Estivill-Rodríguez, P., Carreras-Marcos, B., Montes-Pérez, A., Comps-Vicente, O., Esteve, M., Grasa, M., Rosa, A., Cuesta-Vargas, A. I., Maes, M., Borràs, X., Edo, S., Sanz, A., Feliu-Soler, A., Castaño-Asins, J. R. y Luciano, J. V. (2020). Efficacy, cost-utility and physiological effects of Acceptance and Commitment Therapy (ACT) and Behavioural Activation Treatment for Depression (BATD) in patients with chronic low back pain and depression: Study protocol of a randomised, controlled trial including mobile-technology-based ecological momentary assessment (IMPACT study). *BMJ Open*, *10*(7), e038107. https://doi.org/10.1136/bmjopen-2020-038107

Artículo 3

Sanabria-Mazo, J. P., Colomer-Carbonell, A., Borràs, X., Castaño-Asins, J. R., McCracken, L. M., Montero-Marin, J., Pérez-Aranda, A., Edo, S., Sanz, A., Feliu-Soler, A. y Luciano, J. V. (2023). Efficacy of videoconference group Acceptance and Commitment Therapy (ACT) and Behavioral Activation Therapy for Depression (BATD) for chronic low back pain (CLBP) plus comorbid depressive symptoms: A randomized controlled trial (IMPACT study). *The Journal of Pain, 24*(8), 1522-1540. https://doi.org/10.1016/j.jpain.2023.04.008

Artículo 4

Sanabria-Mazo, J. P., Colomer-Carbonell, A., Gandara-Urrutia, N., Pérez-Sutil, J. M., Noboa-Rocamora, G., Fernández-Vázquez, Ó., Val-Mariano, G., Fontana-McNally, M., Cardona-Ros, G., Feliu-Soler, A., McCracken, L. M., Edo, S., Sanz, A. y Luciano, J. V. (2023). Experiences of patients with chronic low back pain plus comorbid depressive symptoms in a

videoconference group Acceptance and Commitment Therapy or Behavioral Activation Treatment for Depression: A qualitative study. *Disability and Rehabilitation*, 1-12. https://doi.org/10.1080/09638288.2023.2298265

Artículo 5 *

Sanabria-Mazo, J. P., D'Amico, F., Cardeñosa, E., Edo, S., Borràs, X., McCracken, L. M., Feliu-Soler, A., Sanz, A. y Luciano, J. V. (2024). Economic evaluation of Acceptance and Commitment Therapy and Behavioral Activation Therapy for Depression versus usual care among adults with chronic low back pain plus comorbid depressive symptoms. *The Journal of Pain*. https://doi.org/10.1016/j.jpain.2024.01.337

***** El **Artículo 5** se realizó durante una estancia predoctoral en *The London School of Economics and Political Science* (Londres, Reino Unido) entre el 1 de junio y el 31 de agosto de 2023. Por tanto, a través de esta tesis doctoral se opta a la mención de Doctorado Internacional.

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ABREVIATURAS

	En inglés	En español
ACT	Acceptance and Commitment Therapy	Terapia de Aceptación y Compromiso
AET	Adverse Effects of Treatments	Efectos adversos de los tratamientos
ARR	Absolute risk reduction	Reducción del riesgo absoluto
BADS	Behavioral Activation for Depression Scale	Escala de Activación para la Depresión
BATD	Behavioral Activation Treatment for Depression	Terapia de Activación Conductual para la Depresión
BPI-IS	Brief Pain Inventory - Interference Scale	Inventario Breve del Dolor - Escala de Interferencia
CBT	Cognitive Behavioural Therapy	Terapia Cognitivo Conductual
CCA	Complete case analysis	Análisis de casos completos
CEQ	Credibility/Expectancy Questionnaire	Cuestionario de Credibilidad/Expectativas
CHEERS	Consolidated Health Economic Evaluation Reporting Standards	Normas consolidadas para la presentación de informes de evaluación económica sanitaria
CIDI	Composite International Diagnostic Interview	Entrevista Internacional de Diagnóstico Compuesta
CLBP	Chronic low back pain	Dolor lumbar crónico
CONSORT	Consolidated Standards of Reporting Trials	Normas consolidadas de notificación de ensayos
COREQ	Consolidated criteria for Reporting Qualitative research	Criterios consolidados para la presentación de informes investigación cualitativa
COVID-19	Coronavirus disease 2019	Enfermedad por coronavirus 2019
CPAQ	Chronic Pain Acceptance Questionnaire	Cuestionario de Aceptación del Dolor Crónico

CSRI	Client Service Receipt Inventory	Inventario de Recibos de Servicio al Cliente
CTQ	Childhood Trauma Questionnaire	Cuestionario sobre Traumas Infantiles
DALY	Disability-adjusted life year	Año de vida ajustado en función de la discapacidad
DASS	Depression Anxiety Stress Scales	Escalas de depresión, ansiedad y estrés
DSM	Diagnostic and Statistical Manual of Mental Disorders	Manual diagnóstico y estadístico de los trastornos mentales
EMA	Ecological Momentary Assessment	Evaluación ecológica momentánea
EQ-5D-5L	European Quality of Life 5 Dimensions 5 Levels	Calidad de vida europea 5 dimensiones 5 niveles
GLM	Generalized linear mixed models	Modelos lineales mixtos generalizados
ICUR	Incremental cost-utility ratio	Relación coste-utilidad incremental
ICER	Incremental cost-effectiveness ratio	Relación coste-efectividad incremental
ICTRP	International Clinical Trials Registry Platform	Plataforma internacional de registros de ensayos clínicos
IMMPACT	Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials	Iniciativa sobre métodos, medición y evaluación del dolor en ensayos clínicos
ISRCTN	International Standard Randomized Controlled Trial Number register	Registro internacional normalizado de números de ensayos controlados aleatorios
ITT	Intention-to-treat	Intención de tratar
JARS	Journal Article Reporting Standards for Qualitative Research	Normas de notificación de artículos de revistas para la investigación cualitativa

NNT	Number needed-to-treat	Número necesario para tratar
NRS	Numerical Pain Rating Scale	Escala Numérica de Valoración del Dolor
MBI	Mindfulness-based intervention	Intervenciones basadas en Mindfulness
PCS	Pain Catastrophizing Scale	Escala de Catastrofización del Dolor
PGIC	Patient Global Impression of Change	Impresión Global del Paciente sobre el Cambio
PHQ	Patient Health Questionnaire	Cuestionario de Salud del Paciente
PICOS	Population, Intervention, Comparison, Outcomes, and Study	Población, intervención, comparación, variables de resultados y estudio
PPA	Per protocol analysis	Análisis por protocolo
PRESS	Peer Review of Electronic Search Strategies	Revisión inter pares de las estrategias de búsqueda electrónica
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analysis	Elementos de notificación preferidos para revisiones sistemáticas y metaanálisis
PROSPERO	Prospective Register of Systematic Reviews	Registro prospectivo de revisiones sistemáticas
PSIC	Pain Specific Impression of Change	Impresión Específica del Cambio del Dolor
RCT	Randomized controlled trial	Ensayo clínico controlado y aleatorizado
REDCap	Research Electronic Data Capture	Captura electrónica de datos de investigación
RoB	Risk of bias	Riesgo de sesgo

SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials	Elementos estándar del protocolo: recomendaciones para ensayos intervencionistas
SUR	Seemingly unrelated regression	Regresión aparentemente no relacionada
TAU	Treatment-as-usual	Tratamiento habitual
QALY	Quality-adjusted life year	Año de vida ajustado por calidad
WHO	World Health Organization	Organización Mundial de la Salud

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RESUMEN

RESUMEN

Introducción

El dolor lumbar crónico y la depresión son condiciones prevalentes e incapacitantes con elevados costes para el sistema de salud pública y la sociedad. La comorbilidad entre estas condiciones de salud es superior al 60% e implica una disminución significativa en la calidad de vida de las personas afectadas. Además, hay evidencia de que los pacientes con esta comorbilidad son más resistentes a los efectos de las intervenciones y menos adherentes a los tratamientos farmacológicos y no farmacológicos. En los últimos años, identificar intervenciones psicológicas eficaces y eficientes para el manejo del dolor crónico y la depresión ha supuesto un gran desafío para clínicos, investigadores y actores de la gobernanza sanitaria. En este escenario, ensayos clínicos recientes han aportado evidencia sobre el potencial terapéutico de las terapias psicológicas de tercera generación basadas en la aceptación y en la activación conductual para el tratamiento del dolor crónico y de las alteraciones emocionales.

En esta tesis doctoral se revisaron sistemáticamente las evidencias disponibles sobre la eficacia de las terapias cognitivo-conductuales en población con dolor crónico y malestar psicológico. A continuación, se realizó una evaluación clínica y económica de la Terapia de Aceptación y Compromiso (ACT) y de la Terapia de Activación Conductual para la Depresión (TACD) en comparación con el tratamiento habitual en pacientes con dolor lumbar crónico y síntomas de depresión comórbidos clínicamente relevantes. Además, en la evaluación clínica se exploraron las experiencias relatadas por un grupo de pacientes que participaron en estas 2 terapias psicológicas. Hasta donde se sabe, este es el primer compendio de estudios -compuesto por 5 artículos- en realizar una evaluación clínica y económica de un formato grupal de 2 terapias psicológicas de tercera generación (ACT y TACD) administradas mediante videoconferencia en población con esta comorbilidad.

Objetivos

El objetivo general de esta tesis doctoral fue realizar una evaluación clínica y económica de la ACT y de la TACD en pacientes con dolor lumbar crónico y síntomas de depresión. Para cumplir con este propósito, se establecieron los siguientes objetivos específicos:

Artículo 1

- Revisar sistemáticamente la evidencia disponible sobre la eficacia de las terapias cognitivo-conductuales en población con dolor crónico y malestar psicológico clínicamente relevante.

Artículo 2

- Presentar el protocolo de un ensayo clínico controlado y aleatorizado (Proyecto IMPACT) dirigido a pacientes con dolor lumbar crónico y síntomas de depresión comórbidos.

Artículo 3

- Examinar la eficacia de 2 terapias psicológicas de tercera generación (ACT y TACD) en comparación con el tratamiento habitual en pacientes con dolor lumbar crónico y síntomas de depresión comórbidos.
- Analizar el potencial rol mediador de variables de proceso como la aceptación del dolor, la activación conductual y la flexibilidad psicológica en los cambios clínicos a largo plazo (12 meses de seguimiento) obtenidos por 2 terapias psicológicas de tercera generación (ACT y TACD).

Artículo 4

- Explorar las experiencias relatadas por un grupo de pacientes con dolor lumbar crónico y síntomas de depresión comórbidos que participaron en un formato grupal de 2 terapias psicológicas de tercera generación (ACT y TACD) administradas mediante videoconferencia sincrónica a distancia.

Artículo 5

- Investigar la coste-utilidad y la coste-efectividad de 2 terapias psicológicas de tercera generación (ACT y TACD) en comparación con el tratamiento habitual para pacientes con dolor lumbar crónico y síntomas de depresión comórbidos.

Métodos

Estudio de revisión sistemática

El **Artículo 1** reporta una revisión sistemática que se implementó para comparar los resultados de eficacia obtenidos en el Proyecto IMPACT respecto a las evidencias disponibles de otras terapias cognitivo-conductuales en población con dolor crónico y malestar psicológico. La búsqueda sistemática se ejecutó en Medline, PsycINFO, Web of Science y Scopus (desde el origen hasta 18 de marzo de 2023). En este estudio de síntesis 4 revisores realizaron de forma independiente el cribado, la extracción de datos y la evaluación de riesgo de sesgo de los estudios incluidos. En total, 12 ensayos clínicos controlados y aleatorizados y 1 ensayo clínico controlado no aleatorizado examinaron la eficacia de la Terapia Cognitiva Conductual (9 estudios), de las intervenciones basadas en Mindfulness (3 estudios), de la ACT (1 estudio) y de la TACD (1 estudio). Este estudio, que involucró a 1661 participantes, siguió la declaración *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA). Además, el protocolo se registró prospectivamente en el *Prospective Register of Systematic Reviews* (PROSPERO), bajo el número de identificación CRD42021219921.

Estudio de protocolo y estudios empíricos

Los **Artículos 2, 3, 4 y 5** se enmarcan en el Proyecto IMPACT, ensayo clínico controlado, aleatorizado, multicéntrico y simple ciego en el que participaron 234 pacientes con dolor lumbar crónico y síntomas de depresión comórbidos. Como se informa en el protocolo (**Artículo 2**), este ensayo clínico se registró en ClinicalTrials.gov (NCT04140838) y siguió las directrices del *Standard Protocol Items: Recommendations for Interventional Trials* (SPIRIT), del *Consolidated Standards of Reporting Trials* (CONSORT), del *Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials* (IMMPACT) y del *Consolidated Health Economic Evaluation Reporting Standards* (CHEERS). Esta investigación contó también con la aprobación del Comité Ético del Parc Sanitari Sant Joan de Déu (PIC-178-19) y del Hospital del Mar (2019/8866/I).

Los 234 pacientes de este ensayo se reclutaron en la Clínica del Dolor del Parc Sanitari Sant Joan de Déu (Sant Boi de Llobregat) y de la Unidad del Dolor del Hospital del Mar (Barcelona). Después del cribaje y de la evaluación basal, se asignaron aleatoriamente a 1 de las 3 ramas: (1) ACT + tratamiento habitual, (2) TACD + tratamiento habitual y (3) tratamiento habitual. Debido a las restricciones de movilidad ocasionadas por la pandemia de COVID-19, este

ensayo clínico, diseñado inicialmente para presentar las terapias grupales en formato presencial, se adaptó para ser administrado a través de una plataforma de videoconferencia sincrónica a distancia. Aunque no estaba previsto en el protocolo original, se añadió una valoración cualitativa al finalizar las 8 sesiones de las intervenciones para ampliar la interpretación de los hallazgos de esta investigación.

En los estudios empíricos vinculados a este proyecto se realizaron 2 tipos de evaluaciones: una cuantitativa, en la que se analizaron los datos de eficacia (**Artículo 3**) y de coste-utilidad/coste-efectividad (**Artículo 5**) en el total de la muestra (234 pacientes) de las 3 ramas; y otra cualitativa, en la que se exploraron las experiencias (**Artículo 4**) de un subgrupo de la muestra (55 pacientes) que participó en la ACT o en la TACD. Las evaluaciones cuantitativas se realizaron antes de iniciar las intervenciones, después de terminar las intervenciones (2 meses respecto a la evaluación basal) y a largo plazo (12 meses respecto a la evaluación basal); y las evaluaciones cualitativas un mes después de terminar las intervenciones (3 meses respecto a la evaluación basal), con el fin de evitar posibles interferencias temporales con los otros datos recogidos en el proyecto.

Las evaluaciones cuantitativas consistieron en la administración de una batería de instrumentos para evaluar información sociodemográfica (género, edad, estado civil, lugar de residencia, nivel educativo y situación laboral) y clínica (años de diagnóstico, medicación diaria y presencia de un episodio depresivo actual); variables de resultado primarias (interferencia del dolor) y secundarias (intensidad del dolor, síntomas de depresión, ansiedad y estrés y catastrofización del dolor); variables de proceso (aceptación del dolor, activación conductual y flexibilidad psicológica); y variables relacionadas con los costes directos, indirectos y totales (uso de servicios clínicos, medicación y bajas por enfermedad, entre otros) y con la calidad de vida. Por su parte, en las evaluaciones cualitativas se examinaron las experiencias de los pacientes en relación con la terapia y con el uso de la tecnología.

En el protocolo de este ensayo clínico (**Artículo 2**) se presenta una descripción general del plan de análisis de algunos de los estudios empíricos vinculados a esta tesis doctoral. En resumen, el análisis de la eficacia (**Artículo 3**) de las intervenciones se realizó mediante modelos lineales mixtos generalizados. En esta investigación, también, se calculó el número necesario de pacientes a tratar y se ejecutaron modelos de mediación para estudiar el efecto de variables procesos en el cambio a largo plazo de las 2 terapias exploradas. El análisis de las experiencias

(**Artículo 4**) de los pacientes que participaron en las terapias se exploró mediante un análisis temático basado en un enfoque fenomenológico descriptivo, con una aproximación deductiva (temas predefinidos) e inductiva (subtemas derivados de los datos). Por último, la evaluación económica (**Artículo 5)** se computó mediante regresiones aparentemente no relacionadas y se analizó desde la perspectiva gubernamental (coste total) y sanitaria (coste directo). Para ello, se realizaron análisis de coste-utilidad y coste-efectividad, calculados mediante la razón de coste-utilidad incremental basados en los años de vida ajustados por calidad y la razón de coste-efectividad incremental basados en la interferencia de dolor, para identificar la interacción entre los beneficios económicos y clínicos de una intervención en comparación con las otras.

Resultados

Los hallazgos derivados de 1 estudio de revisión de la literatura científica **(Artículo 1)** y de 3 estudios empíricos (**Artículo 3, 4 y 5)** son los siguientes:

Artículo 1

Los resultados de la revisión sistemática indicaron que la terapia cognitivo conductual tradicional mejoró los síntomas de depresión y de ansiedad y la calidad de vida en pacientes con dolor crónico comórbido y malestar psicológico, pero no la intensidad del dolor y la catastrofización del dolor. A pesar de que se presentaron algunas evidencias de los beneficios de las intervenciones basadas en Mindfulness, de la ACT y de la TACD, se necesitan más ensayos clínicos robustos basados en intervenciones de tercera generación para determinar su eficacia en pacientes con esta comorbilidad.

Artículo 3

En comparación con el tratamiento habitual, la ACT y la TACD fueron eficaces para la mejora de la interferencia del dolor, la catastrofización del dolor, la activación conductual y la flexibilidad psicológica en el postratamiento y en el seguimiento de 12 meses en estos pacientes. Adicionalmente, la ACT mostró ser eficaz para la reducción de los síntomas de estrés en el postratamiento. A pesar de que algunas de estas mejoras disminuyeron efecto en el seguimiento, ambas terapias aportaron evidencia sobre sus respectivos beneficios. No se encontraron mejoras significativas en la disminución de la intensidad del dolor y de los síntomas de depresión o de ansiedad en la ACT y en la TACD en ninguno de los momentos de evaluación. La ACT obtuvo una proporción significativamente superior de respondedores que la TACD en el postratamiento y en el seguimiento; sin embargo, no se identificaron diferencias significativas en ninguna variable de resultado entre estas 2 terapias. En ambas terapias, las mejoras en la interferencia del dolor durante el seguimiento se relacionaron significativamente con las mejoras en la flexibilidad psicológica tras el tratamiento.

Artículo 4

En general, los pacientes se mostraron satisfechos tras participar en un formato grupal de la ACT y de la TACD administrado mediante videoconferencia sincrónica a distancia. Los relatos de la mayoría de este grupo de participantes evidenciaron el potencial terapéutico percibido en ambas terapias para su mejoría clínica. Las sesiones de la ACT y de la TACD se reconocieron

como un lugar seguro y sin prejuicios en el que podían expresarse y sentirse comprendidos. En cuanto a la implementación de ambas terapias mediante videoconferencia, se señalaron como barreras, principalmente, la falta de contacto humano y la pérdida de interacción social; y como facilitadores la comodidad de acceso, la flexibilidad para conectarse desde cualquier lugar, la diminución de desplazamiento y el ahorro de tiempo y dinero.

Artículo 5

La ACT y la TACD fueron más eficaces y obtuvieron una mayor reducción de costes que el tratamiento habitual en pacientes con esta comorbilidad. Respecto al tratamiento habitual, la ACT mostró una reducción significativa de los costes totales y la TACD de los costes indirectos y totales. En la ACT y en la TACD se identificó una mejoría significativa en las puntuaciones de interferencia del dolor y de los años de vida ajustados por calidad. No se detectaron diferencias significativas en los costes y en las variables de resultados al comparar la ACT y la TACD. El efecto incremental sobre la interferencia del dolor fue significativo en la ACT y en la TACD en comparación con el tratamiento habitual, pero no sobre los de los años de vida ajustados por calidad en ninguno de los análisis de sensibilidad (casos completos, intención de tratar o por protocolo). No se encontraron diferencias significativas en el coste incremental basado en la interferencia del dolor y en los años de vida ajustados por calidad entre los 3 grupos. En general, la ACT y la TACD fueron eficaces en la reducción de la interferencia del dolor.

Conclusiones

Esta tesis doctoral aporta evidencia sobre la eficacia y la coste-utilidad/coste-efectividad de 2 terapias psicológicas de tercera generación (ACT y TACD) administradas mediante videoconferencia sincrónica a distancia en comparación con el tratamiento habitual en pacientes con dolor crónico y síntomas de depresión comórbidos. Los relatos de un subgrupo de pacientes señalan el potencial terapéutico percibido en ambas terapias para la mejoría clínica y para su implementación en el sistema de salud. Finalmente, se destaca que la resistencia a las terapias podría estar asociada con la combinación del dolor crónico y la depresión, con la administración de las intervenciones mediante videoconferencia, con la disminución de práctica autónoma de los contenidos centrales de ambas terapias y con las interferencias generadas por la pandemia COVID-19. Los resultados de la revisión sistemática arrojan conclusiones poco sólidas en la actualidad y apuntan a la necesidad de realizar más ensayos clínicos controlados y aleatorizados basados en intervenciones de tercera generación. En conjunto, los hallazgos de este trabajo contribuyen al conocimiento sobre la comorbilidad dolor crónico y depresión y sobre su abordaje desde la psicología clínica y de la salud.

ABSTRACT

ABSTRACT

Introduction

Chronic low back pain and depression are prevalent and disabling conditions with high costs for the public health system and society. The comorbidity between these health conditions is higher than 60% and implies a significant decrease in the quality of life of the affected people. In addition, there is evidence that patients with this comorbidity are more resistant to the effects of interventions and less adherent to pharmacological and non-pharmacological treatments. In recent years, identifying effective and cost-effective psychological interventions for the management of chronic pain and depression has been a major challenge for clinicians, researchers, and health governance stakeholders. In this scenario, recent clinical trials have provided evidence for the therapeutic potential of third-generation psychological therapies based on acceptance and behavioral activation for the treatment of chronic pain and emotional disturbances.

This doctoral dissertation systematically reviewed the available evidence on the efficacy of cognitive-behavioral therapies in the population with chronic pain and psychological distress. A clinical and economic evaluation of Acceptance and Commitment Therapy (ACT) and Behavioral Activation Therapy for Depression (BATD) compared to treatment as usual in patients with chronic low back pain and clinically relevant comorbid depressive symptoms was then performed. In addition, the clinical evaluation explored the experiences reported by a group of patients who participated in these 2 psychological therapies. As far as it is known, this is the first compendium of studies -composed of 5 articles- to perform a clinical and economic evaluation of a group format of 2 third-generation psychological therapies (ACT and BATD) administered via videoconferencing in a population with this comorbidity.

Objectives

The general objective of this doctoral dissertation was to carry out a clinical and economic evaluation of ACT and BATD in patients with chronic low back pain and depressive symptoms. To fulfill this purpose, the following specific objectives were established:

Article 1

- To systematically review the available evidence on the efficacy of psychological interventions based on cognitive-behavioral therapies in the population with chronic pain and clinically relevant psychological distress.

Article 2

- To present the protocol of a randomized controlled trial (IMPACT Project) aimed at patients with chronic low back pain and comorbid depressive symptoms.

Article 3

- To examine the efficacy of 2 third-generation psychological therapies (ACT and BATD) compared to treatment as usual in patients with chronic low back pain and comorbid depressive symptoms.
- To analyze the potential mediating role of process variables such as pain acceptance, behavioral activation, and psychological flexibility in long-term clinical changes (12-month follow-up) obtained by 2 third-generation psychological therapies (ACT and BATD).

Article 4

- To explore the experiences reported by a group of patients with chronic low back pain and comorbid depressive symptoms who participated in a group format of 2 third-generation psychological therapies (ACT and BATD) administered via synchronous remote videoconferencing.

Article 5

- To investigate the cost-utility and cost-effectiveness of 2 third-generation psychological therapies (ACT and BATD) compared to treatment as usual for patients with chronic low back pain and comorbid depressive symptoms.

Methods

Systematic review study

Article 1 reports a systematic review that was implemented to compare the efficacy results obtained in the IMPACT Project concerning the available evidence of other cognitive-behavioral therapies in the population with chronic pain and psychological distress. The systematic search was carried out in Medline, PsycINFO, Web of Science, and Scopus (from the inception until March 18, 2023). In this synthesis study, 4 reviewers independently performed screening, data extraction, and risk of bias assessment of the included studies. In total, 12 randomized controlled trials and 1 nonrandomized controlled trial examined the efficacy of Cognitive Behavioral Therapy (9 studies), Mindfulness-based interventions (3 studies), ACT (1 study), and BATD (1 study). This study, which involved 1661 participants, followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. In addition, the protocol was prospectively registered in the Prospective Register of Systematic Reviews (PROSPERO), under the identification number CRD42021219921.

Protocol study and empirical studies

Articles 2, 3, 4, and 5 are part of the IMPACT Project, a randomized, multicenter, single-blind, controlled clinical trial in which 234 patients with chronic low back pain and comorbid depressive symptoms participated. As reported in the protocol (**Article 2**), this clinical trial was registered on ClinicalTrials.gov (NCT04140838) and followed the guidelines of the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT), the Consolidated Standards of Reporting Trials (CONSORT), the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT), and the Consolidated Health Economic Evaluation Reporting Standards (CHEERS). This research was also approved by the Ethics Committee of Parc Sanitari Sant Joan de Déu (PIC-178-19) and Hospital del Mar (2019/8866/I).

The 234 patients in this trial were recruited from the Pain Clinic of Parc Sanitari Sant Joan de Déu (Sant Boi de Llobregat) and the Pain Unit of Hospital del Mar (Barcelona). After screening and baseline assessment, they were randomly assigned to 1 of 3 arms: (1) ACT + treatment as usual, (2) BATD + treatment as usual, and (3) treatment as usual. Due to mobility restrictions caused by the COVID-19 pandemic, this clinical trial, initially designed to administer the group therapies in a face-to-face format, was adapted to be administered via a remote synchronous videoconferencing platform. Although not planned in the original protocol, a qualitative

assessment was added at the end of the 8 sessions of the interventions to broaden the interpretation of the findings of this research.

In the empirical studies linked to this project, 2 types of evaluations were carried out: a quantitative one, in which efficacy (**Article 3**) and cost-utility/cost-effectiveness (**Article 5**) data were analyzed in the total sample (234 patients) of the 3 arms; and a qualitative one, in which the experiences (**Article 4**) of a subgroup of the sample (55 patients) who participated in ACT or BATD were explored. Quantitative assessments were conducted before starting the interventions, after finishing the interventions (2 months from baseline), and in the long term (12 months from baseline); and qualitative assessments one month after finishing the interventions (3 months from baseline), to avoid possible temporal interferences with the other data collected in the project.

Quantitative assessments consisted of the administration of a battery of instruments to assess sociodemographic (gender, age, marital status, place of residence, educational level, and employment status) and clinical information (years of diagnosis, daily medication, and presence of a current depressive episode); primary (pain interference) and secondary outcome variables (pain intensity, depression, anxiety, and stress symptoms, and pain catastrophizing); process variables (pain acceptance, behavioral activation, and psychological flexibility); and variables related to direct, indirect, and total costs (use of clinical services, medication, and sick leave, among others) and quality of life. Qualitative evaluations examined patients' experiences of therapy and the use of technology.

A general description of the analysis plan of some of the empirical studies linked to this doctoral dissertation is presented in the protocol of this trial (**Article 2**). In summary, the efficacy analysis (**Article 3**) of the interventions was performed using generalized linear mixed models. In this research the number needed to treat was calculated and mediation models were run to study the effect of process variables on the long-term change of the 2 therapies explored. The analysis of the experiences (**Article 4**) of the patients who participated in the therapies was explored through a thematic analysis based on a descriptive phenomenological approach, with a deductive (predefined themes) and inductive (subthemes derived from the data) approach. Finally, the economic evaluation (**Article 5**) was computed using seemingly unrelated regressions and analyzed from the governmental (total cost) and healthcare (direct cost) perspectives. For this, cost-utility and cost-effectiveness analyses, computed using the

incremental cost-utility ratio based on quality-adjusted life years and the incremental cost-effectiveness ratio based on pain interference, were performed to identify the interaction between the economic and clinical benefits of one intervention compared to the others.

Results

The findings derived from 1 scientific literature review study (**Article 1**) and 3 empirical studies (**Article 3, 4 and** 5) are as follows:

Article 1

The results of the systematic review indicated that traditional Cognitive Behavioral Therapy improved depressive and anxiety symptoms and quality of life in patients with comorbid chronic pain and psychological distress, but not pain intensity and pain catastrophizing. Although some evidence of the benefits of Mindfulness-based interventions, ACT, and BATD was presented, more robust clinical trials based on third-generation interventions are needed to determine their efficacy in patients with this comorbidity.

Article 3

Compared to treatment as usual, ACT and BATD were effective for the improvement of pain interference, pain catastrophizing, behavioral activation, and psychological flexibility at posttreatment and at 12-month follow-up in these patients. Additionally, ACT was shown to be effective in reducing stress symptoms at post-treatment. Although some of these improvements diminished at follow-up, both therapies provided evidence of their respective benefits. No significant improvements in the reduction of pain intensity and depressive or anxiety symptoms were found in ACT and BATD at either evaluation time point. ACT had a significantly higher proportion of responders than BATD at posttreatment and follow-up; however, no significant differences were identified in any outcome between these 2 therapies. In both therapies, improvements in pain interference at follow-up were significantly related to improvements in psychological flexibility after treatment.

Article 4

Overall, patients were satisfied after participating in a group format of ACT and BATD administered via synchronous remote videoconferencing. The testimonials of most of this group of participants evidenced the perceived therapeutic potential of both therapies for their clinical improvement. The ACT and BATD sessions were recognized as a safe and non-judgmental place where they could express themselves and feel understood. Regarding the implementation of both therapies by videoconference, the main barriers were the lack of human

contact and the loss of social interaction; and the facilitators were the ease of access, the flexibility to connect from anywhere, the reduction of travel, and the time and money savings.

Article 5

ACT and BATD were more effective and obtained a greater cost reduction than treatment as usual in patients with this comorbidity. Compared to treatment as usual, ACT showed a significant reduction in total costs and BATD in indirect and total costs. ACT and BATD showed a significant improvement in pain interference and quality-adjusted life years. No significant differences in costs and outcome variables were detected when comparing ACT and BATD. The incremental effect on pain interference was significant in ACT and BATD compared with treatment as usual, but not on quality-adjusted life-years in any of the sensitivity analyses (complete cases, intention-to-treat, or per protocol). No significant differences were found in incremental cost based on pain interference and quality-adjusted life years among the 3 groups. Overall, ACT and TACD were effective in reducing pain interference.

Conclusions

This doctoral dissertation provides evidence on the efficacy and cost-utility/cost-effectiveness of 2 third-generation psychological therapies (ACT and BATD) delivered via synchronous remote videoconferencing compared to treatment as usual in patients with comorbid chronic pain and depressive symptoms. Testimonials from a subgroup of patients point to the perceived therapeutic potential of both therapies for clinical improvement and implementation in this format in the healthcare system. Finally, it is highlighted that resistance to the therapies could be associated with the combination of chronic pain and depression, with the administration of the interventions by videoconference, with the decrease in autonomous practice of the central contents of both therapies, and with the interferences generated by the COVID-19 pandemic. The results of the systematic review yield weak conclusions at present and point to the need for more randomized controlled trials based on third-generation interventions. Taken together, the findings of this work contribute to the knowledge about chronic pain and depression comorbidity and its approach from clinical and health psychology.

CAPÍTULO 1

Introducción

INTRODUCCIÓN

1. Dolor lumbar crónico

1.1. Aspectos generales

El dolor lumbar crónico se define como un dolor o una tensión muscular focalizada en la parte baja de la espalda que persiste por un período superior a los 3 meses desde su inicio o que se presenta de forma recurrente (Nicholas et al., 2019). Cuando el dolor lumbar cumple este criterio de duración o de recurrencia ya no se considera un síntoma específico (Nieto et al., 2023), sino un trastorno independiente que se mantiene por factores que podrían variar respecto a sus causas iniciales (Kamaleri et al., 2009). En algunos casos el dolor fluctuante o persistente de baja o media intensidad, interrumpido por períodos de ausencia o de exacerbación del dolor, también podría considerase como crónico (Kongsted et al., 2016). Otra característica general de esta condición es que con frecuencia coexiste con dolores en otras regiones del cuerpo (Kamaleri et al., 2009) y con otras enfermedades (Vlaeyen et al., 2018). El dolor crónico afecta a la calidad de vida (Hartvigsen et al., 2018), interfiere en las actividades diarias (Treede et al., 2019) y causa alteraciones físicas, psicológicas y sociales clínicamente relevantes en las personas que lo padecen (Rayner et al., 2016).

1.2. Sistemas de clasificación

La Clasificación Internacional de Enfermedades (CIE-11) categoriza el dolor lumbar crónico como un dolor primario (código MG30.02) cuando es consecuencia de una afección específica y como un dolor musculoesquelético secundario (código MG30.02) cuando es un síntoma de otra enfermedad (Nicholas et al., 2019). Principalmente, existen 2 sistemas de clasificación para caracterizar el dolor lumbar: uno basado en su duración (es decir, en la cantidad de tiempo que ha estado presente) y otro en su origen (es decir, en la causa subyacente del dolor experimentado). Según el sistema de clasificación basado en la duración -adoptado por el *Royal College of General Practitioners* a partir de la definición de Spitzers y colaboradores- este dolor puede ser agudo (menos de 1 mes), subagudo (entre 1 mes y 3 meses) y crónico (más de 3 meses); y según el basado en el origen puede ocasionarse por lesiones previas, enfermedades degenerativas y trastornos psicológicos, entre otras causas (Barrey et al., 2019).

Aunque hay diferentes sistemas de clasificación basados en la duración -como, por ejemplo, el propuesto por *The American Society of Interventional Pain Physicians* que categoriza el dolor como crónico cuando persiste por un tiempo superior a los 6 meses-, en la actualidad el de

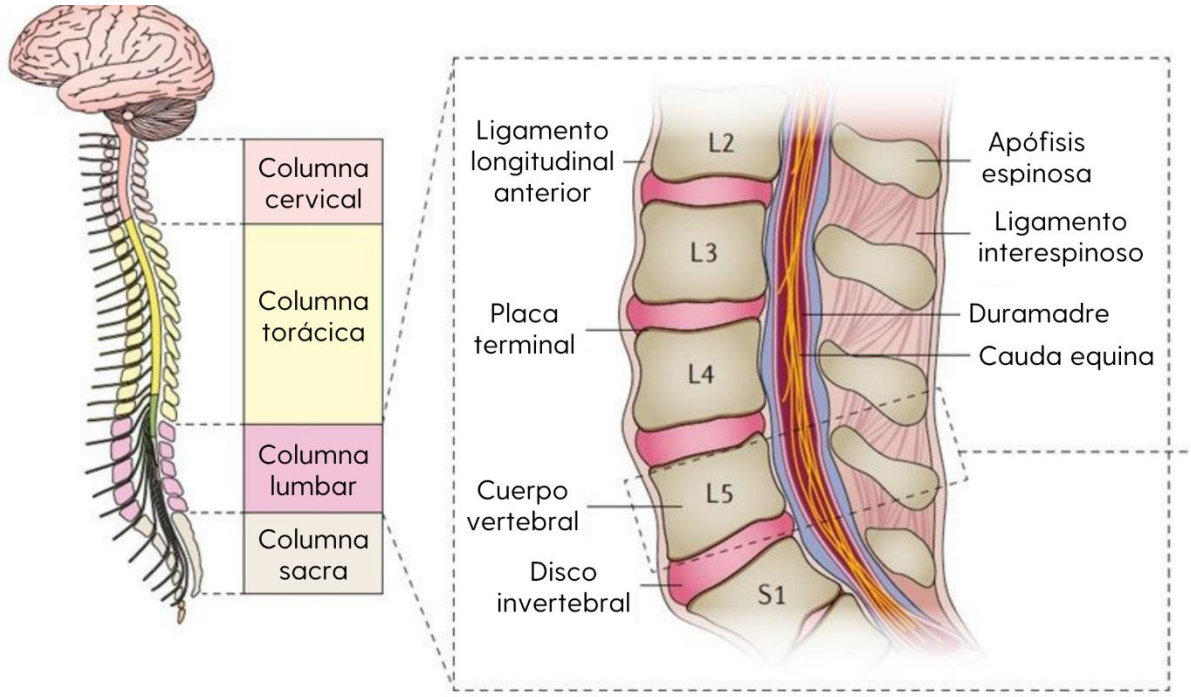
Spitzers y colaboradores sigue siendo el más aceptado por la comunidad científica y clínica (Vlaeyen et al., 2018). Respecto al origen, el dolor lumbar crónico se clasifica como específico cuando se identifica una causa subyacente concreta e inespecífico cuando no existe una causa subyacente definida (Kongsted et al., 2016). Estos 2 sistemas de clasificación son complementarios y especialmente útiles para detectar tratamientos eficaces acordes a las necesidades de atención médicas específicas de las personas con esta condición de salud (Barrey et al., 2019).

1.3. Etiopatogenia

Originalmente, el dolor lumbar se consideraba como el resultado de la asociación entre lesiones específicas provocadas por cargas físicas y por cambios degenerativos estructurales en la columna vertebral o en las estructuras de soporte (Battié et al., 2009). En la actualidad, el dolor lumbar se concibe como una condición de salud con una etiopatogenia compleja y multifactorial en la que interactúan factores físicos, psicológicos y sociales (Treede et al., 2019). De hecho, en los últimos años, se ha reportado que la cronificación del dolor podría estar conectada con alteraciones en los mecanismos de la sensibilización central (Pak et al., 2018). Durante este proceso, el sistema nervioso tiende a sensibilizarse y a reaccionar exageradamente ante estímulos de dolor, incluso en circunstancias en las que no se detecta una lesión tisular periférica desencadenante de este malestar (Treede et al., 2019) o en las que la causa original del malestar (física, psicológica y/o social) ha desaparecido (Kamaleri et al., 2009).

En la Figura 1 se ilustra la anatomía vertebral de una persona. El daño en estructuras dentro de la columna vertebral -ocasionado en algunos casos por lesiones traumáticas, inflamaciones o infecciones (Barrey et al., 2019) y potencializado por expectativas negativas, respuestas emocionales y conductas relacionadas con el dolor (Sharot y Garrett, 2016)- contribuye a la aparición del dolor lumbar, aunque no necesariamente es el motivo desencadenante (Vlaeyen et al., 2018).

Figura 1. Anatomía vertebral. Imagen traducida de Vlaeyen et al. (2018).



Algunos factores de riesgo que aumentan las probabilidades de padecer dolor lumbar (Vlaeyen et al., 2018) están relacionados con lesiones previas (provocadas por estar de pie durante largos períodos, levantar peso, realizar posturas forzadas o mover objetos distanciados del cuerpo), con estilos de vida poco saludables (sedentarismo, tabaquismo y obesidad) y con alteraciones en la salud mental (estrés, ansiedad y depresión). A pesar de que faltan más evidencias sólidas para confirmar o refutar esta hipótesis (Cohen et al., 2022), hay estudios que sugieren que el dolor lumbar inicia en la infancia, continúa en la edad adulta y persiste en las personas mayores (Dunn et al., 2013).

1.4. Diagnóstico

El diagnóstico del dolor lumbar requiere una toma de decisiones clínicamente compleja (Han et al., 2023). Por lo general, este diagnóstico se realiza a partir de una valoración médica en la que se incluyen revisiones de la historia clínica, de los exámenes físicos y de las pruebas de diagnóstico (Allegri et al., 2016). Concretamente, la revisión de la historia clínica permite recopilar información sobre los antecedentes del paciente (posibles factores de riesgo, enfermedades previas y cirugías); los exámenes físicos ayudan a conocer la movilidad de la columna vertebral, la fuerza muscular, los reflejos y la sensibilidad del paciente; y las pruebas

diagnósticas contribuyen a explorar posibles causas subyacentes del dolor (Stevans et al., 2021). Los procedimientos que se utilizan con más frecuencia para diagnosticar dolor lumbar son las pruebas de extensión de las piernas, las pruebas de percusión de apófisis espinosas vertebrales y los exámenes radiológicos (Urits et al., 2019).

En la práctica clínica, el dolor lumbar suele clasificarse en 4 categorías: (1) trastorno visceral, en el que las causas del dolor provienen de los órganos situados en el interior de la cavidad abdominal (por ejemplo, riñón, páncreas o intestinos); (2) enfermedad espinal específica, en la que se reconoce una patología específica de la columna vertebral que causa el dolor (por ejemplo, hernias discales, estenosis espinal, fracturas vertebrales, infecciones o tumores); (3) síndrome radicular, en el que las raíces nerviosas de la columna vertebral causan el dolor percibido en las piernas; o (4) enfermedad lumbar inespecífica, en la que no se detectan fracturas, traumatismos, enfermedades sistémicas o alteraciones nerviosas que expliquen el dolor (Vlaeyen et al., 2018).

Cuando los pacientes experimentan este dolor por un tiempo superior a los 3 meses (Downie et al., 2014), cumplen los criterios del CIE-11 para el diagnóstico de dolor primario crónico (Nicholas et al., 2019). A pesar de que existe evidencia de que muchos de los pacientes que acuden a atención primaria por episodios de dolor lumbar agudo mejoran, se estima que cerca del 15% desarrollan dolor crónico (Maher et al., 2017). Por tanto, la identificación temprana del dolor lumbar es fundamental para evitar su cronificación (Vlaeyen et al., 2018). En los últimos años, instrumentos como el *Örebro Musculoskeletal Pain Screening Questionnaire* (Linton y Boersma, 2003) y el *Start Back Screening Tool* (Hill et al., 2008) se han utilizado en el sistema de salud para evaluar el riesgo de que un paciente que busca atención por dolor agudo desarrolle dolor crónico (Treede et al., 2019).

Además de los instrumentos de cribado empleados para la detección temprana, en la práctica clínica cada vez se utiliza con más frecuencia el modelo de banderas (*flag model*, en inglés). En particular, este sistema, dividido principalmente en 2 categorías (banderas clínicas y banderas psicosociales) permite identificar señales de alerta relacionadas con el dolor lumbar crónico, así como delimitar la ruta de intervención más adecuada a las circunstancias concretas de los pacientes (Downie et al., 2014). Como se observa en la Tabla 1, en esta evaluación inicial se exploran señales de alerta como: (1) sospechas de patología graves (bandera roja), (2) síntomas psiquiátricos (bandera naranja), (3) alteraciones cognitivas, emocionales y

conductuales (bandera amarilla), (4) problemas relacionados con el trabajo (bandera azul) y (5) dificultades asociadas al sistema (bandera negra).

Tabla 1. Modelo de banderas (*flag model*, en inglés). Adaptado y traducido de Vlaeyen et al. (2018).

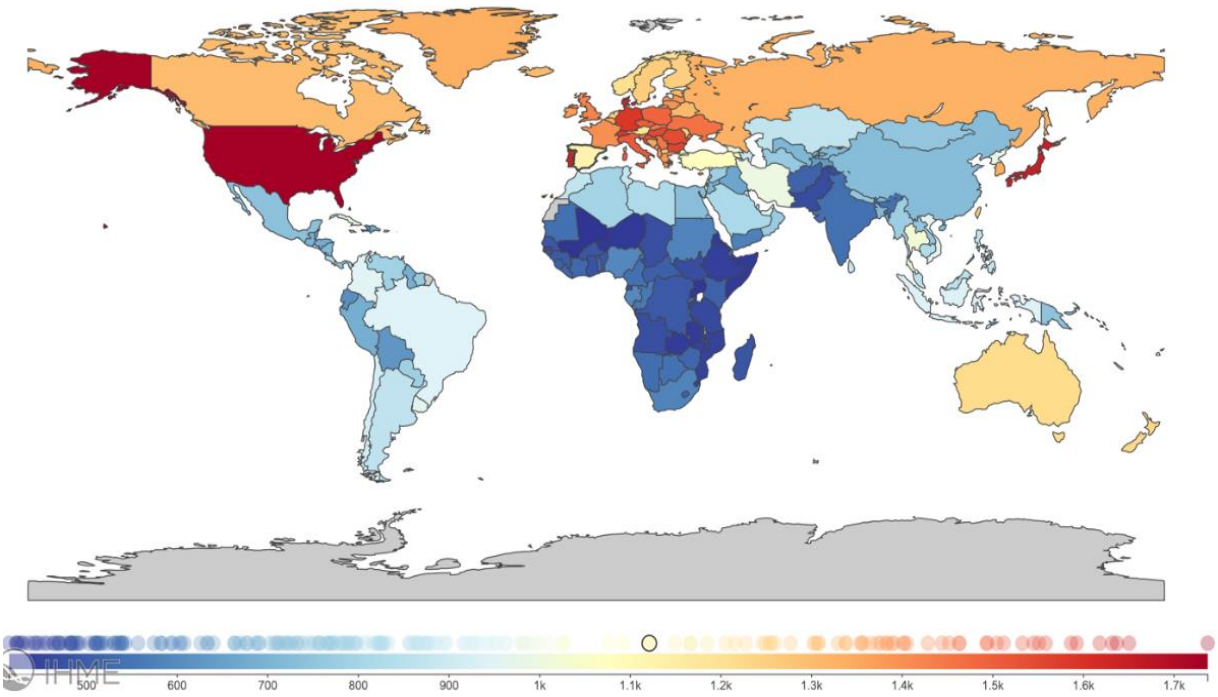
Bandera	**Naturaleza**	**Ejemplos**
Roja	Funciones de alerta presentes que generan sospechas de patología grave.	• Nueva disfunción vesical o intestinal (posible síndrome de cauda equina). • Uso de drogas intravenosas, fiebre o infección reciente (posible infección vertebral). • Antecedentes de cáncer (posibles metástasis vertebrales).
Naranja	Síntomas psiquiátricos.	• Depresión clínica. • Trastorno de la personalidad.
Amarillo	Creencias, valoraciones y juicios.	• Creencias perjudiciales sobre el dolor: interpretación de la lesión como incontrolable o susceptible de empeorar. • Expectativas de malos resultados respecto al tratamiento. • Retraso en la reincorporación al trabajo.
	Respuestas emocionales.	• Angustia que no cumple con los criterios para el diagnóstico de un trastorno mental. • Preocupación. • Miedos. • Ansiedad.
	Comportamiento ante el dolor (incluidas estrategias de afrontamiento).	• Evitación de actividades debido a las expectativas de dolor y a la posibilidad de volver a lesionarse.

		• Excesiva dependencia de tratamientos pasivos.
Azul	Percepciones sobre la relación entre el trabajo y la salud.	• Creencia de que el trabajo es demasiado agotador y puede causar más lesiones. • Creencia de que el supervisor y los compañeros de trabajo no bridan apoyo.
Negro	Obstáculos sistémicos o contextuales.	• Legislación que restringe las opciones de reincorporación al trabajo. • Conflicto con el personal del seguro sobre la reclamación por lesiones. • Familiares y profesionales sanitarios demasiado insistentes.

1.5. Epidemiología

El dolor lumbar crónico representa una carga económica y social significativa (Vlaeyen et al., 2018). De acuerdo con un informe del *Global Burden of Disease Study*, en 2019 este dolor se posicionó como la principal causa de años vividos con discapacidad. En este mismo estudio, el dolor lumbar crónico se clasificó como una de las 10 principales causas de años vividos con discapacidad en los 188 países evaluados (Institute for Health Metrics and Evaluation, 2019). A nivel mundial, la prevalencia del dolor lumbar es cercana al 8% (569 millones de casos), con una afectación del 9% en mujeres (332 millones de casos) y del 6% en hombres (237 millones de casos). La prevalencia del dolor lumbar aumenta con la edad, alcanzando su máximo en las personas mayores de 70 años (20%). En la Figura 2 se presenta un gráfico con los años de vida ajustados por discapacidad registrados en población con dolor lumbar en 2019.

Figura 2. Años de vida ajustados por discapacidad en población con dolor lumbar (datos generales para todas las edades, por cada 100.000). Datos extraídos del *Global Burden of Disease Study* realizado por el Institute for Health Metrics and Evaluation (2019).



Globalmente, el número de casos de personas diagnosticadas con dolor lumbar ha aumentado de forma considerable en los últimos años (Hoy et al., 2012). En 1990 se registraron 377 millones de personas con dolor lumbar y en 2019 -fecha del último informe disponible- esta cifra aumentó a 569 millones (Institute for Health Metrics and Evaluation, 2019). En la Unión Europea, esta cifra incrementó de los 57 millones en 1990 a los 66 millones registrados en 2019. En España -contexto en el que se desarrolló esta investigación- incrementó de los 4 millones en 1990 a los cerca de 5 millones en 2019. En la Tabla 2 se presenta una comparativa de la prevalencia de dolor crónico registrada en países de la Unión Europea en 1990 (primer registro) y en 2019 (último registro disponible), a partir de los datos facilitados por el Institute for Health Metrics and Evaluation (2019).

Tabla 2. Prevalencia de dolor lumbar en países de la Unión Europea. Datos extraídos del *Global Burden of Disease Study* realizado por el Institute for Health Metrics and Evaluation (2019).

País	2019				1990			
	Casos	Prevalencia (%)			Casos	Prevalencia (%)		
		Total	Mujeres	Hombres		Total	Mujeres	Hombres
Alemania	12.173.995	15,1	17,3	12,7	10.682.440	14,1	16,1	11,8
Austria	948.943	11,2	13,2	9,3	818.761	11,2	12,8	9,1
Bélgica	1.392.622	12,9	14,8	10,9	1.164.254	12,4	14,2	10,5
Bulgaria	964.742	14,4	14,9	14,4	1.051.861	12,6	12,3	13,1
Chipre	159.103	12,8	14,1	11,4	79.208	10,9	12,1	9,7
Croacia	585.421	14,3	15,1	13,5	602.908	12,9	13,9	11,8
Dinamarca	847.322	15,5	16,9	13,9	729.266	15,1	16,6	13,4
Eslovaquia	698.962	13,4	13,1	13,8	572.990	11,4	11,1	11,9
Eslovenia	272.110	13,7	13,3	14,1	219.275	11,7	11,4	11,9
España	4.621.840	11,1	12,8	10,2	4.036.017	10,6	11,8	8,2
Estonia	154.230	12,3	13,5	10,9	152.484	10,2	11,1	9,2
Finlandia	625.072	11,9	13,4	10,3	523.555	11,1	12,4	9,7
Francia	8.294.271	13,3	16,1	10,3	6.469.421	11,9	14,2	9,4
Grecia	1.281.973	13,1	15,1	10,8	1.100.335	11,1	12,7	9,4
Hungría	1.342.770	14,5	13,8	15,3	1.201.351	12,1	11,7	12,4
Irlanda	602.267	13,2	14,5	11,8	385.326	11,6	12,8	10,4
Italia	8.207.555	14,1	16,1	11,9	7.086.166	12,9	15,3	10,5
Letonia	240.047	13,1	15,0	10,8	274.255	10,9	12,5	8,8
Lituania	350.548	13,1	14,6	11,2	375.045	10,7	12,1	9,2
Luxemburgo	75.917	13,0	15,8	10,1	46.055	12,8	15,5	9,9
Malta	63.593	15,3	17,6	12,8	43.113	12,5	14,1	10,8
Países Bajos	1.920.886	11,9	13,6	10,1	1.498.330	10,8	12,1	9,3
Polonia	5.116.533	13,9	14,8	13,1	4.300.346	11,9	13,1	10,6
Portugal	1.568.205	15,4	18,5	11,8	1.232.816	12,9	15,2	10,4
Rep. Checa	1.441.297	14,2	14,2	14,2	1.215.512	12,4	12,6	12,2
Rumanía	2.645.553	14,3	14,8	13,7	2.803.974	12,5	13,0	11,9
Suecia	1.156.300	11,9	13,6	10,2	956.911	11,8	13,6	9,9

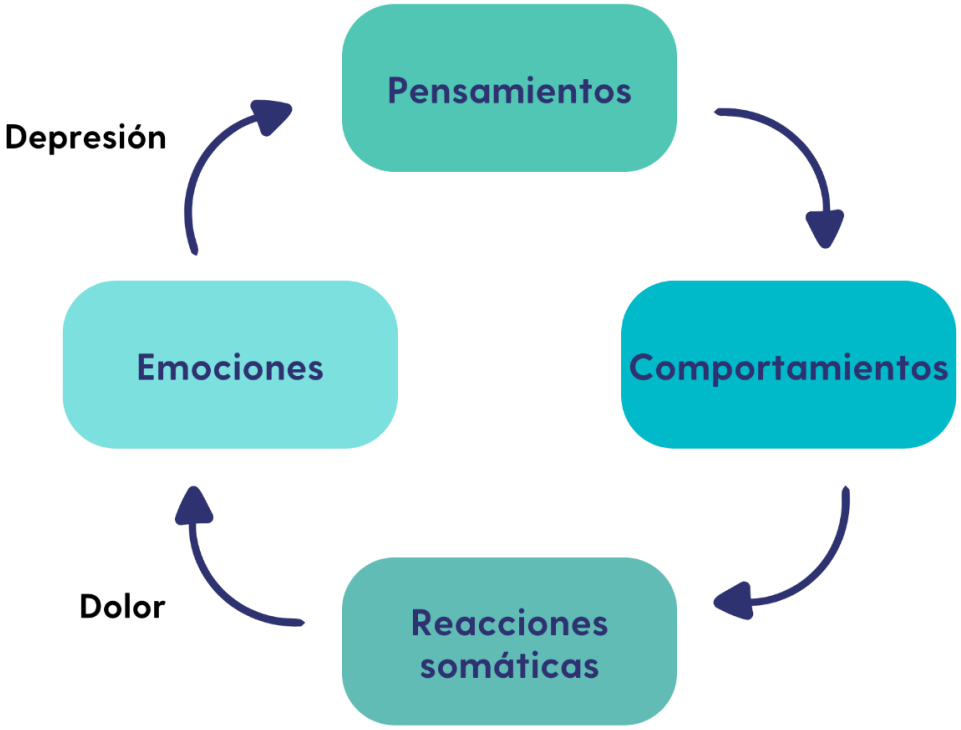
1.6. Comorbilidades

La comorbilidad se define como la presencia de 2 o más trastornos o enfermedades en una misma persona (Rizvi et al., 2021). Las personas diagnosticadas con dolor lumbar crónico conviven con diferentes condiciones de salud (Lim et al., 2020). Un estudio poblacional señaló (Gore et al., 2012) que, en comparación con controles sanos, las personas con dolor lumbar crónico presentaron con más frecuencia trastornos del estado de ánimo (13% frente a 6%), de ansiedad (8% frente a 3%) y del sueño (10% frente a 3%). La coexistencia de distintas condiciones, circunstancia que varía según la persona y la trayectoria del dolor, complejiza el cuadro clínico y obstaculiza las estrategias de intervención en esta población (de Heer et al., 2018).

1.6.1. Dolor crónico y depresión

Debido a su alta prevalencia y a sus repercusiones clínicas, sociales y económicas, la comorbilidad entre el dolor crónico y la depresión ha despertado un interés creciente en la comunidad científica (Holmes et al., 2013). Como se observa en la Figura 3, hasta la fecha se sabe que la relación entre el dolor crónico y la depresión es bidireccional (Kroenke et al., 2011). De acuerdo con las evidencias disponibles, las personas diagnosticadas con dolor crónico tienen más riesgo de desarrollar depresión y, a su vez, las diagnosticadas con depresión tienen mayor riesgo de desarrollar dolor crónico (Gore et al., 2012). De hecho, algunas teorías postulan que el dolor y la depresión comparten mecanismos fisiopatológicos comunes que pueden activar ambas condiciones (Dell'Osso et al., 2015). El rol mediador de las citoquinas y del eje e hipotálamo-hipófisis-adrenal desempeñan a la vez un papel potencialmente crucial en las dolencias crónicas (Sanabria-Mazo et al., 2022) y en las alteraciones emocionales (Lim et al., 2020).

Figura 3. Relación entre el dolor crónico y la depresión. Adaptado y traducido de Zis et al. (2017).



La comorbilidad entre el dolor crónico y la depresión es superior al 60% de los casos que asisten a las unidades de dolor (Rizvi et al., 2021). Como se ha evidenciado en estudios previos, la coexistencia de ambas condiciones de salud afecta negativamente en la calidad de vida (Han et al., 2023), interfiere en el funcionamiento diario (Hartvigsen et al., 2018), aumenta las probabilidades de sufrimiento psicológico (Kongsted et al., 2016) e incrementa el consumo de fármacos (de Heer et al., 2018). Las personas con dolor crónico que experimentan síntomas de depresión tienen más dificultades de recuperación (Wang et al., 2019) y se adhieren menos a los tratamientos prescritos (Mansfield et al., 2016).

Además, informes recientes han señalado que el coste total anual generado por el dolor lumbar es de unos 8945 millones de € (1096 € paciente/año), de los cuales el 75% corresponde a costes indirectos (Alonso-García y Sarría-Santamera, 2020), y por los trastornos de depresión de unos 224 millones (3235 € paciente/año), de los cuales el 82% se atribuyen a costes indirectos (Vierta et al., 2021). Considerando estas repercusiones, intervenir los efectos de esta comorbilidad se constituye como un asunto prioritario para el sistema de salud pública (Schmaling y Nounou, 2019).

2. Psicología y dolor crónico

2.1. Modelos explicativos del dolor

Antes del auge de los modelos psicológicos, los modelos para explicar la experiencia del dolor se enfocaban principalmente en factores biológicos y neurológicos (Turk y Flor, 1984). A partir de 1970, los modelos comenzaron a reconocer la importancia de los factores psicológicos en el estudio y en el tratamiento del dolor crónico (Linton y Shaw, 2011). Desde ese momento hasta la actualidad, varios modelos se han interesado en explorar el papel de los factores emocionales (miedo-ansiedad y tristeza) y cognitivos-conductuales (creencias y actitudes, catastrofización del dolor, miedo-evitación del dolor, expectativas de recuperación y autoeficacia) en la cronificación del dolor (González, 2014).

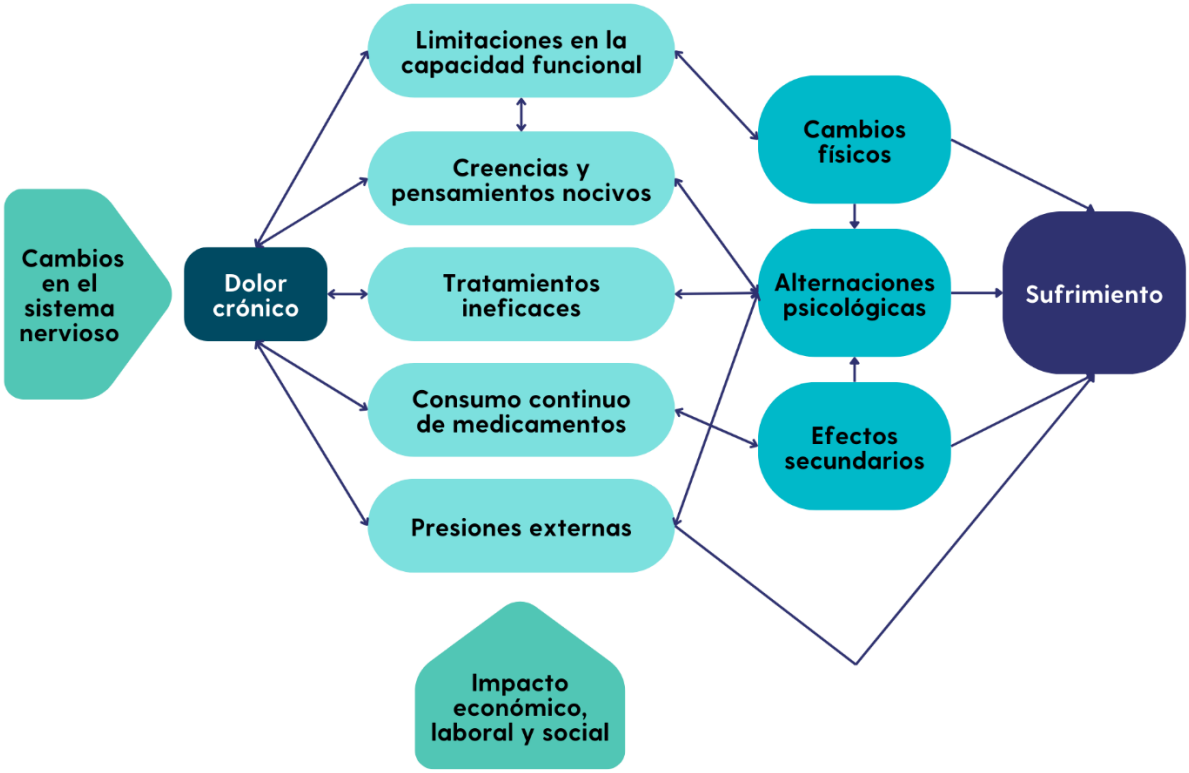
De los propuestos hasta ahora, 2 de los modelos psicológicos con mayor popularidad en el campo del dolor son: (1) el modelo de catastrofización ante el dolor (Sullivan et al., 1995), que sugiere que la catastrofización (formada por las dimensiones de rumiación, magnificación y desesperanza) aumenta la intensidad del dolor y la sensación de incapacidad asociada; y (2) el modelo de miedo-evitación (Vlaeyen y Linton, 2000), que propone que el miedo a experimentar dolor influye en la evitación de actividades que se cree que podría generar dolor, lo que, a su vez, aumenta la sensibilidad al dolor y perpetua el ciclo dolor-miedo-evitación. En común, ambos modelos destacan el papel de los pensamientos y las emociones en la persistencia de la experiencia de dolor crónico (Rogers y Farris, 2022). En la Tabla 3 se presenta una síntesis de algunos modelos psicológicos que han intentado explicar los mecanismos involucrados en la experiencia del dolor.

Tabla 3. Síntesis de modelos psicológicos explorados en el campo del dolor. Adaptado y traducido de Linton y Shaw (2011).

Modelo	Descripción
Modelo de autoeficacia (Bandura, 1986)	La creencia de que una persona puede afrontar el dolor está relacionada con su capacidad de autogestión. La percepción de una baja autoeficacia, en la que se refleja que la persona no se considera capaz de controlar el dolor, causa una disfunción física y psicológica que interfiere en la experiencia del dolor.
Modelo de catastrofización ante el dolor (Sullivan et al., 1995)	Las personas con pensamientos catastróficos amplifican el dolor percibido, anticipan las posibles consecuencias negativas y se sienten vulnerables ante el malestar ocasionado. Este sufrimiento, además, limita su capacidad para hacer frente al dolor experimentado.
Modelo de aceptación y compromiso (Hayes et al., 1999)	Las creencias rígidas, como que el dolor debe desaparecer por completo para ser feliz, pueden bloquear la consecución de objetivos vitales a largo plazo. Reducir los intentos de alcanzar objetivos poco realistas (mediante la aceptación) posibilita flexibilidad y responsabilidad en la búsqueda de objetivos vitales importantes (actitud de compromiso).
Modelo diátesis-estrés (Trask y Sigmon, 1999)	Un estrés psicológico clínicamente relevante y unos recursos de afrontamiento limitados predisponen a las personas a sufrir dolor y a estar menos preparadas para afrontarlo. En estas circunstancias, es más probable que el dolor provoque dificultades funcionales y malestar emocional.
Modelo de miedo-evitación (Vlaeyen y Linton, 2000)	Una lesión dolorosa puede provocar catastrofismo y miedo a realizar determinados movimientos. Este comportamiento, a su vez, conduce a más evitación, disfunción, depresión y, en última instancia, a más dolor.
Modelo de resolución de problemas mal encaminados (Eccleston y Crombez, 2007)	La preocupación cotidiana por el dolor puede implicar que el paciente adopte ciertas formas desadaptativas de resolver el problema. En este caso, el paciente experimenta más preocupación y una visión más restringida sobre la naturaleza de la situación. Esto genera, al mismo tiempo, que sea menos probable que se resuelva.

En la actualidad, el modelo biopsicosocial es el más aceptado para el abordaje del dolor crónico (Miaskowski et al., 2020). Este modelo, propuesto por Engel en 1997, comprende que la salud y la enfermedad son el resultado de la interacción entre factores biológicos, psicológicos y sociales (Bolton, 2022). En el contexto del dolor crónico, este modelo es relevante porque entiende que el dolor no es solo una respuesta física a una lesión, sino que es una consecuencia de los factores psicológicos y sociales involucrados (Cohen et al., 2021). De acuerdo con este modelo, factores psicológicos, como la depresión, la ansiedad o el estrés, podrían aumentar la percepción del dolor; y, a su vez, factores sociales, como el acceso a atención médica o el apoyo social, podrían influir en la forma en la que las personas afrontan la enfermedad (Nicholas, 2022). Como se ilustra en la Figura 4, el modelo biopsicosocial aborda, de forma integral, todos aquellos aspectos relevantes que influyen sobre la toma de decisiones y el bienestar de los pacientes (Nicholas, 2008).

Figura 4. Perspectiva biopsicosocial para comprender el dolor crónico. Adaptado y traducido de Nicholas (2008).



2.2. Factores psicológicos involucrados en el dolor

La experiencia del dolor está condicionada por una serie de factores psicológicos (Linton y Shaw, 2011). De forma consensuada, varios modelos en el campo del dolor señalan que los factores psicológicos -en su interacción continua con procesos biológicos y sociales- cumplen un rol relevante en el desarrollo y en el mantenimiento del dolor persistente (Nicholas, 2022). Como se observa en la Tabla 4, las cogniciones, las emociones y los comportamientos contribuyen a la experiencia del dolor (Vlaeyen et al., 2018).

Tabla 4. Factores psicológicos involucrados en la experiencia del dolor. Adaptado y traducido de Linton y Shaw (2011).

Factores	Posible efecto en el dolor
Cogniciones	La vigilancia puede aumentar la intensidad del dolor.
	La distracción puede disminuir la intensidad del dolor.
Emociones	El miedo puede aumentar el comportamiento de evitación y la discapacidad.
	La ansiedad puede aumentar la discapacidad.
	La depresión puede aumentar la discapacidad.
	La angustia puede aumentar las cogniciones negativas y la discapacidad.
	Las emociones positivas podrían disminuir el dolor.
Conductuales	El comportamiento de evitación puede aumentar la discapacidad.
	La actividad ilimitada (hiperactividad) puede provocar dolor.
	Las conductas de dolor incrementan el dolor.

Por ejemplo, factores cognitivos, como las expectativas sobre la aparición, la magnitud y las consecuencias del dolor -generadas a partir de información previa sobre el estado del cuerpo o de observaciones de otras personas en circunstancias similares-, o factores emocionales, como los síntomas de depresión, ansiedad y estrés, influyen en la capacidad de ajuste de las personas (Wiech, 2016), afectan sus conductas de salud o enfermedad (Vlaeyen et al., 2018) e impactan en su bienestar psicológico (Sharot y Garrett, 2016). A su vez, factores conductuales, como los comportamientos de evitación (*kinesiofobia* o miedo al movimiento) -desarrollados ante la necesidad de protegerse de movimientos o actividades que podrían ocasionar malestar físico o emocional-, contribuyen a aumentar la percepción de incapacidad en las personas con dolor crónico (Trinderup et al., 2018). También, se ha propuesto que los procesos cognitivos, como la autoeficacia, pueden ejercer un efecto modulador del control del dolor (Bandura et al., 1987).

3. Recomendaciones para el abordaje del dolor crónico

Los tratamientos disponibles para el abordaje del dolor crónico tienen como propósito principal mejorar la calidad de vida y la capacidad funcional de las personas con esta condición (Hartvigsen et al., 2018). Un objetivo terapéutico central para cumplir con este fin consiste en reducir la interferencia del dolor en las diferentes dimensiones de la vida de los pacientes (Vlaeyen et al., 2018). Desde hace varios años, existe un consenso acerca de la pertinencia de adoptar una perspectiva biopsicosocial y multidisciplinar para el abordaje del dolor crónico (Schütze et al., 2018). Guías clínicas internacionales de asociaciones como el *International Association for the Study of Pain*, el *American Pain Society*, la *American Academy of Pain Medicine Clinical Practice Guideline*, la *European Pain Federation* y la *International Headache Society* destacan la relevancia de combinar los beneficios de las intervenciones no farmacológicas y farmacológicas para el abordaje integral del dolor crónico (Oliveira et al., 2018).

En general, en estas guías se recomienda que los tratamientos sean personalizados y adaptados según las necesidades específicas de cada paciente (Petersen et al., 2018). Para ello, la ruta de intervención debe iniciar con una valoración clínica general (Vlaeyen et al., 2018). Esta evaluación permite delimitar si el paciente requiere un abordaje conservador (primera opción) o un abordaje invasivo (segunda opción) para la intervención del dolor (Knezevic et al., 2017). El enfoque conservador consiste en la implementación de estrategias farmacológicas (antiinflamatorios, antiepilépticos, opioides y antidepresivos, entre otras) y/o no farmacológicas (fisioterapia, terapias psicológicas y acupuntura, entre otras). Los protocolos de intervención más recientes sugieren adoptar, como primera medida de atención, estrategias no farmacológicas (Abdel-Shaheed et al., 2017). En caso de que el paciente no obtenga la respuesta esperada, se recomienda combinar, de forma paralela, las estrategias farmacológicas con las no farmacológicas (Hartvigsen et al., 2018). Ambas estrategias tienen como propósito común controlar síntomas asociados al dolor, como la rigidez muscular, la fatiga, las alteraciones del sueño, los problemas de concentración y los trastornos emocionales (Urits et al., 2019). Si el enfoque conservador no es efectivo para disminuir estos síntomas, se suelen considerar enfoques más invasivos (Knezevic et al., 2017). Estos enfoques invasivos incluyen procedimientos no quirúrgicos, como las inyecciones epidurales, y/o quirúrgicos, como la discectomía, la artroplastia discal y la fusión vertebral, entre otros (Knezevic et al., 2017).

El abordaje del dolor lumbar debe adaptarse a la respuesta de los pacientes, así como a la valoración clínica del especialista (Traeger et al., 2019). En la Tabla 5 se presentan una serie de recomendaciones expuestas en diferentes guías internacionales especializadas en el manejo del dolor lumbar.

Tabla 5. Recomendaciones generales para el manejo del dolor lumbar, según las directrices de 6 guías internacionales. Adaptado y traducido de Traeger et al. (2019).

	Recomendaciones
1	Adoptar un enfoque escalonado o estratificado para la atención del dolor lumbar, guiado por la respuesta del paciente a la atención previa o a los resultados de las herramientas de predicción del riesgo.
2	Aconsejar a los pacientes que se mantengan activos, educar sobre la naturaleza benigna del dolor lumbar y tranquilizar sobre la ausencia de patología grave.
3	Proponer a los pacientes con dolor agudo terapias físicas (masajes, manipulaciones vertebrales, terapia con vendas térmicas), terapias psicológicas (fisioterapia psicológicamente informada) y/o terapias complementarias (acupuntura).
4	Sugerir a los pacientes con dolor lumbar crónico terapias físicas (ejercicio, masaje, manipulación espinal), terapias psicológicas (terapia cognitivo-conductual) y/o terapias complementarias (yoga, acupuntura, taichí).
5	Iniciar tratamiento multidisciplinar del dolor, en el que se aborden aspectos físicos, psicológicos y sociales asociados al dolor lumbar.
6	Priorizar la atención del dolor lumbar sin medicación, salvo que sea imprescindible para el paciente.
7	Iniciar, cuando sea necesario, los tratamientos farmacológicos con antiinflamatorios no esteroideos a la dosis efectiva más baja durante el menor tiempo posible.
8	Evitar, en lo posible, la prescripción de opiáceos para el abordaje del dolor lumbar crónico.
9	Evitar ofrecer esteroides inyectables a pacientes con dolor lumbar crónico inespecífico.
10	Evitar cirugía a pacientes con dolor crónico inespecífico por fuera de un ensayo clínico controlado y aleatorizado.

3.1. Tratamientos no farmacológicos

Los tratamientos no farmacológicos están compuestos por terapias físicas, psicológicas y complementarias (Vlaeyen et al., 2018). En los últimos años, cada vez son más las guías de dolor que sugieren priorizar los tratamientos no farmacológicos sobre los farmacológicos (Knezevic et al., 2017). Esta tendencia se sustenta considerando las evidencias disponibles sobre los beneficios de los tratamientos no farmacológicos (Traeger et al., 2019) y sobre la preocupación creciente respecto a los posibles efectos nocivos a medio-largo plazo de algunos analgésicos, antinflamatorios y opioides (Dowel et al., 2016). Investigaciones recientes han demostrado que los programas de ejercicios supervisados, como el yoga, el taichí, el pilates y la actividad graduada, o los basados en terapias físicas o psicológicas son beneficiosos para la prevención (Steffens et al., 2016) y el tratamiento del dolor lumbar crónico (Hoffmann et al., 2016).

La atención no farmacológica debe proporcionar educación integral a los pacientes sobre las causas y los mecanismos del dolor, las estrategias de autogestión y las técnicas de autocuidado (Steffens et al., 2016). Concretamente, la educación en neurociencia del dolor se ha posicionado en los últimos años como una herramienta complementaria para ayudar a los pacientes a comprender el origen del dolor (Louw et al., 2016). Si los pacientes requieren cuidados más complejos, se recomienda que, adicionalmente, reciban terapias físicas, como masajes, manipulaciones vertebrales o ejercicios de relajación; psicológicas, como las intervenciones cognitivo-conductuales; y/o complementarias, como la acupuntura (Traeger et al., 2019). En este proceso, es fundamental conocer las necesidades individuales de cada paciente (Vlaeyen et al., 2018).

3.2. Tratamientos farmacológicos

Los tratamientos farmacológicos varían dependiendo de la causa subyacente y de la gravedad del dolor (Chou et al., 2017). El dolor lumbar inespecífico agudo (inferior a 3 meses de duración) y crónico (superior 3 meses de duración) se abordan con tratamientos farmacológicos diferentes (Vlaeyen et al., 2018), aunque ambos de forma escalonada o estratificada. Por ejemplo, en algunas guías de práctica clínica se recomienda prescribir una gama reducida de analgésicos o de relajantes musculares para el dolor lumbar agudo cuando las personas no responden a los tratamientos no farmacológicos sugeridos (Abdel-Shaheed et al., 2017). En estos casos, la primera opción consiste en utilizar una dosis baja de fármacos antiinflamatorios no esteroideos con la dosis efectiva más baja durante el menor tiempo posible (Qaseem et al.,

2017). En cambio, para el dolor lumbar crónico el uso de los fármacos antiinflamatorios no esteroideos debe acompañarse de un seguimiento continuo de los factores de riesgo de los trastornos gastrointestinales de los pacientes (Bernstein et al., 2017). En algunas guías, analgésicos opioides, como el tramadol, y antidepresivos, como la duloxetina, se recomiendan también como opciones farmacológicas de segunda línea cuando el dolor es crónico (Abdel-Shaheed et al., 2017). Los opioides se deben utilizar, exclusivamente, cuando los beneficios potenciales superan los riesgos individuales (Bernstein et al., 2017).

La pauta farmacológica específica para los pacientes con dolor lumbar crónico está sujeta a la valoración y al seguimiento médico del especialista responsable (Knezevic et al., 2017). Los fármacos que se suelen prescribir con más frecuencia en población con dolor lumbar crónico son los analgésicos, los antiinflamatorios no esteroideos, los antiepilépticos, los opioides y/o los antidepresivos (Migliorini et al., 2021). Las pautas farmacológicas de los centros se adaptan a las guías clínicas definidas por los sistemas de salud nacional (Traeger et al., 2019). Aunque existen unas directrices generales para el manejo farmacológico del dolor crónico, las pautas pueden variar dependiendo de la normativa vigente en cada contexto (Urits et al., 2019).

3.3. Tratamiento habitual

En España, contexto en el que se desarrolla el ensayo clínico controlado y aleatorizado vinculado a esta tesis doctoral, los médicos de familia y los reumatólogos suelen manejar el dolor crónico en consultas periódicas (Dueñas et al., 2015). Este tratamiento habitual incluye medicación (analgésicos, ansiolíticos, antiinflamatorios, opioides y/u antidepresivos), psicoeducación y sugerencias de ejercicio aeróbico (Ángel-García et al., 2015).

4. Terapias psicológicas cognitivo-conductuales

4.1. Aspectos generales

El término terapias cognitivo-conductuales hace referencia a un conjunto de intervenciones psicológicas transdiagnósticas con una amplia evidencia empírica (Hofmann et al., 2012). Tradicionalmente, el objetivo principal de estas intervenciones ha consistido en la reducción de los síntomas, en el aumento de la capacidad funcional y en la mejora de la calidad de vida (Hayes et al., 2016). Para cumplir con este propósito, estas terapias se han centrado en reconocer e intervenir la asociación entre las cogniciones, las emociones y las conductas de las personas (Karyotaki et al., 2017). En general, el enfoque de estas terapias parte de un protocolo adaptable en función de las necesidades concretas del paciente, así como de su condición de salud (Wright et al., 2017). El contenido genérico de las terapias cognitivo-conductuales tradicionales se presenta en la Tabla 6.

Tabla 6. Contenido genérico de las terapias cognitivo-conductuales tradicionales. Elaboración propia.

Contenido	Objetivo
Identificación de pensamientos negativos o distorsionados	• Reconocer los patrones de pensamiento negativos o distorsionados que contribuyen al desarrollo de problemas emocionales o comportamentales (Friedberg y Thordarson, 2017).
Reestructuración cognitiva	• Remplazar pensamientos automáticos negativos (como los pensamientos catastrofistas o de autodesvalorización) o creencias irracionales por pensamientos adaptativos o racionales (Wright et al., 2017).
Desarrollo de estrategias de afrontamiento	• Enseñar estrategias de afrontamiento efectivas para manejar los problemas emocionales, incluyendo técnicas de relajación, respiración profunda y resolución de problemas (Lorenzo-Luaces et al., 2016).
Establecimiento de metas y seguimiento	• Definir metas específicas y medibles a corto, medio y largo plazo para trabajar hacia el cambio deseado en el paciente (Hofmann et al., 2012).

Las terapias cognitivo-conductuales, propuestas originalmente por Beck (1970) y Ellis (1962), se han utilizado para tratar una amplia variedad de condiciones de salud, como los trastornos de ansiedad (Carpenter et al., 2018), del estado del ánimo (Păsărelu et al., 2017), de la alimentación (Linardon et al., 2017), del sueño (Ho et al., 2016) y de la personalidad (Hoppen et al., 2021), en diversos grupos poblacionales, como los niños, los adolescentes y los adultos. Debido a su carácter transdiagnóstico, estas terapias han demostrado ser eficaces tanto en población clínica (es decir, personas que están recibiendo tratamiento médico debido a una condición de salud específica) como población no clínica (es decir, personas que no están recibiendo tratamiento médico debido a una condición de salud específica). Estas intervenciones, además, se han administrado en diferentes modalidades (individuales y grupales) y formatos (presencial, internet, telefónico e híbridos), en los que se han utilizado protocolos (breves o completos) combinados o no con componentes de otras terapias (Carpenter et al., 2018).

A lo largo de la historia, estas terapias han ajustado sus técnicas y sus enfoques según las evidencias recopiladas (Hayes y Hofmann, 2017). Actualmente, se identifican 3 generaciones (u olas) principales para diferenciar los fundamentos y los conceptos centrales de las terapias cognitivo-conductuales (Hayes et al., 2016). La primera generación de estas intervenciones (conocidas como terapias conductuales y desarrolladas en los años 40-50) se centró en la aplicación de los principios de aprendizaje para modificar conductas manifiestas; la segunda generación (conocidas como terapias cognitivo-conductuales y desarrolladas en los años 60-70) en intervenir los patrones de pensamiento no adaptativos que influyen en la emoción y el comportamiento; y la tercera generación (conocidas como terapias contextuales y desarrolladas en los años 80-90) en tratar los procesos contextuales que interactúan con los pensamientos, las emociones y las conductas de las personas (Hayes y Hofmann, 2017). Las terapias de tercera generación incluyen intervenciones como la Terapia de Aceptación y Compromiso -en adelante, ACT- (Hayes et al., 1999), la Terapia de Activación Conductual -en adelante, TAC- (Jacobson et al., 1996), la Terapia Cognitiva basada en Mindfulness (Segal et al., 2002), la Terapia Dialéctico Conductual (Linehan, 1993) y la Psicoterapia Analítica Funcional (Kohlenberg y Tsai, 1991), entre otras.

Aunque las bases siguen en progreso, desde hace más de una década algunos autores han mencionado que se aproxima una cuarta generación de terapias cognitivo-conductuales (Callaghan y Darrow, 2015). A diferencia de las terapias de tercera generación, que se centran

en la intervención de los procesos contextuales que interactúan con el malestar psicológico de las personas, esta nueva generación busca integrar las evidencias de los diferentes enfoques terapéuticos para atender de forma personalizada las necesidades individuales de los pacientes (Abreu y Abreu, 2017). Esta generación -aún en desarrollo- engloba una variedad de enfoques terapéuticos recientes (Callaghan y Darrow, 2015).

Finalmente, las terapias basadas en procesos -que en los últimos años han generado un interés creciente en la comunidad científica y clínica- se centran específicamente en los procesos terapéuticos facilitadores del cambio (Hayes et al., 2020). Estas terapias son una concreción de la perspectiva biopsicosocial y se fundamentan en la evidencia de factores etiológicos, factores de cronificación y factores terapéuticos transdiagnósticos. A su vez, implican una superación de criterios diagnósticos y terapéuticos categoriales, sustituyéndolos por una perspectiva dimensional (Hayes et al., 2020). La aceptación, el compromiso, la flexibilidad cognitiva, la atención plena, la activación conductual, la (auto)compasión y la autorregulación emocional, entre otros, son componentes centrales de los modelos psicológicos en los que se soportan estas terapias (Hayes y Hofmann, 2017).

4.2. Eficacia de las terapias cognitivo-conductuales para el dolor crónico

Según la División 12 de la Asociación Americana de Psicólogos, las terapias cognitivo-conductuales se constituyen como el estándar de calidad para el abordaje psicológico del dolor crónico (Hartvigsen et al., 2018). La evidencia disponible señala que muchos factores psicológicos de riesgo para el mantenimiento (Vlaeyen et al., 2018) y la cronificación del dolor lumbar (Linton y Shaw, 2011) están asociados con procesos emocionales (estrés), cognitivos (catastrofización o autoeficacia) o conductuales (comportamientos de evitación). Concretamente, en el campo del dolor, este tipo de intervenciones contribuyen a abordar los factores psicológicos subyacentes al malestar emocional, la percepción de incapacidad, las distorsiones cognitivas y las conductas desadaptativas (Richmond et al., 2015).

Los efectos de las terapias cognitivo-conductuales se han estudiado en poblaciones con diferentes diagnósticos de dolor (Williams et al., 2020), como la fibromialgia (Gilpin et al., 2017), el dolor lumbar crónico (Cherkin et al., 2016), el dolor musculoesquelético crónico (Yarns et al., 2020) o la artritis reumatoide (Shen et al., 2020), entre otros. De forma consistente, distintos metaanálisis han aportado evidencia de que las terapias cognitivo-

conductuales, de segunda y tercera generación, son más beneficiosas para el abordaje del dolor que el tratamiento habitual, especialmente para la mejora de:

- La intensidad del dolor (Gandy et al., 2022; Lai et al., 2023; Ma et al., 2023; Trindade et al., 2021; Rosser et al., 2023; Veehof et al., 2016; Williams et al., 2020; Yang et al., 2022).
- La interferencia del dolor (Trindade et al., 2021; Veehof et al., 2016).
- La capacidad física (Gandy et al., 2022; Lai et al., 2023; Ma et al., 2023; Rosser et al., 2023; Veehof et al., 2016; Williams et al., 2020; Yang et al., 2022).
- Los síntomas de depresión (Gandy et al., 2022; Hughes et al., 2017; Lai et al., 2023; Ma et al., 2023; Pei et al., 2021; Trindade et al., 2021; Veehof et al., 2016).
- Los síntomas de ansiedad (Gandy et al., 2022; Hughes et al., 2017; Lai et al., 2023; Ma et al., 2023; Trindade et al., 2021; Veehof et al., 2016).
- La autoeficacia (Gandy et al., 2022; Yang et al., 2022).
- La calidad de vida (Lai et al., 2023; Ma et al., 2023; Veehof et al., 2016).
- La aceptación ante el dolor (Hughes et al., 2017; Ma et al., 2023; Trindade et al., 2021).
- La flexibilidad psicológica (Hughes et al., 2017; Trindade et al., 2021).

A pesar de que los efectos de estas terapias varían dependiendo del tipo de intervención (terapias cognitivo-conductuales tradicionales o terapias contextuales), del formato de administración (presencial, internet, telefónico e híbridos), de los componentes (combinadas o no con otro tipo de intervenciones) y de las variables exploradas (primarias, secundarias y de procesos), en general sus tamaños de efecto son moderados tras la intervención, con una disminución progresiva en el seguimiento (Martínez-Calderón et al., 2023). En la Tabla 7 se presenta una síntesis de los metaanálisis más recientes en población con dolor crónico.

Tabla 7. Efectos de las terapias cognitivo-conductuales en población con dolor crónico. Elaboración propia.

Autores	Intervención	Estudios incluidos	Población	Resultados
Rosser et al. (2023)	Terapias cognitivo-conductuales y ACT administradas remotamente versus tratamiento habitual.	32 ensayos clínicos controlados y aleatorizados.	Pacientes adultos con dolor crónico (sin incluir dolor de cabeza).	Las terapias cognitivo-conductual fueron superiores al tratamiento habitual en la mejora de la intensidad del dolor (*DME* = -0,28) y de la capacidad física (*DME* = -0,38) tras la intervención, pero no en el seguimiento. No se encontraron diferencias significativas en la calidad de vida tras la intervención y el seguimiento.
Ma et al. (2023)	ACT versus tratamiento habitual.	21 ensayos clínicos controlados y aleatorizados.	Pacientes adultos con dolor crónico.	Las ACT fueron significativamente superiores al tratamiento habitual en la mejora de la aceptación del dolor (*DME* = 0,67), de la calidad de vida (*DME* = 0,43), de la capacidad física (*DME* = -0,88), de la intensidad del dolor (*DME* = -0,45), de la ansiedad (*DME* = -0,35) y de la depresión (*DME* = -0,74) tras la intervención.
Lai et al. (2023)	ACT versus tratamiento habitual.	33 ensayos clínicos controlados y aleatorizados.	Pacientes adultos con dolor crónico.	Las ACT fueron significativamente superiores al tratamiento habitual en la mejora de la intensidad del dolor (*g* = 0,44 a 0,34), de la capacidad física (*g* = 0,59 a 0,56), de la depresión (*g* = 0,43), de la ansiedad (*g* = 0,43 a 0,35) y de la calidad de vida (*g* = 0,45 a 0,43) tras la intervención y el seguimiento.

Gandy et al. (2022)	Terapias cognitivo-conductuales administradas por internet versus otras terapias psicológicas.	36 ensayos clínicos y controlados aleatorizados.	Pacientes adultos con dolor crónico.	Las terapias cognitivo-conductuales administradas por internet fueron significativamente superiores al tratamiento habitual en la mejora de la discapacidad (g = 0,28), la depresión (g = 0,43), la ansiedad (g = 0,32), intensidad del dolor (g = 0,27), la autoeficacia (g = 0,39) y el catastrofismo ante el dolor (g = 0.31). No se encontraron diferencias entre las terapias cognitivo-conductuales tradicionales frente a la ACT.
Yang et al. (2022)	Terapias cognitivo-conductuales tradicionales versus otras terapias psicológicas.	22 ensayos clínicos y controlados aleatorizados.	Pacientes adultos con dolor lumbar crónico.	Las terapias cognitivo-conductuales tradicionales fueron significativamente superiores a otras terapias en la mejora de la discapacidad (*DME* = -0,44), el dolor (*DME* = -0,32), la evitación del miedo (*DME* = -1,24) y la autoeficacia (*DME* = 0,27) tras la intervención, pero no en el seguimiento.
Pei et al. (2021)	Terapias Cognitivas basadas en Mindfulness versus el tratamiento habitual y otras terapias psicológicas.	8 ensayos clínicos y controlados aleatorizados.	Pacientes adultos con dolor lumbar crónico.	Las Terapias Cognitivas basadas en Mindfulness fueron significativamente superiores al tratamiento habitual en la mejora de la depresión (*DME* = -0,72) y del mindfulness (*DME* = 0,51) tras la intervención, pero no en el seguimiento. No se encontraron diferencias significativas en la intensidad del dolor, la inferencia del dolor y la aceptación del dolor tras la intervención y el seguimiento. En comparación con otras

				terapias psicológicas tampoco se encontraron diferencias significativas.
Trindade et al. (2021)	ACT versus tratamiento habitual y otras terapias.	5 ensayos clínicos aleatorizados.	Pacientes adultos con dolor crónico.	Las ACT fueron significativamente superiores al tratamiento habitual y otras terapias en la mejora de la interferencia del dolor (*DME* = -0,50 a -0,69), de la intensidad del dolor (*DME* = 0,14 a 0,21), de la aceptación del dolor (*DME* = 0,63 a 0,55), de la flexibilidad psicológica (*DME* = -0,43 a -0,48), de la acción basada en valores (*DME* = 0,19 a 0,10), del mindfulness (*DME* = 0,29 a 0,33), de la depresión (*DME* = -0,40 a -0,37) y de la ansiedad (*DME* = -0,22 a -0,24) tras la intervención y el seguimiento.
Williams et al. (2020)	Terapias cognitivo-conductuales tradicionales, TACD y ACT versus tratamiento habitual y otras terapias.	59 ensayos clínicos controlados y aleatorizados basados en terapias cognitivo-conductuales tradicionales, 8 en TAC y 5 en ACT.	Pacientes adultos con dolor crónico (sin incluir dolor de cabeza).	Las terapias cognitivo-conductuales tradicionales fueron significativamente superiores a otras terapias en la mejora de la discapacidad (*DME* = -0,12), del dolor (*DME* = -0,09) y del malestar psicológico (*DME* = -0,09) tras la intervención, pero no en el seguimiento. Fueron superiores, también, al tratamiento habitual en la mejora de la discapacidad (*DME* = -0,32), del dolor (*DME* = -0,22) y del malestar psicológico (*DME* = -0,34) tras la intervención, manteniéndose estos efectos en el seguimiento.

				No se encontraron diferencias significativas favorables a la TAC en comparación con otras terapias en la mejora de la discapacidad (*DME* = -0,65), del dolor (*DME* = -0,67) y del malestar psicológico (*DME* = -0,73). Tampoco en la comparación con el tratamiento habitual en la mejora de la discapacidad (*DME* = -0,02), del dolor (*DME* = -0,08) y del malestar psicológico (*DME* = -0,22). No se encontraron diferencias significativas favorables a la ACT en comparación con otras terapias en la mejora de la discapacidad (*DME* = -0,67), del dolor (*DME* = -0,25) y del malestar psicológico (*DME* = -0,30). Sin embargo, aunque con solo dos evidencias disponibles, la ACT fue significativamente superior que el tratamiento habitual en la mejora del dolor (*DME* = -0,83), pero no de la discapacidad (*DME* = -1,39) o del malestar psicológico (*DME* = -1,16) tras la intervención.
Hughes et al. (2017)	ACT versus tratamiento habitual y otras terapias.	11 ensayos clínicos aleatorizados.	Pacientes adultos con dolor crónico.	Las ACT fueron significativamente superiores al tratamiento habitual en la mejora de la aceptación del dolor (*DME* = 0,84 a 0,53), de la flexibilidad psicológica (*DME* = -0,87 a -0,65),

				de la depresión (*DME* = -0,84 a -0,52) y de la ansiedad (*DME* = -0,57 a -0,32) tras la intervención y el seguimiento.
Veehof et al. (2016)	Terapias basadas en la aceptación y el mindfulness versus tratamiento habitual y otras terapias.	25 ensayos clínicos controlados y aleatorizados.	Pacientes adultos con dolor crónico.	Las terapias basadas en la aceptación y el mindfulness fueron significativamente superiores a otras terapias y al tratamiento habitual en la mejora de la intensidad del dolor (*DME* = 0,24 a 0,41), la interferencia del dolor (*DME* = 0,62 a 1,05), la capacidad física (*DME* = 0,40 a 0,39), la depresión (*DME* = 0,43 a 0,50), la ansiedad (*DME* = 0,51 a 0,57) y la calidad de vida (*DME* = 0,44 a 0,66) tras la intervención y el seguimiento.

Nota. *g* = g de Hedges; *DME*: diferencias de medias estandarizadas.

4.3. Terapias cognitivo-conductuales de tercera generación para el dolor crónico

En los últimos años, han sido cada vez más los clínicos y los investigadores que han señalado tanto el potencial terapéutico (Vowles et al., 2020) como la eficiencia de las terapias de tercera generación (Feliu-Soler et al., 2018). En concreto, se ha destacado que las terapias basadas en la aceptación, como la ACT (Hayes et al., 1999), y en la activación conductual, como la TAC (Jacobson et al., 1996), son beneficiosas debido a su capacidad para promover la aceptación del dolor, mejorar las alteraciones emocionales, reducir las conductas de evitación, fortalecer el compromiso de los pacientes con sus valores y proporcionar herramientas prácticas para el manejo del dolor crónico (McCracken et al., 2022).

En general, las nuevas formas de terapias cognitivo-conductuales amplían y fortalecen los supuestos críticos de la terapia cognitivo conductual tradicional, animando a los pacientes a realizar actividades significativas y gratificantes incluso en presencia de dolor (Walsh et al., 2022). Aunque comparten el mismo enfoque empírico, estos nuevos métodos ponen más atención a los aspectos contextuales y experienciales que facilitan los procesos de cambio que a la reducción de los síntomas de las personas (McCracken et al., 2022). Priorizan, además, la promoción holística de la salud y el bienestar, siendo sensibles al contexto y a las funciones de los fenómenos psicológicos y se orientan a la construcción de repertorios amplios, flexibles y eficaces en lugar de adoptar un enfoque eliminativo de problemas definidos (McCracken, 2023).

5. Terapia de Aceptación y Compromiso

5.1. Origen y objetivo

Hayes et al. (1999) desarrollaron la ACT entre los años 80 y 90. Esta terapia, basada en la filosofía del contextualismo funcional -concretamente en la teoría de los marcos relacionales (Hayes et al., 2004)- propone que la conducta humana debe entenderse en su contexto y no de forma aislada (Hayes, 2004). Explora, además, la función que tienen las conductas, las emociones y los pensamientos de las personas en el contexto específico en el que acontecen para, de esta manera, reconocer su significado (Hayes et al., 1999). La teoría de los marcos relacionales, que sostiene que las estructuras mentales generan asociaciones contextuales entre estímulos y eventos, cumple un papel fundamental en el desarrollo de la flexibilidad psicológica en las personas (Hayes, 2004).

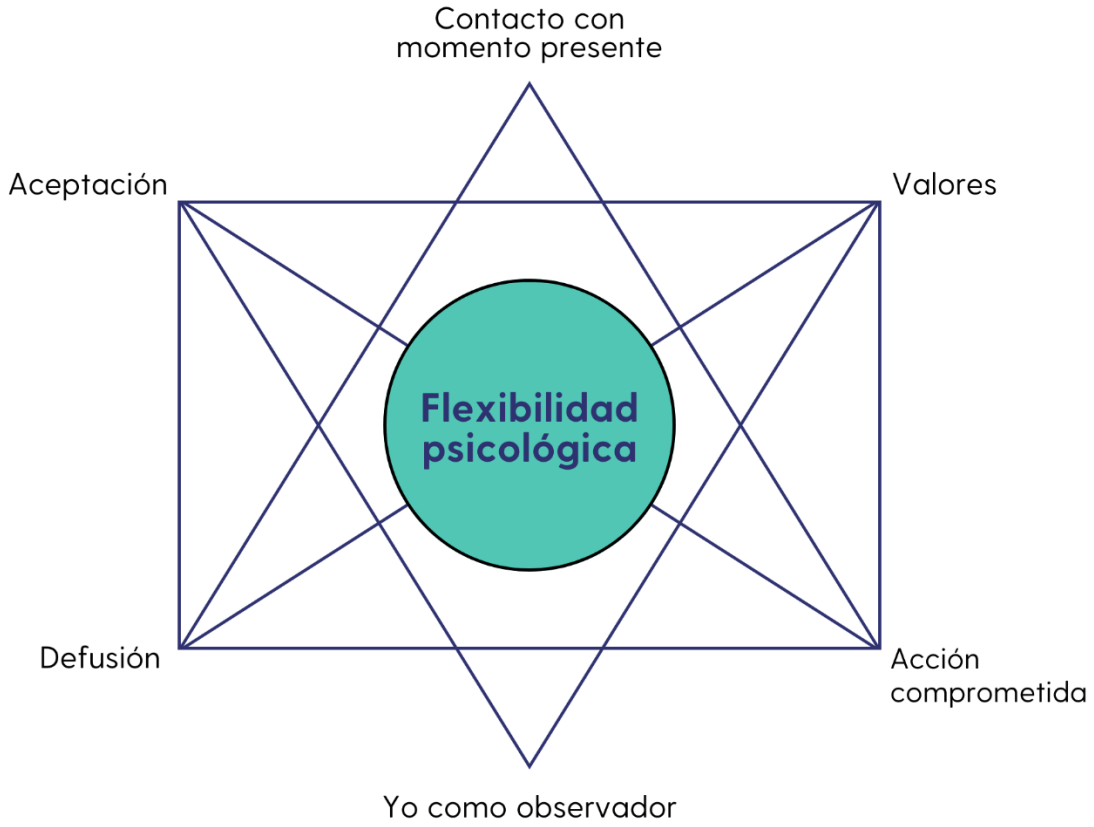
Originalmente, esta terapia surgió como una alternativa para superar las limitaciones de las terapias cognitivo-conductuales tradicionales para abordar ciertos problemas de salud (Hayes et al., 2004). En los fundamentos de esta terapia se proponía que el sufrimiento humano era consecuencia de la evitación y la lucha contra las experiencias internas (Hayes, 2004). Además, se fomentaba la aceptación de las experiencias no deseadas y el compromiso con la acción dirigida a objetivos y basada en valores (Hayes et al., 1999). En la actualidad, el objetivo de esta terapia no consiste en cambiar las experiencias internas, sino en promover habilidades de aceptación que permitan comportamientos basados en valores en presencia de experiencias desagradables (Hayes, 2004). Para ello, se centra especialmente en promover la flexibilidad psicológica como un mecanismo clave del cambio (McCracken et al., 2022).

5.2. Mecanismos psicológicos

La flexibilidad psicológica es el concepto central de la ACT (Hayes et al., 2004). Este constructo se define como la capacidad de adaptarse y de responder a los diferentes desafíos de la vida (Hayes, 2004). La flexibilidad psicológica implica estar en contacto con el momento presente, experimentar sin juicios los pensamientos y emociones, actuar en consonancia con los valores personales y reducir la evitación experiencial (Biglan et al., 2008). Esto conlleva a aceptar las experiencias internas positivas y negativas, así como comprometerse con las metas y los valores personales (Hayes, 2004). De acuerdo con la filosofía de la ACT, esta habilidad se puede desarrollar mediante el entrenamiento de 6 procesos psicológicos (Hayes et al., 2004). Estos procesos se representan en un diagrama hexagonal, conocido en la comunidad científica

y clínica como el modelo *hexaflex*. En la Figura 5 se presentan los componentes de este modelo (Rolffs et al., 2018).

Figura 5. Procesos psicológicos que integran la flexibilidad psicológica. Adaptado y traducido de Rolffs et al. (2018).



Los procesos psicológicos expuestos en el modelo *hexaflex* son fundamentales para promover la flexibilidad psicológica en las personas (Hayes et al., 2022). Estos son: (1) el contacto con el momento presente, que es la capacidad de estar plenamente presente en el aquí y el ahora, sin dejarse llevar por preocupaciones pasadas o futuras; (2) los valores, que es la capacidad de identificar y comprometerse con los valores personales que guían la toma de decisiones sobre aspectos significativos de la vida de las personas; (3) la acción comprometida, que es la capacidad de tomar decisiones alineadas con los valores personales, incluso en momentos complejos; (4) el yo como observador, que es la capacidad que tienen las personas para verse a sí mismas desde una perspectiva más amplia y objetiva, siendo flexibles con sus experiencias

internas; (5) la defusión, que es la capacidad de desvincular de los pensamientos de las emociones, procesándolos como eventos mentales y no como realidades objetivas; y (6) la aceptación, que es la capacidad de reconocer y permitir las experiencias internas (pensamientos y emociones) sin luchar contra ellas.

5.3. Protocolo de intervención

La ACT es una intervención enfocada en objetivos terapéuticos específicos (Hayes et al., 1999). El número de sesiones varía dependiendo de las necesidades individuales de los pacientes y de las metas terapéuticas (Hayes, 2004). Aplicadas de forma grupal, se recomiendan incorporar un mínimo de 8 sesiones, en las que se aborden los 6 procesos psicológicos asociados a la flexibilidad psicológica (Rolffs et al., 2018). El ensayo clínico en el que se enmarca esta tesis doctoral se basó en el protocolo de intervención de la ACT propuesto por Vowles et al. (2008). En la Tabla 8 se presenta una descripción de los componentes abordados durante la intervención.

Tabla 8. Componentes abordados en la ACT, adaptada según el protocolo propuesto por Vowles et al. (2008).

Sesión	Componente	Módulos
1	Psicoeducación	• Fundamentos de la ACT. • Avances científicos en el manejo de los síntomas relacionados con el dolor crónico. • Teorías psicológicas relacionadas con el dolor y el sufrimiento. • Reconocimiento de factores estresores. • Identificación de valores personales. • Exposición de ejercicios de relajación.
2	Análisis de valores 1	• Problemas ocasionados por la evitación experiencial. • La desesperanza creativa a través de metáforas: el control es el problema y no la solución. • Ansiedad, lucha y huida, y sus efectos. • Aceptar el riesgo del viaje vital: experiencias, sentimientos y emociones.

3	Análisis de valores 2	• Leyes del pensamiento y consecuencias del lenguaje. • Mente y desactivación del pensamiento (fusión cognitiva): crear distancia con los pensamientos. • Aprendizaje de técnicas y efectos de la meditación. • Práctica de ejercicios de meditación.
4	Análisis de valores 3	• Barreras y obstáculos psicológicos. • Estrés emocional y sus consecuencias. • Fenómenos emocionales, variables de personalidad y estados de salud. • Descubriendo compromisos con acciones comprometidas.
5	Valores y sentimientos	• Tomar la iniciativa con un "Plan de acción y voluntad". • Flexibilidad psicológica, resiliencia y automotivación. • Ejercicios de expansión y exploración corporal. • Aprender a relajarse.
6	Tomar una dirección	• El yo como contexto, proceso y contenido. • Conciencia del presente: "aquí y ahora". • El cerebro y las emociones: gestión de situaciones y respuestas emocionales abrumadoras.
7	Atrévete y cambia	• Voluntad y determinación. • Autoconocimiento, asertividad y autoestima. • Ejercicios de expansión experiencial: sensaciones sentidas. • La felicidad según la psicología positiva. • Beneficios del ejercicio físico: el movimiento.
8	Avanzando	• Preparado para actuar: mente, cuerpo, pensamientos y sentimientos. • Resumir los conceptos, conclusión y evaluación.

5.4. Evaluación clínica

Esta terapia ha demostrado ser eficaz en población con depresión (Zhao et al., 2023), con ansiedad (Ferreira et al., 2022), con trastorno obsesivo compulsivo (Soondrum et al., 2022),

con trastorno de estrés postraumático (Benfer et al., 2021), con trastornos neurológicos (Han et al., 2023), con trastorno bipolar (Burgos et al., 2022), con trastornos de la conducta alimentaria (Di Sante et al., 2022), con insomnio (Ruan et al., 2022), con adicciones (Lee et al., 2015), con psicosis (Louise et al., 2018), con dolor crónico (Lai et al., 2023), con diabetes (Sakamoto et al., 2022), con cáncer (Fang et al., 2023), con tinitus (Ungar et al., 2023) y con otras condiciones de salud (Herbert et al., 2022). La evidencia empírica indica efectos positivos de esta terapia en el fortalecimiento de los 6 procesos psicológicos relacionados con la flexibilidad psicológica (Han y Kim, 2022). Recientemente, en el campo del dolor crónico, un estudio de síntesis -que integró las evidencias de todos los metaanálisis disponibles hasta la fecha- ha demostrado que esta terapia mejora los síntomas de depresión, los síntomas de ansiedad, el catastrofismo ante el dolor, la aceptación y la flexibilidad psicológica (Martínez-Calderón et al., 2023).

5.5. Evaluación económica

En la última década, ha existido un interés creciente por conocer la eficiencia de la ACT en población diagnosticada con dolor crónico (Aasdahl et al., 2023; Kemani et al., 2015; Luciano et al., 2017) o con trastornos psicológicos (Aasdahl et al., 2023; Finnes et al., 2017; Risør et al., 2022; Witlox et al., 2022). Desde 2015 (primer estudio publicado) hasta 2023 (último estudio publicado), 6 estudios han explorado la relación coste-efectividad de esta terapia respecto a controles activos y/o inactivos. En general, las evaluaciones económicas disponibles en la actualidad señalan que la ACT es coste-efectiva en comparación al tratamiento habitual (Finnes et al., 2017; Luciano et al., 2017; Risør et al., 2022) y a otros tratamientos, como la relajación (Kemani et al., 2015). Aunque se requieren más evidencias, no se ha demostrado una dominancia significativa en las ratios de coste-efectividad incrementales de esta terapia respecto a la terapia cognitivo-conductual tradicional (Witlox et al., 2022) y a la rehabilitación ocupacional multimodal (Aasdahl et al., 2023). En la Tabla 9 se reportan los resultados de las evaluaciones económicas disponibles de la ACT en la actualidad.

Tabla 9. Evidencias sobre la eficiencia de la ACT. Elaboración propia.

Autores	Población	Resultados
Aasdahl et al. (2023)	Ensayo clínico controlado y aleatorizado en el que participaron 164 pacientes en situación de baja por trastornos musculoesqueléticos o mentales comunes (79 recibieron ACT y 85 rehabilitación ocupacional multimodal).	Los costes sanitarios totales fueron 12057 € inferiores en la ACT en comparación con la rehabilitación ocupacional multimodal. La diferencia en pérdidas de producción fue 14725 € inferior en la rehabilitación ocupacional multimodal en comparación con la ACT. Una diferencia de 43 días laborables, a favor de la rehabilitación ocupacional multimodal, dio una razón coste-efectividad incremental de 278 € por un día laborable, inferior al coste de un día de producción (339 €). El beneficio social neto fue de 2667 € durante 2 años de seguimiento. Los cocientes de coste-efectividad incrementales de la rehabilitación ocupacional multimodal fueron dominantes respecto a la ACT.
Risør et al. (2022)	Ensayo clínico controlado y aleatorizado en el que participaron 101 pacientes diagnosticados de ansiedad (53 recibieron ACT y 48 tratamiento habitual con psicoeducación).	No se detectaron diferencias significativas en los costes sanitarios entre la ACT y el tratamiento habitual con psicoeducación; sin embargo, la ACT mostró mejores resultados en todas las variables evaluadas. Desde el punto de vista sanitario, la ACT se asoció con una relación coste-efectividad incremental de 33 € por caso adicional de mejoría clínicamente significativa en comparación con el tratamiento habitual con psicoeducación. Los cocientes de coste-efectividad incrementales de la ACT fueron dominantes respecto al tratamiento habitual con psicoeducación.
Witlox et al. (2022)	Ensayo clínico controlado y aleatorizado en el que	La ACT se asoció con una reducción media de los costes totales por participante de 466 en

	participaron 314 pacientes diagnosticados de ansiedad (150 recibieron ACT y 164 terapia cognitivo-conductual tradicional).	comparación con la terapia cognitivo-conductual tradicional. Desde el punto de vista de la asistencia sanitaria, la ACT se asoció con costes más elevados (71 € por paciente) que la terapia cognitivo-conductual tradicional. No se evidenció una dominancia significativa de la ACT respecto a la terapia cognitivo-conductual tradicional.
Luciano et al. (2017)	Ensayo clínico controlado y aleatorizado en el que participaron 156 pacientes con fibromialgia (51 recibieron ACT, 52 tratamiento farmacológico recomendado y 53 estaban en lista de espera).	La ACT (*M* = 824 €, *DE* = 1063 €) se relacionó con costes directos significativamente menores en comparación con el tratamiento farmacológico recomendado (*M* = 1731 €, *DE* = 1657 €) y con la lista de espera (*M* = 2463 €, *DE* = 2822 €). Los cocientes de coste-utilidad y coste-efectividad incrementales de la ACT fueron dominantes en los análisis de sensibilidad.
Finnes et al. (2017)	Ensayo clínico controlado y aleatorizado en el que participaron 352 pacientes en situación de baja por trastornos mentales (89 recibieron ACT, 87 intervención de diálogo en el lugar de trabajo, 88 ACT junto a intervención de diálogo en el lugar de trabajo y 88 tratamiento habitual).	En los 4 grupos se obtuvieron mejoras significativas en la calidad de vida relacionada con la salud. No hubo diferencias significativas en la calidad de vida relacionadas con la salud o los costes entre los grupos. La probabilidad de rentabilidad de la ACT junto a la intervención de diálogo en el lugar de trabajo fue del 50% en comparación con la ACT sola. Ambas alternativas de tratamiento se consideraron igualmente favorables para los responsables de la toma de decisiones.
Kemani et al. (2015)	Ensayo clínico controlado y aleatorizado en el que participaron 60 pacientes con dolor crónico (30 recibieron ACT	En comparación con el tratamiento basado en la relajación, la ACT mostró mejores resultados en todas las variables evaluadas. Los análisis económicos mostraron que la

	y 30 tratamiento basado en la relajación).	ACT era más rentable que el tratamiento basado en la relajación en la evaluación posterior y a los 3 meses de seguimiento, pero no a los 6 meses de seguimiento. En general, los cocientes de coste-efectividad incrementales de la ACT fueron dominantes respecto al tratamiento basado en la relajación.

6. Terapia de Activación Conductual

6.1. Origen y objetivo

Jacobson et al. (1996) desarrollaron la TAC entre los años 70 y 80. Esta terapia, basada en la filosofía del contextualismo funcional, propone que la depresión se debe entender reconociendo el contexto específico de las personas (Walsh et al., 2022). Según los fundamentos de esta terapia, las intervenciones deben actuar sobre el contexto que provoca la respuesta emocional, así como sobre la función concreta que ejerce la conducta en la persona (Hopko et al., 2016). Los principios de la TAC indican que las personas con depresión desarrollan una serie de comportamientos evitativos ante la falta de refuerzos positivos (Martell et al. 2021); estos comportamientos, a su vez, generan una interrupción sobre las actividades gratificantes, reforzando pensamientos de rumiación que contribuyen a la pérdida de interés, a la disminución del estado de ánimo y al aislamiento social (Twyman, 2007).

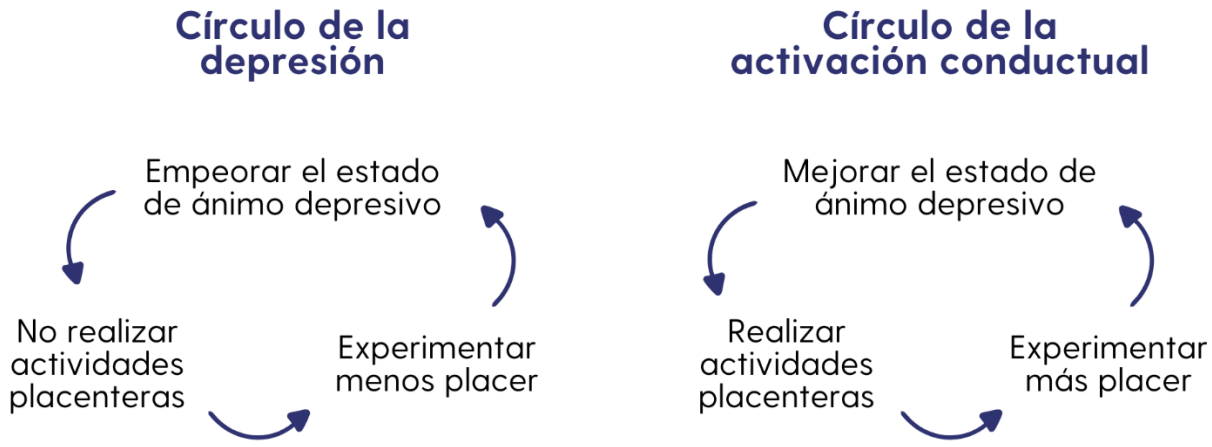
Esta terapia se originó a partir de una exploración experimental de la teoría de cambio propuesta por Beck y colaboradores (Martell et al., 2001). En este experimento se analizaron los efectos del componente conductual de la terapia cognitivo-conductual en comparación a los de la versión completa de esta misma terapia en una muestra de pacientes con depresión mayor (Jacobson et al., 1996). Los hallazgos señalaron que incorporando únicamente las técnicas de modificación conductual en los pacientes se obtenía el mismo nivel de mejoría que en la terapia completa (Martell et al., 2001). Este estudio permitió concluir que las técnicas cognitivas -aunque relevantes para el abordaje de otras condiciones de salud- no eran imprescindibles para el tratamiento de la depresión (Twyman, 2007). Contribuyó, también, para considerar esta terapia como un enfoque independiente para el abordaje de la depresión y de otros trastornos del estado de ánimo (Jacobson et al., 1996).

En la actualidad, el objetivo de la TAC no consiste en modificar las cogniciones y las emociones para que las personas cambien sus conductas, sino en promover actividades gratificantes conectadas con los valores de las personas que actúen como reforzadores (Jacobson et al., 1996). Para cumplir con este propósito, se centra especialmente en promover la activación conductual como un mecanismo clave para romper el ciclo de inactividad que contribuye a la depresión (Martell et al., 2021).

6.2. Mecanismos psicológicos

La activación conductual es el concepto central de la TAC (Jacobson et al., 1996). Este constructo se define como los intentos estructurados de una persona para aumentar las conductas que le permiten contactar con contingencias ambientales reforzantes (Hopko et al., 2016); estas conductas, a su vez, generan mejoras en los pensamientos, en el estado de ánimo y en la calidad de vida (Walsh et al., 2022). La activación conductual implica reconocer y superar patrones de evitación que podrían estar presentes en la depresión (Martell et al., 2001), así como participar progresivamente en actividades gratificantes (sociales, recreativas, laborales u otras) como una forma de mejorar el estado de ánimo (Martell et al., 2021). Existe evidencia de que la activación conductual es un constructo nuclear en el tratamiento de la depresión (Stein et al., 2021). En la Figura 6 se visualiza la conexión entre la activación conductual y la depresión (Lewinsohn, 1974).

Figura 6. Relación entre la activación conductual y la depresión. Adaptado y traducido de van Genugten et al. (2021).



6.3. Protocolo de intervención

La TAC es una intervención enfocada en objetivos terapéuticos específicos (Martell et al., 2001). El número de sesiones fluctúa según las necesidades individuales de los pacientes y de las metas terapéuticas definidas (Lejuez et al., 2001). Implementadas de forma grupal, se sugiere incorporar un mínimo de 8 sesiones en la versión completa (Hopko et al., 2003) y de 3 a 5 sesiones en la versión breve (Lejuez et al., 2011), en las que se aborden gradualmente

dominios relacionados con la activación conductual (Lejuez et al., 2001). En la Tabla 10 se presenta una descripción de los componentes abordados durante la intervención.

Tabla 10. Componentes abordados en la TAC, adaptada según el protocolo propuesto por Lejuez et al. (2001).

Sesión	Componente	Módulos
1	Psicoeducación	• Fundamentos de la TAC. • Evidencias sobre la utilidad de esta intervención para pacientes con síntomas de depresión. • Recolección información inicial acerca de las áreas de actividad y los contextos de interacción de los pacientes. • Entrega de un registro de actividad para obtener una evaluación precisa de las actividades diarias del paciente.
2	Conductas problemáticas y valores personales	• Identificación de información relacionada con conductas depresivas. • Exploración de conductas problemáticas. • Reconocimiento de objetivos y valores personales.
3	Objetivos personales	• Obtención de información complementaria sobre las características del historial de interacciones del paciente. • Reconocimiento de los contextos e interacciones que refuerzan las conductas depresivas. • Establecimiento de objetivos a corto, medio y largo plazo.
4	Cambio terapéutico del comportamiento problemático	• Explicación de las hipótesis sobre los factores asociados al origen, al mantenimiento y al cambio terapéutico de los comportamientos problemáticos. • Selección de 10 actividades personalizadas según las necesidades y deseos de los pacientes.

5	Actividades objetivo	• Registro del progreso semanal de las actividades seleccionadas. • Reconocimiento de los avances logrados. • Resolución de problemas.
6	Satisfacción con actividades	• Exploración de la satisfacción con las actividades. • Discusión grupal sobre las emociones y los sentimientos experimentados durante las actividades.
7	Capacidad de afrontamiento	• Abordaje de las emociones. • Reacciones ante los acontecimientos y las respuestas asociadas a la depresión. • Relación entre las conductas de evitación y el mantenimiento de las dificultades.
8	Nuevos comportamientos	• Examinación de los nuevos comportamientos a incorporar. • Mantenimiento y prevención de recaídas. • Discusión sobre los objetivos alcanzados y las barreras para mantener el plan de actividades semanal.

6.4. Evaluación clínica

Esta terapia ha demostrado ser eficaz en pacientes con depresión (Cuijpers et al., 2023) y con trastorno de estrés postraumático (Etherton y Farley, 2022). Aunque no existe evidencia previa de la eficacia de la TAC en pacientes con dolor crónico (Lejuez et al., 2011), una revisión sistemática recientemente ha señalado algunos motivos por los que esta terapia podría ser potencialmente beneficiosa para mejorar la interferencia del dolor en esta población (Walsh et al., 2022). El primer motivo es que puede mejorar indirectamente los resultados relacionados con el dolor al reducir el impacto negativo de la depresión sobre el dolor; el segundo motivo es que ayuda a identificar y abordar factores que pueden contribuir al mantenimiento de la depresión, como los pensamientos negativos y las conductas de evitación (variables que también contribuyen al mantenimiento de la discapacidad relacionada con el dolor); y el tercer motivo es que puede mejorar la calidad de vida y el funcionamiento en general, lo que indirectamente puede mejorar los resultados del dolor al aumentar la capacidad de la persona para hacer frente al dolor y participar en actividades significativas.

6.5. Evaluación económica

En el último lustro, se ha evidenciado cierto interés por aportar pruebas sobre la eficiencia de la TAC en población diagnosticada con depresión (Egede et al., 2018; Sun et al., 2021) y en población no clínica (Chen et al., 2022). Desde 2018 (primer estudio publicado) hasta 2022 (último estudio publicado), 3 estudios han explorado la relación coste-efectividad de esta terapia respecto a controles activos y/o inactivos. En términos generales, las evaluaciones económicas disponibles en la actualidad han señalado que la TAC es coste-efectiva en comparación al tratamiento habitual (Chen et al., 2022; Sun et al., 2021). Respecto al formato de administración, un estudio ha indicado recientemente que los costes de la TAC en línea son superiores a los de la atención presencial en adultos mayores con depresión. Pese a estas diferencias, la administración de esta terapia tanto en formato presencial como no presencial es coste-efectiva (Egede et al., 2018). En la Tabla 11 se reportan los resultados de las evaluaciones económicas disponibles de la TAC en la actualidad.

Tabla 11. Evidencias sobre la eficiencia de la TAC. Elaboración propia.

Autores	Población	Resultados
Chen et al. (2022)	Ensayo clínico controlado y aleatorizado en el que participaron 277 personas mayores confinadas en casa con bajos ingresos (90 recibieron TAC, 93 Terapia de Resolución de Problemas y 94 acompañamiento basado en el control de la atención).	En comparación con el acompañamiento basado en el control de la atención, la TAC y la Terapia de Resolución de Problema redujeron más costes. Los cocientes de coste-efectividad incrementales de la TAC y la Terapia de Resolución de Problema estuvieron por debajo de los 50000 $, el umbral inferior de rentabilidad. Al comparar con el acompañamiento basado en el control de la atención, tanto la TAC como la Terapia de Resolución de Problema fueron opciones coste-efectivas.
Sun et al. (2021)	Ensayo clínico controlado y aleatorizado en el que participaron 331 pacientes de atención primaria con depresión subumbral (115 recibieron TAC	En comparación al tratamiento habitual, la TAC con mindfulness fue coste-efectiva en la prevención de la progresión de la depresión mayor. Los cocientes de coste-efectividad incrementales fueron de 1046 $ por caso

	con mindfulness y 116 tratamiento habitual).	prevenible de progresión mayor, con una probabilidad de 0,99 de ser coste-efectivo. La TAC con mindfulness se consideró un tratamiento alternativo coste-efectivo para tratar la depresión subumbral.
Egede et al. (2018)	Ensayo clínico controlado y aleatorizado en el que participaron 241 pacientes adultos mayores con depresión (120 recibieron TAC presencial y 121 TAC en línea).	Los adultos mayores tratados presencialmente tuvieron una media de 2998 $ más de costes de utilización de la atención sanitaria, mientras que los tratados en línea tuvieron una media de 871 $. Aunque los costes de intervención en línea fueron superiores a los de la atención presencial, los adultos mayores que recibieron activación conductual en línea registraron menores costes de utilización de servicios sanitarios 1 año después de la intervención que los que recibieron atención en presencial. No se identificaron diferencias significativas en términos de años de vida ajustados por calidad entre ambas administraciones.

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CAPÍTULO 2

Objetivos

OBJETIVOS

El objetivo general de esta tesis doctoral fue realizar una evaluación clínica y económica de la Terapia de Aceptación y Compromiso (ACT) y de la Terapia de Activación Conductual para la Depresión (TACD) en pacientes con dolor lumbar crónico y síntomas de depresión. Para cumplir con este propósito, se establecieron los siguientes objetivos específicos:

Artículo 1

- Revisar sistemáticamente la evidencia disponible sobre la eficacia de las terapias cognitivo-conductuales en población con dolor crónico y malestar psicológico clínicamente relevante.

Artículo 2

- Presentar el protocolo de un ensayo clínico controlado y aleatorizado (Proyecto IMPACT) dirigido a pacientes con dolor lumbar crónico y síntomas de depresión comórbidos.

Artículo 3

- Examinar la eficacia de 2 terapias psicológicas de tercera generación (ACT y TACD) en comparación con el tratamiento habitual en pacientes con dolor lumbar crónico y síntomas de depresión comórbidos.
- Analizar el potencial rol mediador de variables de proceso como la aceptación del dolor, la activación conductual y la flexibilidad psicológica en los cambios clínicos a largo plazo (12 meses de seguimiento) obtenidos por 2 terapias psicológicas de tercera generación (ACT y TACD).

Artículo 4

- Conocer las experiencias relatadas por un grupo de pacientes con dolor lumbar crónico y síntomas depresivos comórbidos que participaron en un formato grupal de 2 terapias psicológicas de tercera generación (ACT y TACD) administradas mediante videoconferencia sincrónica a distancia.

Artículo 5

- Explorar la coste-utilidad y la coste-efectividad de 2 terapias psicológicas de tercera generación (ACT y TACD) en comparación con el tratamiento habitual para pacientes con dolor lumbar crónico y síntomas de depresión comórbidos.

CAPÍTULO 3

Publicaciones

PUBLICACIONES

En total, 4 estudios -reflejados en 5 artículos- formaron parte de esta tesis doctoral. En resumen, en el **Artículo 1** (estudio de revisión) se presentó una revisión sistemática de las evidencias disponibles sobre la eficacia de las terapias cognitivo-conductuales en población con dolor crónico y malestar psicológico comórbido. En el **Artículo 2** (protocolo) se reportó un registro prospectivo del ensayo clínico controlado y aleatorizado (Proyecto IMPACT) en el que se enmarca esta tesis doctoral, en el **Artículo 3** (estudio empírico) los resultados de eficacia, en el **Artículo 4** (estudio empírico) los resultados cualitativos y en el **Artículo 5** (estudio empírico) los resultados de la relación coste-utilidad y coste-efectividad. Estos 5 artículos se presentan a continuación.

1. Artículo 1

Sanabria-Mazo, J. P., Colomer-Carbonell, A., Fernández-Vázquez, Ó., Noboa-Rocamora, G., Cardona-Ros, R., McCracken, L. M., Montes-Pérez, A., Castaño-Asins, J. R., Edo, S., Borràs, X., Sanz, A., Feliu-Soler, A. y Luciano, J. V. (2023a). A systematic review of psychological therapies for comorbid chronic pain and clinically relevant psychological distress. *Frontiers in Psychology, 14*, 1-18. https://doi.org/10.3389/fpsyg.2023.1200685

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A systematic review of cognitive behavioral therapy-based interventions for comorbid chronic pain and clinically relevant psychological distress

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Objective: Chronic pain frequently co-occurs with clinically relevant psychological distress. A systematic review was conducted to identify the efficacy of cognitive behavioral therapy-based interventions for patients with these comorbid conditions.

Methods: The systematic search was carried out in Medline, PsycINFO, Web of Science, and Scopus up to March 18th, 2023. Four reviewers independently conducted screenings, extraction, and quality assessment.

Results: Twelve randomized controlled trials and one non-randomized controlled trial involving 1,661 participants that examined the efficacy of Cognitive Behavioral Therapy (nine studies), Mindfulness-based Interventions (three studies), Acceptance and Commitment Therapy (one study), and Behavioral Activation Therapy for Depression (one study) were included. Compared to treatment as usual, six out of eight studies of traditional Cognitive Behavioral Therapy reported significant differences in the reduction of depressive symptoms at post-treatment (*d* from 1.31 to 0.18) and four out of six at follow-up (*d* from 0.75 to 0.26); similarly, five out of six reported significant differences in the reduction of anxiety symptoms at post-treatment (*d* from 1.08 to 0.19) and three out of four at follow-up (*d* from 1.07 to 0.27). Overall, no significant differences between traditional Cognitive Behavioral Therapy and treatment as usual were reported at post-treatment and follow-up in the studies exploring pain intensity and pain catastrophizing.

Conclusion: The available evidence suggests that traditional Cognitive Behavioral Therapy may produce significant benefits for the improvement of depression, anxiety, and quality of life, but not for pain intensity and pain catastrophizing. More evidence is needed to determine the effects of MBI, ACT, and BATD.

Systematic review registration: PROSPERO, CRD42021219921.

KEYWORDS

cognitive behavioral therapy, chronic pain, distress, depression, anxiety, systematic review

1 Introduction

Chronic pain and psychological distress are common health conditions (Wittchen et al., 2011) with substantial healthcare and social impacts (Chopra and Arora, 2014). The prevalence of chronic pain ranges from 10% to 30% worldwide (Reid et al., 2011), generating a significant public health demand and economic burden (Baumeister et al., 2012). According to epidemiological studies, comorbidity between chronic pain and psychological distress in clinical practice is higher than 60% (Walker et al., 2014). Since this comorbidity is more treatment-resistant than either condition alone (Mansfield et al., 2016) and it generates a significant impact on the quality of life of patients with these conditions (McCracken et al., 2022), it has been considered a growing target for treatment in recent years (McCracken, 2023). The concurrent appearance of chronic pain and significant psychological distress is striking and requires attention from researchers, clinicians, and policymakers, as well as demands effective management strategies to improve the health and well-being of those affected by these conditions (Snyder and Handrup, 2018).

Due to the complexity and multifaceted nature of the construct, many definitions for psychological distress have been proposed in recent years. One of the most widely accepted defines this psychological construct as "state of emotional suffering characterized by the undifferentiated combinations of symptoms of depression (e.g., lost interest, sadness, hopelessness) and anxiety (e.g., restlessness, feeling tense) which are sometimes accompanied by somatic symptoms (e.g., insomnia, headaches, lack of energy)" (Drapeau et al., 2012, p. 125). Generally, psychological distress refers to a range of unpleasant emotional and mental experiences that can impact a person's well-being and ability to function (Bisby et al., 2022; Gasslander et al., 2022). It is also considered a dimensional construct that has been truncated in most studies to employ it as a categorical construct to establish when it is or is not "clinically relevant," with relevant meaning that scores on psychopathological measures exceed specific cut-off points.

Previous studies demonstrate that people with chronic pain are more likely to experience psychological distress, such as anxiety and depression, and individuals with psychological distress are more likely to report chronic pain (Rayner et al., 2016). The relationship between chronic pain and psychological distress is complex and bidirectional (Wittchen et al., 2011). The multidimensional nature of both chronic pain and psychological distress, with sensory, affective, and behavioral dimensions, is a challenge for intervention design and delivery (Roberts et al., 2018). Specifically, the presence of psychological distress in patients with chronic pain increases pain complaints and reduces quality of life (Snyder and Handrup, 2018). Comorbidity between psychological distress and chronic pain generates a higher degree of functional impairment than the presence of either condition alone (Mansfield et al., 2016) and negatively influences the response to pharmacological and non-pharmacological treatments (Kroenke et al., 2011). Chronic pain and clinical psychological distress involve shared neurobiological and psychosocial processes (Hooten, 2016).

Cognitive Behavioral Therapy (CBT) is the most applied psychological approach to chronic pain (McCracken, 2023). Different forms of CBT are frequently applied in chronic pain and related conditions (e.g., anxiety and/or depression), appearing effective when explored independently (Churchill et al., 2013; Cuijpers et al., 2013; Buhrman et al., 2016; Pasarelu et al., 2017). Traditional CBT has beneficial effects in adults with chronic pain (Williams et al., 2020) and is also effective in patients with emotional disorders (Lorenzo-Luaces et al., 2018; López-López et al., 2019). Concretely, recent evidence shows that Mindfulness-based Interventions (MBI), Dialectical Behavior Therapy (DBT), Rational Emotive Behavior Therapy (REBT), Acceptance and Commitment Therapy (ACT), and Behavioral Activation Therapy for Depression (BATD) also produce positive effects in patients with chronic pain (Jorn, 2015; Veehof et al., 2016; Hughes et al., 2017; Boersma et al., 2019; Khoo et al., 2019; Gloster et al., 2020; Pardos-Gascón et al., 2021).

Although the above-mentioned CBT-based interventions have generally demonstrated evidence in the management of chronic pain and related conditions, their specific efficacy in patients with comorbid pain and clinical psychological distress has been scarcely assessed. It appears that this is the first systematic review that aims to examine the efficacy of CBT-based interventions for comorbid chronic pain and clinically relevant psychological distress. Since chronic pain and psychological distress frequently co-occur, worsen one another, and resist therapy effects when they are both present, identifying effective CBT-based interventions for this complex set of conditions is critical work. In this systematic review, randomized controlled trials (RCTs) and non-randomized trials (non-RCTs) were selected for patients with chronic pain plus clinically relevant psychological distress, comparing CBT-based interventions to control conditions (active or inactive). Additionally, this research explored the risk of bias (RoB) of the included studies to assess their methodological quality.

2 Methods

2.1 Protocol and registration

This systematic review was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA; Page et al., 2021). The review protocol was registered in the Prospective Register of Systematic Reviews (PROSPERO), under

identification number CRD42021219921. Supplementary Table S1 indicates some adjustments incorporated into the protocol of this systematic review and includes the PRISMA checklist.

2.2 Data sources and searches

To reduce publication bias, published and unpublished clinical trials were examined. For exploration of published clinical trials, searches were conducted in four electronic databases: Medline (PubMed), Web of Science (Core Collection), PsycINFO (ProQuest), and Scopus (Elsevier). The search strategy identified studies that included combinations of the population terms and the specific terms of psychological therapies. The search terms were selected according to a validation by experts and a review of the search strategies used in previous systematic reviews on CBT-based interventions for chronic pain (Lin et al., 2019; Williams et al., 2020; White et al., 2022). The specific Boolean searches were adjusted according to the Peer Review of Electronic Search Strategies (PRESS) guideline statement (McGowan et al., 2016). The following limits and filters were activated in all databases if possible: publication date (from inception until March 18th, 2023), type of publication (only studies of interest), species (humans), and languages (English and Spanish). The bibliographic database searches are detailed in Table 1.

For the exploration of unpublished clinical trials, a search was conducted in ClinicalTrials.Gov, International Standard Randomized Controlled Trial Number register (ISRCTN), World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP), and PROSPERO (Lin et al., 2019). The reference list of included articles was also examined through a reverse citation search for further analysis. In addition, the reference list of published narrative reviews, systematic reviews, and meta-analyses, as well as grey literature (search carried out in Google Scholar), were consulted to ensure that all eligible studies were included (i.e., Buhrman et al., 2016; Hilton et al., 2017; Ahern et al., 2018; Haugmark et al., 2019; Khoo et al., 2019; López-López et al., 2019; Williams et al., 2020; Fordham et al., 2021; Pardos-Gascón et al., 2021; White et al., 2022).

2.3 Eligibility criteria

To select the eligibility criteria, the "Population," "Intervention," "Comparison," "Outcomes," and "Study" (PICOS) approach was followed. Table 2 details the inclusion and exclusion criteria established in this systematic review.

2.3.1 Participants

The population of interest consisted of adults (≥ 18 years) with the presence of non-oncologic chronic pain (> 12 weeks) and clinically relevant psychological distress, according to the clinical cut-off for depression and/or anxiety reported in the studies. Participants diagnosed with psychiatric disorders other than depression and/or anxiety, other clinically relevant psychiatric symptoms, substance dependence, and neurodegenerative disorders were excluded.

2.3.2 Interventions

CBT-based interventions exploring their efficacy in patients with non-oncologic chronic pain and clinically relevant psychological distress, regardless of their mode of delivery (e.g., face-to-face, online, and blended format). To explore all available evidence in the literature, this systematic review synthesized the efficacy of all CBT-based interventions that met this eligibility criteria. The points analyzed for each outcome were the post-treatment and the follow-up assessment, examining differences between the groups. The combination of pharmacological and CBT-based interventions was excluded.

2.3.3 Comparators

CBT-based interventions were included exclusively when the comparison group received active (i.e., another type of psychological intervention) or inactive treatment (i.e., wait-list, usual care, attention control, and psychological placebo, among others). Given the objective of this study, CBT-based interventions without a control group were excluded.

2.3.4 Outcomes

The selection of outcomes was based on recommendations from the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT; Dworkin et al., 2008). Specifically,

TABLE 1 Bibliographic database searches.

Databases: Medline, Web of Science, PsycINFO, and Scopus	
1	Chronic pain [Title/Abstract] OR eye pain [Title/Abstract] OR neck pain [Title/Abstract] OR nociceptive pain [Title/Abstract] OR facial pain [Title/Abstract] OR shoulder pain [Title/Abstract] OR myofascial pain syndromes [Title/Abstract] OR pelvic pain [Title/Abstract] OR patellofemoral pain syndrome [Title/Abstract] OR pelvic girdle pain [Title/Abstract] OR abdominal pain [Title/Abstract] OR flank pain [Title/Abstract] OR low back pain [Title/Abstract] OR back pain [Title/Abstract] OR musculoskeletal pain [Title/Abstract] OR chest pain [Title/Abstract] OR complex regional pain syndromes [Title/Abstract] OR visceral pain [Title/Abstract] OR neuropath* [Title/Abstract] OR phantom limb [Title/Abstract] OR fantom limb [Title/Abstract] OR spinal cord [Title/Abstract] OR idiopathic [Title/Abstract] OR shoulder [Title/Abstract] OR persistent sciatica [Title/Abstract] OR lumbago [Title/Abstract] OR fibromyalgia [Title/Abstract] OR complex regional pain syndromes [Title/Abstract] OR headache disorders [Title/Abstract]
2	Depress* [Title/Abstract] OR anxi* [Title/Abstract] OR stress [Title/Abstract] OR distress [Title/Abstract] OR mood disorder [Title/Abstract] OR emotional regulation [Title/Abstract] OR emotional dysregulation [Title/Abstract] OR affective disorder [Title/Abstract]
3	Intervention [Title/Abstract] OR treatment [Title/Abstract] OR psychotherapy [Title/Abstract] OR therapy [Title/Abstract] OR clinical trial [Title/Abstract] OR trial [Title/Abstract] OR cognitive behavioral therapy [Title/Abstract] OR mindfulness [Title/Abstract] OR acceptance and commitment therapy [Title/Abstract] OR behavioral activation therapy [Title/Abstract]
((1 AND 2) AND 3)	

The following filters were applied in all databases if possible: type of publication (controlled trials only), species (humans), and languages (English and Spanish).

TABLE 2 Eligibility criteria according to PICOS strategy.

	Inclusion criteria	Exclusion criteria
[P] Participants	Adults (≥ 18 years) with the presence of non-oncologic chronic pain (> 12 weeks) and clinically relevant psychological distress	Adults diagnosed with psychiatric disorders other than depression and/or anxiety, other clinically relevant psychiatric symptoms, substance dependence, and neurodegenerative disorders
[I] Intervention	CBT-based interventions exploring their efficacy in patients with non-oncologic chronic pain and clinically relevant psychological distress	The combination of pharmacological and CBT-based interventions
[C] Comparison	CBT-based interventions compared with active (i.e., another type of psychological intervention) or inactive treatment (i.e., wait-list, usual care, attention control, and psychological placebo, among others)	Interventions without a control group
[O] Outcomes	Pain-related variables (pain interference, pain intensity, pain acceptance, pain catastrophizing, and pain self-efficacy, among others), emotional functioning (depression, anxiety, and stress), health-related quality of life, behavioral activation, and psychological flexibility, among others	Other types of outcomes
[S] Study design	RCTs and non-RCTs	Research with other study designs

pain-related variables (pain interference, pain intensity, pain acceptance, pain catastrophizing, and pain self-efficacy, among others), emotional functioning (depression, anxiety, and stress), health-related quality of life, behavioral activation, and psychological flexibility, among others, were explored in this systematic review.

2.3.5 Study design

RCTs and non-RCTs of any length of follow-up were included. Only data from studies that have received ethical approval and were published in English or Spanish were used. No studies were excluded based on publication status, date, or type (Lin et al., 2019).

2.4 Data management and study selection

Duplicate articles in the databases were automatically removed by Mendeley. Then, four reviewers independently screened all articles in Rayyan QCRI based on their titles and abstracts. The full texts were independently checked for compliance with the eligibility criteria. Finally, the reviewers entered key information from each study into a standardized data extraction form and assessed the RoB of included studies. During each phase, at least two reviewers were employed. No additional reviewer was needed to resolve a disagreement.

2.5 Risk of bias

The RoB of the included studies was assessed using the Cochrane Collaboration's risk of bias assessment tool (Higgins et al., 2011). This tool involves the assessment of RoB arising from each of six domains: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases. Studies were classified as high risk (if at least one domain was assessed as high), unclear (if at least one domain was assessed as unclear and the other domains were low), or low risk of bias (if all individual domains were low).

2.6 Data synthesis

Findings were described according to therapy type (CBT, MBI, ACT, and BATD). A narrative synthesis was carried out to describe the main characteristics of psychological therapies and the results obtained in the comparison of outcomes with control conditions (inactive or active). The statistical significance threshold was set at $p < 0.05$ and the magnitude of Cohen's d was interpreted according to the following rule of thumb criterion (Sawilowsky, 2009): very small (0.10), small (0.20), medium (0.50), large (0.80), very large (1.20), and huge (2.00).

3 Results

3.1 Selection and inclusion of studies

The initial database search yielded a total of 1,230 published articles. As shown in Figure 1, after removing duplicates and screenings, 14 articles based on 12 RCT and 1 non-RCT were included. Two studies were derived from the same sample (De Jong et al., 2016, 2018), although they presented evidence of different outcomes. The 14 articles that were excluded during the full-text screening are presented in Supplementary Table S2.

3.2 Characteristics of all the included studies

The 13 articles included were published between 2011 and 2023. Three studies (23%) were conducted in Sweden, three (23%) in Spain, three (23%) in Germany, two (15%) in the United States of America, one (8%) in Australia, and one (8%) in Iceland. Five studies (38%) assessed patients with chronic pain (CP), three (23%) with chronic low back pain (CLBP), two (15%) with chronic musculoskeletal pain (CMP), one (8%) with chronic back pain (CBP), one (8%) with chronic spinal cord injury, and one (8%) with non-specific chronic pain (NSCP). Nine studies (69%) included CBT, three (23%) MBI, and one ACT and BATD (8%) as the main therapy of interest. Eleven studies (85%) employed inactive control groups (usual care or waitlist). All the studies (100%) carried out the therapy program weekly. The format of the therapy was face-to-face in six studies (46%), entirely online in five (38%), a blended format in one (8%), and combined face-to-face plus online versus online in one (8%).

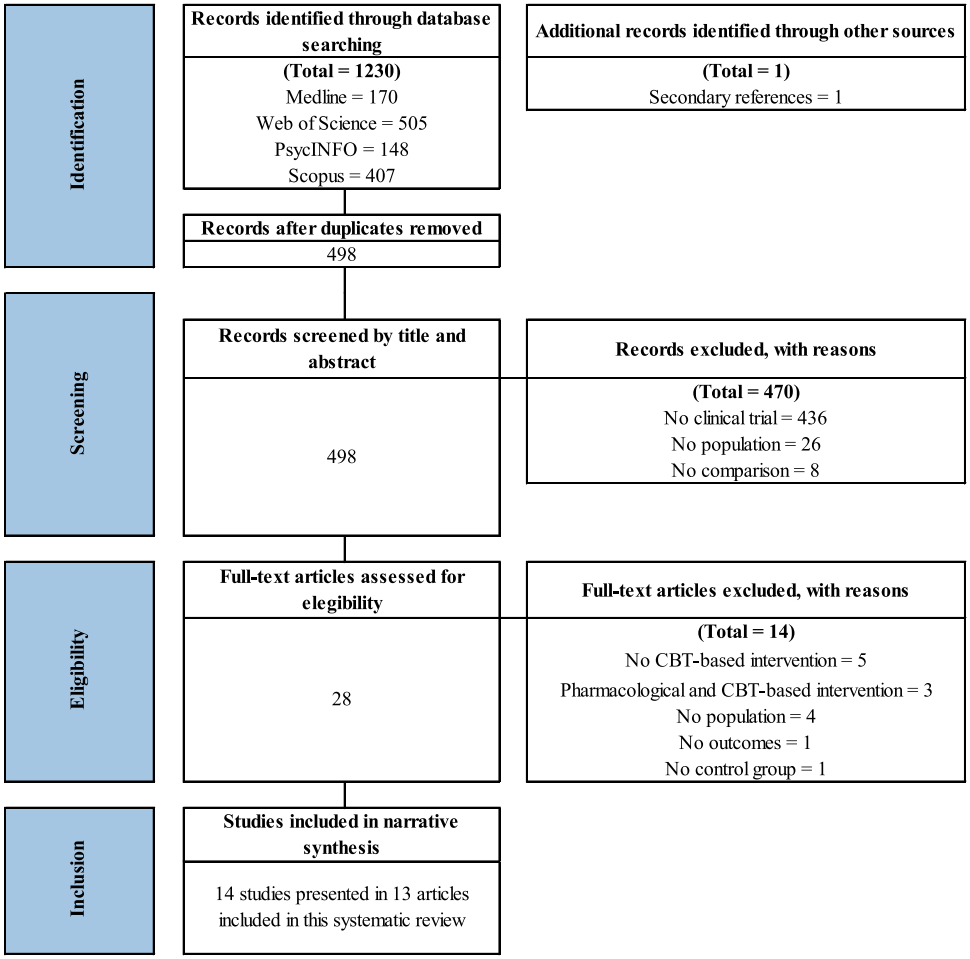

FIGURE 1
Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flowchart from record identification to study inclusion.

The sample size of the study's arms ranged from 26 to 167 in the intervention group (IG) and 24 to 161 in the control group (CG), and the mean age varied from 45 to 61 in IG and 46 to 59 years old in CG. In total, 1,661 participants were involved in this systematic review, of which 850 were in IG and 811 in CG. The proportion of women in all studies was higher than 50%, both in IG and CG, except for the IG in two (43.2% and 26%; Tlach and Hampel, 2011; Migliorini et al., 2016, respectively) and CG in one (32%; Migliorini et al., 2016). The employment status was reported in nine studies (69.2%) and medication consumption in eight studies (61.6%). The dropout rate at the end of the studies ranged from 17 to 67%. The number of sessions ranged from four to thirteen with a minimum duration of 50 min per session and a maximum of 150 min. The therapies were delivered by psychologists in ten studies (77.7%), other professionals in two (27.3%), and without therapists in one (7.7%). Details are described in Table 3.

3.3 Risk of bias assessment

Figure 2 shows the RoB for each included study. Twelve studies (92%) reported an adequate random sequence generation and provided sufficient information on the method of allocation concealment of patients. None of the studies (0%) blinded the participants and personnel to the intervention delivered. However, seven studies (54%) explicitly reported that they were able to blind outcome assessment from knowledge of which intervention a participant received. Incomplete outcome data were adequately managed in all cases (100%), and they were rated as free from selective outcome reporting bias in all included studies (100%). Considering the impossibility of blinding participants in psychological therapies, six studies (46%) reported a high (Tlach and Hampel, 2011; Ólason et al., 2018; Boersma et al., 2019; Schlicker et al., 2020; Baumeister et al., 2021; Torrijos-Zarcero et al., 2021) and seven (54%) an unclear RoB (Buhrman et al., 2015; De Jong et al., 2016, 2018; Migliorini et al., 2016; Aragonès et al., 2019; Gardiner et al., 2019; Gasslander et al., 2022; Sanabria-Mazo et al., 2023).

3.4 Psychological therapies

The specific results of each of the studies included in this systematic review are presented in Supplementary Table S3. Information from these controlled trials is organized according to the type of intervention (CBT, MBI, ACT, and BATD).

TABLE 3 Characteristics of the controlled trials included in the systematic review.

Author (year), country	Target condition (measure), study design	Treatment arms (sample) and delivery period (format)	Groups (intervention and control): age and gender	Components (dropout and adherence rate), sessions (duration), and therapist	Assessments (time horizon)	Primary outcome (instrument)	Secondary outcomes (instruments)
Cognitive behavioral therapy (CBT)							
[1] Tlach and Hampel (2011), Germany	Patients with CLBP and depression (measured with the ADS; cut-off ≥24 points), non-RCT	• *Treatment arms:* CBT + TAU ($n = 44$) and TAU ($n = 40$) • *Delivery period:* weekly (face-to-face)	• *Intervention group*: CBT + TAU. Age: $M = 50.08$ ($SD = 5.4$). Gender: 25 females (43.2%) • *Control group:* TAU. Age: $M = 51.00$ ($SD = 6.3$). Gender: 20 females (50.0%)	• *Components:* a biopsychosocial approach of CBT: cognitive-behavioral pain-management training and cognitive-behavioral training program for the management of depressive symptoms (37% dropout rate at the end of the study; adherence rate was not reported) • *Number of sessions:* 13 (60 min) • *Therapist:* physicians and nurses	Pre, post, follow-up+6, follow-up+12, and follow-up+24 (24 months)	• Depression symptoms (CES-D)	• Anxiety (HADS-A) • Mental quality of life (SF-12)
[2] Buhrman et al. (2015), Sweden	Patients with CP and depression (measured with the MADRS-S; cut-off >10 points), RCT	• *Treatment arms:* CBT + TAU ($n = 28$) and TAU ($n = 24$) • *Delivery period:* weekly (online)	• *Intervention group*: CBT + TAU. Age: $M = 54.1$ ($SD = 11.76$). Gender: 24 females (86%) • *Control group:* TAU. Age: $M = 46.8$ ($SD = 12.9$). Gender: 20 females (83%)	• *Components:* program based on CBT: behavioral activation and psychoeducation (17% dropout rate at the end of the study and 44% completed 100% of the total number of sessions) • *Number of sessions:* 8 (NR minutes) • *Therapist:* graduate students trained in CBT with supervision by a clinical psychologist	Pre, post, and follow-up+12 (12 months)	• Depression symptoms (MADRS-S) • Anxiety symptoms (BAI) • Pain interference (PDI)	• Fear of the symptoms of anxiety (ASI) • Pain catastrophizing (PCS) • Chronic pain acceptance (CPAQ) • Cognitive and behavioral coping strategies (CSQ) • Psychosocial and behavioral consequence of chronic pain (MPI) • Quality of life (QoLI)
[3] Migliorini et al. (2016), Australia	Patients with chronic spinal cord injury and depression or anxiety (measured with the DASS-21; cut-off ≥ was not reported), RCT	• *Treatment arms:* CBT ($n = 34$) and waitlist ($n = 25$) • *Delivery period:* weekly (face-to-face)	• *Intervention group*: CBT. Age: $M = 47.5$ ($SD = 12.2$). Gender: 9 females (26%) • *Control group:* Waitlist. Age: $M = 52.8$ ($SD = 12.9$). Gender: 8 females (32%)	• *Components:* internet program based on CBT: psychoeducation, mindfulness, and positive psychology (32% dropout rate at the end of the study; adherence rate was not reported) • *Number of sessions:* 10 (NR minutes) • *No therapists*	Pre and post	• Depression, anxiety, and stress symptoms (DASS-21)	• Quality of life (PWIA)
[4] Ólason et al. (2018), Iceland	Patients with CP and depression or anxiety (measured with the BDI-II or BAI; cut-off ≥ was not reported), RCT	• *Treatment arms:* CBT + TAU ($n = 39$) and TAU ($n = 38$) • *Delivery period:* weekly (face-to-face)	• *Intervention group*: CBT + TAU. Age: $M = 37.32$ ($SD = 12.16$). Gender: 21 females (59%) • *Control group:* TAU. Age: $M = 35.79$ ($SD = 11.28$). Gender: 26 females (68%)	• *Components:* a biopsychosocial approach of CBT: pain and emotional management training (34% dropout rate at the end of the study; attendance was not reported) • *Number of sessions:* 12 (45 min) • *Therapist:* psychologist, nurses, occupational therapists, and social worker	Pre, post, follow-up+12, and follow-up+36 (36 months)	• Depression symptoms (BDI-II) • Anxiety symptoms (BAI)	• Pain intensity (NRS) • Fear avoidance (FABQ) • Social functioning (SF-36-SR)

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TABLE 3 (Continued)

Author (year), country	Target condition (measure), study design	Treatment arms (sample) and delivery period (format)	Groups (intervention and control): age and gender	Components (dropout and adherence rate), sessions (duration), and therapist	Assessments (time horizon)	Primary outcome (instrument)	Secondary outcomes (instruments)
[5] Aragonès et al. (2019), Spain	Patients with CMP and MDD (measured with the SCID; cut-off was not reported), RCT	• *Treatment arms:* CBT + TAU ($n = 167$) and TAU ($n = 161$) • *Delivery period:* weekly (face-to-face)	• *Intervention group*: CBT + TAU. Age: $M = 61.4$ ($SD = 10.2$). Gender: 138 females (82.6%) • *Control group:* TAU. Age: $M = 59.3$ ($SD = 10.1$). Gender: 134 females (83.2%)	• *Components:* optimized management of major depression, care management, and psychoeducation for chronic pain and depression (17% dropout rate at the end of the study and 49% attendance of at least 50% of the total number of sessions) • *Number of sessions:* 9 (120 min) • *Therapist:* psychologist and physician (primary care)	Pre, post, follow-up+6, and follow-up+12 (12 months)	• Depression symptoms (HSCL-20)	• Pain intensity (BPI) • Pain interference (BPI)
[6] Boersma et al. (2019), Sweden	Patients with CMP and depression, and anxiety (measured with the HADS; cut-off ≥8 points), RCT	• *Treatment arms:* CBT ($n = 57$) and Hybrid ($n = 58$) • *Delivery period:* weekly (online)	• *Intervention group*: CBT. Age: $M = 45$ ($SD = 12$). 44 (72.2) • *Control group:* Hybrid. Age: $M = 44$ ($SD = 12$). Gender: 52 females (89.7%)	• *Components:* CBT: psychoeducation (18% dropout rate at the end of the study and 30% attendance at least 75% of the total number of sessions); Hybrid: exposure *in vivo* and dialectical behavior therapy (DBT; 18% dropout rate at the end of the study and 65% attendance at least 75% of the total number of sessions) • *Number of sessions:* 10–16 (75 min) • *Therapist:* clinical psychologists and clinical psychologists in their post-graduate year	Pre, post, and follow-up+9 (9 months)	• Depression symptoms (MADRS-S) • Anxiety symptoms (GAD-7)	• Pain catastrophizing (PCS) • Pain intensity (MPI) • Pain interference (MPI)
[7] Schlicker et al. (2020), Germany	Patients with CLBP and depression (measured with the CES-D; cut-off ≥16), RCT	• *Treatment arms:* CBT + TAU ($n = 40$) and TAU ($n = 36$) • *Delivery period:* weekly (online)	• *Intervention group*: CBT + TAU. Age: $M = 51.3$ ($SD = 8.6$). Gender: 26 females (65%) • *Control group:* TAU. Age: $M = 50.1$ ($SD = 7.0$). Gender: 29 females (81%)	• *Components:* internet and mobile-based interventions based on CBT and visiting a general practitioner: psychoeducation, behavioral activation, and cognitive restructuring (35% dropout rate at the end of the study and 60% attendance of at least 80% of the total number of sessions) • *Number of sessions:* 7 (45 to 60 min) • *Therapist:* trained psychologists (eCoaches)	Pre, post, and follow-up+6 (6 months)	• Depression symptoms (CES-D and QUIDS)	• Anxiety (HADS-A) • Quality of life (AQoL-6D and EQ-5D-5L) • Social functioning (ODI-fd) • Pain intensity (GPR) • Pain self-efficacy (PSEQ) • Working capacity (SPE)

(Continued)

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TABLE 3 (Continued)

Author (year), country	Target condition (measure), study design	Treatment arms (sample) and delivery period (format)	Groups (intervention and control): age and gender	Components (dropout and adherence rate), sessions (duration), and therapist	Assessments (time horizon)	Primary outcome (instrument)	Secondary outcomes (instruments)
[8] Baumeister et al. (2021), Germany	Patients with CBP and depression (measured with the SCID; cut-off was not reported), RCT	• *Treatment arms:* CBT ($n = 104$) and TAU ($n = 105$) • *Delivery period:* weekly (online)	• *Intervention group*: CBT. Age: $M = 50.3$ ($SD = 9.4$). Gender: 60 females (58%) • *Control group:* TAU. Age: $M = 49.6$ ($SD = 9.3$). Gender: 65 females (62%)	• *Components:* internet and mobile program based on CBT: psychoeducation, behavior activation, and problem-solving (22 to 45%% dropout rate at the end of the study; attendance was not reported) • *Number of sessions:* 6 regular and 3 optional (50 to 60 min) • *Therapist:* trained psychologists (eCoaches)	Pre, post, and follow-up+6	• Depression level (HPRSD)	• Depression symptoms (PHQ-9) • Pain intensity (NRS) • Pain-related disability (ODI) • Pain self-efficacy (PSEQ) • Quality of Life (AQoL-6D) • Work capacity (SPE)
[9] Gasslander et al. (2022), Sweden	Patients with CP and psychological distress (measured according to DSM-5), RCT	• *Treatment arms:* CBT ($n = 95$) and TAU ($n = 92$) • *Delivery period:* weekly (online)	• *Intervention group*: CBT. Age: $M = 45.6$ ($SD = 11.1$). Gender: 70 females (74%) • *Control group:* TAU. Age: $M = 46.2$ ($SD = 11.2$). Gender: 67 females (73%)	• *Components:* internet program based on CBT: psychoeducation, relaxation, stress coping, behavioral activation, and maintenance (61% dropout rate at the end of the study and 35% attendance of at least 75% of the total number of sessions) • *Number of sessions:* 6–13 (not reported) • *Therapist:* psychologists	Pre, post, and follow-up+12 (12 months)*	• Depression symptoms (MADR-S) • Pain interference (MPI-S)	• Depression and anxiety symptoms (HADS) • Pain intensity (MPI-S) • Pain acceptance (CPAQ) • Coping strategies (CSQ-R) • Pain catastrophizing (PCS) • Quality of life (QoLI) • Fear of anxiety symptoms (ASI) • Social functioning (PDI) • Pain self-efficacy (PSEQ-2) • Kinesiophobia (TSK-11)
Mindfulness-based interventions (MBI)							
[10] De Jong et al. (2016, 2018), United States of America	Patients with CP and MDD (measured with the QIDS-C16; cut-off ≥6 points), pilot RCT	• *Treatment arms:* MBCT + TAU ($n = 26$) and TAU ($n = 14$) • *Delivery period:* weekly (face-to-face)	• *Intervention group*: MBI + TAU. Age: $M = 51.3$ ($SD = 11.9$). Gender: 21 females (80.8%) • *Control group:* TAU. Age: $M = 49.9$ ($SD = 11.1$). Gender: 9 females (64.3%)	• *Components:* intervention based on MBI: CBT with a "mindful" approach (17% dropout rate at the end of the study and 73% attendance of at least 50% of the total number of sessions) • *Number of sessions:* 8 (120 min) • *Therapist:* clinical social worker (training in MBI)	Pre and post (2 months)	• Depression symptoms (QIDS-C16 and HRSD17) • Body awareness (MAIA)	• Pain intensity (VAS) • Pain interference (BPI) • Anxiety (BAI) • Quality of life (SF-36) • Pain catastrophizing (PCS)
[11] Gardiner et al. (2019), United States of America	Patients with NSCP and MDD (measured with the PHQ-9; cut-off ≥5 points), RCT	• *Treatment arms:* IMGV + TAU ($n = 76$) and TAU ($n = 79$) • *Delivery period:* weekly (face-to-face and online)	• *Intervention group*: IMGV + TAU. Age: $M = 50$ ($SD = 12.2$). Gender: 64 females (84%) • *Control group:* TAU. Age: $M = 51$ ($SD = 12.4$). Gender: 70 females (89%)	• *Components:* mindfulness techniques, evidence-based integrative medicine, and medical group visits (7% dropout rate at the end of the study and 72% attended at least 50% of the total number of sessions) • *Number of sessions:* 9 (90 min) • *Therapist:* physician and a co-facilitator with training in mindfulness	Pre, post, and follow-up+6 (5 months and 1 week)	• Pain intensity (BPI) • Depression level (PHQ-9)	• Pain self-efficacy (PSEQ) • Quality of life (SF-12) • Behavioral activation (PAM)

(Continued)

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TABLE 3 (Continued)

Author (year), country	Target condition (measure), study design	Treatment arms (sample) and delivery period (format)	Groups (intervention and control): age and gender	Components (dropout and adherence rate), sessions (duration), and therapist	Assessments (time horizon)	Primary outcome (instrument)	Secondary outcomes (instruments)
[12] Torrijos-Zarcero et al. (2021), Spain	Patients with CP and depression and anxiety (measured with the HADS; cut-off ≥8 points), RCT	• Treatment arms: MSC ($n = 62$) and CBT ($n = 61$) • *Delivery period:* weekly (face-to-face)	• *Intervention group*: MSC. Age: $M = 48.29$ ($SD = 10.17$). Gender: 56 females (90.3%) • *Control group:* CBT. Age: $M = 49.25$ ($SD = 11.39$). Gender: 52 females (85.2%)	• *Components:* MSC: formal meditation together with formal and informal self-compassion practices (33% dropout rate at the end of the study; adherence rate was not reported); and CBT: psychoeducation, relaxation, and cognitive restructuring (23% dropout rate; adherence rate was not reported) • *Number of sessions:* 8 (150 min) • *Therapist:* MSC: psychiatrist and art therapist (trained); and CBT: clinical psychologists (trained)	Pre and post	• Self-compassion (SCS)	• Pain interference (BPI) • Pain intensity (PVAS) • Anxiety and depression symptoms (HADS) • Quality of life (SF-36) • Pain catastrophizing (PCS) • Pain acceptance (CPAQ)
Acceptance and Commitment Therapy (ACT) and Behavioral Activation Therapy (BATD)							
[13] Sanabria-Mazo et al. (2023), Spain	Patients with CLBP and depression (measured with the PHQ-9; cut-off ≥10 points), RCT	• Treatment arms: ACT+TAU ($n = 78$), BATD+TAU ($n = 78$), and TAU ($n = 78$) • *Delivery period:* weekly (online)	• *Intervention groups*: ACT+TAU. Age: $M = 54.9$ ($SD = 8.3$). Gender: 54 females (69.2%). BATD+TAU. Age: $M = 54.9$ ($SD = 10.2$). Gender: 53 females (67.9%). • *Control group:* TAU. Age: $M = 53.8$ ($SD = 10.0$). Gender: 51 females (65.4%)	• *Components:* ACT+TAU (67% dropout rate at the end of the post-treatment and 56% at the end of the 12-month follow-up; and 53% attended at least 6 of the 8 sessions); and BATD+TAU (54% dropout rate at the end of the post-treatment and 50% at the end of the 12-months follow-up; and 46% attended at least 6 of the 8 sessions) • *Number of sessions:* 8 (90 min) • *Therapist:* ACT and BATD: clinical psychologists (trained)	Pre, post, during, and follow-up (12 months)	• Pain interference (BPI)	• Pain intensity (NRS) • Depression, anxiety, and stress (DASS-21) • Pain catastrophizing (PCS) • Pain acceptance (CPAQ) • Behavioral activation (BADS-SF) • Psychological inflexibility (PIPS)

ADS, Allgemeine Depressions-Skala (German version of the CES-D); ACT, Acceptance and Commitment Therapy; ASI, Anxiety Sensitivity Index; AQoL-6D, Assessment of Quality of Life; BAI, Beck Anxiety Inventory; BAD-SF, Behavioral Activation for Depression Scale-Short; BATD, Behavioral Activation Therapy for Depression; BDI-II, Beck Depression Inventor; BPI, Brief Pain Inventory; CBP, chronic back pain; CBT, Cognitive Behavior Therapy; CES-D, Centre for Epidemiological Studies–Depression; CLBP, chronic low back pain; CMP, chronic musculoskeletal pain; COMM, Risk of Opioid Misuse; CP, chronic pain; CPAQ, Chronic Pain Acceptance Questionnaire; CSQ, Coping Strategies Questionnaire; DASS-21, Depression Anxiety Stress Scale; DSM-5, Diagnostic and Statistical Manual of Mental Disorders-5; EQ-5D-5L, EuroQol; FABQ, Fear-Avoidance Beliefs Questionnaire; GAD-7, Generalized Anxiety Disorder; GPR, Global Pain Rating; HADS, Hospital Anxiety and Depression Scale; HRSD, Hamilton Rating Scale for Depression; HSCL-20, Hopkins Symptom Checklist; IMGV, integrative medical group visits; MADRS-S, Montgomery–Åsberg Depression Rating Scale; MADRS-S, Montgomery–Åsberg Depression Rating Scale; MAIA, Multidimensional Assessment of Interceptive Awareness; MBCT, Mindfulness-Based Cognitive Therapy; MBI, mindfulness-based intervention; MDD, major depression disorder; MPI, Multidimensional Pain Inventory; MSC, mindful self-compassion; NNT, numbers needed to treat; NRS, Numerical Pain Rating Scale; NSCP, non-specific chronic pain; ODI-fd, Oswestry Disability Index; PAM, Patient Activation Measure; PCS, Pain Catastrophizing Scale; PDI, Pain Disability Index; PHQ-9, Patient Health Questionnaire-9; PIPS, Psychological Inflexibility in Pain Scale; PSEQ, Pain Self-Efficacy Questionnaire; PVAS, Pain Visual Analogue Scale; PWIA, Personal Well-being Index–Adult; QIDS, Quick Inventory of Depressive Symptomatology; QIDS-C16, Quick Inventory of Depressive Symptomatology–Clinician rated for DSM-IV; QoLI, Quality of Life Inventory; SCID, Structured Clinical Interview for DSM-IV; SF-12, 12-Item Short-Form Health Survey; SF-36, 36-Item Short-Form Health Survey; SPE, Subjective Prognosis of Employment Scale; TAU, treatment-as-usual; TSK-1, Tampa Scale of Kinesiophobia; VAS, visual analogue scale. *This study reported the between-group difference in the post-treatment comparison and intra-group difference in the pre-post-treatment and pre-follow-up + 12 comparison. Considering the objectives of this systematic review, only between-group comparisons are reported in this study.

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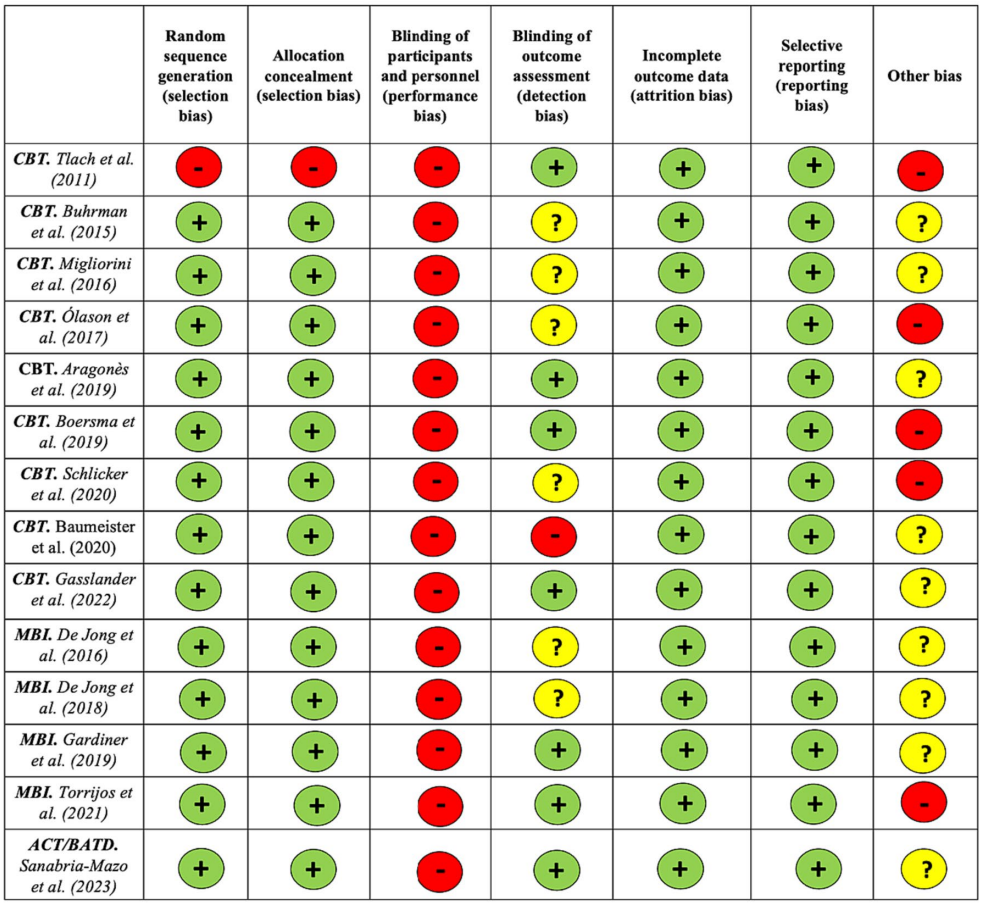

FIGURE 2
Risk of bias assessment for each included study using the Cochrane Collaboration's tool for assessing risk of bias (Higgins et al., 2011).

3.4.1 Cognitive behavioral therapy (CBT)

Five out of the nine studies evaluated CBT as the only therapeutic component therapy (Tlach and Hampel, 2011; Ólason et al., 2018; Boersma et al., 2019; Baumeister et al., 2021; Gasslander et al., 2022) and the remaining four with other components (Buhrman et al., 2015; Migliorini et al., 2016; Aragonès et al., 2019; Schlicker et al., 2020). The time horizon of the assessment of eight out of the nine studies was pre-, post, and follow-up. Except for Tlach and Hampel (2011), Migliorini et al. (2016), and Ólason et al. (2018), all analyses of CBTs were based on ITT. Baseline comparisons were carried out in all nine CBT studies. Less Boersma et al. (2019), all studies compared CBT with an inactive control group (usual care).

All nine studies assessed depressive symptoms as the primary outcome (Buhrman et al., 2015; Migliorini et al., 2016; Ólason et al., 2018; Aragonès et al., 2019; Boersma et al., 2019; Schlicker et al., 2020; Baumeister et al., 2021; Gasslander et al., 2022) and three anxiety symptoms as the co-primary outcome (Tlach and Hampel, 2011; Buhrman et al., 2015; Ólason et al., 2018; Boersma et al., 2019). The characteristics of the CBT are detailed in Table 3 and the specific results of each study are presented in Supplementary Table S3. The evidence for each outcome is presented below.

3.4.1.1 Depression

Six out of eight studies (75%) found significant differences in the reduction of depressive symptoms at post-treatment with very large to very small effect sizes (d ranging from 1.31 to 0.18; Tlach and Hampel, 2011; Buhrman et al., 2015; Migliorini et al., 2016; Schlicker et al., 2020; Baumeister et al., 2021; Gasslander et al., 2022); and four out of six studies (66%) at follow-up with medium to small effect sizes (d ranging from 0.75 to 0.26; Tlach and Hampel, 2011; Ólason et al., 2018; Aragonès et al., 2019; Baumeister et al., 2021) in favor of CBT compared to treatment as usual (TAU).

Another study (Boersma et al., 2019) identified significant differences in the reduction of depressive symptoms at follow-up with a small effect size ($d = 0.25$) in favor of hybrid therapy (exposure *in vivo* and DBT) compared to CBT.

3.4.1.2 Anxiety

Five out of six studies (83%) also showed significant differences in the reduction of anxiety symptoms at post-treatment with large to very small effect sizes (d ranging from 1.08 to 0.19; Tlach and Hampel, 2011; Buhrman et al., 2015; Migliorini et al., 2016; Schlicker et al., 2020; Gasslander et al., 2022); and three out of four studies (75%) at follow-up with large to small effect sizes (d ranging from 1.07 to 0.27; Tlach and Hampel, 2011; Buhrman et al., 2015; Schlicker et al., 2020)

in favor of CBT compared to TAU. No significant differences (0%) between these groups were found at post-treatment in two studies (Buhrman et al., 2015; Gasslander et al., 2022) and at follow-up in one study (Buhrman et al., 2015) exploring the fear of anxiety symptoms.

No significant differences (Boersma et al., 2019) were identified between CBT and hybrid therapy (exposure *in vivo* and DBT) in the reduction of anxiety symptoms at post-treatment and at follow-up.

3.4.1.3 Stress

One out of one study (100%) identified significant differences in improved stress symptoms at follow-up with a small effect size ($d = 0.47$) in favor of CBT compared to TAU (Migliorini et al., 2016).

3.4.1.4 Pain intensity

Significant differences in improved pain intensity were identified at post-treatment in one out of four studies with a small effect size ($d = 0.42$; Baumeister et al., 2021) in favor of CBT compared to TAU. No differences at follow-up were found in any of the four studies exploring pain intensity (Migliorini et al., 2016; Ólason et al., 2018; Aragonès et al., 2019; Schlicker et al., 2020).

Similarly, no significant differences were also found in the study (Boersma et al., 2019) comparing pain intensity after CBT and hybrid therapy (exposure *in vivo* and DBT) at post-treatment and follow-up.

3.4.1.5 Pain interference

Two out of three studies (67%) found significant differences in the reduction of pain interference at post-treatment with small to very small (d ranging from 0.22 to 0.12; Buhrman et al., 2015; Gasslander et al., 2022), but not at the follow-up in the two studies (0%) that explored this outcome (Buhrman et al., 2015; Aragonès et al., 2019), in favor of the CBT compared to TAU.

Another study (Boersma et al., 2019) demonstrated significant changes in the reduction of pain interference in hybrid therapy (exposure *in vivo* and dialectical behavior therapy) compared to CBT at post-treatment with very small effect size ($d = 0.02$) and at follow-up with small effect size ($d = 0.25$).

3.4.1.6 Pain catastrophizing

No significant differences (0%) between CBT and TAU were found at post-treatment in two studies (Buhrman et al., 2015; Gasslander et al., 2022) and at follow-up in one study (Buhrman et al., 2015) exploring pain catastrophizing.

However, another study (Boersma et al., 2019) reported significant differences in the decrease of pain catastrophizing at post-treatment with a small effect size ($d = 0.26$), but not at follow-up, in favor of hybrid therapy (exposure *in vivo* and dialectical behavior therapy) compared to CBT.

3.4.1.7 Pain acceptance

Two out of two studies (100%) indicated significant differences in increased pain acceptance at post-treatment (Buhrman et al., 2015; Gasslander et al., 2022) with very small ($d = 0.12$) and small effect size ($d = 0.30$), but not at follow-up in one out of one study (0%) that explored this outcome, in favor of CBT compared to TAU.

3.4.1.8 Pain self-efficacy

Significant differences between CBT and TAU were found at post-treatment in one out of three studies (33%) with a small effect size ($d = 0.39$; Baumeister et al., 2021) and at follow-up in one out of two studies (50%) with small effect size ($d = 0.33$; Baumeister et al., 2021).

No significant differences (0%) between CBT and TAU were found post-treatment in two studies (Schlicker et al., 2020; Gasslander et al., 2022) and at follow-up in one study (Schlicker et al., 2020) exploring pain self-efficacy.

3.4.1.9 Quality of life

Four out of six studies (67%) found significant differences in improving quality of life at post-treatment with medium to invaluable effect sizes (d ranging from 0.78 to 0.02; Tlach and Hampel, 2011; Migliorini et al., 2016; Baumeister et al., 2021; Gasslander et al., 2022) and two out of four studies (50%) at follow-up with medium to small effect size ($d = 0.78$ and $d = 0.33$; Tlach and Hampel, 2011 and Baumeister et al., 2021, respectively) in favor of CBT compared to TAU.

3.4.1.10 Social functioning

One out of one study (100%) identified significant differences in improved social functioning at follow-up with a medium effect size ($d = 0.51$) in favor of CBT compared to TAU (Ólason et al., 2018). No differences were found between these groups at post-treatment in the three studies (Ólason et al., 2018; Schlicker et al., 2020; Gasslander et al., 2022) exploring this outcome.

3.4.1.11 Other outcomes

One out of two studies (50%) indicated significant differences in coping strategy of ignoring and catastrophizing at post-treatment (Gasslander et al., 2022) with small effect sizes ($d = 0.38$ and $d = 0.34$), but not at follow-up in one out of one study (0%) that explored cognitive and behavioral coping strategies (Buhrman et al., 2015), in favor of CBT compared to TAU. One out of one study (100%) identified significant differences in improved pain-related disability at post-treatment with a small effect size ($d = 0.35$) in favor of CBT compared to TAU (Baumeister et al., 2021), but not at follow-up.

No differences were found between CBT and TAU in one out of one study examining kinesiophobia (Gasslander et al., 2022), fear avoidance (Ólason et al., 2018), and life control (Gasslander et al., 2022) at post-treatment. Two studies explored work capacity at post-treatment and follow-up (Schlicker et al., 2020; Baumeister et al., 2021), but neither found significant differences (0%).

3.4.2 Mindfulness-based interventions (MBI)

One of the MBI assessed the effects of Mindfulness-Based Cognitive Therapy (MBCT; De Jong et al., 2016, 2018), one of Integrative Medicine Group Visits (IMGV) with mindfulness techniques (Gardiner et al., 2019), and one of Mindful Self-Compassion (MSC) program (Torrijos-Zarcero et al., 2021). Two out of three studies evaluated MBI as the only therapeutic component (De Jong et al., 2016, 2018; Torrijos-Zarcero et al., 2021) and the remaining one as a multi-component (Gardiner et al., 2019) integrating mindfulness techniques, evidence-based integrative medicine, and medical group visits (Gardiner et al., 2019). The time horizon of the assessment of two of these studies was pre- and post (De Jong et al., 2016, 2018; Torrijos-Zarcero et al., 2021). All the analyses of MBIs were based on ITT. The efficacy of one study was tested in one RCT with results reported in two different publications (De Jong et al., 2016, 2018). Baseline comparisons were carried out in all MBI studies. Except for

Torrijos-Zarcero et al. (2021), all studies compared MBI with an inactive control group (TAU).

Two studies assessed depressive symptoms as the primary outcome (De Jong et al., 2016, 2018; Gardiner et al., 2019); and one evaluated self-compassion (Torrijos-Zarcero et al., 2021) as the primary outcome and depressive and anxiety symptoms as the secondary outcome. The characteristics of the MBI are detailed in Table 3 and the specific results of each study are presented in Supplementary Table S3. The evidence for each outcome is detailed below.

3.4.2.1 Depression

One study out of two (50%) identified significant differences in the reduction of depressive symptoms at post-treatment (De Jong et al., 2016, 2018) with a very small effect size ($d = 0.13$) in favor of MBI compared to TAU. The only study (Gardiner et al., 2019) that assessed depressive symptoms at follow-up found no significant difference between MBI and TAU.

No significant differences were identified in the study (Torrijos-Zarcero et al., 2021) comparing depressive symptoms at post-treatment between MBI and CBT.

3.4.2.2 Anxiety

No differences were found between CBT and TAU in one out of one study examining anxiety symptoms at post-treatment and at follow-up (De Jong et al., 2016, 2018).

In contrast, one study (Torrijos-Zarcero et al., 2021) reported significant differences in the reduction of anxiety symptoms at post-treatment with a very small effect size ($d = 0.17$) in favor of MBI compared to CBT.

3.4.2.3 Pain intensity

No significant differences between MBI and TAU (De Jong et al., 2016, 2018) and MBI and CBT (Torrijos-Zarcero et al., 2021) were reported at post-treatment in the reduction of pain intensity.

3.4.2.4 Pain interference

Neither of the two studies comparing pain interference between MBI and TAU at post-treatment (De Jong et al., 2016, 2018; Gardiner et al., 2019) and at follow-up (Gardiner et al., 2019) showed significant differences.

However, one study (Torrijos-Zarcero et al., 2021) indicated significant differences in the reduction of pain interference at post-treatment with a very small effect size ($d = 0.07$) in favor of MBI compared to CBT.

3.4.2.5 Pain catastrophizing

There was also no significant difference in the comparison between MBI and TAU in the reduction of pain catastrophizing in the only study (De Jong et al., 2016, 2018) that explored it at post-treatment.

One study (Torrijos-Zarcero et al., 2021) reported significant differences in decreasing pain catastrophizing at post-treatment with a very small effect size ($d = 0.12$) in favor of MBI compared to CBT.

3.4.2.6 Pain acceptance

One study (Torrijos-Zarcero et al., 2021) reported significant differences in increasing pain acceptance at post-treatment with a very small effect size ($d = 0.19$) in favor of MBI compared to CBT.

3.4.2.7 Pain self-efficacy

No significant differences between MBI and TAU (De Jong et al., 2016, 2018) were reported at post-treatment and follow-up in the reduction of pain self-efficacy.

3.4.2.8 Quality of life

One study (De Jong et al., 2016, 2018) out of two found significant differences in improving quality of life at post-treatment with a very small effect size ($d = 0.19$); and one (Gardiner et al., 2019), the only one featuring this comparison, found a significant effect at follow-up ($RR = 1.07$) in favor of MBI compared to TAU.

In contrast, no significant differences in quality-of-life improvement were identified (Torrijos-Zarcero et al., 2021) between MBI and CBT.

3.4.2.9 Mindfulness

One study (De Jong et al., 2016, 2018) showed significant differences in increased self-regulation with a large effect size ($d = 0.91$) and emotional awareness with a medium effect size ($d = 0.57$) at post-treatment.

Another study (Torrijos-Zarcero et al., 2021) identified significant differences in self-compassion with a very small effect size ($d = 0.05$) at post-treatment in favor of the MBI compared to CBT.

3.4.2.10 Behavioral activation

No significant differences between MBI and TAU (De Jong et al., 2016, 2018) were reported at post-treatment and follow-up in the reduction of behavioral activation.

3.4.3 Acceptance and commitment therapy (ACT) and behavioral activation therapy for depression (BATD)

One study explored the efficacy of ACT and BATD compared to TAU (Sanabria-Mazo et al., 2023). The time horizon of the assessment of this study was pre-, post, and follow-up and the analyses were based on ITT. Baseline comparisons were carried out in this study. This study assessed pain interference as the primary outcome. The characteristics of the ACT and BATD are detailed in Table 3 and the specific results of these studies are presented in Supplementary Table S3. The evidence for each outcome is detailed below.

3.4.3.1 Depression, anxiety, and stress

Significant differences were detected in the improvement of stress symptoms at post-treatment with medium effect size ($d = 0.69$), but not at follow-up, in favor of ACT compared to TAU. However, no significant differences between these groups were found in depressive and anxiety symptoms. Similarly, no significant differences between BATD and TAU and between ACT and TAU were found in the improvement of depressive, anxiety, and stress symptoms.

3.4.3.2 Pain interference, pain intensity, and pain catastrophizing

Significant differences between ACT and TAU were identified in the improvement of pain interference at post-treatment with a medium effect size ($d = 0.64$) and at follow-up with a medium effect size ($d = 0.73$). BATD was only statistically superior to TAU at follow-up with a medium effect size ($d = 0.66$). No significant differences between ACT and TAU, between BATD and TAU, and

between ACT and BATD were found in pain intensity. A significant reduction in pain catastrophizing was reported by patients assigned to ACT and BATD at post-treatment with small and medium effect sizes ($d = 0.45$ and $d = 0.59$, respectively) and at follow-up with medium effect sizes ($d = 0.59$, in both) compared to TAU.

3.4.3.3 Pain acceptance

Significant differences were found in the improvement of pain acceptance at post-treatment with a small effect size ($d = 0.34$) and at follow-up with a small effect size ($d = 0.42$) in ACT compared to TAU. In contrast, no significant differences between BATD and TAU and between ACT and BATD were found in pain acceptance.

3.4.3.4 Psychological flexibility

Significant differences were identified in the improvement of psychological flexibility at post-treatment with a medium effect size ($d = 0.52$) and at follow-up with a small effect size ($d = 0.37$) in ACT compared to TAU. Similarly, significant differences between BATD and TAU were found in psychological flexibility with a small effect size ($d = 0.40$), but not at follow-up. No significant differences between ACT and BATD were found in psychological flexibility.

3.4.3.5 Behavioral activation

Significant differences between ACT and TAU and between BATD and TAU were found in behavioral activation at post-treatment with small effect sizes ($d = 0.30$ and $d = 0.46$, respectively), but not at follow-up. No significant differences between ACT and BATD were found in behavioral activation.

3.5 Summary of results

Table 4 details a synthesis of all the evidence identified in the comparison between CBT, MBI, ACT, or BATD and TAU.

3.6 Upcoming RCT

One upcoming RCT was identified. This RCT will evaluate the efficacy of internet-delivered ACT and internet-delivered CBT compared to attention control in patients with chronic non-cancer pain and major depression (Bell et al., 2020). The general characteristics of this study are detailed in Supplementary Table S4.

4 Discussion

Depression and anxiety are among the most diagnosed mental health conditions in people with chronic pain. Identification of effective therapies is needed because of the poorer prognosis and higher therapy resistance entailed in comorbid pain and psychological distress compared to either condition considered alone. However, to date, no published systematic reviews have attempted to synthesize the efficacy of these interventions in patients with these combined conditions. The current systematic review demonstrates positive, but modest, results from CBT-based interventions for patients with chronic pain and clinically relevant psychological distress. A total of twelve RCTs and one non-RCT published between 2011 and 2023 were included in the analyses. In addition, it was noted that one RCT is upcoming that will explore the efficacy of ACT and traditional CBT in patients with chronic non-cancer pain and major depression, and results are expected soon (Bell et al., 2020). Taken together, the published and upcoming studies signal an increasing interest in examining how CBT-based therapies (CBT, MBI, ACT, and BATD) can improve the functional status and quality of life in patients with chronic pain experiencing clinically relevant depressive and/or anxiety symptoms. There is also an increasing interest in recognizing potential beneficial therapeutic processes of change in patients with this comorbidity in the second and third wave of CBTs (Hayes and Hofmann, 2021), such as acceptance of pain, psychological flexibility, and behavioral activation (Buhrman et al., 2015; Bell et al., 2020; Gasslander et al., 2022; Sanabria-Mazo et al., 2023).

Compared to TAU, traditional CBT reported significant differences in the reduction of depressive and anxiety symptoms and in the increase of quality of life at post-treatment and at follow-up, with very large to small effect sizes. These results are consistent with the reported efficacy of CBT-based interventions for depression or chronic pain in previous systematic reviews (Lorenzo-Luaces et al., 2018; López-López et al., 2019; Williams et al., 2020), but with a more modest magnitude. Nevertheless, in general, no significant differences between traditional CBT and TAU were identified at post-treatment and follow-up in the studies exploring pain intensity and pain catastrophizing. Although with a limited number of studies, there is also evidence that CBT could be beneficial in improving pain interference and pain acceptance (Buhrman et al., 2015; Gasslander et al., 2022) at posttreatment, but not at follow-up, with small effect sizes. In other pain-related variables, such as pain self-efficacy, pain-related disability, fear avoidance, kinesiophobia, working capacity, and social functioning, inconsistent results or insufficient evidence were obtained.

As in previous research in chronic pain (Veehof et al., 2016; Hilton et al., 2017; Khoo et al., 2019), compared to TAU, MBI produced a significant reduction at post-treatment in depressive symptoms, in one out of two studies (De Jong et al., 2018), and an increase in emotional awareness and self-regulation, in the one study that addressed this (De Jong et al., 2016). However, this evidence comes from a pilot RCT with a small sample size (De Jong et al., 2016, 2018). More evidence is needed to determine the overall efficacy of MBI in depression, anxiety, pain, and quality of life for populations with this comorbidity. Results from a single study (Torrijos-Zarcero et al., 2021) indicated significant differences in anxiety, pain interference, pain acceptance, pain catastrophizing, and self-compassion at post-treatment in favor of MBI compared to CBT.

Findings from a recent RCT provided evidence of the clinical utility of including remote synchronous video group-based ACT or BATD as adjuncts to TAU for the improvement of pain interference and pain catastrophizing after treatment and in the follow-up to patients with chronic low back pain (CLBP) and comorbid depressive symptoms. However, no significant differences in depressive or anxiety symptoms were found in ACT and BATD compared to TAU at any assessment time points. In both active therapies, improvements in pain interference at follow-up were significantly mediated by improvements at post-treatment in psychological flexibility (Sanabria-Mazo et al., 2023). Investigating the mediating role of psychological flexibility in the third wave of CBTs for chronic pain patients is important for understanding the mechanisms of change underlying

TABLE 4 Synthesis of all evidence identified in the comparison between CBT or MBI and TAU.

Outcome	Studies (*n*)	IG (*n*)	CG (*n*)	Significant* differences at posttreatment IG vs. CG (*n*, %)	Significant* differences at follow-up IG vs. CG (*n*, %)
Cognitive behavioral therapy (CBT)					
Depression	8 [1–5,7–9]	551	521	(6/8, 75%) [1–3,7–9]	(4/6, 67%) [1,4,5,8]
Anxiety	6 [1–4,7,9]	270	255	(5/6, 83%) [1,2,3,7,9]	(3/4, 75%) [1,4,7]
Stress	1 [3]	34	25	(1/1, 100%) [3]	–
Fear of anxiety	2 [2,9]	123	116	(0/2, 0%)	(0/1, 0%)
Fear-avoidance	1 [4]	39	38	(0/1, 0%)	–
Pain intensity	5 [4,5,7–9]	445	432	(1/5, 20%) [8]	(0/4, 0%)
Pain interference	4 [2,5,9]	290	277	(2/3, 67%) [2,9]	(0/2, 0%)
Pain catastrophizing	2 [2,9]	123	116	(0/2, 0%)	(0/1, 0%)
Pain acceptance	2 [2,9]	123	116	(2/2, 100%) [2,9]	(0/1, 0%)
Pain self-efficacy	3 [7–9]	239	232	(1/3, 33%) [8]	(1/2, 50%) [8]
Pain related disability	1 [8]	104	105	(1/1, 100%) [8]	(0/1, 0%)
Kinesiophobia	1 [9]	95	92	(0/1, 0%)	–
Coping strategy	2 [2,9]	123	116	(1/2, 50%) [9]	(0/1, 0%)
Life control	1 [9]	95	92	(1/1, 100%) [9]	-
Working capacity	2 [7,8]	144	141	(0/2, 0%)	(0/2, 0%)
Quality of life	6 [1–3,7–9]	345	322	(4/6, 67%) [1,3,8,9]	(2/4, 50%) [1,8]
Social functioning	3 [4,7,9]	174	166	(0/3, 0%)	(1/1, 100%) [4]
Mindfulness-based interventions (MBI)					
Depression	2 [10,11]	102	93	(1/2, 50%) [10]	(0/1, 0%)
Anxiety	1 [10]	26	14	(0/1, 0%)	(0/1, 0%)
Pain intensity	2 [10,11]	88	75	(0/2, 0%)	-
Pain interference	2 [10,11]	102	93	(0/2, 0%)	(0/1, 0%)
Pain catastrophizing	1 [10]	26	14	(0/1, 0%)	-
Pain self-efficacy	1 [10]	26	14	(0/1, 0%)	(0/1, 0%)
Quality of life	2 [10,11]	102	93	(1/2, 50%) [10]	(1/1, 100%) [10]
Self-regulation	1 [10]	26	14	(1/1, 100%) [10]	-
Emotional awareness	1 [10]	26	14	(1/1, 100%) [10]	-
Behavioral activation	1 [10]	26	14	(0/1, 0%)	(0/1, 0%)
Acceptance and commitment therapy (ACT)					
Depression	1 [13]	78	78	(0/1, 0%)	(0/1, 0%)
Anxiety	1 [13]	78	78	(0/1, 0%)	(0/1, 0%)
Stress	1 [13]	78	78	(1/1, 100%)	(0/1, 0%)
Pain intensity	1 [13]	78	78	(0/1, 0%)	(0/1, 0%)
Pain interference	1 [13]	78	78	(1/1, 100%)	(1/1, 100%)
Pain catastrophizing	1 [13]	78	78	(1/1, 100%)	(1/1, 100%)
Pain acceptance	1 [13]	78	78	(1/1, 100%)	(1/1, 100%)
Behavioral activation	1 [13]	78	78	(1/1, 100%)	(0/1, 0%)
Psychological inflexibility	1 [13]	78	78	(1/1, 100%)	(1/1, 100%)
Behavioral activation therapy for depression (BATD)					
Depression	1 [13]	78	78	(0/1, 0%)	(0/1, 0%)
Anxiety	1 [13]	78	78	(0/1, 0%)	(0/1, 0%)
Stress	1 [13]	78	78	(0/1, 100%)	(0/1, 0%)

TABLE 4 (Continued)

Outcome	Studies (*n*)	IG (*n*)	CG (*n*)	Significant* differences at posttreatment IG vs. CG (*n*, %)	Significant* differences at follow-up IG vs. CG (*n*, %)
Pain intensity	1 [13]	78	78	(0/1, 0%)	(0/1, 0%)
Pain interference	1 [13]	78	78	(1/1, 100%)	(1/1, 100%)
Pain catastrophizing	1 [13]	78	78	(1/1, 100%)	(1/1, 100%)
Pain acceptance	1 [13]	78	78	(0/1, 100%)	(0/1, 100%)
Behavioral activation	1 [13]	78	78	(1/1, 100%)	(0/1, 0%)
Psychological inflexibility	1 [13]	78	78	(1/1, 100%)	(0/1, 0%)

This table presents the evidence obtained in the exclusive comparison between CBT, MBI, ACT, or BATD and TAU. The evidence from the studies of [6] Boersma et al. (2019), a comparison of CBT and hybrid therapy (exposure in vivo and DBT), and [12] Torrijos-Zarcero et al. (2021), a comparison of MSC and CBT, is indicated in the text. The numbering of the synthesized evidence is indicated in brackets. [1] Tlach and Hampel (2011), [2] Buhrman et al. (2015), [3] Migliorini et al. (2016), [4] Ólason et al. (2018), [5] Aragonès et al. (2019), [7] Schlicker et al. (2020), [8] Baumeister et al. (2021), [9] Gasslander et al. (2022), [10] De Jong et al. (2016, 2018), [11] Gardiner et al. (2019), [13] Sanabria-Mazo et al. (2023). *$p < 0.05$.

treatment effectiveness, identifying effective treatment components, and enhancing treatment outcomes (McCracken et al., 2022). The results of the Bell et al. (2020) study, when available, could help provide stronger evidence for the findings known so far in the population with this comorbidity.

In most of the studies explored in this systematic review, CBT-based interventions were more effective than control groups in improving depression, anxiety, and quality of life, at both post-treatment and at follow-up, but not in the improvement of pain intensity. However, the findings of this systematic review should be interpreted with some caution, as they are based on few studies with high heterogeneity in terms of mode of delivery (e.g., face-to-face, online, and blended format), number of sessions, intervention components, compliance, and characteristics of therapists, among others. It is also important to consider the potential bias arising from studies with samples smaller than 50 participants per arm and the lack of information on the adverse effects of therapies (Moore et al., 2010). A recent Delphi study has pointed out the importance of recognizing what the main contents of CBT are. In this regard, three main components have been highlighted: (1) pain education; (2) increased activity; and (3) some form of cognitive challenge (Sharpe et al., 2020). In the studies included, there were also some differences in the types of CBT methods used or in the primary and secondary outcomes, which complicates the generalizability of these results.

Like previous meta-analyses in chronic pain (Williams et al., 2020) and depression (Lorenzo-Luaces et al., 2018), the efficacy of CBT-based interventions for comorbid pain and depression is clinically relevant on average (Sanabria-Mazo et al., 2020). As the findings of this study point out, the effects of CBT targeting the population with chronic pain and comorbid psychological distress are more modest than targeting one of the two conditions separately (Sanabria-Mazo et al., 2020). Psychological distress could potentially impact adherence to pain management interventions, leading to decreased engagement in self-care activities, and treatment plan compliance among patients with depression or anxiety, ultimately affecting treatment outcomes. Hence, it is crucial to evaluate and tackle depression in chronic pain populations for better treatment outcomes.

While the results of this systematic review fit with a wider conclusion that traditional CBT is beneficial for many varied conditions (Fordham et al., 2021), there appears substantial room for improvement. Considering the effects identified, it would be interesting to explore, when more robust evidence is available, the efficacy of third-generation therapies in patients with chronic pain and comorbid psychological stress. Although evidence is beginning to emerge on the effects of third-wave CBT therapies compared with TAU (De Jong et al., 2016, 2018; Gardiner et al., 2019; Bell et al., 2020; Torrijos-Zarcero et al., 2021; Sanabria-Mazo et al., 2023), more research is needed to compare which therapy is most effective, in which circumstances, and for whom.

4.1 Limitations and strengths

These findings must be interpreted to understand the following limitations and strengths. First, given the lack of trials with low RoB, it might be premature to conclude the magnitude of the efficacy of CBT-based interventions for this comorbidity. Second, since the heterogeneity of available data in the included studies (e.g., mode of delivery, number of sessions, intervention components, and characteristics of therapists, among others), it was not possible to compute a meta-analysis. Third, although published and unpublished studies were explored, only published studies in English or Spanish were finally included in this systematic review, so other otherwise relevant evidence could have been omitted. Fourth, due to the limited number of RCTs, it was not possible to examine whether specific forms of CBT are more effective than others. The strengths of this study are the number of databases explored, the compliance with PRISMA guidelines, the validation of the Boolean searches according to PRESS guidelines, the use of Rayyan as a tool to minimize possible loss of evidence, and the consensual review between reviewers in the different phases of screening, extraction of the data, and RoB.

4.2 Future research

Further research is needed in this area when more studies are available. The need to identify the core elements of psychosocial therapies that drive their therapeutic effects is critical. To extend the knowledge on the relevant topic examined in this study, future studies should explore the ingredients that are indeed effective and for which patients, as well as what amount of variance is explained by universal factors shared by all therapies. These interventions should also strive to employ adequately powered randomized

designs and compare the efficacy of psychological therapies to other empirically supported therapies.

5 Conclusion

The comorbidity of chronic pain and psychological distress represents a complex problem or set of problems, perhaps best conceived as having a multifactorial aetiology. Psychological research and treatment should address these because when they appear together, they cause substantial health and social impacts. This study shows that traditional CBT improves depression, anxiety, and quality of life in patients with comorbid chronic pain and clinically relevant psychological distress, but not for pain intensity and pain catastrophizing. Although some evidence is presented in this systematic review, more RCTs based on MBI, ACT, and BATD are needed to determine the overall efficacy of this intervention in these patients.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

JL, AS, SE, and JS-M designed the study. JS-M, AC-C, ÓF-V, and GN-R performed the eligibility criteria, data extraction, and study coding. JS-M and AC-C performed the data analysis and synthesized all extracted data. JS-M drafted the manuscript. GC-R, AM-P, JC-A, SE, XB, AS, AF-S, and JL revised and approved the final version of the manuscript. LM critically revised and supervised the final draft. All authors commented on, revised, and approved the draft and the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2023.1200685/full#supplementary-material

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2. Artículo 2

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ABSTRACT

Introduction The IMPACT study focuses on chronic low back pain (CLBP) and depression symptoms, a prevalent and complex problem that represents a challenge for health professionals. Acceptance and Commitment Therapy (ACT) and Brief Behavioural Activation Treatment for Depression (BATD) are effective treatments for patients with persistent pain and depression, respectively. The objectives of this 12 month, multicentre, randomised, controlled trial (RCT) are (i) to examine the efficacy and cost-utility of adding a group-based form of ACT or BATD to treatment-as-usual (TAU) for patients with CLBP and moderate to severe levels of depressive symptoms; (ii) identify pre–post differences in levels of some physiological variables and (iii) analyse the role of polymorphisms in the *FKBP5* gene, psychological process measures and physiological variables as mediators or moderators of long-term clinical changes.

Methods and analysis Participants will be 225 patients with CLBP and moderate to severe depression symptoms recruited at Parc Sanitari Sant Joan de Déu (St. Boi de Llobregat, Spain) and Hospital del Mar (Barcelona, Spain), randomly allocated to one of the three study arms: TAU vs TAU+ACT versus TAU+BATD. A comprehensive assessment to collect clinical variables and costs will be conducted pretreatment, post-treatment and at 12 months follow-up, being pain interference the primary outcome measure. The following physiological variables will be considered at pretreatment and post-treatment assessments in 50% of the sample: immune-inflammatory markers, hair cortisol and cortisone, serum cortisol, corticosteroid-binding globulin and vitamin D. Polymorphisms in the *FKBP5* gene (rs3800373, rs9296158, rs1360780, rs9470080 and rs4713916) will be analysed at baseline assessment. Moreover, we will include mobile-technology-based ecological momentary assessment, through the Pain Monitor app, to track ongoing clinical status during ACT and BATD treatments. Linear mixed-effects models using restricted maximum likelihood, and a full economic evaluation applying bootstrapping techniques, acceptability curves and sensitivity analyses will be computed.

Ethics and dissemination This study has been approved by the Ethics Committee of the Fundació Sant Joan de Déu and Hospital del Mar. The results will be actively disseminated through peer-reviewed journals, conference presentations, social media and various community engagement activities.

Trial registration number NCT04140838

Strengths and limitations of this study

- This is thought to be the first study comparing the efficacy and cost-utility of Acceptance and Commitment Therapy and Behavioural Activation Treatment for Depression in addition to treatment as usual (TAU) versus TAU alone for the management of comorbid chronic low back pain (CLBP) and depression.
- The IMPACT protocol combines assessment with classical legacy measures and ecological momentary assessment to obtain more precise information on the dynamics of the variables to be assessed.
- Besides self-report measures, this study will include physiological variables such as cortisol, cytokines and vitamin D levels, in order to know the impact of treatments on these stress-related biological variables.
- As far as we know, this study represents the first attempt to explore the predictive role of *FKBP5* gene and distal or proximal stressful experiences in response to psychological treatments for CLBP and depression.
- Blinding of patients and therapists will not be possible. This represents a fundamental problem in randomised controlled trials with psychological treatments.

INTRODUCTION

Recent systematic reviews have estimated that more than 10% of the general population worldwide suffers chronic pain.[1 2] Among chronic pain conditions, chronic low back pain (CLBP) is one of the most prevalent and costly.[3 4] Depression is by far the most common psychiatric problem associated with CLBP.[5 6]

The relationship between pain and depression is bidirectional.[7] Some theories postulate that pain and depression share common physiopathological mechanisms and that one can lead to the other via activation of these mechanisms. This could include mediators of the inflammatory and immune response and the role they play in endogenous nociceptive regulation and affective regulation.[8] In particular, cytokines appear to have a crucial role in chronic pain conditions, so that a high expression of proinflammatory mediators can alter the physiopathology of chronic pain.[9] At the same time, inflammatory mediators of innate immunity and cell-mediated immunity cooperate in the onset and expression of depression.[10] On the other hand, a clear correlation between vitamin D deficiency and the presence of chronic pain and depression has been described in recent years.[11] Vitamin D substantially modulates the inflammatory response by controlling cytokine expression, inhibiting proinflammatory, and increasing anti-inflammatory ones. Vitamin D deficiency could affect the response of patients with chronic pain to the treatments applied.[12–15]

Chronic stress appears to play a pivotal role in mental and physical health and leads to hypothalamic–pituitary–adrenal axis (HPA) dysregulation which in turn impairs the stress response.[16 17] Genetic, epigenetic and early stress exposure, among other factors, shape individual resilience and vulnerability, as well as HPA activity.[18 19] In this regard, the FKB506 binding protein 51 gene (FKBP5) is a critical regulator of glucocorticoid receptor activity (and thus HPA function too) and its interaction with distal and proximal stressors has not been previously examined in comorbid chronic pain and depression. This interaction could be key for understanding the etiological mechanisms involved in such conditions, as well as for identifying potential therapeutic mechanisms.[20–26] In addition, hair cortisol reflecting long-term HPA activity has recently emerged as a potential predictor of treatment response in anxiety and depression.[19]

The therapeutic options available for chronic pain management are very extensive. Interestingly, a number of psychological treatments have shown positive effects at the psychological, neuroendocrine and immune levels in a wide range of pain-related conditions, as well as for depression.[27] These generally comprise forms of Cognitive Behavioural Therapy (CBT), including treatments that focus on mindfulness, and Acceptance and Commitment Therapy (ACT). In a meta-analysis of 11 clinical trials in patients with chronic pain,[28] ACT was better than the control conditions in improving pain acceptance, functional impairment, anxiety, depression and pain intensity. In addition, another form of CBT, Behavioural Activation Treatment for Depression (BATD), has proved to be as effective as classical CBT in reducing depressive symptoms in a meta-analysis.[29]

Both treatments, ACT and BATD, are potentially cost-effective for the management of chronic pain and depression, respectively, according to a recent systematic review carried out by the team of the present project.[30] In our opinion, it is important to demonstrate their cost-utility for the management of a complex problem as relevant as comorbid CLBP and depression, to characterise the psychological and physiological mechanisms through which they exert their therapeutic effect, and identify potential predictors of treatment response.

The objectives of the IMPACT (*Improving Pain and Depression with ACT and BATD*) study are (i) to examine the efficacy and cost-utility of adding ACT or BATD to treatment-as-usual (TAU) in the management of patients with CLBP and moderate to severe depression for improving pain interference (primary outcome) and depressive, anxious and stress symptoms, pain catastrophising and quality of life (secondary outcomes); (ii) to identify pre–post differences in levels of different physiological variables (immune-inflammatory markers, hair cortisol and cortisone, serum cortisol, corticosteroid-binding globulin (CBG) and vitamin D) and correlate these changes with those observed at self-report measures and (iii) analyse the role of polymorphisms in the *FKBP5* gene, psychological process measures and physiological variables as mediators or moderators of long-term clinical changes.

METHODS AND ANALYSIS

Trial design

The RCT protocol has been developed following the Standard Protocol Items: Recommendations for Interventional Trials.[31] For reporting, we will follow the

guidelines of the Consolidated Standards of Reporting Trials (CONSORT)[32] and the Consolidated Health Economic Evaluation Reporting Standards statement.[33] IMPACT is a 12-month multicentre RCT with three treatment arms: TAU, TAU+ACT and TAU+BATD. Therefore, patients in three arms will receive TAU, and ACT and BATD will be complementary treatments to the standard one provided in the Spanish National Health System.

Recruitment strategy

Potential participants are those patients with CLBP diagnosis seeking services currently or in the last 3 years at Parc Sanitari Sant Joan de Déu (St. Boi de Llobregat, Spain) or Hospital del Mar (Barcelona, Spain). These patients will be screened to evaluate their current pain intensity and the Patient Health Questionnaire (PHQ-9) will be administered to confirm the presence of moderate to severe active depression.

Sample size

Sample size was estimated considering a target power of 80%, an alpha level of 0.05 and was calculated taking the primary outcome measure into account (Brief Pain Inventory-Interference Scale (BPI-IS)). The estimate was based on a one-way analysis of variance (followed by Dunn–Bonferroni post-hoc tests) for between-group differences in the change from baseline to subsequent assessment, assuming no systematic baseline or other covariate group differences after randomisation. The minimal clinically significant difference for the BPI-IS is 1 point (SD of improvement of 2 points).[34] This calculation yielded a suggested sample size of 64 patients per study arm. Allowing for a potential attrition rate of 15% our final sample size was 75 participants per group.

Eligibility criteria

All participants will meet the following inclusion criteria: male or female aged 18–70 years; diagnosis of CLBP (≥3 months) according to medical history; pain intensity ≥4 points out of 10 points on a numeric pain rating scale in the past week; moderate to severe depressive symptoms according to PHQ-9 (total score ≥10); fluent in Spanish language and provision of written informed consent to participate (a copy of the consent form is provided as an (online supplementary document). Only participants with a score of at least 60% on the question 'Which situation describes your pain over the past 4 weeks the best? 100% of the pain in the low back; 80% of the pain in the low back and 20% in the leg(s); 60% of the pain in the low back and 40% in the leg(s); 50% of the pain in the low back and 50% in the leg(s); 40% of the pain in the low back and 60% in the leg(s); or 20% of the pain in the low back and 80% in the leg(s)' will be included. With this question, we will be able to differentiate dominant leg pain from dominant CLBP, avoiding the likelihood of recruitment of participants suffering dominant radiculopathy.[35]

Potential participants will be excluded according to the following exclusion criteria (based on previous RCTs):[36] the presence of cognitive impairment; previous (last year) or current psychological treatment; presence of severe psychiatric disorder (eg, psychotic disorder), substance dependence/abuse or presence of degenerative medical disease (eg, Alzheimer's dementia); patients involved in litigation with the health system; patients with scheduled surgical intervention or other interventions and inability to attend group treatment sessions. For the biomarkers substudy (50% of patients in each study arm), the following exclusion criteria will be added: cold/infection symptoms on the day of blood collection; needle phobia; BMI>30 kg/m^2 or weight >110 kg; consumption >8 units of caffeine per day (maximum one drink with caffeine on the day of testing); smoker >5 cigarettes a day; hair length <3 cm, use of glucocorticoid medication or anticytokine drugs and being pregnant or breastfeeding.

Procedure and randomisation

A list of potential participants (with contact telephone number) will be presented to the study team at each centre. This list will pass to the clinicians, so that they carry out the telephone screening and set an appointment for the first face-to-face interview (performed by health psychologists) with all those who agree to participate and meet the eligibility criteria. After obtaining informed written consent, the evaluators will conduct the baseline interview using battery of computer-administered measures. Patients will be contacted again after 3–5 days to obtain peripheral blood and hair samples. These extractions will be performed at a preset time (8.00–9.00 AM) to reduce circadian variability in the levels of the immune and endocrine markers evaluated. In order to limit the effects of medication on the study variables, patients will be asked to refrain from taking analgesic or anti-inflammatory drugs within 72 hours prior to obtaining the biological samples.

Random assignment of participants to study arms will be executed after baseline assessments as recommended by the CONSORT guidelines.[32] Randomisation will be planned and executed by a statistician with no involvement in screening, enrolment or treatment processes. Once written consent and baseline assessment have been completed, study participants will be given a unique personal code and randomised by means of an online randomisation programme. The computer-generated randomisation will apply a permuted block design to ensure that the groups are balanced taking biomarkers substudy eligibility criteria into account. The randomisation list will remain with the clinical trials committee of Fundació Sant Joan de Déu (FSJD) for the full duration of the RCT. This list will be stored in an encrypted file on a password-protected computer in the clinical trials supervisor's office to assure concealment of allocation. Participants' assignments will be communicated to administrative personnel of each centre by the clinical trials supervisor via e-mail. Patients will be informed of

their group allocation by the administrative personnel, who will send a notification in sealed, opaque numbered envelopes.

Two subsequent face-to-face assessments will be carried out at the end of the 8 weeks of treatment (post-treatment) and at 12 months follow-up (56 weeks after randomisation). To obtain the biological samples at post-treatment, the same procedure as in the baseline assessment will be followed. See figure 1 for patients' flow chart.

Treatments

Treatment-as-usual

In Spain, chronic pain management is mainly carried out by general practitioners (GPs) in regular consultations, commonly consisting of face-to-face visits (5–10 min) to monitor the physical and emotional status of the patient. GPs usually provide advice, and prescribe pharmacotherapy (pain medications, hypnotics and antidepressants) or make onward referrals to pain units in hospitals when more specialised pain management procedures are required. The frequency of consultations is based on the type and stage of disease of each patient. For this study, usual care will be the same as in routine daily practice, without any modifications.

Treatment-as-usual+Acceptance and commitment therapy

The ACT treatment component includes, as the name implies, methods to promote acceptance (non-avoidance) of unwanted experiences, and engagement in goal-directed and values-based action. Alternatively, ACT is focused on promoting psychological flexibility, or the ability to develop behaviour patterns *open, aware and engaged*[37] (see table 1). Patients suffering from pain recurrently use avoidance as a coping strategy, and at its most basic level, this therapy is designed to address that by providing a broader set of skills. There is now considerable evidence for the therapeutic model underlying ACT[38] and for the treatment approach itself as applied to chronic pain. Recent meta-analyses supported the effectiveness of ACT in patients with chronic pain.[28 39]

Treatment-as-usual+Behavioural activation treatment for depression

BATD is based on the application of learning principles to the pattern of withdrawn or reduced behaviour activity associated with depression (see table 2). Its objective is to counteract depressive symptoms and, as a consequence, to ensure that patients regain a productive and emotionally satisfying life. Its methodology essentially consists in 'activating' subjects with depression through programming

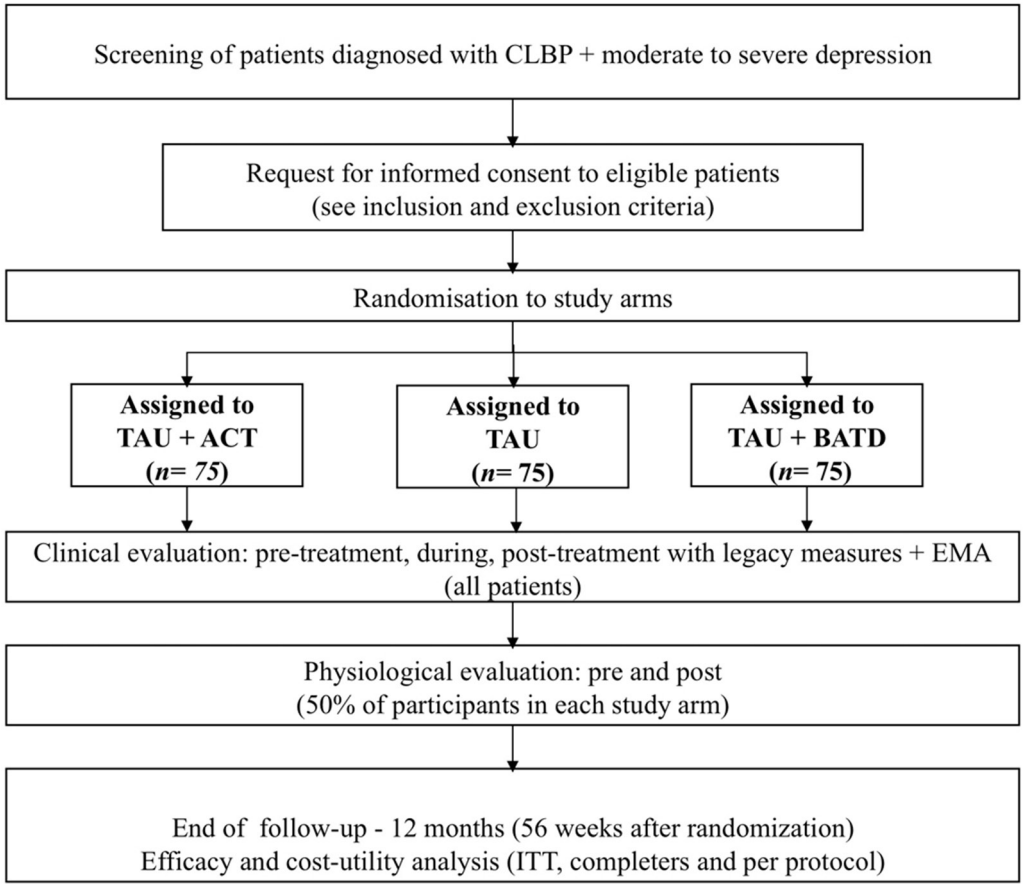

Figure 1 Flowchart of the IMPACT study based on the Consolidated Standards of Reporting Trials guidelines. ACT, Acceptance and Commitment Therapy; BATD, Brief Behavioural Activation Treatment for Depression; CLBP, chronic low back pain; EMA, ecological momentary assessment; ITT, intention-to-treat; TAU, treatment as usual.

Table 1 Outline of ACT group treatment sessions

Session	ACT
1	Participants' and clinician's presentation. Psychoeducation and introduction to ACT (ACT basics; scientific advances in chronic pain and depression management; psychological theories of pain, suffering and stress; stressors, fears and indicators; identification of values; breathing exercises).
2	Value analysis I. Problems of experiential avoidance. Creative hopelessness through metaphors: control is the problem and not the solution. Anxiety, fight and flight, and its effects. Accepting the risk of the life's journey: experiences, feelings and emotions.
3	Value analysis II. Objectives. Laws of thought and consequences of language. Mind and deactivation of thought (cognitive defusion): creating distance with thoughts. Learning meditation techniques and effects. Practicing meditation exercises.
4	Value analysis III. Psychological barriers and obstacles. Emotional distress and its consequences. Emotional phenomena, personality variables and health states. Discovering commitments with committed actions.
5	Values and feelings. Taking the initiative with a 'Plan of action and willingness'. Psychological flexibility, resilience and self-motivation. Expansion and body scan exercises. Learning to relax.
6	Taking a direction. The self as context, process and content. Awareness of the present: 'here and now'. The brain and emotions: managing situations and overwhelming emotional responses.
7	Dare and change: willingness and determination. Self-awareness, assertiveness and self-esteem. Experiential expansion exercises: felt sensations. Happiness according to positive psychology. Benefits of physical exercise: movement.

At the beginning of each session, time will be taken to briefly go over what was discussed in the previous session and every person's weekly records will be collected and briefly commented on.
ACT, Acceptance and Commitment Therapy.

and conduct of behaviours that are likely to increase the experiences of directly positively reinforcing qualities in their current context. A meta-analysis supported the effectiveness of behavioural activation in patients with depression.[29]

Both psychological treatments (ACT and BATD) will be administered in a group format of 8 weekly 1.5 hour sessions. In RCTs of psychological treatment, it is recommend that more than one therapist deliver each treatment to create a more realistic and generalisable impression of

Table 2 Outline of BATD group treatment sessions

Session	Description
1	Participants' and clinician's presentation. Collection of information related with areas of activity and interaction contexts. Delivery of activity log to obtain an accurate assessment of the patient's daily activities, which is useful for: providing a baseline measure and comparing their progress when their activity level increases later in the treatment.
2	Identification of information related to depressive behaviours. Exploration of problematic behaviours and identification of patients' objectives regarding treatment.
3	Obtaining complementary information regarding the characteristics of the history of patient interactions and any contexts and interactions that reinforce depressive behaviours. Establishment of short-term, medium-term and long-term goals.
4	Explanation of the hypotheses of factors associated with the origins, maintenance and therapeutic change of problematic behaviour. In this session, 10 personalised activities are selected according to each person's own needs and desires, without any particular order. With the selected activities, a ranking is then generated that goes from the least difficult to the most difficult activity.
5	Once the 10 target activities have been identified, a record is made to track their progress weekly, including the number of times they would like to complete the activity in a period of 1 week (the ideal frequency). The number of activities varies each week, but they always range between three and five activities.
6	Discussion of what was obtained from the records in general. Exploration of the satisfaction with the activities.
7	Coping abilities. How to approach emotions and reactions to events and responses associated with depression. Relationship between avoidance behaviours and maintenance of difficulties.
8	Examination of new behaviours to be incorporated. Discussion about the goals achieved and the barriers to maintain the weekly activity plan. Farewell.

BATD, Brief Behavioural Activation Treatment for Depression.

effectiveness,[40] so each therapy will be conducted by at least three different therapists. In addition to prior experience delivering ACT or BATD, all therapists will do a 3-hour 'refresher' training prior to starting the RCT with the aim also to assure simultaneous fidelity to the manual with flexibility within sessions. Finally, to monitor treatment fidelity within ACT and BATD, research assistants will video-tape all sessions. Two independent experts in both treatments have been selected for his expertise in the delivery of these therapies. They will rate adherence to treatment using videotapes of therapy sessions. A random sample of tapes, stratified by therapist and therapy session will be rated using the instruments described below.

Study measures

All participants will be assessed with a computer-administered battery of measures, using the software Research Electronic Data Capture (REDCap) (see table 3).

Measures for sociodemographic characteristics, clinical features and screening

Sociodemographic Questionnaire. Information about gender, date of birth, marital status, living arrangements, educational level, income level and employment status.

Clinical data. Ad hoc interview collecting data about history and duration of CLBP and depression symptoms,

Table 3 Time points at which measures and data are collected

Measures	Pre	During	Post	1-year follow-up
Sociodemographic, clinical and screening measures				
Sociodemographic data (gender, date of birth, marital status)	X			
Clinical data (years of evolution, comorbidities)	X			
PHQ-9 (depression symptoms)	X			
CIDI (diagnosis of depression)	X			
CTQ-SF (childhood trauma)	X			
Primary outcome measure				
BPI-IS (pain interference)	X		X	X
Secondary outcome measures				
NRS (pain intensity)	X		X	X
DASS-21 (anxiety, depression and stress)	X		X	X
PCS (pain catastrophising)	X		X	X
Process measures				
CPAQ-8 (pain acceptance)	X		X	X
BADS-SF (behavioural activation for depression)	X		X	X
Other measures				
EQ-5D-5L (quality of life)	X		X	X
CEQ (credibility and expectations regarding treatments)	X		X	
CSRI (medication consumption and service receipt)	X			X
AET (negative effects of psychological treatments)			X	
PGIC and PSIC (impression of change)			X	
ACT-FM (fidelity measure)		X	X	
QBAS (fidelity measure)		X	X	
Pain Monitor app		X		
Physiological variables				
Immune-inflammatory markers	X		X	
HPA and vitamin D markers	X		X	
FKBP5 polymorphisms	X			

ACT-FM, Acceptance and Commitment Therapy Fidelity Measure; AET, Adverse Effects of Treatments checklist; BADS-SF, Behavioural Activation for Depression Scale (short form); BPI-IS, Brief Pain Inventory-Interference Scale; CEQ, Credibility/Expectancy Questionnaire; CIDI, Composite International Diagnostic Interview—depression section; CPAQ-8, Chronic Pain Acceptance Questionnaire (8-item version); CSRI, Client Service Receipt Inventory; CTQ-SF, Childhood Trauma Questionnaire–Short Form; DASS-21, Depression Anxiety Stress Scales-21; EQ-5D-5L, EuroQoL; HPA, hypothalamic–pituitary–adrenal; NRS, Numerical Pain Rating Scale; PCS, Pain Catastrophising Scale; PGIC, Patient Global Impression of Change; PHQ-9, Patient Health Questionnaire; PSIC, Pain Specific Impression of Change; QBAS, Quality of Behavioral Activation Scale.

and family history of medical/mental illness. Information regarding comorbidity with other diagnosed physical–psychiatric conditions and the type and dose of current drugs will be consulted in medical records.

The *Patient Health Questionnaire* (PHQ-9).[41 42] Each of the nine PHQ items corresponds to one of the DSM-IV Diagnostic Criterion A symptoms for major depressive disorder. Response options are 'not at all', 'several days', 'more than half the days' and 'nearly every day', scored as 0, 1, 2 and 3, respectively. In addition, the PHQ-9 has a functional impairment question (item 10) that asks how much the symptoms they endorse in the first nine items interfere with daily functioning. The questionnaire can be used algorithmically for the probable diagnosis of a depressive disorder, or as a continuous measure of scores ranging from 0 to 27, with cut-off points of 5, 10, 15 and 20, which set the levels of symptoms of depression as mild, moderate, moderately severe or severe. In the present work, if potential participants obtain a score ≥2 at item 9 (risk of suicide), additional assessment will be undertaken to explore the real risk of suicide. The telephone-administered version of the PHQ-9 showed adequate reliability (α=0.82),[43] therefore it seems highly recommendable for our telephone-based screening of concomitant depression symptomatology.

The *Composite International Diagnostic Interview—depression section* (CIDI V.3.0).[44] The CIDI is a fully structured diagnostic interview developed and validated by the WHO to be used with the general population by trained lay interviewers. The interview will be used to confirm the presence of major depression. The psychometric properties of the CIDI have been examined extensively and are highly sound.[44]

The *Childhood Trauma Questionnaire–Short Form* (CTQ-SF).[45] The CTQ-SF is a 28-item retrospective questionnaire designed to capture five dimensions of childhood maltreatment (each scale includes five items): physical abuse; emotional abuse; sexual abuse (SA); physical neglect and emotional neglect (EN). Additionally, there is a three-item minimisation/denial scale. Items are scored from 1 to 5 in order to reflect the frequency of maltreatment experiences ('never true' to 'very often true'). Higher scores indicate greater child abuse and neglect. The Spanish CTQ-SF obtained Cronbach's α values ranging from 0.66 for EN to 0.94 for SA.[46]

Primary outcome measure

The *Brief Pain Inventory-Interference Scale* (BPI-IS).[47] The BPI-IS is a seven-item self-report measure that assesses the extent to which pain interferes with general activity, walking, work outside and inside the home, sleep, mood, enjoyment of life and relationships, each rated on a 0 ('does not interfere') to 10 ('completely interferes') scale. Scoring is done by computing the arithmetic mean of all items, such that higher scores indicate greater pain interference. A reduction of 1 point on the BPI-IS is considered as a clinically meaningful change. The BPI-IS is highly recommended as an outcome in clinical trials of patients with chronic pain and the psychometric properties are well-established (α>0.80).[48]

Secondary outcome measures

The *Numeric Rating Scale* (NRS).[49] The NRS is a unidimensional measure of pain intensity mainly used for adults. The most used version is an 11-point numeric scale (a horizontal bar or line) with 0 representing 'no pain' and 10 representing 'worst pain imaginable'. Time frames vary between studies. In the present work, respondents will be asked to report average pain intensity over the last week.

The *Depression Anxiety Stress Scales-21* (DASS-21).[50] The DASS-21 is a self-report measure developed to differentiate between features of depression (low positive affect), anxiety (physical arousal) and stress (psychological tension/agitation) in clinical and non-clinical samples. In addition, the DASS has been validated in clinical chronic pain samples.[51] Responders are required to indicate the presence of a symptom over the previous week. Each item is scored from 0 ('did not apply to me at all over the last week') to 3 ('applied to me very much or most of the time over the past week'). There are seven items on each of the three subscales (Depression, Anxiety and Stress). Therefore, total scores in each scale can range from 0 to 21. Higher scores indicate more severe levels of depression, anxiety and stress. The Spanish version obtained adequate internal consistency (0.84, 0.70 and 0.82 for the depression, anxiety and stress scales, respectively).[52]

The *Pain Catastrophising Scale* (PCS).[53] The PCS will be used to assess the pain catastrophising thoughts. It is a 13-item measure that captures three dimensions: rumination over pain, magnification of pain and helplessness in the face of pain symptoms. Each item is answered on a rating scale of 5 points (0 = 'never', 4 = 'almost always'). Total scores on each scale can range from 0 to 52, with higher scores indicating more pain catastrophising thoughts. The Spanish PCS has shown good internal consistency (α=0.79) and test–retest reliability (r=0.84).[54]

Process measures

The *Chronic Pain Acceptance Questionnaire* (CPAQ-8).[55] The CPAQ-8 is a self-report measure reflecting engagement in important activities with pain and willingness to experience pain. The eight items are rated on a 7-point scale (0= 'never true', 6= 'always true'). Higher total scores reflect greater acceptance. The Spanish CPAQ-8 has adequate internal consistency, a Cronbach α values of 0.75.[56]

The *Behavioural Activation for Depression Scale—short form* (BADS-SF).[57 58] Behavioural activation is conceptualised as a key therapeutic process in BATD. The BADS-SF assesses this construct by means of a 9-item scale. Items are answered on a Likert scale of 7 points ranging from 0 ('not at all') to 6 ('completely'). Higher scores indicate greater behavioural activation in depressed individuals. The BADS-SF has shown adequate internal consistency (α=0.82).[57]

Other measures

The *EuroQoL* (version EQ-5D-5L).[59] The EQ-5D-5L is a health-related quality of life questionnaire that consists of two parts: in the first part, the individual's difficulties concerning mobility, self-care, pain/discomfort and anxiety/depression are evaluated; and in the second part, the current state of perceived health is assessed by a Visual Analogue Scale (VAS) ranging from 0 to 100. The EQ-5D-5L scores will be used to calculate the Quality-Adjusted Life Years (QALYs) during the follow-up period, adjusting the duration of time affected by the health outcome by the value of the utility.

The *Credibility/Expectancy Questionnaire* (CEQ).[60] The CEQ is a quick and easy to complete measure widely used to assess credibility and expectations regarding treatments. The CEQ contains six items: three of them focused on *therapy credibility* (the extent to which the treatment appears logical; the extent to which the treatment appears useful and the confidence with which the patient would recommend the treatment to a friend having the same problem) and three items assessing *expectations* (the extent to which the patient thinks an improvement will occur; the extent to which the patient feels that therapy will help him/her and the extent to which the patient feels an improvement will occur). The CEQ has demonstrated satisfactory psychometric properties.[60]

The *Client Service Receipt Inventory* (CSRI).[61] The CSRI will be used to collect retrospective data on medication consumption and service receipt. Regarding medication intake, patients are asked to bring their daily medication prescriptions and the following information for pain-related drugs (ie, analgesics, anti-inflammatories, opioids, muscle relaxants, antidepressants) is recorded: the name of the drug, the dosage, the total number of prescription days and the daily dosage consumed. Concerning service receipt, patients are asked about the total visits to accident and emergency services, the total number of general inpatient hospital admissions, the number of diagnostic tests administered and the total visits to healthcare professionals for pain management, including family physicians, nurses, social workers, psychologists, psychiatrists, group psychotherapy and other community healthcare professionals, specifying in each case if these services were provided by the public or by the private sector. The CSRI will be administered on two occasions: at baseline and at 12-month follow-up, both referring to the previous 12 months. Medical records will be checked to verify the accuracy of the collected data.

Ad-hoc measure of *Adverse Effects of Treatments*. It was developed in a previous RCT[36] and will be used to check the presence of negative effects of ACT and BATD. The item reads as follows: *Have you experienced, during the course of the psychological treatment, any unwanted symptom that you think might be directly or indirectly associated with the psychological intervention?*

The *Patient Global Impression of Change* (PGIC) and the *Pain Specific Impression of Change* (PSIC).[62] Patient impression of change measures are frequently used as indicators of meaningful change in treatments for chronic pain. The most frequently used scale is a 7-point numerical scale (from 1= 'Much better' to 7= 'Much worse'). The PGIC is one item referred to the perception of global improvement, whereas the PSIC asks about the impression of change in more specific domains: physical and social functioning, work-related activities, mood and pain. These scales will be completed by the participants who are assigned to ACT and BATD.

The *Acceptance and Commitment Therapy Fidelity Measure* (ACT-FM).[63] The ACT-FM is a recently developed 25-item measure that captures four areas: therapist stance, open response style, aware response style and engaged response style (each split into ACT consistent and ACT inconsistent items, making eight sections in all). Items are rated on a 4-point scale from 0 ('behaviour never occurred') to 3 ('therapist consistently enacts this behaviour').

The *Quality of Behavioural Activation Scale* (QBAS).[64] The QBAS is a 14-item scale designed to assess ability in implementing behavioural activation. Items are rated using a 7-point Likert-type scale with higher scores indicating higher implementation quality (total score range 0–96). A score of 3 on each item corresponds to satisfactory skill in implementing the BA component delineated by that item. Preliminary psychometric analysis of this instrument yielded adequate inter-rater reliability (intraclass correlation coefficient=0.72).

Ecological momentary assessment (EMA)

Pain severity and other pain-related variables included in the study (eg, mood symptoms and health-related quality of life, to name some examples) can fluctuate during the day and across days depending on many factors, such as environmental stressors. Additionally, retrospective evaluation is known to be susceptible to memory bias.[65] Retrospective evaluation can lead to overestimation of the symptomatology, which can be avoided by frequent evaluations of the present symptomatology. Moreover, the prospective and repeated evaluation over time substantially improves the accuracy, reliability and quality of research.[66] While EMA has been difficult for decades due to the problems associated with paper diaries, the availability of smartphones and the explosion of apps is making EMA easiest than ever.[67] There is growing evidence indicating that well-designed smartphone can be very easy to use and well accepted even in relatively old pain populations, and compliance rates with daily assessment have been as high as 75%.[66] In the present study, we will use the Monitor del Dolor (Pain Monitor) app, which has been recently validated in an empirical study[68] that assessed a number of biopsychosocial constructs twice a day during 4 weeks. In the present work, we will assess daily (twice a day: once in the morning and once in the evening, at convenient times) the items listed in table 4 during the 8-week treatment period.

Table 4 List of items administered via pain monitor app

Items	Morning	Evening
Pain intensity	X	X
Fatigue	X	X
Perceived control over pain	X	X
Openness to thoughts and feelings	X	X
Focused in the present moment	X	X
Guided by goals and values	X	X
Perceived competence	X	X
Activity level	X	X
Perceived stress	X	X
Perceived social support	X	X
Rumination	X	X
Magnification	X	X
Helplessness	X	X
Sleep disturbance	X	
Interference with leisure activities	X	X
Interference with work-related activities	X	X
Rescue medications	X	X

The Pain Monitor app informs patients automatically when to respond (by default, at 11 AM and 7 PM) using a push notification system, but patients can change the assessment times with a flexibility of 2 hours from given times. Collected data are stored on a secure server at the Jaume I University, Spain. The app and the data are stored on different servers with different domain names and connected locally only (the server containing the data does not have Internet access).[69]

Physiological variables

Immune-inflammatory markers. After drawing the blood, it will be allowed to coagulate for a minimum of 30 min at room temperature and then centrifuged for 10 min at 1000 g. The resulting serum will be stored at −80°C during the same morning of extraction until it is ready to be analysed. All samples (pre and post) will be analysed in a single analytical batch to reduce inter-assay variability (approx. 15%). The serum levels of cytokines IL-6, CXCL-8, IL-10, TNF-α, IL-1β and high-sensitivity C-reactive protein will be evaluated. For the quantification of the cytokines, the Milliplex reagents from the company MerckMillipore will be used and analysed using a Luminex platform. The high sensitivity multiplex kit will be used: Human High Sensitivity T Cell, catalogue number: HSTCMAG-28SPMX11 adapted to the aforementioned cytokines. The hs-PCR will be quantified using turbidimetry in an Olympus AU5400 auto-analyser.

Hair cortisol and cortisone, blood cortisol, CBG and vitamin D. Hair samples will be obtained from the middle-lower back area of the head as it is less exposed to environmental conditions such as sunlight, which affect the hormone levels in hair and as close as possible to the scalp. No products such as gels, lacquers or softeners will be used during the 3 days prior to obtaining the sample. A strand about 10 mm thick from the posterior vertex will be taken, packed in foil to avoid light impact and stored at room temperature. For the hormones determination only the 1 cm of hair closest to the scalp will be analysed. The extraction of hormones will be done from pre–post samples in the Nutrition and Obesity Laboratory of the Biochemistry and Molecular Medicine Department (University of Barcelona, UB), as they are obtained. The protocol consists, after hair samples weighing, of a previous wash with 5 mL of isopropanol to remove accumulated dirt and sweat, detergent residue or cosmetic products. Then, hair samples are dried at 37°C and minced. Cortisol and cortisone are extracted in 2 mL liquid chromatography with tandem mass spectrometry (LC–MS) grade methanol and stirring overnight at room temperature in the presence of deuterated Cortisol-d4 and Cortisone-d8 (Sigma Aldrich solution C-113 and 900170). The methanol is transferred to test tubes and evaporated in a dry bath at 50°C under a stream of N_2. The dried tubes are stored at −20°C until the quantification of cortisol and cortisone by LC-MS/MS at the Scientific and Technological Centres of the UB (CCiTUB). The levels of vitamin D and cortisol in serum will be determined by ELISA (DRG EIA-5396, EIA-1887R and EIA-3647) and CBG by RIA125I (IBL KIP1809) in a radioactive facility situated at the UB.

Polymorphisms in the FKBP5 gene. A blood sample of 4 mL will be collected in a vial with EDTA anticoagulant (BD Vacutainer; BD, NJ, USA). Specifically, the analysis of the genetic variants of the FKBP5 gene will be carried out in the Molecular Genetics Laboratory of the Anthropology Unit (UB). The samples will be coded, preserved and the DNA will be extracted with the Real Extraction DNA kit (Durviz S.L.U., Valencia, Spain). Quality of the DNA will be tested using the Nanodrop D1000 (Thermoscientific, Wilmington, DE). The genotyping of the five proposed SNP polymorphisms in the *FKBP5* gene will be carried out using TaqMan 5′ exonuclease assay (Applied Biosystems) technology at the Scientific and Technological Centres of the UB (CCiTUB): rs3800373 (SNP1), rs9296158 (SNP2), rs1360780 (SNP3), rs9470080 (SNP4) and rs4713916 (SNP5). The PCR reaction will be carried out on the ABI PRISM 7900HT instrument thermal cycler and genotype analysis will be carried out using SDS V.2.1 software (Applied Biosystems). For accuracy of genotyping, 15% of the samples, randomly selected, will be genotyped twice. Finally, the estimation of haplotypes will be conducted in order to increase the power to detect genetic associations.[69] Linkage disequilibrium between the five polymorphisms in the *FKBP5* gene will be examined by pair-wise comparisons of r2 and D' using Haploview V.4.2.[70] Estimation of *FKBP5* haplotype combination per subject will be conducted using a Bayesian approach implemented with PHASE software.[71]

Statistical analysis

The main analysis will compare the effect of the treatments on the primary outcome (pain interference at 12 months follow-up). All data analyses will be carried out

following an intention-to-treat (ITT) principle, that is, regardless of protocol adherence. Then, we will compute analysis of the primary outcome post-treatment and analysis of the secondary and treatment process outcomes at post-treatment and at 12-month follow-up. The analyses will be replicated from a per-protocol approach. Multi-level, linear mixed models will be created using the restricted maximum likelihood method for the estimation of parameters. The effect sizes will be calculated according to Cohen's *d*. No interim analysis is planned for this RCT. A 5% significance level will be used in all two-tailed tests, applying the Benjamini-Hochberg correction for multiple comparisons (to reduce the risk of false positives). For these analyses, we will use SPSS V.24.0.

To examine whether the effects of ACT and BATD in addition to usual care on primary and secondary outcomes at 12-month follow-up are mediated through pre–post changes in pain acceptance (CPAQ-8), and behaviour activation (BADS-SF), respectively, we will calculate pre–post changes in the total scores of the CPAQ-8 and the BADS-SF and pre-follow-up change scores in the primary and secondary outcomes. Then, bivariate Pearson correlations will be computed between the pre–post change in the process variables and the pre-follow-up change in the outcomes to detect potential significant relationships. Finally, we will explore the direct and indirect associations between the treatment condition (TAU+ACT vs TAU and TAU +BATD vs TAU as independent variable), CPAQ-8 and BADS-SF (mediators), and primary and secondary outcomes (dependent variables) using path analyses. The direct paths between the treatment condition and clinical outcomes and the indirect effect path through CPAQ-8, and BADS-SF will be tested in all models. Regression coefficients (B) of bias-corrected bootstrapped indirect effects will be calculated as well as their SEs and 95% CIs. Parameters of indirect effects are considered statistically significant when the 95% CI does not include 0. The MPlus V.7.4 will be used to compute the mediation models.

Regarding analyses of the EMA data, Group (TAU+ACT vs TAU+BATD vs TAU), Time (each of the EMA measurement points; up to two assessments per day × 60 days) and the Group × Time interaction will be the primary fixed effects of interest.

Regarding the economic evaluation, when the cost-utility of two or more therapeutic options is compared, it is necessary to calculate the relationship between the costs of each treatment and its consequences in the form of QALYs, a measure designed for assessing both quantity of life (years) and health-related quality of life (ie, a year lived with the maximum quality of life would be transformed into 1 QALY; a year lived with half the maximum quality of life would be transformed into 1/2 QALY). This relative value will be called the incremental cost-utility ratio (ICUR), and it will express the relationship between the costs and the effects of one option compared with another. The QALYs obtained in the 12 months after the start of the treatments will be calculated by the area under the curve.

The direct costs will be calculated by adding together the costs derived from the medication and the use of the health services. The cost of medications will be calculated by multiplying the price per milligram by the total daily dose consumed (in milligrams) and the number of days that the treatment is received. The cost arising from the use of the health services (primary care, specialist and accident and emergency consultations and hospital admissions) will be obtained from the eSalud database (http://www.oblikue.com/en/esalud.html). The indirect costs will be calculated based on the days off work, which will be multiplied by the official minimum wage during the study period. The effect of the treatments will be estimated using ordinary least squares multivariate regression, adjusting for the baseline differences between groups. In order to manage uncertainty in the sampling distribution of the ICUR, non-parametric bootstrapping will be applied, with 1000 replications in each comparison. Cost-utility analyses will be conducted with STATA V.16.0.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting or dissemination of our research.

ETHICS AND DISSEMINATION

All procedures performed in this study will be in accordance with the 1964 Helsinki declaration and its last amendments (seventh revision, adopted by the 64th World Medical Association General Assembly, Fortaleza, Brazil). Signed informed consent will be obtained from all patients once they have been informed of the study procedures, potential risks and their right to withdraw at any time from the RCT. The FSJD Ethics Committee Board evaluated and approved the study protocol in September 2019 (PIC-178-19). The Hospital del Mar Ethics Committee Board evaluated and approved the study protocol in November 2019 (2019/8866/I). Only the principal investigator (JVL) will have full access to the final trial data set.

Once the RCT is completed, we will publish our results in international peer-reviewed biomedical journals and present them at national and international conferences. In addition, we will send participating patients a short report of our findings. A copy of the report will also be sent to Institute of Health Carlos III (main funding body). The principal investigator will organise an end-of-study knowledge translation seminar. The main objective of this activity will be to share the study findings with stakeholders in order to discuss how to maximise uptake of the findings in patient treatment and clinical practice, and to determine future research directions.

DISCUSSION

The present manuscript describes the design and protocol of an RCT that aims to assess the efficacy, cost-utility and physiological effects of adding ACT or BATD to TAU for the management of CLBP and moderate to severe levels of depressive symptoms. If the results are strong enough in terms of cost-utility, in one or both of the evaluated treatments (ACT and BATD), they could be considered for inclusion in the public healthcare system to treat patients with CLBP and depression, and could be used to treat similar conditions if such general applicability is demonstrated. The fact that these treatments are performed in groups can make them more cost-effective, and therefore of interest for health managers.[72] Additionally, if the results are positive, these treatments could also be tested in similar chronic conditions (eg, fibromyalgia, irritable bowel syndrome, or chronic fatigue syndrome) that also frequently present with comorbid depression symptoms.

This study has some strengths that should be highlighted. The inclusion of a large sample and the inclusion of a comprehensive set of measures will allow us to explore important pain-related outcomes and treatment mediators. Our study will both focus on the clinical effects of ACT and BATD as add-on treatments in the long-term, and also on the psychological constructs and physiological variables that may be involved in the changes experienced by patients after treatment. On the whole, our study explores genetic, neuroendocrine (HPA axis) and immune-inflammatory (cytokines) pathways with a combination of technologies which may lead to a characterisation of biochemical markers and targets relevant to increase our understanding of both chronic pain and depression, new therapeutic interventions to manage these disorders, and a better prediction of treatment results based on individual variations of these biomarkers in the line of personalised medicine. In addition, this study will use a smartphone app to monitor the treatments' effects ecologically, which is a novel approach into the pain literature exploring the effectiveness of psychological interventions.

It is important to mention that we will analyse five different polymorphisms in the *FKBP5* gene whose interest relies on its implication in HPA axis stress response regulating glucocorticoid receptor affinity and signalling. Previous gene-environment studies have found associations between the variability of this gene and early trauma with depression[73 74] and anxiety.[75] Based on these findings, our main aim is to explore, for the first time, the moderator role of the interaction between *FKBP5* gene polymorphisms and childhood trauma on the response to psychological treatments for chronic pain and depression.

There are some potential limitations that should be acknowledged. First, there may be a higher than expected dropout rate due to the length of the study (1 year). Second, there is a risk that not all recruited patients have a smartphone or that completion rates may be unsatisfactory, so EMA might not be possible or effective for all participants. Participants who do not engage will not be excluded, but the analyses will be limited to the classical assessments. Finally, we have to note the lack of blinding of patients and therapists, a typical bias in RCTs of psychological treatments.

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Contributors JVL, AF-S and JRC-A designed the major outlines of the study. PC-N, CS-R, AG-P, AC-C, AP-A, LA-R, LMMcC, FD'A, PE-R, BC-M, AM-P, OC-V, ME, MG, AR, AIC-V, MM, XB, SE, AS and AF-S contributed to the study design. PE-R, JRC-A, AM-P and OC-V will include patients in the study. JVL, CGF and FD'A carried out the sample size calculation. JPS-M wrote the first draft of the manuscript together with JVL, AF-S, JRC-A and CS-R. All authors read and approved the final version of the manuscript.

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Competing interests None declared.

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3. Artículo 3

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Efficacy of Videoconference Group Acceptance and Commitment Therapy (ACT) and Behavioral Activation Therapy for Depression (BATD) for Chronic Low Back Pain (CLBP) Plus Comorbid Depressive Symptoms: A Randomized Controlled Trial (IMPACT Study)

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Abstract: This study examined the efficacy of adding a remote, synchronous, group, videoconference-based form of acceptance and commitment therapy (ACT) or behavioral activation therapy for depression (BATD) to treatment-as-usual (TAU) in 234 patients with chronic low back pain (CLBP) plus comorbid depressive symptoms. Participants were randomly assigned to ACT, BATD, or TAU. Compared to TAU, ACT produced a significant reduction in pain interference at posttreatment (*d* = .64) and at follow-up (*d* = .73). BATD was only superior to TAU at follow-up (*d* = .66). A significant reduction in pain catastrophizing was reported by patients assigned to ACT and BATD at posttreatment (*d* = .45 and *d* = .59, respectively) and at follow-up (*d* = .59, in both) compared to TAU. Stress was significantly reduced at posttreatment by ACT in comparison to TAU (*d* = .69). No significant between-group differences were found in depressive or anxiety symptoms. Clinically relevant number needed to treat (NNT) values for reduction in pain interference were obtained at posttreatment (ACT vs TAU = 4) and at follow-up (ACT vs TAU = 3; BATD vs TAU = 5). In both active therapies, improvements in pain interference at follow-up were significantly related to improvements at posttreatment in psychological flexibility. These findings suggest that new forms of cognitive-behavioral therapy are clinically useful in improving pain interference and pain catastrophizing. Further research on evidence-based change processes is required to understand the therapeutic needs of patients with chronic pain and comorbid conditions.

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Supplementary data accompanying this article are available online at www.jpain.org and www.sciencedirect.com.
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Perspective: **Group videoconference-based ACT and BATD showed greater efficacy than TAU for reducing pain interference and pain catastrophizing in patients with CLBP plus clinically relevant depression. Psychological flexibility appeared to be the main contributor to treatment effects for both ACT and BATD.**

Key words: *Chronic low back pain, depression, acceptance and commitment therapy, behavioral activation, eHealth*

Chronic low back pain (CLBP) is one of the most prevalent chronic pain conditions, and it is associated with substantial healthcare and social impact.[1] It is also connected with effects on mental health, including major depression.[2] Overall, the prevalence of depression in the context of chronic pain exceeds 60%, generating a significant healthcare and societal burden.[3,4] Chronic pain usually exacerbates depression and depression, in turn, exacerbates chronic pain, resulting in a greater overall burden of disability and suffering.[5,6] Due to its high prevalence, treatment resistance,[7-9] and particularly significant burden during recent time,[10] comorbid chronic pain and depression represents an important treatment priority.[11-14] This complex problem is a significant challenge for clinicians and may require greater treatment intensity, duration, complexity, or new approaches.[1,2,8]

The coronavirus disease (COVID-19) pandemic and related lockdowns significantly impacted public healthcare systems around the world, including usual patient care in pain management centers.[15] The physical and mental health conditions of chronic pain patients worsened during the pandemic,[10,16-18] and therapists were forced to adapt the format of interventions based on available resources, including available technology solutions.[19-21] Consequently, eHealth increased in clinical practice from 7 to 85% during this period.[22] The exponential growth of remote-delivered psychotherapies, designed to provide a similar outcome to face-to-face therapies, highlights the relevance of technology as a resource for treating chronic pain patients.[23,24]

Internet- or remote-delivered forms of psychotherapy seem to be effective for both chronic pain and depression management.[25-28] Ease of access, relative ease of delivery, and decrease in social costs position them as alternative or complementary resources to face-to-face therapies.[21,22] Cognitive-behavioral therapy (CBT) is an umbrella term that includes a wide variety of psychotherapies.[13,29] Several forms of CBT such as acceptance and commitment therapy (ACT)[30,31] and behavioral activation therapy for depression (BATD)[32,33] have been developed and appear beneficial. Results from systematic reviews and meta-analysis support the efficacy of Internet-based ACT for chronic pain patients in improving emotional distress and pain-related outcomes.[1,28] The effectiveness of BATD for patients with depression is well-established,[34,35] but as far it is known there is a lack of studies testing its effects in individuals with chronic pain and comorbid depression. Therefore, this is the first randomized controlled trial (RCT) to provide evidence for its efficacy in a remote-delivered form.

Currently, there are no RCTs analyzing the efficacy of adding remote-delivered form of ACT or BATD to treatment-as-usual (TAU) in patients with CLBP plus depression.[36] In Spain, TAU for chronic pain is managed by general practitioners in periodic consultations and includes prescription of medication and recommendations for aerobic exercise.[37] Therefore, the objectives here were 1) to conduct an RCT to examine the efficacy of adding a remote, synchronous, group videoconference-based form of ACT or BATD to TAU in patients with CLBP plus clinically relevant depression for improving pain interference (primary outcome), pain intensity, depression, anxiety, and stress symptoms, and pain catastrophizing (secondary outcomes); and 2) to analyze the effect of pain acceptance, behavioral activation, and psychological flexibility (process outcomes) on clinical changes at long term. Larger improvements in outcomes were expected for ACT[1,28] and BATD[28] when compared to TAU (hypothesis 1). Moreover, improvements in pain interference were expected to be related to increases in psychological flexibility and pain acceptance in ACT[38-40] and by behavioral activation in BATD[38] (hypothesis 2).

Methods

Design

A 12-month, multicenter, single-blinded RCT was conducted with random allocation of patients to 3 arms: 1) ACT + TAU (hereafter, ACT), 2) BATD + TAU (hereafter, BATD), and 3) TAU alone. This RCT was registered on ClinicalTrials.gov (NCT04140838) and followed the guidelines issued by the "Standard Protocol Items: Recommendations for Interventional Trials" (SPIRIT) and the "Consolidated Standards of Reporting Trials" (CONSORT). A detailed description of the study protocol can be found elsewhere.[41]

This RCT, initially designed to deliver the therapies in a face-to-face format,[41] was adapted to be delivered via

a remote, synchronous, videoconferencing platform (ie, Zoom). Data collection was conducted at baseline, at posttreatment (2 months after baseline), and at follow-up (12 months after baseline). This research was carried out in accordance with the 1964 Declaration of Helsinki and subsequent revisions and was approved by the Ethics Committee of the Fundació Sant Joan de Déu (PIC-178-19) and the Hospital del Mar (2019/8866/I). Informed consent was obtained from all participants involved in the study. None of the patients received any financial incentive for participating in this study.

Sample Size

The sample size was estimated through R with RStudio. To detect a medium effect size on the primary outcome (Brief Pain Inventory-Interference Scale, BPI-IS)[42] for either ACT or BATD versus TAU, a total of 63 participants were required for α = .05 (2-tailed) and 1 – β = .80. Considering a possible attrition rate of 20%,[14,43] the stipulated minimum sample size was approximately 78 patients per group.

Participants

Patients with a diagnosis of CLBP who sought services at the Pain Unit of the Parc Sanitari Sant Joan de Déu (Sant Boi de Llobregat, Spain) or Hospital del Mar (Barcelona, Spain) in the last 3 years were invited to participate in this RCT. A total of 234 patients with CLBP who met the selection criteria, including the presence of moderate-to-severe depressive symptoms, were recruited between September 2020 and May 2021. As shown in Fig 1, these patients were randomly allocated into the 3 study arms: ACT (n = 78), BATD (n = 78), and TAU alone (n = 78).

Inclusion criteria were 1) aged between 18 and 70 years old; 2) diagnosis of CLBP (ie, presence of tension, soreness, or stiffness in the lower back pain)[1] ≥3 months according to medical history; 3) pain intensity > 4 points out of 10 points on a Numeric Rating Scale (NRS) in the last week; 4) moderate-to-severe depressive symptoms (≥10 points out of 27 points) in the last 2 weeks according to Patient Health Questionnaire (PHQ-9); and 5) able to understand Spanish language. Exclusion criteria were 1) presence of cognitive impairment according to medical history; 2) previous (last year) or current participation in psychological therapy; 3) diagnosis of severe psychiatric disorder or substance dependence/abuse; 4) radiculopathy; 5) involvement in litigation with the healthcare system; and 6) patients with scheduled surgical intervention and inability to attend group sessions.

Procedure

Patients who met the eligibility criteria attended a baseline face-to-face interview at the hospitals with trained clinical psychologists. Before providing informed consent and administering the battery of self-report measures (see below), patients were informed of the study purpose and confidentiality agreements. They were also notified that they were free to withdraw from the study at any time with the assurance that they could continue to receive their usual treatment. Randomization of patients to treatment arms was performed after the completion of baseline clinical assessments as recommended by the CONSORT guidelines.[44] Following Ost's recommendations,[45] patients were randomly assigned to ACT and BATD therapists to control possible therapist effects on the outcome. This allocation process was performed by a statistician who was not involved in any other research or treatment delivery procedures. Patients were assigned a list of alphanumeric codes and then randomly assigned to groups using SPSS (v26). In this process, stratified randomization was performed

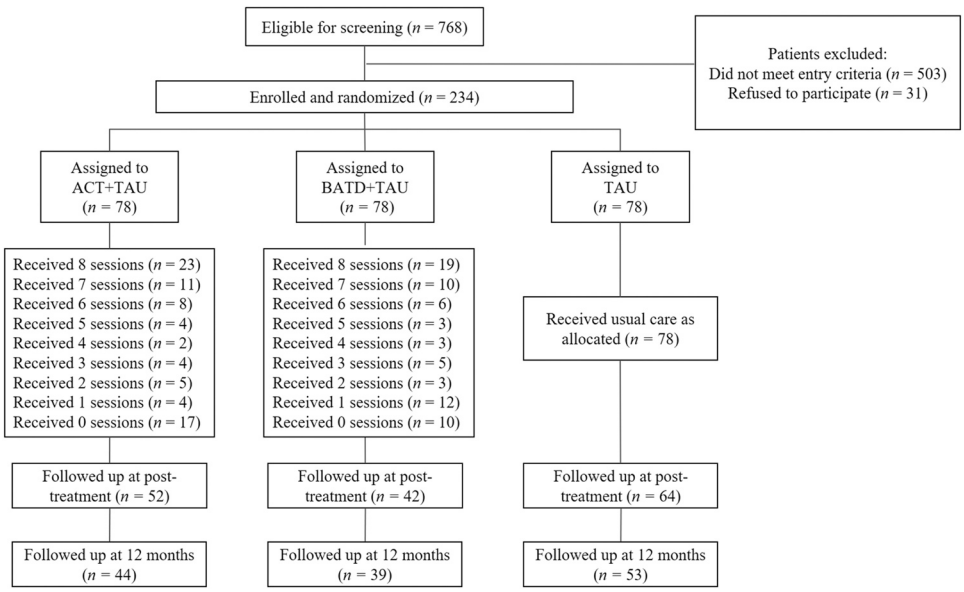

Figure 1. Flowchart of participants in the RCT.

considering baseline pain (NRS; ≥7 points out of 10 points) and depressive symptom (PHQ-9; ≥15 points out of 27 points) scores to ensure comparable clinical severity ratings between groups.

Interventions

Prior to the start of the RCT, all therapists received a 3-hour training to ensure fidelity to the protocol and homogeneity in their intervention. This training was led by 2 therapists with experience in ACT and BATD. Three different therapists guided the groups in each therapy (1 therapist per group with a total of 6). The therapists were technically supported by a research assistant during the 8 sessions. The research assistant was responsible for noting patients' attendance and recording relevant aspects identified during the interventions. A qualitative study nested within this RCT reported the experiences of a group of patients who received the online group form of ACT or BATD.[46]

Study participants were not asked to stop their usual medication regimen during the study period (12 months). After the first session, participants received a homework document to reinforce the main concepts of the therapies. They received weekly reminders with the link to access the therapy session. Both therapies were administered in group format (range: 7–13 participants) and consisted of 8 weekly 1.5-hour sessions via remote synchronous videoconference. ACT and BATD programs were conducted in 3 waves: October to December 2020 (first wave), February to April 2021 (second wave), and May to July 2021 (third wave). This study was conducted during a partial relaxation of the COVID-19 lockdown measures adopted by the Spanish authorities. During this period, people residing in Spain were able to move around, access health services, and go to work, although with some mobility restrictions that were especially stricter during the first and second waves.

Acceptance and Commitment Therapy

ACT promotes acceptance of unwanted experiences and engagement in goal-directed and value-based action. The aim of ACT is not to change internal experiences, but to promote acceptance skills to enable values-based behaviors in the presence of unpleasant experiences.[47] This psychotherapy, developed by Hayes et al,[38] focuses particularly on promoting psychological flexibility and is increasingly used as a treatment for chronic pain.[40] Psychological flexibility is defined as "the ability to contact the present moment more fully as a conscious human being and to change or persist in behavior when doing so serves valued ends" (p. 140).[30] According to Hayes et al (2022),[31] ACT interventions target 3 core pillars[30,47] to build psychological flexibility: 1) openness, 2) awareness, and 3) active engagement. ACT is supported in evidence as treatment for chronic pain.[1,40,48,49] ACT was based on the Vowles et al protocol.[50] An outline of the ACT sessions is detailed in Table 1.

Behavioral Activation Therapy for Depression

BATD applies learning principles to the pattern of withdrawal or reduction of behavioral activity related to depression. The aim of BATD is to reduce depressive symptoms and consequently to enable patients to achieve a satisfying life. This therapy primarily seeks to activate patients diagnosed with depression by scheduling and performing behaviors that are likely to increase experiences of direct positive qualities in their current context. BATD focuses on aspects of activation such as daily monitoring, identification of core life values, selection and planning of valued activities, and social support.[51] Behavioral activation is defined as "structured attempts to increase overt behaviors likely to bring patients into contact with reinforcing environmental contingencies and corresponding improvements in thoughts, mood, and quality of life" (p. 700).[52] It is an effective treatment in patients with depression[34] and other mental health problems. This can lead to increased physical activity, improved sleep, and decreased stress, which can all have positive effects on pain outcomes. This therapy was based on the Lejuez et al protocol.[32] An outline of BATD sessions is detailed in Table 1.

Although there is no prior evidence of the efficacy of BATD in patients with CLBP and comorbid depression, there are several reasons why BATD might be beneficial in improving pain interference in these individuals. First, BATD may indirectly improve pain-related outcomes by reducing the negative impact of depression on pain. Second, this therapy helps to identify and address factors that may contribute to the maintenance of depression, such as negative thinking and avoidance behaviors (variables that also contribute to the maintenance of pain-related disability). Third, it can improve the overall quality of life and functioning, which may indirectly improve pain outcomes by enhancing an individual's ability to cope with pain and engage in meaningful activities.[9,24,32]

Treatment-as-usual

All study patients received TAU. Patients randomized exclusively to TAU did not receive any additional active treatment during the study period. In Spain, chronic pain is managed by general practitioners in regular consultations of approximately 10 minutes to monitor the patient's health.[37] Standard treatment of chronic pain includes medication prescription (analgesics, anxiolytics, antidepressants, anti-inflammatories, and/or opioids) and recommendations for aerobic exercise. For this study, usual care was the same as in routine clinical practice, without any modification. Upon completion of the study's follow-up assessments, patients in the TAU group were given the opportunity to receive the therapy that had demonstrated the highest efficacy.

Study Measures

Patients were assessed with a computer-administered battery of measures, using Research Electronic Data

Table 1. Outline of the Interventions ACT and BATD

SESSION	ACT	BATD
1	*Participants' and clinician's presentation*. Psychoeducation and introduction to ACT (ACT basics; scientific advances in chronic pain and depression management; psychological theories of pain, suffering and stress; stressors, fears, and indicators; identification of values; breathing exercises).	*Participants' and clinician's presentation.* Collection of information related with areas of activity and interaction contexts. Delivery of activity log to obtain an accurate assessment of the patient's daily activities, which is useful for providing a baseline measure and comparing their progress when their activity level increases later in the treatment.
2	*Value analysis I.* Problems of experiential avoidance. Creative hopelessness through metaphors: control is the problem and not the solution. Anxiety, fight and flight, and its effects. Accepting the risk of the life's journey: experiences, feelings, and emotions.	*Problematic behaviors, patients' aims, and personal values.* Identification of information related to depressive behaviors. Exploration of problematic behaviors, identification of patients' objectives regarding treatment, and recognition of personal values.
3	*Value analysis II.* Objectives. Laws of thought and consequences of language. Mind and deactivation of thought (cognitive defusion): creating distance with thoughts. Learning meditation techniques and effects. Practicing meditation exercises.	*Establishing personal goals.* Obtaining complementary information regarding the characteristics of the history of patient interactions and any contexts and interactions that reinforce depressive behaviors. Establishment of short-term, medium-term, and long-term goals.
4	*Value analysis III.* Psychological barriers and obstacles. Emotional distress and its consequences. Emotional phenomena, personality variables and health states. Discovering commitments with committed actions.	*Therapeutic change of problematic behavior*. Explanation of the hypotheses of factors associated with the origins, maintenance, and therapeutic change of problematic behavior. In this session, 10 personalized activities are selected according to each person's own needs and desires, without any order. With the selected activities, a ranking is then generated that goes from the least difficult to the most difficult activity.
5	*Values and feelings.* Taking the initiative with a "Plan of action and willingness." Psychological flexibility, resilience, and self-motivation. Expansion and body scan exercises. Learning to relax.	*Target activities.* Once the 10 target activities have been identified, a record is made to track their progress weekly, including the number of times they would like to complete the activity in a period of 1 week (the ideal frequency). The number of activities varies each week, but they always range between 3 and 5 activities.
6	*Taking a direction.* The self as context, process, and content. Awareness of the present: "here and now." The brain and emotions: managing situations and overwhelming emotional responses.	*Satisfaction with activities.* Discussion of what was obtained from the records in general. Exploration of the satisfaction with the activities.
7	*Dare and change:* willingness and determination. Self-awareness, assertiveness, and self-esteem. Experiential expansion exercises: felt sensations. Happiness according to positive psychology. Benefits of physical exercise: movement.	*Coping abilities*. How to approach emotions and reactions to events and responses associated with depression. Relationship between avoidance behaviors and maintenance of difficulties.
8	*Moving forward.* Prepared to act with ACT: mind, body, thoughts, and feelings. Summarizing the concepts, conclusion, and evaluation.	*New behaviors.* Examination of new behaviors to be incorporated. Discussion about the goals achieved and the barriers to maintain the weekly activity plan. Farewell.

Capture (REDCap) software.[53] Table 2 shows the measures administered at each time point.

Sociodemographic and Clinical Characteristics

A sociodemographic and clinical questionnaire was used to obtain the patient's general information (gender, age, marital status, living arrangement, educational level, and employment status) and clinical characteristics (years of diagnosis and daily medication). Furthermore, the *Composite International Diagnostic Interview* (CIDI v3)[54] was used to evaluate the presence of a current depressive episode.

Primary Outcome Measure

The *BPI-IS* was used to measure pain interference during the last week.[55,56] The BPI-IS is composed of 7 items (general activity, mood, walking ability, normal work/housework, relations with other people, sleep, and enjoyment of life), which are answered on a 0 ("*does not interfere*") to 10 ("*completely interferes*") scale. The total score (0–10) is calculated as the arithmetic mean of all items, with higher scores indicating greater pain interference. Internal consistency in this study was good (Cronbach's alpha [α] = .86).

Secondary Outcome Measures

The *NRS* was used to measure pain intensity during the last week. The NRS is a unidimensional measure composed of only one item that is answered on a 0 ("*no pain*") to 10 ("*worst pain imaginable*") scale.

The *Depression Anxiety Stress Scales-21* (DASS-21) was used to measure depressive, anxiety, and stress symptoms during the last week.[57,58] The DASS-21 is composed of 21 items, which are answered on a 0 ("*did not apply to me at all*") to 3 ("*applied to me very much or most of the time*") scale. One example of DASS-21 items

Table 2. Study Periods at Which Measures and Data Are Collected

MEASURES	PRE	POST	FOLLOW-UP
Screening			
PHQ-9 (depression symptoms)	X		
NRS (pain intensity)	X		
General information			
Sociodemographic data (gender, age, marital status, etc.)	X		
Clinical data (years of diagnosis and daily medication)	X		
CIDI (current episode of depression)	X		
Primary outcome			
BPI-IS (pain interference)	X	X	X
Secondary outcomes			
NRS (pain intensity)	X	X	X
DASS-21 (anxiety, depression, and stress symptoms)	X	X	X
PCS (pain catastrophizing)	X	X	X
Process measures			
CPAQ-8 (pain acceptance)	X	X	X
BADS-SF (behavioural activation for depression)	X	X	X
PIPS (psychological inflexibility)	X	X	X
Other measures			
CEQ (credibility and expectations regarding treatments/technology)	X	X	
AET (negative effects of psychological treatments)		X	
PGIC and PSIC (impression of change)		X	

Abbreviations: AET, Adverse Effects of Treatments checklist; BADS-SF, Behavioural Activation for Depression Scale (short form); BPI-IS, Brief Pain Inventory-Interference Scale; CEQ, Credibility/Expectancy Questionnaire; CIDI, Composite International Diagnostic Interview; CPAQ-8, Chronic Pain Acceptance Questionnaire (8-item version); DASS-21, Depression Anxiety Stress Scales-21; NRS, Numerical Pain Rating Scale; PGIC and PSIC, Patient Global Impression of Change and Pain Specific Impression of Change; PCS, Pain Catastrophizing Scale; PHQ-9, Patient Health Questionnaire.

for depression is *"I found it difficult to work up the initiative to do things,"* for anxiety is *"I felt scared without any good reason,"* and for stress is *"I found it difficult to relax."* Scores range from 0 to 21 for each scale, with higher scores indicating greater depressive, anxiety, or stress symptoms. Internal consistency in the present study for depressive ($\alpha = .89$), anxiety ($\alpha = .75$), and stress ($\alpha = .92$) symptoms was acceptable to excellent.

The *Pain Catastrophizing Scale* (PCS) was used to measure pain catastrophizing.[59,60] The PCS is composed of 13 items, which are answered on a 0 ("*never*") to 5 ("*almost always*") scale. Two examples of PCS items are *"It's awful and I feel that it overwhelms me"* and *"I become afraid that the pain will get worse."* Scores range from 0 to 52, with higher scores indicating more pain catastrophizing. Internal consistency in this study was excellent ($\alpha = .92$).

Process Variables

The *Chronic Pain Acceptance Questionnaire* (CPAQ-8) was used to measure pain acceptance.[61,62] The CPAQ-8 is composed of 8 items, which are answered on a 0 ("*never true*") to 6 ("*always true*") scale. Two examples of CPAQ-8 items are *"Keeping my pain level under control takes first priority whenever I am doing something"* and *"I lead a full life even though I have chronic pain."* Scores range from 0 to 48, with higher scores indicating more pain acceptance. Internal consistency in this study was acceptable (Cronbach's $\alpha = .68$).

The *Behavioral Activation for Depression Scale-Short Form* (BADS-SF) was used to measure behavioral activation.[63,64] The BADS-SF is composed of 9 items, which are answered on a 0 ("*not at all*") to 6 ("*completely*") scale. Two examples of BADS-SF items are "*I am content with the amount and types of things I did*" and "*I spent a long time thinking over and over about my problems.*" Scores range from 0 to 54, with higher scores indicating greater behavioral activation. Internal consistency in this study was acceptable ($\alpha = .73$).

The *Psychological Inflexibility in Pain Scale* (PIPS) was used to measure psychological inflexibility towards pain.[65,66] The PIPS is composed of 12 items, which are answered on a 1 ("*never true*") to 7 ("*always true*") scale. Two examples of PIPS items are *"I cancel planned activities when I am in pain"* and *"I avoid doing things when there is a risk it will hurt or make things worse."* Scores range from 12 to 84, with higher scores indicating greater psychological inflexibility in pain. Internal consistency in this study was excellent ($\alpha = .90$).

Other Measures

The adapted version of the *Credibility/Expectancy Questionnaire* (CEQ) was used to measure credibility and expectancy regarding treatments and technology use.[67] Originally, the CEQ contained 3 items to assess therapy credibility and 3 items for expectancies. In addition, 7 items were included in this study to assess technology use. In this version, credibility and expectancy about therapies (eg, *"To what extent does this therapy seem logical to you?"* and *"To what extent do you think this therapy could be useful in treating other problems or diseases?"*) and technology use (eg, *"To what extent do you feel motivated to do this therapy non-face-to-face?"* and *"To what extent do you think that doing this therapy in a non-face-to-face setting will be useful to you?"*) were assessed at the end of the first and last ACT and BATD sessions. All items were measured on a scale of 0 ("*not at all*") to 10 ("*completely*").

The *Patient Global Impression of Change* (PGIC) and the *Pain Specific Impression of Change* (PSIC) were used to measure the impression of change.[68] The PGIC is composed of 1 item (eg, perception of global improvement) and the PSIC is composed of 5 items (eg, physical functioning, social functioning, work-related activities, mood, and pain), which are answered on a 1 ("*much better*") to 7 ("*much worse*") scale. These scales were only completed by patients who were assigned to the ACT or BATD intervention arms.

The *Adverse Effects of Treatments*[69] was used to measure the potential presence of negative effects of ACT and BATD. This ad hoc instrument is composed of 1 item ("*Have you experienced, during the psychological*

treatment, any unwanted symptom that you think might be directly or indirectly associated with the psychological intervention?"), with a "yes" or "no" answer option. Previous RCTs have used this question to explore adverse events (eg, headaches, dizziness, sleep problems, etc.) across the interventions.[69]

An ad hoc questionnaire was used to identify the characteristics of the therapists who conducted the sessions. Specifically, the therapists' training and experience in the therapies (theoretical concepts, knowledge of the protocol, years of experience as a therapist, years of experience in group therapies, years of experience in individual therapies, and years of experience in non-face-to-face therapies) were described.

Statistical Analyses

Descriptive analyses were calculated for all study measures and presented as means (M) and standard deviations (SD) for continuous variables and as frequencies (n) and percentages (%) for categorical variables. Baseline between-group differences (ACT, BATD, and TAU) in sociodemographic and clinical characteristics were examined by applying the analysis of variance (ANOVA) for continuous variables and the χ^2 test for categorical variables. Following CONSORT recommendations, potential baseline differences in sociodemographic characteristics are considered irrelevant and therefore were not included as covariates in the analyses of study outcomes.[70] Moreover, Student's t-test was used to examine differences in credibility and expectancy (CEQ) regarding therapy and technology use between the ACT and BATD groups at the end of the first session. As this RCT was conducted in 3 waves (in different circumstances of restricted movement and pandemic risk situation), it was also assessed whether there were differences between waves in terms of attrition.

The between-group analysis to assess the therapy effect on primary and secondary outcomes and process variables was carried out on an intention-to-treat (ITT). Generalized linear mixed models (GLM) were used in which restricted maximum likelihood regression was computed. Treatment effects on outcomes and process variables were estimated using these models, accounting for within-patient correlations between repeated measurements. Twisk et al[71] provided evidence that multiple imputation for missing data is not necessary before computing longitudinal mixed models. The set of linear mixed models included random intercept adjusted with the baseline score, as well as time and the interaction between *"group × time."* When the number of observations within each group is relatively small, it is advisable to include a random intercept in the model. This allows for the within-group variability and reference level of the response variable between groups to be accounted for, leading to more accurate parameter estimates and better model predictions.[71] Regression coefficients (β) and 95% confidence intervals (95% CI) were calculated for the *"group × time"* interaction between groups at posttreatment and at 12-month follow-up. The effect sizes were calculated according to Cohen's *d* for each comparison, using the pooled baseline SD to weight the differences in the pre-post or pre-follow-up mean values and to correct the population estimate.[72] The rule of thumb criterion was as follows[73]: very small (.10), small (.20), medium (.50), large (.80), very large (1.20), and huge (2.00).

The Benjamini-Hochberg procedure[74] is designed to control the false discovery rate, which is the expected proportion of false discoveries among all the discoveries conducted. The false discovery rate is calculated as the ratio of false positives to the total number of discoveries, and it provides a more flexible approach to controlling the error rate than the family-wise error rate, which controls the probability of at least one false positive among all the comparisons.[74] The Benjamini-Hochberg procedure works as follows: 1) rank the *P*-values from smallest to largest; 2) define a significance threshold or alpha level, which represents the desired false discovery rate; 3) reject all null hypotheses for which the corresponding *P*-value is less than or equal to the Benjamini-Hochberg critical value.[74] In this study, the threshold for statistical significance was set at $P < .05$. Adjusting the rate helps to prevent apparent significance from emerging by chance, avoiding Type I errors (false positives).[74] This procedure corrected for multiple comparisons by adjusting the significance threshold for each comparison based on the number of comparisons and the rank of the *P*-value.

To assess the clinical significance of improvements in the primary outcome (BPI-IS), patients were classified into 2 categories: responders and nonresponders to treatment.[75,76] Following the IMMPACT recommendations to establish a clinically significant improvement, a 1-point reduction in the pre-post and the pre-follow-up BPI-IS total score at posttreatment and at follow-up as the response criterion was used as a response criterion.[77] This categorization was also used to estimate the number needed to treat (NNT) in ACT and BATD compared to the other arms. A 95% CI for each NNT was calculated at posttreatment and at follow-up. In addition, baseline, post, and follow-up between-group differences in sociodemographic, clinical characteristics, and outcomes were explored for responders versus nonresponders, and for completers (defined here as patients who attended a minimum of 6 therapy sessions out of 8) versus noncompleters. Differences between groups were evaluated using the χ^2 and Student's t-test for categorical and continuous variables, respectively. The differences between active groups regarding patient global and pain-specific impressions of change (PGIC and PSIC) were evaluated using the χ^2 test with continuity correction.

Finally, it was examined whether the effects of ACT and BATD in addition to TAU on primary and secondary outcomes at 12-month follow-up were related to pre-post changes in process variables. Specifically, pre-post change in CPAQ-8, BADS-SF, and PIPS total scores, and pre-follow-up change scores in primary (BPI-IS) and secondary outcomes (NRS, DASS-21, and PCS) were calculated. To detect possible significant relationships, bivariate Pearson correlations were explored between pre-post change in process variables and pre-follow-up

change in primary and secondary outcomes. Direct and indirect associations between treatment conditions (ACT vs TAU and BATD vs TAU, as independent variables), significant process measures according to correlations, and primary and secondary outcomes were explored through path analysis. Regression coefficients (β) reflecting bias-corrected bootstrapped indirect effects based on 10,000 bootstrap samples were calculated, as well as their SEs and 95% CIs. Parameters of indirect effects were considered statistically significant when the 95% CI did not include 0.

SPSS (v26) and MPlus (v7) were used to compute the analysis. A 5% significance level was used in all 2-tailed tests.

Results

Patients Flow and Compliance

Of the 768 potential patients who were eligible, 503 were excluded at the screening phone interview because they did not meet the selection criteria and 31 refused to participate for personal reasons. In total, 234 patients comprised the sample of this RCT, with 78 patients randomly assigned per arm. The mean number of sessions attended in the ACT group was 4.65 (SD = 3.23) and in the BATD group was 4.42 (SD = 3.16). This difference was not statistically significant. As shown in Fig 1, 17 (21.8%) patients assigned to ACT and 10 (12.8%) to BATD did not attend any sessions. The rate of retention for ACT was 66.6 and 56.4% at posttreatment and at 12-month follow-up, respectively. In BATD, the rate of retention was 53.8 and 50% at posttreatment and at 12 months follow-up, respectively. Finally, TAU had an 82% rate of retention at posttreatment and 67.9% at 12 months follow-up.

The dropouts were significantly higher at posttreatment ($P = .001$) in BATD compared to TAU and ACT, but not at 12-month follow-up. Overall, there was a significant difference ($P = .011$) in the dropouts at the end of the study in the third wave (55.3%) compared to the first (38.8%) and second waves (32.1%). Schedule incompatibility for medical procedures (34.2%), loss of interest (28.9%), and perception that the therapy would not be useful (18.4%) were the main reasons for dropping out at posttreatment. In contrast, the main causes for dropping out at 12-month follow-up were inability to contact patients (45.5%), loss of interest (31.8%), and schedule incompatibly for medical procedures (22.7%). No significant differences in reasons for dropout were identified at posttreatment and at 12-month follow-up.

Furthermore, baseline differences (see Supplementary Table 1) were identified in marital status between ACT completers versus noncompleters (7.1% of completers vs 30.6% of noncompleters were separated/divorced; $P = .035$) and in age between BATD completers (M = 59.13, SD = 7.63) and noncompleters (M = 51.25, SD = 10.77, $P < .001$). No significant differences were observed at posttreatment and at 12-month follow-up.

Baseline Sociodemographic and Clinical Characteristics

Most patients were middle-aged women who had completed at least primary education. They mostly lived with their partner and were in paid employment at the start of this study. Most of them had a current episode of depression (70–81%), based on the CIDI, and were prescribed analgesics and antidepressants as part of their daily medication. The mean time with diagnosed chronic pain was >10 years. As shown in Table 3, no significant differences in sociodemographic and baseline clinical characteristics were found between the 3 study arms.

Description of the Therapists' Characteristics

All 6 therapists had postgraduate degrees. All had specialized health training as psychologists in Spain and 3 were studying or had a PhD. As shown in Supplementary Table 2, the mean years of experience in group therapy, individual therapy, and specific therapy of the RCT were higher for ACT therapists than for BATD therapists. In contrast, mean years of non-face-to-face therapy experience were higher in BATD than in ACT. Based on a scale of 0 to 10, ACT therapists reported higher scores than BATD therapists in knowing the core theoretical concepts of their respective therapy and in knowing how to apply the therapeutic protocol. However, none of the differences mentioned were statistically significant.

Expectancies and Technology Use at the End of the First Session

Focusing on the therapies, ACT patients reported higher scores on expecting the therapy to be satisfactory, recommendable, useful for treating other problems, and personally useful. In contrast, BATD patients scored higher on expecting therapy to be logical and not aversive. No significant differences in these scores were identified between the 2 therapies (see Supplementary Table 3).

In terms of technology use, ACT patients scored higher on knowing how to use the electronic device (phone, tablet, or computer) they would use during therapy, having little technical support during therapy, and considering that their electronic device was adequate to follow the therapy, while BATD patients scored higher on having little need for technical support during therapy and on believing that following the therapy non-face-to-face would make it difficult for them to attend or participate. However, these differences were not significant. Compared to BATD patients, ACT patients indicated a significantly greater perceived ability to follow

Table 3. Baseline Characteristics of Patients by Therapy Group

VARIABLES	ACT (N = 78)	BATD (N = 78)	TAU (N = 78)	P
Gender (women), n (%)	54 (69.2)	53 (67.9)	51 (65.4)	.87
Age, mean (SD)	54.9 (8.3)	54.9 (10.2)	53.8 (10.0)	.73
Marital status, n (%)				.54
Single	9 (11.5)	12 (15.4)	6 (7.7)	
Married/living with partner	49 (62.8)	50 (64.1)	53 (67.9)	
Separated/divorced	14 (17.9)	12 (15.4)	17 (21.8)	
Widowed	6 (7.7)	4 (5.1)	2 (2.6)	
Living arrangement, n (%)				.60
Living alone	11 (14.1)	7 (9.0)	9 (11.5)	
Living with partner	67 (85.9)	71 (91.0)	69 (88.5)	
Education level, n (%)				.81
Illiterate	2 (2.6)	0 (.0)	1 (1.3)	
Did not graduate from primary school	2 (2.6)	3 (3.8)	3 (3.8)	
Primary studies	18 (23.1)	20 (25.6)	16 (20.5)	
Secondary studies	42 (53.8)	46 (59.0)	43 (55.1)	
University	14 (17.9)	9 (11.5)	15 (19.2)	
Employment status, n (%)				.33
Homemaker	3 (3.8)	4 (5.1)	2 (2.6)	
Paid employment	20 (25.6)	24 (30.8)	32 (41.0)	
Paid employment but in sick leave	5 (6.4)	4 (5.1)	4 (5.1)	
Unemployed with subsidy	14 (17.9)	10 (12.8)	4 (5.1)	
Unemployed without subsidy	5 (6.4)	4 (5.1)	4 (5.1)	
Retired/pensioner	9 (11.5)	12 (15.4)	14 (17.9)	
Temporal disability	4 (5.1)	8 (10.3)	9 (11.5)	
Others	18 (23.1)	12 (15.4)	9 (11.5)	
Clinical variables				
Years of diagnosis, M (SD)	10.9 (7.9)	11.1 (8.7)	11.2 (8.0)	.98
Current episode of depression, n (%)*	60 (76.9)	63 (80.8)	55 (70.5)	.32
Daily medication, n (%)				
Analgesics	35 (50.7)	33 (50.0)	35 (50.7)	.99
Anti-inflammatory	16 (23.2)	19 (29.2)	16 (23.2)	.58
Opioids	15 (23.1)	18 (27.7)	12 (17.4)	.36
Antiepileptic	11 (16.9)	15 (23.1)	13 (18.8)	.66
Muscle relaxant	6 (9.4)	11 (16.9)	11 (15.9)	.41
Antidepressants	19 (29.7)	24 (36.9)	29 (42.0)	.33
Anxiolytics	12 (18.8)	11 (16.9)	13 (18.8)	.95

Abbreviations: ACT, acceptance and commitment therapy; BATD, behavioral activation therapy for depression; TAU, treatment-as-usual.
*CIDI, Composite International Diagnostic Interview.

the therapy in online format ($P = .026$, $d = .41$) and in believing that doing this therapy non-face-to-face would be useful to them ($P = .041$, $d = .37$; see Supplementary Table 3).

Effects on Pain Interference (Primary Outcome)

Table 4 shows descriptive statistics and between-group analyses for pain interference (BPI-IS) according to the ITT approach. After applying the Benjamini-Hochberg correction for multiple comparisons, ACT achieved a significantly greater reduction in pain interference compared to TAU at posttreatment ($\beta = -1.22$, $P = .001$) and at 12 months follow-up ($\beta = -1.41$, $P < .001$). Likewise, BATD showed greater reduction in pain interference compared to TAU at 12 months follow-up ($\beta = -1.29$, $P = .001$). No significant differences in pain interference reduction were identified in the comparison between ACT and BATD at any assessment point.

Effects on Pain Intensity, Depressive, Anxiety, Stress Symptoms, and Pain Catastrophizing (Secondary Outcomes)

Descriptive statistics and between-group analyses for pain severity (NRS), depression-anxiety-stress (DASS-21), and pain catastrophizing (PCS) are shown in Table 4 according to the ITT approach. After applying the Benjamini-Hochberg correction, no significant differences in pain intensity, depressive and anxiety reductions were found at posttreatment and at 12-month follow-up for any pairwise comparison. Significantly greater reductions were detected in stress symptoms for ACT compared to TAU at posttreatment ($\beta = -2.74$, $P = .001$). Finally, significantly greater reductions were identified in pain catastrophizing for ACT compared to

Table 4. Descriptive Statistics and Between-Group Analyses for Primary and Secondary Outcomes and Process Variables (ITT Approach)

	ACTM (SD)	*BATDM (SD)*	*TAUM (SD)*	*ACT VS TAU*			*BATD VS TAU*			*ACT VS BATD*		
				D	*T (P)*	*B (95% CI)*	*D*	*T (P)*	*B (95% CI)*	*D*	*T (P)*	*B (95% CI)*
Primary outcome												
BPI-IS (0–10)*												
Baseline	6.71 (1.72)	6.46 (2.07)	6.49 (1.91)									
Posttreatment	4.89 (2.26)	5.03 (2.44)	5.84 (2.43)	.64	**−3.41 (.001)**	−1.22 (−1.93 to −.52)	.39	**−2.17 (.030)**†	−.81 (1.54 to −.08)	.20	1.08 (.281)	.41 (−.34 to 1.17)
Follow-up	5.30 (2.42)	5.07 (2.36)	6.42 (2.16)	.73	**−3.88 (< .001)**	−1.41 (−2.12 to −.69)	.66	**−3.48 (.001)**	−1.29 (−2.02 to −.56)	.01	.30 (.764)	.11 (−.64 to .86)
Secondary outcome												
NRS (0–10)*												
Baseline	6.88 (1.74)	6.54 (1.68)	6.95 (1.69)									
Posttreatment	5.96 (1.93)	5.54 (1.98)	6.03 (2.00)	.01	−.15 (.880)	−.05 (−.77 to .66)	.05	.07 (.943)	.03 (−.72 to −1.22)	.05	.21 (.833)	.08 (−.68 to .84)
Follow-up	6.16 (2.41)	6.91 (1.65)	6.74 (1.88)	.30	−1.95 (.052)	−.71 (−1.43 to .01)	.34	−1.32 (.189)	−.49 (−1.22 to .24)	.63	.57 (.568)	.22 (−.53 to .97)
DASS-21-A (0–21)*												
Baseline	5.85 (4.05)	5.87 (4.37)	5.81 (4.65)									
Posttreatment	3.92 (3.63)	3.90 (3.15)	5.61 (5.02)	.39	**−2.00 (.046)**†	−1.32 (−2.62 to −.02)	.39	−1.50 (.135)	−1.03 (−2.37 to .32)	.01	.42 (.677)	.29 (−1.09 to 1.68)
Follow-up	4.93 (4.58)	4.51 (4.11)	6.87 (5.52)	.45	−1.90 (.058)	−1.25 (−2.55 to .04)	.53	−1.80 (.072)	−1.22 (−2.54 to .11)	.10	.05 (.959)	.03 (−1.33 to 1.40)
DASS-21-D (0–21)*												
Baseline	7.29 (5.47)	6.77 (5.26)	7.62 (6.07)									
Posttreatment	5.27 (5.75)	4.67 (4.63)	7.28 (6.30)	.29	−1.80 (.073)	−1.53 (−3.20 to .14)	.31	−1.72 (.086)	−1.51 (−3.25 to .22)	.01	.01 (.988)	.01 (−1.77 to 1.79)
Follow-up	6.68 (5.94)	5.44 (5.08)	9.06 (6.51)	.35	−1.52 (.128)	−1.31 (−3.01 to .38)	.48	**−2.08 (.038)**†	−1.83 (−3.57 to −.10)	.13	−.57 (.565)	−.52 (−2.30 to 1.26)
DASS-21-S (0–21)*												
Baseline	9.31 (4.72)	8.92 (5.24)	8.82 (5.00)									
Posttreatment	6.04 (4.15)	7.74 (4.75)	8.91 (5.59)	.69	**−3.42 (.001)**	−2.74 (−4.32 to −1.17)	.25	−1.27 (.203)	−1.06 (−2.69 to .57)	.42	**1.97 (.049)**†	1.68 (.01–3.36)
Follow-up	8.00 (5.08)	7.92 (5.34)	9.60 (5.30)	.43	−1.50 (.133)	−1.22 (−2.82 to .37)	.35	−1.74 (.083)	−1.45 (−3.08 to .19)	.06	−.26 (.796)	−.22 (−1.90 to 1.46)
PCS (0–52)*												
Baseline	24.88 (11.74)	24.22 (11.75)	24.14 (12.82)									
Posttreatment	17.29 (13.17)	14.83 (10.06)	22.09 (13.38)	.45	**−2.47 (.014)**	−4.25 (−7.63 to −.87)	.59	**−3.35 (.001)**	−5.99 (−9.50 to −2.48)	.15	−.95 (.344)	−1.74 (−5.35 to 1.87)
Follow-up	17.41 (12.03)	16.74 (11.69)	23.98 (13.95)	.59	**−2.83 (.005)**	−4.81 (−8.16 to −1.47)	.59	**−3.09 (.002)**	−5.39 (−8.81 to −1.96)	.01	−.32 (.749)	−.57 (−4.10 to 2.95)
Process variables												
CPAQ-8 (0–48)*												
Baseline	18.08 (7.25)	19.14 (6.98)	18.53 (6.41)									
Posttreatment	20.27 (8.08)	19.67 (5.95)	18.36 (6.42)	.34	**3.03 (.003)**	2.91 (1.03–4.80)	.10	.73 (.464)	.73 (−1.23 to 2.69)	.23	**−2.13 (.034)**†	−2.18 (−4.20 to −.17)
Follow-up	19.41 (6.94)	18.90 (7.62)	16.94 (6.98)	.42	**3.06 (.002)**	2.90 (1.03–4.76)	.20	.55 (.580)	.54 (−1.37 to 2.45)	.22	**−2.36 (.019)**†	−2.36 (−4.33 to −.39)
BADS-SF (0–54)*												
Baseline	29.05 (10.44)	27.94 (8.81)	27.46 (9.59)									
Posttreatment	32.84 (11.10)	32.95 (10.19)	28.22 (10.85)	.30	**2.26 (.024)**	3.79 (.49–7.09)	.46	**2.31 (.021)**	4.01 (.60–7.42)	.13	.12 (.903)	.22 (−3.30 to 3.73)
Follow-up	31.89 (11.79)	32.41 (10.98)	27.36 (12.38)	.29	1.69 (.091)	2.91 (−.47 to 6.28)	.49	1.95 (.051)	3.43 (−.02 to 6.88)	.17	.29 (.771)	.52 (−3.02 to 4.07)

Table 4 (*Continued*)

	ACTM (SD)	BATDM (SD)	TAUM (SD)	ACT VS TAU			BATD VS TAU			ACT VS BATD		
				D	*T* (*P*)	*B* (95% CI)	*D*	*T* (*P*)	*B* (95% CI)	*D*	*T* (*P*)	*B* (95% CI)
PIPS (12–84)*												
Baseline	57.53 (16.92)	56.05 (15.14)	56.47 (16.64)									
Posttreatment	48.38 (15.27)	49.26 (13.98)	56.02 (15.25)	.52	**−4.55 (<.001)**	−9.63 (−13.79 to −5.47)	.40	**−2.48 (.013)**	−5.46 (−9.78 to −1.14)	.15	1.85 (.065)	4.17 (−.26 to 8.61)
Follow-up	51.50 (15.52)	50.23 (15.17)	56.70 (16.56)	.37	**−2.63 (.009)**	−5.59 (−9.77 to −1.41)	.38	−1.85 (.065)	−4.02 (−8.30 to .25)	.01	.70 (.485)	1.57 (−2.83 to 5.97)

Abbreviations: *B*, regression coefficients; CI, confidence interval; *d*, Cohen's *d* as an effect size measure; ITT, intention-to-treat; ACT, acceptance and commitment therapy; BATD, behavioral activation therapy for depression; TAU, treatment-as-usual; BADS- SF, Behavioural Activation for Depression Scale (short form); BPI-IS, Brief Pain Inventory-Interference Scale; CPAQ-8, Chronic Pain Acceptance Questionnaire; DASS-21, Depression Anxiety Stress Scales; PCS, Pain Catastrophizing Scale; NRS, Numeric Rating Scale; PIPS, Psychological Inflexibility in Pain Scale.
NOTE. The baseline level of the variable was controlled. M and SD are not adjusted.
*The baseline level of the variable is a significant covariate in the model.
†When the Benjamini-Hochberg correction was applied to correct for multiple comparisons, the following effects were no longer significant: ACT versus TAU in DASS-21-A (post $P = .069$); BATD versus TAU in BPI-IS (post $P = .090$) and in DASS-21-D (follow-up $P = .076$); ACT versus BATD in DASS-21-S (post $P = .294$) and in CPAQ-8 (post $P = .102$; follow-up $P = .056$). The number of participants varied across assessment periods due to dropouts (see flowchart). Significant values ($P < .05$) are shown in bold.

TAU at posttreatment ($\beta = -4.25$, $P = .014$) and at 12-month follow-up ($\beta = -4.81$, $P = .005$); and for BATD compared to TAU at posttreatment ($\beta = -5.99$, $P = .001$) and at 12-month follow-up ($\beta = -5.39$, $P = .006$). No significant differences in pain catastrophizing were found when comparing ACT and BATD.

Effects on Pain Acceptance, Behavioral Activation, and Psychological Inflexibility (Process Variables)

Table 4 shows descriptive statistics and between-group analyses for pain acceptance (CPAQ-8), behavioral activation (BADS-SF), and psychological inflexibility (PIPS) according to the ITT approach. After applying the Benjamini-Hochberg, significant differences were detected in pain acceptance in ACT compared to TAU at posttreatment ($\beta = 2.91$, $P = .003$) and at 12-month follow-up ($\beta = 2.90$, $P = .002$). No significant differences in pain acceptance were found when comparing BATD and TAU and ACT and BATD. Compared to TAU, ACT ($\beta = 3.79$, $P = .024$) and BATD ($\beta = 4.01$, $P = .021$) showed significant increases in behavioral activation at posttreatment. No significant differences in behavioral activation were found when comparing ACT and BATD. Finally, significantly greater reductions in psychological inflexibility were detected for ACT compared to TAU at posttreatment ($\beta = -9.63$, $P < .001$) and at 12-month follow-up ($\beta = -5.59$, $P = .009$). In addition, there were significantly greater reductions in psychological inflexibility for BATD compared to TAU at posttreatment ($\beta = -5.46$, $P = .013$). No significantly different reductions in psychological inflexibility were found in the comparison between ACT and BATD.

Number Needed to Treat

At posttreatment, a total of 35 patients (67.3%) in ACT, 19 patients (45.2%) in BATD, and 23 patients (35.9%) in TAU reached the criterion 1-point reduction in pain interference (ie, "responders"), with this difference being significant ($P = .003$). Baseline differences between responders and nonresponders were analyzed for all variables (see Supplementary Table 4). In both ACT and BATD, there were no significant differences between responders and nonresponders on sociodemographic or clinical variables. Regarding outcomes, nonresponders in the ACT group scored significantly lower than responders on baseline pain acceptance ($P = .041$, $d = .64$). No significant differences between responders and nonresponders were observed at posttreatment or at 12-month follow-up for any of the variables.

At posttreatment, the absolute risk reduction (ARR) in ACT versus TAU was 31.4% (95% CI 14–48.7%) with NNT = 4 (95% CI 2.1–7.1), meaning that 4 patients would need to be treated with ACT for one of them to become a responder, who would not have done so in the TAU group (see Supplementary Table 5). The ARR obtained with BATD versus TAU was 9.3% (95% CI −9.8 to 28.4%) with NNT = 11; in this case, because the 95% CI for the

ARR extends from a negative number (BATD may harm) to a positive number (BATD may benefit), the NNT result is unreliable. This means that it is not possible to say with 95% certainty whether BATD has no effect or is useful compared to TAU. Comparisons between ACT and BATD also indicated an unreliable NNT result.

At the 12-month follow-up, a total of 26 patients (59.1%) in ACT, 19 patients (48.7%) in BATD, and 13 patients (24.5%) in TAU reached the criterion 1-point reduction in pain interference ($P = .002$). A significant ARR was found for ACT versus TAU (AAR = 34.6%, 95% CI = 15.9–53.1%) with NNT = 3 (95% CI 1.9–6.3) and BATD versus TAU (AAR = 24.2%, 95% CI = 4.7–43.7%) with NNT = 5 (95% CI 2.3–21.3). Finally, comparisons between ACT and BATD showed an unreliable NNT result (see Supplementary Table 5).

Indirect Effects: the Role of Pain Acceptance, Behavioral Activation, and Psychological Inflexibility

Bivariate correlational analyses were calculated between baseline-follow-up differences in primary and secondary outcomes and pre-post-treatment differences in process variables within the ACT group (see Supplementary Table 6) and the BATD group (Supplementary Table 7). Only those variables showing significant correlations were considered in the subsequent path analyses. The results of the path analyses are detailed in Table 5 and Table 6 and illustrated in Fig 2 by a generic example.

Regarding ACT, 1 out of the 3 models with significant effects yielded indirect paths between the study arm and clinical outcome. Specifically, in the model for pain interference, ACT produced a change in psychological inflexibility ($P = .043$), which in turn was associated with a change in pain interference scores at follow-up ($P = .001$). As shown in Table 5, no indirect effects were identified for pain intensity and pain catastrophizing changes in their respective models.

Focusing on BATD, 1 out of the 2 tested models yielded significant indirect paths between the study arm clinical outcome. As shown in Table 6, in the model for pain interference, BATD produced reductions in psychological inflexibility at posttreatment ($P = .001$), which in turn predicted improvements in pain interference scores at follow-up ($P = .001$). In contrast, no indirect effects were found for pain catastrophizing in the model.

Table 5. Direct and Bootstrap Indirect Effects in the Mediational of ACT Versus TAU [Effects of Pre-to-post-changes in Process Variables on Pre-to-follow-up Changes in Primary and Secondary Outcomes]

	DIRECT EFFECTS				INDIRECT EFFECTS			
OUTCOME AND PROCESS VARIABLE (R^2)	PATH	COEFF.	SE	P	PATH	BOOT.	SE	95% CI
BPI-IS (.20)	a	−7.705	2.319	**.001**				
PIPS (.10)	b	.460	.096	**.001**	a × b	−3.542	1.310	−6.700 to −1.432
	c	−1.655	2.382	.487				
NRS (.07)	a	−7.705	2.313	**.001**				
PIPS (.10)	b	−.032	.018	.065	a × b	.250	.152	.040 to .682
	c	−1.011	.467	**.031**				
PCS (.06)	a	2.412	1.071	**.024**				
CPAQ-8 (.05)	b	−.325	.205	.113	a × b	−.785	.675	−2.654 to .062
	c	−3.384	1.946	.082				

Abbreviations: CI, confidence interval; BPI-IS, Brief Pain Inventory-Interference Scale; CPAQ-8, Chronic Pain Acceptance Questionnaire; PCS, Pain Catastrophizing Scale; NRS, Numeric Rating Scale; PIPS, Psychological Inflexibility in Pain Scale.
NOTE. A generic example of a multiple model (with 1 process variable) is displayed in Fig. 2. Significant values (*P < .05) are shown in bold.*

Table 6. Direct and Bootstrap Indirect Effects in the Models of BATD Versus TAU [Effects of Pre-to-post-changes in Process Variables on Pre-to-follow-up Changes in Primary and Secondary Outcomes]

	DIRECT EFFECTS				INDIRECT EFFECTS			
OUTCOME AND PROCESS VARIABLE (R^2)	PATH	COEFF.	SE	P	PATH	BOOT.	SE	95% CI
BPI-IS (.18)	a	−4.707	2.321	**.043**				
PIPS (.04)	b	.477	.102	**.001**	**a × b**	−2.247	1.348	−5.453 to −.150
	c	−1.355	2.488	.586				
PCS (.06)	a	−4.707	2.344	**.045**				
PIPS (.04)	b	.090	.131	.490	**a × b**	−.425	.712	−2.252 to .648
	c	−4.729	2.362	**.045**				

Abbreviations: CI, confidence interval; BPI-IS, Brief Pain Inventory-Interference Scale; PCS, Pain Catastrophizing Scale; PIPS, Psychological Inflexibility in Pain Scale.
NOTE. A generic example of a multiple model (with 1 process variable) is displayed in Fig. 2. Significant values ($P < .05$) are shown in bold.

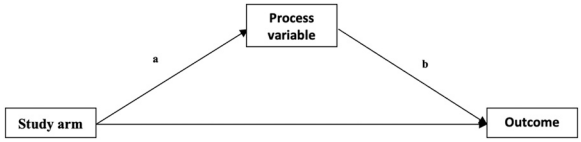

Figure 2. Generic example of a multiple direct and indirect effects model.

Other Clinical Results

Impression of Change

Regarding ACT, 3 patients (5.9%) felt "very much improved," 13 patients (25.5%) felt "much improved," 17 patients (33.3%) reported that they had "minimally improved," and 18 patients (35.3%) reported "no changes." No patient reported feeling worse. Focusing on BATD, only 1 patient (2.4%) felt "very much improved," 11 patients (26.8%) experienced "much improved," 17 patients indicated (41.5%) "minimal improvement," 11 patients (26.8%) reported feeling "no changes," and 1 patient felt "much worse" (2.4%). No significant between-group differences were identified in this analysis.

Most patients attending BATD groups felt improvement to some degree (minimal, much, or very much) in physical activities (43.9%), social activities (43.9%), and work-related activities (31.7%). Except in mood (68.6% vs 63.4% in BATD) and pain (25.4% vs 19.5% in BATD), ACT achieved lower percentages in the remaining areas: physical activities (41.2%), social activities (43.1%), and work-related activities (27.4%). These results are presented in Supplementary Table 8.

Credibility About the Interventions

Patients in the ACT and BATD arms, respectively, considered the therapy as highly recommendable ($M = 8.44$, $SD = 1.47$ vs $M = 8.17$, $SD = 1.62$). Moreover, after completing the sessions, ACT and BATD patients, respectively, showed high scores in knowing how to use the electronic device (phone, tablet, or computer) to receive non-face-to-face therapies ($M = 8.24$, $SD = 2.10$ vs $M = 8.60$, $SD = 1.52$) and the ability to follow this therapy via videoconference ($M = 8.78$, $SD = 1.49$ vs $M = 8.86$, $SD = 1.52$). The differences in scores for the 2 therapies were not significant.

Adverse Effects

In total, 6 patients in the ACT group and 2 in the BATD group reported unpleasant events at posttreatment. In the ACT group, 5 patients described increased emotional distress (depressive, anxiety, or stress symptoms) during body awareness exercises and 1 patient reported increased pain at the end of one therapeutic exercise. In the case of the BATD group, 2 patients mentioned an increase in depressive and anxiety symptoms after the end of the therapy sessions.

Discussion

This RCT examined the efficacy of adding a remote, synchronous, group, videoconference-based form of ACT or BATD to TAU for the psychological management of patients with CLBP plus comorbid depressive symptoms. In addition, the role of theoretically relevant process variables as facilitators of long-term clinical changes was analyzed. Compared to TAU, ACT yielded significantly greater improvements in pain interference (primary outcome) at posttreatment and at follow-up, and BATD yielded greater improvements than TAU at follow-up.

Significantly greater improvements were identified in pain catastrophizing (secondary outcome) in ACT and BATD, compared to TAU, at posttreatment and at follow-up. In addition, ACT showed significantly greater reductions in stress symptoms at posttreatment compared to TAU. Contrary to hypothesis 1, no significant differences in pain intensity, depressive, or anxiety symptoms were found in ACT and BATD compared to TAU at any of the time points. Previous systematic reviews provide evidence for the efficacy of Internet-based ACT in chronic pain patients in reducing pain intensity and emotional distress,[28,78] but with small effects. Treatment resistance associated with the combination of chronic pain and depression could be one of the explanations for the more moderate results obtained by this work compared to previous studies.[7,8]

According to Walsh et al,[9] BATD is a potentially useful treatment for patients with pain because it can help to reduce pain interference and other pain-related variables by its positive effects, namely by increasing self-efficacy (a sense of mastery), and experiencing rewards derived from carrying out actions and achieving goals. Although in this trial, BATD was effective for the improvement of pain interference, pain catastrophizing, behavioral activation, and psychological flexibility (variables relevant to the maintenance of pain-related disability), it did not have the expected effects in this population for decreasing depressive, anxiety, and stress symptoms.[9,24,32] Therefore, the results of the current study would suggest that the improvement in pain-related outcomes would not be as closely linked to the relief of negative symptoms (sadness, anxiety) as to the promotion of positive affectivity through cognitive and motivational mechanisms. Moreover, it is possible that the exceptional conditions under which the trial was developed (which forced a change in the format of delivery of interventions) had a greater impact on the success of BATD compared to ACT.

In addition, some differences observed in therapists' mastery, technological capabilities, and expectations about therapy in patients in favor of ACT could explain why the therapeutic results of BATD were more modest than those obtained with ACT. As far as it is known, the efficacy of BATD in a face-to-face and remote-delivered form had not been explored in patients with chronic pain and comorbid depression, so its effects should be further investigated in the future in other RCTs. Further evidence on the role of comorbidity between depression and chronic pain is needed to know more precisely the therapeutic potential of BATD. In any case, this future

research should clarify whether, as the results of this study suggest, improvements in pain-related outcomes are associated more with the positive than the negative effects of BATD on depression.

Overall, these findings are relevant because they indicate that pain interference and pain catastrophizing are moderately improved in both ACT and BATD compared to TAU, with small differences between the 2 active therapies. Notwithstanding this, some superiority of ACT over BATD and TAU was observed in the proportion of responders (67% vs 45% vs 35%, respectively) and clinically relevant NNT values at posttreatment compared to TAU (NTT = 4). In the same way, differences in the proportion of responders (59% vs 49% vs 24%) were in favor of ACT compared to BATD and TAU at 12 months follow-up. Furthermore, clinically relevant NNT values at 12 months follow-up were observed in ACT (NTT = 3) and BATD (NTT = 5) compared to TAU. It is important to highlight that nonresponders in the ACT group scored significantly lower than responders at baseline in pain acceptance. There were no significant differences between responders and nonresponders in BATD regarding sociodemographic, clinical or outcomes variables.

Retention in trial at posttreatment and at 12-month follow-up was lower than expected in ACT (about 67 and 56%, respectively) and BATD (about 54 and 50%, respectively) and higher than expected in TAU (about 82 and 68%, respectively). Moreover, the dropouts were significantly higher in BATD compared to ACT at posttreatment, although no differences were identified in the clinical improvement perceived by patients in both groups. The dropouts were significantly higher in the third (May to July 2021) than in the first and second waves of the RCT, when mobility restrictions due to the COVID-19 pandemic were relaxed and the preholiday period began in Spain. The adherence problems identified are consistent with those reported in Internet or remote-delivered therapies in patients with chronic pain and psychological distress.[79-81] Furthermore, as indicated in a qualitative study nested within this RCT,[46] barriers identified by these patients such as losing face-to-face contact, missing out on different physical intervention spaces, leaving home, and moments of informal socialization, may have affected their engagement, attendance, and adherence to therapies. Although the benefits of this format are identified (eg, ease of access, flexibility, avoidance of the need to travel, and resources savings), there is a need to improve the technical and social aspects of implementing videoconferencing-based therapies, as well as to strengthen guidelines for adequate support for patients and therapists.[46]

Consistent with hypothesis 2, significant differences were found in decreased psychological inflexibility and increased pain acceptance in ACT[38-40] both at posttreatment and at 12 months follow-up; and in improved behavioral activation in BATD[38] at posttreatment. However, unexpected significant differences were identified in increased behavioral activation in ACT and improved psychological inflexibility in BATD at posttreatment. Changes in pain interference at follow-up were associated with changes in psychological inflexibility in ACT.[39,40,82] Even though BATD is not based on the psychological flexibility model, in this sample changes in pain interference were also related to increases in psychological inflexibility.

Regarding this finding, psychological inflexibility has been found as a nonspecific contributor of the effects of new forms of CBT.[83-86] Thus, this indirect effect may be because "third-wave" psychotherapies commonly address some facets that overlap with the primary components (eg, mindfulness, acceptance, values, goals, and defusion) of psychological flexibility, as reported in a recent systematic review.[40] Committed action and values are at least implicit aspects in more recent forms of CBTs, including but not limited to ACT, Mindfulness-Based Cognitive Therapy, Behavioral Activation, Motivational Interviewing, and Solution-Focused Brief Therapy. All these therapies have in common a focus on helping individuals identify and align their actions and values with their goals and desires and develop strategies for making meaningful changes in their lives.

There are some potential reasons for the loss of efficacy of ACT and BATD in the long term, such as the fact that patients were no longer attending weekly group treatment, reduction of programmed home exercises in both therapies, and possible interferences generated by the COVID-19 pandemic. Specifically, 41% of patients in ACT and 38% in BATD received 4 or fewer sessions (out of 8), making it difficult to perform an accurate analysis of the short- and long-term effects of both therapies under optimal adherence conditions. As reported in a meta-analysis,[87] it is possible that the outcomes of home-practice therapies, such as ACT, BATD, and other forms of CBT, decrease according to patients' frequency of practice. It would be interesting for future research to explore how improving the frequency and assessment of practice in both therapies, which in this RCT was not systematically monitored, could be beneficial for better outcomes. Smartphones are increasingly being included as clinical resources to help address this issue.[85,88] Also, the practice of skills outside the group has been highlighted as a relevant element to improve outcomes in this type of therapy.[87]

The direct and indirect health problems generated by the COVID-19 pandemic are relevant to consider.[10,19,23] This context, combined with the technical and social difficulties related to the implementation of Internet-based therapies,[79] may also have contributed to the decrease in attendance and adherence and, in turn, to the relative loss of overall effects. Even though patients received continuous and personalized technical support, new models of using remote telehealth technologies are needed to help improve the coordination of pain management services and facilitate meaningful patient engagement.[15] In this sense, the implementation of remote synchronous video group form therapies in public healthcare requires improving access to the necessary resources (a private place, an adequate Internet connection, and a suitable device) and facilitating greater technical support for patients and therapists, especially those without prior technical experience.[20,29]

Although the therapists delivering the ACT and BATD modules (3 different therapists per active group) were

trained prior to the start of the RCT, in this study it was not possible to conduct an external assessment of the therapist fidelity and competence due to budget limitations. Therapists in this RCT were selected for their expertise, both in group and individual formats, and received technical support from the research team to adapt their interventions to a videoconferencing format. Furthermore, aspects related to implementation in routine clinical practice were considered in this selection, so that therapists with different years of experience in the therapy and age profiles were included. In terms of expectancy and credibility about therapy, no differences were identified between therapists or groups. In line with some research, future studies should continue to explore the potential role of the therapist profile in improving outcomes.[89,90]

Side effects are often not assessed in RCTs of psychological therapies, but some exercises such as focus on the present moment sometimes can have adverse effects.[91] Some common side effects of ACT include an increased awareness of one's thoughts and emotions, which can initially lead to increased discomfort or distress. However, this is typically short-lived, and over time, individuals typically report decreased distress. In this RCT, 6 participants in the ACT and 2 in the BATD groups reported emotional discomfort related to the therapeutic exercises. Adverse effects related to body awareness or behavioral activation exercises in this population should be further investigated. Specifically, more information is required on the potential impact these effects might exert on adherence and dropouts from both therapies. Finally, it may be necessary to take an individualized approach to adverse effects detected in the therapies administered in group format, including during the intervention sessions, to prevent possible dropouts and improve group adherence.

These findings should be interpreted with the following limitations in mind. First, as mentioned, there was no external assessment of treatment fidelity and therapist competence. Second, treatment adherence in home exercises was not specifically monitored. Third, the inclusion of a random intercept in the GLM was necessary in this study to consider within-group variability; however, estimating this intercept in patients with only one data point could partially lead to overfitting the model. Fourth, the dropout rate was higher than expected, which could have an impact on an accurate analysis of the short- and long-term effects of both therapies under optimal adherence conditions. Specifically, due to the low retention rate at follow-up, path analyses based on change scores were probably underpowered to detect some small indirect effects.

Conclusions

This 12-month, multicenter, single-blind RCT has demonstrated the clinical utility of including remote synchronous video group-based ACT or BATD as adjuncts to usual care for the improvement of pain interference (primary outcome) and pain catastrophizing (secondary outcome) at posttreatment and at 12-month follow-up in patients with CLBP plus comorbid depressive symptoms. Unexpectedly, no significant differences in depressive or anxiety symptoms were found in ACT and BATD compared to TAU at any of the time points. The superiority of ACT versus BATD and TAU was only detected by the significant difference in the proportion of responders at posttreatment and at follow-up. However, no significant differences in any outcome were identified between the 2 active arms. Finally, the reported attrition rates emphasize the importance of finding strategies to increase retention and adherence in therapies delivered via videoconferencing in this type of population. Even though this study was initially designed to deliver the therapies in a face-to-face format, the benefits identified in distance delivery suggest that it is an effective solution that transcends a temporary need generated by the COVID-19 pandemic.

Author Contributions

JPS-M: Data curation, software, formal analysis, methodology, visualization, and writing the original draft. **SE** and **AS:** Methodology, supervision, and writing – review & editing. **AC-C**, **JRC-A**, **LMM**, **JM-M**, **AP-A**, **XB**, and **AF-S:** Writing – review & editing. **JVL**: Conceptualization, funding acquisition, investigation, project administration, methodology, formal analysis, supervision, writing – review & editing.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jpain.2023.04.008.

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4. Artículo 4

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RESEARCH ARTICLE

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Experiences of patients with chronic low back pain plus comorbid depressive symptoms in a videoconference group acceptance and commitment therapy or behavioral activation treatment for depression: a qualitative study

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ABSTRACT

Purpose: To explore the experiences of patients with chronic low back pain (CLBP) plus comorbid depressive symptoms who received a remote synchronous videoconference group form of Acceptance and Commitment Therapy (ACT) or Behavioral Activation Treatment for Depression (BATD).

Methods: A qualitative study (IMPACT-Q) was nested within a randomized controlled trial (RCT) designed to assess the efficacy and the cost-utility/cost-effectiveness of two therapies in the management of CLBP and depression. Fifty-five patients with CLBP plus depression were selected from the RCT. Twelve focus group sessions, each approximately 60–90 min long, were audio-recorded, transcribed verbatim, and analyzed by six coders through a thematic analysis (deductive and inductive) based on a descriptive phenomenological approach.

Results: Patients perceived behavioral, affective, and cognitive improvements after completing group sessions. Overall, psychotherapy was perceived as a safe and non-judgmental place to express emotions and feel understood. The main barriers reported were lack of human contact and loss of social interaction. In contrast, ease of access, flexibility in the ability to connect from anywhere, avoidance of the need to travel, and savings in time and money were key facilitators to increase attendance and adherence to therapy.

Conclusion: This study provided support for the acceptability of videoconference-delivered ACT or BATD in patients with CLBP plus comorbid depressive symptoms.

IMPLICATIONS FOR REHABILITATION

- Overall, patients reported behavioral, affective, and cognitive improvements after Acceptance and Commitment Therapy and Behavioral Activation Treatment for Depression group sessions.
- Acceptance and Commitment Therapy and Behavioral Activation Treatment for Depression delivered via videoconference platform were perceived as a facilitator for therapy attendance rather than a barrier.
- The findings indicate that group therapy on videoconferencing is perceived favorably as an alternative for managing patients with chronic pain and comorbid depression.
- Technical and social aspects of implementing videoconferencing therapies should be improved, as well as guidelines for adequate support for patients and therapists should also be provided.

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Chronic pain; depression; acceptance and commitment therapy; behavioral activation treatment for depression; eHealth; qualitative study

Introduction

Chronic low back pain (CLBP) and depression are common conditions that represent a great challenge for healthcare systems [1]. The prevalence of CLBP worldwide ranges from 4% to 20% [2] and depression among pain patients ranges from 12% to 72% [3], being greater than that reported for the general population [4]. Overall, comorbidity between chronic pain and depression is over 60% [5], creating a significant economic burden [6] and social impact [7]. Depression in the context of chronic pain is associated with reduced psychological well-being, daily activities, social relationships, and quality of life [8]. In addition, this comorbidity negatively affects treatment adherence and response [9], requiring a multidimensional and specialized approach for its management [10].

Significant developments in psychotherapies for chronic pain and depression in recent years include new forms of Cognitive Behavioral Therapy (CBT), such as Acceptance and Commitment

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Therapy (ACT) or Behavioral Activation Treatment for Depression (BATD). The potential of ACT and BATD to improve pain interference, pain acceptance, and behavioral activation in patients with chronic pain and depression has been empirically evidenced [11–13]. The efficacy of ACT and BATD patients in improving emotional distress is also well established [14–18]. However, some studies have shown that when these conditions coexist, they are more resistant to treatment [9,19–21] as compared to depression alone [22–24].

The experience of the coronavirus disease 2019 (COVID-19) pandemic has highlighted the need for digital technologies and their testing to treat health conditions. In this regard, eHealth, defined as the practice of healthcare delivered via digital tools (computers or smartphones) in the prevention, treatment, promotion, and maintenance of health, has never been more important [25,26]. Previous studies have concluded that internet- and remote-delivered forms of CBT are beneficial for improving depression and chronic conditions [8,27–29]. Specifically, recent meta-analyses demonstrated the benefits of internet-based ACT in chronic pain patients for improving pain acceptance, anxiety, depression, catastrophizing, pain interference, distress, pain intensity, pain disability, and fear avoidance [30,31].

The use of eHealth in clinical practice increased from 7% to 85% during the COVID-19 pandemic, and over the next few years, it is expected that approximately 30% of psychotherapy will be delivered via this format [32]. Particularly, internet- and remote-delivered therapies are highlighted as a useful resource for people with chronic pain due to their easy accessibility [30,31,33,34]. A recent systematic review [35], which included 21 qualitative studies exploring the experiences of chronic pain patients, found that the main facilitators of participation in eHealth interventions were flexibility and patient empowerment, while barriers were lack of contact, technological challenges, irrelevant content, and limited digital (health) literacy. Strengthening internet- and remote-delivered therapies as a complementary or alternative health intervention resource, in addition to face-to-face therapy, requires a detailed exploration of patients' and therapists' opinions, to assure its successful implementation [36–38].

Systematic reviews and meta-analyses to date provide insight into the efficacy of online psychotherapies. However, it appears that there are limited studies of the experiences of using videoconferencing platforms for delivering third-wave CBT, particularly studies that recognize potential barriers and facilitators that could affect adherence and efficacy in group format. Thus, the main objective of this qualitative study (IMPACT-Q), nested within a randomized controlled trial (RCT) [39], was to explore the experiences reported by a group of patients with CLBP plus comorbid depressive symptoms that had participated in ACT or BATD delivered via remote synchronous videoconferencing.

Methods

Study protocol

The main purpose of the IMPACT study was to examine the efficacy and the cost-utility/cost-effectiveness of adding a group-based form of ACT or BATD to treatment-as-usual (TAU) for patients with CLBP plus comorbid depressive symptoms [39,40]. Due to the COVID-19 pandemic, this 12-month, multicenter, RCT, initially designed to deliver therapies in a face-to-face format, was adapted to be delivered through a remote synchronous videoconference platform (Zoom). Among the various technological options available, this one was chosen because it guaranteed a synchronous and bidirectional interaction, consistent with the needs of both therapies and their group-based delivery format. This RCT was registered in ClinicalTrial.gov (NCT04140838), following the guidelines issued by the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) and Consolidated Standards of Reporting Trials (CONSORT).

In brief, both therapies (ACT and BATD) were administered in a group format (maximum 13 patients per therapy) including eight weekly 1.5-h sessions via remote synchronous videoconference. Three different therapists guided the groups in each therapy (one therapist per group for ACT and BATD), with technical support from a researcher during the therapy. This study was conducted in accordance with the 1964 Helsinki Declaration and was approved by the Ethics Committee of the Fundació Sant Joan de Déu (PIC-178-19) and the Hospital del Mar (2019/8866/I). None of the patients received any financial incentive for participating in this study. A published study protocol is available [41].

Study design

IMPACT-Q study, which was not contemplated in the original study protocol [41], arose out of the research team's interest in exploring the experiences of patients who participated in these group forms of ACT or BATD administered via videoconferencing during this period of global emergency. A qualitative thematic analysis based on a descriptive phenomenological approach was used to explore patients' experiences after completing ACT or BATD group sessions [42]. Two general topics were explored in this research: (1) patients' experiences related to the therapy and (2) patients' experiences related to the use of technology. This study followed the checklist of Consolidated Criteria for Reporting Qualitative Research [43] and the guidelines of the Journal Article Reporting Standards for Qualitative Research (JARS) [44].

Study context

Patients were recruited between September 2020 and May 2021 [39]. The ACT and BATD programs were conducted in three waves: October to December 2020 (first wave), February to April 2021 (second wave), and May to June 2021 (third wave). The focus groups were conducted no later than one month after the end of each of these waves. It is important to note that this qualitative study was conducted during a fluctuating period of the COVID-19 confinement measures adopted by the Spanish authorities, which encompassed phases of increased (first and second waves) and decreased mobility restriction (third wave). For example, it was identified that a significant proportion of the patients who did not complete the ACT or BATD program or decided not to participate in the focus groups, presented in the third wave (when the mobility restrictions due to the pandemic were relaxed and the pre-holiday period in Spain began). The pandemic created a unique context in which the interventions were delivered. For this reason, the social and health context in which this study was implemented was a relevant element to consider in the exploration and interpretation of patients' experiences.

Participants

A total of 234 patients participated in the RCT: 78 were assigned to ACT, 78 to BATD, and 78 to TAU [39]. Of the 156 patients who participated in the active interventions (ACT or BATD), 94 completed the group sessions (ACT = 52 and BATD = 42). The 62

patients who did not complete the active interventions program (ACT = 26 and BATD = 36) did not participate in the qualitative study due to the impossibility of contacting them or their lack of interest in continuing to contribute to the project. All 94 eligible patients were invited by telephone and email to participate in this qualitative study, but 23 did not respond. As shown in Figure 1, from the 71 patients who initially agreed to participate in the focus groups delivered via Zoom, 16 ultimately did not participate due to time availability. Finally, 55 patients completed the focus groups: 31 from ACT and 24 from BATD

The selection of patients for this study was intentionally established. Specifically, the experiences of all patients who completed the active intervention sessions and agreed to participate in this qualitative study were explored. Because the purpose of this qualitative study was to explore the experiences of a significant set of patients with these therapies, it was decided not to use saturation as a criterion for determining data collection. This decision was also supported by the arguments recently published by Braun and Clarke [45] regarding the relevance of saturation in thematic analyses.

Interventions

This study explored the experiences of a group of patients who participated in ACT or BATD. ACT is an intervention that promotes acceptance of unwanted experiences and commitment to goal-oriented and value-based actions [46], whereas BATD applies learning principles to the pattern of withdrawal or reduction of behavioral activity related to depression [47]. The ACT sessions were based on the protocol proposed by Vowles et al. [48] and the BATD sessions on the protocol proposed by Lejuez et al. [49]. Patients who received these interventions continued with their usual treatment during the RCT. Following the Spanish standards [50], TAU consists of medication (analgesics, anxiolytics, anti-inflammatories, opioids, and/or antidepressants), psychoeducation, and suggestions for aerobic exercise. A more detailed description of the characteristics of both interventions is available in Sanabria-Mazo et al. [39,40].

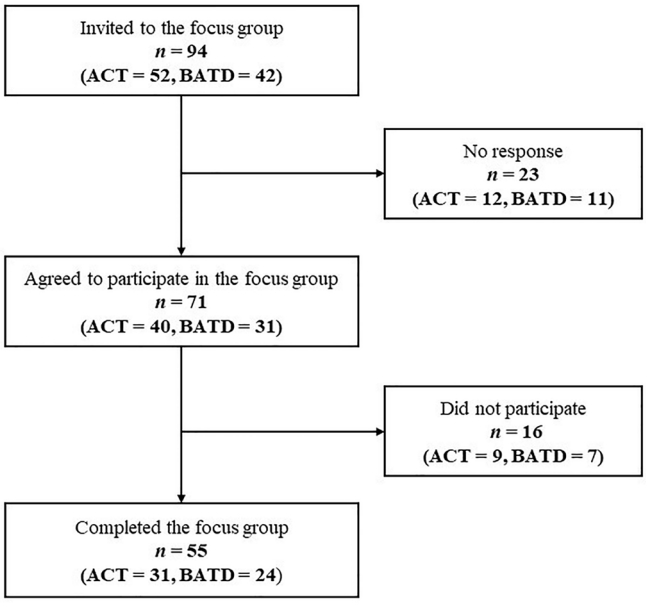

Figure 1. Flowchart of patients who participated in IMPACT-Q.

Data collection

The focus groups were conducted via Zoom by five researchers, of which three were female (NGU, GNR, and GVM) and two were male (JMPS and ÓFV). Before starting the focus groups, these researchers were previously trained in qualitative data collection and analysis procedures. All had master's degrees in health psychology and worked as psychologists specializing in mental health. The focus groups were led by the researchers who provided technical support to patients and therapists during the eight sessions of each therapy group. Because patients were familiar with the researchers this is likely to have enhanced rapport, and because the researchers had not delivered the treatment this may have encouraged participant responses. Focus groups were used as an interactive data collection technique to reflect on the experiences of the patients who participated in the group therapies [51,52].

The objective of this qualitative study was explained at the beginning of the focus group. In total, 12 focus groups (six for ACT and six for BATD) were conducted between January and July 2021. These included three to six patients (who were part of the same therapy group in which they participated), lasted between 45 and 90 min, and were completed one month after the post-treatment assessment, to avoid temporal interference with the other assessment points of the IMPACT study [39]. The questions used in the focus groups were validated by five project researchers (JPSM, AFS, SE, AS, and JVL) and approved by all the authors of this article, considering the main objectives of the study. Two leading questions were included for open exploration of participants' experiences with therapy (*how was your experience participating in this therapy?*) and technology use (*how was your experience participating in this therapy via videoconference?*). The list of main questions addressed during this study is included in Supplementary Table 1. During the focus groups, the five researchers noted down all the observations they considered relevant to this study. These notes, as indicated below, were used to complement the interpretation of the results.

Data analysis

The focus group sessions were audio-recorded, transcribed verbatim, and analyzed by six coders (JPSM, ACC, NGU, JMPS, GVM, and MFM) using Atlas.Ti (v. 7.5). During this process the patients' names were replaced by a code to ensure the confidentiality of their data. The data were analyzed by open, axial, and selective coding, applying thematic analysis (deductive and inductive) [53]. At first, coders independently designated relevant fragments and coded them using deductive analysis (i.e., from predefined themes) [54,55]. These themes, defined by the research team (composed entirely of clinical and health psychologists) to explore the main purpose of this study, were: (1) patients' experiences related to the therapy and (2) patients' experiences related to the use of technology. The analysis was performed independently to reinforce the rigor of data processing. Subsequently, inductive analysis (i.e., subthemes derived from data, instead of predefined themes) was used to classify all fragments into subthemes.

After analyzing each focus group, the coders (JPSM, ACC, NGU, JMPS, GVM, and MFM) met to discuss the identified subthemes and redefine the coding scheme (when discrepancies were detected). When all codes were obtained, coding schemes with example codes were developed by constantly comparing similarities and dissimilarities in the data. The final coding was validated by the research team after completion of the analysis. After that, the final analysis was adjusted according to the consensus themes

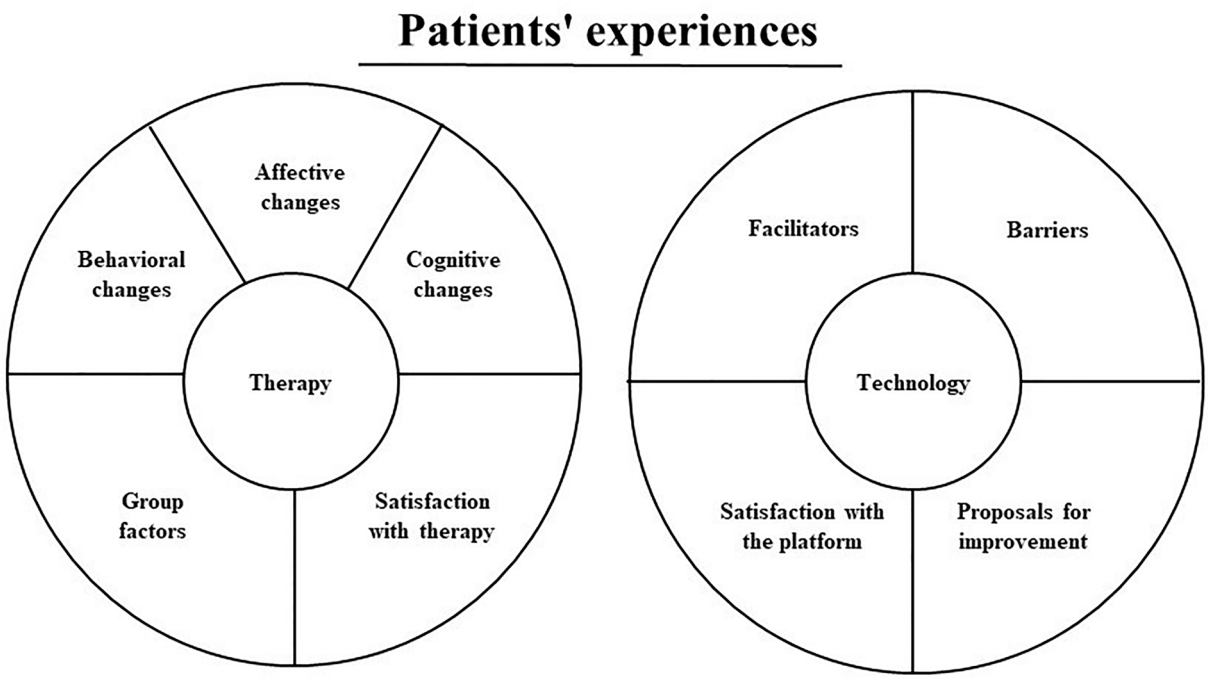

Figure 2. Themes and subthemes of analysis of this study.

and subthemes (see Figure 2). The final interpretation and synthesis of the results presented below were carried out by the first author (JPS-M). To reinforce the rigor of the interpretation of the results, the five researchers in charge of the focus groups (NGU, JMPS, GNR, ÓFV, and GVM) were asked to validate the final interpretation. The purpose of this final validation was to contrast the interpretation of the results with the notes that they collected during the focus groups, which were in turn based on the information they already knew about the patients' participation during the therapies [53].

Reflexivity

The research team reflected on possible ideas that could have influenced the data collection and analysis [56]. Following the AMEE Guide No. 149, personal (i.e., expectations, assumptions, and reactions to contexts, participants, and data), interpersonal (i.e., the influence of the relationships surrounding the research), methodological (i.e., consideration of researchers' paradigmatic orientations and decisions), and contextual reflexivity (i.e., social, cultural, and historical factors in which the study was implemented) was especially considered during this analytical process [57].

Reflexivity was adopted in all phases of the study to ameliorate the potential impact of subjective influences on the exploration of this phenomenon [56]. After completing the interpretation of the results, a group reflective discussion was held to recognize specific aspects that may have influenced this study [57]. In general, four elements were considered during the exploration and interpretation of the phenomenon: (1) the expectations of the research team (personal factor), which could be indirectly associated with the quantitative results of the RCT; (2) the social desirability of the participants (interpersonal factor), which could have facilitated favorable responses regarding the therapies due to the previous bond between the patients and some of the researchers; (3) the collective nature of the discussion during the focus groups (methodological factor), in which dominant perspectives are more easily socially articulated ("collective sense-making"); and (4) the implementation of the therapies by videoconference due to the COVID-19 pandemic (contextual factor), which could have influenced the meanings attributed to the experience or the type of connection of the participants toward the interventions.

Data synthesis

The selected quotes below were used to support the qualitative analysis and were labeled according to patient identification code (ID) to facilitate recognition of sociodemographic characteristics. Considering that the purpose of this study was to explore patient experiences of these two third-wave CBT therapies (i.e., ACT and BATD), some results are presented in parallel, except as specified in the description. Although some results regarding experiences with the therapies are presented in parallel to expand on the narratives of the patient groups, it was not the aim of this study to compare the two interventions, but rather to gain an integrated understanding of the experiences reported by participants.

Results

Sample description

A total of 55 patients with CBLP and comorbid depressive symptoms participated in the IMPACT-Q study: 31 in ACT and 24 in BATD groups. The age range of ACT patients was 35 to 70 ($M = 57.32$; $SD = 7.96$) and of BATD was 44 to 69 ($M = 59.38$; $SD = 8.13$). The time since diagnosis of chronic pain as communicated by ACT patients ranged from 2 to 30 years ago ($M = 10.55$; $SD = 9.13$) and by BATD patients from 1 to 35 years ago ($M = 13.88$; $SD = 10.58$). The number of sessions attended by ACT patients fluctuated from 3 to 8 sessions ($M = 7.13$; $SD = 1.18$) and by BATD patients from 6 to 8 sessions ($M = 7.46$; $SD = 0.72$). Overall, 71% of ACT and 84% of BATD patients were female. At the time of the study, 48% of ACT and 25% of BATD patients were unemployed.

Table 1. Socio-demographic characteristics of the patients.

Patient ID	Therapy	Sessions attended	Years of diagnosis	Age	Gender	Civil status	Education level	Work status
01	ACT	6	16	54	Male	Married or paired	University	Unemployed
02	ACT	8	8	49	Male	Married or paired	University	Employee on sick leave
03	ACT	8	7	70	Female	Widow	Secondary	Retired
04	ACT	8	30	60	Male	Married or paired	Primary	Unemployed
05	ACT	8	2	43	Male	Single	Primary	Unemployed
06	ACT	8	7	66	Female	Married or paired	Secondary	Active
07	ACT	5	2	55	Female	Married or paired	Secondary	Unemployed
08	ACT	8	9	58	Female	Married or paired	Secondary	Unemployed
09	ACT	6	29	64	Female	Married or paired	Secondary	Unemployed
10	ACT	7	3	55	Female	Married or paired	No studies	Household
11	ACT	8	10	48	Female	Married or paired	Secondary	Active
12	ACT	8	5	61	Female	Single	University	Active
13	ACT	8	25	67	Female	Married or paired	Primary	Retired
14	ACT	7	5	52	Female	Single	Secondary	Unemployed
15	ACT	7	3	53	Female	Widow	Secondary	Unemployed
16	ACT	7	36	68	Female	Married or paired	Primary	Retired
17	ACT	3	6	54	Female	Married or paired	Secondary	Unemployed
18	ACT	8	15	55	Male	Married or paired	Secondary	Unemployed
19	ACT	7	17	51	Male	Married or paired	Primary	Unemployed
20	ACT	6	2	57	Female	Married or paired	Secondary	Active
21	ACT	6	11	65	Female	Married or paired	Primary	Household
22	ACT	6	5	58	Female	Widow	Secondary	Unemployed
23	ACT	8	5	64	Female	Married or paired	University	Employee on sick leave
24	ACT	8	7	35	Male	Married or paired	Secondary	Active
25	ACT	6	4	46	Female	Single	Secondary	Active
26	ACT	8	6	57	Female	Married or paired	University	Unemployed
27	ACT	7	8	60	Male	Married or paired	Primary	Unemployed
28	ACT	8	4	65	Female	Separated or divorced	Secondary	Unemployed
29	ACT	8	21	63	Female	Married or paired	Secondary	Active
30	ACT	7	3	58	Female	Married or paired	Secondary	Employee on sick leave
31	ACT	8	16	66	Male	Separated or divorced	University	Retired
32	BATD	8	10	55	Female	Married or paired	Secondary	Unemployed
33	BATD	7	25	54	Female	Married or paired	University	Unemployed
34	BATD	8	5	69	Female	Widow	Primary	Retired
35	BATD	8	10	68	Female	Married or paired	Secondary	Retired
36	BATD	8	30	62	Female	Married or paired	Primary	Active
37	BATD	7	30	56	Female	Married or paired	Secondary	Unemployed
38	BATD	7	7	63	Female	Single	Secondary	Active
39	BATD	8	35	65	Female	Married or paired	Secondary	Active
40	BATD	8	6	50	Female	Married or paired	Secondary	Unemployed
41	BATD	8	5	64	Female	Widow	Primary	Household
42	BATD	6	20	69	Male	Married or paired	Secondary	Retired
43	BATD	8	23	67	Female	Married or paired	University	Active
44	BATD	8	34	56	Female	Married or paired	University	Unemployed
45	BATD	8	16	64	Female	Separated or divorced	Primary	Active
46	BATD	8	6	65	Male	Married or paired	Secondary	Retired
47	BATD	8	6	60	Female	Married or paired	University	Active
48	BATD	6	3	59	Female	Separated or divorced	Secondary	Employee on sick leave
49	BATD	7	1	66	Female	Widow	Primary	Retired
50	BATD	6	8	46	Male	Married or paired	Secondary	Employee on sick leave
51	BATD	7	6	69	Female	Married or paired	Primary	Retired
52	BATD	7	10	44	Female	Married or paired	Secondary	Employee on sick leave
53	BATD	8	18	62	Female	Married or paired	Primary	Household
54	BATD	8	3	47	Male	Married or paired	Secondary	Unemployed
55	BATD	7	16	45	Female	Single	Secondary	Active

All patients resided in Catalonia and were mostly white Europeans. The characteristics of each patient are detailed in Table 1.

Experiences related to the therapy

The patients' experiences related to the therapy mainly reflected: (1) behavioral changes, (2) affective changes, (3) cognitive changes, (4) group factors, and (5) satisfaction with the therapy.

Behavioral changes

Patients allocated to ACT reported that they learned to be more proactive, to be open to new experiences, and to set healthy limits to improve their quality of life. Some patients also informed that setting small daily goals allowed them to make an overall assessment that helped them to improve their health status.

> I try to do my things little by little every day. When you achieve small results, it helps you to believe that you can improve. Now I try to focus on the positive aspects. If I go out for half an hour, I count that as progress (Patient ID 19: female, 63 years old).

Similarly, BATD patients learned to define their weekly goals, incorporate healthy habits into their lives, express their emotions more freely, be less strict with themselves, and reconnect with pleasurable activities they avoided because of pain. Several patients agreed that being more organized, structured, and flexible

with their personal goals helped them to improve their well-being and quality of life.

> I am doing things that I had stopped doing a long time ago, and that makes me feel very good. I'm not giving anything up now, I'm trying to do as much as I can. Now I walk every day, which I had given up, and that is helping me to break the negative dynamic I was in (Patient ID 38: male, 51 years old).

Affective changes

Almost all ACT patients perceived an improvement in their mood. They pointed out that releasing blocked emotions, managing their resources, acknowledging their experience of pain to others, and feeling understood by people with the same health condition helped them to feel more comfortable. Specifically, one patient reported increased empathy for the pain experiences of others.

> On the days when there was a session, my morale was very high. The fact that I was interacting with more people like me, with people with pain and problems like mine, made me feel less lonely and more accompanied. It was a great help (Patient ID 05: male, 43 years old).

Most BATD patients described that being more active in their daily lives helped them to feel in a better mood. Others highlighted that after completing the therapy they had learned not to let their pain get the better of them. For some of them, finding that they could return to pleasurable activities was synonymous with empowering themselves to "move on." In this regard, one participant reported that participating in the sessions allowed her to feel "alive again."

> This therapy has helped me to feel that I am alive again. It has reminded me that I must not give up and must keep fighting every day to stay ahead. Being part of this group has been a very enriching experience for me (Patient ID 37: female, 56 years old).

Cognitive changes

Many ACT patients reported changes in their relationship and stance with their health condition. Particularly, they described learning to be in contact with the present moment, to be more compassionate about their situation, to accept chronic pain as part of their life, and to be more tolerant of daily difficulties. Some patients described developing strategies such as turning their attention away from the pain and boosting their positive attitude.

> It is easy to say: "I feel so bad", and then fall into depression. So, you have two problems: pain and depression. But if you realize that with a positive attitude, you can do a lot for yourself, you can improve your quality of life (Patient ID 08: female, 58 years old).

Some BATD patients mentioned acting for themselves to break the negative spiral between pain level and depression symptoms, to become aware of the harmful effects of disruptive thoughts, and to recognize that they can carry out activities even with some restrictions. Others remarked that although the therapy had not helped them to reduce their pain intensity, it allowed them to reconnect with themselves and avoid judging their emotions.

> I have learned to find strength in those moments when I am most lacking in enthusiasm and happiness. Even though it is hard to break the negative spiral, I now try to give a little more of myself. Doing more things than before, makes me feel much better (Patient ID 33: female, 54 years old).

Group factors

ACT and BATD patients highlighted that being connected to weekly sessions helped them create a space to express all their progress. They revealed that recognizing that there are other people struggling with pain helped them feel more understood and less judged. In addition, having a place to share their experiences was an opportunity to free themselves from the frustration of feeling isolated. Similarly, as an emergent issue, they highlighted that participating in these sessions had been helpful as a source of social activity in times of mobility restrictions imposed during the pandemic.

> I was in a bad state of mind. It helped me to share my current health conditions with the group, especially in these times of pandemic. Attending these sessions and having a space to express my emotions has been positive for me. This came at the right time (Patient ID 02: male, 49 years old).

Satisfaction towards therapy

Beyond the therapy type, all patients indicated that they were satisfied and grateful to participate in the therapy sessions. Repeatedly, they expressed they would like to engage in a more extensive therapeutic program to deepen their experience of specific components of the therapy and to be provided with individual space to address personal issues. Some patients in ACT pointed out they would like to have more practical tasks in sessions, and fewer metaphors, to make it easier for everyone to comprehend.

> I enjoyed the therapy, although I found it a bit short. I think that what they teach us in each session is very useful for our mental health. The simple fact that you must connect to the weekly sessions and talk, forces you to move, to be better (Patient ID 36: female, 62 years old).

Additionally, one BATD patient suggested that creating groups according to pain severity could help all patients feel more comfortable and understood. Other BATD patients perceived an overload of information during the sessions. Therefore, they suggested simplifying the content of each session into more specific educational and psychological components. Almost all patients agreed with the implementation of these therapies in the public health system for chronic pain and comorbid depressive symptoms to promote adequate emotional regulation.

Experiences related to the use of technology

The patients' experiences related to the use of the technology indicate: (1) barriers, (2) facilitators, (3) satisfaction with the platform, and (4) proposals for improvement.

Facilitators

The majority of ACT and BATD patients indicated that this was the first time they participated in a group-based therapy delivered via videoconferencing. The positive aspects of participating in therapy via this platform were avoiding additional journeys, having the flexibility to be connected from elsewhere according to their daily needs, saving time and money in transport, increasing their proactive ability to participate in the groups, and facilitating their attendance and adherence. In addition, many patients stated that these therapies are especially useful for people with chronic pain, as well as in times of pandemics, to avoid the risk of contagion.

> I like that you can connect at any time, and you don't have to move. It's very comfortable and flexible: you can connect from your mobile, tablet, or computer, no matter if you're in your car or home. Moreover, it is very practical for people with chronic pain (Patient ID 52: female, 44 years old).

Barriers

In contrast, the negative aspects identified were losing face-to-face contact during the sessions, losing the opportunity to set off from home and change the usual space, and missing the moments of social interaction before and after the sessions. Some patients also described that lack of resources, such as a private place to attend the sessions, an adequate internet connection, a suitable device (smartphone, tablet, or computer), or having limited technological knowledge, interfered sometimes during therapy.

> I would have liked the sessions to be face-to-face so I could go out, move around, change spaces… Connecting from home is not bad, but I prefer direct contact with people because it helps me to distract myself and, above all, socialize (Patient ID 29: female, 63 years old).

Satisfaction with the platform

Beyond the specific therapy received, patients acknowledged the advantages of participating in therapy groups delivered via videoconferencing, but several indicated a preference for face-to-face treatment if available. One of the main positive points for some of them was the feeling of increased self-competence for being able to use a technology that was unfamiliar to them. In other words, they perceived an increase in their digital literacy. Overall, they recognized that implementing eHealth in the public health system would contribute to savings in healthcare costs.

> Applying therapies in this format is a way to save time, space, and costs. This allows you to start a therapy and finish it, according to your needs and your rhythms. Because it is online, you can reach more people with pain, no matter where they are in the world (Patient ID 14: female, 52 years old).

Proposals for improvements

Some patients suggested that blended therapies combining face-to-face and online sessions could be a strategy to bring out the strengths of each modality. As mentioned above, other potential improvements identified by some patients would be to create groups according to pain severity. Some recommended reducing the number of patients per group to encourage participation and facilitate a more personalized intervention. Others suggested scheduling an initial technology training session to help them adapt to the online sessions. Similarly, one patient stated that it was also important to train therapists in the use of technological platforms.

> I would be in favor of combined therapy: two or three online sessions to get to know each other and, afterward, some face-to-face sessions to have contact with the group. Alternating face-to-face with online sessions would help to make it more dynamic (Patient ID 44: female, 56 years old).

Discussion

This qualitative study (IMPACT-Q) was nested within an RCT investigating the efficacy and cost-utility/cost-effectiveness of two third-wave treatments for patients with CLBP plus depression. Beyond the therapy type, patients perceived behavioral, affective, and cognitive improvements after completing their treatment, and overall improvements in emotion management and quality of life. The perception of changes reported by patients in both therapies is partially consistent with the results obtained in the RCT efficacy study, which identified a statistically significant improvement in pain interference, pain catastrophizing, pain acceptance, behavioral activation, and psychological flexibility, but not in the reduction of depression, anxiety, and stress symptoms [39]. The differences identified in the improvement of emotional disturbances, where a marginal trend towards significance was observed in the RCT, is a relevant contribution of this qualitative study, which recognizes the importance of participants' experiences in understanding the therapeutic potential of both therapies.

Another relevant finding of this qualitative study is that patients highlighted that being part of these therapy sessions promoted a group identity that helped them to feel more understood and accompanied in their health condition, especially during restrictions imposed during the COVID-19 pandemic. Moreover, most of the patients agreed on the benefits of freely sharing their emotions related to their health care condition, in a therapeutic context, without feeling that they are overwhelming their relatives and other close personal relationships. Particularly, the non-judgmental environment of therapy encouraged compassion toward self and others within the groups. In this regard, a growing body of research suggests that group cohesion is a factor with great potential to improve individual patient outcomes [58,59]. Specifically, group identification and cohesion have been identified as a therapeutic mechanism that contributes to the improvement of personal control and thus facilitates the management of chronic pain in patients [60].

Patients who participated in psychotherapy sessions delivered via a videoconferencing platform expressed satisfaction with the therapy and strengthened confidence in using this technology. This may be a result of the synchronized two-way interactions provided here, as in conventional group therapy. Having met others with a similar clinical problem in the online sessions, patients experienced an enhanced sense of well-being. At the same time, patients agreed to receive in-person therapy is also important. Even though some barriers were identified in the technological implementation of these therapies (such as losing face-to-face contact, missing out on physically different intervention spaces, going out from home, and dispensing with moments of socialization), both were generally perceived to be psychologically beneficial for people with chronic pain and depression. In this regard, the most important benefits were to avoid additional journeys and to save time and money on transport, as well as the ability to connect from different settings according to their needs. Taken together these were seen to facilitate attendance and adherence to the therapy.

As mentioned above, patients in both therapies perceived positive psychological changes after completing the groups, which are consistent with those obtained in the RCT efficacy study [39]. Like previous studies with chronic pain samples, the patients perceived a positive impact of ACT and BATD on mood, social relationships, behavioral activation, and self-care [15,17,30,31,61]. Although several patients in both groups perceived no change in pain intensity, they reported a decrease in pain catastrophizing, as well as an increase in pain acceptance [9,21] and quality of life [20,24]. Consistent with other studies, ACT patients reported more improvements related to pain acceptance [30,31,36] and BATD patients to behavioral activation [19,38], partially consistent with the main intervention target and theoretical orientation of each therapy [19].

In line with previous qualitative studies, patients commented that being part of a therapeutic group had allowed them to feel understood and less judged [36,38,62,63]. They also indicated that attending the sessions was an opportunity to talk about their daily problems, reinforce acquired habits, evaluate progress toward goals, and feel less lonely [64,65]. In this sense, numerous studies have shown that feeling listened to by others contributes to both the acceptance of pain and the development of active coping strategies [36,38,62,66], a typical unspecific effect of joining a psychotherapy group. Even though several patients indicated that the virtual format facilitated greater emotional openness during the sessions, some expressed that the lack of face-to-face contact and moments of socialization interfered with their attention to the therapy. The findings of this qualitative study are consistent with experiences described in other group interventions delivered via videoconferencing [35,36,38].

Repeatedly, patients highlighted the relevance of offering group therapy via videoconferencing during the COVID-19 pandemic to increase patient care coverage, decrease costs, and reduce potential risks of contagion [37]. Results from the RCT indicate that group-based forms of ACT or BATD delivered via videoconferencing are potentially cost-effective interventions [40]. The quantitative and qualitative findings of the IMPACT study [39–41] highlight the importance of continuing to investigate the clinical and economic benefits of therapies administered by videoconference in the chronic pain population, especially in terms of costs, accessibility, convenience, flexibility, and effectiveness. As mentioned in other studies, the need for further development of digital resources for adequate monitoring and treatment of pain is increasingly evident [25,26].

Further research is needed to identify the benefits and costs of videoconferencing therapies in group format [67,68]. It appears that undertreated chronic pain due to the pandemic situation created widespread feelings of isolation in patients and indirectly impacted the overload of the public health care system [69]. The investment of digital resources that guarantee adequate monitoring of pain development and promote eHealth appears indispensable in this pandemic era [25,26]. According to the findings of this qualitative study, the implementation of therapies in this format in the public health system requires ensuring access to the necessary resources (a private place, an adequate internet connection, or a suitable device) and more technical support for patients and therapists, especially those without previous technological experience [37]. Other important aspects for the implementation of both therapies are to increase the number of sessions, suggest more practical tasks between sessions, include additional sessions to strengthen specific psychoeducational components, and provide spaces for individual intervention.

Limitations

These findings must be interpreted with caution. First, as this was a purposive sample, not all patients who participated in the RCT were included. However, the considerable number of patients included in this study contributed to the exploration of experiences related to both therapies. Second, the experiences of patients who did not complete the ACT or BATD program or therapists were not explored in this research, which could add more depth to the interpretation of these findings. Similarly, it would have been valuable to explore the views of invited patients who did not participate in the qualitative study, and who had the lowest attendance in the groups. Third, in this qualitative study based on a descriptive phenomenological approach, focus groups (rather than in-depth interviews) were used to explore individual experiences, which may have affected the interactional nature of the situation and, therefore, the data produced. The collective nature of the discussion ("collective sense-making"), the fact that individual narratives can get lost in the dialogue between participants, and the social situations that focus groups represent (in which for instance dominating perspectives are socially most easily articulated) are relevant aspects to consider.

Fourth, the fact that five different researchers conducted the focus groups may have impacted the standardized exploration of patients' experiences. Nevertheless, to minimize these effects, all interviewers were trained in the collection of the data, and all researchers reached an agreement regarding the analysis procedure of the qualitative data for this project. Fifth, considering that patients had a prior relationship with their interviewers, there is a possibility that responses were influenced by social desirability. Finally, patients were not included in the final validation of the analyses in this study, which could have helped to gain a more reliable perspective on the interpretation reported by the research team. It is suggested that future qualitative studies integrate participants to ensure a more reliable interpretation of their experiences.

Strengths

It appears that this is the first qualitative study to investigate the experiences of patients with chronic pain plus comorbid depressive symptoms who participated in a remote synchronous videoconference group form of ACT or BATD. The strengths of this study were the large number of patients who shared their experiences in the focus groups, the three waves of data collection to minimize the potential influence associated with the specific timing of data collection, and the adherence to COREQ guidelines. Another aspect to highlight is that the five researchers in charge of the focus groups received prior training in qualitative data collection and analysis. This training, added to the previous relationship with the patients (which was established while providing technical support to the therapists), was an element of great relevance in enriching the interpretation of the results of this study.

Future research lines

The findings of this qualitative study could be transferable to populations with similar demographic and clinical characteristics who participated in interventions during the COVID-19 pandemic. There is a possibility that some therapeutic effects of ACT and BATD—documented in previous clinical trials—such as improvement in emotional disturbances (depression, anxiety, and stress), were diminished by the implementation of these interventions via videoconferencing, as well as by the high percentage of patients withdrawing from the intervention (which were like those of other studies conducted during the pandemic). Considering the emergency context in which this study was developed, it is recommended to continue exploring the experiences of patients with this comorbidity in group forms of these therapies administered by videoconference. Findings from future studies could help expand information about the role the COVID-19 pandemic played in these experiences and on the overall satisfaction with the implementation of these group therapies via videoconferencing.

Methodological rigor

This qualitative study followed the four criteria defined by Lincoln and Guba to guarantee the credibility, transferability, dependability,

and confirmability of the reported findings [70]. To ensure credibility, an accurate presentation of all methods used in the data collection and analyses of this study was reported. In this process, aspects relevant to the interpretation of the results were acknowledged, such as the intentional selection of patients for both therapies. To ensure transferability, information was provided on the demographic and clinical characteristics of patients on both therapies, as well as information on the unique context in which this research was developed (which, as mentioned above, arose in response to the therapeutic demands of the COVID-19 pandemic). To ensure reliability, information was provided about the procedures carried out for the design and execution of this qualitative study nested to an RCT, thus facilitating the replicability of the methods. Finally, to ensure confirmability, the strategies implemented to detect the possible influence of the research team's preconceptions (reflexivity) in the interpretation of the findings were recognized [71].

Conclusions

The COVID-19 pandemic has highlighted the importance of videoconferencing as a tool to assist patients with chronic pain. The implementation of eHealth in the public health system is a growing challenge for both therapists and patients. Overall, the findings of this study provided support for the acceptability of remote synchronous videoconferencing in patients with CLBP plus comorbid depressive symptoms. In addition, the importance of group identification and cohesion is highlighted as a mechanism that contributes to disease management in patients with chronic pain. Even though the experiences with this therapy format were perceived as beneficial for this profile of patients, further technical improvements are needed for its implementation in healthcare settings. For this purpose, more research is required to identify the specific needs of patients, therapists, and healthcare institutions.

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Author contributions

Conceptualization: JPSM, ACC, and JVL; *data curation*: JPSM and ACC; *formal analysis*: JPSM, ACC, JMPS, NGU, GVM, and MF-M; *funding acquisition*: JVL; *investigation*: JPSM and ACC; *methodology*: JPSM, ACC, and JVL; *project administration*: JPSM and JVL; *resources*: JVL; *software*: JPSM and ACC; *supervision*: AS, SEI, and JVL; *validation*: AFS, LMM, AS, SEI, and JVL; *visualization*: JPSM; *writing – original draft*: JPSM; *writing—review and editing*: JPSM, ACC, NGU, JMPS, GNR, OFV, GVM, MF-M, GCR, AFS, LMM, AS, SEI, and JVL. All authors have read and agreed to the published version of the manuscript.

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Informed consent statement

Informed consent was obtained from all participants involved in the study.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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5. Artículo 5

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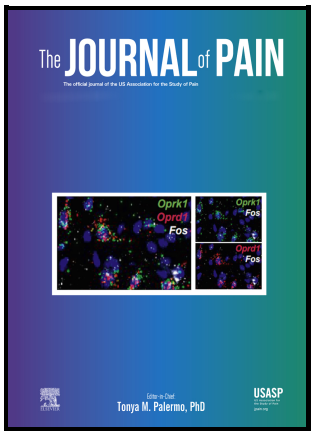

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Economic evaluation of videoconference group Acceptance and Commitment Therapy and Behavioral Activation Therapy for Depression versus usual care among adults with chronic low back pain plus comorbid depressive symptoms

Short-running title: Economic evaluation of ACT and BATD

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Abstract

Chronic pain and depression are frequently comorbid conditions associated with significant healthcare and social costs. This study examined the cost-utility and cost-effectiveness of videoconference-based group forms of Acceptance and Commitment Therapy (ACT) and Behavioral Activation Therapy for Depression (BATD), as a complement to treatment-as-usual (TAU), for patients with chronic low back pain (CLBP) plus depressive symptoms, compared to TAU alone. A trial-based economic evaluation (n = 234) was conducted from a governmental and healthcare perspective with a time horizon of 12 months. Primary outcomes were the Brief Pain Inventory–Interference Scale (BPI-IS) and Quality Adjusted Life Year (QALY). Compared to TAU, ACT achieved a significant reduction in total costs (d = 0.47), and BATD achieved significant reductions in indirect (d = 0.61) and total costs (d = 0.63). Significant improvements in BPI-IS (d = 0.73 and d = 0.66, respectively) and QALY scores (d = 0.46 and d = 0.28, respectively) were found in ACT and BATD compared to TAU. No significant differences in costs and outcomes were found between ACT and BATD. In the intention-to-treat analyses, from the governmental and healthcare perspective, no significant differences in cost reduction and incremental effects were identified in the comparison between ACT, BATD, and TAU. However, in the complete case analysis, significant incremental effects of ACT (ΔBPI-IS = -1.57 and -1.39, respectively) and BATD (ΔBPI-IS = -1.08 and -1.04, respectively) compared with TAU were observed. In the per-protocol analysis, only the significant incremental effects of ACT (ΔBPI-IS = -

1.68 and -1.43, respectively) compared to TAU were detected. In conclusion, ACT and BATD might be efficient options in the management of CLBP plus comorbid depression symptoms as compared to usual care. However, no clear difference was found in the comparison between the two active therapies regarding cost-effectiveness or cost-utility.

Trial number: NCT04140838

Perspective: The economic evaluation of psychological therapies for the management of complex conditions is crucial as can be used in decision-making and resource allocation. This study provides evidence that videoconference group-based forms of ACT and BATD are more effective and involve a greater reduction in costs than usual care in the management of CLBP plus comorbid depressive symptoms. Both psychological therapies seem to offer good value for money to the Spanish national health service and the government.

Keywords: Chronic low back pain; group therapy; acceptance and commitment therapy; behavioral activation therapy; cost-utility; cost-effectiveness

1. Introduction

Chronic low back pain (CLBP) and depression are both prevalent and disabling conditions associated with considerable healthcare and societal costs.[1-4] According to the Global Burden of Disease Study, CLBP is one of the most significant contributors to years of living with disability.[5,6] Globally, CLBP affects 4% to 20% of the population[7] and depression affects 12% to 72%,[4] with a co-occurrence of both conditions exceeding 60%.[1] Patients with this comorbidity are more resistant to treatment than those with only one of them.[4] In Spain, the estimated total annual cost of low back pain is around 8945 M€ (1096 € patient/year), of which 75% corresponds to indirect costs (absenteeism and

presentism)[8]; and for depression, the estimated cost is around 224 M€ (3235 € patient/year)[9], 82% of which represents indirect costs.

Effective management of chronic pain and comorbid depression is a priority given their prevalence, resistance to therapy, and economic burden.[10-13] For some years now, forms of cognitive-behavioral therapy (CBT) have demonstrated efficacy in the improvement of the quality of life and functional status of individuals with chronic pain, depression, anxiety, or stress.[12,14,16,17] In fact, there is evidence that Acceptance and Commitment Therapy (ACT) is effective in patients with chronic pain[18-20] and that Behavioral Activation Therapy for Depression (BATD) is effective in patients with depression.[21-24]

In Spain, a 12-month, multicenter, single-blind, randomized controlled trial (RCT), involving 234 patients with CLBP plus depressive symptoms, provided evidence for the efficacy of group and remote-delivered forms of ACT and BATD. Results indicated that patients receiving ACT and BATD showed significant improvements in pain interference, pain catastrophizing, behavioral activation, and psychological flexibility compared to those undergoing treatment-as-usual (TAU), with moderate effect sizes at post-treatment and follow-up.[25,26] Compared to the findings of other studies that evaluated the efficacy of ACT or BATD in patients with chronic pain or depression[21,23,24,27-29], more modest results were obtained, suggesting that resistance to treatment associated with the combination of chronic pain and depression,[30-33] videoconference delivery,[34,35] or psychological impact generated by the COVID 19 pandemic[34,36-40] might have reduced treatment effects[16,19,41,42]

Economic evaluations are fundamental for policy decision-making.[43-45] Economic resources for public health are limited, so it is necessary to prioritize among different interventions for different conditions.[46] The evidence for the cost-effectiveness of

cognitive-behavioral approaches for individuals with CLBP and comorbid depression remains limited, especially when compared to the significant burden reflected in these combined conditions.[4,32,47] This article extends the evidence from the IMPACT (*Improving Pain and Depression with ACT and BATD*) study on the clinical efficacy of ACT and BATD in patients with CLBP and depressive symptoms[26] by conducting an economic evaluation from a healthcare and governmental perspective. This study examined, for the first time, the cost-utility and cost-effectiveness of both therapies, delivered via videoconferencing, compared to TAU. It was hypothesized that ACT and BATD, as add-on treatments combined with usual care, would lead to decreased pain interference, increased quality of life, and reduced costs compared to TAU. Based on previous results, no superiority of one therapy over the other was expected in the economic analysis.

2. Method

2.1. Design

This economic study was based on the data collected in the IMPACT study.[26] Details on the design and methods of the trial can also be found elsewhere.[25] The research was approved by the Ethics Committee of the Fundació Sant Joan de Déu (PIC-178-19) and the Hospital del Mar (2019/8866/I) and was performed by the 1964 Declaration of Helsinki.

Briefly, a 12-month, multicenter, single-blinded RCT was performed with random allocation (using a computer-generated randomization list) of patients to 3 arms: ACT+TAU (hereafter, ACT), BATD+TAU (hereafter, BATD), and TAU alone. All recruited patients signed an informed consent (explaining the purpose of the study and the confidentiality agreements) to participate in this RCT voluntarily and with no

financial incentive. Data were collected at baseline, at post-treatment (2 months after baseline), and at follow-up (12 months after baseline).

2.2. Participants

After a multistage recruitment process, a total of 234 adult patients diagnosed with CLBP plus clinically relevant depressive symptoms were recruited from the Pain Unit of the Parc Sanitari Sant Joan de Déu (Sant Boi de Llobregat, Spain) or Hospital del Mar (Barcelona, Spain) between September 2020 and May 2021. Participant flow through the study phases is shown in Figure 1, including allocation into 3 study arms (1:1:1 ratio): ACT (*n* = 78), BATD (*n* = 78), and TAU alone (*n* = 78).

Insert Figure 1

Inclusion criteria were aged between 18 and 70 years old; diagnosis of CLBP (i.e., presence of tension, soreness, or stiffness in the lower back pain)[3] equal to or greater than 3 months according to medical history; pain intensity > 4 points out of 10 points on a Numeric Rating Scale (NRS) in the last week;[48] moderate-to-severe depressive symptoms (≥ 10 points out of 27 points) in the last 2 weeks according to Patient Health Questionnaire (PHQ-9);[49] and able to understand Spanish language. Exclusion criteria were the presence of cognitive impairment, and/or diagnosis of severe psychiatric disorder or substance dependence/abuse according to medical history; previous (last year) or current participation in psychological therapy; radiculopathy; involvement in litigation with the healthcare system; and patients with scheduled surgical intervention, or inability to attend group sessions.

2.3. Procedure

Patients who met the eligibility criteria were scheduled for a first face-to-face interview at the hospitals with a trained clinical psychologist blind to intervention. This interview was conducted using the Research Electronic Data Capture (REDCap) web-based

application. The assessments consisted of the administration of a battery of measures to assess sociodemographic (gender, age, marital status, living arrangement, educational level, and employment status) and clinical information (years of diagnosis, daily medication, and presence of a current depressive episode); primary (pain interference) and secondary outcomes (pain intensity, depressive/anxiety/stress symptoms, and pain catastrophizing); process variables (pain acceptance, behavioral activation, and psychological inflexibility); and quality of life and cost-related outcomes (use of clinical services, medication, and sick leaves, among others). Randomization of patients to arms was performed by a statistician (who was not involved in any other research procedures) upon completion of baseline clinical assessments.[29,50]

2.4. Psychological therapies

ACT and BATD contents were based on the Vowles et al[51] and Lejuez et al[52] protocols, respectively. Both programs consisted of eight weekly 1.5-hour sessions via a remote synchronous videoconferencing platform (i.e., Zoom) and included a homework document to reinforce the main concepts of the therapy. The therapies were administered in group format (range: 7 to 13 participants), and each group was run by a different properly trained ACT/BATD therapist.[26] Patients were asked to keep the prescribed medication regimen stable during the study. Patients randomized to TAU did not receive any psychological therapy during the study period.

2.4.1. Acceptance and Commitment Therapy (ACT)

ACT is a form of CBT that adopts an acceptance-based approach to unwanted thoughts and feelings and a change-oriented approach in support of goal-directed values-based action. It is designed to be generally applicable to a wide range of conditions. The main direct focus of ACT is to improve people's psychological flexibility.[14,53-55] This psychological process is defined as "the ability to contact the present moment more fully

as a conscious human being and to change or persist in behavior when doing so serves valued ends" (p. 140).[56] ACT is an empirically supported intervention for the chronic pain population[14,18-20,27,47] and the chronic pain population with comorbid depression.[26]

2.4.2. Behavioral Activation Therapy for Depression (BATD)

BATD is an approach within CBT that was developed specifically to treat depression. The main aim of BATD is to help people improve their mood and quality of life through participation in meaningful and rewarding activities.[52] This psychological process is defined as "structured attempts to increase overt behaviors likely to bring patients into contact with reinforcing environmental contingencies and corresponding improvements in thoughts, mood, and quality of life" (p. 700).[57] There is strong evidence that BATD is an effective intervention for patients with depression.[21,24] It appears that the efficacy of BATD in individuals with CLBP and comorbid depression has only been explored in the RCT being further analyzed here.[26] Although the findings of this study indicate that this therapy is potentially beneficial in reducing pain interference, further evidence on the efficacy of BATD in the chronic pain population is needed.[58,59]

2.4.3. Treatment-as-usual (TAU)

The usual care of chronic pain includes medication prescriptions (analgesics, antidepressants, anti-inflammatories, and/or opioids), education, and recommendations for aerobic exercise.[60] In this study, no changes were made to the usual care received by patients in routine clinical practice. For ethical reasons, participants assigned to the TAU arm were offered to participate in ACT groups via videoconferencing once the trial had ended.

2.5. Study measures

Patients were assessed by in-person interviews at baseline, post-treatment, and 12-month follow-up. Responses to the battery of measures in this study were included directly in REDCap during the interviews.

2.5.1. Sociodemographic and clinical characteristics

A self-report questionnaire was used to obtain information about the patient's sociodemographic and clinical characteristics. In addition, the *Composite International Diagnostic Interview* (CIDI v3)[61] was administered to evaluate the presence of a current depressive episode. Both questionnaires were administered only at baseline.

2.5.2. EuroQol Questionnaire (EQ-5D-5L)

The *EuroQoL Questionnaire (EQ-5D-5L)* was used to evaluate health-related quality of life.[62] The EQ-5D-5L consists of two parts: (1) the individual's difficulties in five domains (i.e., mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and (2) the current state of perceived health. The first part is answered on a 5-point rating scale (EQ-5D) ranging from 1 (*"no problems"*) to 5 (*"extreme problems"*), with higher scores indicating greater individual difficulties. The combination of the answers given in the five domains results in 3125 (5^5) different health states. The second part is assessed by a Visual Analogue Scale (EQ-VAS) ranging from 0 (*"worst imaginable health"*) to 100 (*"best imaginable health"*), with a higher score representing greater perceived health. The EQ-5D-5L (i.e., EQ-5D and EQ-VAS) was administered at baseline, post-treatment, and 12-month follow-up. For the economic analyses conducted in this study, only baseline and 12-month follow-up information were used.

In this study, EQ-5D utility values were calculated using the Spanish tariffs of EQ-5D-5L.[63] The EQ-5D utility scores were used to calculate the quality-adjusted life years (QALYs) during the follow-up period (12 months), adjusting the duration of time

affected by the health outcome by the value of the utility. In terms of QALYs, a year of perfect health is worth 1 and a year of less than perfect health is worth less than 1.

2.5.3. Brief Pain Inventory-Interference Scale (BPI-IS)

The *Brief Pain Inventory-Interference Scale (BPI-IS)* was used to evaluate pain interference during the last week.[64,65] The BPI-IS is composed of 7 items (i.e., general activity, mood, walking ability, normal work/housework, relations with other people, sleep, and enjoyment of life), which are answered on an 11-point rating scale ranging from 0 ("*does not interfere*") to 10 ("*completely interferes*"). Higher mean scores (from 0 to 10) indicate greater pain interference. Internal consistency in the general sample of the RCT was good (Cronbach's alpha [α] = .86). The BPI-IS was administered at baseline, post-treatment, and 12-month follow-up. For the economic analyses conducted in this study, only baseline and 12-month follow-up information were used.

2.5.4. Client Service Receipt Inventory (CSRI)

The *Client Service Receipt Inventory* (CSRI) was used to collect retrospective information on medication consumption and service receipt.[66] Information on pain-related medications (i.e., analgesics, anti-inflammatories, opioids, muscle relaxants, anxiolytics, and antidepressants) was recorded from the patient's daily medication prescriptions; specifically, the name of the medication, dosage, total number of prescription days, and daily dose consumed was registered. Data were also collected on total visits to accident and emergency departments; total days of general hospital admission; the number of diagnostic tests administered; and total visits to health professionals (general practitioner, nurse, social worker, psychologist, psychiatrist, group psychotherapy, and others), specifying in each case if the public or private sector provided these services. The CSRI was administered at baseline and 12-month follow-up, both referring to the previous 12 months.

2.6. Statistical analyses

STATA (v17) and SPSS (v29) were used to compute the analysis. The economic evaluation of this study is reported following the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement[67] and adheres to the Good Research Practices for Cost-Effectiveness Analysis Alongside Clinical Trials.[68] The CHEERS checklist is available in Supplementary Table 1.

2.6.1. Description of the costing procedure

Costs were estimated from the point of view of government and healthcare. For this purpose, the previous year (last 12 months) was considered as the time frame for each economic evaluation (baseline and follow-up) in this RCT. From the governmental perspective, the direct (without considering those associated with private insurance) and indirect costs related to productivity losses (based on absenteeism) assumed by the Spanish government were quantified; and from the healthcare perspective, only direct health costs were examined.

2.6.1.1. Direct costs

Direct costs were calculated by adding the costs of primary healthcare services, specialized healthcare services, medical tests, and pain-related medications (i.e., analgesics, anti-inflammatories, opioids, muscle relaxants, anxiolytics, and antidepressants). In the Catalan health system, patients have access to their medical records through a digital app ("La Meva Salut"). This digital app allows them to access detailed information on the medication prescribed by specialists (name of the medication, daily dose, duration of treatment, etc.). Retrospective information (last 12 months) on medication consumption and receipt of services was recorded at the CSRI. This information was collected by face-to-face interview (using REDCap) at baseline and at 12-month follow-up. During the interviews, patients were asked about the medications

they had consumed in the past 12 months. This information was recorded from data reported by patients, who consulted the "La Meva Salut" to obtain accurate direct information and reduce the loss of relevant data.

The SOIKOS database of healthcare costs[69] was used as a source of unit cost data for the use of healthcare services and medical tests. The total cost of the interventions (ACT and BATD) considered the price per patient and group session for the healthcare professional who delivered the sessions. Attendance at sessions of both therapies was queried using the therapists' records. The cost of treatment sessions and resources was the same for all sessions and groups. As in previous studies,[70,71] the costs of both psychological therapies were adjusted according to the number of sessions attended by the patients. The cost of the medications was estimated by consulting the price per milligram in the Vademecum International (with data from 2022). The value-added tax was included in this estimate. Total medication costs were estimated by multiplying the price per milligram by the total daily dose consumed and the number of days the pharmacological treatment was administered.

2.6.1.2. Indirect costs

This study collected information on productivity loss based on absenteeism and presenteeism. However, because a high percentage of the sample was on sick leave, unemployed, or pensioner/retired and because a reduction in productivity due to presenteeism is less tangible, in the end indirect cost analysis were based on absenteeism alone. Indirect costs (lost productivity based on absenteeism) were calculated from the human capital approach. The minimum daily wage in Spain for 2022 was multiplied by the number of days of sick leave declared by each patient in the CSRI. Finally, total costs were obtained by adding direct and indirect costs. As shown in Table 1, unit costs were reported in € based on 2022 prices.

Insert Table 1

2.6.2. Descriptive analyses

Descriptive analyses were calculated for continuous variables (means and standard deviations) and categorical variables (frequencies and percentages). According to the Consolidated Standards of Reporting Trials (CONSORT) recommendations, it is not necessary to include as covariates the possible baseline differences identified in the sociodemographic and clinical characteristics.[72]

2.6.3. Between-group analyses of costs and outcomes

Direct and indirect costs were not normally distributed in this sample. However, after calculating the analyses with a nonparametric test (Kruskal-Wallis), it was determined that the conclusions obtained in the comparisons between the three groups (ACT, BATD, and TAU) yielded similar results at baseline and follow-up. Since no differences were detected between parametric (analysis of variance [ANOVA]) and nonparametric (Kruskal Wallis) tests, the parametric analyses were preferred. A generalized linear mixed model (GLM) was used to explore costs and outcomes. This is consistent with the methods used in the analyses of clinical outcomes for this trial.[26] An advantage in using GLM is that it allows modeling relationships between variables that do not follow a normal distribution. By incorporating random effects, GLM helps to examine the correlation between observations within groups, which is common in longitudinal data. Supplementary Table 2 shows the results of the parametric (ANOVA) and non-parametric (Kruskal-Wallis) tests.

A restricted maximum likelihood regression was calculated.[73] Therapy effects on costs and outcomes were assessed using these models, considering within-patient correlations between repeated measurements. The GLM included the random intercept adjusted for baseline score, as well as time and the interaction between “group × time”.

Regression coefficients (β) and 95% confidence intervals (95% CI) were estimated for the "group × time" interaction between groups (ACT vs TAU, BATD vs TAU, and ACT vs BATD) at the 12-month follow-up. The criteria for estimating effect sizes (Cohen's *d*) were as follows: very small (0.10), small (0.20), medium (0.50), large (0.80), very large (1.20), and huge (2.00).[74] Finally, differences between groups (ACT and BATD) regarding the therapy costs were explored by applying the t-test. The threshold for statistical significance was set at $p < .05$.

2.6.4. Cost-utility and cost-effectiveness analyses

Cost-utility and cost-effectiveness are approaches to examine the relationship between the resources used (i.e., costs) and the health outcomes (i.e., effects, in terms of utilities, or benefits, in terms of effectiveness) of an intervention. Cost-utility analyses examine the specific association between the resources used and the effects of an intervention (typically measured according to QALYs), whereas cost-effectiveness analyses assess the resources used and the benefits of an intervention (measured according to the primary outcome, which in this study was the BPI-IS). These analyses naturallycomplement each other and are widely used for public health decision-making.[43-46]

For the cost-utility analyses, response to therapy was defined as an improvement in the QALYs mean scores (regarding the interpretation, an increase in QALY scores means that an intervention is beneficial); and for the cost-effectiveness, as an improvement in the BPI-IS mean score (regarding the interpretation, a reduction in BPI-IS scores means that an intervention is beneficial). It appears that there are no evidence-based cut-off points for considering clinically relevant changes according to the QALYs. The criterion recommended by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) for defining clinically relevant changes consists of a 1-point reduction in the BPI-IS between pre-post or pre-follow-up scores.[75]

The incremental cost-utility ratio (ICUR) and the incremental cost-effectiveness ratio (ICER) were examined, these being the ratios between incremental costs and incremental effects measured on QALYs and BPI-IS, respectively.[76]

Four potential scenarios were considered for the comparison between the intervention groups (ACT, BATD, and TAU) in the frame of economic evaluation results.[77] A description of the four scenarios for each intervention is presented in Table 2.

Insert Table 2

For decision-making, the first two scenarios (1 and 2) show strong dominance; however, the other two scenarios (3 and 4) depend on the ICUR or ICER. The investment ceiling for cost-utility for an intervention in Spain is 25,000 euros per QALY.[43]

Incremental costs and incremental effects were explored using Zellner's seemingly unrelated regression (SUR) model.[78] The use of the SUR method to explore cost-utility or cost-effectiveness involves using a bivariate system of regressions that includes both costs and outcomes (QALYs or BPI, depending on the model considered) as dependent variables of the two separate equations. Therefore, the cost and outcome regressions are part of two regressions on the intercept arm assignment (i.e., ACT, BATD, or TAU) plus an additional set of control variables (measured at baseline): gender, age, marital status, living arrangement, educational level, employment status, year of diagnosis, current episode of depression, costs, and outcomes.[43,77] Estimates of incremental cost and incremental effect values using the SUR method were obtained with 1000 bootstrap replicates to address possible skewness in the distribution of the dependent variable.

The cost-utility and cost-effectiveness of the interventions were evaluated by considering one main analysis, intention-to-treat (ITT), and two sensitivity analyses, complete case analysis (CCA) and (3) per-protocol analysis (PPA). In the ITT, missing

values at 12-month follow-up were imputed using multiple imputation methods with the chained equations approach.[79] The imputation model incorporated all major sociodemographic and prognostic variables associated with the outcome variables and the other variables containing missing values. Data were assumed to be missing at random. Regarding the CCA, only patients who were evaluated at both baseline and 12-month follow-up were included. The PPA was estimated on a sample that included only patients who completed the interventions (i.e., who attended at least 6 of the 8 therapy sessions). In this study, there were no missing baseline data on any of the measures. Missing data in the follow-ups corresponded to dropouts registered during the RCT.

3. Results

3.1. Sample characteristics

As shown in Table 3, most patients were middle-aged women who had completed at least primary school. All patients spoke Spanish and resided in Catalonia (Spain). They mostly lived with their partner and were in paid employment. According to the CIDI diagnostic criteria, most of them (76%) had a current episode of depression. The mean time with diagnosed chronic pain was greater than 10 years.

Insert Table 3

3.1. Costs and outcomes

Table 4 presents descriptive statistics and between-group analyses (ACT, BATD, and TAU) for costs and outcomes according to the ITT approach. In total, 58% and 51% of the participants completed the ACT and the BATD videoconferencing sessions, respectively. Mean attendance for ACT sessions was higher than for BATD sessions (*M* = 4.65 vs. 4.08), but this difference not statistically significant.

Insert Table 4

3.1.1. Costs

ACT yielded a significantly greater reduction in total costs (β = -2387.65, p = .032) compared to TAU at 12 months follow-up. In ACT an average reduction in total costs of €1329 was observed. In contrast, TAU incurred an average increase of €1059. BATD showed a greater reduction in indirect costs (β = -2915.88, p = .004) and total costs (β = -3266.69, p = .004) compared to TAU at 12 months follow-up. Specifically, in BATD an average reduction in indirect costs of €1775 and total costs of €2208 was reported at follow-up compared to baseline. In TAU there was an average increase in indirect costs of €1141 and total costs of €1059. No significant differences were found in the costs of primary care services, specialized healthcare services, medical tests, pain-related medications, and psychological therapies in the comparison between ACT and BATD.

3.1.2. Outcomes

The analyses yielded significant improvements in EQ-5D utility (β = 0.11, p = .003), QALYs (β = 0.02, p = .017), and BPI-IS (β = -1.47, p < .001) scores in ACT compared to TAU at 12-month follow-up, but not in the current state of EQ-VAS score. Meanwhile, significant improvements were obtained in BATD in EQ-VAS (β = 7.80, p = .023), QALYs (β = 0.02, p = .036), and BPI-IS (β = -1.25, p < .001) scores when compared to TAU at follow-up, but not in EQ-5D utility score. No significant differences in any outcome were found when comparing ACT and BATD.

3.2. Cost-utility (QALYs as the outcome) and cost-effectiveness (BPI-IS mean score as the outcome) analysis

The results identified in the comparison between the three groups (ACT vs TAU, BATD vs TAU, and ACT vs BATD) are presented in Tables 5 and 6.

Insert Tables 5 and 6

Although in the main analysis (ITT) less incremental costs and more incremental effects on BPI-IS and QALYs were observed in ACT and BATD compared to TAU, these differences were not statistically significant from a governmental (total cost) and healthcare perspective (direct costs). ACT demonstrated less incremental costs and more incremental effects on BPI-IS, but not on QALYs, compared to BATD; however, these differences were also not significant.

From the governmental (total cost) and healthcare (direct costs) perspective, in the CCA, a significant incremental effect on BPI-IS was observed in ACT (Δ = -1.57 and -1.39, respectively) and BATD (Δ = -1.08 and -1.04, respectively) compared to TAU, but not on QALYs. In PPA, only a significant incremental effect on BPI-IS was identified in ACT (Δ = -1.68 and -1.43, respectively) compared to TAU, although not on QALYs. No significant decrease in incremental costs was found in ACT and BATD compared to TAU in any of the sensitivity analyses (CCA and PPA). There were also no significant differences in incremental costs and incremental effects between ACT and BATD in these sensitivity analyses (CCA and PPA).

Finally, Supplementary Figures 1, 2, and 3 show the degree of uncertainty around differences in costs and QALYs and Supplementary Figures 4, 5, and 6 show uncertainty around differences in costs and BPI-IS scores between study arms from a governmental and healthcare perspective (ITT, CCA, and PPA, respectively).

4. Discussion

This study appears to be the first to document the cost-utility and cost-effectiveness of two forms of CBT (ACT and BATD) delivered via videoconferencing for the treatment of a population with a complex condition of back pain and clinically relevant depressive symptoms. The economic evaluation reported here extends the results obtained in the IMPACT study,[26] which demonstrated the effectiveness of both therapies for improving

pain interference. Firstly, the differences in costs (direct, indirect, and total) and outcomes (QALYS and BPI-IS scores) between the three study arms (ACT, BATD, and TAU) and the two evaluation time points (baseline and 12-month follow-up) were explored. Then, cost-utility and cost-effectiveness analyses, calculated using QALY-based ICURs and BPI-IS-based ICERs, were performed to identify the interaction between the economic and clinical benefits of one intervention over another.

Between-group analyses indicated that ACT (added to TAU) and BATD (added to TAU) were associated with reduced costs compared to TAU. Moreover, a significant improvement in BPI-IS and QALYs scores was also found in both ACT and BATD compared to TAU. The effect sizes of these detected differences were moderate. No significant differences in cost and outcomes were detected between ACT and BATD. The reduction of costs (direct, indirect, and total) is a priority objective in interventions aimed at the treatment of chronic pain and depression, considering their relevant contribution to the health economic burden.[80] As reported in other studies,[44,81] it appears that the cost reduction in the chronic pain population is related to the interaction between improvement of pain-related symptoms, increase in health-related quality of life, and return to work activities.

Cost-utility and cost-effectiveness analyses, explored from both governmental and healthcare perspectives, indicated that according to the main analysis (ITT), no significant differences in incremental effects were identified in the comparison between ACT, BATD, and TAU. However, it was found that in the sensitivity analyses the incremental effect on BPI-IS scores was significant in ACT compared to TAU alone, based on CCA and PPA, and in BATD compared to TAU alone, based on CCA, but not on QALYs. These differences could be related to the fact that in the chronic pain population, BPI-IS (based on pain interference) is generally the primary outcome,

whereas QALYs (based on health-related quality of life) is a secondary outcome that is indirectly addressed in this type of intervention.

No significant differences were found in the comparison between ACT, BATD, and TAU in the incremental costs, based on BPI-IS and QALY, in the main analysis (ITT) and sensitivity analyses (CCA and PPA). Although according to these analyses, ACT showed some superiority compared to TAU and BATD, the differences observed were not significant in terms of higher costs and effects. The variance of the costs reported in this study was high, with a reduced sample power due to the high percentage of dropouts from the RCT,[82] which was conducted in restrictive phases of the COVID-19 pandemic and delivered by videoconference. These limitations may underlie the failure to detect statistically significant differences associated with increased costs.[83,84]

The results obtained in this study are consistent with the cost reductions observed in other studies in CBT-based psychological therapies compared to TAU.[43,76,81,85,86] Previous studies have provided evidence on the cost-utility and cost-effectiveness of ACT[43,87-89] and BATD[90,91] compared to TAU, both in populations with chronic pain[43,85] and other health conditions.[87,89] Specifically, ACT and BATD have been identified as effective in reducing emotional disturbances and improving quality of life, resulting in long-term healthcare cost savings.[89,91] In previous RCTs, ACT and BATD have consistently achieved a significant incremental effect,[43,87-91,] but also higher incremental costs than TAU or active control conditions. In general, previous RCTs conducted to analyze the economic evaluation of ACTs and BATDs have had relatively small sample sizes to assess incremental costs and effects, limiting the scope for robust conclusions.[83] In sum, the available evidence highlights the therapeutic potential of these approaches for the management of chronic pain and/or depression.[16-24]

The study findings confirm a favorable increased clinical effect of ACT over BATD when compared to TAU, both from the governmental and healthcare perspective. However, no clear preference between ACT and BATD was identified from a cost reduction perspective. While ACT produced superior benefits in pain interference (priority intervention target in the chronic pain population)[92] compared with BATD, neither of these two psychological therapies significantly decreases costs compared to the other, nor compared to TAU. From a strictly clinical point of view, ACT is perhaps preferable for a population with chronic pain and comorbid depression, based on the greater number of responders identified in the RCT.[26]

Although the findings reported in this sample appear more favorable toward ACT, the choice of the most appropriate treatment for other populations should be based on ethical and practical considerations, as well as on the preferences of both the patients and the therapists.[87] In this context, the therapist-patient shared decision-making model promotes therapeutic adherence and improves outcomes by connecting the choice of therapies according to each patient's preferences and values.[93,94] As mentioned above, this is the first RCT to explore an economic evaluation in a population with both health conditions. Therefore, larger RCTs with cost-utility and cost-effectiveness analyses are needed to draw more solid conclusions.[44]

The current findings should be interpreted considering five main limitations. First, some sociodemographic data, such as race and ethnicity, and clinical data, such as the presence of insomnia, were not collected in this study, which could have provided valuable information for the analyses. Second, a considerably low follow-up rate (44% in ACT and 50% in BATD) resulted in considerable missing cost-effectiveness data at the 12-month follow-up assessment. Even though the regression models included bootstrapping with 1000 replications to address the skewness of the data, the sample size

in each arm of the study and the wide confidence intervals detected may have affected the robust estimation of effect sizes. The possible interferences generated by the COVID-19 pandemic (the context in which this RCT was developed) probably influenced the number of dropouts recorded. Third, a random intercept was included in the GLM to account for within-group variability; nevertheless, estimating this intercept in patients with a single data point could represent a risk of overfitting the model. Fourth, productivity loss related to presenteeism was collected in the RCT, but not considered in this study due to the challenges in measuring reduced productivity whilst at work via a self-report measure**.** Fifth, although some studies have provided evidence that self-reported data have the same validity as data collected by public registries in health and economic evaluation,[81,95] to obtain greater assurance around these results it is advisable to contrast the information reported retrospectively (last 12 months) by patients with public registries. However, due to limitations of accessibility to this information, it was not possible to perform this verification. Direct non-health costs (e.g., out-of-pocket expenses, costs of paid and unpaid help, travel expenses, and the use of non-prescription medications and other treatments, among others) were not estimated.

5. Conclusions

The findings of this economic evaluation indicate that videoconference ACT or BATD for people with CLBP and clinically relevant depression symptoms are more effective and involve a greater reduction in costs than usual care. In public healthcare systems, there are many competing demands and limited resources to address these demands. These results suggest that investment in new forms of CBT delivered via videoconferencing for individuals with CLBP plus depression represents good value for money compared to usual care. Even though the results are promising, it is important to consider that the therapies were delivered in a pandemic context with high social

restrictions. The unprecedented context of this study is relevant for the interpretation of the scope and limitations of the results. For this reason, it is recommended that future studies continue to seek evidence for the cost-utility and cost-effectiveness of these therapies administered in group format via videoconferencing in patients with CLBP and comorbid mental problems.

Disclosures

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Author contributions

Juan P. Sanabria-Mazo: data curation, software, formal analysis, methodology, visualization, and writing the original draft. Francesco D'Amico: formal analysis, methodology, and writing – review & editing. Eugenia Cardeñosa, Monserrat Ferrer-Forés, Sílvia Edo, Xavier Borràs, Lance M. McCracken, Albert Feliu-Soler, and Antoni Sanz: writing – review & editing. Juan V. Luciano: conceptualization, funding acquisition, investigation, project administration, supervision, writing – review & editing.

Data availability statement

The data supporting this study's findings are available from the corresponding author upon reasonable request.

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Figure 1. Trial flowchart describing the recruitment process of all three study arms. Note: ACT = Acceptance and Commitment Therapy; BATD = Behavioral Activation Therapy for Depression; TAU = Treatment-as-usual; ITT = intention-to-treat; PPA = per protocol analysis.

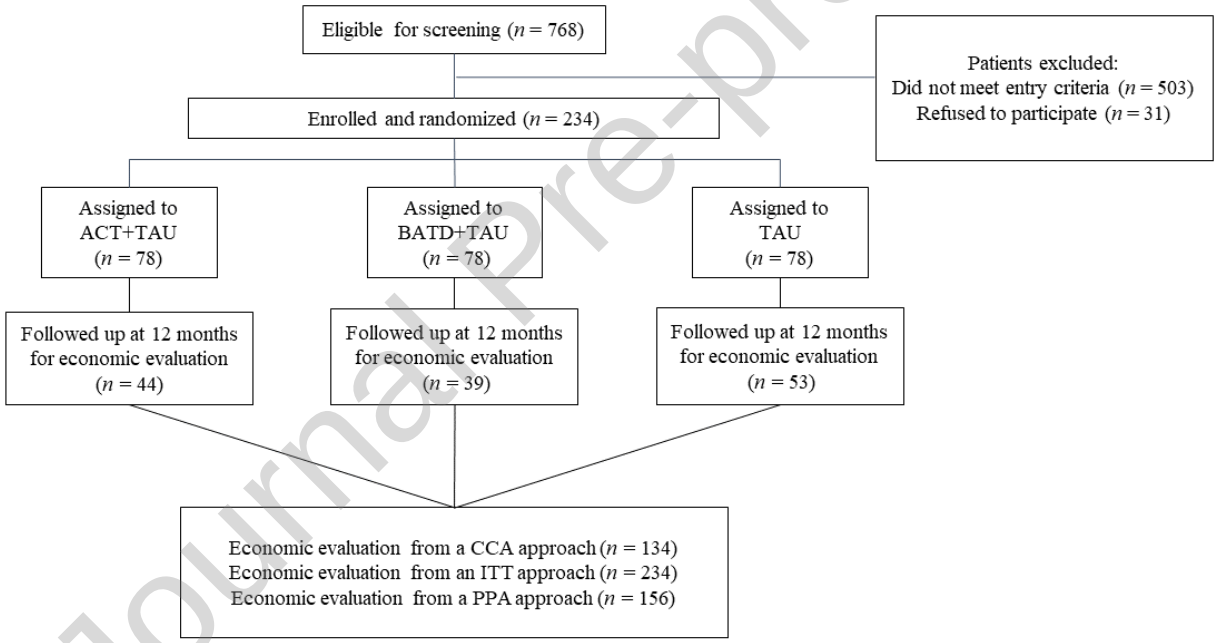


Table 1. Unit costs used in the calculations of direct and indirect costs (Financial Year 2022; values in €).

Service (unit)	Cost (€)
Healthcare (direct costs)	
General practitioner (per appointment)	44
Nurse/psychiatric nurse (per appointment)	41
Social worker (per appointment)	43
Clinical Psychologist (per appointment)	54
Psychiatrist (per appointment)	54
Other medical specialists (per appointment)	52
Accident and emergency in hospital (per attendance)	118
Hospital stay (per night)	133
Diagnostic tests (range)	7-543

Pharmacological treatment (per daily dose) *	Various
ACT and BATD (per participant per group session)	54
Productivity loss (indirect costs)	
Absenteeism from work (minimum daily wage)	33

Note: The unit costs were applied to each resource used to calculate the total cost of the resources used by each participant. All unit costs were for the year 2022. * The cost of prescribed medications was calculated by determining the price per milligram according to the Vademecum International (Red Book; edition 2022) and included the value-added tax.

Table 2. Description of the four scenarios for each intervention.

Intervention	Scenario
ACT	1. ACT costs less and is more effective than the alternatives (TAU and/or BATD). 2. ACT costs more and is less effective than the alternatives (TAU and/or BATD). 3. ACT costs less, but is less effective than the alternatives (TAU and/or BATD). 4. ACT costs more, but is more effective than the alternatives (TAU and/or BATD).
BATD	1. BATD costs less and is more effective than the alternatives (TAU and/or ACT). 2. BATD costs more and is less effective than the alternatives (TAU and/or ACT). 3. BATD costs less, but is less effective than the alternatives (TAU and/or ACT). 4. BATD costs more, but is more effective than the alternatives (TAU and/or ACT).
TAU	1. TAU costs less and is more effective than the alternatives (ACT and/or BATD). 2. TAU costs more and is less effective than the alternatives (ACT and/or BATD). 3. TAU costs less, but is less effective than the alternatives (ACT and/or BATD). 4. TAU costs more, but is more effective than the alternatives (ACT and/or BATD).

Note: For decision-making, the first two scenarios (1 and 2) show strong dominance; however, the other two scenarios (3 and 4) depend on the ICUR or ICER.

Table 3. Baseline characteristics of participants by treatment arm**.**

Variables	ACT (*n* = 78)	BATD (*n* = 78)	TAU (*n* = 78)
Gender (women), *n* (%)	54 (69.2)	53 (67.9)	51 (65.4)
Region of residence (Catalonia), *n* (%)	78 (100)	78 (100)	78 (100)
Language spoken (Spanish), *n* (%)	78 (100)	78 (100)	78 (100)
Age, mean (SD)	54.9 (8.3)	54.9 (10.2)	53.8 (10.0)
Marital status, *n* (%)			
Single	9 (11.5)	12 (15.4)	6 (7.7)
Married/living with partner	49 (62.8)	50 (64.1)	53 (67.9)
Separated/divorced	14 (17.9)	12 (15.4)	17 (21.8)
Widowed	6 (7.7)	4 (5.1)	2 (2.6)
Living arrangement, *n* (%)			
Living alone	11 (14.1)	7 (9.0)	9 (11.5)
Living with partner	67 (85.9)	71 (91.0)	69 (88.5)
Education level, *n* (%)			
Illiterate	2 (2.6)	0 (0.0)	1 (1.3)
Did not graduate from primary school	2 (2.6)	3 (3.8)	3 (3.8)
Primary studies	18 (23.1)	20 (25.6)	16 (20.5)
Secondary studies	42 (53.8)	46 (59.0)	43 (55.1)
University	14 (17.9)	9 (11.5)	15 (19.2)
Employment status, *n* (%)			
Homemaker	3 (3.8)	4 (5.1)	2 (2.6)

Paid employment	20 (25.6)	24 (30.8)	32 (41.0)
Paid employment but in sick leave	5 (6.4)	4 (5.1)	4 (5.1)
Unemployed with subsidy	14 (17.9)	10 (12.8)	4 (5.1)
Unemployed without subsidy	5 (6.4)	4 (5.1)	4 (5.1)
Retired/pensioner	9 (11.5)	12 (15.4)	14 (17.9)
Temporal disability	4 (5.1)	8 (10.3)	9 (11.5)
Others	18 (23.1)	12 (15.4)	9 (11.5)
Clinical variables			
Years of diagnosis, *M* (*SD*)	10.9 (7.9)	11.1 (8.7)	11.2 (8.0)
Current episode of depression, *n* (%) [a]	60 (76.9)	63 (80.8)	55 (70.5)
Daily medication, *n* (%)			
Analgesics	35 (50.7)	33 (50.0)	35 (50.7)
Anti-inflammatory	16 (23.2)	19 (29.2)	16 (23.2)
Opioids	15 (23.1)	18 (27.7)	12 (17.4)
Antiepileptic	11 (16.9)	15 (23.1)	13 (18.8)
Muscle relaxant	6 (9.4)	11 (16.9)	11 (15.9)
Antidepressants	19 (29.7)	24 (36.9)	29 (42.0)
Anxiolytics	12 (18.8)	11 (16.9)	13 (18.8)

Note: ACT, Acceptance and commitment therapy; BATD, Behavioral activation therapy for depression; TAU, Treatment-as-usual. [a] CIDI, Composite International Diagnostic Interview.

Table 4. Summary statistics of the costs (total and disaggregated in components) and outcomes according to treatment arm (ITT approach).

	ACT	**BATD**	**TAU**	**ACT vs TAU**			**BATD vs TAU**			**ACT vs BATD**		
	***M* (*SD*)**	***M* (*SD*)**	***M* (*SD*)**	***d***	***t* (*p*)**	***B* (95% *CI*)**	***d***	***t* (*p*)**	***B* (95% *CI*)**	***d***	***t* (*p*)**	***B* (95% *CI*)**
Cost												
Primary healthcare services *												
Baseline	217.88 (263.99)	206.14 (321.61)	218.48 (245.44)									
Follow-up	116.17 (171.70)	154.07 (223.67)	188.05 (272.53)	0.28	-1.29 (.198)	-71.29 (-180.21 to 37.62)	0.07	-0.39 (.696)	-21.63 (-130.55 to 87.28)	0.17	0.90 (.370)	49.66 (-59.25 to 158.57)
Specialized healthcare services *												
Baseline	591.95 (1091.89)	534.14 (583.86)	572.54 (668.34)									
Follow-up	407.86 (1321.69)	369.46 (733.15)	534.22 (964.63)	0.16	-0.81 (.418)	-145.78 (-499.83 to 208.27)	0.20	-0.70 (.483)	-126.36 (-480.41 to 227.69)	0.02	0.11 (.914)	19.42 (-334.63 to 373.47)

Medical tests *												
Baseline	503.84 (669.87)	483.24 (587.78)	500.03 (580.60)									
Follow-up	319.96 (664.68)	385.09 (683.40)	552.28 (1497.65)	0.37	-1.40 (.163)	-236.13 (-568.68 to 96.42)	0.26	-0.89 (.374)	-150.40 (-482.95 to -182.15)	0.13	0.51 (.612)	85.73 (-246.82 to 418.28)
Pain-related medications *												
Baseline	208.26 (274.10)	212.89 (284.99)	219.38 (293.52)									
Follow-up	100.38 (204.12)	94.92 (195.64)	153.82 (303.23)	0.15	-0.79 (.429)	-42.32 (-147.52 to 62.87)	0.18	-0.98 (.327)	-52.41 (-157.60 to 52.79)	0.04	-0.19 (.850)	-10.08 (-115.28 to 95.11)
Direct costs *												
Baseline	1516.89 (1624.22)	1444.90 (1001.25)	1505.59 (1228.97)									
Follow-up	939.31 (1975.38)	1012.04 (1460.22)	1423.53 (2435.95)	0.34	-1.52 (.130)	-495.53 (-1137.25 to -146.20)	0.31	-1.08 (.283)	-350.80 (-992.53 to -290.92)	0.11	0.44 (.657)	144.73 (-496.99 to 786.45)
Indirect costs *												
Baseline	2975.68 (4924.51)	3302.37 (5302.61)	2584.45 (4131.37)									
Follow-up	2224.29 (4541.62)	1527.22 (4248.59)	3725.19 (5229.07)	0.41	-1.91 (.057)	-1892.12 (-3844.27 to 60.03)	0.61	-2.94 (**.004**)	-2915.88 (-4868.04 to -963.73)	0.20	-1.03 (.303)	-1023.76 (-2975.91 to 928.39)
Total costs *												
Baseline	4504.18 (5572.49)	4700.78 (5710.52)	4126.53 (4548.60)									
Follow-up	3175.21 (5330.91)	2492.78 (4913.01)	5185.21 (6659.91)	0.47	-2.15 (**.032**)	-2387.65 (-4573.	0.63	-2.94 (**.004**)	-3266.69 (-5452.9	0.15	-0.79 (.429)	-879.03 (-3065.2

						88 to -201.43)			1 to -1080.46)			6 to 1307.19)
Outcomes												
EQ-5D utility (0-1) *												
Baseline	0.57 (0.22)	0.57 (0.22)	0.57 (0.26)									
Follow-up	0.59 (0.22)	0.55 (0.31)	0.48 (0.33)	0.45	3.05 (**.003**)	0.11 (0.04 to 0.18)	0.29	1.86 (.064)	0.07 (-0.01 to 0.14)	0.18	-1.10 (.274)	-0.04 (-0.11 to -0.03)
EQ-VAS (0-100) *												
Baseline	55.90 (18.56)	55.68 (19.00)	55.90 (18.65)									
Follow-up	55.10 (19.97)	57.34 (15.97)	49.76 (23.44)	0.29	1.59 (.113)	5.34 (-1.26 to 11.95)	0.39	2.28 (**.023**)	7.80 (1.07 to 14.54)	0.13	0.70 (.483)	2.46 (-4.44 to 9.36)
QALY (0-1) *												
Baseline	0.83 (0.06)	0.83 (0.07)	0.83 (0.07)									
Follow-up	0.84 (0.07)	0.83 (0.08)	0.81 (0.08)	0.46	2.40 (**.017**)	0.02 (0.01 to 0.04)	0.28	2.11 (**.036**)	0.02 (0.01 to 0.04)	0.15	-0.24 (.811)	-0.01 (-0.02 to 0.02)
BPI-IS (0-10) *												
Baseline	6.71 (1.72)	6.46 (2.07)	6.49 (1.91)									
Follow-up	5.30 (2.42)	5.07 (2.36)	6.42 (2.16)	0.73	-4.40 (**<.001**)	-1.47 (-2.13 to -0.81)	0.66	-3.65 (**<.001**)	-1.25 (-1.92 to -0.57)	0.01	0.65 (.519)	0.23 (-0.46 to 0.91)

Baseline level of the variable was controlled. M and SD are not adjusted. The number of participants varied across assessment periods due to dropouts (see flow chart). Significant values ($p < 0.05$) are shown in bold. *B*, regression coefficients; CI, confidence interval; *d*, Cohen`s *d* as an effect size measure; ITT, intention-to-treat; ACT, Acceptance and commitment therapy; BATD, Behavioral activation therapy for depression; TAU, Treatment-as-usual; BPI-IS = Brief Pain Inventory-Interference Scale; EQ-5D = EuroQol five-dimensional classification; EQ-VAS = visual analogue scale; QALY = quality-adjusted life years.

Table 5. Incremental cost, effect, and cost-utility ratios from the government perspective (total costs).

	Incremental cost *M* **(95% Bootstrap CI)**	**Incremental effect** *M* **(95% Bootstrap CI)**	**Dominant treatment (ICER/ICUR)**
Main analysis (ITT)			
ACT vs TAU (n = 156)			
QALY (0-1)	-2301.69 (-5437.08 to 833.70)	0.02 (-0.02 to 0.06)	ACT dominant[1]
BPI-IS (0-10)	-2302.34 (-5398.89 to 794.20)	-0.98 (-2.25 to 0.29)	ACT dominant[1]
BATD vs TAU (*n* = 156)			
QALY (0-1)	-1983.38 (-4390.40 to 423.64)	0.02 (-0.02 to 0.07)	BATD dominant[2]

BPI-IS (0-10)	-1198.46 (-4373.35 to 400.42)	-0.69 (-1.92 to 0.54)	BATD dominant[2]
ACT vs BATD (*n* = 156)			
QALY (0-1)	-318.30 (-2702.91 to 2066.30)	-0.01 (-0.06 to 0.04)	No dominant (ICUR = 59,719)[3]
BPI-IS (0-10)	-315.88 (-2678.89 to 2047.13)	-0.29 (-1.92 to 1.34)	ACT dominant[4]
Sensitive analysis (CCA)			
ACT vs TAU (*n* = 95)			
QALY (0-1)	-3134.57 (-6397.40 to 633.37)	0.02 (-0.01 to 0.10)	ACT dominant[1]
BPI-IS (0-10)	-3380.68 (-7136.53 to -145.83)	**-1.57** (-5.53 to -0.84)	ACT dominant[1]
BATD vs TAU (*n* = 91)			
QALY (0-1)	-1129.88 (-4963.58 to 2081.59)	0.02 (-0.01 to 0.09)	BATD dominant[2]
BPI-IS (0-10)	-1283.88 (-4587.46 to 2345.27)	**-1.08** (-5.44 to -0.01)	BATD dominant[2]
ACT vs BATD (*n* = 82)			
QALY (0-1)	-2004.69 (-5332.05 to 1325.84)	-0.01 (-0.11 to 0.05)	No dominant (ICUR = 359,565)[3]
BPI-IS (0-10)	-2096.80 (-5483.52 to 1556.56)	-0.49 (-5.01 to 0.32)	ACT dominant[4]
Sensitive analysis (PPA)			
ACT vs TAU (n = 120)			
QALY (0-1)	-3318.10 (-7170.74 to 1617.23)	0.02 (-0.02 to 0.22)	ACT dominant[1]
BPI-IS (0-10)	-3547.83 (-7676.82 to 719.42)	**-1.68** (-5.88 to -0.30)	ACT dominant[1]
BATD vs TAU (*n* = 114)			
QALY (0-1)	-1014.04 (-6134.94 to 3575.27)	0.02 (-0.04 to 0.21)	BATD dominant[2]
BPI-IS (0-10)	-1151.70 (-5964.10 to 3355.96)	-0.90 (-5.91 to 1.39)	BATD dominant[2]
ACT vs BATD (*n* = 78)			
QALY (0-1)	-2304.06 (-7213.87 to 2482.64)	0.01 (-0.13 to 0.14)	ACT dominant[4]
BPI-IS (0-10)	-2396.13 (-7193.15 to 2716.75)	-0.78 (-10.92 to 1.86)	ACT dominant[4]

Note: Significant values ($p < 0.05$) are shown in bold. Covariates: gender, age, marital status, living arrangement, educational level, employment status, year of diagnosis, current episode of depression, and costs or outcome at baseline, depending on the equation considered. CCA = complete case analysis; ICER = incremental cost-effectiveness ratio; ICUR = incremental cost-utility ratio; ITT = intention-to-treat (ITT); PPA = per-protocol analysis. CCA (*N* = 134), ITT (*N* = 234), and PPA (*N* = 156). In terms of interpretation, an increase in the QALY score (positive values) and a decrease (negative values) in the BPI-IS score, respectively, means that the intervention is beneficial.
[1] Dominant because ACT costs less and is more effective or useful than TAU.
[2] Dominant because BATD costs less and is more effective or useful than TAU.
[3] No dominant because ACT costs less than BATD, but BATD is more effective or useful than ACT.
[4] Dominant because ACT costs less and is more effective or useful than BATD.

Table 6. Incremental cost, effect, and cost-utility ratios from the healthcare perspective (direct costs).

	Incremental cost *M* **(95% Bootstrap CI)**	**Incremental effect** *M* **(95% Bootstrap CI**	**Dominant treatment (ICER/ICUR)**
Main analysis (ITT)			
ACT vs TAU (n = 156)			
QALY (0-1)	-628.89 (-2386.73 to 1128.94)	0.02 (-0.02 to 0.05)	ACT dominant[1]
BPI-IS (0-10)	-629.22 (-2385.55 to 1127.12)	-1.01 (-2.22 to 0.21)	ACT dominant[1]
BATD vs TAU (*n* = 156)			
QALY (0-1)	-309.62 (-1888.97 to 1269.72)	0.03 (-0.01 to 0.06)	BATD dominant[2]

BPI-IS (0-10)	-308.85 (-1890.41 to 1272.71)	-0.81 (-2.12 to 0.49)	BATD dominant[2]
ACT vs BATD (*n* = 156)			
QALY (0-1)	-319.27 (-1577.14 to 938.59)	-0.01 (-0.06 to 0.04)	No dominant (ICUR = 25,641)[3]
BPI-IS (0-10)	-320.37 (-1577.56 to 936.83)	-0.19 (-1.91 to 1.53)	ACT dominant[4]
Sensitive analysis (CCA)			
ACT vs TAU (*n* = 95)			
QALY (0-1)	-300.91 (-1347.75 to 994.98)	0.01 (-0.01 to 0.13)	ACT dominant[1]
BPI-IS (0-10)	-231.53 (-1260.69 to 1031.73)	**-1.39** (-5.84 to -0.47)	ACT dominant[1]
BATD vs TAU (*n* = 91)			
QALY (0-1)	-82.52 (-1300.26 to 957.84)	0.01 (-0.01 to 0.10)	BATD dominant[2]
BPI-IS (0-10)	-28.08 (-1111.09 to 993.48)	**-1.04** (-6.36 to -0.01)	BATD dominant[2]
ACT vs BATD (*n* = 82)			
QALY (0-1)	-218.38 (-1054.11 to 972.42)	-0.01 (-0.11 to 0.05)	No dominant (ICUR = 25,428)[3]
BPI-IS (0-10)	-203.45 (-1066.74 to 1022.72)	-0.35 (-5.01 to 0.56)	ACT dominant[4]
Sensitive analysis (PPA)			
ACT vs TAU (n = 120)			
QALY (0-1)	-585.78 (-1581.49 to 285.17**)**	0.02 (-0.03 to 0.13)	ACT dominant[1]
BPI-IS (0-10)	-486.87 (-1526.72 to 376.53)	**-1.43** (-6.54 to -0.01)	ACT dominant[1]
BATD vs TAU (*n* = 114)			
QALY (0-1)	60.64 (1002.88 to 1108.33)	0.02 (-0.05 to 0.20)	BATD dominant[2]
BPI-IS (0-10)	134.09 (-914.92 to 1095.52)	-0.77 (-5.96 to 1.75)	No dominant (ICER = 173)[2*]
ACT vs BATD (*n* = 78)			
QALY (0-1)	-646.42 (-1934.27 to 547.46)	-0.01 (-0.14 to 0.13)	No dominant (ICUR = 2,096,696)[3]
BPI-IS (0-10)	-620.95 (-1942.73 to 374.65)	-0.66 (-8.24 to 2.00)	ACT dominant[4]

Note: Significant values ($p < 0.05$) are shown in bold. Covariates: gender, age, marital status, living arrangement, educational level, employment status, year of diagnosis, current episode of depression, and costs or outcome at baseline, depending on the equation considered. CCA = complete case analysis; ICER = incremental cost-effectiveness ratio; ICUR = incremental cost-utility ratio; ITT = intention-to-treat (ITT); PPA = per-protocol analysis. CCA (N = 134), ITT (N = 234), and PPA (N = 156). In terms of interpretation, an increase in the QALY score (positive values) and a decrease (negative values) in the BPI-IS score, respectively, means that the intervention is beneficial.

[1] Dominant because ACT costs less and is more effective or useful than TAU.

[2] Dominant because BATD costs less and is more effective or useful than TAU.

[3] No dominant because ACT costs less than BATD, but BATD is more effective or useful than ACT.

[4] Dominant because ACT costs less and is more effective or useful than BATD.

[*]The sign of the ICER has been inverted since the result is positive when the change is negative.

Highlights

- Chronic pain and depression are comorbid conditions with significant costs.
- New forms of CBT have demonstrated efficacy for chronic pain and depression.
- ACT and BATD are more effective than usual care.
- ACT and BATD involve a greater reduction in costs than usual care.

CAPÍTULO 4

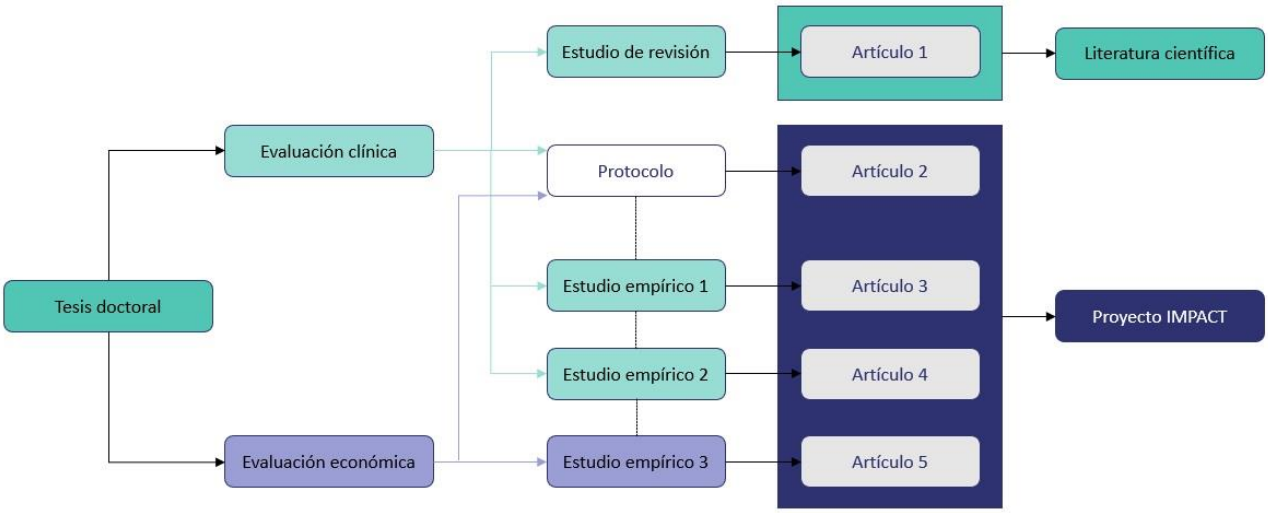
Resultados y discusión

RESULTADOS Y DISCUSIÓN

1. Aspectos generales

Como se ilustra en la Figura 7, esta tesis doctoral por compendio de publicaciones estuvo compuesta por 4 estudios, representados en 5 artículos. En el **Artículo 1** (Sanabria Mazo et al., 2023a) se realizó una revisión sistemática para comparar los resultados de eficacia del ensayo clínico respecto a las evidencias disponibles de otras terapias cognitivo-conductuales en poblaciones con dolor crónico y malestar psicológico clínicamente relevante. En el **Artículo 2** (Sanabria-Mazo et al., 2020) se presentó el protocolo de un ensayo clínico controlado y aleatorizado (Proyecto IMPACT) dirigido a pacientes con dolor lumbar crónico y síntomas de depresión. En el **Artículo 3** (Sanabria-Mazo et al., 2023b) se examinó la eficacia de añadir una forma grupal de Terapia de Aceptación y Compromiso (ACT) y de Terapia de Activación Conductual para la Depresión (TACD) administrada por videoconferencia al tratamiento habitual de pacientes con esta comorbilidad, así como el papel de variables de proceso teóricamente relevantes en los cambios clínicos a largo plazo. En el **Artículo 4** (Sanabria-Mazo et al., 2023c) se exploraron las experiencias relatadas por un grupo de pacientes que participaron en estas 2 terapias psicológicas de tercera generación. Por último, en el **Artículo 5** (Sanabria-Mazo et al., 2024) se investigó la relación coste-utilidad/coste-efectividad de ambas terapias.

Figura 7. Estudios vinculados a la tesis doctoral. Elaboración propia.



En las siguientes líneas se exponen los resultados y la discusión general de la evaluación clínica (**Artículos 1, 3 y 4**) y económica (**Artículo 5**) de ambas terapias psicológicas. Con el propósito de facilitar la lectura de la información que se reporta a continuación, los hallazgos de estos 4 estudios se integran en 2 apartados principales, que, a su vez, se dividen en subapartados que dan respuesta a los objetivos planteados en esta tesis doctoral.

2. Evaluación clínica

2.1. Revisión de la literatura

En el **Artículo 1** (Sanabria-Mazo et al., 2023a) se revisó sistemáticamente la eficacia de las terapias cognitivo-conductuales para el abordaje del dolor crónico y del malestar psicológico. Se incluyeron un total de 12 ensayos clínicos controlados y aleatorizados -entre los que se reportan los resultados del Proyecto IMPACT del **Artículo 3** (Sanabria-Mazo et al., 2023b)- y 1 ensayo clínico controlado no aleatorizado. En estos 13 ensayos clínicos, publicados entre el 2011 y el 2023, participaron 1661 pacientes. En total, 9 ensayos clínicos evaluaron la eficacia de la terapia cognitivo conductual tradicional, 3 de las intervenciones basadas en Mindfulness, 1 de la ACT y 1 de la TACD.

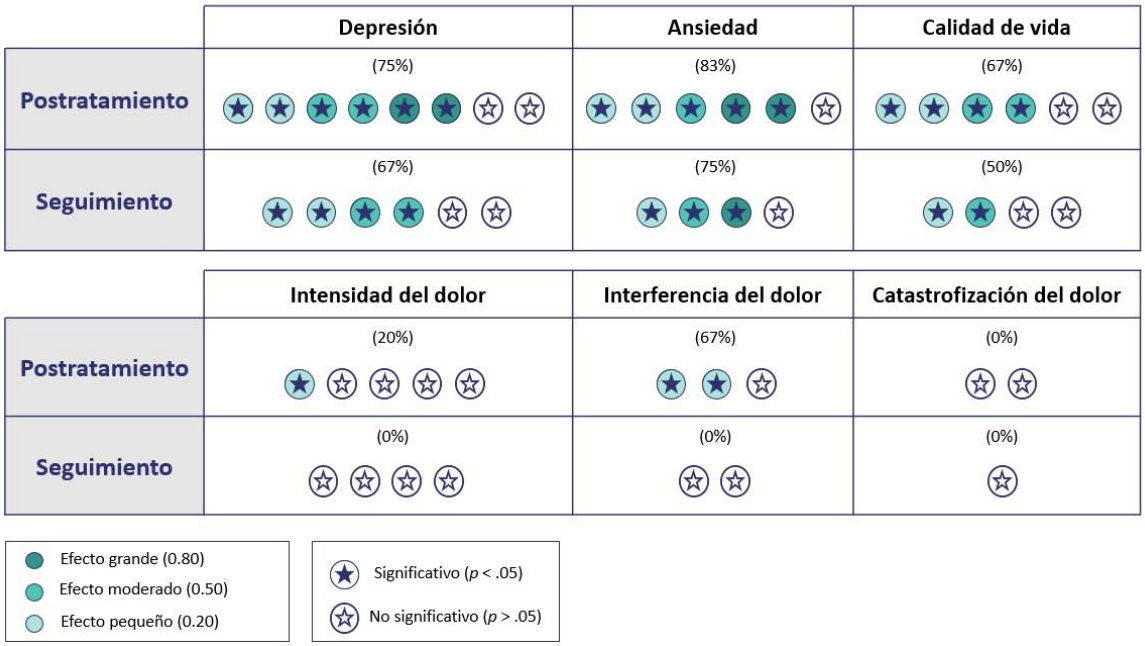
Los 13 estudios publicados -y el que se publicará próximamente (Bell et al., 2020)- señalan un creciente interés en examinar cómo las terapias cognitivo-conductuales podrían mejorar el estado funcional y la calidad de vida en pacientes con esta comorbilidad. Del mismo modo, se observó cierto interés en reconocer variables de proceso que podrían ser potencialmente beneficiosas para estos pacientes en las terapias cognitivo-conductuales de segunda y tercera generación (Hayes y Hofmann, 2021), como la aceptación del dolor, la flexibilidad psicológica y la activación conductual (Bell et al., 2020; Buhrman et al., 2015; Gasslander et al., 2022).

En comparación con el tratamiento habitual, 6 de 8 (75%) terapias cognitivo-conductuales tradicionales redujeron significativamente los síntomas de depresión de los pacientes en el postratamiento (*d* de 0,18 a 1,31) y 4 de 6 (67%) en el seguimiento (*d* de 0,26 a 0,75); también, 5 de 6 (83%) de estas intervenciones disminuyeron los síntomas de ansiedad en el postratamiento (*d* de 0,19 a 1,08) y 3 de 4 (75%) en el seguimiento (*d* de 0,27 a 1,07). En esta misma comparación, 4 de 6 (67%) intervenciones mejoraron significativamente la calidad de vida en el postratamiento (*d* de 0,02 a 0,78) y 2 de 4 (50%) en el seguimiento. Aunque con un número limitado de estudios, 2 de 3 (67%) intervenciones mejoraron la interferencia del dolor (*d* de 0,12 a 0,22) y 2 de 2 (100%) la aceptación del dolor (*d* de 0,12 a 0,30) en el postratamiento, aunque no en el seguimiento.

Contrario a lo reportado en otros estudios de síntesis (Gandy et al., 2022; Lai et al., 2023; Ma et al., 2023; Trindade et al., 2021; Veehof et al., 2016; Williams et al., 2020; Yang et al., 2022), solo 1 de 5 (20%) intervenciones basadas en terapias cognitivo-conductuales tradicionales

disminuyó significativamente la intensidad del dolor de los pacientes en el postratamiento y ninguna de 5 (0%) en el seguimiento. Como se muestra en la Figura 8, ninguna de las 2 intervenciones (0%) mejoró significativamente la catastrofización del dolor en los pacientes en el postratamiento y tampoco lo hizo 1 intervención (0%) en el seguimiento. Se requieren un mayor número de evidencias robustas para reconocer la eficacia de estas intervenciones sobre otras variables relacionadas con el dolor, como la autoeficacia para el dolor, la discapacidad relacionada con el dolor, la evitación del miedo, la kinesiofobia y el funcionamiento social. En términos generales, estos hallazgos son consistentes con la eficacia reportada de las terapias cognitivas-conductuales para la depresión o el dolor crónico en revisiones sistemáticas previas (Buhrman et al., 2015; Gasslander et al., 2022; Hilton et al., 2017; Khoo et al., 2019; López-López et al., 2019; Lorenzo-Luaces et al., 2018; Williams et al., 2020), pero con tamaños de efecto más modestos.

Figura 8. Resultados de la revisión sistemática. Elaboración propia.



Los hallazgos del **Artículo 3** (Sanabria-Mazo et al., 2023b) -incluidos en esta revisión sistemática y analizados con más detalle en los siguientes apartados- aportaron pruebas sobre la utilidad clínica de la ACT y de la TACD para la mejora de la interferencia del dolor, después del tratamiento y en el seguimiento, aunque no para la disminución del dolor. Estos resultados fueron consistentes con las evidencias reportadas en las terapias cognitivo-conductuales tradicionales. Sin embargo, a diferencia de las terapias cognitivo-conductuales tradicionales,

no se encontraron diferencias significativas en la ACT y en la TACD en la reducción de los síntomas de depresión o de ansiedad en comparación con el tratamiento habitual, pero sí en la reducción de la catastrofización del dolor después del tratamiento y en el seguimiento. En ambas terapias, las mejoras en la interferencia del dolor durante el seguimiento estuvieron significativamente mediadas por las mejoras en la flexibilidad psicológica tras el tratamiento.

Al igual que los metaanálisis previos en dolor crónico (Williams et al., 2020) y depresión (Lorenzo-Luaces et al., 2018), la eficacia de las terapias cognitivo-conductuales para el abordaje de la comorbilidad dolor y la depresión fue clínicamente relevante. Los efectos de estas terapias dirigidas al abordaje de esta comorbilidad fueron más modestos que los dirigidos a una de las 2 condiciones por separado. Considerando estos hallazgos, se plantea que el malestar psicológico podría afectar a la adhesión a las intervenciones de tratamiento del dolor y que esto, a su vez, podría reducir la participación en actividades de autocuidado y el cumplimiento del plan de tratamiento, lo que afectaría a los resultados de las intervenciones. Además, se destaca la necesidad de continuar investigando el papel mediador de la flexibilidad psicológica para comprender los mecanismos de cambio subyacentes a la eficacia de los tratamientos, identificar los componentes eficaces de las intervenciones y mejorar los resultados clínicos (McCracken et al., 2022).

2.2. Eficacia de la ACT y la TACD

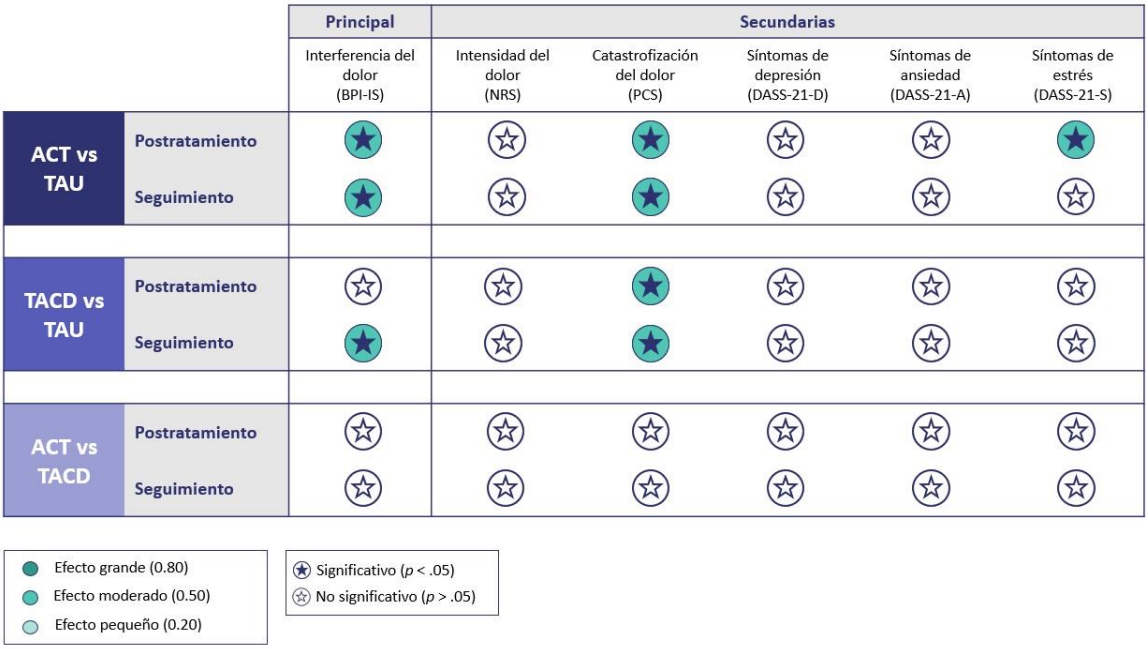
En el **Artículo 2** (Sanabria-Mazo et al., 2020) se presentan las características principales del protocolo del Proyecto IMPACT, ensayo clínico controlado, aleatorizado, multicéntrico y simple ciego en el que participaron 234 pacientes con dolor lumbar crónico y síntomas de depresión comórbidos. Para evaluar la eficacia de las terapias de este ensayo clínico, se exploraron 6 variables de resultado: 1 principal (interferencia del dolor) y 5 secundarias (intensidad del dolor, síntomas de depresión, ansiedad y estrés y catastrofización del dolor).

En general, los resultados del **Artículo 3** (Sanabria-Mazo et al., 2023b) aportan evidencia sobre la eficacia de la ACT y de la TACD en pacientes con esta comorbilidad. En comparación con el tratamiento habitual, la ACT redujo significativamente la interferencia del dolor (variable de resultado principal) en el postratamiento (d = 0,64) y en el seguimiento (d = 0,73), mientras que la TACD únicamente en el seguimiento (d = 0,66); ambas terapias también redujeron significativamente la catastrofización del dolor (variables de resultado secundarias) en el postratamiento (d = 0,45 y d = 0,59, respectivamente) y en el seguimiento (d = 0,59, en ambas).

Además, la ACT redujo significativamente los síntomas de estrés (variable de resultado secundaria) en el postratamiento (d = 0,69), pero no en el seguimiento, en comparación con el tratamiento habitual. Al comparar ambas terapias psicológicas, no se encontraron diferencias significativas en ninguna de las variables exploradas.

Contrario a lo reportado en evidencias previas, no se encontraron diferencias significativas en la reducción de la intensidad del dolor o de los síntomas de depresión o de ansiedad (variables de resultado secundarias) tras participar en la ACT o en la TACD en comparación con el tratamiento habitual en ninguno de los momentos de evaluación. Como se indica en la introducción de esta tesis doctoral, estudios de síntesis anteriores han aportado evidencia sobre la eficacia de la ACT administrada en línea en pacientes con dolor crónico para reducir la intensidad del dolor y los síntomas de depresión y ansiedad (Trindade et al., 2021; Vugts et al., 2018), aunque con tamaños de efectos de pequeños a moderados. A pesar de que la TACD fue eficaz para la mejora de la interferencia del dolor y la catastrofización del dolor, no tuvo los efectos esperados en pacientes con esta comorbilidad para la disminución de la depresión y de la ansiedad (Karyotaki et al., 2021; Walsh et al., 2022). En la Figura 9 se presenta una síntesis de estos resultados.

Figura 9. Resultados de ACT y TACD respecto a las variables clínicas. Elaboración propia.



Considerando los hallazgos mencionados, se plantea que la resistencia al tratamiento asociada a la combinación de dolor crónico y depresión, la implementación de las terapias mediante videoconferencia o el impacto psicológico generado por la pandemia de COVID-19 podrían haber reducido los efectos de estas 2 terapias de tercera generación en comparación con la evidencia reportada en la literatura (Mansfield et al., 2016; Snyder y Handrup, 2018).

2.3. Respondedores a la ACT y la TACD

La ACT y la TACD redujeron significativamente la interferencia del dolor (variable de resultado principal) de los pacientes en el postratamiento y en el seguimiento. Siguiendo las recomendaciones de la *Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials* (IMMPACT), se definió como criterio de respuesta a las intervenciones una reducción de 1 punto en la puntuación total de la interferencia del dolor (medida a partir del *Brief Pain Inventory* [BPI-IS]) respecto a la puntuación basal (Dworkin et al., 2008). Esta categorización también se utilizó para estimar el número necesario de pacientes a tratar (NNT) en la ACT y en la TACD.

Como se indica en el **Artículo 3** (Sanabria-Mazo et al., 2023b), en el postratamiento, se observó superioridad en la proporción de respondedores en la ACT (67%) sobre la TACD (45%) y el tratamiento habitual (35%). Estas diferencias también fueron favorables a la ACT (59%) en comparación con la TACD (49%) y el tratamiento habitual (24%) en el seguimiento. Del mismo modo, los valores del NNT fueron favorables a la ACT en comparación al tratamiento habitual. Respecto al tratamiento habitual, se registraron valores de NNT clínicamente relevantes en el postratamiento y en el seguimiento en la ACT (NTT = 4 y NTT = 3, respectivamente) y únicamente en el seguimiento en la TACD (NTT = 5). En la Tabla 12 se presentan los resultados de estos análisis.

Tabla 12. Número de pacientes necesario a tratar (NTT) y reducción del riesgo absoluto (ARR, por sus siglas en inglés) según el criterio de respondedores.

	Postratamiento		**Seguimiento**	
	NNT (IC 95%)	**ARR (IC 95%)**	**NNT (IC 95%)**	**ARR (IC 95%)**
ACT+TAU vs. TAU	**4** (2.1 to 7.1)	31,37% (14,03 a 48,71)	**3** (1,9 a 6,3)	34,56% (15,98 a 53,14)
BATD+TAU vs TAU	**11***	9,30% (-9,80 a 28,40)	**5** (2,3 a 21,3)	24,19% (4,69 a 43,69)
ACT+TAU vs. BATD+TAU	**6***	17,31% (-2,47 a 37,09)	**6***	10,37% (-11,01 a 31,75)

Nota. Criterio para definir a los respondedores = 1 punto de mejora en la interferencia del dolor (variable de resultado principal, que se midió a partir del BPI-IS) respecto a la puntuación basal. * Debido a que el intervalo de confianza del 95% para la reducción del riesgo absoluto se extiende desde un número negativo (el tratamiento puede dañar) hasta un número positivo (el tratamiento puede beneficiar), no es confiable calcular un IC del 95% para el NNT.

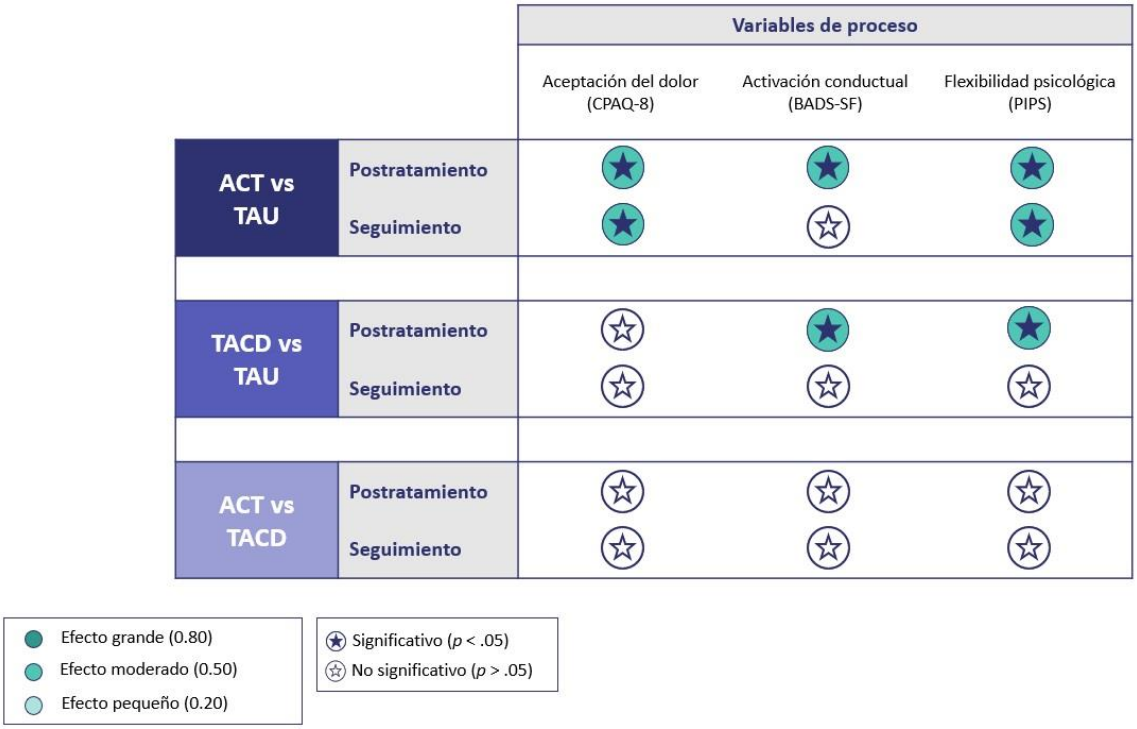
Resulta relevante destacar que los no respondedores del grupo de la ACT obtuvieron puntuaciones basales significativamente más bajas que los respondedores en la aceptación del dolor. Esta variable de proceso, como se menciona más adelante, cumple un rol relevante en los cambios clínicos a largo plazo en la ACT (McCracken et al., 2022). Finalmente, no se registraron diferencias significativas entre los pacientes que respondieron y los que no respondieron a la TACD según las variables sociodemográficas, clínicas o de resultados.

2.4. Impacto de la ACT y la TACD en las variables de proceso

En el **Artículo 3** (Sanabria-Mazo et al., 2023b) se analizó el rol de 3 variables de proceso: aceptación del dolor, flexibilidad psicológica y activación conductual. Comparado con el tratamiento habitual, la ACT aumentó la aceptación del dolor en el postratamiento y en el seguimiento (d = 0,34 y d = 0,42, respectivamente), incrementó significativamente la flexibilidad psicológica en el postratamiento y en el seguimiento (d = 0,52 y d = 0,37, respectivamente) y mejoró la activación conductual (d = 0,30) únicamente en el postratamiento. Por su parte, la TACD incrementó la flexibilidad psicológica (d = 0,40) y aumentó la activación conductual (d = 0,46) en el postratamiento. En consonancia con otras investigaciones, los pacientes que participaron en grupos de la ACT obtuvieron mejoras relacionadas con la aceptación del dolor (Bendelin et al., 2020; Trindade et al., 2021; Vugts et al., 2018) y los

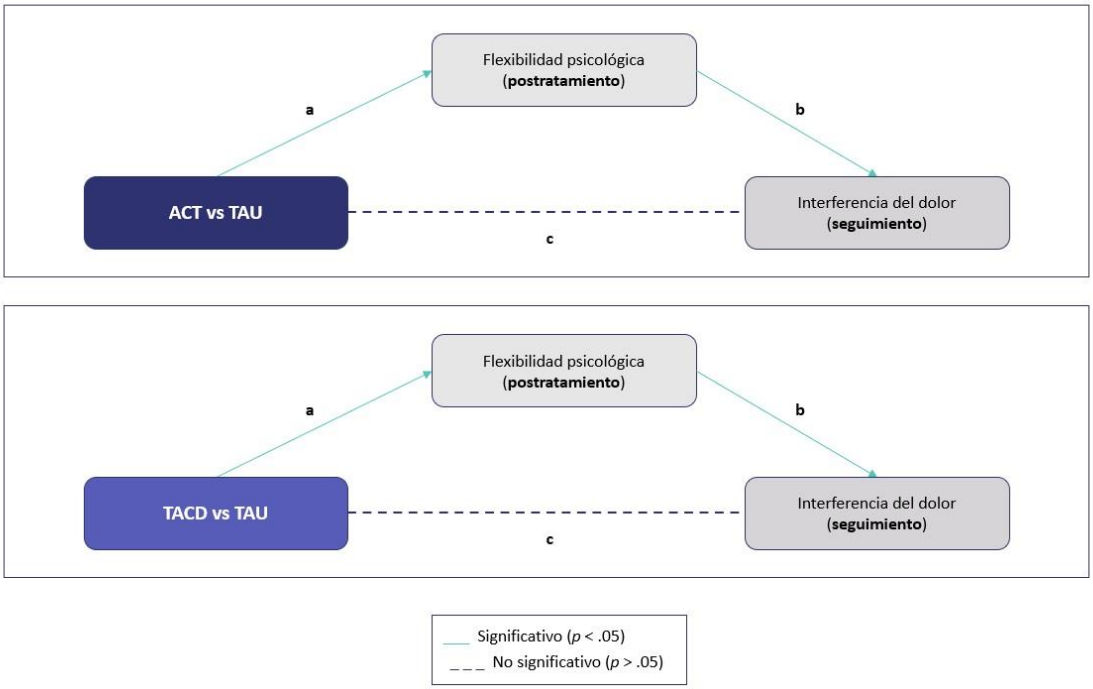
pacientes que participaron en grupos de la TACD con la activación conductual (Amick et al., 2015; Ly et al., 2015), siendo parcialmente coherentes con el objetivo principal de intervención y la orientación teórica de cada terapia (Amick et al., 2015). En la Figura 10 se presenta una síntesis de estos hallazgos.

Figura 10. Resultados de ACT y TACD respecto a las variables de proceso. Elaboración propia.



Aunque en general los resultados de ambas terapias son congruentes con los reportados en estudios previos (Hayes et al., 2011; McCracken et al., 2022; McCracken y Morley, 2014), se identificaron diferencias significativas inesperadas en el aumento significativo de la activación conductual en la ACT y en la mejora significativa de la flexibilidad psicológica en la TACD. Como se observa en la Figura 11, los cambios clínicos en la interferencia del dolor a largo plazo se asociaron con la mejora de la flexibilidad psicológica en el postratamiento en la ACT (McCracken et al., 2022; Probst et al., 2018) y en la TACD. Si bien la TACD no se basa en el modelo de flexibilidad psicológica, en esta muestra los cambios clínicos en la interferencia del dolor también se relacionaron con la mejora en la flexibilidad psicológica en el postratamiento.

Figura 11. Efecto moderador de la flexibilidad psicológica en la ACT y la TACD. Elaboración propia.



En relación con este hallazgo, se ha descubierto que la flexibilidad psicológica contribuye de forma transdiagnóstica como mediador de los efectos de las terapias cognitivo-conductuales de tercera generación (Ciarrochi et al., 2010; Montero-Marín et al., 2018; Pidgeon et al., 2014). Por tanto, este efecto podría deberse a que estas terapias abordan algunas facetas que se solapan con los componentes primarios de la flexibilidad psicológica (p. ej., contacto con el momento presente, aceptación, valores, acción comprometida y defusión), como se informó en una revisión sistemática reciente (McCracken et al., 2022). La acción comprometida y los valores son aspectos implícitos en las formas más recientes de las terapias cognitivo-conductuales, entre las que se incluyen la ACT, la TACD y la Terapia Cognitiva basada en Mindfulness, entre otras. Todas estas terapias se centran en ayudar a las personas a identificar y alinear sus acciones y valores con sus objetivos y deseos, así como a desarrollar estrategias para realizar cambios significativos en sus vidas.

2.5. Adhesión en la ACT y la TACD

La tasa de abandonos en el postratamiento y en el seguimiento fue superior al esperado en la ACT (33% y 44%, respectivamente) y en la TACD (46% y 50%, respectivamente) e inferior al esperado en el tratamiento habitual (28% y 32%, respectivamente). La tasa de abandonos reportada en el **Artículo 3** (Sanabria-Mazo et al., 2023b) fue significativamente mayor en la

TACD en comparación con la ACT en el postratamiento. Respecto al momento de implementación de las terapias, la tasa de abandonos fue significativamente mayor en la tercera ola (mayo a julio de 2021) que en la primera (octubre a diciembre de 2020) y la segunda ola (febrero a abril de 2021) del ensayo clínico, meses que coinciden con la relajación de las restricciones de movilidad asociadas a la pandemia de COVID-19 y con el periodo prevacacional en España. Los problemas de adhesión identificados en el **Artículo 3** (Sanabria-Mazo et al., 2023b) son consistentes con los reportados en terapias administradas por internet o a distancia en pacientes con dolor crónico y malestar psicológico (Gasslander et al., 2021, 2022; Rickardsson et al., 2021).

2.6. Experiencias de los pacientes

En el **Artículo 4** (Sanabria-Mazo et al., 2023c) se exploraron las experiencias relatadas por un grupo de pacientes que participaron en la ACT o en la TACD. Al igual que en otras investigaciones (Gloster et al., 2020; van de Graaf et al., 2021; Vugts et al., 2018; Zhang et al., 2018), se identificó que los pacientes percibieron mejoras psicológicas (conductuales, afectivas y cognitivas) tras finalizar ambas terapias, así como mejoras generales en la gestión de las emociones y en la calidad de vida. La percepción de cambios reportada por los pacientes en ambas terapias fue parcialmente consistente con los resultados cuantitativos presentados en el **Estudio 2** (Sanabria-Mazo et al., 2023a), en el que se identificó una mejora significativa en la interferencia del dolor (variable de resultado principal), la catastrofización del dolor (variable de resultado secundaria) y la aceptación del dolor, la activación conductual y la flexibilidad psicológica (variables de proceso), pero no en la reducción del dolor o de los síntomas de depresión y de ansiedad (variables de resultado secundarias). Las diferencias identificadas en la mejora de las alteraciones emocionales, en las que se observó una tendencia marginal hacia la significación estadística en el ensayo clínico, es una contribución relevante del estudio cualitativo, que destaca la importancia de las experiencias de los participantes para comprender el potencial terapéutico de estas terapias.

En línea con estudios cualitativos previos, los pacientes comentaron que formar parte de un grupo terapéutico les ayudó a sentirse más comprendidos y menos juzgados por su condición de salud, especialmente durante las restricciones impuestas durante la pandemia de COVID-19 (Bendelin et al., 2020; Finning et al., 2017; Ly et al., 2015). Del mismo modo, indicaron que asistir a las sesiones de terapia era una oportunidad para conversar sobre sus problemas cotidianos, reforzar sus nuevos hábitos, evaluar el progreso hacia sus objetivos y sentirse menos

solos (Caeiro et al., 2019; Doukani et al., 2020). Al respecto, un gran número de estudios han demostrado que sentirse escuchado por los demás contribuye tanto a la aceptación del dolor como al desarrollo de estrategias activas de afrontamiento (Bendelin et al., 2020; Callesen et al., 2020; Finning et al., 2017; Ly et al., 2015). También, se ha observado que el entorno seguro generado en las terapias fomenta la compasión en los pacientes y en el grupo. En concordancia con otras investigaciones, la identificación y la cohesión grupal se señalan como mecanismos terapéuticos que contribuyen a la mejora del control personal y del abordaje del dolor (Dolgin et al., 2020; Haslam et al., 2022; Woodland et al., 2022).

La mayoría de los pacientes expresaron su satisfacción con la terapia en formato virtual y una mayor confianza en el uso de esta tecnología al finalizar el ensayo clínico. Sin embargo, estuvieron de acuerdo en que recibir terapia en persona sigue siendo importante. Estos hallazgos son consistentes con las experiencias descritas en otras intervenciones grupales realizadas mediante videoconferencia (Bendelin et al., 2020; Fernandes et al., 2022; Ly et al., 2015). A pesar de que se identificaron algunas barreras en la implementación virtual de estas terapias (como perder el contacto cara a cara, perderse espacios de intervención presenciales y prescindir de momentos de socialización), ambas se percibieron como psicológicamente beneficiosas para las personas con dolor crónico y síntomas de depresión. Los beneficios principales fueron evitar desplazamientos adicionales, ahorrar tiempo y dinero en transporte y la posibilidad de conectarse desde diferentes entornos en función de sus necesidades.

3. Evaluación económica

En el **Artículo 5** (Sanabria-Mazo et al., 2024) se realizó una evaluación económica (coste-utilidad y coste-efectividad) de la ACT y de la TACD respecto al tratamiento habitual, desde la perspectiva sanitaria y gubernamental. Esta evaluación amplió los resultados cuantitativos y cualitativos reportados en el **Artículo 3** (Sanabria-Mazo et al., 2023b) y en el **Artículo 4** (Sanabria-Mazo et al., 2023c), respectivamente. En comparación con el tratamiento habitual, la ACT logró una reducción significativa en los costes totales (d = 0,47), mientras que la TACD en los costes indirectos (d = 0,61) y totales (d = 0,63). En ambas terapias, además, se encontraron mejoras significativas en la interferencia del dolor (d = 0,73 y d = 0,66, respectivamente) y en los años de vida ajustados por calidad (d = 0,46 y d = 0,28, respectivamente). Al comparar ambas terapias activas, no se hallaron diferencias significativas en los costes y en las variables de resultados (interferencia de dolor y años de vida ajustados por calidad). Considerando la alta carga económica y sanitaria que supone el abordaje del dolor crónico y de la depresión (Becker, 2012), la reducción de costes (directos, indirectos y totales) y el incremento en paralelo de los efectos clínicos es un asunto prioritario (Hedman-Lagerlöf et al., 2019) para los gestores sanitarios en el ámbito público.

Los análisis de coste-efectividad (basados en la interferencia del dolor) y de coste-utilidad (basados en los años de vida ajustados por calidad [AVACs]) -explorados desde la perspectiva sanitaria y gubernamental- indicaron que el efecto incremental sobre la interferencia del dolor fue significativo en la ACT (Δ = -1,57 y -1,39, respectivamente) y en la TACD (Δ = -1,08 y -1,04, respectivamente) en comparación con el tratamiento habitual, pero no sobre los AVACs. En común, los efectos fueron significativos en el análisis de casos completos (pacientes que completaron ambos momentos de evaluación del estudio), aunque no en el análisis por intención de tratar. Se plantea que las diferencias detectadas entre los resultados de coste-utilidad y de coste-efectividad podrían relacionarse con que en esta población la interferencia del dolor es generalmente la variable de resultado principal, mientras que los AVACs es una variable de resultado secundaria.

Desde la perspectiva sanitaria y gubernamental, no se observaron diferencias significativas -en ninguno de los análisis explorados en este estudio (intención de tratar, casos completos y por protocolo)- en el coste incremental basado en la interferencia del dolor y en los AVACs. Aunque según estos análisis, la ACT mostró cierta superioridad en comparación con la TACD.

Se hipotetiza que la alta variabilidad observada en los costes informados en este estudio y el tamaño muestral mermado por la elevada tasa de abandonos registrados en el ensayo clínico controlado y aleatorizado (Faria et al., 2014) pudo influir en la falta de detección de diferencias significativas asociadas con mayores costes (Al et al., 1998; Bader et al., 2018).

Las reducciones de costes son consistentes con las observadas en las terapias cognitivo-conductuales (Hedman-Lagerlöf et al., 2019; Luciano et al., 2013, 2017; Richardson y Manca, 2004; Schröder et al., 2017). Como se menciona en la introducción de esta tesis doctoral, existe evidencia sobre la eficacia y la eficiencia de la ACT (Kemani et al., 2015; Luciano et al., 2017; Risør et al., 2022; Witlox et al., 2022) y de la TACD (Chen et al., 2022; Sun et al., 2021) en comparación con el tratamiento habitual, tanto en poblaciones con dolor crónico (Luciano et al., 2013, 2017) como con otras condiciones de salud (Risør et al., 2022; Witlox et al., 2022). En ensayos clínicos anteriores, ambas terapias han logrado efectos incrementales significativos (Chen et al., 2022; Kemani et al., 2015; Luciano et al., 2017; Risør et al., 2022; Sun et al., 2021; Witlox et al., 2022), aunque también se han identificado costes incrementales más altos que el tratamiento habitual.

En la ACT y en la TACD se observaron efectos clínicos relevantes en comparación con el tratamiento habitual. No obstante, no se evidenció una preferencia clara entre ambas terapias desde una perspectiva de reducción de costes. Si bien la ACT obtuvo mejores resultados en la interferencia del dolor -variable de resultado de intervención principal en población con dolor crónico (Buchbinder et al., 2018)- en comparación con la TACD, ninguna de estas 2 terapias disminuyó significativamente los costes en comparación con la otra, así como tampoco en comparación con el tratamiento habitual. Desde un punto de vista estrictamente clínico, la ACT parece preferible para una población con dolor crónico y depresión comórbida, considerando que obtuvo un mayor número de respondedores en el **Artículo 3** (Sanabria-Mazo et al., 2023b).

Por último, se propone que la elección de la terapia más apropiada para otras poblaciones se base en consideraciones éticas y prácticas, así como en las preferencias tanto de los pacientes como de los terapeutas (Luciano et al., 2017). En este contexto, el modelo de toma de decisiones compartida terapeuta-paciente promueve la adhesión terapéutica y mejora los resultados al conectar la elección de terapias de acuerdo con las preferencias y los valores de cada paciente (Joosten et al., 2008). Hasta donde se sabe, este es el primer ensayo clínico que explora una evaluación económica en una población con la comorbilidad dolor crónico y

depresión. Se necesitan, así pues, más ensayos clínicos que analicen la relación coste-utilidad y la relación coste-efectividad de estas terapias para tener unas conclusiones más sólidas (Feliu-Soler et al., 2018).

4. Fortalezas y limitaciones

Los hallazgos que se reportan en esta tesis doctoral deben interpretarse reconociendo las limitaciones y las fortalezas de los estudios que la componen. En la Tabla 13 se presenta una síntesis de aspectos metodológicos principales a considerar en los 4 estudios -reflejados en 5 artículos- incluidos en este trabajo.

Tabla 13. Limitaciones y fortalezas de los artículos incluidos en esta tesis doctoral.

	Limitaciones	**Fortalezas**
Artículo 1	• La falta de ensayos clínicos aleatorizados y no aleatorizados con riesgo de sesgo bajo dificultó concluir con solidez la magnitud de la eficacia de las terapias cognitivo-conductuales para el abordaje de la comorbilidad dolor crónico y malestar psicológico.	• En la revisión sistemática se incluyeron 4 bases de datos principales (Medline, PsycINFO, Web of Science y Scopus) y se siguieron las directrices de la declaración *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA).
	• La alta heterogeneidad detectada en los estudios incluidos en la revisión sistemática (por ejemplo, modo de ejecución, número de sesiones, componentes de la intervención y características de los terapeutas, entre otros) impidió ejecutar los metaanálisis previstos.	• Las búsquedas booleanas se validaron según las pautas de la *Peer Review of Electronic Search Strategies* (PRESS).
	• Solamente se incluyeron estudios publicados en inglés o español, por lo que se podrían haber omitido otras evidencias relevantes.	• Para minimizar la posible pérdida de evidencias, se utilizó la herramienta Rayyan QCRI.
	• No fue posible examinar si formas específicas de las terapias cognitivo-conductuales eran más efectivas que otras.	• En este estudio se contó con una revisión consensuada entre revisores en las diferentes fases de cribado, extracción de datos y evaluación de riesgo de sesgo.

Artículos 2 y 3	• Por limitaciones presupuestarias, no fue posible realizar una evaluación externa de la fidelidad a las intervenciones de este ensayo clínico y una valoración de las competencias de los terapeutas a cargo de los programas.	• El protocolo del ensayo clínico se registró prospectivamente en *ClinicalTrials.gov* (NCT04140838).
	• No se monitorizó el cumplimiento que tuvieron los pacientes sobre los ejercicios o las actividades que debían realizar en casa.	• Se siguieron las recomendaciones del *Standard Protocol Items: Recommendations for Interventional Trials* (SPIRIT) y del *Consolidated Standards of Reporting Trials* (CONSORT).
	• La tasa de abandono fue mayor de la registrada en otros ensayos clínicos, lo que pudo influir en un análisis preciso de los efectos a corto y largo plazo de ambas terapias en condiciones óptimas de adhesión.	• Se utilizaron las sugerencias de la *Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials* (IMMPACT) para establecer la mejoría clínica de los pacientes después de la terapia y tras el seguimiento.
	• Debido a la alta tasa de abandono en el seguimiento, es posible que los análisis de caminos no tuvieran el poder estadístico suficiente para detectar pequeños efectos mediacionales.	• Se incluyó una muestra amplia con un conjunto de medidas clínicas validadas que facilitó explorar resultados importantes relacionados con la experiencia del dolor.
Artículo 4	• No se pudo incluir todos los pacientes que participaron en el ensayo clínico, solamente a aquellos que confirmaron su interés.	• Este estudio se adhirió a las directrices de *Consolidated Criteria for Reporting Qualitative Research* (COREQ) y de *Journal Article Reporting Standards for Qualitative Research* (JARS).

	• En este estudio no se exploraron las experiencias de los pacientes que no completaron las sesiones de la ACT o de la TACD, así como tampoco la experiencia de los terapeutas, algo que podría haber agregado más solidez a la interpretación de los hallazgos.	• Se contó con una cantidad significativa de pacientes que participaron en este proyecto y que compartieron sus experiencias en los grupos focales.
	• No se realizaron entrevistas en profundidad individuales como técnica de recolección de datos complementaria a los grupos focales.	• Se utilizó la guía AMEE No. 149 para explorar elementos clave de la reflexividad, como los factores personales, interpersonales, metodológicos y contextuales.
	• Considerando que los pacientes tenían una relación previa con sus entrevistadores, existe la posibilidad de que las respuestas estuvieran influenciadas por la deseabilidad social.	• Los 5 investigadores responsables de los grupos focales recibieron formación previa en la recogida y en el análisis de datos cualitativos.
	• Los pacientes no se incluyeron en la validación final de los resultados, lo que podría haber ayudado a obtener una perspectiva interpretativa más fiable.	• La codificación y los análisis de los datos se validó con la participación de todo el equipo de investigación.
Artículo 5	• La alta tasa de abandono contribuyó a una considerable falta de datos de eficiencia en la evaluación de seguimiento a los 12 meses.	• La evaluación económica de este estudio se realizó siguiendo la *Consolidated Health Economic Evaluation Reporting Standards* (CHEERS) y se adhirió a las buenas prácticas de investigación para el análisis económico de los ensayos.
	• Aunque se incluyó una intersección aleatoria en los modelos lineales generalizados para considerar la	• Se utilizó la base de datos SOIKOS (con datos actualizados de 2022) de costes sanitarios como fuente para

	variabilidad dentro de cada grupo, estimar este intercepto en pacientes con un solo punto de datos pudo representar un riesgo de sobreajuste en los modelos.	estimar el uso de servicios sanitarios y pruebas médicas.
	• Debido a limitaciones de accesibilidad, no se contrastó la información sobre costes reportada retrospectivamente (último 12 meses) por los pacientes con las historias clínicas informatizadas.	• El coste de los medicamentos se estimó consultando el precio por miligramo en el Vademécum Internacional, con datos de 2022.
	• No se estimaron los costes directos no relacionados con la salud (por ejemplo, gastos del propio bolsillo, costes de asistencia remunerada y no remunerada, gastos de viaje y el uso de medicamentos sin receta y otros tratamientos, entre otros).	• Se implementaron 3 oleadas de recopilación de datos para minimizar la posible influencia asociada con el momento específico de ejecución del estudio.

5. Futuras líneas de investigación

En esta tesis doctoral se realizó una evaluación clínica y económica de la ACT y de la TACD en pacientes con dolor lumbar crónico y síntomas de depresión. En conjunto, los 4 estudios de este trabajo -reflejados en 5 artículos- aportan evidencia, por primera vez, acerca de la eficacia y de la eficiencia de estas terapias cognitivo-conductuales de tercera generación para el abordaje de esta comorbilidad. A pesar de que en general los hallazgos de este trabajo destacan los beneficios de ambas terapias, existen distintos aspectos aún por explorar. En la Tabla 14 se presenta una propuesta de posibles futuras líneas de investigación.

Tabla 14. Propuesta de futuras líneas de investigación.

	Recomendaciones
1	Las terapias exploradas en este ensayo clínico se implementaron en una fase restrictiva de la pandemia. Considerando los posibles efectos del contexto particular en el que se desarrolló este trabajo, se recomienda que futuros estudios continúen evaluando la eficacia y la eficiencia de la ACT y de la TACD en pacientes con dolor crónico y síntomas de depresión.
2	La inversión en recursos digitales que garanticen un acompañamiento adecuado tanto a los pacientes con dolor crónico como a los terapeutas parece indispensable tras la pandemia. Así pues, se necesitan más investigaciones que contribuyan a identificar los beneficios clínicos y económicos de las terapias cognitivo-conductuales de tercera generación implementadas mediante videoconferencia en formato grupal.
3	La alta tasa de abandonos reportada en este ensayo clínico influyó directamente en la potencia estadística de los análisis explorados. Futuras líneas de investigación podrían aportar más evidencia acerca de los factores sociodemográficos, clínicos y contextuales que podrían influir en la adhesión de los pacientes en terapias psicológicas con características similares.
4	Los terapeutas del ensayo clínico contaban con experiencia acreditada para la implementación de estas terapias psicológicas. Al igual que en la práctica clínica habitual, estos terapeutas tenían diferentes años de experiencia en las intervenciones y perfiles de

	edad. Se recomienda que futuras investigaciones exploren el papel potencial de las características de los terapeutas en la mejora de los resultados clínicos.
5	Una pequeña submuestra de pacientes experimentó efectos adversos al realizar ejercicios que implicaban una mayor conciencia de los pensamientos y las emociones, lo que condujo a un malestar transitorio de corta duración. Analizar más a fondo los efectos adversos relacionados los ejercicios de ambas terapias podría ser clínicamente relevante para mejorar la adhesión.
6	Aunque están empezando a reportarse evidencias acerca de los efectos de terapias de tercera generación, como las aquí analizadas, en pacientes con dolor crónico y malestar psicológico comórbido, es importante continuar comparando qué terapia es más eficaz, en qué circunstancias y para qué perfil o clúster de pacientes.
7	En general, la elección de las terapias psicológicas más adecuadas para el dolor crónico y la depresión se derivan de la comparación sistemática de los tamaños del efecto reportados en los ensayos clínicos. A pesar de que los ensayos siguen siendo el diseño de referencia para evaluar los efectos terapéuticos, es pertinente empezar a investigar estos efectos de forma longitudinal y desde una perspectiva individualizada a través de diseños alternativos, como los diseños de caso único.
8	Los hallazgos de este ensayo clínico indican que algunos procesos psicológicos están significativamente relacionados con los cambios clínicos en la interferencia del dolor en pacientes con dolor lumbar crónico y síntomas de depresión. Examinar la relación en el transcurso del tiempo entre variables de procesos, como la flexibilidad psicológica o la activación conductual, podría ser de gran utilidad clínica.

6. Referencias

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Capítulo 5

Conclusiones

CONCLUSIONES

Las conclusiones derivadas de la evaluación clínica (**Artículos 1, 3 y 4**) y económica (**Artículo 5)** de la Terapia de Aceptación y Compromiso (ACT) y de la Terapia de Activación Conductual para la Depresión (TACD) en pacientes con dolor lumbar crónico y síntomas de depresión comórbidos son las siguientes:

Artículo 1

- La terapia cognitivo conductual tradicional mejora los síntomas de depresión y de ansiedad, así como aumenta la calidad de vida, en pacientes con dolor crónico comórbido y malestar psicológico clínicamente relevante, pero no reduce ni la intensidad del dolor ni la catastrofización del dolor. Aunque en esta revisión sistemática se obtuvieron algunas evidencias de los beneficios de las intervenciones basadas en Mindfulness, de la ACT y de la TACD, se necesitan más ensayos clínicos controlados y aleatorizados basados en intervenciones de tercera generación para determinar la eficacia general de estas terapias en estos pacientes con esta comorbilidad.

Artículo 3

- En comparación con el tratamiento habitual, los datos obtenidos apoyan la eficacia de la ACT y la TACD en la mejora de la interferencia del dolor, la catastrofización del dolor, la activación conductual y la flexibilidad psicológica en el postratamiento y en el seguimiento de 12 meses en pacientes con dolor lumbar crónico y síntomas de depresión comórbidos. Además, la ACT mostró ser eficaz para la reducción de los síntomas de estrés en el postratamiento. Aunque algunas de las mejoras reportadas disminuyeron parcialmente su efecto en el seguimiento, ambas terapias mostraron beneficios. En contraposición a evidencias previas, no se encontraron mejoras significativas en la disminución del dolor y de los síntomas de depresión o de ansiedad en ninguno de los momentos de evaluación de ambas terapias.
- La ACT obtuvo una proporción significativamente superior de respondedores que la TACD en el postratamiento y en el seguimiento; sin embargo, no se identificaron diferencias significativas en la variable principal o las secundarias entre estas 2 terapias. En ambas terapias, las mejoras en la interferencia del dolor durante el seguimiento se relacionaron significativamente con las mejoras en la flexibilidad psicológica tras el tratamiento.

Artículo 4

- Los pacientes con dolor lumbar crónico y síntomas de depresión comórbidos mostraron su satisfacción con participar en un formato grupal y por videoconferencia de la ACT y de la TACD. En sus relatos la mayoría destacaron el potencial terapéutico de ambas terapias para su mejoría clínica. En general, las sesiones de las 2 terapias se percibieron como un lugar seguro y sin prejuicios en el que podían expresar sus emociones y sentirse comprendidos. Respecto la implementación de ambas terapias mediante videoconferencia, se señalaron como principales barreras la falta de contacto humano y la pérdida de interacción social; y como facilitadores la comodidad de acceso, la flexibilidad para conectarse desde cualquier lugar, la diminución de desplazamiento y el ahorro de tiempo y dinero.

Artículo 5

- La ACT y la TACD fueron más eficaces e implicaron una mayor reducción de costes que el tratamiento habitual en pacientes con dolor lumbar crónico y síntomas de depresión comórbidos. En comparación con el tratamiento habitual, la ACT mostró una reducción significativa de los costes totales y la TACD de los costes indirectos y totales. En ambas terapias también se encontró una mejoría significativa en las puntuaciones de interferencia del dolor y de los años de vida ajustados por calidad (AVACs). No se detectaron diferencias significativas en los costes y los resultados al comparar las 2 terapias activas entre sí. El efecto incremental sobre la interferencia del dolor fue significativo para la ACT y la TACD en comparación con el tratamiento habitual, pero no sobre los AVACs en ninguno de los análisis de sensibilidad (casos completos, intención de tratar y por protocolo). No se encontraron diferencias significativas en el coste incremental basado en la interferencia del dolor y en los AVACs entre los 3 grupos. En general, la ACT y la TACD fueron eficaces en la reducción del efecto incremental de la interferencia del dolor, pero no en términos de la razón coste-utilidad incremental y de la razón coste-efectividad incremental.

CAPÍTULO 5

Conclusions

CONCLUSIONS

The conclusions derived from the clinical (**Articles 1, 3, and 4**) and economic (**Article 5**) evaluation of Acceptance and Commitment Therapy (ACT) and Behavioral Activation Therapy for Depression (BATD) in patients with chronic low back pain and comorbid depressive symptoms are as follows:

Article 1

- Traditional Cognitive Behavioral Therapy improves symptoms of depression and anxiety, as well as increases quality of life, in patients with comorbid chronic pain and clinically relevant psychological distress, but does not reduce either pain intensity or pain catastrophizing. Although some evidence for the benefits of Mindfulness-based interventions, ACT, and BATD was obtained in this systematic review, more randomized controlled trials based on third-generation interventions are needed to determine the overall efficacy of these therapies in these patients with this comorbidity.

Article 3

- Compared to treatment as usual, the data obtained support the efficacy of ACT and BATD in improving pain interference, pain catastrophizing, behavioral activation, and psychological flexibility at post-treatment and at 12-month follow-up in patients with chronic low back pain and comorbid depressive symptoms. In addition, ACT was shown to be effective in reducing stress symptoms at post-treatment. Although some of the reported improvements partially diminished their effect at follow-up, both therapies showed benefits. In contrast to previous evidence, no significant improvements in decreasing pain and depression or anxiety symptoms were found at either evaluation time point for both therapies.
- ACT had a significantly higher proportion of responders than BATD at posttreatment and follow-up; however, no significant differences in the primary or secondary endpoint were identified between these 2 active therapies. In both therapies, improvements in pain interference at follow-up were significantly related to improvements in psychological flexibility after treatment.

Article 4

- Patients with chronic low back pain and comorbid depressive symptoms showed their satisfaction with participating in a group and videoconference format of ACT and BATD. In their narratives most highlighted the therapeutic potential of both therapies for their clinical improvement. In general, the sessions of the 2 therapies were perceived as a safe and non-judgmental place where they could express their emotions and feel understood. Regarding the implementation of both therapies by videoconference, the main barriers were the lack of human contact and the loss of social interaction; and as facilitators, the ease of access, the flexibility to connect from anywhere, the reduction of travel, and the savings in time and money.

Article 5

- ACT and BATD were more effective and involved a greater cost reduction than treatment as usual in patients with chronic low back pain and comorbid depressive symptoms. Compared to treatment as usual, ACT showed a significant reduction in total costs and BATD in indirect and total costs. Significant improvement in pain interference scores and quality adjusted life year (QALYs) was also found in both therapies. No significant differences in costs and outcomes were detected when comparing the 2 active therapies with each other. The incremental effect on pain interference was significant for ACT and BATD compared with treatment as usual, but not on QALYs in any of the sensitivity analyses (complete cases, intention-to-treat, and per-protocol). No significant differences were found in incremental cost based on pain interference and QALYs among the 3 groups. Overall, ACT and BATD were effective in reducing the incremental effect of pain interference, but not in terms of incremental cost-utility ratio and incremental cost-effectiveness ratio.

ANEXOS

Otros estudios relacionados con el Proyecto IMPACT

ANEXOS

Estos son otros estudios directamente relacionados con IMPACT, proyecto en el que se enmarca esta tesis doctoral:

1. Sanabria-Mazo, J. P., Colomer-Carbonell, A., Carmona-Cervelló, M., Feliu-Soler, A., Borràs, X., Grasa, M., Esteve, M., Maes, M., Edo, S., Sanz, A. y Luciano, J. V. (2022). Immune-inflammatory and hypothalamic-pituitary-adrenal axis biomarkers are altered in patients with non-specific low back pain: A systematic review. *Frontiers in Immunology, 13*, 945513. https://doi.org/10.3389/fimmu.2022.945513
2. Sanabria-Mazo, J. P., Giné-Vázquez, I., Cristóbal-Narváez, P., Suso-Ribera, C., García-Palacios, A., McCracken, L. M., Hayes, S. C., Hofmann, S. G., Ciarrochi, J. y Luciano, J. V. (s.f.). Relationship between outcomes and processes in patients with chronic low back pain plus depressive symptoms: Idiographic analyses within a randomized controlled trial (IMPACT study). *Under review*.

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