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**A LOW-INTENSITY INTERNET-BASED INTERVENTION FOCUSED ON
THE PROMOTION OF POSITIVE AFFECT FOR THE TREATMENT OF
DEPRESSION IN PRIMARY CARE: A RANDOMIZED CONTROL TRIAL**

TESIS DOCTORAL

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*“Normality is a paved road: It’s comfortable to walk,
but no flowers grow on it”.*
Vincent Van Gogh

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VALENCIAN SUMMARY

RESUM EN VALENCIÀ

1. Introducció

La depressió és un dels trastorns mentals més comuns a tot el món. Està associada amb costos significants de tipus personal (p.e. en termes de qualitat de vida i benestar) i social (p.e. en termes de despeses econòmiques i ús de serveis) (Gustavsson et al., 2011; Kessler, 2012; Mrazek, Hornberger, Altar, i Degtiar, 2014; Parés-Badell et al., 2014). En especial, la prevalença de depressió en l'Atenció Mèdica Primària espanyola es troba entre el 13.9% i el 29% (Alonso et al., 2004; Roca et al., 2009) i menys del 50% de la gent rep el tractament adequat (p.e. Aragonès, Piñol, Labad, Folch, i Mèlich, 2004).

Tot i que actualment existeixen tractaments efectius per a la depressió (medicació, psicoteràpia o ambdós) (Cuijpers, van Straten, van Oppen, i Andersson, 2008; Cuijpers et al., 2013; Huhn et al., 2014) no arriben al nombre creixent de gent que els necessita (Kazdin i Blase, 2011). Les causes poden ser els llargs períodes de llistes d'espera en l'Atenció Primària, el temps limitat d'atenció al pacient, l'estigma social associat a les malalties mentals i la falta de professionals ben qualificats, entre altres (Gaston, Abbott, Rapee, i Neary, 2006; Harvey i Gumport, 2015; Sartorius, 2002; Wittchen et al., 2011). Així doncs, cal incorporar ferramentes noves que proporcionen tractaments basats en l'evidència per a tractar la depressió amb l'objectiu de respondre de manera efectiva a aquesta necessitat.

Les intervencions de baixa intensitat podrien ser una bona alternativa per a superar aquestes limitacions (Bockting, Williams, Carswell, i Grech, 2016). En particular, les intervencions basades en Internet són un exemple d'aquest tipus d'intervencions que han rebut evidència empírica com opcions adequades dins del model d'atenció escalonada (Bennett-Levy, Richards, i Farrand, 2010). De fet, alguns meta-anàlisis suggereixen que la depressió pot ser tractada de manera efectiva amb psicoteràpia breu (de 6 a 8 sessions),

en concret amb teràpia cognitiva conductual (TCC), teràpia de resolució de problemes (Nieuwsma et al., 2012) i orientació (Cape, Whittington, Buszewicz, Wallace, i Underwood, 2010). Però, es necessiten més estudis sobre l'eficàcia i assajos controlats aleatoris per analitzar els efectes d'aquestes intervencions emprant una condició de control actiu com a comparació.

S'han proposat les intervencions basades en Internet com una opció assequible que pot ajudar a reduir la diferència entre la demanda i l'oferta de tractaments (Andersson & Titov, 2014; Cuijpers, Kleiboer, Karyotaki, i Riper, 2017; Holst et al., 2018). Un considerable nombre d'estudis han demostrat la seua eficàcia i acceptabilitat en el tractament de la depressió (Andersson i Cuijpers, 2009; Andersson, 2016; Andrews, Cuijpers, Craske, McEvoy, i Titov, 2010; Karyotaki et al., 2018). A més a més, alguns estudis han demostrat que les intervencions basades en Internet són més eficaces quan són guiades (des de recordatoris automàtics fins *feedback* per correu electrònic, missatges de text o breus trucades), cosa que emfatitza la relació positiva entre l'assistència terapèutica i els índexs de millora (Baumeister, Reichler, Munzinger, i Lin, 2014; Berger, Hämmerli, Gubser, Andersson, i Caspar, 2011; Johansson i Andersson, 2012; Richards i Richardson, 2012). Finalment, s'han trobat magnituds d'efecte similars entre intervencions basades en Internet i teràpies cara a cara (Andersson, Cuijpers, Carlbring, Riper, i Hedman, 2014; Andersson, Topooco, Havik, i Nordgreen, 2016).

Fins el moment, moltes intervencions basades en Internet per a la depressió estan basades principalment en TCC (Andersson, 2009; Hedman, Ljótsson, i Lindefors, 2012) i en altres aproximacions terapèutiques com la teràpia de resolució de problemes (van Straten et al., 2008), teràpia interpersonal (Donker et al., 2013), teràpia d'acceptació i compromís (Glendenning, Hoon, i John, 2016), teràpia psicodinàmica (Johansson et al., 2012) o activació conductual (Nyström et al., 2017). Tot i que aquestes aproximacions

són eficaces per al tractament de la depressió, no tots els pacients es beneficien d'elles. La causa podria ser que molts tractaments estàndard paren més atenció a trastorns mentals específics sense tindre en compte la presència de comorbiditats (p.e. trastorns d'ansietat) o trastorns no especificats (Fairburn, Cooper, i Shafran, 2003; Kring i Sloan, 2009). Una aproximació alternativa que podria contribuir a resoldre aquesta limitació és la perspectiva transdiagnòstica (Sauer-Zavala et al., 2017).

La perspectiva transdiagnòstica es centra principalment en allò que tenen en comú els trastorns emocionals (TEs) (p.e. depressió i ansietat) en compte d'allò que és específic i diferencial (Sandín, 2012). En aquesta línia, Brown i Barlow (2009) han suggerit que els TEs tenen en comú una estructura latent amb dues dimensions (afecte negatiu o inhibició conductual i afecte positiu o activació conductual) que, associades amb diferents factors d'estrès, poden resultar en símptomes d'ansietat o depressió. Aquesta conceptualització dels TEs ha permès el disseny i la implementació dels protocols transdiagnòstics amb components de tractaments comuns a través d'un marc més parsimoniós com és el Protocol Unificat (Barlow et al., 2011) i la teràpia grupal transdiagnòstica TCC (Norton, 2012). Estudis recents i meta-anàlisis han demostrat que els tractaments transdiagnòstics són efectius en TEs respecte als grups en llista d'espera o al tractament habitual (Reinholt i Krogh, 2014) i fins i tot en comparació amb les intervencions destinades a trastorns específics (Pearl i Norton, 2017). Així mateix, l'eficàcia d'aquests resultats pot ser transferida al camp de les intervencions basades en Internet (Newby, McKinnon, Kuyken, Gilbody, i Dalgleish, 2015; Newby, Twomey, Yuan Li, i Andrews, 2016; Păsărelu, Andersson, Bergman Nordgren, i Dobrean, 2017).

Fins el moment, la majoria dels tractaments psicològics per als TEs (p.e. TCC o transdiagnòstic) s'han centrat, principalment, en intervencions dissenyades per a la dimensió d'afecte negatiu i han parat menys atenció a construir recursos positius. Alguns

estudis proposen que el sistema d'afecte positiu podria ser la clau per a facilitar la recuperació dels trastorns d'ansietat i depressió (Dunn, 2012; Fredrickson, 2013; Garland et al., 2010; Layous, Chancellor, i Lyubomirsky, 2014). Si tenim en compte el paper de l'afecte positiu en TEs, és necessari incloure aquesta dimensió com una estratègia d'intervenció especialment als tractaments transdiagnòstics (Carl, Soskin, Kerns, i Barlow, 2013).

Una perspectiva que va emergir amb força amb l'objectiu de reforçar el funcionament emocional positiu humà, i particularment l'afecte positiu, és la psicologia positiva (Seligman i Csikszentmihalyi, 2000). Aquesta pretén augmentar o generar una sèrie de factors protectors (p.e. benestar, resiliència, satisfacció amb la vida) que preparen la persona per a lidiar amb situacions d'estrès que pot trobar en el present o que poden aparèixer en el futur (Fredrickson, 2001; Tugade i Fredrickson, 2007; Vázquez i Hervás, 2008).

La psicologia positiva és especialment rellevant per a aquells que pateixen depressió. Per exemple, Santos et al. (2013) van concloure que les intervencions amb psicologia positiva redueixen tant els símptomes de depressió com la possibilitat de recaiguda durant els subseqüents períodes de depressió. A més a més, diversos meta-anàlisis han demostrat la seua efectivitat a l'hora de reduir la simptomatologia depressiva i d'incrementar el benestar (Bolier et al., 2013a; Chakhssi, Kraiss, Sommers-Spijkerman, i Bohlmeijer, 2018; Sin i Lyubomirsky, 2009; Weiss, Westerhof, i Bohlmeijer, 2016) emfatitzant el seu paper juntament amb tractaments convencionals per a la depressió clínica (Johnson i Wood 2015).

Pel que fa a les intervencions basades en Internet i les intervencions de psicologia positiva, la literatura ha posat de manifest resultats desiguals en relació amb la millora de la simptomatologia de la depressió (Bolier i Abello, 2014; Mitchell, Vella-Brodrick, i

Klein, 2010). Alguns estudis mostren que les intervencions de psicologia positiva *online* podrien augmentar el benestar dels participants i reduir la seua depressió en comparació de les condicions de control (Bolier et al., 2013b; Mitchell, Stanimirovic, Klein, i Vella-Brodrick, 2009; Seligman et al., 2005; Shapira i Mongrain, 2010; Wellenzohn, Proyer, i Ruch, 2016). Tot i això, altres estudis no ho fan (Abbott, Klein, Hamilton, i Rosenthal, 2009; Gander, Proyer, Ruch, i Wyss, 2013; Mitchell et al., 2009; Mongrain i Anselmo-Matthews, 2012; Woodworth, O'Brien-Malone, Diamond, i Schüz, 2016). A part d'això, la majoria de les intervencions de psicologia positiva *online* han emprat exercicis curts d'una setmana de durada si es comparen amb els tractaments convencionals, els qual usen sèries de mòduls i exercicis. Fins el moment, hi ha pocs estudis que inclouen programes més llargs i molts d'ells incorporen exercicis de psicologia positiva i d'altres disciplines com la teràpia cognitiva (Abbott et al., 2009; Bolier et al., 2013b; Roepke et al., 2015).

Així doncs, és necessari desenvolupar més estudis que investiguen l'eficàcia d'intervencions basades en Internet més complexes basades en la perspectiva transdiagnòstica i la psicologia positiva per tal de verificar la seua eficàcia (Görges, Oehler, von Hirschhausen, Hegerl, i Rummel-Kluge, 2018). En aquesta línia, Taylor, Lyubomirsky, i Stein (2017) i González-Robles, García-Palacios, Baños, Quero, i Botella (2017) avaluaren l'eficàcia de dos noves intervencions transdiagnòstiques basades en la psicologia positiva per augmentar l'afecte positiu en casos d'ansietat i depressió i obtingueren prometedors resultats d'eficàcia per al tractament de TEs. A més, Díaz-García et al. (2017) també desenvoluparen una intervenció basada en Internet i transdiagnòstica amb un component particular per abordar l'afecte positiu. El tractament de protocol va consistir en 16 mòduls que van incloure elements per reduir l'afecte negatiu, elements convencionals del tractaments basats en l'evidència per a TEs i elements per promoure l'afecte positiu. Aquesta intervenció també formà part d'un assaig controlat

aleatori amb dues altres condicions (un protocol a través d'Internet i transdiagnòstic sense un component d'afecte positiu i un grup de control en llista d'espera). Aquest projecte està en curs i no s'han publicat resultats per a aquest estudi.

2. Objectius

Atès que les intervencions de baixa intensitat basades en Internet, la perspectiva transdiagnòstica i les intervencions de psicologia positiva han començat a acumular evidència empírica per al tractament de la depressió, és necessari realitzar més estudis per demostrar la seua eficàcia en la pràctica d'Atenció Primària. Aquest estudi pretén explorar l'eficàcia i la cost-efectivitat d'un tractament habitual millorat (THM) per part del metge amb una intervenció computeritzada de baixa intensitat a través d'Internet centrada en la promoció de l'afecte positiu (THM+IPAP) comparada amb només el THM (només-THM), per al tractament de la depressió en centres espanyols d'Atenció Primària. Aquest assaig forma part del projecte FIS de l'Institut de Salut Carlos III del Ministeri d'Economia i Competitivitat espanyol (ETES n° PI13/00982; PSI2010-17563), el qual inclou un assaig controlat aleatori multicèntric en quatre condicions paral·leles: a) un programa psicoeducacional d'estil de vida saludable, b) un programa centrat en la promoció de l'afecte positiu, c) una breu intervenció basada en el *mindfulness* i d) un THM en l'Atenció Primària.

Només la informació clínica relacionada amb les condicions THM+IPAP i només-THM es tindran en compte en aquest estudi. Els objectius concrets són:

1. Examinar l'eficàcia de ambdues intervencions (THM+IPAP i només-THM) en la severitat de la depressió i altres variables secundàries (afecte, qualitat de vida en relació amb la salut, benestar i *mindfulness*) després del tractament i als seguiments (de 6 i 12 mesos).

2. Analitzar si ambdues intervencions (THM+IPAP i només-THM) són tractaments psicològics cost-efectius per a la depressió en un entorn d'Atenció Primària.
3. Observar l'opinió dels participants sobre el tractament rebut.
4. Analitzar si l'efecte de la condició (THM+IPAP vs. només-THM) varia en la severitat de la depressió a causa de l'afecte positiu.
5. Explorar si les variables sociodemogràfiques (sexe, edat, estat civil, nivell d'estudis, treball i nivell d'ingressos) i les variables clíniques de la línia base (severitat de la depressió, qualitat de vida en relació amb la salut, benestar i *mindfulness*) moderen els efectes de la severitat de la depressió després del tractament i els seguiments.

En concret, les **hipòtesis** d'aquest estudi són:

H1. La condició THM+IPAP serà més eficaç comparada amb la condició només-THM en la millora de la severitat de la depressió i altres variables secundàries (afecte, qualitat de vida en relació amb la salut, benestar i *mindfulness*) després del tractament i dels seguiments (de 6 a 12 mesos).

H2. La condició de THM+IPAP serà més cost-efectiva comparada amb la condició només-THM en termes de l'ús dels serveis sanitaris i socials (visites al metge de família, visites al servei d'urgències, absències al treball, deixar tasques habituals inacabades i reducció en la qualitat de tasques habituals per causa de problemes de salut) en el seguiments.

H3. L'opinió de l'usuari sobre el tractament (lògica, satisfacció, recomanació a altres i utilitat) serà millor per a la condició THM+IPAP en tots els moments de l'avaluació.

H4. Els participants de la condició THM+IPAP (comparats amb el control) tindran un major canvi en l'afecte positiu (després del tractament i el seguiments) donant lloc a una major reducció de la severitat de la depressió (després del tractament i el seguiments).

H5. No es generen hipòtesis específiques sobre quines variables moderadores (sociodemogràfiques i variables clíniques en la línia base) podrien ser significatives en l'efecte de la condició (THM + IPAP vs. només-THM) sobre la severitat de la depressió després del tractament i seguiments, a causa de l'exploratori naturalesa de les anàlisis.

3. Metodologia

3.1. Disseny

S'ha portat a terme un assaig controlat aleatori accessible amb avaluacions contínues (pre-tractament, post-tractament, 6 mesos de seguiment, 12 mesos de seguiment) i en dues condicions: THM+IPAP i només-THM (grup de control) en un entorn d'Atenció Primària.

3.2. Mostra

La mostra va ser estimada mitjançant G*Power 3 (Faul, Erdfelder, Lang, i Buchner, 2007). Es va requerir una mostra de 52 participants (26 per condició) tenint en compte una potència de 0.80, un nivell alfa de 0.05 i una magnitud de l'efecte baixa-mitja ($f = 0.20$ d'acord amb els estudis de Bolier et al., 2013b i Meyer et al., 2015). Segons la literatura sobre intervencions a través d'Internet, s'espera una taxa d'abandó d'entre el 20-30% (Spek et al., 2007; van Ballegooijen et al., 2014). Així doncs, el nombre total de participants que era necessari reclutar va ser 66.

3.3. Població estudiada, reclutament, criteris d'eligibilitat i aleatoritat

El reclutament va ser posat en pràctica en centres espanyols d'Atenció Primària de les regions d'Aragó, Andalusia i les Illes Balears. Va començar en maig de 2015 i va finalitzar en maig de 2017. El metge de família va completar un informe de derivació psicològica on descrivia les característiques generals del pacient per què l'investigador local contactés amb el participant. Tots els pacients interessats van haver de signar un informe de consentiment per poder formar part de l'estudi. Per confirmar els criteris d'inclusió (> de 18 anys, conèixer els criteris diagnòstics per al Trastorn Depressiu Major o el Trastorn de Depressió Persistent), l'investigador va administrar instruments d'avaluació a través d'una entrevista telefònica: la entrevista neuropsiquiàtrica internacional per a diagnòstic -MINI versió 5- (Ferrando et al., 1998), el qüestionari sobre la salut del pacient-9 (PHQ-9) (Diez-Quevedo, Rangil, Sanchez-Planell, Kroenke, i Spitzer, 2001) i un breu qüestionari sobre variables sociodemogràfiques.

Després de la realització del diagnòstic, els pacients van ser assignats aleatòriament a una de les dues condicions (THM+IPAP o només-THM). L'assignació va ser duta a terme per un investigador independent pertanyent a la REDIAPP (Red d'Investigació d'Activitats Preventives i Promoció de la Salut) que no va participar en l'estudi.

3.4. Intervencions

Tots els pacients que van participar en l'estudi (independentment del grup on van ser aleatòriament assignats) van ser tractats pels seus metges de família.

3.4.1. Tractament habitual millorat

El tractament habitual va ser millorat perquè els metges de família que participaren van rebre un programa d'entrenament sobre com diagnosticar i tractar la depressió. El

programa estava basat en la guia espanyola per al tractament de la depressió en l'Atenció Primària (Fernández et al., 2006). En cas de risc de suïcidi, disfunció social severa o empitjorament dels símptomes, es va recomanar derivar el pacient al servei de salut mental.

3.4.2. Tractament habitual millorat amb una intervenció computeritzada de baixa intensitat a través d'Internet centrada en la promoció de l'afecte positiu

Sessió cara a cara

A banda de rebre tractament per part del metge de família, els participants van participar en una sessió cara a cara de 90 minuts de durada (3-5 pacients) dirigida per un psicòleg clínic. L'objectiu de la sessió era explicar l'estructura del programa i els components principals del tractament, deixar clares les instruccions d'ús de la plataforma *online* i motivar els participants al canvi. En últim lloc, l'objectiu últim era reforçar el compromís i l'adhesió al tractament.

Programa d'intervenció online

El programa auto-guiat *online* va consistir en 4 mòduls terapèutics (60 minuts per mòdul aproximadament). La durada del programa podia variar entre els usuaris, però normalment va ser completat entre 4 i 8 setmanes (com a màxim 2 setmanes per mòdul). Aquests mòduls contenien elements multimèdia (vídeos, imatges, textos) que proporcionaven informació sobre la depressió i estratègies d'afrontament. Els mòduls eren seqüencials per avançar pas a pas al llarg del programa. Una volta acabat, l'usuari podia repassar els continguts.

En concret, aquesta intervenció seguia la perspectiva transdiagnòstica i estava basada en tècniques de la psicologia positiva. Va ser dissenyada principalment per disminuir la

severitat de la depressió i previndre recaigudes mitjançant la promoció del benestar i l'afecte positiu.

Per a més informació sobre el protocol per a la promoció de l'afecte positiu consulteu el capítol de García-Palacios, Mira, Mayoral, Baños, i Botella (2017) i el protocol de l'estudi de Castro et al. (2015).

3.5. Mesures

3.5.1. Mesura principal

Severitat de la depressió: Qüestionari sobre la Salut del Pacient-9 (PHQ-9; Kroenke, Spitzer, i Williams, 2001).

3.5.2. Mesures secundàries

Entrevista de diagnostic: entrevista neuropsiquiàtrica internacional per a diagnòstic versió 5.0 (M.I.N.I. 5.0; Ferrando et al., 1998; Sheehan et al., 1998).

Afecte: escala de l'afecte positiu i negatiu (PANAS; Sandín et al., 1999; Watson, Clark, i Tellegen, 1988).

Qualitat de vida en relació a la salut: qüestionari de salut SF-12 (SF-12; Vilagut et al., 2008; Ware, Kosinski, i Keller, 1996).

Benestar: L'índex de felicitat de Pemberton (PHI; Hervás i Vázquez, 2013).

Facetes del mindfulness: qüestionari de les cinc facetes del mindfulness (FFMQ; Baer, Smith, Hopkins, Krietemeyer, i Toney, 2006; Cebolla et al., 2012).

3.5.3. Altres indicadors

Ús dels serveis sanitaris i socials: qüestionari *ad hoc* de 5 preguntes per a les despeses relacionats amb l'ús dels serveis sanitaris i socials, la pèrdua de productivitat al treball, i l'impacte de la malaltia en les tasques habituals dels usuaris.

Informació sociodemogràfica: sexe, estat civil, nivell educatiu, ocupació i nivell d'ingressos.

Opinió sobre el tractament rebut.

3.6. Anàlisi de dades

Totes les anàlisis estadístiques van ser realitzades amb el software SPSS 24.0 (IBM) per a Windows.

Les anàlisis per intenció de tractar de models mixtos sense imputació *ad hoc* van ser emprats per afrontar la pèrdua d'informació (Chakraborty i Gu, 2009). La hipòtesi de què la informació faltava de manera completament aleatòria (MCAR) va ser avaluada amb el Little's MCAR test. Per tal d'analitzar l'efecte de la condició en els indicadors primaris (severitat de la depressió) i secundaris (afecte, qualitat de vida en relació amb la salut, benestar recordat i experimentat i facetes del *mindfulness*), així com la relació cost-efectivitat i l'opinió dels participants, s'implementaren 29 models mixtos lineals.

L'índex de canvi fiable (ICF) (Jacobson i Truax, 1991) per a la severitat de la depressió va ser calculat en la mostra completa.

Per analitzar els canvis en la severitat de la depressió i l'afecte tot tenint en compte l'assessorament posterior al mòdul en la condició THM+IPAP, es desenvoluparen 3 models mixtos lineals.

Finalment, per explorar les variables de mediació i moderació, es realitzaren les anàlisis de mediació i moderació mitjançant el procediment descrit per Hayes (2013) del PROCESS macro (versió 2.16). Es van elegir els models 4 i 1, respectivament.

4. Resultats

4.1. Participants i abandons

En principi, 113 participants van interessar-se per l'estudi, dels qual 47 van ser exclosos del procés. Finalment, es van incloure a l'estudi 66 participants, que foren aleatòriament assignats a cada condició (THM+IPAP, $n = 40$; només-THM, $n = 26$). El 25% dels participants de la condició THM+IPAP i el 19% de la condició només-THM van abandonar durant el post-tractament. El 47.5% dels participants de la condició THM+IPAP i el 23.07% de la condició només-THM abandonaren durant els 6 mesos de seguiment. Finalment, el 55% dels participants de la condició THM+IPAP i el 30.76% de la condició només-THM abandonaren durant els 12 mesos de seguiment.

Respecte el percentatge de participants que completaren cada mòdul en la condició THM+IPAP, només el 45% completaren tots els mòduls del tractament; el 65% va completar tres mòduls; el 72.5%, dos mòduls; i el 77.5%, un mòdul.

4.2. Diferències d'eficàcia entre les dues condicions del tractament

Severitat de la depressió (PHQ-9)

Va haver-hi un efecte principal significat amb el pas del temps en la severitat de la depressió, $F(3, 130.68) = 20.90, p < .001$, cosa que indica que ambdues condicions van ser eficaces en la disminució de la severitat en el temps. Però, no es va produir cap efecte significatiu de la interacció condició x temps en la severitat de la depressió, $F(3, 130.68) = 1.64, p = .182$.

Afecte (PANAS)

Va haver-hi un efecte principal significant amb el pas del temps en l'afecte positiu $F(3, 133.48) = 12.16, p < .001$, i l'afecte negatiu, $F(3, 130.30) = 9.14, p < .001$, cosa que indica que els dos grups van ser eficaços en l'increment de l'afecte positiu i la disminució de l'afecte negatiu en el temps. Però, no es va produir cap efecte significatiu de la interacció condició x temps en l'afecte positiu, $F(3, 133.48) = 0.57, p = .636$, i l'afecte negatiu, $F(3, 130.30) = 0.20, p = .896$.

Qualitat de vida en relació amb la salut (SF-12)

Va haver-hi un efecte principal significant amb el pas del temps en la salut en general $F(3, 125.79) = 3.53, p < .05$; dolor corporal, $F(3, 129.39) = 6.64, p < .001$; rol físic, $F(3, 133.41) = 5.54, p < .001$; salut mental, $F(3, 137.27) = 10.09, p < .001$; rol emocional, $F(3, 135.76) = 15.18, p < .001$; funcionament social, $F(3, 128.25) = 12.71, p < .001$; i vitalitat, $F(3, 135.75) = 7.85, p < .001$, excepte en la variable del funcionament físic, $F(3, 125.25) = 1.84, p = .143$. Aquests resultats indiquen que les dues condicions van ser eficaces a l'hora de millorar la qualitat de vida amb la salut física i mental en el temps. Però, no es va produir cap efecte significatiu de la interacció condició x temps en la salut general, $F(3, 125.79) = 2.07, p = .108$; dolor corporal, $F(3, 129.39) = 1.39, p = .247$; rol físic, $F(3, 133.41) = 0.62, p = .602$; funcionament físic, $F(3, 125.25) = 0.37, p = .777$; salut mental, $F(3, 137.27) = 0.85, p = .47$; rol emocional, $F(3, 135.76) = 2.30, p = .080$; funcionament social, $F(3, 128.25) = 1.55, p = .204$; i vitalitat, $F(3, 135.75) = 1.48, p = .224$.

Benestar (PHI)

Va haver-hi un efecte principal significant amb el pas del temps en el benestar total, $F(2, 75.75) = 17.84, p < .001$; benestar recordat, $F(2, 75.74) = 16.63, p < .001$; i benestar experimentat, $F(2, 95.74) = 3.29, p < .05$, cosa que indica que ambdues condicions van ser eficaces en l'increment del benestar en el temps. Però, no es va produir cap efecte significatiu de la interacció condició x temps en el benestar total, $F(2, 75.75) = 1.57, p = .215$; benestar recordat, $F(2, 75.74) = 1.51, p = .228$; i benestar experimentat, $F(2, 95.74) = 0.42, p = .661$.

Facetes del mindfulness (FFMQ)

Va haver-hi un efecte principal significant amb el pas del temps en la variable d'observar, $F(2, 77.14) = 9.49, p < .001$; actuar de manera conscient, $F(2, 78.35) = 5.05, p < .01$; no jutjar l'experiència interior, $F(2, 79.92) = 5.28, p < .01$; i no reaccionar a l'experiència interior, $F(2, 80.99) = 6.10, p < .01$, excepte en descriure, $F(2, 78.88) = 1.81, p = .170$. Aquests resultats indiquen que les dues condicions del tractament van ser eficaces a l'hora de millorar les facetes del *mindfulness* en el temps. Però, no es va produir cap efecte significatiu de la interacció condició x temps en observar, $F(2, 77.14) = 0.36, p = .697$; descriure, $F(2, 78.88) = 1.25, p = .293$; actuar de manera conscient, $F(2, 78.35) = 0.55, p = .581$; no jutjar l'experiència interior, $F(2, 79.92) = 0.59, p = .553$; i no reaccionar a l'experiència interior, $F(2, 80.99) = 0.57, p = .568$.

4.2.1. Canvi clínicament significant en la severitat de la depressió (PHQ-9)

En general, ambdues condicions del tractament mostraren un alt percentatge de participants "sense canvis" durant el post-tractament, participants "millorats" durant el seguiment 1 i participants "sense canvis" durant el seguiment 2.

4.3. Diferències en la relació cost-efectivitat entre les dues condicions del tractament

No va haver-hi un efecte principal significat amb el pas del temps en el nombre de visites al metge de família durant els últims 3 mesos $F(2, 53.19) = 2.96, p = .061$; el nombre de visites a emergències durant els últims 3 mesos, $F(2, 16.51) = 1.33, p = .292$; el nombre de dies de treball durant l'últim any, $F(2, 25.17) = 0.18, p = .839$; i el nombre de dies en què les tasques habituals no es van finalitzar per causa de problemes de salut durant l'últim mes, $F(2, 47) = 1.48, p = .239$, excepte en el nombre de dies en què la qualitat de les tasques habituals es va veure reduïda per causa de problemes de salut durant l'últim mes. Però, no es va produir cap efecte significatiu de la interacció condició x temps en el nombre de visites al metge de família durant els últims tres mesos, $F(2, 53.19) = 0.11, p = .897$; el nombre de visites a emergències durant els últims 3 mesos, $F(2, 16.51) = 0.54, p = .591$; el nombre de dies de treball durant l'últim any, $F(2, 25.17) = 2.29, p = .122$; el nombre de dies en què les tasques habituals no es van finalitzar per causa de problemes de salut durant l'últim mes, $F(2, 47) = 0.81, p = .451$; i el nombre de dies en què la qualitat de les tasques habituals es va veure reduïda per causa de problemes de salut durant l'últim mes, $F(2, 47.55) = 1.38, p = .262$.

4.4. Opinió dels participants sobre el tractament rebut

Va haver-hi un efecte principal significat en la lògica del tractament, $F(1, 60.24) = 12.67, p \leq .001$; el grau de satisfacció amb el tractament, $F(1, 61.61) = 12.91, p \leq .001$; la recomanació del tractament a altres persones, $F(1, 62.54) = 15.97, p \leq .001$; la utilitat del tractament en el cas propi, $F(1, 60.77) = 10.97, p \leq .001$; i la utilitat del tractament per a altres problemes psicològics, $F(1, 62.24) = 8.54, p < .01$.

Va haver-hi un important efecte principal de la condició en la lògica del tractament, $F(1, 60.24) = 12.67, p \leq .001$; el grau de satisfacció amb el tractament, $F(1, 61.61) =$

12.91, $p \leq .001$; la recomanació de tractament als altres, $F(1, 62.54) = 15.97$, $p \leq .001$; utilitat del tractament en el cas propi, $F(1, 60.77) = 10.97$, $p \leq .001$; i la utilitat del tractament per a altres problemes psicològics, $F(1, 62.24) = 8.54$, $p < .01$, indicant que els participants en la condició THM+IPAP van mostrar una millor opinió sobre el tractament rebut en tots els punts del temps que els participants de la condició només-THM.

Però, no es va produir cap efecte significatiu de la interacció condició x temps en relació a la lògica del tractament, $F(1, 54.99) = 2.69$, $p = .107$; el grau de satisfacció amb el tractament, $F(1, 54.46) = 2.45$, $p = .123$; i la utilitat del tractament per a altres problemes psicològics, $F(1, 53.78) = 1.24$, $p = .27$, excepte en la recomanació del tractament a altres persones, $F(1, 56.41) = 5.66$, $p < .05$; i la utilitat del tractament en el cas propi, $F(1, 54.49) = 5.83$, $p < .05$.

4.5. Afecte positiu com a mediador

No hi va a ver efectes indirectes significants en cap dels models, cosa que indica que el canvi en l'afecte positiu, (resultats del post-tractament, seguiment 1 i seguiment 2-PANAS) no va afectar a la relació entre la condició i la severitat de la depressió (resultats del post-tractament, seguiment 1 i seguiment 2-PHQ-9). Ni els efectes directes ni l'efecte total dels models van resultar significants.

4.6. Models de moderació

Variables sociodemogràfiques

Les anàlisis mostraren que les variables sociodemogràfiques no van moderar l'efecte de la condició en els resultats posteriors al qüestionari PHQ-9 ($p > .05$).

*Variables clíniques de la línia base**Severitat de la depressió (PHQ-9)*

La mesura PHQ-9 no va moderar l'efecte de la condició en els resultats posteriors (post-tractament i en el seguiments) al PHQ-9 ($p > .05$).

Qualitat de vida en relació amb la salut (SF-12)

La variable de funcionament físic va moderar l'efecte de la condició en els resultats al PHQ-9 en el post-tractament. Els participants del THM+IPAP amb altes puntuacions en el funcionament físic en el pre-tractament aconseguiren una menor puntuació en el PHQ-9 durant el post-tractament, $b = 6.11$, 95% CI [2.41, 9.80], $t = 3.32$, $p = .002$.

A més, la variable rol emocional va moderar l'efecte de la condició en els resultats al PHQ-9 en el post-tractament. Els participants de la condició THM+IPAP que partiren amb baixes puntuacions en el rol emocional en el pre-tractament aconseguiren una menor puntuació en el PHQ-9 durant el post-tractament, $b = 3.46$, 95% CI [0.11, 6.81], $t = 2.08$, $p = .043$.

Finalment, la variable funcionament social va moderar l'efecte de la condició en els resultats al PHQ-9 en el seguiment 1 (6 mesos), però de forma marginalment significativa. Els participants de la condició THM+IPAP que partiren amb baixes puntuacions en el funcionament social en el pre-tractament aconseguiren una menor puntuació en el PHQ-9 durant el seguiment 1, $b = 6.04$, 95% CI [0.42, 11.66], $t = 2.19$, $p = .036$.

La resta de variables del SF-12 no van moderar l'efecte de la condició sobre les puntuacions del PHQ-9 en el post-tractament i en els seguiments.

Benestar (PHI)

Cap variable de la mesura PHI va moderar l'efecte de la condició en els resultats posteriors (post-tractament i en el seguiments) al PHQ-9: benestar total, benestar recordat i benestar experimentat ($p > .05$).

Facetes del mindfulness (resultats FFMQ)

La variable observar va moderar de manera marginal significant l'efecte de la condició en els resultats posteriors al PHQ-9. Els participants de la condició THM+IPAP que partiren amb baixes puntuacions en observar en el pre-tractament aconseguiren una menor puntuació en el PHQ-9 durant el post-tractament, $b = 3.93$, 95% CI [0.59, 7.26], $t = 2.37$, $p = .022$.

A banda d'això, la variable descriure va moderar l'efecte de la condició en els resultats posteriors al PHQ-9. Els participants de la condició THM+IPAP que partiren amb baixes puntuacions en la variable descriure en el pre-tractament aconseguiren una menor puntuació en el PHQ-9 durant el post-tractament $b = 6.87$, 95% CI [2.71, 11.04], $t = 3.32$, $p = .002$.

La resta de variables del FFMQ no van moderar l'efecte de la condició sobre les puntuacions del PHQ-9 en el post-tractament i en el seguiments.

5. Discussió i conclusions

5.1. Eficàcia dels tractaments per a la depressió en atenció primària

La primera hipòtesi proposada va ser que la condició THM+IPAP seria més eficaç comparada amb la condició només-THM respecte a la millora de la severitat de la depressió i altres variables secundàries (afecte, qualitat de vida en relació amb la salut, benestar i *mindfulness*) després del tractament i els seguiments. Aquesta hipòtesi no es va confirmar.

Ambdues intervencions van resultar igualment eficaces a l'hora de reduir la severitat de la depressió i l'afecte negatiu, així com d'incrementar la resta de variables relatives al funcionament positiu (afecte positiu, qualitat de vida en relació a la salut, benestar i facetes del *mindfulness*) fins el mes 12 del seguiment. L'índex d'adherència va ser major en la condició només-THM.

Tot i que no hi hagueren diferències estadísticament significatives entre els tractaments, ens agradaria subratllar dos aspectes: en primer lloc, sembla que la condició THM+IPAP va produir millores més ràpides i amb unes magnituds de l'efecte del tractament majors a curt termini. I en segon lloc, sembla que la condició només-THM va resultar més eficaç a l'hora de generar i mantenir els canvis a llarg termini (excepte per a les variables del *mindfulness*).

En relació amb l'alt índex d'abandonament de la condició THM+IPAP, ens agradaria matissar que aquest tractament va ser més eficaç a curt termini, cosa que ens fa considerar si aquesta gran eficàcia podria ser la responsable dels abandonaments del tractament en un context amb una adherència tan limitada a l'ordinador.

Per tal d'explicar els resultats sobre l'eficàcia i els abandonaments, en agradaria considerar altres possibles factors (p.e. la duració i el nombre de mòduls, la teràpia de suport) (Sin, Della Porta, i Lyubomirsky. 2011). Aquest factors seran detallats a continuació.

Duració i nombre dels mòduls dels tractaments: Algunes evidències demostren que les intervencions de psicologia positiva amb una major duració (més setmanes) són més eficaces a l'hora de reduir la simptomatologia de la depressió i d'incrementar el benestar que les intervencions més curtes (Sin i Lyubomirsky, 2009). En aquest sentit, les intervencions més llargues poden permetre que els pacients tinguin més temps de practicar activitats, ajudant, així, a convertir-les en hàbits.

La majoria dels estudis sobre les intervencions de psicologia positiva *online* normalment empen exercicis curts d'una setmana de duració en comparació amb els tractaments estàndard, que usen una sèrie de mòduls i exercicis (Görges et al., 2018). Així doncs, és necessari dur a terme més investigacions per determinar la duració apropiada (més llarga o més curta) dels programes del tractament basats en la psicologia positiva i així aconseguir que segueixen eficaces a llarg termini.

Inclusió del suport del terapeuta en la intervenció basada en Internet: S'ha observat que les intervencions basades en Internet són més eficaces quan s'ofereix més suport per part del terapeuta (Baumeister et al., 2014; Berger et al., 2011; Richards i Richardson, 2012). En una línia similar, s'ha comprovat que les intervencions de psicologia positiva sense suport per part d'un terapeuta no són tan eficaces com la teràpia individual o en grup (Sin i Lyubomirsky, 2009).

Auto-selecció i motivació en relació al tractament assignat: Les probes mostren que les intervencions en què les persones elegeixen lliurement participar tendeixen a tindre

més èxit que les intervencions en què les persones han sigut assignades (Sin i Lyubomirsky, 2009). Possiblement, aquestes persones estaven més motivades i, per tant, mantenien una actitud més responsable i entusiasta a l'hora de seguir les directrius de les intervencions.

Implicació del metge de família en el tractament: El grup de control en aquest estudi va consistir en un THM, cosa que significa que el metge de família va haver d'aplicar un tractament mèdic (p.e. medicació) i també seguir les directrius recomanades pel tractament per a la depressió en l'Atenció Primària segons les guies. És possible que aquesta indicació, sumada al fet de saber que estaven participant en un estudi de prova controlat, haja afavorit el seguiment efectiu de les directrius i per això la condició només-THM va resultar tan eficaç.

Finalment, tenint en compte *el grau d'implicació dels participants en el tractament*, la realització del THM+IPAP va implicar que tingueren un paper més actiu en relació amb la seua resposta al tractament. A més de rebre un THM (medicació, sessions amb el seu metge de família) hagueren de dur a terme una intervenció a través d'Internet. Açò podria donar com a resultat un nivell d'implicació millor per part dels participants (en matèria de temps, activitat, ocupació) en comparació als participants de la condició només-THM.

5.2. Cost-efectivitat de les dues condicions del tractament

La segona hipòtesi proposava que la condició THM+IPAP resultaria més cost-efectiva que la condició només-THM en termes de l'ús dels serveis sanitaris i socials (visites al metge de família, visites al servei d'urgències, absències al treball, deixar tasques habituals inacabades i reducció en la qualitat de tasques habituals per causa de problemes de salut) en els seguiments. Aquesta hipòtesi no es va confirmar i els resultats

només mostraren que ambdós tractaments (THM+IPAP i només-THM) van resultar igualment eficaços a l'hora de produir canvis en la qualitat de tasques quotidianes (nombre de dies en què la qualitat de les tasques quotidianes s'havien reduït a causa de problemes de salut durant l'últim mes) al llarg del temps.

Aquests resultats se situen en la mateixa línia que estudis similars com el de Duarte et al. (2017) el qual va demostrar que no sembla que les intervencions amb suport i a través d'Internet siguen més cost-efectives que el tractament del metge des d'una perspectiva sanitària. A més a més, Kenter et al. (2015) confirmaren que l'assistència combinada (intervencions a través d'Internet en combinació amb sessions cara a cara) era més cara en comparació amb els tractaments cara a cara establerts i no s'aconseguien millors resultats en termes de funcionament general.

5.3. Anàlisis post-mòduls en la condició THM+IPAP: Canvis en la severitat de la depressió i l'afecte

La IPAP va ser eficaça en la reducció de la severitat de la depressió i l'afecte negatiu i en l'increment de l'afecte positiu al llarg dels mòduls del tractament. Tot i això, l'efecte dels mòduls va ser millor entre l'1 i el 2. Així doncs, sembla que les intervencions basades en Internet tenen un impacte inicial important en totes les variables, cosa que reforça la idea d'una trajectòria més ràpida en la millora de la simptomatologia.

Pel que fa al percentatge de participants que van completar cada mòdul, només el 45% dels participants van completar tots els mòduls del tractament, el 65% van completar tres mòduls, el 72.5% dos mòduls i el 77.5% un mòdul. Com es va esmentar anteriorment, la disminució del nombre de participants per mòdul podria explicar-se pel grau d'implicació que aquest tractament els suposava, en comparació amb la condició només-

THM. A més, la severitat de la depressió dels participants i la millora de la simptomatologia també poden influir en la resposta als mòduls del tractament.

5.4. Opinió dels participants sobre el tractament rebut

La tercera hipòtesi proposava que l'opinió dels participants sobre el tractament seria millor en la condició THM+IPAP. Aquesta hipòtesi es va confirmar, ja que els participants de THM+IPAP van mostrar una millor opinió sobre el tractament rebut (en termes de lògica, satisfacció, recomanació a altres persones, utilitat per al problema en el cas propi, i la utilitat per a altres problemes psicològics) en tots els moments d'avaluació.

5.5. Afecte positiu com a mediador

La quarta hipòtesi proposava que els participants de THM+IPAP incrementarien més el seu afecte positiu (després del tractament i els seguiments), donant lloc a una major reducció en la severitat de la depressió (després del tractament i els seguiments). Aquesta hipòtesi no es va confirmar perquè l'efecte de la condició en les puntuacions de la severitat de la depressió després del tractament i els seguiments no es va veure mediat pel canvi en l'afecte positiu en qualsevol moment de l'avaluació. Aquest resultat suggereix que la IPAP no era tan eficaç a l'hora de produir canvis en l'afecte positiu. Com es va explicar anteriorment, no es van trobar diferències estadísticament significatives entre els tractaments, i la inclusió de la IPAP no va donar com a resultat majors grandàries de l'efecte en comparació amb la condició de control per a reduir els símptomes de depressió a llarg termini.

Encara que les intervencions de psicologia positiva s'han utilitzat sovint per promoure el benestar i regular l'afecte positiu en l'individu, les seues implicacions en l'àmbit clínic semblen qüestionables segons la literatura (p.e., Mongrain i Anselmo-

Matthews, 2012). Per exemple, en alguns estudis no s'han trobat diferències entre les intervencions de psicologia positiva *online* i els grups placebo per augmentar la felicitat i reduir la depressió (Woodworth, O'Brien-Malone, Diamond, i Schütz, 2016a). És important seguir investigant els factors mediadors dels efectes en aquest tipus d'intervencions sobre la severitat de la depressió (Woodworth, O'Brien-Malone, Diamond, i Schütz, 2016b).

5.6. Models de moderació

No es van generar hipòtesis específiques sobre quines variables moderadores (variables sociodemogràfiques i clíniques) podrien ser significatives en l'efecte de la condició (THM+IPAP vs. només-THM) sobre la severitat de la depressió (després del tractament i els seguiments), a causa de la naturalesa exploratòria de les anàlisis.

Els resultats van mostrar que les variables sociodemogràfiques (sexe, estat civil, nivell educatiu, ocupació i nivell d'ingressos) i algunes variables clíniques de la línia base com la severitat de la depressió, la qualitat de vida relacionada amb la salut (salut en general, dolor corporal, rol físic, salut mental i vitalitat), el benestar (el benestar total, el benestar recordat i el benestar experimentat) i les facetes de *mindfulness* (actuant de manera conscient, no jutjar l'experiència interior i no reaccionar a l'experiència interior) no van moderar l'efecte de la condició sobre les puntuacions de la severitat de la depressió després del tractament i els seguiments. A continuació veurem algunes excepcions.

Els participants de la condició de THM+IPAP amb una puntuació basal més alta en la variable de funcionament físic i més baixa en la variable de rol emocional van aconseguir puntuacions més baixes en la severitat de la depressió després del tractament. A més, els participants amb una puntuació basal més baixa en la variable de funcionament

social van aconseguir puntuacions més baixes en la severitat de la depressió en el seguiment de 6 mesos.

El bon funcionament físic (com a factor protector de depressió) dels participants en el pretractament podria haver contribuït a una major adhesió a les directrius de la IPAP (una de les quals es va centrar en el paper de l'activitat en el benestar) (Warburton, Nicol, i Bredin, 2006). A més, altres estratègies terapèutiques de la IPAP (p.e. la regulació emocional o el suport social) podrien haver ajudat a millorar la seua funció emocional (intel·ligència emocional) i funcionament social (habilitats socials), cosa que va comportar en una millora de la severitat de la depressió al llarg del temps. Aquests resultats recolzen la idea que la regulació emocional (Extremera i Rey, 2015) i el suport social (Chou i Chi, 2001) poden moderar l'efecte de la depressió.

Pel que fa a les facetes del *mindfulness*, els participants de la condició de THM+IPAP amb una puntuació basal més baixa en les variables observar i descriure van aconseguir puntuacions més baixes en la severitat de la depressió després del tractament. Per tant, la inclusió de la IPAP com a tractament complementari (centrat també en aspectes relacionats amb el *mindfulness*) va permetre als participants assistir a les seues experiències internes i externes (p.e. sensacions, pensaments o emocions), i també etiquetar-les amb paraules, contribuint així a la millora de la severitat de la seua depressió. Aquests resultats indiquen que és important considerar les habilitats del *mindfulness* dins de les intervencions de psicologia positiva per a reduir la simptomatologia depressiva (Cebolla, Enrique, Alvear, Soler, i García-Campayo 2017; Sin et al., 2011).

Es necessiten més estudis per identificar els moderadors potencials de les intervencions de psicologia positiva *online* per a la depressió en un context d'Atenció Primària.

5.7. Limitacions

Cal assenyalar algunes limitacions de l'estudi actual:

En primer lloc, la taxa d'abandonaments en ambdues condicions i especialment en la condició THM+IPAP podria haver afectat la potència estadística i, per tant, en la resta de les anàlisis (eficàcia, cost-efectivitat, opinió, mediació i moderació) del present estudi.

En segon lloc, no tenim informació sobre els motius d'abandonament dels participants. És rellevant explorar les seues raons per trobar maneres d'abordar aquest problema. La perspectiva qualitativa podria ajudar a analitzar aquestes experiències d'una manera més clara i profunda (Fernández-Álvarez et al., 2017).

En tercer lloc, no tenim cap registre sobre les sessions amb el metge per temes de la depressió i tampoc sobre la dosi de la medicació. Caldria considerar aquestes variables en el futur i analitzar si els participants sota una intervenció basada en Internet reben menys atenció mèdica i, per tant, aquesta podria ser una variable d'eficàcia en aquest tractament.

En quart lloc, no tenim informació sobre el diagnòstic de possibles trastorns comòrbids de depressió. Hauria estat interessant saber si els tractaments també eren eficaços en produir canvis respecte a altres simptomatologies com l'ansietat. D'aquesta manera, podríem haver obtingut més informació sobre el paper que jugava la IPAP, que es basava en la perspectiva transdiagnòstica.

En cinquè lloc, la informació sobre la història anterior de depressió dels participants no s'ha tingut en compte en aquest estudi. Aquestes dades són importants perquè la possible cronicitat o familiaritat amb els tractaments (mèdics o psicològics) podria haver influït en els resultats (p.e. Görge et al., 2018).

Finalment, aquest estudi no va utilitzar un instrument de mesura validat per analitzar la relació cost-efectivitat dels tractaments avaluats. És important que tots els assajos controlats incloguen els mateixos instruments o similars per analitzar la seua evidència d'una manera més sistemàtica.

5.8. Línies futures

En aquest estudi, incloem alguns elements relacionats amb el suport terapèutic per augmentar l'adhesió a la intervenció basada en Internet. En concret, hi va haver una sessió grupal cara a cara amb un terapeuta per explicar la intervenció. A més, incloem missatges setmanals de text i correus electrònics per animar els participants a continuar amb el programa i realitzar tasques. La investigació futura podria explorar altres tipus de suport terapèutic (per exemple, assistència telefònica setmanal, ús de terapeutes en línia) per analitzar si hi ha una major participació i una major adherència al tractament informatitzat. Fins ara, s'ha demostrat que el suport terapèutic s'associa positivament amb una major eficàcia i una menor taxa d'abandonament de les intervencions basades en Internet (p.e. Johansson i Andersson, 2012; Richards i Richardson, 2012).

Un altre aspecte que seria interessant analitzar en el futur és la inclusió d'altres components psicoterapèutics destinats a la regulació del afecte negatiu (p.e. TCC) juntament amb la IPAP, com en altres estudis (p.e. Díaz et al., 2017). Això ens permetria saber si la IPAP seria més eficaç pel que fa a la simptomatologia depressiva i altres variables relacionades amb el funcionament positiu.

Altres estudis podrien incloure intervencions adaptades a les característiques, necessitats i preferències dels pacients amb depressió i possibles trastorns comòrbids (Batterham, Calear, Farrer, McCallum, i Cheng, 2018). D'aquesta manera, els

professionals de la salut (metges de capçalera i psicòlegs) tractarien de manera més eficaç la depressió (Johansson et al., 2012).

A més, es necessiten dissenys híbrids per avançar en l'eficàcia clínica (per proporcionar tractaments basats en l'evidència) i en la implementació (tenint en compte processos com planificar, educar, finançar, reestructurar, gestionar la qualitat i context de política) per millorar la seua traducció a la rutina d'assistència sanitària per al tractament de la depressió (Powell et al., 2012).

Fins ara, la majoria dels tractaments basats en l'evidència (*online*) per a la depressió s'han dispensat a través d'ordinadors. Els estudis futurs també haurien de tenir en compte altres tecnologies innovadores (per exemple, telèfons intel·ligents, avatars i realitat virtual) per millorar l'accés a aquests tractaments i, fins i tot, els seus efectes (Cuijpers et al., 2017). Una metaanàlisi recent mostra que els dispositius intel·ligents són una eina prometedora d'autogestió per a la depressió (Firth et al., 2017). Es necessiten més estudis sobre l'aplicació d'aquestes tecnologies en un entorn d'Atenció Primària.

5.9. Conclusions

Aquest és el primer estudi a Espanya que analitza l'eficàcia i la relació cost-efectivitat d'una intervenció basada en Internet de baixa intensitat centrada en la perspectiva transdiagnòstica i la psicologia positiva combinada amb el THM per part del metge i en comparació amb el només-THM, per al tractament de la depressió en un context d'Atenció Primària. A més, aquest treball proporciona dades sobre l'eficàcia d'ambdues intervencions al llarg del temps en relació amb els canvis aconseguits després del tractament (seguiment de 6 i 12 mesos).

Les principals conclusions sobre els objectius d'aquesta tesi es presenten en els següents punts:

- La inclusió d'una intervenció basada en Internet no va millorar substancialment els resultats de la severitat de la depressió en comparació amb el només-THM. Tanmateix, els nostres resultats recolzen l'ús d'intervencions basades en Internet de baixa intensitat per promoure millores més ràpides en la depressió, juntament amb el THM. La seua implementació en centres d'Atenció Primària ajudaria tant al pacient (que sovint no rep un tractament adequat o es troba a la llista d'espera) i el metge de capçalera (que no té prou temps de consulta per oferir un tractament adequat) per reduir la bretxa entre la demanda i l'oferta del tractament.
- El nostre estudi no va recolzar la idea que la intervenció basada en Internet de baixa intensitat, juntament amb el THM, era més cost-efectiva en comparació amb el només-THM. Ambdós tractaments van ser igualment cost-efectius només pel que fa a la qualitat del rendiment de les tasques habituals.
- Pel que fa a l'opinió dels participants sobre el tractament rebut, el THM+IPAP es va valorar millor que el només-THM des del tractament previ al tractament posterior. Això suggereix que les tecnologies podrien ser una eina atractiva per al tractament de la depressió en l'Atenció Primària.
- El afecte positiu no era una variable medidora per a la relació entre la condició i la severitat de la depressió.
- Algunes variables de la qualitat de vida relacionada amb la salut (funcionament físic, rol emocional, funcionament social) i les facetes de *mindfulness* (observar i descriure) van ser variables moderadores associades a un millor pronòstic en la depressió després del THM+IPAP.

És important continuar investigant el paper de les intervencions basades en Internet de baixa intensitat guiades per a la depressió i en un context d' Atenció Primària, tenint en compte la perspectiva transdiagnòstica, la psicologia positiva, els programes personalitzats, les estratègies d'implementació i altres dispositius tecnològics, com els telèfons intel·ligents.

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INTRODUCTION

Depression is the most common mental disorder in the health care services. Specifically, 60% of patients with depression are attended to in primary care centers (Fernández et al., 2006).

This psychological problem presents a high rate of comorbidity with other disorders, and if not treated correctly, its course tends to become chronic, interfering significantly in different areas of the individual's functioning (Wittchen et al., 2011). Therefore, effective treatments that can be easily applied and disseminated are needed (Collins et al., 2011).

So far, there are numerous evidence-based psychological treatments (e.g., cognitive-behavioral therapy) for depression (Cuijpers, van Straten, van Oppen, Andersson, 2008; Cuijpers et al., 2013; Huhn et al., 2014). However, despite the existence of these treatments, the provision of mental health services is considerably low in terms of access and quality (Kazdin & Blase, 2011). In fact, less than 50% of people receive appropriate treatment, due to the cost, time required or lack of well-trained professionals (Gaston, Abbot, Rapee, & Neary, 2006). A fundamental challenge in research is the dissemination of these treatments, that is, making them available to all those who need them. Numerous studies have already shown that it is possible to apply these treatments via the Internet without losing their effectiveness (Andersson & Cuijpers, 2009; Andersson, 2016; Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010). In addition, several meta-analyses show that these treatments have effects comparable to those of face-to-face treatments (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014; Andersson, Topooco, Havik, & Nordgreen, 2016). Moreover, low-intensity psychological interventions, applied by Information and Communication Technologies could be an efficacious and cost-effective therapeutic option for the treatment of depression in primary care, given their potentialities (Donker et al., 2015).

Finally, although good efficacy data are available, further efforts are needed to find ways to treat depression in its different manifestations (e.g., degree of severity) and in different healthcare settings (e.g., primary care, specialized care).

In recent years, the transdiagnostic perspective (Sauer-Zavala et al., 2017) has received considerable importance as one of the approaches to improve the understanding and treatment of emotional disorders, including depression and anxiety. This perspective emphasizes the role of emotional regulation as a key concept in understanding and treating emotional disorders (Brown & Barlow, 2009).

It is worth to consider, in addition, a relevant aspect proposed to improve the currently available treatments: the promotion of positive affect. Thus far, psychological treatments for emotional disorders have focused primarily on the dimension of negative affect. Taking into account the central factors defended from the transdiagnostic perspective to explain the vulnerability of the emotional disorders, it is necessary to improve the intervention strategies for the positive affect dimension (Carl, Soskin, Kerns, & Barlow, 2013). Another perspective that emerged precisely with the aim of enhancing the positive aspects of the human being is the Positive Psychology movement (Seligman & Csikszentmihalyi, 2000). This perspective is especially relevant to people suffering from depression (e.g., Santos et al., 2013).

Therefore, the general objective of this dissertation is to investigate the efficacy and cost-effectiveness of an improved treatment as usual (ITAU) with a low-intensity Internet-based computerized intervention focused on the promotion of positive affect (ITAU+IPPA) for the treatment of depression, compared to only the ITAU (only-ITAU) in Spanish primary care (PC) settings. Concretely, this dissertation is composed by the following chapters:

In **chapter 1** “Depression and new psychotherapeutic approaches”, a review of the scientific literature will be carried out to frame the topic of study, a key process in this research.

In **chapter 2** “Efficacy and cost-effectiveness of a low-intensity Internet-based intervention focused on the promotion of positive affect for the treatment of depression in primary care: a randomized control trial”, the experimental study of this dissertation will be presented.

Finally, in **chapter 3** “General discussion”, the main findings, limitations and future lines of research will be discussed.

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CHAPTER

1

DEPRESSION AND NEW PSYCHOTHERAPEUTIC APPROACHES

1. Depression

1.1. Concept and diagnosis

Depression is a term that refers both to a transient mood state and a clinical syndrome or disorder characterized by the presence of a variety of *behavioral* (e.g., psychomotor agitation or retardation, avoidance behaviors in daily tasks and social interactions), *cognitive* (e.g., inability to concentrate, ruminations, dysfunctional beliefs), *emotional* (e.g., sadness, frustration, irritability, feeling of failure or emptiness), *motivational* (e.g., anhedonia, apathy or indifference), and *somatic* (e.g., sleeping problems, appetite and weight changes, fatigue) manifestations (Carrobbles, 2011; Vázquez & Sanz, 2008). The range and severity of symptoms varies from individual to individual and over time. Depression is also associated with an increased risk of mortality (Cuijpers & Smit, 2002), and it can lead to suicide (Li et al., 2017).

To diagnose depression, the criteria most commonly used in both clinical and research settings are those contained in the Diagnostic and Statistical Manual of Mental Disorders (DSM) of the American Psychiatric Association (APA), and in the International Classification of Diseases (ICD) of the World Health Organization (WHO) (Evans et al., 2013).

According to the DSM-5 (APA, 2013), the diagnosis of a Major Depressive Episode (MDE) is established by the presence of at least five of the nine symptoms listed, with at least one of them being depressed mood or loss of interest or pleasure in activities. Moreover, the symptoms must be maintained for at least two weeks and cause clinically significant distress or impairment in social, occupational, or other important areas of the person's activity. Table 1 shows the diagnostic criteria for Major Depressive Disorder (MDD) according to the DSM-5 (APA, 2013).

Table 1. Diagnostic criteria for MDD according to DSM-5 (APA, 2013, p. 160).

Major Depressive Disorder

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning: at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective reports (e.g., feels sad, empty, hopeless) or observations made by others (e.g., appears tearful).
(Note: In children and adolescents, it can be irritable mood).
2. Markedly diminished interest or pleasure in all or almost all activities most of the day, nearly every day (as indicated by either subjective accounts or observations).
3. Significant weight loss when not dieting, or weight gain (e.g., a change of more than 5% of body weight in a month), or a decrease or increase in appetite nearly every day.
(Note: In children, consider failure to make expected weight gain).
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective accounts or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

Note: Criteria A-C represent a major depressive episode.

Note: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual's history and the cultural norms for the expression of distress in the context of loss.

D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum or other psychotic disorders.

E. There has never been a manic episode or a hypomanic episode.

Note: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

Table 1. Continued

Specifiers for the number of episodes:

- Single episode.
- Recurrent episode.

Severity/course specifier:

- Mild.
- Moderate.
- Severe.
- With psychotic features.
- In partial remission.
- In full remission.
- Unspecified.

Specifiers for the current episode:

- With anxious distress.
 - With mixed features.
 - With melancholic features.
 - With atypical features.
 - With mood-congruent psychotic features.
 - With mood-incongruent psychotic features.
 - With catatonia.
 - With peripartum onset.
 - With seasonal pattern (recurrent episode only).
-

The diagnosis of Persistent Depressive Disorder (Dysthymia) represents a consolidation of DSM-IV-defined chronic MDD and dysthymic disorder (APA, 2013). The symptoms of dysthymia are similar to those of an MDE, but they tend to be less intense and last longer. Table 2 shows the diagnostic criteria for Persistent Depressive Disorder (Dysthymia) according to the DSM-5 (APA, 2013).

Table 2. Diagnostic criteria for Persistent Depressive Disorder (Dysthymia) according to the DSM-5 (APA, 2013, p. 168).

Persistent Depressive Disorder (Dysthymia)

A. Depressed mood for most of the day, for more days than not, as indicated by either subjective accounts or observations by others, for at least 2 years.

Note: In children and adolescents, mood can be irritable and duration must be at least 1 year.

B. Presence, while depressed, of two (or more) of the following:

1. Poor appetite or overeating.
2. Insomnia or hypersomnia.
3. Low energy or fatigue.
4. Low self-esteem.
5. Poor concentration or difficulty making decisions.
6. Feelings of hopelessness.

C. During the 2-year period (1 year for children or adolescents) of the disturbance, the individual has never been without the symptoms in Criteria A and B for more than 2 months at a time.

D. Criteria for a major depressive disorder may be continuously present for 2 years.

E. There has never been a manic episode or a hypomanic episode, and criteria have never been met for cyclothymic disorder.

F. The disturbance is not better explained by a persistent schizoaffective disorder, schizophrenia, delusional disorder, or other specified or unspecified schizophrenia spectrum or other psychotic disorder.

G. The symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g. hypothyroidism).

H. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Note: Because the criteria for a major depressive episode include four symptoms that are absent from the symptom list for persistent depressive disorder (dysthymia), a very limited number of individuals will have depressive symptoms that have persisted longer than 2 years but will not meet the criteria for persistent depressive disorder. If all the criteria for a major depressive episode have been met at some point during the current illness episode, they should be given a diagnosis of major depressive disorder. Otherwise, a diagnosis of other specified depressive disorder or unspecified depressive disorder is warranted.

Table 2. Continued

Specify if:

- With anxious distress.
- With mixed features.
- With melancholic features.
- With atypical features.
- With mood-congruent psychotic features.
- With mood-incongruent psychotic features.
- With peripartum onset.

Specify if:

- In partial remission.
- In full remission.

Specify if:

- Early onset: If onset is before 21 years old.
- Late onset: If onset is at 21 years or older.

Specify if (for most recent 2 years of persistent depressive disorder):

- With pure dysthymic syndrome: Full criteria for a major depressive episode have not been met in at least the preceding 2 years.
- With persistent major depressive episode: All the criteria for a major depressive episode have been met throughout the preceding 2-year period.
- With intermittent major depressive episodes, with current episode: All the criteria for a major depressive episode are currently met, but there have been periods of at least 8 weeks in at least the preceding 2 years with symptoms below the threshold for a full major depressive episode.
- With intermittent major depressive episodes, without current episode: All the criteria for a major depressive episode are not currently met, but there has been one or more major depressive episode in at least the preceding 2 years.

Specify current severity:

- Mild.
 - Moderate.
 - Severe.
-

Other diagnostic categories of depressive disorders, according to the DSM-5 (APA, 2013), are: Disruptive Mood Dysregulation Disorder; Premenstrual Dysphoric Disorder; Substance/Medication-Induced Depressive Disorder; Depressive Disorder Due to another Medical Condition; Other Specified Depressive Disorder, and Unspecified Depressive Disorder.

The common characteristics of the spectrum of depressive disorders are the presence of sadness, empty or irritable mood, accompanied by somatic and cognitive changes that significantly affect the individual's ability to function. The difference between them lies in their duration, chronology, or etiology (APA, 2013).

Regarding ICD-11 (WHO, 2018), the following diagnostic categories are included in the epigraph of Mood Disorders: Single Episode Depressive Disorder, Recurrent Depressive Disorder, Dysthymic Disorder, and Mixed Depressive and Anxiety Disorder. Table 3 shows the description of each diagnostic category according to the ICD-11 (WHO, 2018).

Table 3. Description of principal diagnostic categories of Mood Disorders according to ICD-11 (WHO, 2018).

Single Episode Depressive Disorder

Single episode depressive disorder is characterized by the presence or history of one depressive episode when there is no history of prior depressive episodes. A depressive episode is characterized by a period of almost daily depressed mood or diminished interest in activities, lasting at least two weeks and accompanied by other symptoms such as difficulty concentrating, feelings of worthlessness or excessive or inappropriate guilt, hopelessness, recurrent thoughts of death or suicide, changes in appetite or sleep, psychomotor agitation or retardation, and reduced energy or fatigue. There have never been any prior manic, hypomanic, or mixed episodes that would indicate the presence of a bipolar disorder.

Recurrent Depressive Disorder

Recurrent depressive disorder is characterized by a history of or at least two depressive episodes separated by at least several months without significant mood disturbance. A depressive episode is characterized by a period of almost daily depressed mood or diminished interest in activities, lasting at least two weeks and accompanied by other symptoms such as difficulty concentrating, feelings of worthlessness or excessive or inappropriate guilt, hopelessness, recurrent thoughts of death or suicide, changes in appetite or sleep, psychomotor agitation or retardation, and reduced energy or fatigue. There have never been any prior manic, hypomanic, or mixed episodes that would indicate the presence of a Bipolar disorder.

Dysthymic Disorder

Dysthymic disorder is characterized by a persistent depressive mood (i.e., lasting 2 years or more) for most of the day, on more days than not. In children and adolescents, depressed mood can manifest as pervasive irritability. The depressed mood is accompanied by additional symptoms, such as markedly diminished interest or pleasure in activities, reduced concentration and attention or indecisiveness, low self-worth or excessive or inappropriate guilt, hopelessness about the future, disturbed sleep or increased sleep, diminished or increased appetite, or low energy or fatigue. During the first two years of the disorder, there has never been a 2-week period during which the number and duration of symptoms were sufficient to meet the diagnostic requirements for a Depressive Episode. There is no history of Manic, Mixed, or Hypomanic Episodes.

Mixed Depressive and Anxiety Disorder

Mixed depressive and anxiety disorder is characterized by symptoms of both anxiety and depression more days than not for a period of two weeks or more. Neither set of symptoms, considered separately, is sufficiently severe, numerous, or persistent to justify a diagnosis of a depressive episode, dysthymia, or an anxiety and fear-related disorder. Depressed mood or diminished interest in activities must be present, accompanied by additional depressive symptoms, as well as multiple symptoms of anxiety. The symptoms result in significant distress or significant impairment in personal, family, social, educational, occupational or other important areas of functioning. There have never been any prior manic, hypomanic, or mixed episodes that would indicate the presence of a bipolar disorder.

As can be observed, there are some differences between the two principal classification systems, for example: ICD-11 continues to maintain the diagnosis of mixed anxiety-depressive disorder (in the DSM-5, anxiety is a specifier of MDD), and bereavement is maintained as an exclusion criterion for MDD (in the DSM-5, it is withdrawn as an exclusion criterion for MDD). The bereavement exclusion in the DSM-5 was removed and replaced with much more descriptive guidance about the distinction between symptoms characteristic of normal grief and symptoms indicative of a clinical disorder (Zisook et al., 2012).

In general, although the current main classification systems are eminently categorical, it seems that an important effort is being made to include the advantages of the dimensional approach in the new versions of the diagnostic classification.

1.2. Depression as a public health problem

1.2.1. Prevalence

The WHO highlights that depression will be the third cause of disability in 2030, and it estimates that 4.4% were depressed in 2015, with this being more common in females (5.1%) than males (3.6%) (WHO, 2017). Prevalence rates vary by age and more prevalent in older adulthood (over 7.5% in females aged 55-74 years and over 5.5% in males). Depression also emerges in children and adolescents (<15 years), but at a lower level than older age groups (WHO, 2017). The regions of South-East Asia and the Western Pacific present a higher prevalence rate than the African region. Table 4 shows the percentages of cases with depressive disorder in different regions.

Table 4. Percentage of cases of depressive disorders by WHO Region (WHO, 2017).

Regions	%
African	9
Eastern Mediterranean	16
European	12
Region of the Americas	15
South-East Asia	27
Western Pacific	21

In Spain, it has been estimated that 10.6% of the population has suffered from MDD at some point in their lives (Alonso et al., 2002). Another Spanish community-based study estimated a 12-month prevalence of 6% (Navarro-Mateu et al., 2015) and a point prevalence ranging from 1.5% (Calvó-Perxas, Garre-Olmo, & Vilalta-Franch, 2015) to 1.8% (Ayuso-Mateos, 2001).

1.2.2. Course and development

The course of a depressive episode is quite variable. In general, it begins during the second and third decades of life (Kessler et al., 2003), although it can also begin earlier, during childhood. The average duration of an MDE in the general population is three months (Eaton et al., 2008; Spijker et al., 2002). Approximately 53% of the cases of untreated depression remit within 12 months (Whiteford et al., 2013), and in less than 10% of the cases, depression persists or becomes chronic (Kessler et al., 2003). The risk of recurrence of major depression is high. It has been estimated that at least 60% of people who have had one episode of depression will suffer another (APA, 2002). In addition, the risk of recurrence in the long term is high, with a percentage of recurrence after 20 years of around 42% (Hardeveld, Spijker, De Graaf, Nolen, & Beekman, 2013). Finally, one

variable that can affect the course of depression is the presence of comorbid psychiatric or medical illnesses (Richards, 2011).

1.2.3. Comorbidity

Important North American studies such as the National Comorbidity Study (Kessler et al., 1996) and the Epidemiologic Catchment Area (Andrade, Eaton, & Chilcoat, 1994) reveal that depression has a high rate of comorbidity with anxiety disorders. Specifically, between 40% and 80% of patients with panic disorder (PD) and 49% of patients with generalized anxiety disorder (GAD) suffer from depression. Along the same lines, the Spanish study by Aragonès, Piñol, and Labad (2009) observed that 45.7% of patients with MDD also had another mental disorder, such as GAD (55.2%), PD (33.8%), dysthymia (15.7%), or somatization disorder (6.6%). Moreover, depression presents comorbidities with other mental disorders, such as eating disorders (Campos & Martínez-Larrea, 2002), obsessive-compulsive disorder, (Vallejo, 2002), alcohol dependence (Santodomingo & Rubio, 2000), and substance abuse (Andrade et al., 1994).

Depressive disorders are also characterized by a high rate of comorbidity with other medical conditions. Specifically in patients with cancer, stroke, and acute coronary syndrome (Kang et al., 2015), depression can affect the course of these diseases, which are accompanied by poor quality of life, worse medical outcomes, and a higher mortality rate (Moussavi et al., 2007).

Finally, it is important to highlight that the psychiatric comorbidity of depression implies a worse prognosis, that is, a greater probability of resistance to treatment and recurrence. It also entails a greater risk of suicide, difficulties in clinical management, and costs of health resources (Aragonès et al., 2009).

1.2.4. Sociodemographic correlates

In the majority of the countries and the international data collected, a number of sociodemographic patterns are associated with depression, for example: problems in role transitions (e.g., poor academic performance, marital separation, unemployment), reduced role functioning (e.g., lower marital quality, lower work performance), high risk of a wide range of secondary disorders, and high risk of early mortality due to physical disorders and suicide (Kessler & Bromet, 2013).

1.2.5. Societal costs

As mentioned above, if depression is not treated correctly, its course will tend to become chronic, influencing people's health, well-being, quality of life and functioning in different areas (e.g., personal, academic, professional) (Judd et al., 2000; Plaisier et al., 2010; Saarnin et al., 2007). In Spain, it is the main specific cause of adjusted years of life due to disability (Génova-Maleras, Álvarez-Martín, Morant-Ginestar, de Larrea-Baz, & Catalá-López, 2012).

This psychological problem also causes serious economic costs. In the United States, only in the year 2000, the total economic cost of depression was estimated at around 83.000 \$ million (Greenberg et al., 2003). Of that amount, 26.100 \$ million were direct medical costs, 5.400 \$ million were costs related to mortality due to suicides, and 51.500 \$ million were indirect costs related to lost productivity. In Europe it is estimated that the treatment of depression represents an annual cost of 118.000 € million, of which 61% is due to indirect costs related to workers' lost productivity and sick leave, and the remaining 39% to direct costs (Sobocki, Jönsson, Angst, & Rehnberg, 2006). In Spain in 2010, the societal cost was estimated at 10.763 € million (4.546 € million as direct healthcare costs,

1.410 € million as non-medical costs, and 4.807 € million as indirect costs) and 3584 € per patient/year (Parés-Badell et al., 2014).

1.3. Prevalence and diagnosis of depression in primary care

Between 10% and 16% of primary care (PC) patients meet the criteria for MDD (King et al., 2008; Serrano-Blanco et al., 2010), and over 60% of patients with depression are treated in PC settings (Fernández et al., 2006). The Diagnostic and Assessment Study of Mental Disorders in Primary Care (DASMAP), based on 3.815 patients from PC centers in Spain, showed that almost 30% reported a lifetime history of MDD, with 9.6% experiencing MDD in the past 12 months (Serrano-Blanco et al., 2010).

Patients with depression who are treated at PC settings do not usually demand attention for their psychological symptoms, and they usually report more somatic or physical complaints without referring directly to their emotional problems. Some studies have shown that the probability of presenting symptoms of muscle, head, or stomach pain is between 4 and 7 times higher in patients diagnosed with depression (Means-Christensen, Roy-Byrne, Sherbourne, Craske, & Stein, 2008). Therefore, it is not always easy to make a correct diagnosis (Cano-Vindel, Salguero, Mae-Wood, Dongil, & Latorre, 2012).

The scientific literature points out two difficulties in the diagnosis of depression: underdiagnosis (not diagnosing depression in people who really suffer from depression, thus leading to false negatives), and overdiagnosis (diagnosing depression in people who do not really suffer from depression, thus leading to false positives). In fact, the Spanish study by Fernández et al. (2010) showed that nearly 78% of patients with depression are misdiagnosed, indicating that only about 1/4 of the cases diagnosed as depressed by general practitioners (GPs) are correctly diagnosed. Some obstacles that prevent a correct

diagnosis are: the time available for the patient, keeping the patient from expressing him/herself in a more comprehensive and detailed manner (Mitchell, Vaze, & Rao, 2009); whether the type of diagnosis is made for research or clinical purposes (Fernández et al., 2010); and the attitude of GPs towards the recognition of depression. The attitudes related to the possibility of successfully treating depression or to the effectiveness of psychotherapy have been shown to be associated with greater accuracy in the diagnosis (Gask, Dixon, May, & Dowrick, 2005). Therefore, a correct diagnosis is necessary for adequate treatment.

2. Evidence-based treatments for depression

2.1. Effectiveness of evidence-based treatments

Currently, there are evidence-based treatments (EBTs) for depression, both pharmacological and psychological, that have been accumulating empirical support for their effectiveness. Numerous randomized controlled trials (RCTs) and meta-analyses have shown that psychotherapies such as cognitive behavioral therapy (CBT), interpersonal therapy (IPT), problem solving therapy (PST), behavioral activation (BA), and Psychodynamic psychotherapy are effective treatment strategies for depression on average, with effect sizes between 0.56-0.82 compared to control conditions (Churchill et al., 2002; Cuijpers et al., 2013; Cuijpers et al., 2011; Cuijpers, van Straten, & Warmerdam, 2007; Driessen et al., 2010; Ekers, Richards, & Gilbody, 2008). In addition, these psychotherapies have been shown to be as effective as pharmacological treatments such as selective serotonin reuptake inhibitors (SSRIs), selective norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCIs), and monoamine oxidase inhibitors (MAOIs) (Amick et al., 2015; Cuijpers, van Straten, van Oppen, & Andersson, 2008; Dobson, 1989; Kirsch et al., 2008).

Given the effectiveness and success of EBTs, the National Institute for Health and Care Excellence (NICE) included them as the main guidelines for the treatment of depression (NICE, 2017). Table 5 shows the type of first-line treatments depending on the severity of the depression.

Table 5. First-line treatments according to the severity of the depression (NICE, 2017).

Severity	First-line treatment
	Lower intensity psychological interventions
<p>LESS SEVERE DEPRESSION</p> <p>Subthreshold symptoms</p> <p>Mild depression</p> <p>Lower half of moderate depression</p>	<ul style="list-style-type: none"> • Group-based CBT specific to depression as the initial treatment. • Individual self-help with support for people who do not want group CBT. • Physical activity program specifically designed for people with depression who do not want group CBT or self-help with support.
	Pharmacological interventions
	<ul style="list-style-type: none"> • SSRIs or mirtazapine for people who choose not to have psychological interventions, or based on previous treatment history confirming depression had a positive response to SSRIs or mirtazapine or a poor response to psychological interventions.
	Higher intensity psychological interventions
<p>MORE SEVERE DEPRESSION</p> <p>Upper half of moderate depression</p> <p>Severe depression</p>	<ul style="list-style-type: none"> • Individual CBT or BA. • IPT if the person would like help for interpersonal difficulties that focus on role transitions or disputes or grief. • Counselling if the person would like help for significant psychosocial, relationship, or employment problems. • Short-term psychodynamic therapy if the person would like help for emotional and developmental difficulties in relationships. • Individual CBT in combination with an SSRI or mirtazapine as the initial treatment. • If the person does not want to take medication, offer: group CBT, or individual CBT or BA if the person does not want group therapy. • If the person does not want psychological therapy, offer an SSRI or mirtazapine. • Short-term psychodynamic psychotherapy, alone or in combination with an SSRI or mirtazapine, for the person who would like help for emotional and developmental difficulties in relationships.

Note. BA, Behavioral Activation; CBT, Cognitive Behavioral Therapy; IPT, Interpersonal Therapy; SSRIs, Selective Serotonin Reuptake Inhibitors.

2.2. Treatment of depression in primary care

In Spain, approximately 1/3 of patients with MDD do not receive minimally adequate treatment (Fernández et al., 2006). This can have significant health consequences, affecting the course of treatment (Kravitz, Bloom, & Fawcett, 2000), increasing suicidal acts (Oquendo et al., 2002), decreasing quality of life (Mendlowicz & Stein, 2000), and increasing societal costs (Lépine, 2002). Thus far, pharmacological treatment is the standard recommendation in a PC, including for mild depression. The most commonly used drugs by GPs are SSRIs (98.3%) and anxiolytics (73.4%) (Martin-Agueda et al., 2007). A meta-analysis showed that the effect of antidepressants is non-existent or negligible in patients with mild or moderate symptoms (Fournier et al., 2010). Clinical guidelines for depression recommend active monitoring of symptoms or collaborative strategies with specialized services, along with a stepped model of care in which psychological treatments play a very important role (NICE, 2009). In fact, several studies suggest that patients prefer psychological treatments to medication (McHugh, Whitton, Peckham, Welge, & Otto, 2013; Raue, Schulberg, Heo, Klimstra, & Bruce, 2009).

Psychological treatment in PC has been shown to be more effective than conventional treatment (Bortolotti, Menchetti, Bellini, Montaguti, & Berardi, 2008), even when in the case of brief interventions (Cape, Whittington, Buszewicz, Wallace, & Underwood, 2010). A meta-analysis by Cuijpers, van Straten, van Schaik, and Andersson (2009) found that psychological treatment was more effective when GPs referred patients with depression for treatment.

All these data suggest that psychological intervention is a very important variable in the treatment of depression in the context of PC. The use of psychological (e.g., CBT, physical activity) or pharmacological treatments is recommended in moderate cases, as well as the application of combined treatments or access to specialized services when the

symptomatology does not improve or the symptoms are very severe (e.g., suicidal ideation, psychotic symptoms, or serious personal neglect) (NICE, 2017).

2.3. Limitations of evidence-based psychological treatments

Although there are evidence-based psychological treatments (EBPTs) for depression, these treatments present a series of limitations.

The provision of mental health services is generally less than adequate in terms of accessibility and quality (Kazdin & Blase, 2011), and especially in PC (Bower & Gilbody 2005). Findings have shown that less than 50% of people with depression receive the correct treatment due to the economic cost, the time required for its application, and or the lack of well-trained professionals (Andrade et al., 2003; Gaston, Abbott, Rapee, & Neary, 2006; Harvey & Gumport, 2015). Specifically, difficulty in accessing facilities or professionals, ethnic and cultural barriers, geographical barriers (e.g., living in rural areas or small towns), and other obstacles (e.g., transport, babysitting, elderly people) are some of the factors that make it difficult for people to receive EBPTs (Harvey & Gumport, 2015; Hinrichsen, 2010; Institute of Medicine, 2008; Kazdin & Blase, 2011).

Social stigma about mental health problems or about being treated by mental health professionals may also be another factor that complicates access to treatment (Sartorius, 2002; Weissman et al., 1996). This can lead many people to decide not to seek help or to have difficulties in seeking help (Bebbington et al., 2000; Gaston et al., 2006), or they may only receive it after the problem has produced adverse effects in their lives (Kessler & Greenberg, 2002).

The therapist's beliefs about EBPTs may have an adverse impact on the therapeutic relationship. EBPTs may be too structured and technique-focused, and they may not necessarily yield a better outcome (Harvey & Gumport, 2015).

The existence of an excessive range of EBPTs may hinder their dissemination and implementation (Weisz, Ng, & Bearman, 2014). It is very difficult for a therapist to be able to master all the EBPTs. The need for training in a variety of single-disorder treatments may be unrealistic (McHugh & Barlow, 2012). In addition, most EBPTs focus on specific mental disorders, regardless of the presence of comorbidities (Fairburn, Cooper, & Shafran, 2003; Kring & Sloan, 2009).

Another limitation of EBPTs is the high dropout rate from all forms of psychotherapy. Swift and Greenberg (2012) found that 1 in every 5 patients drops out of therapy prematurely.

In the following sections, we will focus on the need to continue to work towards innovating EBPTs, while also solving these limitations in order to contribute to their dissemination. We review new therapeutic approaches for depression and Internet as an innovative tool to deliver treatments.

3. Other therapeutic approaches for depression

3.1. Transdiagnostic perspective

Recently, a strong emergence of alternative approaches has been observed, some of which are crystallizing into a different way to understand mental disorders (Mansell, Harvey, Watkins, & Shafran, 2009). The problems with subclinical forms point to the difficulty of establishing diagnostic thresholds, the high rates of comorbidity between disorders, the increase in "not specified" diagnoses, the overlapping of symptoms, and the greater intra-subject variability in the longitudinal evolution of clinical manifestations. These issues raise an important question: perhaps there is a more parsimonious structure, and the different diagnostic entities are in fact small variations of a broader syndrome

(Barlow, Sauer-Zavala, Carl, Bullis, & Ellard, 2013). Therefore, instead of highlighting the differences between the wide variety of mental disorders, the emphasis is on studying what they have in common (Barlow, Allen, & Choate, 2004; Harvey, Watkins, Mansell, & Shafran, 2004).

This perspective, called the “transdiagnostic perspective” (TP), has received considerable interest from clinicians and researchers in recent years (Sauer-Zavala et al., 2017). From the point of view of psychopathology, the “TP consists in understanding mental disorders based on a range of cognitive and behavioral etiopathogenic processes that cause and/or maintain most mental disorders or consistent groups of mental disorders” (Sandín, Chorot, & Valiente, 2012, p. 187). Thus, this approach focuses primarily on what these disorders have in common, rather than on what is specific and differential (Sandín, 2012).

Regarding emotional disorders (EDs), empirical evidence shows the existence of an overlap between the latent structures and the clinical characteristics of anxiety disorders and mood disorders, both forming EDs (Brown, 2007; Brown & Barlow, 2009; Wilamowska et al., 2010). The nature of EDs shows that the common aspects in terms of their etiology are greater than their differences, and they present a high rate of comorbidity (Allen et al., 2010; Brown, Campbell, Lehman, Grisham, & Mancill, 2001; Kessler, Berglund, & Demler, 2003; Kessler et al., 2008). Psychological treatments for anxiety disorders often produce additional improvements in other anxiety disorders or in co-morbid mood disorders to which the treatment is not specifically directed (Allen et al., 2010; Borkovec, Abel, & Newman, 1995; Brown, Antony, & Barlow, 1995; Tsao, Lewin, & Craske, 1998; Tsao, Mystkowski, & Zucker, 2002). Moreover, there is evidence of the existence of shared neurobiological mechanisms between them (Etkin & Wager, 2007; Porto et al., 2009; Shin & Liberzon, 2010).

Barlow (2000, 2002) proposed three vulnerabilities that contribute to the etiology of EDs: 1) *general biological vulnerability* (e.g., dimensions of temperament such as neuroticism and extraversion); 2) *general psychological vulnerability* (e.g., perceived control over life stress and emotional states); and 3) *disorder-specific psychological vulnerability* (e.g., anhedonia in MDD). It is argued that the two generalized vulnerabilities work as direct risk factors for the development of an ED, which, associated with the third specific vulnerability, allow it to crystallize into one or disorder or another (Brown, 2007).

Later, Brown and Barlow (2009) suggest that EDs have a common latent structure with two dimensions: a) "*anxiety / neuroticism / behavioral inhibition or negative affect (NA)*" (associated with generalized chronic discomfort, perception of uncontrollability about threatening and challenging future events, attentional hypervigilance, and low self-confidence and self-efficacy in coping with future threatening events), which is present in most EDs; and b) "*positive affect (PA) / BA*" (associated with low enthusiasm and interest and a predominant pessimism), which seems to be more specific to some disorders (e.g., depression). In addition, these authors also highlight various fundamental transdiagnostic processes that underlie the ED (e.g., emotional problems, avoidance behaviors, rumination, etc.).

Moreover, these ED dimensions are related to the neuropsychological constructs pointed out by Gray and McNaughton (2000): the behavioral inhibition system (BIS) and the behavioral activation system (BAS). It is proposed that the individual will experience several levels of severity of neuroticism-BIS and extroversion-BAS. Neuroticism is related to chronic stress that includes the hypothalamic-pituitary-adrenal axis. Low PA is related to reduced BAS activity. This vulnerability, associated with stressors, can lead to anxious or depressive symptoms.

People with EDs have higher levels of NA and experience negative emotions more intensely and more frequently (Brown & Barlow, 2009; Campbell-Sills, Barlow, Brown, & Hofman, 2006; Mennin, Heimberg, Turk, & Fresco, 2005). In fact, this population shows greater intolerance to uncertainty and ambiguity, or situations that are perceived as uncontrollable, which leads to an increase in NA (Boelen, Vrinssen, & van Tulder, 2010; Boswell et al., 2013; Lee, Orsillo, Roemer, & Allen, 2010). All these ways of interpreting and responding to negative emotions, paradoxically, serve to increase and maintain them. Therefore, this pathological reaction to emotional experience is considered the phenotypic core of EDs (Barlow et al., 2013).

Several constructs have been identified as problematic reactions to emotions that may be involved in the development and maintenance of different ED: sensitivity to anxiety (Reiss, 1991), avoidance of internal experience (Hayes, Wilson, Gifford, Follette, & Strosahl, 1996), deficits in mindfulness (Rasmussen & Pidgeon, 2011), the suppression of emotion (Abramowitz, Tolin, & Street, 2001), rumination (Aldao, Nolen-Hoeksema, & Schweizer, 2010), and behavioral avoidance (Manos, Kanter, & Busch, 2010).

In summary, the TP seem to propose the role of emotional regulation as a key factor in understanding the development of EDs.

3.1.1. Main transdiagnostic treatments for emotional disorders

Taking into account the considerable overlap among anxiety and mood disorders, the etiology of ED, the shared neurobiological mechanisms, the high rates of diagnostic comorbidity, and some generalization of the treatment response, the TP could be a powerful option in the field of psychological treatments.

From the point of view of psychopathology, there are different ways of understanding what makes a transdiagnostic treatment. For example, McEvoy, Nathan, and Norton (2009) have defined them as “those that apply the same underlying treatment principles across mental disorders without tailoring the protocol to specific diagnoses” (p. 21), whereas Mansell, Harvey, Watkins, and Shafran (2008) defined them as “a therapy that is made available to individuals with a wide range of diagnoses, and that does not rely on knowledge of these diagnoses to operate effectively” (p. 14). Some authors propose different treatment approaches within the TP.

For example, Sauer-Zavala et al. (2017) propose three categories to classify transdiagnostic treatments: a) *universally applied therapeutic principles* (top-down approach): these include all interventions that start from a theoretical model or therapy orientation (e.g., humanistic, psychodynamic, cognitive therapy) whose therapeutic strategies (e.g., unconditional acceptance, transfer process, cognitive restructuring) are applied to all the problems, without explicitly considering if all the disorders treated with this technique are maintained by similar processes. Clear examples would be client-centered therapy (Rogers, 1951), psychodynamic psychotherapy focused on resolving psychic conflicts (Gabbard, 2000; Shedler, 2010), or cognitive therapy (Beck, 1976); b) *modular treatments*: these allow the clinician to choose from an organized bank of empirically validated therapeutic strategies, assembling a treatment that maps the problems presented by the patient, independently of the diagnosis. This type of

intervention represents an empirical approach, instead of a theoretical one, because it uses strategies that show a reduction in the symptoms, but without necessarily addressing the basic psychopathological mechanisms. The use of this type of intervention has been tested in the therapeutic approach to anxiety problems in children (Chorpita, Taylor, Francis, Moffitt, & Austin, 2004) and in mental health problems in adults from countries with a low-medium socioeconomic level (Murray et al., 2014); and c) *treatments of shared mechanisms* (bottom-up approach): these are based on theoretical models of psychopathology, and not on universally applied therapeutic principles, with the aim of treating psychological processes that are involved in the development and maintenance of disorders. Two examples of this type of treatment are: the Unified Protocol (UP) for EDs by Barlow et al. (2004, 2011) and transdiagnostic group CBT for anxiety (T-GCBT) by Norton (2012).

3.1.1.1. The Unified protocol

The UP is a transdiagnostic, emotion-focused CBT designed to be applicable to all anxiety and unipolar mood disorders, and possibly other disorders with strong emotional components, such as many somatoform and dissociative disorders (Allen, McHugh, & Barlow, 2008; Barlow et al., 2004, 2011). It addresses core temperamental factors that maintain EDs, specifically frequent and acute NA and the perception of negative emotion as intolerable. Therefore, its final objective is to extinguish distress in response to the experience of strong emotion.

This protocol includes aspects from traditional empirically supported CBT (Barlow & Cerny, 1988; Barlow & Craske, 2006; Beck, 1976), but incorporating advances in research on modern learning theory, cognitive neuroscience, and ER literatures (Barlow et al., 2004). It is based on three basic therapeutic components: 1) *targeting antecedent*

cognitive appraisals; 2) *reducing and preventing avoidance of dysregulated emotions*; and 3) *encouraging actions that are inconsistent with disordered emotional states* (Barlow et al., 2004). Moreover, UP consists of eight modules, with five of these modules forming the core treatment components in a maximum of 18 1-hr individual sessions (Farchione et al., 2012; Wilamowska et al., 2010). Table 6 shows the UP modules.

Table 6. Modules of the UP for transdiagnostic treatment of EDs.

Module	Title
1	Motivation Enhancement
2	Psychoeducation and Treatment Rationale
3	Emotion Awareness Training*
4	Cognitive Reappraisal*
5	Emotion Driven Behaviors and Emotional Avoidance*
6	Awareness and Tolerance of Physical Sensations*
7	Interoceptive and Situational Exposure*
8	Relapse Prevention

Note. *Indicates core UP module.

A unified transdiagnostic treatment approach could help in the dissemination of treatment and training of professionals by providing a single set of therapeutic principles rather than numerous specific protocols. Moreover, this type of treatment could increase the availability of psychological interventions for anxiety and depression disorders, thus meeting a significant public health need (Wilamowska et al., 2010).

3.1.1.2. Transdiagnostic group cognitive-behavioral therapy

The T-GCBT consists of 12 weekly 2-hr sessions in groups of six to eight individuals with any anxiety disorder. Treatment highlights the excessive or irrational fear of a particular thing (e.g., somatic symptoms), as opposed to having a particular diagnosis (e.g., PD), so that patients are seen as sharing the same basic pathology, even though the specific stimuli that trigger the fear/anxiety and the associated behavioral responses may differ (García-Escalera, Chorot, Valiente, Reales, & Sandín, 2016; Norton, 2012). The T-GCBT incorporates psychoeducation, cognitive restructuring, graduated in-session exposure and response prevention, cognitive restructuring of core beliefs, and relapse prevention. Table 7 shows the T-GCBT sessions.

Table 7. T-GCBT sessions.

Module	Title
1	Psychoeducation and group socialization
2	Psychoeducation and introduction of cognitive restructuring
3	Cognitive restructuring
4-9	Graduated in-session exposure and response prevention
10-11	Cognitive restructuring of core beliefs
12	Termination and relapse prevention

3.1.2. Effectiveness of transdiagnostic treatments

One of the big questions that the TP must answer is about its effectiveness compared to waitlist groups or the usual treatment. Nevertheless, it is also very important to find out if it is at least as effective as the specific treatments for specific disorders. Currently, there is already some accumulated evidence about the effectiveness of these treatments, both in individual and group formats. Below, we present a series of recent reviews about this question.

The review by Rector, Man, and Lerman (2014) was carried out with studies that applied transdiagnostic CBT (T-CBT) for anxiety and depression. They found preliminary empirical evidence suggesting that this treatment modality is effective in reducing both primary and comorbid symptoms, and it has an impact on shared psychological mechanisms. However, these authors concluded that the empirical literature remains provisional because most of the studies used a small sample, made direct comparisons with the disorder-specific CBT, and only compared specific disorders with the mechanisms of shared action in the treatment. Based on their results, these authors concluded that T treatments should be considered complementary to specific CBT.

Reinholt and Krogh (2014) analyzed the overall efficacy of T-CBT for anxiety disorders compared to waitlist conditions, usual treatment, and disorder-specific CBT. The results of 11 controlled trials highlighted the potential of T-CBT in comparison with the aforementioned conditions, even obtaining positive effects in the follow-ups. However, the pooled estimate showed a moderate treatment effect, but with differences between the included studies. These authors suggested that T-CBT can be a very promising, affordable, and pragmatic pathway for anxiety disorders, and it may be a specialized intervention for comorbid and unspecified anxiety disorders.

Other studies that will be explained in more detail in the next section are those by Newby, McKinnon, Kuyken, Gilbody, and Dalgleish (2015); Newby, Twomey, Yuan Li, and Andrews (2016); and Păsărelu, Andersson, Bergman Nordgren, and Dobrean (2017). These authors carried out a systematic review and meta-analysis about clinician-guided Internet/computerized and face-to-face transdiagnostic treatments.

Norton and Paulus (2016) reviewed the empirical evidence on two of the most widely used transdiagnostic treatments in anxiety and mood disorders: the T-GCBT by Norton (2012), and the UP by Barlow et al. (2004, 2011). Some studies suggest that group T-CBT is effective in reducing anxiety symptoms (Norton et al., 2013), and comorbid depression (Norton, Hayes, & Hope, 2004), compared to disorder-specific CBT. Along the same lines, the UP showed positive results in the reduction of primary (Farchione et al., 2012) and comorbid (Davis, Barlow, & Smith, 2010) symptoms, in the improvement of subjective quality of life (Gallagher et al., 2013), and in two personality factors, neuroticism and extraversion (Carl, Gallagher, Sauer-Zavala, Bentley, & Barlow, 2014). These authors concluded that despite the boom and empirical support for these treatments, more controlled trials and more information about their long-term effects (e.g., results after completing the intervention) are still needed to ensure their effectiveness and efficiency.

Finally, Pearl and Norton (2017) carried out a meta-analysis to compare T-CBT with disorder-specific CBT, and investigate the differential impact of comorbidity on the effect size. To do this, they compared the pre- and post-scores of primary anxiety measures in 83 treatment conditions taken from studies aimed mainly at anxiety disorders. They found that both types of CBT entailed large effect sizes and overlapping confidence intervals, and that the two were similar. In addition, they found that comorbidity rates did not appear to influence the results of T-CBT treatment.

In conclusion, although the reviews are still scarce and preliminary, their results are very promising and encouraging, and it seems that we are in a position to encourage the promotion and dissemination of transdiagnostic treatments, at least for EDs, in clinical settings.

3.1.3. Advantages of transdiagnostic treatment

The advantages of a transdiagnostic treatment are threefold: 1) It is possible to focus the treatment on the maintenance of the symptoms across multiple disorders, rather than on the large number of specific disorders proposed in the DSM. This would contribute to more effective and efficient treatments. 2) Treating processes that are common across the comorbidities provides a path toward improving clinical outcomes. This would avoid the dilemma about which disorder to prioritize for treatment. 3) It is possible to reduce the time and effort of clinicians, who must otherwise learn multiple disorder-focused protocols, often with common theoretical underpinnings and interventions (Harvey et al., 2004; Mansell et al., 2009).

For more information about TP see our chapter “Transdiagnostic as an alternative” (Baños, Vara, Miragall, 2017).

3.2. Interventions focused on positive affect

In order to improve the current available treatments, the enhancement of PA has been considered a relevant variable (Algoe, Fredrickson, & Chow 2011; Carl, Soskin, Kerns, & Barlow, 2013).

Watson and Tellegen (1985) proposed *the factorial model of affection* and established that the structure of affectivity was composed of two independent dimensions

(PA and NA). This means that the absence of negative feelings is not equivalent to the presence of positive ones.

Thus far, psychological treatments for EDs have focused primarily on interventions designed for the NA dimension. Therefore, it is necessary to improve the intervention strategies for the PA dimension (Carl et al., 2013).

In the next sections, some treatment alternatives are examined whose main work axis lies in the promotion of PA for the treatment of depression.

3.2.1. Positive affect in the transdiagnostic treatments

As shown in the previous section, the UP has received great interest as a treatment for EDs, and especially for the regulation of negative emotions (Barlow et al., 2013). However, the main objective of this treatment is to train patients in NA regulation, paying less attention to the inclusion of treatment components directly targeting PA regulation. Likewise, this also occurs with other types of transdiagnostic treatments for anxiety disorders (e.g., Norton, 2012) and mixed anxiety and depression (e.g., Berger, Boettcher, & Caspar, 2014).

The literature suggests that there is a link between the maladaptive strategies used by depressed people to regulate PA and the rest of the depressive symptoms (Gilbert, 2012; Gilbert, Nolen-Noeksema, & Gruber, 2013; Werner-Seidler, Banks, Dunn, & Moulds, 2013), and that deficits in PA regulation are associated with a worse depression prognosis (Shankman, Nelson, Harrow, & Faull, 2011). In addition, a theoretical review on positive emotional regulation concluded that there are transdiagnostic disturbances in the strategies used to regulate positive emotions that may provide the explanation for the low levels of PA in depression and several anxiety disorders (Carl et al., 2013).

Moreover, the research reveals that EDs (e.g., Dunn, 2012; Kashdan, Weeks, & Savostyanova, 2011) are associated with aberrant functioning of the positive emotional system, including low levels of PA (e.g., Brown, Chorpita, & Barlow, 1998), decreased approach motivation and behavior (e.g., Campbell et al., 2009), biased processing of reward-related signals (e.g., Joormann & Gotlib, 2007), and reduced behavioral and neural reactivity to rewards (e.g., Carl et al., 2013; Pizzagalli, Iosifescu, Hallett, Ratner, & Fava, 2008).

Some studies suggest that the PA system may be the key to facilitating recovery from anxiety and depression (Dunn, 2012; Fredrickson, 2013; Garland et al., 2010; Layous, Chancellor, & Lyubomirsky, 2014). In this regard, positive emotions fulfill a number of functions that mitigate the adverse effects of negative emotions by promoting PA, resilience, and psychological well-being (e.g., Fredrickson & Levenson, 1998; Fredrickson, Mancuso, Branigan, & Tugade, 2000).

Thus, several theories have suggested the adaptive value of positive emotions in cognition and action processes. For instance, the *Broaden and Build Theory* proposed by Fredrickson (1998, 2001, 2013) asserts that certain positive emotions, such as joy, interest, contentment, pride and love, share the ability to broaden people's momentary thought-action repertoires, inciting them to accomplish a wider range of thoughts and actions (i.e., to play, explore, savor, and integrate current life circumstances, or envision future achievements) that lead to creating enduring personal resources (i.e., physical, intellectual, social, or psychological resources).

Finally, the regulation of PA can have important implications in the treatment of ED (Carl et al., 2013) because it has been observed that high PA is associated with better physical and psychological health, healthier lifestyles, and better general functioning (Cohen & Pressman, 2006; Fredrickson, 2001; Livingstone & Srivastava, 2012; Pressman

& Cohen, 2005; Quoidbach, Berry, Hansenne, & Mikolajczak, 2010; Tugade & Fredrickson, 2007).

Taking into account the role of PA in EDs, it is necessary to include this dimension as an intervention strategy, especially in the transdiagnostic treatments (Carl et al., 2013).

3.2.2. Positive psychology and depression treatments

A recent perspective that emerged strongly with the aim of enhancing positive emotional human functioning, and especially PA, is positive psychology (PP) (Seligman & Csikszentmihalyi, 2000). PP emerged to unite disparate theory and knowledge on positive human functioning and advance the work on positive mental health and well-being (Seligman, Steen, Park, & Peterson, 2005). Psychological well-being is understood as “both the absence of mental illness and the presence of positive psychological resources, such as PA and satisfaction with one’s life (Diener, 1984), autonomy, competence, relatedness (Ryan & Deci, 2001), self-acceptance, purpose, and personal growth (Ryff, 1989)” (Sin, Della Porta, & Lyubomirsky, 2011, p. 79).

To date, treatments for depression seem to have focused more on relieving mood, paying less attention to building positive resources. According to a frequently mentioned analogy, many therapies have only focused on increasing the mental health of people from -5 to 0 (neutral), without aiming to elevate these people to +5 or higher. Psychological interventions should strive to work on the well-being of an individual, instead of focusing only on improving depressive symptomatology (Lyubomirsky, 2008).

The benefits of positive emotions are especially relevant to those suffering from depression. Santos et al. (2013) concluded that positive psychology interventions (PPIs) reduce both symptoms of depression and the potential for relapse into subsequent periods of depression. Consequently, many studies have demonstrated the effectiveness of PPIs

such as the exercise of counting your blessings (Emmons & McCullough, 2003; Seligman et al., 2005), practicing kindness (Otake, Shimai, Tanaka-Matsumi, Otsui, & Fredrickson, 2006), setting personal goals (Green, Oades, & Grant, 2006; Sheldon, Kasser, Smith, & Share, 2002), expressing gratitude (Seligman et al., 2005; Sheldon & Lyubomirsky, 2006) and using personal strengths to improve well-being and improve or relieve depressive symptoms (Seligman et al., 2005). The meta-analysis by Sin and Lyubomirsky (2009) showed that PPIs can indeed be effective in enhancing well-being (Cohen's $d = 0.61$) and helping to reduce depressive symptom levels in clinical samples (Cohen's $d = 0.65$). Along the same lines, the meta-analysis by Bolier et al. (2013a) revealed that PPIs produced a small but significant treatment efficacy on variables of subjective well-being (Cohen's $d = 0.34$), psychological well-being (Cohen's $d = 0.20$), and depression (Cohen's $d = 0.23$). A later meta-analysis conducted by Weiss, Westerhof, and Bohlmeijer (2016) also showed that PPIs are effective. Finally, other authors have found that PPIs may help individuals with other EDs and somatic disorders (Chakhssi, Kraiss, Sommers-Spijkerman, & Bohlmeijer, 2018).

Another very promising way to increase well-being and PA is to engage individuals in valuable and enjoyable activities. The contemporary BA approach tries to make patients commit to their life again, increase their experiences of well-being, and get involved in behaviors that give them a greater sense of self-efficacy and that are consistent with their values (Kanter, Puspitasari, Santos, & Nagy, 2012). A meta-analysis about BA interventions for well-being showed that these interventions can increase the well-being of participants, and that they are equally effective regardless of depression severity (Mazzucchelli, Kane, & Rees, 2010). The moderate effect size (Hedges's $g = 0.52$) was comparable in size to the mean effect on measures of well-being achieved by PPIs (0.61;

Sin & Lyubomirsky, 2009). This finding suggests that BA could be added to the growing number of interventions in the field of PP.

In summary, it seems that the inclusion of PPIs in existing CBT interventions (e.g., transdiagnostic interventions) may help to increase the effect on PA, and thus, lead to better and longer-lasting outcomes of positive emotional functioning and well-being (González-Robles, García-Palacios, Baños, Quero, & Botella, 2017).

3.2.3. Transdiagnostic interventions based on positive psychology

Recently, Taylor, Lyubomirsky, and Stein (2017) evaluated the efficacy of a pilot study about a new transdiagnostic intervention based on PP to upregulate PA in anxiety and depression. Participants with clinically impairing symptoms of anxiety and/or depression were randomly allocated to two conditions: 1) 10 1-hr sessions of an individual therapist-delivered protocol comprised of positive activity intervention (PAI) (13 modules) and 2) a waitlist (WL) (N=13). Table 8 shows the modules and goals of the PAI protocol.

Table 8. Modules of the PAI protocol for EDs.

Module	Goal
1. Psychoeducation	Present treatment rationale; self-monitoring of emotions.
2. Noticing and amplifying positive events	Train attention towards and increase awareness of positive events; intensify and prolong positive emotional experiences.
3. Gratitude: Counting one's blessings	Direct attention to positive events.
4. Acts of kindness	Increase prosocial behaviors.
5. Pleasurable, engaging, and meaningful activities	Increase participation in rewarding activities, both hedonic and eudaimonic.
6. Strengths	Increase awareness of personal strengths and opportunities to use those strengths.
7. Affirming values	Strengthen commitment to personal values.
8. Optimism: Best possible future	Promote future-oriented positive cognitions and behaviors.
9. Make someone else happier	Increase investment in relationships; increase prosocial behaviors and connection with others.
10. Live this month like it's your last in this area	Promote increased engagement in positive activities; increase anticipation, appreciation, and sustained responsiveness to positive events.
11. Gratitude: Gratitude letter	Direct attention to another person's role in positive events; strengthen social connections.
12. Develop personalized positive activity plan	Maximize person-activity fit and continued engagement in activities; translate activities into habits.
13. Termination plan	Consolidate learning; develop plan to maintain/enhance gains.

The results show that the PAI group presents significantly greater improvements in PA and psychological well-being from pre- to post-treatment compared to the WL group. The PAI group also shows significant reductions in NA, as well as in anxiety and depression symptoms, compared to WL. Improvements across all outcomes (positive and negative emotions, psychological well-being, and symptoms) were large in magnitude and maintained over a 6-month follow-up period. Therefore, these findings support the idea of explicitly treating positive emotions in disorders classically defined and conceptualized according to heightened negative emotions.

Other study carried out by members of our research group Labpsitec (González-Robles et al., 2017), analyzed the preliminary effects of positive affectivity in the transdiagnostic treatment of ED. This study differs from the previous treatment because it also includes strategies for downregulating NA. These authors develop a transdiagnostic protocol (T-protocol) for EDs based on the UP (Barlow et al., 2011) and some strategies for ER from dialectical behavior therapy (DBT, Linehan, 1993) (12 modules). Another version of this protocol also includes a specific component mainly based on PPIs to directly address PA regulation (T-protocol+PA) (11 modules + 4 specific modules of PP). Participants with ED were randomly allocated to 12 to 15 1-hr sessions of individual therapist-delivered T-protocol (N = 12) or to 16 to 19 1-hr sessions of individual therapist-delivered T-protocol+PA (N= 12). Table 9 shows the modules in both conditions: T-protocol and T-protocol+PA.

Table 9. Modules of the T-protocol and T-protocol+PA for EDs.

Module	Title
1	Introduction to treatment
2	Motivation for change and goal-setting
3	Understanding the role of emotions (psychoeducation about emotions and goal-setting)
4	Nonjudgmental emotional awareness and acceptance of emotional experiences
5	Practicing present-focused awareness: Physical sensations, thoughts, emotions, and daily activities
6	Learning to be flexible (identification of thinking traps)
7	Practicing cognitive flexibility (cognitive reappraisal and evaluation of intrusive thoughts)
8	Emotional avoidance
9	Emotion-driven behaviors
10	Accepting and facing physical sensations
11	Facing emotions in the contexts in which they occur
12	Relapse prevention Learning to move on (e.g., BA)*
13	Learning to enjoy (e.g., the importance of smiling, savoring)*
14	Learning to live (e.g., identifying individual's own psychological strengths, meaningful activities linked to personal values)*
15	Living and learning (e.g., gratitude, hope, curiosity)*
16	Relapse prevention*

Note. * Modules included in T-protocol+PA; BA, Behavioral Activation.

The results reveal that both interventions (T-protocol and T-protocol+PA) led to improvements in all measures (anxiety, depression, positive and negative affectivity, and quality of life) at post-treatment, and these changes were maintained at the 3-month follow-up, with large effect sizes. Moreover, the effect sizes for the PA were larger in the condition that included the component to upregulate positive affectivity. Once again, the potential impact of including therapeutic components directly addressing PA regulation in the treatment for EDs is shown.

All of these findings suggest that transdiagnostic treatments focused on the regulation of PA may be a promising solution for the management of EDs. However, this field is quite new, and more research is needed.

4. The use of the Internet in the application of psychological treatments

4.1. The inclusion of Information and Communication Technologies (ICTs) in the application of psychological treatments

The importance of disseminating EBPTs has been mentioned in previous sections. Many studies show that not all depressed PC patients are receiving adequate treatment for depression (Uebelacker, Smith, Lewis, Sasaki, & Miller, 2009). Therefore, it is a priority to change the way of delivering psychological treatments. In recent years, a need to radically change the way psychological treatments are applied has been detected.

The work by Kazdin and Blase (2011) has proposed something as drastic as "rebooting" the research and practice of psychotherapy to reduce the burden of mental illness. In the opinion of these authors, a radical change in perspective is necessary, an approach that goes beyond individual one-to-one psychotherapy. We need to offer the best treatment, but without excessively increasing the costs or reducing the effectiveness

of the intervention. To do this, it is necessary to analyze other treatment frameworks as alternatives to the traditional ones that, without altering the essence of the clinician-patient relationship, involve a different mode of interaction from those of traditional face-to-face therapy, with changes in the specific responsibilities of each party (e.g., a more active role on the part of the patient) (Botella, Quero, Baños, & Garcia-Palacios, 2009). For this purpose, the inclusion of Information and Communication Technologies (ICTs) could be very useful (Kazdin & Blase, 2011). ICTs (e.g., virtual reality, augmented reality, Internet) are becoming very useful tools for delivering and improving the application of therapeutic services, making it possible to expand the axis of the effectiveness or clinical utility of EBPTs, and promoting the power to reach everyone who needs them (Botella et al., 2009; Kazdin & Rabbit, 2013). ICTS contribute to the five dimensions postulated by the RE-AIM model (reach, efficacy/effectiveness, adoption, implementation, and maintenance), which has received considerable empirical support from a large body of science (Glasgow, McKay, Piette, & Reynolds, 2001).

Specifically, some literature suggests that the Internet can be used for the assessment and treatment of clinical conditions (Andersson, 2016).

4.2. Internet-based interventions for mental disorders

In the past 20 years, Internet-based interventions (IBIs) have emerged as a useful alternative for coping with the challenge of disseminating psychological treatments (Andersson & Titov, 2014). The IBIs, also referred to as e-therapy, online interventions, or computerized psychotherapy, are defined as therapeutic programs with specific health objectives delivered mainly using the Internet (Barak, Klein, & Proudfoot, 2009).

Prior to the development of IBIs, the first computer-based interventions were not online, such as the programs *Overcoming Depression* (Williams, Taylor, Aubin, Harkin, & Cottrell, 2002) and *Blues Begone* (Purves, Bennett, & Wellman, 2009).

IBIs can be classified into six categories (Barak et al., 2009): a) *web-based education interventions*; b) *self-guided web-based therapeutic interventions*; c) *human-supported web-based therapeutic interventions*; d) *online counseling* (e.g., chat, video-based); e) *Internet-operated therapeutic software* (e.g., robotic simulation, gaming); and f) *other online activities* (e.g., blogs, podcasts). Moreover, each category of IBI is described taking into account four major types of components: 1) *content* (e.g., educational or directed to behavior change); 2) *multimedia* (e.g., text, images, videos); 3) *interactive online activities* (e.g., online quizzes, homework); and 4) *guidance and supportive feedback* (e.g., automatic reminders, professional feedback).

In some IBIs, psycho-educational information through text is presented in a sequential order, whereas in others, simulated dialogues with content tailored to a user's response are included (e.g., *Deprexis*; Meyer et al., 2009, 2015). Some IBIs may be used without registration (e.g., *MoodGym*; Christensen, Griffiths, & Jorm, 2004), whereas others require registration or involve careful prior evaluation (e.g., *Smiling is fun*; Botella et al., 2012). Some of them are often offered without therapist guidance (unguided interventions), but can be combined with minimal but regular contact with the therapist (guided interventions) (Andersson, 2009). Contact with the therapist is limited to providing support and, if necessary, clarifying questions about standardized treatment, and it can be provided in person, by telephone, or by e-mail (Cuijpers & Schuurmans, 2007). The involvement of the therapist may take different forms and vary in terms of the time spent with the patient (Andersson, Carlbring, Berger, Almlöv, & Cuijpers, 2009). Finally, there are blended treatments, which are a combination of guided IBI and regular

contact with a therapist at different points in time during the therapeutic process (Wentzel, van der Vaart, Bohlmeijer, & van Gemert-Pijnen, 2016).

In the following section, the types of IBIs for depression will be discussed in more detail.

4.2.1. Internet-based Interventions for depression

Through IBIs, patients work from a self-help guide adapted for the Internet and based on EBPT protocols. The patient systematically completes several online lessons, which usually present the same information and therapeutic strategies used in traditional face-to-face therapy, often with the support of a therapist who is trained to do so (Titov, 2011).

As discussed in previous sections, there are several forms of effective psychotherapy for the treatment of depression (e.g., CBT, IPT, PST) (e.g., Cuijpers et al., 2013). These structured psychological treatments seem to work better than unstructured or non-directive therapeutic approaches (Cuijpers et al., 2012). In addition, it has become clear that EBPTs can be transferable to the Internet format, especially CBT (ICBT), without losing their effectiveness (Andersson, 2009). One of the most important aspects of IBIs is the possibility of improving cost-effectiveness compared to face-to-face traditional therapy (Andersson, 2016).

4.2.1.1. Unguided Internet-based computerized interventions

Unguided ICBT programs represent an attractive way to optimize the benefits of traditional CBT because they are eminently scalable and can be disseminated quickly (Leykin, Muñoz, Contreras, & Latham, 2014). Table 10 shows the main unguided ICBT programs for depression that have accumulated empirical evidence during these years (Andersson, 2014, p. 45).

Table 10. List of the main unguided ICBT programs for depression.

Program, country of origin, and authors	Number of modules	Description
ODIN (Overcoming depression on the Internet) United States (Clarke et al., 2002)	7	- Program based on training and the use of cognitive restructuring techniques.
MoodGYM Australia (Christensen, Griffiths, & Jorm 2004)	5	- Program based on CBT, IPT and relaxation therapy. - It is also designed to prevent depression. - It has also been tested as guided treatment (Farrer et al., 2011).
Deprexis Germany (Meyer et al., 2009)	10	- Program based on CBT but also includes other approaches such as PP and mindfulness. - It has also been tested as guided treatment (Berger et al., 2011).
Living life to the Full United Kingdom (William & Chellingsworth, 2010)	8	- Program based on CBT through the five areas approach (people and events, thinking, feelings, physical symptoms, and behavior or activity levels).

Note. CBT, Cognitive Behavioral Therapy; IPT, Interpersonal Therapy; PP, Positive Psychology.

4.2.1.2. Guided Internet-based computerized interventions

So far, many guided IBIs for the treatment of depression have been proposed, and their number has steadily increased. As can be seen, all these programs differ in content but share common CBT components. Table 11 shows the main guided ICBT programs for depression (Andersson, 2014, p. 81).

Table 11. List of the main guided ICBT programs for depression.

Program, country of origin, and authors	Number of modules	Therapeutic components
Beating the Blues United Kingdom (Proudfoot et al., 2003)	8	Cognitive and behavioral techniques.
Out of Depression (DAVID) Sweden (Andersson et al., 2005)	5 Later: 7 adapted modules (Vernmark et al., 2010)	Psychoeducation, BA, cognitive techniques, insomnia, and relapse prevention.
Sadness program Australia (Perini et al., 2009)	6	BA, cognitive restructuring, PST, and assertiveness skills.
Interapy depression Netherlands (Ruwaard et al., 2009)	8	Inducing awareness, structuring activities, cognitive restructuring, positive self-verbalization, social skills, and relapse prevention.
Relapse prevention program (ISIDOR) Sweden (Holländare et al., 2011)	9 7 optional advanced modules	Psychoeducation, positively reinforced activities, cognitive restructuring, improving sleep, mindfulness, reducing anxiety, physical activity, and long-term goals.
Well-being program Australia (Titov et al., 2011)	8	Transdiagnostic with a focus on depression. Psychoeducation, cognitive therapy, control of physical symptoms, BA, graded exposure, beliefs, PST, and relapse prevention.
Tailored Internet intervention for depression (Taylor) Sweden (Johansson et al., 2012)	25 that are prescribed according to symptom profile 4 modules are fixed: psychoeducation, cognitive restructuring, and relapse prevention	Psychoeducation, cognitive restructuring, and relapse prevention (fixed contents). Also: PST, mindfulness, and relaxation.
Depressionshjälpen Sweden (Carlbring et al., 2013)	7	Psychoeducation, activity and well-being, understanding other activities and the role of reinforcement.

Note. BA, Behavioral Activation; PST, Problem Solving Therapy.

4.2.2. Effectiveness of Internet-based interventions for depression

The empirical evidence show that IBIs are effective for the treatment of depression (Richards & Richardson, 2012). Several meta-analyses indicate that IBIs (e.g., CBT, IPT) produce larger effect sizes than control groups, ranging from 0.5 to 0.8 (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010, Richards & Richardson, 2012). Moreover, there are no major differences between the types of psychological therapy or the types of intervention format (Barth et al., 2013). The meta-analysis by Cuijpers, Donker, van Straten, Li, & Andersson (2010) examined whether guided IBIs and other conventional methods (e.g., self-help books with telephone support) for depressive and anxiety disorders were as effective as face-to-face treatments. The results revealed that there were no significant differences between them (differential effect size $d = 0.02$), even in the follow-ups at 3, 6 and 12 months (Cuijpers & Riper, 2014). Nor has it been found that the risk of dropping out from treatment is greater or lesser in guided IBIs than in face-to-face treatments (Cuijpers & Riper, 2014). In another meta-analysis focused only on guided IBIs and face-to-face therapies for EDs and other problems (e.g., body dissatisfaction), no significant differences were found (Cohen's $d = 0.01$) (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014). Finally, all these results are also confirmed in some meta-analyses of individual patient data (e.g., Karyotaki et al., 2017).

Regarding unguided IBIs (interventions without any kind of human support), the effect sizes are significantly smaller than those for the guided IBIs (Andersson & Cuijpers, 2009; Richards & Richardson, 2012). A meta-analysis about unguided IBIs for depression reported a small effect size (Cohen's $d = 0.28$) (Cuijpers, Donker, Johansson, Mohr, van Straten, & Andersson, 2011). This finding suggests that guidance has a facilitating effect on adherence, keeping users engaged in the IBI (Baumeister, Reichler, Munzinger & Lin, 2014). However, these types of interventions are currently being

examined because they could be more cost-effective (Gerhards et al., 2010), especially in low and middle income countries without an infrastructure for mental health care (Cuijpers, Riper, & Andersson, 2015). The use of interactive tools such as automatic messages, videos, audios, mobile features, and feedback systems could help improve adherence of this type of treatment (Ritterband, Thorndike, Cox, Kovatchev, & Gonder-Frederick, 2009).

In summary, guided IBIs can be considered an evidence-based first step option in the treatment of depression.

4.2.3. Effectiveness of Internet-based interventions for depression in primary care

Although there is empirical evidence supporting IBIs for the treatment of depression, it has yet to be shown that results can be transferred to routine clinical practice (Schröder, Berger, Westermann, Klein, & Moritz, 2016). Most of the randomized trials on IBIs have been carried out with self-referred depressed people recruited through advertisements, leaflets, and the Internet (Cuijpers et al., 2015). However, several groups in Europe, the US, and Australia are working on examining IBIs in PC settings (Riper et al., 2010, Andrews et al., 2018). For example, Watts, Newby, Mewton, & Andrews (2012) found that the ICBT program prescribed by GPs in PC reduced suicidal ideation. Another uncontrolled trial on a guided IBI implemented in routine care showed that depressive symptomatology decreased after treatment, remaining at the 1-year follow-up (Ruwaard, Lange, Schrieken, Dolan, & Emmelkamp, 2012). Along the same lines, another Australian study showed positive results in individuals with severe depression (Williams & Andrews, 2013). Finally, the recent systematic review and meta-analysis by Wells et al. (2018) reported that therapist-supported computer-assisted CBT in PC settings could

increase treatment efficiency, reduce costs, and provide access to effective interventions for depression.

It is important for the research to prioritize how to implement IBIs in PC settings in order to reach a greater number of people, beyond the efficacy and effectiveness studies (Drozd et al., 2016).

4.3. Internet-based interventions focused on positive affect for depression

As explained above, it is important for psychological treatments to not only focus on reducing NA and also consider the promotion of PA as another essential aspect that can contribute to the therapeutic approach to depression.

The Internet seems to be promising tool for delivering interventions to enhance PA in clinical population. Several IBIS will be described below, focusing on TP and PP.

4.3.1. Internet-based transdiagnostic interventions

Internet-delivered transdiagnostic-CBT (T-CBT) can be an alternative to standard treatments for EDs (Titov et al., 2011). Newby et al. (2015), through a systematic review and meta-analysis, showed that transdiagnostic treatments were effective in reducing symptoms of anxiety and depression. In addition, the modality of treatment delivery was found to be an important moderator, with transdiagnostic face-to-face and online-delivered treatments being better than group-delivered treatments. Another meta-analysis showed that T-CBT computerized interventions for anxiety and depression are just as effective as disorder-specific interventions (Newby et al., 2016). A recent meta-analysis by Păsărelu et al. (2017) synthesized the effects of the Internet-delivered transdiagnostic and tailored CBT, taking into account the comorbidity of anxiety and depression. The results showed that these treatments produce large effects on measures of anxiety and

depression, and a moderate effect on comorbidities. Moreover, when compared to disorder-specific interventions, there were no differences in anxiety outcomes, but there were differences in depression outcomes, with the results favoring the Internet-delivered T-CBT.

Table 12 shows some of the main studies of Internet-based transdiagnostic interventions for EDs.

Table 12. Summary of some principal studies of Internet-based transdiagnostic interventions for anxiety and depression.

Study and program	Treatment target	Sample	Therapeutic approach	Control	Number of modules and duration
Day, McGrath and Wojtowicz (2013) Modified version of <i>Feeling Better</i>	Symptoms of anxiety, depression, stress	University students (18 years of age or older)	T-CBT	WL	5 (6 weeks)
Mullin et al. (2015) <i>UniWell-being course</i>	Symptoms of anxiety and depression	University students (18 years of age or older)	T-CBT	WL	5 (6 weeks)
Newby et al. (2013) <i>Depression and Anxiety Program</i>	Symptoms of anxiety and depression	Patients in PC setting (18 years of age or older)	T-CBT	WL	6 (10 weeks)
Newby, Mewton, and Andrews (2017) <i>Depression and Anxiety Program</i>	Symptoms of anxiety and depression	Patients in PC setting (18 years of age or older)	T-CBT	DS	6 (90 days)
Titov et al. (2011) <i>Well-being Program</i>	Mixed anxiety and depression	Adults (18 years of age or older)	T-CBT	WL	8 (10 weeks)
Titov et al. (2013) <i>Well-being Course</i>	Mixed anxiety and depression symptoms	Adults (18 years of age or older)	T-CBT and interpersonal therapy	WL	5 (8 weeks)
Titov et al. (2015) <i>Mood Course and Well-being course</i>	Major depression and comorbid anxiety	Adults (18 years of age or older)	T-CBT and interpersonal therapy	DS	5 (8 weeks)
Titov et al. (2016) <i>Well-being Plus Course</i>	Mixed anxiety and depression symptoms	Older adults (at least 60 years of age)	T-CBT	SG	5 (8 weeks)
Tulbure, Rusu, Sava, Salagean, and Farchione (2018) <i>Web-based Transdiagnostic Intervention</i>	Affective and mood disorders	Adults (18 years of age or older)	Adaptation of the UP protocol	WL	9 (10 weeks)

Note. T-CBT, Transdiagnostic-Cognitive Behavioral Therapy; WL, Waitlist; DS, disorder-specific; SG, self-guided.

4.3.2. Internet-based positive technologies

There are several ways to capture the relationship between PPIs and ICTs, and some possible definitions. For example, Riva, Baños, Botella, Wiederhold, and Gaggioli (2012) and Botella, Riva, Gaggioli, Wiederhold, Alcañiz, and Baños (2012) proposed the term of *Positive Technologies* to refer to the “scientific and applied approach that uses technology to improve the quality of our personal experience with the goal of increasing wellness and generating strengths and resilience in individuals, organizations, and society”. The positive technologies could be a great tool in the evaluation and treatment of EDs.

Online PPIs have shown mixed results regarding the improvement of depressive symptomatology (Bolier & Abello, 2014; Mitchell, Vella-Brodrick, & Klein, 2010). Some studies showed that online PPIs could increase participants’ happiness and decrease their depression compared to the control condition (e.g., waiting list, placebo) (Bolier et al., 2013b; Seligman et al., 2005; Shapira & Mongrain, 2010; Wellenzohn, Proyer, & Ruch, 2016). However, other studies did not (Abbott, Klein, Hamilton, & Rosenthal, 2009; Gander, Proyer, Ruch, & Wyss, 2013; Mitchell, Stanimirovic, Klein, & Vella-Brodrick, 2009; Mongrain & Anselmo-Matthews, 2012; Woodworth, O’Brien-Malone, Diamond, & Schüz, 2016). It seems that all the interventions (including placebo) were a consequence of the activation of positive and self-relevant information in participants, rather than the possibilities of the exercises themselves (Mongrain & Anselmo-Matthews, 2012).

Studies about online PPIs usually use short one-week exercises, compared to standard treatments, which use a series of modules and exercises. Thus far, there are very few studies that include longer programs, and most of them incorporate PP exercises and

other disciplines such as cognitive therapy (Abbott et al. 2009; Bolier et al., 2013b; Roepke et al., 2015), with mixed results (see table 13). One exception is the pilot study by Görge, Oehler, von Hirschhausen, Hegerl, and Rummel-Kluge (2018) that developed a more complex online program (*Get.happy*) consisting solely of PP exercises to analyze its efficacy and acceptability in a sample of patients with depression. The preliminary results showed that participants were satisfied with the program but less satisfied with its impact on the problems they were trying to solve. In addition, symptom severity decreased over time with mild to moderate effect sizes.

Overall, online PPIs have been shown to be effective in reducing depressive symptoms in non-clinical samples (e.g., Carpenter et al., 2016). However, empirical evidence about their efficacy in clinical samples does not allow clear and firm conclusions to be drawn about their use (Görge et al., 2018). It seems that the clinical features of depression (e.g., apathy, concentration problems) may be an important factor that could explain this result showing that participants lean toward more complex programs that require more active involvement and response (Linden & Schermuly-Haupt, 2014).

Taking all of the above into account, it is necessary to develop more studies that investigate the efficacy of more complex IBIs based entirely on PP in order to verify their usefulness.

Table 13. Summary of some principal studies of online PPIs for depression.

Study and program	System's description	Outcomes
Abbott et al. (2009) <i>ResilienceOnline</i>	Internet-based program of seven resilience core skills (“learning your ABCs”, “avoiding thinking traps”, “detecting icebergs”, “challenging beliefs”, “putting in perspective”, “calming and focusing”, and “real-time resilience”) to improve ability to cope with challenges and setbacks in a sample of sales managers.	There was no significant reduction in anxiety or depression due to small sample sizes and high attrition rates.
Bolier et al. (2013b) <i>Psyfit</i>	Online self-intervention based on principles of PP and elements of mindfulness, CBT, and PST in six modules (“personal mission statement and setting your goals”, “positive emotions”, “positive relations”, “mindfulness”, “optimistic thinking”, and “mastering your life”) to enhance well-being or mental fitness for mildly depressed adults.	A small reduction in depression symptoms was found after treatment, remaining at the 6-month follow-up, compared to the waitlist control group. However, the majority of participants completed only one of the six modules.
Roepke et al. (2015) <i>SuperBetter</i>	Computer and smartphone-based self-help program consisting of two modules, one of which incorporated CBT exercises (“cognitive restructuring” and “BA”), whereas the second one included PP exercises (“the 3 good things”, “identification of personal strengths”, and “guidance on using strengths in new ways”), to reduce depressive symptoms.	There was a significant reduction in depression symptoms when participants completed the entire treatment program. However, exploratory analyses showed no advantage of the PP module over the waitlist control group.

Note. PPI, Positive Psychology Intervention; CBT, Cognitive Behavioral Therapy; PST, Problem Solving Therapy; BA, Behavioral Activation.

4.3.3. Internet-based transdiagnostic interventions based on positive psychology

To date, there are very few studies on IBIs that integrate TP and PP for the treatment of depression. For example, Díaz-García et al. (2017) developed a transdiagnostic IBI for

EDs with a specific component to address PA. It is an adapted intervention based on UP (Barlow et al., 2004; Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010) and some strategies from Marsha Linehan's protocol (Linehan, 1993). The treatment protocol consists of 16 modules (with a maximum period of 18 weeks) that includes the following components: a) *elements addressed to down-regulate NA*: present-focused emotional awareness and acceptance, cognitive flexibility, behavioral and emotional avoidance patterns, and interoceptive and situational exposure; b) *traditional elements of evidence-based treatment for EDs*: psychoeducation, motivation for change, and relapse prevention; and c) *elements to promote PA*: BA strategies (e.g., pleasant and significant activities linked to values and life goals) and some aspects of Fredrickson's Broaden and Build Theory (Fredrickson, 2001). This intervention is designed and carried out by our research group Labpsitec (<http://www.labpsitec.uji.es/esp/index.php>). It is also part of a RCT with other two conditions (transdiagnostic Internet-based protocol without a PA component and a waitlist control group). This work is in progress, and no efficacy results have been published for this study.

Another related study that we have also developed in our research team, and that is part of the European ECOMPARED project (European 7FP, N° Agreement; 603,098), is the one by Vara et al. (2018). This project includes several randomized controlled non-inferiority trials in both PC and specialized care in eight European countries, in an effort to obtain clinically significant data. Specifically, we designed a blended CBT online intervention for depression. The aim of this study is to explore the clinical- and cost-effectiveness of this intervention compared to treatment as usual. Online treatment follows a TP and is based on CBT techniques, including PP strategies. As in the previous study, no results have been published yet.

So far, little research has focused on alternative methods of treatment to CBT for depression. Therefore, further research is needed into other therapeutic approaches, such as transdiagnostic and PP, whose main objective is to treat symptomatology through the promotion of PA.

4.4. Low-intensity Internet-delivered psychological interventions

In recent years, work has been carried out to integrate psychotherapy in the PC setting. In particular, efforts are being made to ensure that patients with depression receive EBPTs (DeLeon, Rossomando, & Smedley, 2004).

One of the most important barriers to providing EBPTs is that many of them consist of at least 12 to 20 weekly 1-hour sessions (Beck, 1995; Weissman, Markowitz, & Klerman, 2000). Although this treatment length is considered quite abbreviated compared to older approaches, it has been argued that it is still too intense for implementation in PC settings. As explained in previous sections, the lack of time and resources are important difficulties in the application of these types of treatments. Therefore, brief or low-intensity psychological treatments for depression are a good alternative to overcome these limitations (Castro et al., 2015). In fact, some meta-analyses suggest that depression can be effectively treated with brief psychotherapy (6 to 8 sessions), specifically with CBT, PST (Nieuwsma et al., 2012), and counselling approaches (Cape et al., 2010).

Therefore, it is necessary to have a stepped-care model that recommends low-intensity interventions as the first option before referral to high-intensity interventions (Clark et al., 2009). In fact, Bockting, Williams, Carswell, and Grech (2016) propose low-intensity interventions, the use of transdiagnostic-based treatment protocols, and the use of technologies as accessibility and implementation strategies that would contribute to reducing the big "mental health gap" in many countries.

Both guided and unguided IBIs are examples of low-intensity interventions that have received evidence as appropriate options within the stepped-care model (Bennett-Levy, Richards, & Farrand, 2010). More efficacy studies and RCTs are needed to analyze the effects of these interventions, using an active control condition as a comparison, in order to ensure their dissemination.

Low-intensity. Internet-delivered interventions could be a simple, cost-effective method for treating depression in PC settings (Donker et al., 2015).

5. Outline of this dissertation

As shown in previous sections, depression is one of the most common mental disorders in PC and Psychiatric health care settings. It has a high rate of comorbidity with other disorders (e.g., anxiety). If not treated correctly, it will tend to become chronic, reducing people's functioning in different areas (personal, academic, professional, etc.) and leading to high economic and social costs worldwide. Therefore, it is necessary to have effective and efficient treatments that can be spread easily, in order to address this major public health problem.

Depression can be treated effectively with psychotherapy (especially CBT), pharmacological interventions, or a combination of the two. Until now, most of the scientific literature has focused more attention on more traditional therapeutic currents such as CBT, the gold standard psychological treatment for depression. However, standard treatments are not always the best option because they tend to be very specific to the disorder, focus mainly on down-regulating NA, and they are often longer (e.g., in terms of the time spent by the patient or clinician), without taking into account other important aspects such as the high rate of comorbidity between disorders, the role of up-regulating PA, and the characteristics of the patient (e.g., motivation, stigma, lack of time,

problems with accessibility to treatment) and the clinician (e.g., level of training and experience in the different psychological treatments).

Transdiagnostic treatments, PPIS, the use of Internet, and the low-intensity treatments could be good alternative approaches to treating depression. In recent years, these approaches have begun to accumulate empirical evidence, although more research is still needed, particularly in PC settings. Therefore, the **general objective** of this dissertation is to analyze in an RCT the efficacy and cost-effectiveness of an improved treatment-as-usual with a low-intensity Internet-based computerized intervention focused on the promotion of positive affect (ITAU+IPPA), compared to only improved treatment-as-usual (only-ITAU) in Spanish PC settings.

The **specific objectives** of this dissertation are:

1. To examine the efficacy of both interventions (ITAU+IPPA and only-ITAU) in decreasing depression severity and increasing other secondary variables (affect, health-related quality of life, well-being and mindfulness) after treatment and follow-ups (6 and 12 months).
2. To analyze whether both interventions (ITAU+IPPA and only-ITAU) are cost-effective psychological treatments for depression in PC settings.
3. To analyze the participants' opinions of the treatment received.
4. To explore the possible mediator and moderator roles of several relevant variables in the effect of the condition on the depression severity.

In the following chapter, the objectives described above will be analyzed in depth.

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CHAPTER

2

**EFFICACY AND COST-EFFECTIVENESS
OF A LOW-INTENSITY INTERNET-
BASED INTERVENTION FOCUSED ON
THE PROMOTION OF POSITIVE
AFFECT FOR THE TREATMENT OF
DEPRESSION IN PRIMARY CARE: A
RANDOMIZED CONTROL TRIAL**

1. Introduction

Depression is one of the most prevalent mental disorders worldwide, and it is associated with significant personal (e.g., in terms of quality of life or well-being) and social (e.g., in terms of economic expenditure and use of services) costs (Gustavsson et al., 2011; Kessler, 2012; Mrazek, Hornberger, Altar, & Degtiar, 2014; Parés-Badell et al., 2014). Specifically, the prevalence of depression in Spanish Primary Care (PC) is between 13.9 and 29% (Roca et al., 2009; Alonso et al., 2004), and less than 50% of these patients receive the appropriate treatment (e.g., Aragonès, Piñol, Labad, Folch, & Mèlich, 2004).

Although there are currently effective treatments for depression (medication, psychotherapy, or both) (Huhn et al., 2014; Cuijpers, van Straten, van Oppen, Andersson, 2008; Cuijpers et al., 2013), these treatments do not reach the growing number of people who need them (Kazdin & Blase, 2011). This situation may be due to long waiting list periods in PC settings, reduced clinician time to assist to the patient, social stigma about mental illness, and lack of well-trained professionals, among others (Gaston, Abbott, Rapee, & Neary, 2006; Harvey & Gumport, 2015; Sartorius, 2002; Wittchen et al., 2011). Therefore, it is necessary to incorporate new tools to provide evidence-based treatments (EBT) for depression in order to respond effectively to this need.

Low-intensity interventions could be a good alternative to overcome these limitations (Bockting, Williams, Carswell, & Grech, 2016) and bring an adequate assistance to those who need it. Particularly, Internet-based interventions (IBIs) received empirical evidence as an appropriate option to deliver interventions within the stepped-care model (Bennett-Levy, Richards, & Farrand, 2010). In fact, some meta-analyses suggested that depression can be effectively treated with brief psychotherapy (from 6 to 8 sessions). Specifically,

this intervention are based on cognitive behavioral therapy (CBT), problem-solving therapy (Nieuwsma et al., 2012), and counseling approaches (Cape, Whittington, Buszewicz, Wallace, & Underwood, 2010). However, none of them have proven its efficacy in comparative to an active condition, therefore more efficacy studies and randomized controlled trials (RCTs) are needed to analyze the effects of these interventions using an active control condition as a comparison.

The IBIs have been proposed as a useful option that can help to reduce the gap between treatment demands and supply (Andersson & Titov, 2014; Cuijpers, Kleiboer, Karyotaki, & Riper, 2017; Holst et al., 2018). Several studies have demonstrated their effectiveness and acceptability in treating depression (Andersson & Cuijpers, 2009; Andersson, 2016; Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Karyotaki et al., 2018). Moreover, some reviews have shown that IBIs are more effective when patients received a guidance (automated reminders to motivate and feedback by e-mail, text messages, or brief telephone calls), emphasizing the positive relationship between therapist support and the improvement rates (Baumeister, Reichler, Munzinger, & Lin, 2014; Berger, Hämmerli, Gubser, Andersson, & Caspar, 2011; Johansson & Andersson, 2012; Richards & Richardson, 2012). In addition, a systematic review about the economic cost of IBIs in mental health showed that IBIs were more likely to be less cost-effectiveness compared to non-guided interventions, waiting list, routine care, group CBT, and telephone counseling (Donker et al., 2015). Finally, similar effect sizes have been found between IBIs and face-to-face therapies (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014; Andersson, Topooco, Havik, & Nordgreen, 2016).

So far, most IBIs for depression have been based primarily on CBT (Andersson, 2009; Hedman, Ljótsson, & Lindefors, 2012), and other therapeutic approaches such as problem-solving therapy (van Straten et al., 2008), interpersonal therapy (Donker et al.,

2013), acceptance and commitment therapy (Brown, Glendenning, Hoon, & John, 2016), psychodynamic therapy (Johansson et al., 2012), or behavioral activation (Nyström et al., 2017). Although these approaches are effective for depression, not all patients benefit from these types of treatments, perhaps because most standard treatments focus on more specific mental disorders without taking into account the presence of comorbidities (e.g., anxiety disorders) or unspecified disorders (Fairburn, Cooper, & Shafran, 2003; Kring & Sloan, 2009). An alternative approach that could contribute to resolving these limitations is the transdiagnostic perspective (TP) (Sauer-Zavala et al., 2017).

The TP focuses primarily on what the emotional disorders (such as depression and anxiety) have in common, rather than on what is specific and differential (Sandín, 2012). Along these lines, Brown and Barlow (2009) suggested that emotional disorders share a common latent structure with two dimensions (negative affect (NA) or behavioral inhibition and positive affect (PA) or behavioral activation), which, associated with different stressors, can lead to anxious or depressive symptoms. This conceptualization of emotional disorders led to the design and implementation of transdiagnostic protocols with common treatment components within a more parsimonious framework, such as the Unified Protocol (Barlow et al., 2011) and transdiagnostic group CBT (Norton, 2012). Recent reviews and meta-analyses have shown that transdiagnostic treatments are effective for emotional disorders compared to waiting list groups or treatment as usual (Reinholt & Krogh, 2014), and even compared to disorder-specific interventions (Pearl & Norton, 2017). Furthermore, these effectiveness results can be transferred to the field of IBIs (Newby, McKinnon, Kuyken, Gilbody, & Dalgleish, 2015; Newby, Twomey, Yuan Li, & Andrews, 2016; Păsărelu, Andersson, Bergman Nordgren, & Dobrea, 2017).

Thus far, the majority of psychological treatments (e.g., CBT or transdiagnostic) for emotional disorders have focused primarily on interventions designed for the NA

dimension, paying less attention to building positive resources. Some studies suggest that the PA system may be the key to facilitating recovery from anxiety and depression disorders (Dunn, 2012; Fredrickson, 2013; Garland et al., 2010; Layous, Chancellor, & Lyubomirsky, 2014). Taking into account the role of PA in the emotional disorders, it is necessary to include this dimension as an intervention strategy, especially in the transdiagnostic treatments (Carl, Soskin, Kerns, & Barlow, 2013).

A perspective that emerged strongly with the aim of enhancing positive emotional human functioning, and especially PA, is positive psychology (PP) (Seligman & Csikszentmihalyi, 2000). PP aims to enhance or generate a series of protective factors (e.g., well-being, resilience, satisfaction with life) that prepare the person to deal with stressful situations that s/he may find in the present or that may appear in the future (Fredrickson, 2001; Tugade & Fredrickson, 2007; Vázquez & Hervás, 2008).

PP is especially relevant to people suffering from depression. For example, Santos et al. (2013) concluded that positive psychology interventions (PPIs) reduce both symptoms of depression and the potential for relapse into subsequent periods of depression. Furthermore, several meta-analyses have demonstrated their effectiveness in reducing depressive symptomatology and increasing well-being (Bolier et al., 2013; Chakhssi, Kraiss, Sommers-Spijkerman, & Bohlmeijer, 2018; Sin & Lyubomirsky, 2009; Weiss, Westerhof, & Bohlmeijer, 2016), emphasizing their role alongside standard treatments for clinical depression (Johnson & Wood, 2015).

Regarding IBIs and PPIs, the literature has shown mixed results regarding the improvement of depressive symptoms (Bolier & Abello, 2014; Mitchell, Vella-Brodrick, & Klein, 2010). Some studies showed that online PPIs could increase participants' well-being and decrease their depression, compared to the control conditions (Bolier et al., 2013; Mitchell, Stanimirovic, Klein, & Vella-Brodrick, 2009; Seligman et al., 2005;

Shapira & Mongrain, 2010; Wellenzohn, Proyer, & Ruch, 2016), whereas other studies did not (Abbott, Klein, Hamilton, & Rosenthal, 2009; Gander, Proyer, Ruch, & Wyss, 2013; Mitchell et al., 2009; Mongrain & Anselmo-Matthews, 2012; Woodworth, O'Brien-Malone, Diamond, & Schütz, 2016). In addition, most of the online PPIs have used short one-week exercises, compared to standard treatments, which use a series of modules and exercises. Thus far, there are very few studies that include longer programs, and most of them incorporate PP exercises and other disciplines such as cognitive therapy (Abbott et al. 2009; Bolier et al., 2013b; Roepke et al., 2015).

Therefore, it is necessary to develop more studies that investigate the efficacy of more complex IBIs based on TP and PP in order to verify their effectiveness (Görges, Oehler, von Hirschhausen, Hegerl, & Rummel-Kluge, 2018). In this regard, Taylor, Lyubomirsky, and Stein (2017) and González-Robles, García-Palacios, Baños, Quero, and Botella (2017) evaluated the efficacy of two new transdiagnostic interventions based on PP to upregulate PA in anxiety and depression, finding promising efficacy results for the treatment of the emotional disorders. Furthermore, Díaz-García et al. (2017) also developed a transdiagnostic IBI with a specific component to address PA. The treatment protocol consisted of 16 modules that included elements to down-regulate NA, traditional elements of EBT for the emotional disorders, and elements to promote PA. This intervention was also part of an RCT with other two conditions (transdiagnostic IBI protocol without a PA component and a waitlist control group). This work is in progress, and no efficacy results have been published for this study.

Given that low-intensity IBIs, TP, and PPIs have begun to accumulate empirical evidence for the treatment of depression, more studies are needed to demonstrate their efficacy and cost-effectiveness in routine clinical practice. Therefore, the present study aims to explore the efficacy and cost-effectiveness of an improved treatment as usual

(ITAU) with a low-intensity Internet-based computerized intervention focused on the promotion of positive affect (ITAU+IPPA) for the treatment of depression, compared to only the ITAU (only-ITAU) in Spanish PC centers. This trial is part of the FIS project from the Carlos III Health Institute of the Spanish Ministry Economy and Competitiveness (ETES n° PI13/00982; PSI2010-17563), which includes a multicenter RCT in four parallel conditions: a) a healthy lifestyle psychoeducational program, b) a program focused on positive affect promotion, c) a brief intervention based on mindfulness, and d) ITAU in PC.

Only clinical data related to the ITAU+IPPA and only-ITAU conditions will be taken into account in this study. The specific objectives are:

1. To examine the efficacy of the two interventions (ITAU+IPPA and only-ITAU) in improving depression severity and other secondary variables (affect, health-related quality of life, well-being, and mindfulness) after treatment and follow-ups (6 and 12 months).
2. To analyze whether the two interventions (ITAU+IPPA and only-ITAU) are cost-effective psychological treatments for depression in a PC setting.
3. To observe the participants' opinions of the treatment received.
4. To analyze whether the effect of condition (ITAU+IPPA vs. only-ITAU) on depression severity is mediated by the change in PA.
5. To explore whether sociodemographic (sex, age, marital status, educational level, occupation, and income level) and baseline clinical variables (depression severity, health-related quality of life, well-being, and mindfulness) moderate the effect of the condition on depression severity.

Specifically, the **hypotheses** of this study are:

H1. The ITAU+IPPA condition will be more efficacious than the only-ITAU condition in improving depression severity and other secondary variables (affect, health-related quality of life, wellbeing, and mindfulness) after treatment and follow-ups (6 and 12 months).

H2. The ITAU+IPPA condition will be more cost-effective than the only-ITAU condition in terms of health and social services use (visits to the GP, visits to the emergency room, absence from work, leaving the usual tasks unfinished, and reduction in the quality of usual tasks due to health problems) in the follow-ups.

H3. The user's opinion about the treatment (rationale, satisfaction, the recommendation to others, and usefulness) will be better in the ITAU+IPPA condition at all moments of the assessment.

H4. Participants in the ITAU+IPPA condition (compared to control) will have a greater change in PA (both after treatment and follow-ups), leading to a greater reduction in depression severity (both after treatment and follow-ups).

H5. No specific hypotheses are generated about which moderator variables (sociodemographic and baseline clinical variables) could be significant in the effect of the condition (ITAU+IPPA vs. only-ITAU) on depression severity after the treatment and follow-ups, due to the exploratory nature of the analyses.

2. Method

2.1. Study design

A two-arm randomized controlled and cost-effectiveness trial was carried out, with repeated measures (baseline, post-treatment, 6-month follow-up, 12-month follow-up) and two conditions: IPPA+ITAU and only-ITAU (control group) in a PC setting. The

study followed the CONSORT 2010 statement (Consolidated Standards of Reporting Trials, <http://www.consort-statement.org>) (Schulz et al., 2010), the CONSORT-eHEALTH guidelines (Eysenbach et al., 2011), and the Recommendations for Interventional Trials (SPIRIT) (Chan et al., 2013).

2.2. Sample size

The sample size was estimated using G*Power 3 (Faul, Erdfelder, Lang, & Buchner, 2007). A required sample size of 52 participants (26 per condition) was calculated, taking into account a power of 0.80, an alpha level of 0.05, and a small-medium effect size ($f = 0.20$, according to the studies by Bolier et al. 2013b and Meyer et al. 2015). Based on the literature on Internet-based interventions, a dropout rate of between 20-30% is expected (Spek et al., 2007; van Ballegooijen et al., 2014). Thus, a total of 66 participants had to be recruited.

2.3. Study population, recruitment, eligibility criteria, and randomization

Patients who reported depressive symptoms to their general practitioner (GP) were invited to participate in this trial. The GPs explained the characteristics of the study to the patients. The recruitment was implemented in Spanish PC centers in the regions of Aragon, Andalusia, and the Balearic Islands, and it started on May 2015 and ended on May 2017. The GPs completed a referral report describing general patient characteristics including the personal data, so the local researcher could contact the participant. All the interested patients signed an informed consent to take part in the study. To confirm inclusion/exclusion criteria (see Table 1), the researcher administered the psychological assessment instruments through a telephone interview: the MINI International Neuropsychiatric Interview for diagnosis version 5 (Ferrando et al., 1998), Patient Health

Questionnaire-9 (PHQ-9) (Diez-Quevedo, Rangil, Sanchez-Planell, Kroenke, & Spitzer, 2001), and sociodemographic variables.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Minimal criteria of 18 years	Presence of serious psychiatric comorbidities (substance dependence, bipolar affective disorder, obsessive compulsive disorder, psychotic illness)
Meeting the DSM-5 diagnostic criteria for Major Depressive Disorder or Persistent Depressive Disorder (Dysthymia)	High risk of suicide
Ability to understand and read Spanish	Receiving psychological treatment for depression at the moment of recruitment
Access to the Internet and having an email account	An increase and/or change in the pharmacological treatment (in the case of receiving) during the study period
Providing written informed consent	Presence of severe physical illness

After the confirmation of the diagnosis, patients were randomly assigned to one of the two conditions (ITAU+IPPA and only-ITAU). The allocation was carried out by an independent researcher who belonged to the REDIAPP (Research Network on Preventative Activities and Health Promotion) and who was not involved in the study. The method used to implement the random allocation sequence was a central telephone. The sequence was concealed until interventions were assigned. The patients agreed to

participate before the random assignment and without knowing what treatment would be assigned to them. The researchers (who conducted the psychological assessments) and the GPs (who applied the ITAU treatment following the recommendations of the guidelines for the treatment of depression) were blind to the participants' treatment conditions.

The assigned condition was communicated to the participants via phone call. In this call, a clinical psychologist (a professional with Master's degree in Clinical Psychology, with at least two years of experience in the diagnosis, psychological evaluation, and treatment) explained the procedure before starting the assigned intervention.

Before and after the interventions, the participants filled out the assessments via telephone or online. Online follow-up assessments were programmed at 6 and 12 months.

2.4. Ethics

The study followed the guidelines of the Helsinki Declaration (World Medical Association, 2013). All the researchers followed the guidelines for Good Clinical Practice (Food Drug Administration, 1997). All the participants were volunteers, and they did not receive any compensation for their participation. Participants were able to withdraw from the study at any time, without giving any reason and with no consequences. The study was registered in the ISRCTN registry under the number: ISRCTN82388279 (<http://www.isrctn.com/ISRCTN82388279>).

2.5. Interventions

All the patients included in the study (regardless of the treatment group to which they were randomly assigned) were treated by their GPs.

2.5.1. Improved treatment as usual (ITAU)

The Treatment as Usual in PC settings was improved because the participating GP received a training program on how to diagnose and treat depression in PC, based on the Spanish Guide for the Treatment of Depression in Primary Care (Fernández et al., 2006). In the case of suicide risk, severe social dysfunction, or worsening of symptoms, it was recommended to refer the patient to mental health services.

Criteria for minimally adequate treatment were: receiving medication for at least 2 months, plus at least 4 visits with a GP lasting an average of 30 minutes (Fernández et al., 2006).

2.5.2. Improved treatment as usual with a low-intensity Internet-based computerized intervention focused on the promotion of positive affect (ITAU+IPPA)

2.5.2.1. Face-to-face session

In addition to the treatment provided with the GP, the participants also received a 90-minute (3-5 patients) group face-to-face session conducted by a clinical psychologist. The objective of this session was to explain the program structure and main components of treatment, clarify the instructions for the use of the online platform, and motivate participants to change. Ultimately, the final goal was to reinforce commitment and adherence to treatment.

2.5.2.2. Online intervention program

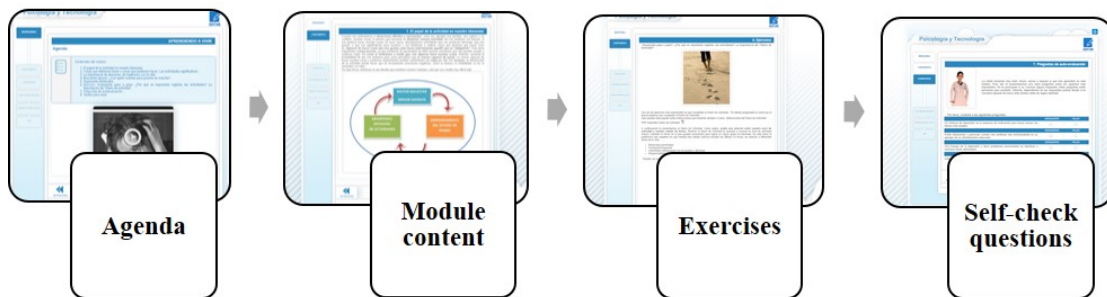
The online self-guided program consisted of 4 therapeutic modules (60 minutes per module). The duration of the program could vary among the users, but it was usually

completed in 4 to 8 weeks (maximum 2 weeks per module). These modules contained multimedia elements (videos, images, texts) that provided information about depression and coping strategies (see Figure 1). These modules were sequential in order to move step by step through the program. Moreover, users could review the module contents once they were finished. Figure 2 shows the schema of the structure of the program modules.

Figure 1. Screenshot of module 4 “Living and learning”.



Figure 2. Schema of the structure of the program modules.



Specifically, this intervention followed the TP and was based on PP techniques. It was mainly designed to decrease depression severity and prevent relapses using the promotion of well-being and PA. Each module, with its objectives, specific content, and empirical source, is shown in Table 2.

Additionally, the online platform included two interactive tools that are available for the patients during the intervention: 1) *Activity Diary*, where the users had to register their activities performed in relation to social areas, work, and leisure, considering their influence on mood and enjoyment. 2) *Feedback Section*, where users could visualize their progress in their mood through different graphs (weekly and pre/post/follow-up moments) (see Figure 3). Moreover, the program also included an assessment protocol at different moments (pre-treatment, post-module, post-treatment, and follow-ups).

Figure 3. Screenshot of the feedback section.



We used the web platform *psicologiaytecnologia* to deliver the intervention designed by our research team (<http://www.labpsitec.uji.es/esp/index.php>).

The participants received two weekly, automated mobile phone messages, encouraging them to proceed with the program and reminding them of the importance of doing the homework tasks. In addition, the participants received automated e-mails encouraging them to continue with the modules if they had not accessed the program for a week.

For more information on the protocol for the promotion of PA, see the chapter written by García-Palacios, Mira, Mayoral, Baños, and Botella (2017) and the protocol study by Castro et al. (2015).

Table 2. Modules, objectives, therapeutic content, and empirical sources of the online program.

Module	Objectives	Therapeutic content	Empirical sources
1. Learning to live	<ul style="list-style-type: none"> - Understanding the role of activity in mood regulation and our well-being. - Establishing and maintaining an adequate activity level and the relevance of choosing activities that are significant, with a personal meaning for the individual. - Learning the procedure to follow to schedule meaningful activities in daily life. 	<ol style="list-style-type: none"> 1. The role of activity in our well-being. 2. Things we should do and things we can do: meaningful activities. 3. The importance of daring, of getting involved with life. 4. Seeking social support. 5. Overcoming obstacles. 	<p>Ekers, Richards, McMillan, Bland, and Gilbody (2011)</p> <p>Kanter, Puspitasari, Santos, and Nagy (2012)</p>
2. Learning to enjoy	<ul style="list-style-type: none"> - Learning about the effect of positive emotions in our lives. - Learning procedures to increase the likelihood of experiencing positive emotions, promoting the occurrence of pleasant activities in order to learn to enjoy the present moment. 	<ol style="list-style-type: none"> 1. Positive emotions such as seeds or life anchors. 2. Satisfaction with the present. 3. Learning to generate good moments. 4. The importance of smiling. 5. Learn to identify, capture and save good times. 	<p>Bryant, Chadwick, and Kluwe (2011)</p> <p>Ekman, Davidson, and Friesen (1990)</p> <p>Catalano and Fredrickson (2011)</p> <p>Soussignan (2002)</p>
3. Accepting life	<ul style="list-style-type: none"> - Focusing on positive emotions related to the past (e.g., gratitude) or the future (e.g., optimism). - Identification and management of beliefs and behaviors that disturb the good moments. 	<ol style="list-style-type: none"> 1. Satisfaction with the past. 2. Satisfaction with the future. 3. Psychological well-being as a result of being active and practicing learned strategies. 	<p>Rash, Matsuba, and Prkachin (2011)</p> <p>Seligman et al. (2005)</p> <p>Sheldon and Lyubomirsky (2006)</p>
4. Living and learning	<ul style="list-style-type: none"> - Understanding life as a continuous process of learning and personal growth. - Emphasizing training in strategies to promote psychological strengths, resilience, and meaningful goals linked to important values. 	<ol style="list-style-type: none"> 1. Finding psychological well-being. 2. Potential, talents, and life goals. 3. Living with others, finding support in others. 4. What do I want my future to be like? 	<p>Sheldon and Lyubomirsky (2006)</p>

2.6. Measures

The study measures and assessment times (online and by phone) are summarized in Table 3.

2.6.1. Primary outcome

Depression severity: The Patient Health Questionnaire-9 (PHQ-9; Kroenke, Spitzer, Williams, 2001) is a 9-item self-administered test for screening, diagnosing, monitoring and measuring depression severity. Participants describe their state taking into account the last two weeks prior to evaluation. Items are rated from 0 to 3 denoting “not at all”, “several days”, “more than half the days” and “nearly every day”, respectively. Cut-offs of 5, 10, 15 and 20 represent mild, moderate, moderately severe, and severe depression, based on the criteria identified by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR; APA, 2000). The Spanish version has been shown to have good psychometric properties (for the diagnosis of any disorder, $k = .74$; overall accuracy, 88%; sensitivity, 87%; specificity, 88%) (Diez-Quevedo, Rangil, Sanchez-Planell, Kroenke, & Spitzer, 2001).

2.6.2. Secondary outcomes

Diagnostic interview: The MINI International Neuropsychiatric Interview version 5.0 (M.I.N.I. 5.0; Sheehan et al., 1998) is used at the screening to assess current depression and comorbid disorders. This measure is a structured diagnostic interview based on the DSM-IV (DSM-IV, 1994) and on International Classification of Diseases-10 (ICD-10; World Health Organization, 1993) criteria. The Spanish version (Ferrando et al., 1998) was used for this study.

Affect: The Positive and Negative Affect Scale (PANAS; Watson, Clark, Tellegen, 1988) consists of 20 items that evaluate two independent dimensions: PA (10 items) and NA (10 items). The total score for each subscale ranges from 5 to 50, using a 5-point Likert-type scale (1=very slightly or not at all, 5 = very much). The Spanish version by Sandín et al. (1999) showed adequate internal consistency (Cronbach's α between .87 and .91). The "state" version was used in the post-module assessment, and the "trait" version in the pre-treatment, post-treatment, and follow-up (6 and 12 months) assessments.

Health-related quality of life: The Short Form 12 Health Survey (SF-12; Ware, Kosinski, Keller, 1996) is a 12-item questionnaire that measures aspects of health-related quality of life from the patient's perspective. It contains eight domains in two dimensions: physical health (general health, bodily pain, role-physical, physical functioning) and mental health (mental health, role-emotional, social-functioning, vitality). Scores > 50 represent better physical or mental health than the mean, and scores < 50 represent worse physical or mental health than the mean. The Spanish validated version (Gandek et al., 1998) was used. This instrument has been found to be a valid and reliable measure, showing good internal consistency (Cronbach's $\alpha > .70$) (Vilagut et al., 2008).

Well-being: The Pemberton Happiness Index (PHI; Hervás & Vázquez, 2013) consists of 11 items related to different domains of remembered well-being (general, hedonic, eudaimonic and social well-being), each with an 11-point Likert-type scale (0 = fully disagree, 10 = fully agree), and 10 items related to experienced well-being (positive and negative emotional events that possibly happened the day before), with dichotomous response options (yes/no). The remembered well-being score is calculated with the mean score of the 11 items and varies from 0 to 10. The items for experienced well-being are transformed into a single score from 0 (zero positive experiences and 5 negative experiences) to 10 (5 positive experiences and no negative experiences). The sum of the

remembered and experienced well-being scores results in a combined well-being index (total well-being) ranging from 0 to 10. The validated Spanish version showed adequate psychometric properties (Cronbach's $\alpha > .80$) (Hervás & Vázquez, 2013).

Facets of mindfulness: The Five Facet Mindfulness Questionnaire (FFMQ; Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006) comprises 39 items, rated on a 5-point Likert-type scale (1 = never or very rarely true, 5 = very often or always true), that assess five facets or factors of mindfulness: observing (tendency to attend to internal and external experiences such as sensations, emotions, sounds), describing (tendency to describe and label these experiences with words), acting with awareness (tendency to give full awareness and attention to current activities or experiences), not judging inner experience (tendency for a nonevaluative stance toward inner experiences), and not reacting to inner experience (tendency to allow thoughts and feelings to come and go, without getting caught up in them). The Spanish version demonstrated good internal consistency (Cronbach's $\alpha > .80$) (Cebolla et al., 2012).

2.6.3. Cost outcomes

Health and social services use: An ad hoc 5-item questionnaire to assess costs related to the use of health and social services (“number of visits to the GP in the past three months”, “number of visits to the emergency room in the past three months”), lost productivity at work (“number of days off work in the past year”), and the impact of illness on the usual tasks (“number of days that usual tasks have been left unfinished due to health problems in the past month”, “number of days when the quality of usual tasks has been reduced due to health problems in the past month”).

2.6.4. Other outcomes

Sociodemographic data: Personal data that includes information such as age, marital status, educational level, occupation, and income level.

Opinion about the treatment received: An ad hoc 5-item questionnaire rated on a 10-point Likert-type scale (0 = fully disagree, 10 = fully agree) to measure aspects related to the treatment received in terms of: rationale behind the treatment, satisfaction with the treatment, recommendation of treatment to others, usefulness of the treatment in your case, and usefulness of the treatment for other psychological problems.

Table 3. The study measures and assessment times (online and by phone).

Variable	Instrument	Pre-treatment		Post-treatment		Follow-up 1 (6 months)		Follow-up 2 (12 months)	
		Online	Phone	Online	Phone	Online	Phone	Online	Phone
Primary outcome									
Depression severity	PHQ-9*		x	x		x		x	
Secondary outcomes									
Diagnostic interview	M.I.N.I.		x						
Affect	PANAS*	x		x		x		x	
Health-related quality of life	SF-12	x				x		x	
Well-being	PHI	x				x		x	
Facets of mindfulness	FFMQ	x				x		x	
Cost outcomes									
Health and social services use	Ad hoc		x				x		x
Other outcomes									
Sociodemographic data			x						
Opinion about the treatment received	Ad hoc	x		x					

*Note.**This instrument was also administered in the post-module assessments. PHQ-9, Patient Health Questionnaire-9; M.I.N.I, MINI International Neuropsychiatric Interview; PANAS, Positive and Negative Affect; SF-12, Short Form 12 Health Survey; PHI, Pemberton Happiness Index; FFMQ, Five Facet Mindfulness Questionnaire.

2.7. Data analyses

All statistical analyses were performed using the software package SPSS 24.0 (IBM) for Windows. Group differences in participants' sociodemographic, clinical, and cost-effectiveness data were examined using independent-samples t-tests (t) for continuous variables and chi-square tests (χ^2) for categorical variables. When the contrast χ^2 with the typical asymptotic method was not reliable –because more than 20% of the cells had an expected frequency of less than 5–, the Monte Carlo method was used with 10,000 samples and a 99% confidence level.

Intent-to-treat mixed-model analyses without any ad hoc imputations were used to handle missing data (Chakraborty & Gu, 2009). This approach is appropriate for RCTs with multiple time points and pre-to-post-only designs, and it does not assume that the last measurement is stable (the last observation carried forward assumption). This method is conducted using all the available observations (Gueorguieva & Krystal, 2004; Salim, Mackinnon, Christensen, & Griffiths, 2008). The assumption that data were missing completely at random (MCAR) was evaluated using Little's MCAR test. To analyze the effect of condition on the primary (depression severity) and secondary outcomes (affect, health-related quality of life, remembered and experienced well-being, and facets of mindfulness), as well as on the cost-effectiveness and opinions of the participants, 29 linear mixed models were implemented with Time (pre-treatment, post-treatment, 6-month and 12-month follow-ups) as within-group factor and Group (ITAU+IPPA and only-ITAU) as between-group factor, using the MIXED procedure with 1 random intercept per subject, in order to analyze the effect of time and the condition x time interaction effect. In addition, effect sizes (*Cohen's d*; 95% confidence interval, CI) were calculated for within-group comparisons (pre vs. post; pre vs. follow-up-1; pre vs. follow-up-2) for each condition to analyze the size of the change from pre-treatment to post-

treatment and follow-up scores for each condition independently, as well as between-group comparisons at each point to analyze the size of the differences between conditions at post-treatment, at follow-up-1, and at follow-up-2 (Ausina & Meca, 2015; Cumming, 2013; Cumming & Calin-Jageman, 2016). Based on Cohen's logic (1988), a standardized mean difference of $d = 0.2$ represents a “small” effect size, $d = 0.5$ a “medium” effect size, and $d = 0.8$ a “large” effect size.

The Reliable Change Index (RCI) (Jacobson & Truax, 1991) for depression severity was calculated in the completer sample. The RCI was calculated to make sure that the change indicated by the PHQ-9 total score was not due to measurement error, but rather to a reliable and real change in the level of depression severity. Criterion C was chosen to determine whether the participant's score was within the functional population distribution ($C = (M_{\text{dysfunctional}} \times SD_{\text{functional}} + M_{\text{functional}} \times SD_{\text{dysfunctional}}) / SD_{\text{dysfunctional}} + SD_{\text{functional}}$). Participants were classified as: (a) "recovered" when the RCI was $\geq |1.96|$ and their total PHQ-9 score was within the range of the functional distribution; (b) "improved" when the RCI was $\geq |1.96|$, but their total PHQ-9 score was not within the range of the functional level; (c) "unchanged" when the RCI was $< |1.96|$; and (d) “deteriorated” when the RCI was $\geq |1.96|$, but their total PHQ-9 was in the direction of a deterioration (McGlinchey, Atkins, & Jacobson, 2002). Chi-square tests (χ^2) were performed to evaluate group differences in RCI rates.

In order to analyze changes in depression severity and affect taking into account post-module assessments in the ITAU+IPPA condition, 3 linear mixed models were conducted for the ITAU+IPPA condition with Time (pre-treatment, post-modules, and post-treatment) as a within-group factor, using MIXED procedure.

Finally, to explore the mediator and moderator variables, mediation and moderator analyses were performed using the procedure described by Hayes (2013) with the PROCESS macro (version 2.16), choosing models 4 and 1, respectively. First, three simple mediation analyses¹ were performed to test whether the effect of condition on the post, follow-up-1, and follow-up-2-PHQ-9 scores was mediated by the change in positive affect PANAS scores (post, follow-up-1, and follow-up-2-PANAS scores). Change in PA was calculated using the pre-PHQ-9 score and post-follow-up-1 and follow-up-2-PHQ-9 scores, where positive values for change in positive affect PANAS scores reflected an improvement. Bias-corrected bootstrap 95% CIs based on 5,000 samples were used to assess the indirect effects. CIs that did not include the zero-value indicated a significant indirect effect, meaning that the effects of the condition on the post-follow-up-1 and or follow-up-2-PHQ-9 scores were mediated by the changes in PA. Second, 21 moderation analyses were carried out to examine whether the relationship between the condition and the post-follow-up-1 and follow-up-2-PHQ-9 scores was moderated by sociodemographic (sex, age, marital status, educational level, occupation, and income level) and baseline clinical variables (depression severity PHQ-9, health-related quality of life SF-12, well-being PHI, and mindfulness FFMQ). Tests of significance ($p < .05$) or a CI (not including zero) in the interaction between independent variables (condition) and the moderator variables (sociodemographic variables and clinical variables) indicated whether these variables moderated the effect of condition on post-follow-up-1 and follow-up-2-PHQ-9 scores. We examined the conditional effect of condition on the post-follow-up-1 and follow-up-2-PHQ-9 at medium (the mean), low ($-1 SD$), and high ($+1 SD$) levels of sociodemographic variables and clinical variables using the “pick-a-point approach” (or analysis of the simple slopes).

¹ These analyses were conducted only with completers.

3. Results

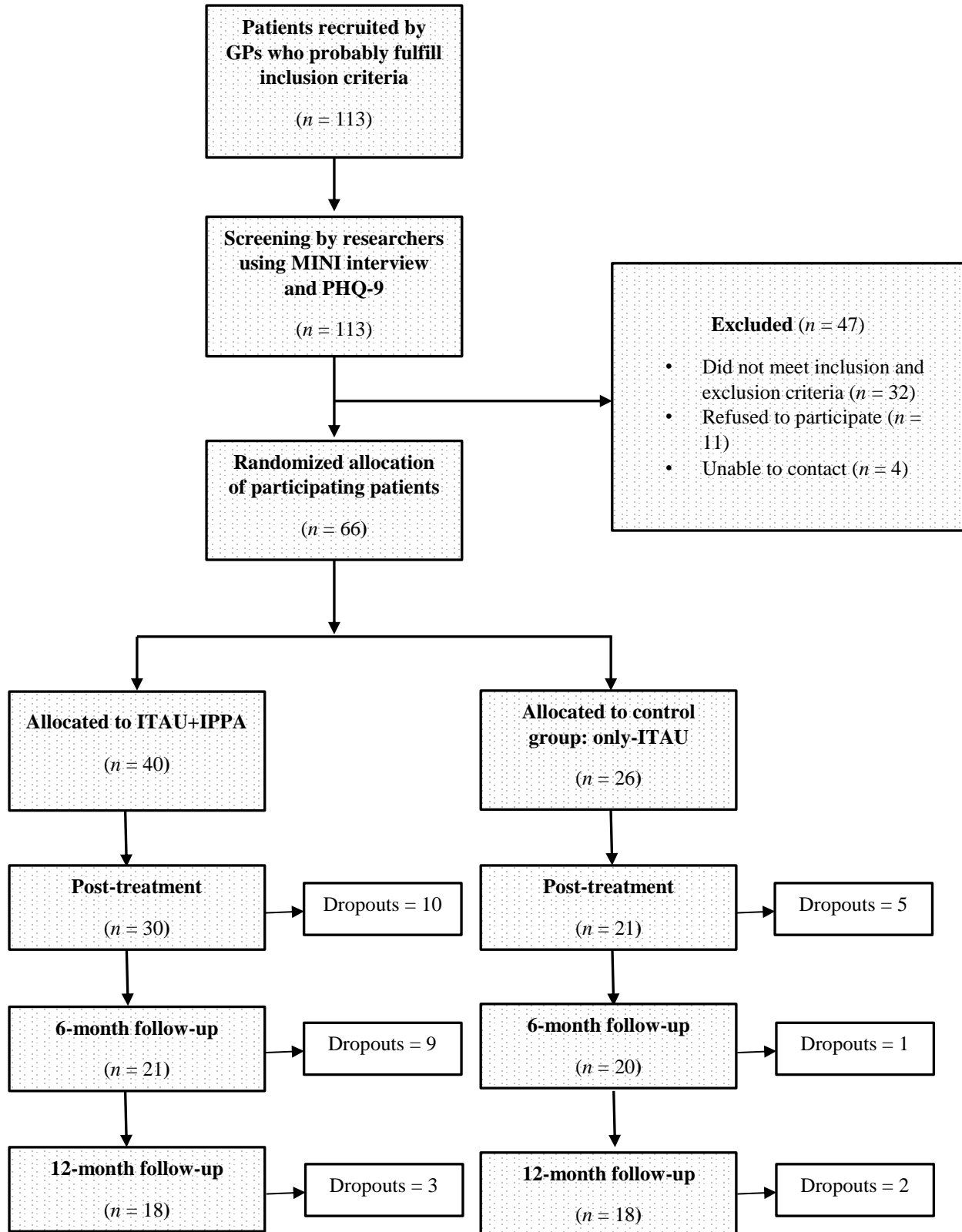
3.1. Participants flow and attrition

Initially, as the flow diagram shows (Figure 4), 113 participants were interested in the study, and 47 were excluded from the trial. Finally, 66 participants were included in the study, and they were randomly allocated to each condition (ITAU+IPPA, $n = 40$; only-ITAU, $n = 26$). Thus, 25% of participants from the ITAU+IPPA condition and 19% from the only-ITAU condition dropped out of the post-treatment, and 47.5% of participants from the ITAU+IPPA condition and 23.07% from the only-ITAU condition dropped out during the 6-month follow-up. Finally, 55% of participants from the ITAU+IPPA condition and 30.76% from the only-ITAU condition dropped out during the 12-month follow-up. Data were missing completely at random (MCAR) ($p > .05$). Regarding the depression severity of those participants who dropped out before ITAU+IPPA post-treatment, 2 participants showed mild depression severity, 1 participant showed moderate severity, and 8 participants showed moderate-severe severity. Concerning to the participants of the only-ITAU condition, 1 participant showed mild depression severity, 1 participant showed moderate severity, and 3 participants showed moderate-severe severity.

With respect to the percentage of participants who completed each module in the ITAU+IPPA condition, only 45% of participants completed all the treatment modules, 65% completed three modules, 72.5% two modules, and 77.5% one module. Specifically, 2 participants dropped out after post-module 1, showing a moderate and severe depression severity. 3 participants dropped out after post-module 2, showing a mild, moderate and severe depression severity; and 8 participants dropped out after post-module 3, showing

a mild (4 participants), moderate (2 participants), and moderate-severe depression severity (2 participants).

Figure 4. Patient flow diagram.



3.2. Baseline sociodemographic and clinical characteristics

Table 4 shows participants' sociodemographic data for each condition. There were no statistically significant differences between groups on sociodemographic data: age, $t(64) = -0.39, p = .700$; sex, $\chi^2(1, N = 66) = 1.35, p = .245$, Cramer's $V = 0.14$; marital status, $\chi^2(3, N = 54) = 5.12, p = .144$, Cramer's $V = 0.29$; educational level, $\chi^2(3, N = 54) = 2.46, p = .514$, Cramer's $V = 0.22$; occupation, $\chi^2(8, N = 60) = 6.31, p = .702$, Cramer's $V = 0.32$, and income level, $\chi^2(3, N = 41) = 6.53, p = .083$, Cramer's $V = 0.39$.

Table 4. Sociodemographic data for each condition.

	ITAU+IPPA <i>n</i> = 40	only-ITAU <i>n</i> = 26
Age <i>M(SD)</i>	45.50 (10.48)	46.62 (12.57)
Sex (%)		
Male	25.00	38.50
Female	75.00	61.50
Marital status (%)		
Single	15.80	19.00
Married/in a relationship	63.20	81.00
Separated/divorced	18.40	0.00
Widowed	2.60	0.00
Educational level (%)		
No studies	2.80	0.00
Primary studies	19.40	27.80
Secondary studies	47.20	27.80
University studies	30.60	44.40
Occupation (%)		
Student	5.10	4.80
Employed	48.70	52.30
Subsidized unemployed	5.10	9.50
Unemployed without benefits	18.00	0.00
Time off work	10.30	14.30
Permanent disability	5.10	4.80
Retired	5.10	14.3
Others	2.60	0.00
Income level (%)		
< NMW ^a	25.80	10.00
1-2 NMW	38.70	60.00
2-4 NMW	35.50	30.00

Note. ^aNational Minimum Wage. ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual.

Table 5 shows participants' clinical data for each condition. There were also no statistically significant differences between groups on the clinical outcomes (depression severity, affect, health-related quality of life, well-being, and mindfulness) ($p > .05$).

Table 5. Clinical data and significant differences between conditions.

	ITAU+IPPA <i>n</i> = 40 <i>M(SD)</i>	only-ITAU <i>n</i> = 26 <i>M(SD)</i>	Statistics
Depression severity			
<i>PHQ-9</i>	15.83 (5.94)	14.32 (4.85)	$t(63) = 1.06, p = .291$
Affect			
<i>PANAS</i>			
Positive affect	18.13 (6.35)	18.64 (6.09)	$t(63) = -0.32, p = .748$
Negative affect	27.65 (8.22)	29.80 (8.66)	$t(63) = -1.01, p = .319$
Health-related quality of life			
<i>Physical Health SF-12</i>			
General health	31.88 (21.92)	39.00 (19.20)	$t(63) = -1.33, p = .186$
Bodily pain	47.50 (32.91)	56.00 (30.00)	$t(63) = -1.04, p = .299$
Role-physical	23.75 (37.53)	32.00 (43.01)	$t(63) = -0.81, p = .418$
Physical functioning	60.00 (32.91)	65.00 (29.76)	$t(63) = -0.61, p = .539$
<i>Mental Health SF-12</i>			
Mental Health	35.75 (17.38)	42.80 (18.62)	$t(63) = -1.54, p = .126$
Role-emotional	18.75 (33.37)	22.00 (35.59)	$t(63) = -0.37, p = .711$
Social-functioning	38.13 (25.31)	43.00 (21.06)	$t(63) = -0.80, p = .424$
Vitality	19.50 (17.82)	24.00 (21.61)	$t(63) = -0.91, p = .365$
Well-being			
<i>PHI</i>			
Total well-being	4.37 (1.79)	4.70 (1.93)	$t(62) = -0.67, p = .501$
Remembered well-being	4.37 (1.82)	4.80 (2.03)	$t(62) = -0.67, p = .500$
Experienced well-being	4.38 (2.49)	4.58 (2.45)	$t(62) = -0.32, p = .745$
Facets of mindfulness			
<i>FFMQ</i>			
Observing	19.88 (5.32)	21.54 (7.16)	$t(62) = -1.06, p = .292$
Describing	22.78 (7.20)	26.00 (7.77)	$t(62) = -1.68, p = .097$
Acting with awareness	22.93 (5.62)	22.79 (6.94)	$t(62) = 0.08, p = .933$
Not judging inner experience	22.30 (6.34)	21.17 (9.46)	$t(62) = 0.57, p = .568$
Not reacting to inner experience	17.28 (4.56)	17.63 (5.06)	$t(62) = -0.28, p = .776$

Note. ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual; PHQ-9, Patient Health Questionnaire-9; PANAS, Positive and Negative Affect; SF-12, Short Form 12 Health Survey; PHI, Pemberton Happiness Index; FFMQ, Five Facet Mindfulness Questionnaire.

3.3. Differential efficacy of two treatments conditions

3.3.1. Change in primary outcome

Depression severity (PHQ-9 scores)

There was a significant main effect of time on depression severity, $F(3, 130.68) = 20.90, p < .001$, indicating that both conditions were efficacious in decreasing depression across time. Moreover, there was no significant condition x time interaction effect on depression severity, $F(3, 130.68) = 1.64, p = .182$.

Effect sizes for within-group comparisons for each condition (pre vs. post; pre vs. follow-up-1; pre vs. follow-up-2) confirmed significant reductions in depression severity because medium and large effect sizes were found for both conditions (see Table 6 for details). Moreover, effect sizes for between-group comparisons at each point in time were small at post-treatment and follow-ups (6 and 12 months) (see Table 7 for details).

Figure 5 shows the changes in depression severity in both conditions (ITAU+IPPA and only-ITAU) at pre-treatment, post-treatment, and follow-up assessments.

Table 6. Descriptive statistics and within-group effect sizes for each condition on primary outcomes (PHQ-9) at pre-treatment, post-treatment, and follow-ups (6 and 12 months).

Measure	Condition	M(SD)				Within-group effect size, <i>d</i> [95% CI]			
		Pre	Post	FW-1	FW-2	Pre vs. post	Pre vs. FW-1	Pre vs. FW-2	
Depression severity PHQ-9	ITAU+IPPA	15.83 (5.94)	10.93 (6.53)	7.67 (5.00)	11.39 (6.01)	0.81 [0.45, 1.17]	1.35 [0.89, 1.80]	0.73 [0.31, 1.16]	
	only-ITAU	14.32 (4.85)	11.95 (5.22)	10.05 (6.64)	9.06 (5.89)	0.47 [0.11, 0.84]	0.85 [0.41, 1.29]	1.05 [0.50, 1.60]	

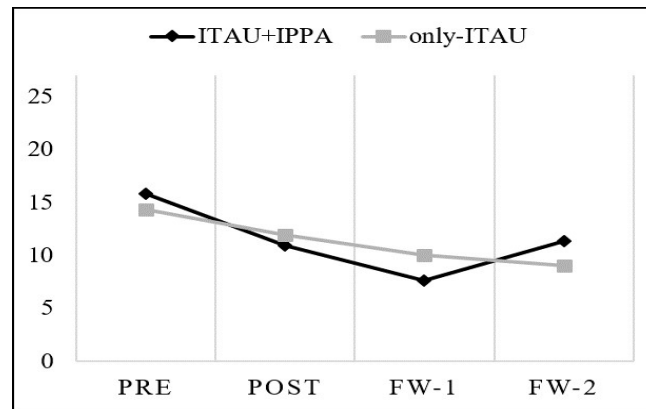
Note. *d*, Cohen's *d*; CI, Confidence Interval; Pre, Pre-treatment; Post, Post-treatment; FW-1, Follow-up-1 (6 months); FW-2, Follow-up-2 (12 months); ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual; PHQ-9, Patient Health Questionnaire-9.

Table 7. Between-group (ITAU+IPPA versus only-ITAU) comparison effect sizes at each point in time on primary outcome (PHQ-9) at post-treatment and follow-ups (6 and 12 months).

Measure	Post-treatment		6-month follow-up		12-month follow-up	
	Mean dif.	Between-group effect size, <i>d</i> [95% CI]	Mean dif.	Between-group effect size, <i>d</i> [95% CI]	Mean dif.	Between-group effect size, <i>d</i> [95% CI]
Depression severity PHQ-9	-1.18	-0.16 [-0.72, 0.39]	-2.08	-0.40 [-1.02, 0.22]	1.03	0.38 [-0.28, 1.04]

Note. Mean dif, Mean differences; *d*, Cohen's *d*; CI, Confidence Interval; PHQ-9, Patient Health Questionnaire-9.

Figure 5. Changes in depression severity (PHQ-9 scores) in both conditions (ITAU+IPPA and only-ITAU) at pre-treatment, post-treatment and follow-up (6 and 12 months) assessments.



Note. Pre, Pre-treatment; Post, Post-treatment; FW-1, Follow-up-1 (6 months); FW-2, Follow-up-2 (12 months); ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual.

3.3.2. Change in secondary outcomes

Affect (PANAS scores)

There was a significant main effect of time on PA, $F(3, 133.48) = 12.16, p < .001$, and NA, $F(3, 130.30) = 9.14, p < .001$, indicating that both treatments were efficacious in increasing PA and decreasing NA across time. In addition, there was no significant condition x time interaction effect on PA, $F(3, 133.48) = 0.57, p = .636$, and NA, $F(3, 130.30) = 0.20, p = .896$.

Effect sizes for within-group comparisons for each condition (pre vs. post; pre vs. follow-up-1; pre vs. follow-up-2) confirmed significant increases in PA with medium and large effect sizes, and decreases in NA with medium effect sizes for both conditions (see Table 8 for details). Furthermore, effect sizes for between-group comparisons at each point in time were small at post-treatment and follow-ups (6 and 12 months) (see Table 9 for details).

Figure 6 (a, b) shows the changes in affect in both conditions (ITAU+IPPA and only-ITAU) at pre-treatment, post-treatment, and follow-up assessments.

Table 8. Descriptive statistics and within-group effect sizes for each condition for PANAS outcomes at pre-treatment, post-treatment, and follow-ups (6 and 12 months).

Measure	Condition	<i>M(SD)</i>						Within-group effect size, <i>d</i> [95% CI]			
		Pre	Post	FW-1	FW-2	Pre vs. post	Pre vs. FW-1	Pre vs. FW-2			
Affect											
<i>PANAS</i>											
Positive affect	ITAU+IPPA	18.13 (6.35)	21.40 (6.43)	25.59 (6.33)	22.72 (9.68)	-0.50 [-0.83, -0.17]	-1.15 [-1.55, -0.76]	-0.71 [-1.07, -0.34]			
	only-ITAU	18.42 (6.07)	24.40 (9.99)	25.74 (10.10)	25.82 (11.10)	-0.96 [-1.40, -0.51]	-1.17 [-1.72, -0.62]	-1.18 [-1.79, -0.58]			
Negative affect	ITAU+IPPA	27.65 (8.22)	22.13 (7.87)	21.68 (8.03)	22.72 (9.21)	0.66 [0.36, 0.95]	0.71 [0.39, 1.03]	0.59 [0.25, 0.92]			
	only-ITAU	29.81 (8.49)	26.20 (9.08)	24.26 (8.78)	24.76 (9.20)	0.41 [0.41, 0.82]	0.63 [0.63, 0.98]	0.58 [0.58, 0.96]			

Note. *d*, Cohen's *d*; CI, Confidence Interval; Pre, Pre-treatment; Post, Post-treatment; FW-1, Follow-up-1 (6 months); FW-2, Follow-up-2 (12 months); ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual; PANAS, Positive and Negative Affect.

Table 9. Between-group (ITAU+IPPA versus only-ITAU) comparison effect sizes at each point in time on PANAS outcomes at post-treatment and follow-ups (6 and 12 months).

Measure	Post-treatment			6-month follow-up			12-month follow-up		
	Mean dif.	Between-group effect size, <i>d</i> [95% CI]		Mean dif.	Between-group effect size, <i>d</i> [95% CI]		Mean dif.	Between-group effect size, <i>d</i> [95% CI]	
Affect									
<i>PANAS</i>									
Positive affect	2.59	-0.36 [-0.92, 0.20]	0.18	-0.02 [-0.63, 0.59]	-1.53	-0.29 [-0.95, 0.37]			
Negative affect	-3.30	-0.48 [-1.04, 0.09]	-1.43	-0.30 [-0.92, 0.31]	-2.35	-0.22 [-0.87, 0.44]			

Note. Mean dif, Mean differences; *d*, Cohen's *d*; CI, Confidence Interval; PANAS, Positive and Negative Affect.

Figure 6 (a, b). Changes in affect (PANAS scores) in both conditions (ITAU+IPPA and only-ITAU) at pre-treatment, post-treatment, and follow-up (6 and 12 months) assessments.

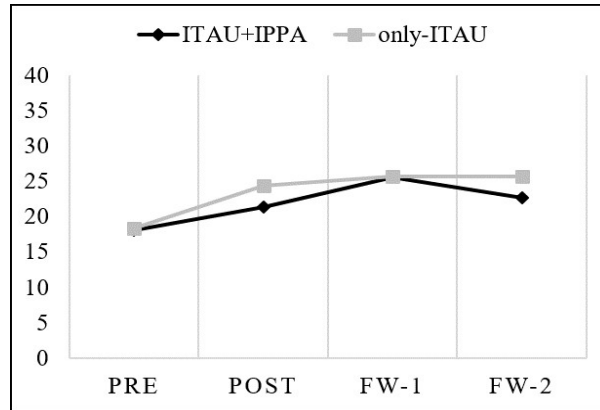


Fig 6a. Positive affect

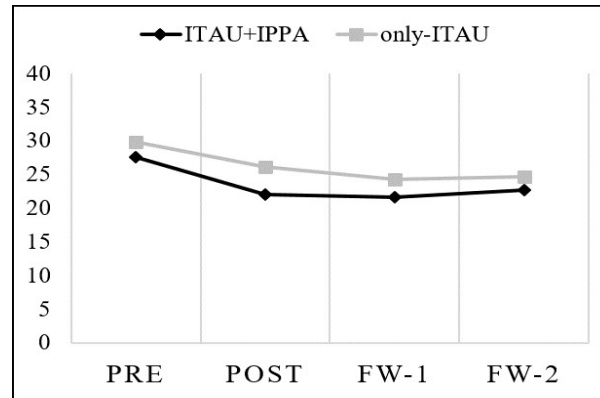


Fig 6b. Negative affect

Note. Pre, Pre-treatment; Post, Post-treatment; FW-1, Follow-up-1 (6 months); FW-2, Follow-up-2 (12 months); ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual.

Health-related quality of life (SF-12 scores)

There was a significant main effect of time on general health, $F(3, 125.79) = 3.53, p < .05$; bodily pain, $F(3, 129.39) = 6.64, p < .001$; role-physical, $F(3, 133.41) = 5.54, p < .001$; mental health, $F(3, 137.27) = 10.09, p < .001$; role-emotional SF-12, $F(3, 135.76) = 15.18, p < .001$; social-functioning, $F(3, 128.25) = 12.71, p < .001$; and vitality, $F(3, 135.75) = 7.85, p < .001$, except on the variable of physical functioning, $F(3, 125.25) = 1.84, p = .143$. These results indicated that the two conditions were efficacious in improving physical and mental health across time. Moreover, there was no significant condition x time interaction effect on general health, $F(3, 125.79) = 2.07, p = .108$; bodily pain, $F(3, 129.39) = 1.39, p = .247$; role-physical, $F(3, 133.41) = 0.62, p = .602$; physical functioning, $F(3, 125.25) = 0.37, p = .777$; mental health, $F(3, 137.27) = 0.85, p = .47$; role-emotional, $F(3, 135.76) = 2.30, p = .080$; social-functioning, $F(3, 128.25) = 1.55, p = .204$; or vitality, $F(3, 135.75) = 1.48, p = .224$.

Effect sizes for within-group comparisons for each condition (pre vs. follow-up-1; pre vs. follow-up-2) confirmed significant increases in all variables of the SF-12, with medium and large effect sizes found for both conditions (see Table 10 for details). Moreover, effect sizes for between-group comparisons at each point in time were small at follow-ups (6 and 12 months) on all variables of the SF-12 survey, except physical functioning (Cohen's $d = -0.73$), role-emotional (Cohen's $d = -0.52$), and vitality (Cohen's $d = -0.59$) with medium effect sizes, and social-functioning (Cohen's $d = -0.93$) with a large effect size at the 12-month follow-up (see Table 11 for details).

Figure 7 (a-h) shows the changes in health-related quality of life in both conditions (ITAU+IPPA and only-ITAU) at pre-treatment and follow-up assessments.

Well-being (PHI scores)

There was a significant main effect of time on total well-being, $F(2, 75.75) = 17.84$, $p < .001$; remembered well-being, $F(2, 75.74) = 16.63$, $p < .001$; and experienced well-being, $F(2, 95.74) = 3.29$, $p < .05$, indicating that both conditions were efficacious in increasing well-being across time. In addition, there was no significant condition x time interaction effect on total well-being, $F(2, 75.75) = 1.57$, $p = .215$; remembered well-being, $F(2, 75.74) = 1.51$, $p = .228$; or experienced well-being, $F(2, 95.74) = 0.42$, $p = .661$.

Effect sizes for within-group comparisons for each condition (pre vs. follow-up-1; pre vs. follow-up-2) confirmed significant increases in all the variables of the PHI, with medium and large effect sizes found for both conditions (see Table 10 for details). Furthermore, effect sizes for between-group comparisons at each point in time were small at follow-ups (6 and 12 months) (see Table 11 for details).

Figure 8 (a-c) shows the changes in well-being in both conditions (ITAU+IPPA and only-ITAU) at pre-treatment and follow-up assessments.

Facets of mindfulness (FFMQ scores)

There was a significant main effect of time on observing, $F(2, 77.14) = 9.49$, $p < .001$; acting with awareness, $F(2, 78.35) = 5.05$, $p < .01$; not judging inner experience, $F(2, 79.92) = 5.28$, $p < .01$; and not reacting to inner experience, $F(2, 80.99) = 6.10$, $p < .01$, but not describing, $F(2, 78.88) = 1.81$, $p = .170$. These results showed that the two treatment conditions were efficacious in improving the facets of mindfulness across time. Moreover, there was no significant condition x time interaction effect on observing, $F(2, 77.14) = 0.36$, $p = .697$; describing, $F(2, 78.88) = 1.25$, $p = .293$; acting with awareness,

$F(2, 78.35) = 0.55, p = .581$; not judging inner experience, $F(2, 79.92) = 0.59, p = .553$; and not reacting to inner experience, $F(2, 80.99) = 0.57, p = .568$.

Effect sizes for within-group comparisons for each condition (pre vs. follow-up-1; pre vs. follow-up-2) confirmed significant increases in all variables of the FFMQ, with small and medium effect sizes found for both conditions (see Table 10 for details). Moreover, effect sizes for between-group comparisons at each point in time were small at follow-ups (6 and 12 months) in all facets of the FFMQ, except the observing facet (Cohen's $d = -0.53$) with a medium effect size at 6-month follow-up (see Table 11 for details).

Figure 9 (a-e) shows the changes in the facets of mindfulness in both conditions (ITAU+IPPA and only-ITAU) at pre-treatment and follow-up assessments.

Table 10. Descriptive statistics and within-group effect sizes for each condition on secondary outcomes at pre-treatment and follow-ups (6 and 12 months).

Measure	Condition	<i>M(SD)</i>		Within-group effect size, <i>d</i> [95% CI]	
		Pre	FW-1	FW-1	Pre vs. FW-2
Health-related quality of life					
<i>Physical Health SF-12</i>					
General health	ITAU+IPPA	31.88 (21.91)	47.73 (23.03)	43.06 (23.96)	-0.71 [-1.12, -0.30]
	only-ITAU	38.46 (19.01)	42.11 (16.78)	47.06 (21.44)	-0.19 [0.48, 0.11]
Bodily pain	ITAU+IPPA	47.50 (32.91)	69.32 (30.79)	70.83 (30.01)	-0.65 [-1.01, -0.29]
	only-ITAU	56.00 (30.00)	68.42 (27.44)	67.65 (32.79)	-0.40 [-0.88, 0.08]
Role-physical	ITAU+IPPA	23.75 (37.53)	50.00 (43.64)	38.89 (43.91)	-0.69 [-1.09, -0.28]
	only-ITAU	32.00 (43.01)	60.53 (45.88)	61.76 (48.51)	-0.64 [-1.12, -0.16]
Physical functioning	ITAU+IPPA	60.00 (32.91)	71.59 (38.80)	58.33 (40.22)	-0.04 [-0.65, 0.10]
	only-ITAU	65.00 (29.76)	72.37 (27.50)	83.82 (26.43)	-0.24 [-0.65, 0.17]
<i>Mental Health SF-12</i>					
Mental Health	ITAU+IPPA	35.75 (17.38)	59.52 (14.99)	53.89 (22.79)	-1.34 [-1.85, -0.83]
	only-ITAU	42.80 (18.60)	55.79 (21.68)	53.53 (26.44)	-0.68 [-1.09, -0.26]
Role-emotional	ITAU+IPPA	18.75 (33.37)	63.64 (41.35)	36.11 (47.91)	-1.32 [-1.82, -0.81]
	only-ITAU	22.00 (35.59)	63.16 (46.67)	61.76 (48.50)	-1.12 [-1.61, -0.63]
Social-functioning	ITAU+IPPA	38.13 (25.31)	61.36 (26.42)	52.78 (28.29)	-0.90 [-1.29, -0.51]
	only-ITAU	43.00 (21.06)	61.84 (33.71)	76.47 (21.21)	-0.87 [-1.37, -0.36]
Vitality	ITAU+IPPA	19.50 (17.82)	37.27 (20.74)	28.89 (24.94)	-0.98 [-1.42, -0.54]
	only-ITAU	24.00 (21.60)	44.21 (26.31)	44.71 (26.95)	-0.91 [-1.40, -0.41]

Table 10. Continued.

Measure	Condition	Pre	M(SD)		Within-group effect size, <i>d</i> [95% CI]	
			FW-1	FW-2	Pre vs. FW-1	Pre vs. FW-2
Well-being						
<i>PHI</i>						
Total well-being	ITAU+IPPA	4.37 (1.80)	5.82 (1.65)	5.72 (2.11)	-0.79 [-1.09, -0.49]	-0.74 [-1.08, -0.38]
	only-ITAU	4.50 (1.93)	5.71 (1.89)	6.33 (2.08)	-0.61 [-0.96, -0.25]	-0.92 [-1.34, -0.49]
Remembered well-being	ITAU+IPPA	4.37 (1.82)	5.83 (1.68)	5.78 (2.21)	-0.79 [-1.08, -0.49]	-0.76 [-1.12, -0.40]
	only-ITAU	4.70 (2.03)	5.73 (2.01)	6.35 (2.16)	-0.49 [-0.83, -0.15]	-0.79 [-1.19, -0.39]
Experienced well-being	ITAU+IPPA	4.38 (2.49)	5.68 (2.90)	5.22 (2.26)	-0.51 [-0.98, -0.04]	-0.33 [-0.66, 0.01]
	only-ITAU	4.58 (2.45)	5.39 (2.35)	6.06 (2.98)	-0.32 [-0.96, 0.32]	-0.59 [-1.23, 0.06]
Facets of mindfulness						
<i>FFMQ</i>						
Observing	ITAU+IPPA	19.88 (5.32)	21.73 (5.77)	24.11 (7.74)	-0.34 [-0.61, -0.07]	-0.78 [-1.16, -0.40]
	only-ITAU	21.54 (7.15)	25.56 (8.15)	25.75 (7.73)	-0.55 [-0.88, -0.21]	-0.57 [-0.94, -0.20]
Describing	ITAU+IPPA	22.78 (7.20)	26.14 (7.27)	26.50 (9.36)	-0.46 [-0.75, -0.17]	-0.51 [-0.81, -0.21]
	only-ITAU	26.00 (7.69)	27.61 (10.24)	27.63 (10.09)	-0.20 [-0.42, 0.01]	-0.21 [-0.48, 0.07]
Acting with awareness	ITAU+IPPA	22.93 (5.62)	27.32 (8.18)	23.89 (6.70)	-0.77 [-1.09, -0.44]	-0.17 [-0.48, 0.14]
	only-ITAU	22.79 (6.94)	25.53 (7.87)	25.63 (7.11)	-0.38 [-0.75, -0.02]	-0.40 [-0.93, 0.14]
Not judging inner experience	ITAU+IPPA	22.30 (6.34)	26.41 (6.71)	26.00 (8.21)	-0.64 [-1.05, -0.22]	-0.57 [-0.93, -0.21]
	only-ITAU	21.17 (9.46)	22.78 (8.11)	22.94 (9.30)	-0.17 [-0.44, 0.11]	-0.18 [-0.46, 0.10]
Not reacting to inner experience						
Not reacting to inner experience	ITAU+IPPA	17.28 (4.56)	18.55 (4.56)	20.11 (4.82)	-0.27 [-0.55, 0.01]	-0.61 [-1.00, -0.22]
	only-ITAU	17.63 (5.06)	20.06 (5.39)	21.25 (6.19)	-0.47 [-0.89, 0.04]	-0.69 [-1.07, -0.32]

Note. *d*, Cohen's *d*; CI, Confidence Interval; Pre, Pre-treatment; FW-1, Follow-up-1 (6 months); FW-2, Follow-up-2 (12 months); ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual; SF-12, Short Form 12 Health Survey; PHI, Pemberton Happiness Index; FFMQ, Five Facet Mindfulness Questionnaire.

Table 11. Between-group (ITAU+IPPA versus only-ITAU) comparison effect sizes at each point in time on secondary outcome measures at follow-ups (6 and 12 months).

Measure	6-month follow-up		12-month follow-up	
	Mean dif.	Between-group effect size, <i>d</i> [95% CI]	Mean dif.	Between-group effect size, <i>d</i> [95% CI]
Health-related quality of life				
<i>Physical Health SF-12</i>				
General health	9.41	0.27 [-0.34, 0.89]	0.58	-0.17 [-0.83, 0.48]
Bodily pain	4.12	0.03 [-0.58, 0.64]	10.50	0.09 [-0.55, 0.75]
Role-physical	-10.86	-0.23 [-0.84, 0.38]	-20.16	-0.48 [-1.15, 0.18]
Physical functioning	-1.58	-0.02 [-0.63, 0.59]	-10.28	-0.73 [-1.40, -0.06]
<i>Mental Health SF-12</i>				
Mental Health	3.29	0.20 [-0.42, 0.81]	0.53	0.01 [-0.64, 0.67]
Role-emotional	-2.02	0.01 [-0.60, 0.62]	-29.41*	-0.52 [-1.18, 0.14]
Social-functioning	-1.27	-0.01 [-0.63, 0.60]	-19.59*	-0.93 [-1.61, -0.24]
Vitality	-4.83	-0.29 [-0.90, 0.33]	-13.82	-0.59 [-1.26, 0.07]
Well-being				
<i>PHI</i>				
Total well-being	0.42	0.06 [-0.55, 0.67]	-0.27	-0.28 [-0.94, 0.37]
Remembered well-being	0.42	0.05 [-0.56, 0.67]	-0.28	-0.25 [-0.91, 0.40]
Experienced well-being	0.31	0.11 [-0.50, 0.72]	-0.74	-0.31 [-0.97, 0.35]
Facets of mindfulness				
<i>FFMQ</i>				
Observing	-2.50	-0.53 [-1.16, 0.09]	-0.91	-0.21 [-0.86, 0.45]
Describing	-1.13	-0.16 [-0.78, 0.45]	-0.15	-0.11 [-0.77, 0.54]
Acting with awareness	1.46	0.22 [-0.39, 0.83]	-0.99	-0.25 [-0.90, 0.41]
Not judging inner experience	2.94	0.48 [-0.14, 1.10]	3.43	0.34 [-0.32, 1.00]
Not reacting to inner experience	-1.68	-0.30 [-0.91, 0.32]	-1.77	-0.20 [-0.85, 0.45]

Note. Mean dif, Mean differences; *Statistically Significant; *d*, Cohen's *d*; CI, Confidence Interval; SF-12, Short Form 12 Health Survey; PHI, Pemberton Happiness Index; FFMQ, Five Facet Mindfulness Questionnaire.

Figure 7 (a-h). Changes in health-related quality of life (SF-12 scores) in both conditions (ITAU+IPPA and only-ITAU) at pre-treatment and follow-up (6 and 12 months) assessments.

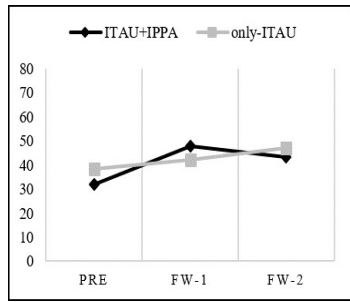


Fig 7a. General health

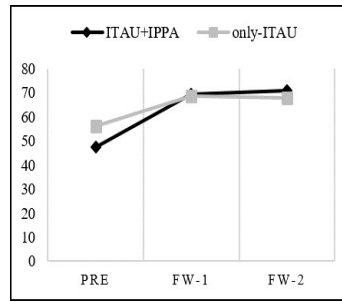


Fig 7b. Bodily pain

Physical Health

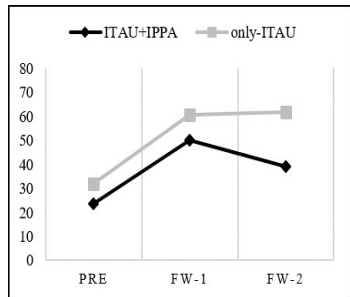


Fig 7c. Role-physical

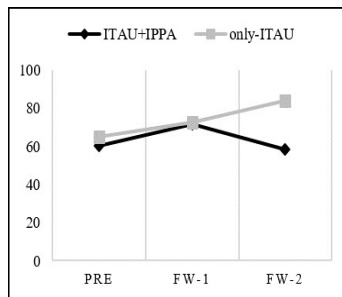


Fig 7d. Physical functioning

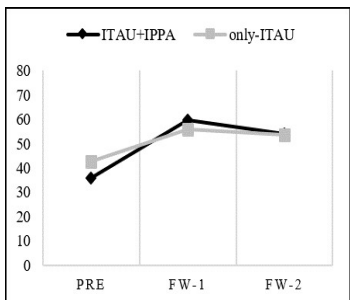


Fig 7e. Mental health

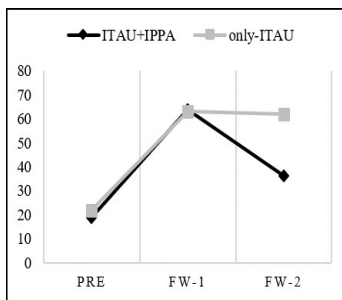


Fig 7f. Role-emotional

Mental Health

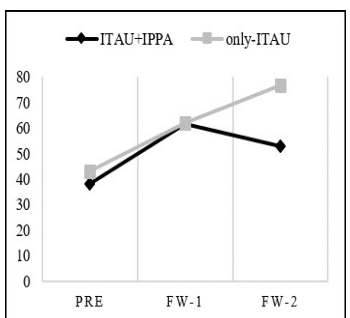


Fig 7g. Social-functioning

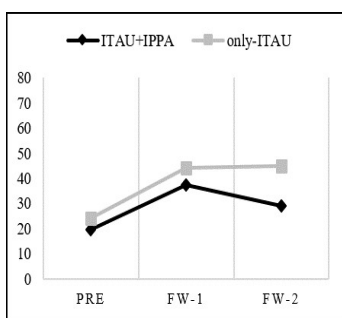


Fig 7h. Vitality

Note. Pre-treatment; FW-1, Follow-up-1 (6 months); FW-2, Follow-up-2 (12 months); ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual.

Figure 8 (a-c). Changes in well-being (PHI scores) in both conditions (ITAU+IPPA and only-ITAU) at pre-treatment and follow-up (6 and 12 months) assessments.

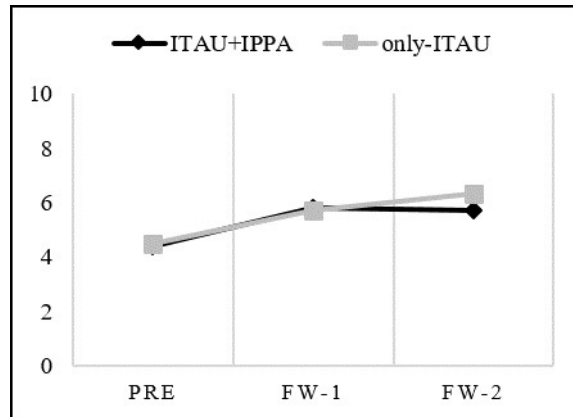


Fig 8a. Total well-being

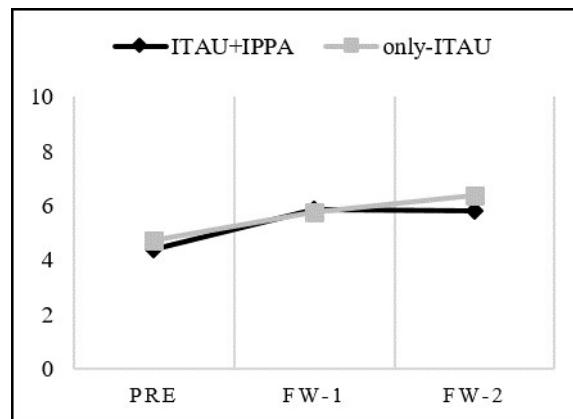


Fig 8b. Remembered well-being

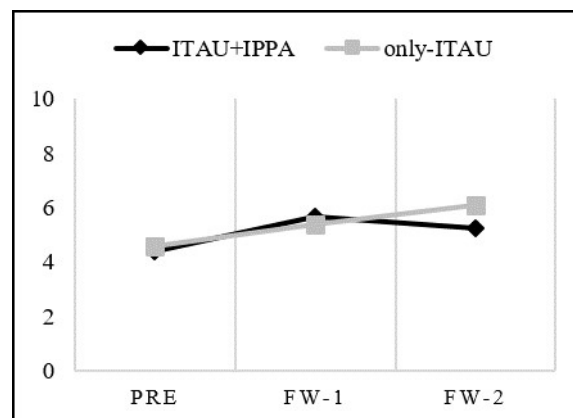


Fig 8c. Experienced well-being

Note. Pre-treatment; FW-1, Follow-up-1 (6 months); FW-2, Follow-up-2 (12 months); ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual.

Figure 9 (a-e). Changes in the facets of mindfulness (FFMQ scores) in both conditions (ITAU+IPPA and only-ITAU) at pre-treatment and follow-up (6 and 12 months) assessments.

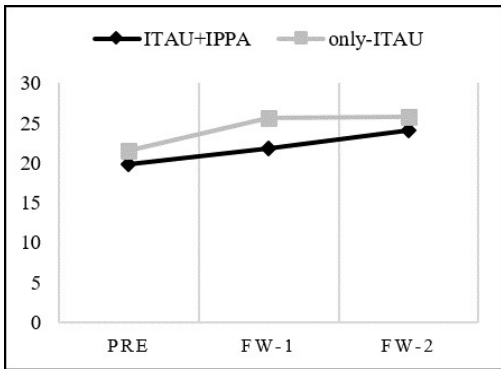


Fig 9a. Observing

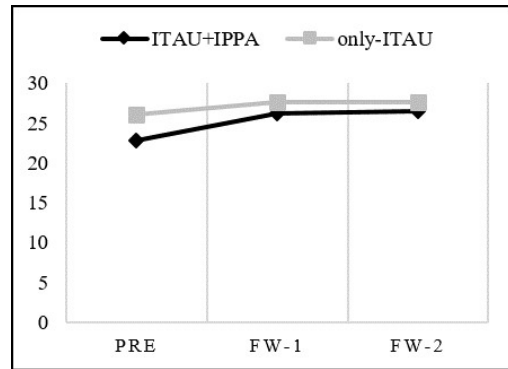


Fig 9b. Describing

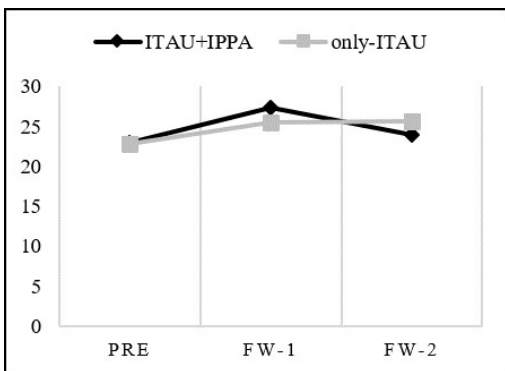


Fig 9c. Acting with awareness

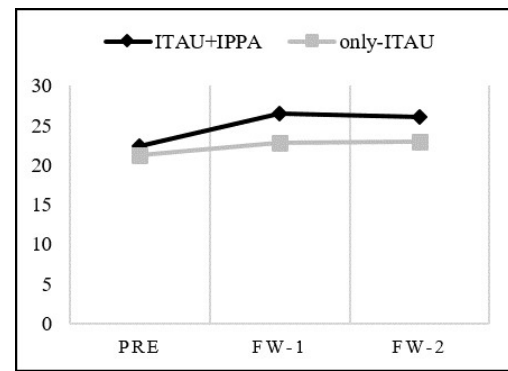


Fig 9d. Not judging inner experience

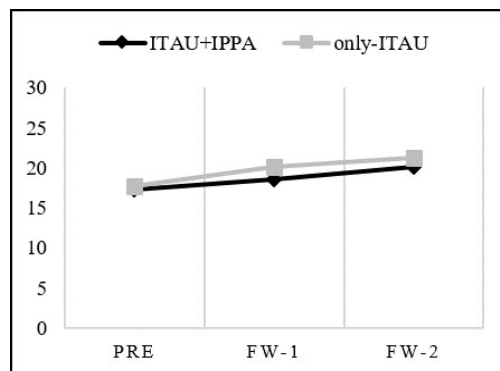


Fig 9e. Not reacting to inner experience

Note. Pre-treatment; FW-1, Follow-up-1 (6 months); FW-2, Follow-up-2 (12 months); ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual.

3.3.3. Clinically significant change in depression severity (PHQ-9)

Figure 10 presents the proportion of completers in each condition who were classified as “recovered”, “improved”, “unchanged”, or “deteriorated” at post-treatment (Fig 7a) and follow-ups (6 and 12 months) (Fig 7b and 7c) on depression severity.

There were no statistically significant differences between groups (ITAU+IPPA and only-ITAU) in the clinically meaningful improvement in depression at post-treatment, $\chi^2(3, N = 66) = 1.94, p = .672$, Cramer’s $V = 0.19$; follow-up-1 (6 months), $\chi^2(2, N = 41) = 0.12, p = .941$, Cramer’s $V = 0.06$, and follow-up-2 (12 months), $\chi^2(2, N = 36) = 1.88, p = .459$, Cramer’s $V = 0.23$.

Overall, both treatment conditions showed high percentages of “unchanged” participants during post-treatment, “improved” participants during follow-up-1, and “unchanged” participants during follow-up-2.

Figure 10. Clinical significance of changes in depression severity (PHQ-9 scores) in both conditions (ITAU+IPPA and only-ITAU) at post-treatment (Fig 7a) and follow-up (6 and 12 months) assessments (Fig 7b and 7c).

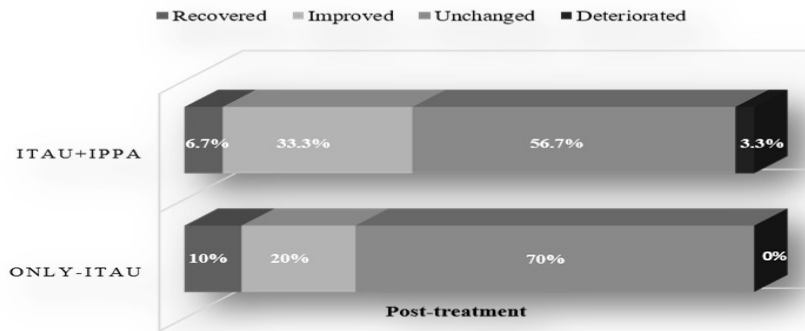


Fig 10a

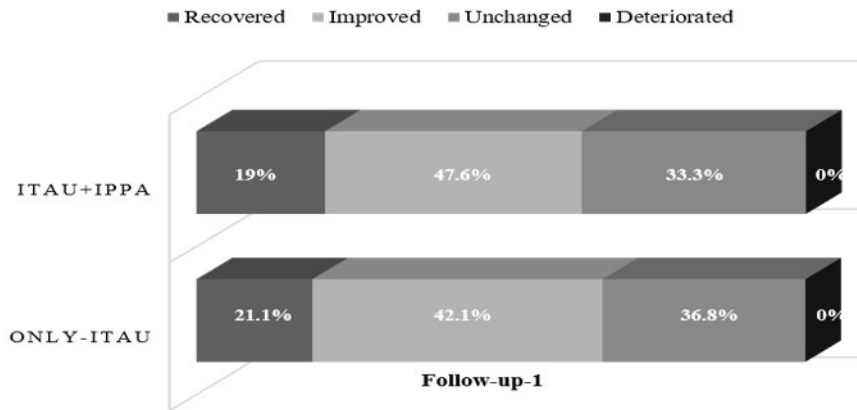


Fig 10b

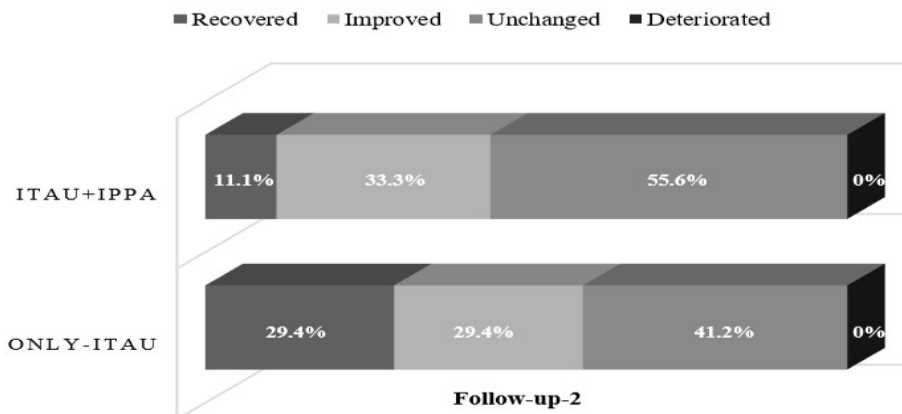


Fig 10c

Note. Percentage of the completer sample in each condition corresponding to recovered, improved, unchanged, or deteriorated. ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual.

3.4. Differential cost-effectiveness of two treatment conditions

There were no statistically significant differences between groups on the cost-effectiveness outcomes at baseline: number of visits to the GP in the past three months, $t(55) = 0.80, p = .428$; number of visits to the emergency room in the past three months, $t(37) = 0.97, p = .330$; number of days off work in the past year, $t(35) = 1.59, p = .121$; number of days that usual tasks have been left unfinished due to health problems in the past month, $t(23) = 0.21, p = .833$; and number of days when the quality of usual tasks has been reduced due to health problems in the past month, $t(22) = -1.89, p = .072$.

There was no significant main effect of time on the number of visits to the GP in the past three months, $F(2, 53.19) = 2.96, p = .061$; number of visits to the emergency room in the past three months, $F(2, 16.51) = 1.33, p = .292$; number of days off work in the past year, $F(2, 25.17) = 0.18, p = .839$; and number of days that usual tasks have been left unfinished due to health problems in the past month, $F(2, 47) = 1.48, p = .239$, but there was on the number of days when the quality of usual tasks was reduced due to health problems in the past month, $F(2, 47.55) = 9.48, p < .001$, indicating that both conditions were only cost-effective in terms of the quality of the usual tasks across time. Moreover, there was no significant condition x time interaction effect on the number of visits to the GP in the past three months, $F(2, 53.19) = 0.11, p = .897$; number of visits to the emergency room in the past three months, $F(2, 16.51) = 0.54, p = .591$; number of days off work in the past year, $F(2, 25.17) = 2.29, p = .122$; number of days that usual tasks have been left unfinished due to health problems in the past month, $F(2, 47) = 0.81, p = .451$; and number of days when the quality of usual tasks was reduced due to health problems in the past month, $F(2, 47.55) = 1.38, p = .262$.

Effect sizes for within-group comparisons for each condition (pre vs. follow-up-1; pre vs. follow-up-2) confirmed a reduction in health and social services use, as small and medium effect sizes were found for both conditions, except on the last variable (number of days when the quality of usual tasks was reduced due to health problems in the past month) with large effect size in follow-up 2 (12 months) (see Table 12 for details). In addition, effect sizes for between-group comparisons at each point in time were large at follow-up-1 (6 months) for the variable of the number of days that usual tasks have been left unfinished due to health problems in the past month (Cohen's $d = -0.80$), and at follow-up-2 (12 months) for the variable of the number of days off work in the last year (Cohen's $d = 1.20$) (see Table 13 for details).

Figure 11 (a-e) shows the changes in cost-effectiveness in both conditions (ITAU+IPPA and only-ITAU) at pre-treatment and follow-up assessments.

Table 12. Descriptive statistics and within-group effect sizes for each condition for cost-effectiveness outcomes at pre-treatment and follow-ups (6 and 12 months).

Measure	Condition	<i>M(SD)</i>		Within-group effect size, <i>d</i> [95% CI]	
		Pre	FW-1	Pre vs. FW-1	Pre vs. FW-2
Health and social services use					
Number of visits to the GP in the past three months	ITAU+IPPA	9.62 (11.87)	7.13 (9.91)	0.21 [-0.22, 0.63]	0.32 [-0.09, 0.73]
	Only-ITAU	7.30 (8.71)	3.85 (4.06)	0.38 [-0.11, 0.88]	0.58 [0.03, 1.13]
Number of visits to the emergency room in the past three months	ITAU+IPPA	2.69 (3.86)	1.33 (0.58)	0.35 [0.01, 0.69]	0.43 [0.08, 0.77]
	only-ITAU	1.54 (2.33)	1.00 (1.00)	0.22 [0.05, 0.40]	0.22 [0.05, 0.39]
Number of days off work in the past year	ITAU+IPPA	79.06 (115.32)	69.17 (116.37)	0.08 [-0.33, 0.49]	-0.47 [-0.84, -0.09]
	only-ITAU	33.05 (50.07)	34.36 (43.29)	-0.03 [-0.58, 0.53]	0.64 [0.05, 1.23]
Number of days that usual tasks have been left unfinished due to health problems in the past month	ITAU+IPPA	7.33 (11.11)	0.33 (0.58)	0.62 [0.11, 1.12]	0.40 [-0.09, 0.89]
	only-ITAU	6.38 (11.10)	7.78 (13.02)	-0.12 [-0.68, 0.44]	0.47 [-0.11, 1.05]
Number of days when the quality of usual tasks has been reduced due to health problems in the past month	ITAU+IPPA	6.55 (10.42)	0.63 (2.01)	0.56 [0.30, 0.81]	0.46 [0.27, 0.65]
	only-ITAU	15.77 (13.05)	5.56 (10.14)	0.76 [0.32, 1.19]	0.99 [0.50, 1.48]

Note. *d*, Cohen's *d*; CI, Confidence Interval; Pre, Pre-treatment; FW-1, Follow-up-1 (6 months); FW-2, Follow-up-2 (12 months); ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual.

Table 13. Between-group (ITAU+IPPA versus only-ITAU) comparison effect sizes at each point in time on cost-effectiveness outcomes at follow-ups (6 and 12 months).

Measure	6-month follow-up		12-month follow-up	
	Mean dif.	Between-group effect size, d [95% CI]	Mean dif.	Between-group effect size, d [95% CI]
Health and social services use				
Number of visits to the GP in the past three months	3.59	0.42 [-0.20, 1.04]	4.07	0.51 [-0.15, 1.18]
Number of visits to the emergency room in the last three months	1.51	0.40 [-0.22, 1.02]	1.34	0 [-0.65, 0.65]
Number of days off work in the past year	78.17	0.38 [-0.23, 1.00]	142.77*	1.20 [0.49, 1.91]
Number of days that usual tasks have been left unfinished due to health problems in the past month	-7.44	-0.80 [-1.44, -0.17]	2.78	0.32 [-0.34, 0.98]
Number of days when the quality of usual tasks has been reduced due to health problems in the past month	-5.41	-0.67 [-1.30, -0.04]	-1.35	-0.20 [-0.86, 0.45]

Note. Mean dif, Mean differences; *Statistically Significant; d , Cohen's d ; CI, Confidence Interval.

Figure 11 (a-e). Changes in cost-effectiveness outcomes in both conditions (ITAU+IPPA and only-ITAU) at pre-treatment and follow-up (6 and 12 months) assessments.

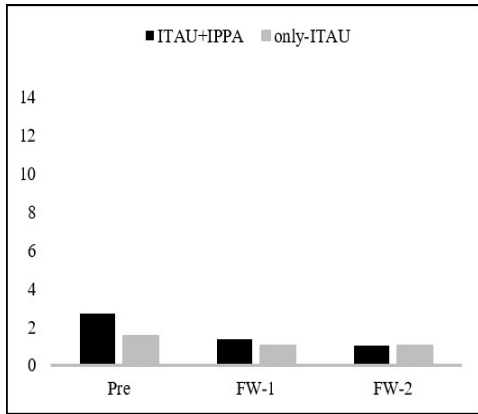


Fig 11a. Number of visits to the GP in the past three months

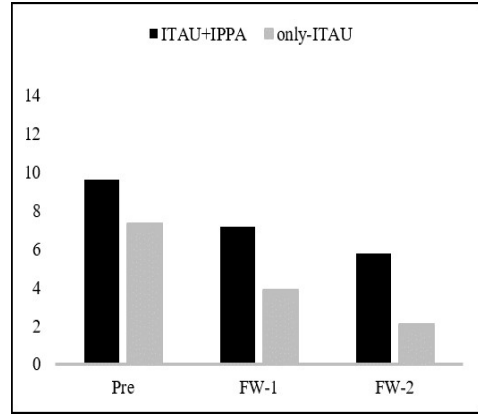


Fig 11b. Number of visits to the emergency room in the past three months

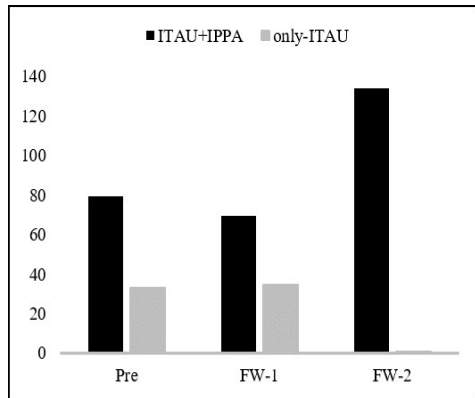


Fig 11c. Number of days off work in the past year

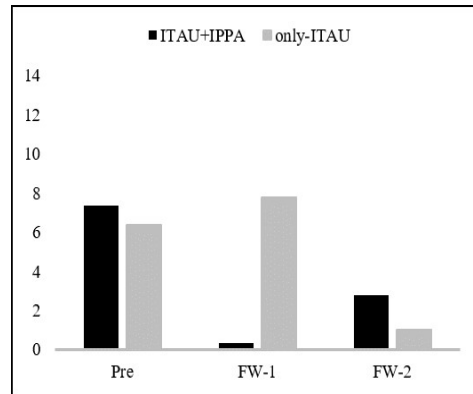


Fig 11d. Number of days that usual tasks have been left unfinished due to health problems in the past month

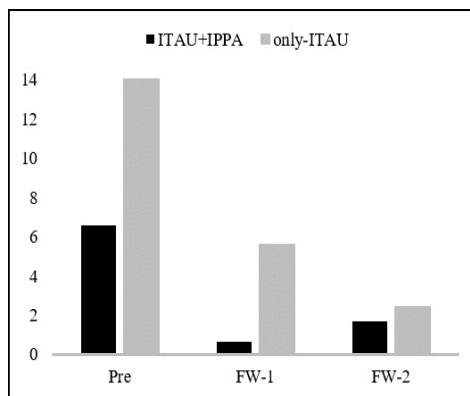


Fig 11e. Number of days when the quality of usual tasks has been reduced due to health problems in the past month

Note. Pre-treatment; FW-1, Follow-up-1 (6 months); FW-2, Follow-up-2 (12 months); ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual.

3.5. Post-module analyses in ITAU+IPPA condition: Changes in depression severity and affect

Depression severity (PHQ-9 scores)

There was a significant main effect of time on depression severity, $F(5, 44.56) = 834.01, p < .01$, indicating that ITAU+IPPA was efficacious in decreasing depression severity across the modules of the treatment. Within-group comparisons showed a medium effect size from post-module 1 to post-module 2, and small effect sizes from post-module 2 to post-module 3, as well as from post-module 3 to post-module 4 (see Table 14 for details).

Affect (PANAS scores)

There was a significant main effect of time on PA, $F(5, 55.49) = 2.61, p < .05$, and NA, $F(5, 45.52) = 3.95, p < .01$, indicating that ITAU+IPPA was efficacious in increasing PA and decreasing NA across the modules of the treatment. Within-group comparisons showed medium effect sizes from post-module 1 to post-module 2, and small effect sizes from post-module 2 to post-module 3, as well as from post-module 3 to post-module 4, for both positive and negative affect outcomes (see Table 14 for details).

Figure 12 (a-c) shows the changes in depression severity and PA and NA during treatment (pre-treatment, post-modules, and post-treatment).

It is worth to mention that some participants accessed the web platform after finishing the treatment period. Specifically, 13 participants accessed to the web platform approximately 4 times from post-treatment to 6-month follow-up ($M = 3.85, SD = 2.70$), and 9 participants accessed nearly 2 times from 6-month follow-up to the 12-month follow-up ($M = 1.77, SD = 2.55$).

Table 14. Descriptive statistics and within-group effect sizes in ITAU+IPPA condition for primary outcomes at pre-treatment, post-treatment, and post-module times.

	<i>M(SD)</i>							Within-group effect size, <i>d</i> [95% CI] ^a		
	Pre	Post-m1	Post-m2	Post-m3	Post-m4	Post	Post-m1 vs. Post-m2	Post-m2 vs. Post-m3	Post-m3 vs. Post-m4	
Depression severity										
<i>PHQ-9</i>	15.83 (5.94)	15.06 (6.03)	11.28 (5.84)	12.38 (5.16)	11.44 (5.05)	10.93 (6.53)	0.61 [0.35, 0.87]	-0.18 [-0.43, 0.06]	0.18 [-0.09, 0.36]	
Affect										
<i>PANAS</i>										
Positive affect	18.13 (6.35)	18.87 (6.57)	22.14 (6.85)	22.35 (7.12)	22.22 (5.90)	21.40 (6.43)	-0.50 [-0.81, -0.15]	-0.03 [-0.30, 0.24]	0.02 [-0.30, 0.33]	
Negative affect	27.65 (8.22)	26.45 (8.33)	22.62 (8.49)	22.81 (7.94)	19.83 (7.13)	22.13 (7.87)	0.48 [0.21, 0.69]	-0.02 [-0.29, 0.25]	0.36 [-0.04, 0.69]	

Note. *d*, Cohen's *d*; CI, Confidence Interval; ^a, Within-group effect size only in post-modules; Pre, Pre-treatment; Post-m1, Post-module 1; Post-m2, Post-module 2; Post-m3, Post-module 3; Post-m4, Post-module 4; Post, Post-treatment; PHQ-9, Patient Health Questionnaire-9; PANAS, Positive and Negative Affect.

Figure 12. Changes in depression severity (PHQ-9 scores) (Fig 9a) and positive and negative affect (PANAS scores) (Fig 9b and 9c) during treatment (pre-treatment, post-modules, and post-treatment).

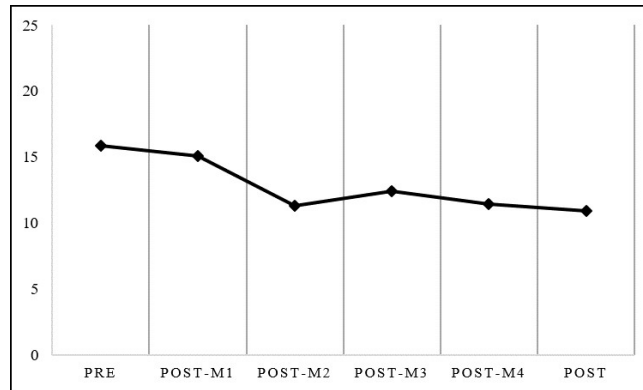


Fig 12a. Depression severity

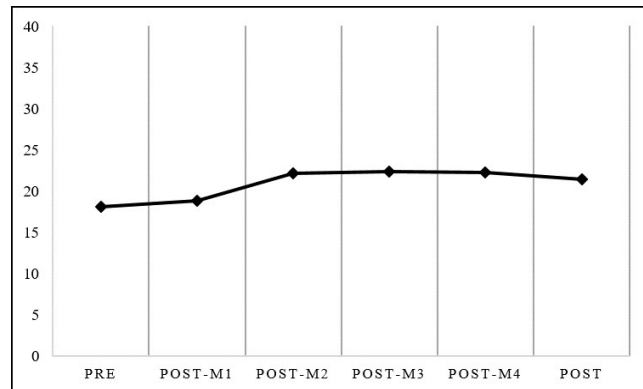


Fig 12b. Positive affect

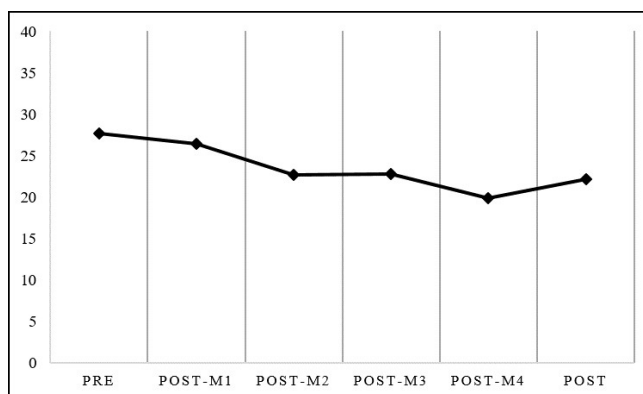


Fig 12c. Negative affect

Note. Pre, Pre-treatment; Post-m1, Post-module 1; Post-m2, Post-module 2; Post-m3, Post-module 3; Post-m4, Post-module 4; Post, Post-treatment.

3.6. Opinion about the treatment received

There was a significant main effect of time on rationale behind the treatment, $F(1, 54.99) = 4.35, p < .05$; satisfaction with the treatment, $F(1, 54.46) = 8.18, p < .01$; and usefulness of the treatment in the person's own case, $F(1, 54.49) = 10.97, p < .01$, but not on recommendation of treatment to others, $F(1, 56.41) = 3.67, p = .06$, and usefulness of the treatment for other psychological problems, $F(1, 53.78) = 0.59, p = .445$, indicating that both conditions (ITAU+IPPA and only-ITAU) were efficacious in decreasing the participants' opinion (in terms of rationale, satisfaction, and usefulness for the problem itself) about the treatment received from pre-treatment (once the treatment has already been explained to the participant) to post-treatment.

There was a significant main effect of condition² on the rationale behind the treatment, $F(1, 60.24) = 12.67, p \leq .001$; satisfaction with the treatment, $F(1, 61.61) = 12.91, p \leq .001$; recommendation of treatment to others, $F(1, 62.54) = 15.97, p \leq .001$; usefulness of the treatment in the person's own case, $F(1, 60.77) = 10.97, p \leq .001$; and usefulness of the treatment for other psychological problems, $F(1, 62.24) = 8.54, p < .01$, indicating that participants in the ITAU+IPPA condition showed a better opinion about the treatment received overall across all points in time than the participants in only-ITAU.

There was no significant condition x time interaction effect on rationale behind the treatment, $F(1, 54.99) = 2.69, p = .107$; satisfaction with the treatment, $F(1, 54.46) = 2.45, p = .123$, and usefulness of the treatment for other psychological problems, $F(1, 53.78) = 1.24, p = .27$, but there was significant differences on recommendation of treatment to

² A significant effect of condition was expected because we expected differences from pre-treatment, as both treatments had already been explained before filling out these measures at pre-treatment.

others, $F(1, 56.41) = 5.66, p < .05$; and usefulness of the treatment in the person's own case, $F(1, 54.49) = 5.83, p < .05$.

Within-group comparisons for each condition (pre vs. post) revealed changes in the participants' opinions with small effect sizes in the ITAU+IPPA condition, and medium effect sizes in the only-ITAU condition (see Table 15 for details). Moreover, effect sizes for between-group comparisons were large at post-treatment (see Table 16 for details).

Figure 13 (a-e) shows the participants' opinions about the treatment received.

Table 15. Descriptive statistics and within-group effect sizes for each condition for the opinion outcomes at pre-treatment and post-treatment.

Measure	Condition	<i>M(SD)</i>		Within-group effect size, <i>d</i> [95% CI]	
		Pre	Post	Pre vs. Post	
Opinion about the treatment	ITAU+IPPA	7.35 (1.67)	7.13 (2.58)	0.13 [-0.27, 0.53]	
	only-ITAU	6.17 (2.43)	4.85 (2.91)	0.53 [0.09, 0.96]	
Rationale behind the treatment	ITAU+IPPA	7.43 (1.55)	6.97 (2.36)	0.29 [-0.06, 0.64]	
	only-ITAU	6.00 (2.60)	4.50 (3.69)	0.56 [0.13, 0.98]	
Satisfaction with the treatment	ITAU+IPPA	7.58 (1.85)	7.77 (2.44)	-0.10 [-0.43, 0.23]	
	only-ITAU	6.21 (2.70)	4.55 (4.06)	0.59 [0.11, 1.08]	
Recommendation of treatment to others	ITAU+IPPA	7.00 (1.69)	6.70 (2.41)	0.17 [-0.20, 0.55]	
	only-ITAU	6.00 (3.15)	3.80 (3.46)	0.68 [0.20, 1.15]	
Usefulness of the treatment in the person's own case	ITAU+IPPA	7.10 (1.92)	7.17 (2.41)	-0.04 [-0.34, 0.27]	
	only-ITAU	5.79 (2.65)	5.25 (3.38)	0.20 [-0.18, 0.58]	
Usefulness of the treatment for other psychological problems	ITAU+IPPA	7.10 (1.92)	7.17 (2.41)	-0.04 [-0.34, 0.27]	
	only-ITAU	5.79 (2.65)	5.25 (3.38)	0.20 [-0.18, 0.58]	

Note. *d*, Cohen's *d*; CI, Confidence Interval; Pre, Pre-treatment; Post, Post-treatment; ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual.

Table 16. Between-group (ITAU+IPPA versus only-ITAU) comparison effect sizes at each point in time on opinion outcomes at post-treatment.

Note. Mean dif, Mean differences; *Statistically Significant; *d*, Cohen's *d*; CI, Confidence Interval.

Measure	Post-treatment	
Opinion about the treatment	Mean dif.	Between-group effect size, <i>d</i> [95% CI]
Rationale behind the treatment	2.43*	0.83 [0.24, 1.41]
Satisfaction with the treatment	2.58*	0.82 [0.23, 1.41]
Recommendation of treatment to others	3.36*	0.99 [0.40, 1.59]
Usefulness of the treatment in the person's own case	2.95*	0.99 [0.39, 1.59]
Usefulness of the treatment for other psychological problems	2.08*	0.66 [0.09, 1.25]

Note. Mean dif, Mean differences; *Statistically Significant; *d*, Cohen's *d*; CI, Confidence Interval.

Figure 13 (a-e). Participants' opinion of the treatment received.

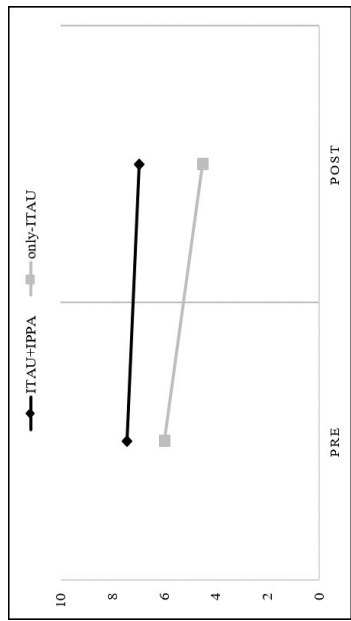


Fig 13a. Rationale behind the treatment

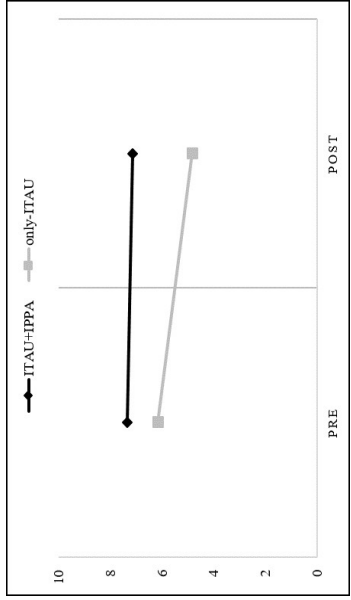


Fig 13b. Satisfaction with the treatment

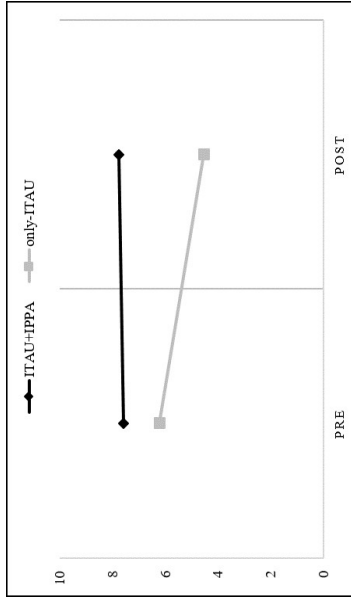


Fig 13c. Recommendation of treatment to others

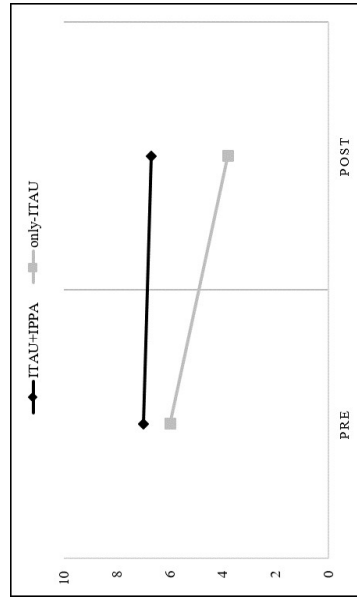


Fig 13d. Usefulness of the treatment in the person's own case

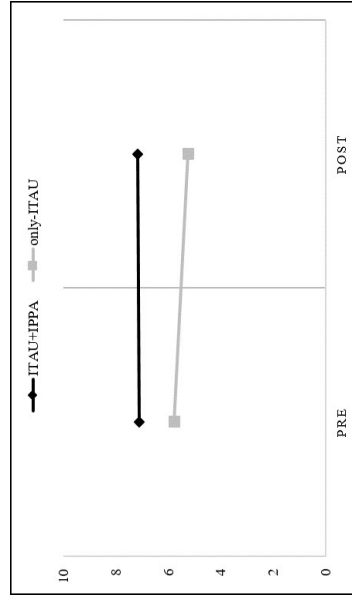


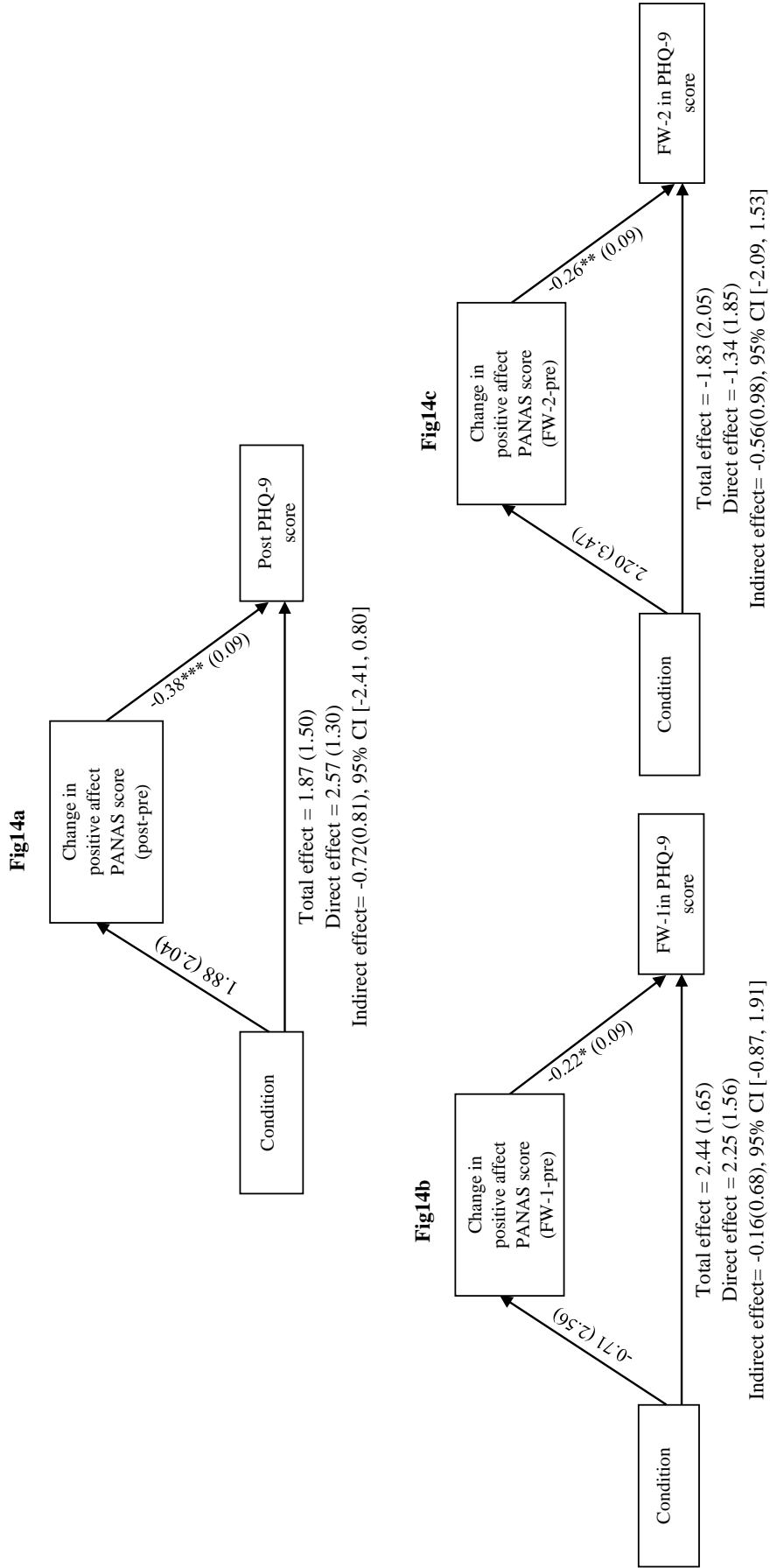
Fig 13e. Usefulness of the treatment for other psychological problems

Note. Pre, Pre-treatment; Post, Post-treatment; ITAU+HPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual.

3.7. Positive affect as mediator: Is the effect of the condition on the post, follow-up-1, and follow-up-2-PHQ-9 scores mediated by changes in positive affect PANAS scores (post, follow-up-1 and follow-up2-PANAS scores)?

Unstandardized regression coefficients, standard errors in parenthesis, and confidence intervals of the direct, total, and indirect effects are shown in Figure 14 (a-c). The indirect effects for all the models were not significant, indicating that the change in positive affect (post, follow-up-1, and follow-up-2-PANAS scores) did not mediate the relationship between the condition and depression severity (post, follow-up-1, and follow-up-2-PHQ-9 scores). Neither the direct effects nor the total effects were significant in any of the models.

Figure 14 (a-c). Simple mediation analyses.



Note. All coefficients represent unstandardized regression coefficients (standard errors in parenthesis); * $p < .05$; ** $p < .01$; *** $p < .001$; FW-1, Follow-up-1 (6 months); Pre, Pre-treatment; Post, Post-treatment; FW-2, Follow-up-2 (12 months); PHQ-9, Patient Health Questionnaire-9; PANAS, Positive and Negative Affect.

3.8. Do the sociodemographic (sex, age, marital status, educational level, occupation, and income level) and baseline clinical variables (depression severity, health-related quality of life SF-12, well-being PHI, and mindfulness FFMQ) moderate the effect of the condition on the post, follow-up-1, and follow-up-2-PHQ-9 scores?

3.8.1. Post-treatment moderation models

a) Sociodemographic variables

Moderation analyses showed that the sociodemographic variables did not moderate the effect of condition on the post-PHQ-9 scores: sex, $F(1, 45) = 0.24, p = .627$; age, $F(1, 45) = 2.67, p = .109$; marital status, $F(1, 45) = 3.31, p = .076$; educational level, $F(1, 45) = 1.38, p = .249$; occupation, $F(1, 45) = 3.38, p = .073$; and income level, $F(1, 45) = 1.95, p = .174$.

b) Clinical variables

Depression severity (baseline PHQ-9 scores)

No variables of the baseline PHQ-9 measure moderated the effect of condition on the post-PHQ-9 scores: $F(1, 45) = 0.24, p = .626$.

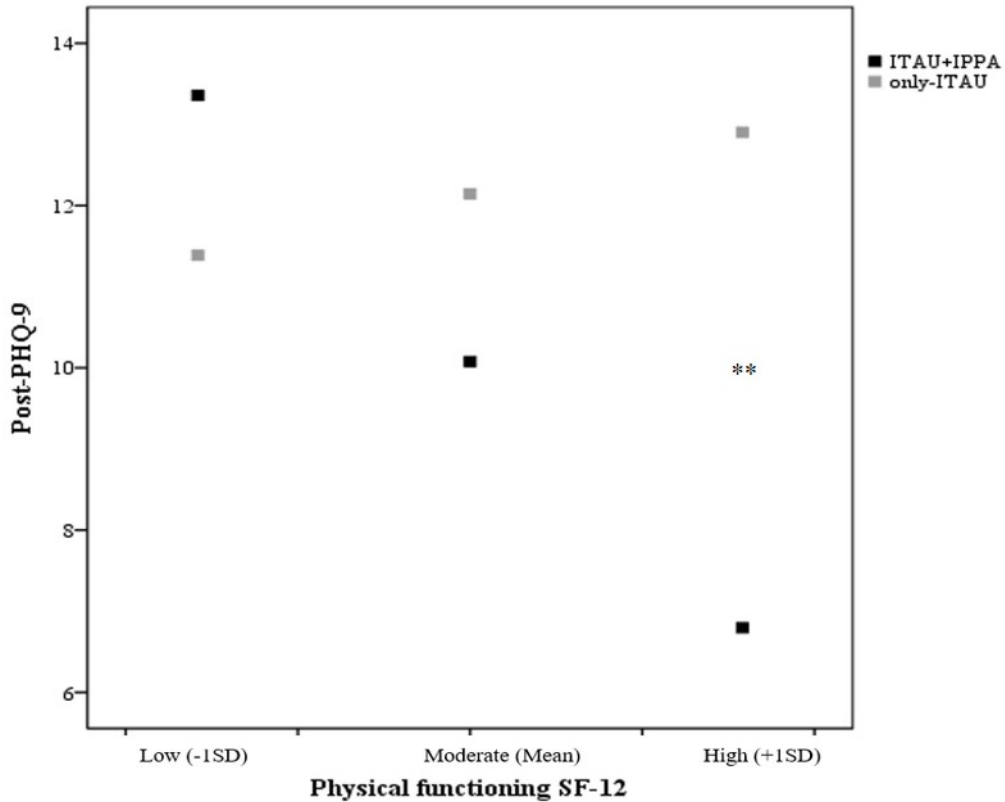
Health-related quality of life (baseline SF-12 scores)

The following variables did not moderate the effect of condition on the post-PHQ-9 scores: general health, $F(1, 45) = 0.66, p = .420$; bodily pain, $F(1, 45) = 0.01, p = .958$; role-physical, $F(1, 45) = 1.83, p = .183$; mental health, $F(1, 45) = 0.25, p = .622$; social functioning, $F(1, 45) = 0.01, p = .963$; and vitality, $F(1, 45) = 0.02, p = .876$.

By contrast, the physical functioning variable moderated the effect of condition on the post-PHQ-9 score. The overall model explained 48.44% of the variance, $F(4, 45) = 10.09$, $p < .001$. The interaction between condition and physical functioning did not include the zero value in the CI, $F(1, 45) = 7.93$, $p < .01$, 95% CI [0.04, 0.22], accounting for 9.58% of the variance. Analyses of simple slopes showed that there was a significant positive relationship between the condition and the physical functioning variable when the physical functioning was “high”, $b = 6.11$, 95% CI [2.41, 9.80], $t = 3.32$, $p = .002$. Participants in the ITAU+IPPA condition with higher baseline physical functioning SF-12 scores achieved lower scores on the post-PHQ-9 (see Figure 15).

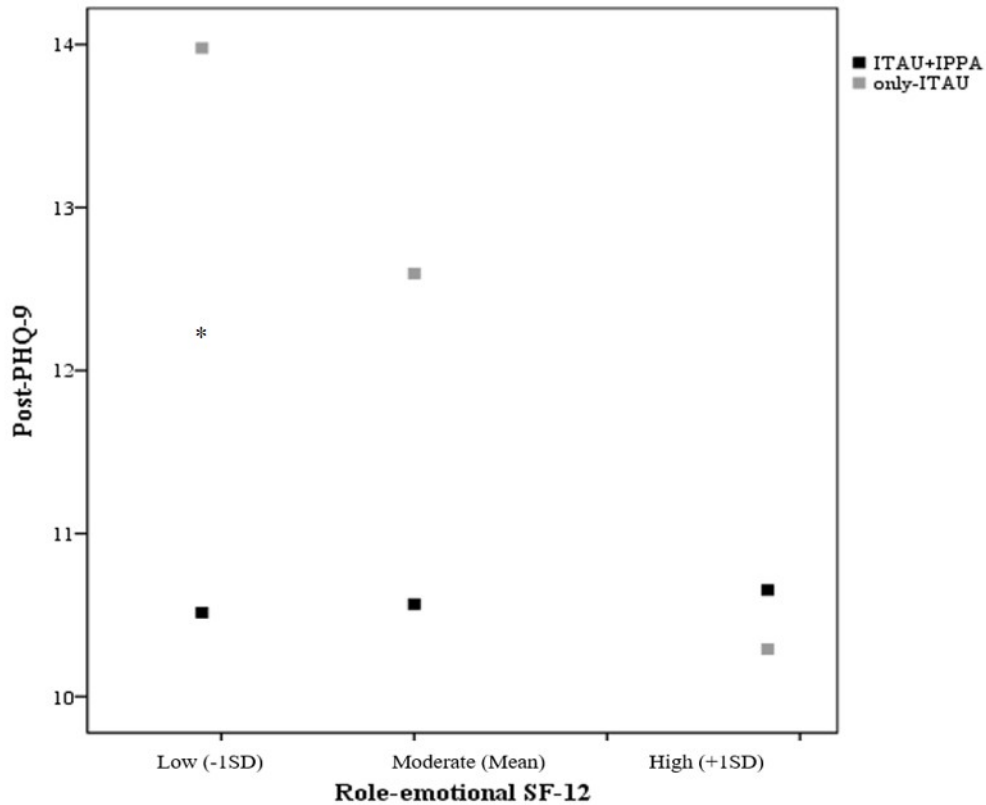
Moreover, the role-emotional variable moderated the effect of condition on the post-PHQ-9 scores. The overall model explained 36.44% of the variance, $F(4, 45) = 9.67$, $p < .001$. The interaction between condition and role-emotional did not include the zero value in the CI, $F(1, 45) = 5.61$, $p < .05$, 95% CI [-0.12, -0.01], accounting for 3.64% of the variance. Analyses of simple slopes showed that there was a significant positive relationship between condition and the role-emotional variable when the role-emotional was “low”, $b = 3.46$, 95% CI [0.11, 6.81], $t = 2.08$, $p = .043$. Participants in the ITAU+IPPA condition with lower baseline role-emotional SF-12 scores achieved lower scores on the post-PHQ-9 (see Figure 16).

Figure 15. Simple slopes graph of the regression of condition on the post-PHQ-9 scores at three levels of baseline physical functioning SF-12 (low, medium, high).



Note. Post, post-treatment; PHQ-9, Patient Health Questionnaire-9; SF-12, Short Form 12 Health Survey; ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual. “Low”, “medium” and “high” levels of the moderators represent the mean and ± 1 standard deviation (SD) (physical functioning SF-12: 61.92 ± 31.59). Significant p-values (* $p < .05$, ** $p < .01$) represent the level of the moderator in which the conditional effect of condition on post-PHQ-9 scores is significant. Baseline score is entered as a covariate.

Figure 16. Simple slopes graph of the regression of condition on the post-PHQ-9 score at three levels of the baseline role-emotional SF-12 (low, medium, high).



Note. Post, post-treatment; PHQ-9, Patient Health Questionnaire-9; SF-12, Short Form 12 Health Survey; ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual. “Low”, “medium” and “high” levels of the moderators represent the mean \pm 1 standard deviation (SD) (role-emotional SF-12: 20.00 ± 34.00). Significant p-values (* $p < .05$, ** $p < .01$) represent the level of the moderator in which the conditional effect of condition on the post-PHQ-9 score is significant. Baseline score is entered as a covariate.

Well-being (baseline PHI scores)

No variables of the baseline PHI measure moderated the effect of condition on the post-PHQ-9 scores: total well-being, $F(1, 45) = 1.64, p = .207$; remembered well-being, $F(1, 45) = 1.97, p = .168$; and experienced well-being, $F(1, 45) = 0.06, p = .809$.

Facets of mindfulness (baseline FFMQ scores)

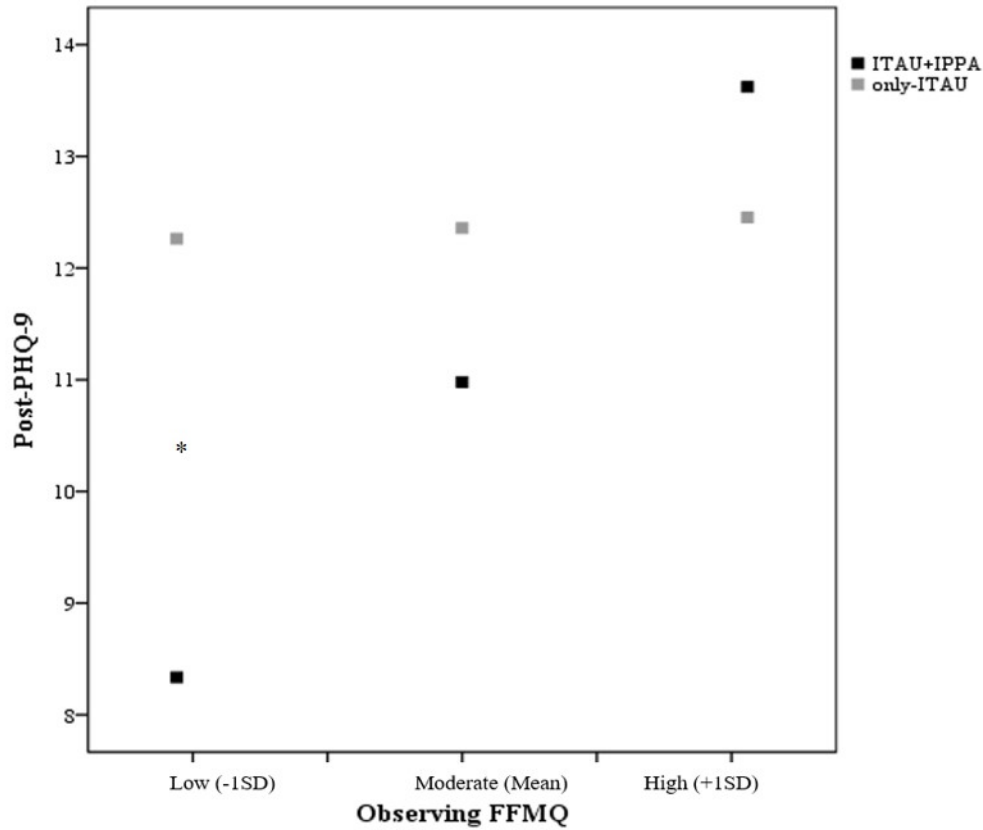
The following variables did not moderate the effect of condition on the post-PHQ-9 scores: acting with awareness, $F(1, 45) = 0.13, p = .715$; not judging inner experience, $F(1, 45) = 0.21, p = .649$; and not reacting to inner experience, $F(1, 45) = 0.60, p = .443$.

However, the observing variable moderated the effect of condition on the post-PHQ-9 score, but the moderation was only marginally significant. The overall model explained 38.75% of the variance, $F(4, 45) = 8.88, p < .001$. The interaction between the condition and observing did not include the zero value in the CI, $F(1, 45) = 3.88, p = .054$, 95% CI [-0.81, 0.01], accounting for 4.26% of the variance. Analyses of simple slopes showed that there was a significant positive relationship between condition and the observing variable when the observing was “low”, $b = 3.93$, 95% CI [0.59, 7.26], $t = 2.37, p = .022$. Participants in the ITAU+IPPA condition with lower baseline observing FFMQ scores achieved lower scores on the post-PHQ-9 (see Figure 17).

In addition, the describing variable moderated the effect of condition on the post-PHQ-9 score. The overall model explained 44.08% of the variance, $F(4, 45) = 10.01, p < .001$. The interaction between condition and describing did not include the zero value in the CI, $F(1, 45) = 6.58, p < .05$, 95% CI [-1.06, -0.13], accounting for 13.69% of the variance. Analyses of simple slopes showed that there was a significant positive relationship between the condition and the describing variable when the describing was “low”, $b = 6.87$, 95% CI [2.71, 11.04], $t = 3.32, p = .002$. Participants in the ITAU+IPPA

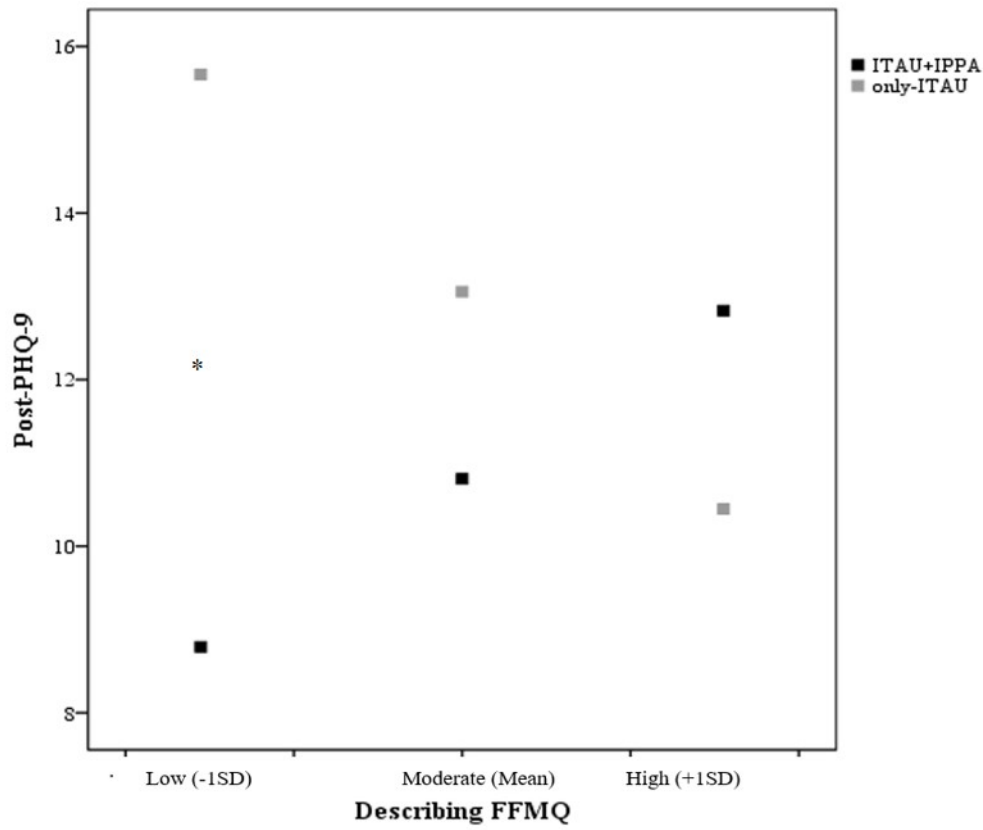
condition with lower baseline describing FFMQ scores achieved lower scores on the post-PHQ-9 (see Figure 18).

Figure 17. Simple slopes graph of the regression of condition on the post-PHQ-9 scores at three levels of the baseline observing FFMQ (low, medium, high).



Note. Post, post-treatment; PHQ-9, Patient Health Questionnaire-9; FFMQ, Five Facet Mindfulness Questionnaire; ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual. “Low”, “medium” and “high” levels of the moderators represent the mean and ± 1 standard deviation (SD) (observing FFMQ: 20.50 ± 6.07). Significant p-values (* $p < .05$, ** $p < .01$) represent the level of the moderator at which the conditional effect of the condition on the post-PHQ-9 score is significant. Baseline score is entered as a covariate.

Figure 18. Simple slopes graph of the regression of condition on the post-PHQ-9 score at three levels of the baseline describing FFMQ (low, medium, high).



Note. Post, post-treatment; PHQ-9, Patient Health Questionnaire-9; FFMQ, Five Facet Mindfulness Questionnaire; ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual. “Low”, “medium” and “high” levels of the moderators represent the mean and ± 1 standard deviation (SD) (describing FFMQ: 23.98 ± 7.53). Significant p-values (* $p < .05$, ** $p < .01$) represent the level of the moderator at which the conditional effect of the condition on the post-PHQ-9 score is significant. Baseline score is entered as a covariate.

3.8.2. Follow-up-1 (6 months) moderation models

a) Sociodemographic variables

Moderation analyses showed that the sociodemographic variables did not moderate the effect of the condition on the follow-up-1-PHQ-9 score: sex, $F(1, 35) = 0.03, p = .863$; age, $F(1, 35) = 1.44, p = .238$; marital status, $F(1, 35) = 0.03, p = .855$; educational level, $F(1, 35) = 2.92, p = .098$; occupation, $F(1, 35) = 0.73, p = .396$; and income level, $F(1, 35) = 0.08, p = .787$.

b) Clinical variables

Depression severity (baseline PHQ-9 scores)

No variables of the baseline PHQ-9 measure moderated the effect of condition on the follow-up-1-PHQ-9 scores: $F(1, 35) = 0.55, p = .462$.

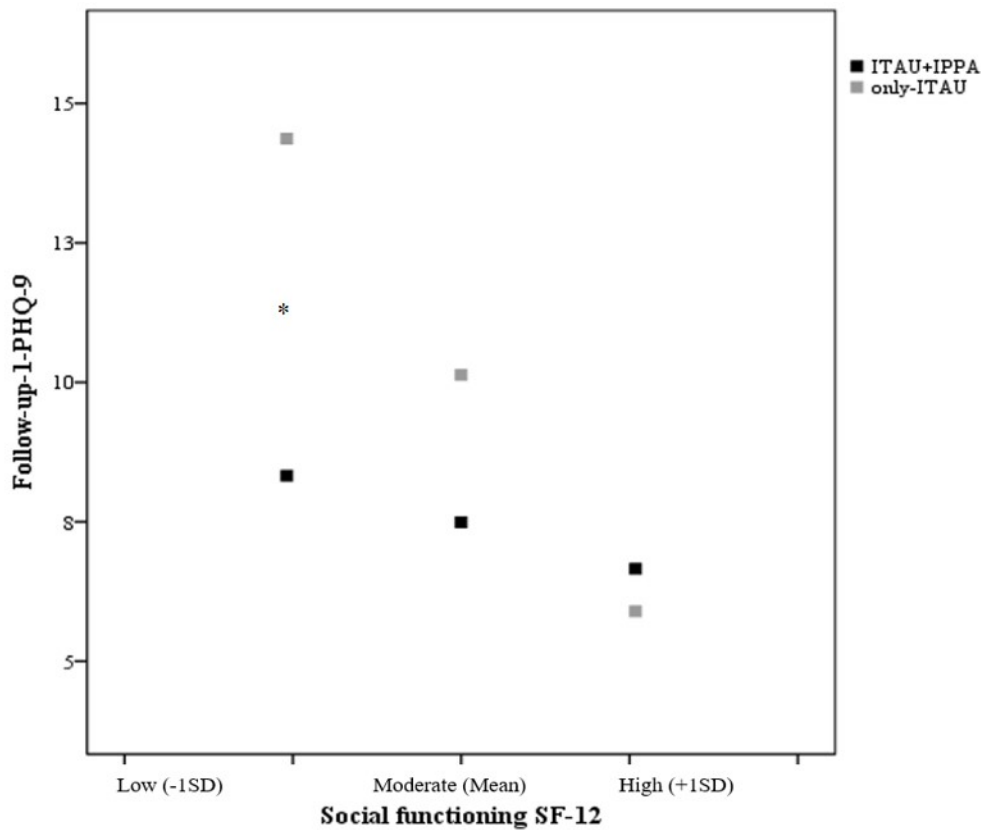
Health-related quality of life (baseline SF-12 scores)

The following variables did not moderate the effect of the condition on the follow-up-1-PHQ-9 scores: general health, $F(1, 35) = 0.18, p = .678$; bodily pain, $F(1, 35) = 0.25, p = .618$; role-physical, $F(1, 35) = 1.18, p = .284$; physical functioning, $F(1, 35) = 0.13, p = .719$; mental health, $F(1, 35) = 3.33, p = .077$; role-emotional, $F(1, 35) = 0.68, p = .416$; and vitality, $F(1, 35) = 1.55, p = .221$.

Nevertheless, the social functioning variable marginally significantly moderated the effect of the condition on the follow-up-1-PHQ-9 score. The overall model explained 41.91% of the variance, $F(4, 35) = 5.61, p = .052$. The interaction between condition and social functioning did not include the zero value in the CI, $F(1, 35) = 4.03, p = .052$, 95% CI [-0.33, 0.01], accounting for 7.81% of the variance. Analyses of simple slopes showed that there was a significant positive relationship between the condition and the social

functioning variable when social functioning was “low”, $b = 6.04$, 95% CI [0.42, 11.66], $t = 2.19$, $p = .036$. Participants in the ITAU+IPPA condition with lower baseline social functioning SF-12 scores achieved lower scores on the follow-up-1-PHQ-9 (see Figure 19).

Figure 19. Simple slopes graph of the regression of condition on the follow-up-1-PHQ-9 scores at three levels of baseline social functioning SF-12 (low, medium, high).



Note. Post, post-treatment; PHQ-9, Patient Health Questionnaire-9; SF-12, Short Form 12 Health Survey; ITAU+IPPA, Improved Treatment as Usual with Intervention focused on the Promotion of Positive Affect; only-ITAU, only-Improved Treatment as Usual. “Low”, “medium” and “high” levels of the moderators represent the mean and ± 1 standard deviation (SD) (social functioning SF-12: 40.00 ± 23.72). Significant p-values (* $p < .05$, ** $p < .01$) represent the level of the moderator at which the conditional effect of the condition on the follow-up-1-PHQ-9 score is significant. Baseline score is entered as a covariate.

Well-being (baseline PHI scores)

No variables of the baseline PHI measure moderated the effect of condition on the follow-up-1-PHQ-9 scores: total well-being, $F(1, 35) = 0.22, p = .639$; remembered well-being, $F(1, 35) = 0.14, p = .712$; and experienced well-being, $F(1, 35) = 1.62, p = .211$.

Facets of mindfulness (baseline FFMQ scores)

No variables of the baseline FFMQ moderated the effect of the condition on the follow-up-1-PHQ-9 scores: observing, $F(1, 35) = 0.15, p = .704$; describing, $F(1, 35) = 2.79, p = .104$; acting with awareness, $F(1, 35) = 0.34, p = .562$; not judging inner experience, $F(1, 35) = 0.32, p = .576$; and not reacting to inner experience, $F(1, 35) = 0.11, p = .742$.

3.8.3. Follow-up-2 (12 months) moderation models*a) Sociodemographic variables*

Moderation analyses showed that the sociodemographic variables did not moderate the effect of the condition on the follow-up-2-PHQ-9 scores: sex, $F(1, 30) = 0.01, p = .907$; age, $F(1, 30) = 2.57, p = .119$; marital status, $F(1, 35) = 0.17, p = .680$; educational level, $F(1, 35) = 2.92, p = .098$; occupation, $F(1, 35) = 0.73, p = .396$; and income level, $F(1, 35) = 3.40, p = .078$.

*b) Clinical variables**Depression severity (baseline PHQ-9 scores)*

No variables of the baseline PHQ-9 measure moderated the effect of condition on the follow-up-2-PHQ-9 scores: $F(1, 30) = 0.18, p = .674$.

Health-related quality of life (baseline SF-12 scores)

No variables of the baseline SF-12 measure moderated the effect of the condition on the follow-up-2-PHQ-9 scores: general health, $F(1, 30) = 0.38, p = .541$; bodily pain, $F(1, 30) = 0.48, p = .828$; role-physical, $F(1, 30) = 0.46, p = .501$; physical functioning, $F(1, 30) = 0.74, p = .395$; mental health, $F(1, 30) = 0.02, p = .901$; role-emotional, $F(1, 30) = 0.13, p = .721$; social functioning, $F(1, 30) = 0.01, p = .910$; and vitality, $F(1, 30) = 0.15, p = .700$.

Well-being (baseline PHI scores)

No variables of the baseline PHI measure moderated the effect of the condition on the follow-up-2-PHQ-9 scores: total well-being, $F(1, 30) = 0.85, p = .365$; remembered well-being, $F(1, 30) = 0.88, p = .356$; and experienced well-being, $F(1, 30) = 0.03, p = .862$.

Facets of mindfulness (baseline FFMQ scores)

No variables of the baseline FFMQ moderated the effect of the condition on the follow-up-2-PHQ-9 scores: observing, $F(1, 30) = 0.17, p = .682$; describing, $F(1, 30) = 0.75, p = .395$; acting with awareness, $F(1, 30) = 0.11, p = .743$; not judging inner experience, $F(1, 30) = 0.01, p = .928$; and not reacting to inner experience, $F(1, 30) = 0.13, p = .725$.

In next chapter, the main findings will be summarized and the main results will be discussed in relation to previous literature. Moreover, the limitations and future directions of this study will be presented.

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CHAPTER

3

GENERAL DISCUSSION

The general objective of this study was to investigate the efficacy and cost-effectiveness of an improved treatment as usual (ITAU) with a low-intensity Internet-based computerized intervention focused on the promotion of positive affect (ITAU+IPPA) for the treatment of depression, compared to only the ITAU (only-ITAU) in Spanish primary care (PC) settings.

The specific objectives of this dissertation were:

1. To examine the efficacy of both interventions (ITAU+IPPA and only-ITAU) in decreasing depression severity and increasing other secondary variables (affect, health-related quality of life, well-being and mindfulness) after treatment and follow-ups (6 and 12 months).
2. To analyze whether both interventions (ITAU+IPPA and only-ITAU) are cost-effective psychological treatments for depression in PC settings.
3. To analyze the participants' opinions of the treatment received.
4. To explore the possible mediator and moderator roles of several relevant variables in the effect of the condition on the depression severity.

In the following subsections, a general discussion will be presented.

1. Efficacy of treatments for depression in primary care settings

The first hypothesis proposed that the condition of ITAU+IPPA would be more efficacious compared to the only-ITAU condition in improving depression severity and other secondary variables (affect, health-related quality of life, well-being and mindfulness) after treatment and follow-ups (6 and 12 months). This hypothesis was not confirmed, and the results showed that both treatments (ITAU+IPPA and only-ITAU)

were equally efficacious in producing changes in all the variables after treatment and follow-ups.

Although there were no statistically significant differences between treatments, information regarding treatment effect sizes will be discussed for each condition in all measurement variables.

1.1. Depression severity

Both treatments were efficacious in reducing depression severity across time. Participants in the ITAU+IPPA condition presented a moderate-severe baseline depression, which changed to moderate after the treatment, and to mild at follow-up 1, returning to moderate at follow-up 2. Participants in the only-ITAU condition presented a moderate baseline depression, remained the same after treatment and follow-up 1, and changed to mild at follow-up 2.

Although depression severity decreased in all participants, it is observed that the change in the severity was faster in the ITAU+IPPA condition, with larger effect sizes compared to only-ITAU at post-treatment. Moreover, the percentage of participants classified as recovered and improved was higher (but not significantly) in the ITAU+IPPA condition (40%) compared to the only-ITAU condition (30%) after the treatment. This result suggests that the Internet-based psychological intervention (IPPA) as an adjunct to the ITAU, could impact depression outcomes in a faster way than the only-ITAU.

In addition, these findings are consistent with the results of the meta-analysis by Bower et al. (2013), which showed the influence of initial depression severity on the effectiveness of low-intensity psychological interventions (in traditional and online

format). Specifically, the outcomes of this study revealed that patients with more severe baseline depression had larger treatment effects than those who were less severely depressed, but not significantly. Thus, our results on the use of low-intensity Internet-based interventions are encouraging, even in more severe disorders in the short term.

Regarding follow-ups, the results showed that depression severity continued to decrease and with greater effect sizes for the ITAU+IPPA condition compared to the ITAU+IPPA at follow-up 1, but the difference was not significant. However, the outcomes showed slightly greater effect sizes for the only-ITAU condition compared to ITAU+IPPA at follow-up 2. There were also better percentages of recovered, improved, and unchanged participants in the only-ITAU condition during follow-ups. This result suggests that both treatment conditions have different time evolutions. More studies are needed to investigate the appropriate dose of psychological treatments to make them more efficacious in the long term (National Institute for Health and Care Excellence, 2017). Overall, the efficacy results are consistent with other studies that have examined the role of Internet-based interventions as an adjunct to the treatment provided in PC for adults with depression. For example, Gilbody et al. (2015) found that supported Internet-delivered cognitive behavioral therapy (ICBT) (Beating the Blues or MoodGYM) was not more efficacious in reducing depressive symptomatology than usual medical care alone. Montero-Marín et al. (2016) also found no differences between a guided or self-guided ICBT compared to ITAU at 3-month follow-up. Norlund et al. (2018) also found that computerized guided ICBT was not better than TAU in reducing depression symptoms in a sample of patients who had suffered a myocardial infarction. Finally, in a systematic review and meta-analysis on the effectiveness of Internet-based interventions in a sample of young adults, they were also not found to be more efficacious in reducing depression severity, compared to usual care (Ye et al., 2014).

1.2. Affect, health-related quality of life, well-being, and facets of mindfulness

Affect

Both treatments were efficacious in increasing positive affect (PA) and decreasing negative affect (NA) across time, and there were no statistical differences between the two conditions. However, regarding NA, the effect size was slightly greater for the ITAU+IPPA condition, especially at post-treatment and follow-up 1, whereas effect sizes for PA were greater in the only-ITAU condition compared to the ITAU+IPPA condition at post-treatment and follow-up 2.

These results may be controversial because the opposite pattern was expected, considering that the Internet-based intervention was specifically designed to regulate PA. However, our results support the idea that the positive psychological interventions (PPIs) could also have a relevant impact on the regulation of NA, coinciding with other studies (e.g., Pietrowsky, & Mikutta, 2012; Seligman, Rashid, & Parks, 2006; Sin & Lyubomirsky 2009; Taylor, Lyubomirsky, & Stein, 2017; Walsh, Cassidy, & Priebe, 2016). Therefore, positive psychology techniques may lead to transdiagnostic treatment strategies for depression.

Health-related quality of life

Both treatments were also efficacious in increasing health-related quality of life in all variables (general health, bodily pain, role-physical, mental health, role-emotional, social-functioning, and vitality), except physical functioning (all participants had high baseline scores). The treatment effect size was greater for the ITAU+IPPA condition compared to the only-ITAU condition in the general health, bodily pain, mental health, role-emotional, and vitality variables at follow-up 1. However, and in the same line of depression severity, the treatment effect increased for the only-ITAU condition at follow-

up 2 in the following variables: general health, role-physical, role-emotional, social-functioning, and vitality. Here, we again find some different time trajectories of both treatment conditions.

Well-being

Both treatments were efficacious in increasing well-being (total well-being, remembered well-being, and experienced well-being) across time. The treatment effect was greater for ITAU+IPPA compared to the only-ITAU condition at follow-up 1. However, the treatment effect decreased for ITAU+IPPA and increased for the only-ITAU condition at follow-up 2. Once again, it seems that ITAU+IPPA was more efficacious in producing well-being changes in the short term compared to only-ITAU, which was more efficacious in the long term, but not significantly.

Facets of mindfulness

Both treatments were efficacious in increasing the facets of mindfulness (observing, describing, acting with awareness, not judging inner experience, and not reacting to inner experience) across time. The treatment effect was greater for the ITAU+IPPA condition in the describing, acting with awareness, and not judging inner experience variables at follow-up 1, and for only-ITAU, the observing and not reacting to inner experience variables. Moreover, these effects were maintained at follow-up 2, except for the observing and not reacting to inner experience variable (which increased for ITAU+IPPA), and the acting with awareness (which decreased for ITAU+IPPA).

Therefore, the ITAU+IPPA condition seems to be more efficacious in producing changes in some facets of mindfulness in both the short and long term. This finding is relevant because the psychological intervention also addressed aspects related to the

ability of mindfulness (e.g., the importance of living and enjoying the present moment, savoring) to regulate PA.

Cebolla, Enrique, Alvear, Soler, and García-Campayo (2017) argue that mindfulness is congruent with many principles proposed by PP, such as the development of kindness, compassion, and positive emotions. In fact, many PPIs include mindfulness to promote well-being and mental health and reduce depression, obtaining good results (Baskin & Enrigh, 2004; Fredrickson, Cohn, Coffey, Pek, & Finkel, 2008; Kuyken et al., 2008). Therefore, although no differences between treatments were found, it appears that the ITAU+IPPA condition plays an influential role in attentional self-regulation for the treatment of depression in the short and long term.

1.3. Attrition rates

The percentage of dropouts after treatment was higher for the ITAU+IPPA condition (25%) than for the only-ITAU condition (19%), and also at follow-ups. These results agree with the literature on Internet-based interventions and similar studies, which usually reported between 20-30% of treatment dropouts (e.g., Gilbody et al., 2015; Spek et al., 2007; van Ballegooijen et al., 2014).

1.4. Summary of findings

Both interventions were equally efficacious in reducing depression severity and NA, and increasing the other variables related to positive functioning (PA, health-related quality of life, well-being, and facets of mindfulness) until the 12-month follow-up. The adherence rate was higher for the only-ITAU condition.

Although there are no statistically significant differences between treatments, we would like to highlight two aspects: first, it seems that the ITAU+IPPA condition

produced faster improvements with larger treatment effect sizes in the majority of the variables in the short term. And second, it seems that the only-ITAU condition was more efficacious in generating and maintaining changes in the long term (except for the mindfulness variables).

Regarding the higher rate of dropouts in the ITAU+IPPA condition, we would like to emphasize that this treatment condition was more efficacious in the short term, and this result leads us to wonder if this greater efficacy in the short term could not be responsible for dropouts of treatment in a context with so little adherence as PC.

To explain the results on efficacy and dropouts, we would like to take into consideration other possible factors (e.g., duration and number of treatment modules, therapist support) (Sin, Della Porta, & Lyubomirsky, 2011). These factors will be described below.

Duration and number of treatment modules: Some evidence shows that PPIs with longer duration (more weeks) are more efficacious in the long term, both in reducing depressive symptomatology and in increasing well-being, than shorter interventions (Sin & Lyubomirsky, 2009). In this way, longer interventions can allow patients to have more time to practice activities, thus helping them to form habits. Moreover, the majority of the Internet-based interventions that were efficacious for the treatment of depression (e.g., CBT, transdiagnostic) included a larger number of modules such as Deprexis (Meyer et al., 2009), the Well-being program (Titov et al., 2011), or the Unified Protocol (Barlow, Allen, & Choate, 2004). However, most studies on online PPIs use short one-week exercises, compared to standard treatments, which use a series of modules and exercises (Görge, Oehler, von Hirschhausen, Hegerl, & Rummel-Kluge, 2018). Therefore, more

research is needed to better determine the appropriate duration (longer or shorter) for PP treatment programs to be efficacious in the long term.

Inclusion of therapist support in the Internet-based intervention: It has been observed that Internet-based interventions are more efficacious when more support is offered by the therapist (Baumeister, Reichler, Munzinger, & Lin, 2014; Berger, Hämmerli, Gubser, Andersson, & Caspar, 2011; Richards & Richardson, 2012). In a similar line, it has been found that PPIs without therapist support are not as efficacious as individual therapy or group therapy (Sin & Lyubomirsky, 2009).

Self-selection and motivation towards the assigned treatment: Previous data show that the interventions tend to be more successful when people freely choose to participate in them than interventions to which people are assigned (Sin & Lyubomirsky, 2009). Possibly, these people are more motivated and thus more responsible and enthusiastic in following the intervention guidelines.

Involvement by GPs in the treatment: The control group in this study consisted of an ITAU, which means that the GPs had to apply the medical treatment (e.g., medication) and follow the recommended guidelines for the treatment of depression in PC. It is possible that this indication and knowing that they were participating in a controlled trial encouraged them to effectively follow the guidelines, and, thus, the ITAU was very efficacious.

Finally, considering the *involvement by the participants in the treatment*, the performance of the ITAU+IPPA implied that the participants had a more active role in their response to the treatment. In addition to receiving an ITAU (medication, sessions with their GP), they had to perform the Internet-based intervention. This could result in a

greater degree of involvement by the participants (in terms of time, activity, occupation) compared to the participants in only-ITAU.

2. Cost-effectiveness of two treatment conditions

The second hypothesis proposed that the ITAU+IPPA condition would be more cost-effective than the only-ITAU condition in terms of health and social services use (visits to the GP for any reason, visits to the emergency room, absence from work, leaving the usual tasks unfinished, and reduction in the quality of usual tasks due to health problems). This hypothesis was not confirmed, and the results only showed that both treatments (ITAU+IPPA and only-ITAU) were equally efficacious in producing changes in terms of the quality of usual tasks (number of days when the quality of usual tasks had been reduced due to health problems in the last month) across time.

Although there was no significant change in hardly any of the variables related to health and social services (except on the item related to quality of usual tasks) from pre-treatment to the follow-ups, it was observed that the number of visits to the GP (for any reason, not specifically psychological problems) and the emergency room, and the number of usual tasks left unfinished due to health problems, decreased in both conditions during the follow-ups, with small and medium treatment effects. However, the number of days off work decreased for the only-ITAU at follow-ups, and increased for the ITAU+IPPA condition at follow-up 2, with small and medium treatment effects. Finally, the number of days when the quality of usual tasks had been reduced due to health problems in the last month decreased in both conditions, but with a greater treatment effect in the only-ITAU condition at follow-ups.

These results are consistent with similar studies, such as Duarte et al. (2017), who showed that technically supported interventions did not appear to be more cost-effective

than usual GP care from a healthcare perspective and outcomes measured using quality-adjusted life years (QALYs) over 2 years. In addition, Kenter et al. (2015) showed that blended care (Internet-based interventions in combination with face-to-face sessions) was more expensive compared to established face-to-face treatments and did not lead to better outcomes in terms of general functioning.

So far, systematic reviews of the cost-effectiveness of Internet-based interventions for the treatment of depression show a lack of consistency in the data, and most studies differ in the method used to estimate costs (Donker et al., 2015; Hedman, Ljotsson, & Lindfors, 2012; Tate, Finkelstein, Khavjou, & Gustafson, 2009). To overcome these limitations, Kolovos et al. (2018) evaluated the cost-effectiveness of guided Internet-based interventions compared to control conditions in a sample of adults with depression through an individual-participant data meta-analysis. Their results indicated that guided Internet-based interventions were not considered more cost-effective compared to controls (care as usual, waiting list). However, these authors included a minority of randomized control trials (RCTs) that had evaluated cost-effectiveness. Therefore, it is important to collect more data on cost-effectiveness in order to draw more robust conclusions.

3. Post- module analyses in ITAU+IPPA condition: Changes in depression severity and affect

Overall, ITAU+IPPA was efficacious in decreasing depression severity and NA, and increasing PA, across the modules of the treatment. However, the effect of the modules was greater between modules 1 and 2. Therefore, it seems that the Internet-based interventions have an important initial impact on all variables, supporting the idea of a faster trajectory of symptomatology improvement.

Regarding the percentage of participants who completed each module in the ITAU+IPPA condition, only 45% of participants completed all the treatment modules, 65% completed three modules, 72.5% two modules, and 77.5% one module. As mentioned above, the decrease in the number of participants per module could be explained by the degree of involvement that this treatment required, compared to only-ITAU. Moreover, participants' depression severity and symptomatology improvement may also influence their response to treatment modules.

It is worth mentioning that some participants accessed the web platform after finishing the treatment period.

4. Participants' opinion of the treatment received

The third hypothesis proposed that the users' opinions about the treatment would be better in the ITAU+IPPA condition. This hypothesis was confirmed, as participants in the ITAU+IPPA showed a better opinion about the treatment received (in terms of rationale, satisfaction, recommendation to others, usefulness for the problem itself, and usefulness for other psychological problems) overall, across all points in time (from pre-treatment to post-treatment), than the participants in the only-ITAU condition. Although opinions of both treatments decreased over time from pre-treatment (once the treatment has already been explained to the participant) to post-treatment, the ITAU+IPPA participants showed better outcomes on recommending the treatment to others and the usefulness of the treatment for the problem itself, compared to the only-ITAU.

Overall, the ITAU+IPPA participants' opinion scores were higher at all assessment moments.

It appears that participants expressed a better opinion of the Internet-based intervention. This finding is encouraging because few studies have analyzed patients' opinions about different types of treatment (e.g., medical treatment, Internet psychological intervention) for depression in a PC setting. One exception is the work by Dorow, Löbner, Pabst, Stein, and Riedel-Heller (2018), who examined preferences for depression treatments (medication, psychotherapy, combined treatment, talking to friends and family, exercise, self-help literature, and Internet-based interventions) in a sample of PC patients. Their results showed that the patients had strong preferences for psychotherapy, talking to friends and family, and exercise. In addition, they found that 1/5 patients considered Internet-based interventions to be a good treatment for depression (especially younger patients). Recently, Walsh, Szymczynska, Taylor, and Priebe (2018) analyzed the acceptability of an online intervention based on positive psychology for the treatment of depression, finding greater acceptance of this treatment among participants who considered it relevant to their depression (own problem), consistent with our results.

Future studies should continue to investigate aspects related to opinions or treatment preferences for depression, taking into account different types of intervention (in traditional or online format) in a PC setting. Specifically, 13 participants accessed the web platform approximately 4 times from post-treatment to 6-month follow-up, and 9 participants accessed nearly 2 times from 6-month follow-up to the 12-month follow-up. This may indicate a positive aspect of the Internet-based interventions, given that information is always available when the patient needs it, even if s/he has dropped out of treatment or completed it (with or without success), something that is not available in traditional interventions.

5. Positive affect as mediator variable

The fourth hypothesis proposed that participants in the ITAU+IPPA condition (compared to control) would have a greater change in PA (both after treatment and follow-ups), leading to a greater reduction in the depression severity (both after treatment and follow-ups). This hypothesis was not confirmed because the effect of condition on depression severity scores at post-treatment and follow-ups was not mediated by the change in PA at any assessment time. This result suggests that the IPPA was not as effective in producing changes in the PA. As explained above, no statistically significant differences were found between treatments, and the inclusion of IPPA did not result in larger effect sizes, compared to the control condition, in reducing depression symptoms in the long term.

Although PPIs have often been used to promote well-being and up-regulate PA in the individual, their implications in the clinical setting seem questionable according to the literature (e.g., Mongrain & Anselmo-Matthews, 2012). For example, in some studies no differences have been found between online PPIs and placebo groups in increasing happiness and reducing depression (Woodworth, O'Brien-Malone, Diamond, & Schütz, 2016a). Therefore, it is necessary to investigate these interventions in a theoretical framework that identifies possible mediating factors of their effects on depression severity (Woodworth, O'Brien-Malone, Diamond, & Schütz, 2016b).

6. Sociodemographic and baseline clinical variables as moderators

No specific hypotheses were generated about which moderator variables (sociodemographic and baseline clinical variables) could be significant in the effect of the condition (ITAU+IPPA vs. only-ITAU) on depression severity after treatment and follow-ups, due to the exploratory nature of the analyses.

The results showed that the sociodemographic variables (sex, marital status, educational level, occupation, and income level) and some baseline clinical variables of depression severity, health-related quality of life (general health, bodily pain, role-physical, mental health, and vitality), well-being (total well-being, remembered well-being, and experienced well-being), and facets of mindfulness (acting with awareness, not judging inner experience, and not reacting to inner experience) did not moderate the effect of the condition on the depression severity scores at post-treatment and follow-ups.

By contrast, the physical functioning and the role-emotional (health-related quality of life variables) moderated the effect of the condition on the depression severity scores at post-treatment. Specifically, the participants in the ITAU+IPPA condition with higher baseline physical functioning and lower baseline role-emotional scores achieved lower depression severity scores at post-treatment. Moreover, social functioning (another health-related quality of life variable) moderated the effect of the condition on the depression severity scores at 6-month follow-up, but in a marginally significant way. The participants in the ITAU+IPPA condition with lower baseline social functioning scores achieved lower depression severity scores at 6-month follow-up. It seems that participants with better physical functioning but worse role-emotional and social functioning benefited more from ITAU+IPPA in decreasing their depression severity.

Good physical functioning (as a protective factor of depression) of participants in pre-treatment could have contributed to greater adherence to the IPPA guidelines (one of which focused on the role of activity in well-being) (Warburton, Nicol, & Bredin, 2006). Moreover, other therapeutic strategies of the IPPA (e.g., emotional regulation or social support) could have helped them to improve their role-emotional (emotional intelligence) and social functioning (social skills), resulting in an improvement in their depression severity across time. These findings support the idea that emotional regulation (Extremera

& Rey, 2015) and social support (Chou & Chi, 2001) may moderate the effect of depression.

Taking into account the baseline facets of mindfulness, the observing and describing variables moderated the effect of the condition on the depression severity scores at post-treatment. Specifically, the participants in the ITAU+IPPA condition with lower baseline observing and describing scores achieved lower depression severity scores at post-treatment. It appears that participants with more difficulties in observing and describing benefited more from ITAU+IPPA in decreasing their depression severity. Therefore, the inclusion of the IPPA as adjunct treatment (focused also on aspects related to mindfulness) allowed the participants to attend to their internal and external experiences (e.g., sensations, thoughts or emotions) and label them with words, thus contributing to the improvement of their depression severity. These findings indicate that it is important to consider the mindfulness abilities within PPIs to reduce depressive symptomatology (Cebolla et al., 2017; Sin et al., 2011).

More studies are needed to identify potential moderators of the response to online PPIs in depression, and also in PC settings.

7. Limitations

Some limitations of the current study should be pointed out:

First, the dropout rate in both conditions, and especially in the ITAU+IPPA condition, could have affected the statistical power, and therefore in the rest of the analyses (efficacy, cost-effectiveness, opinion, mediation and moderation) of the present study.

Second, we do not have information about the reasons for participant dropout. It is relevant to explore the reasons to find ways to address this problem. The qualitative perspective could help to analyze these experiences of treatment dropout in a clearer and deeper way (Fernández-Álvarez et al., 2017).

Third, we do not have any record of the number of sessions directed to depression problems with the GP and the medication dose related to ITAU adherence. It would be necessary to consider these variables in the future, and analyze whether participants in Internet-based interventions receive less medical attention, which could be a cost-effectiveness variable of this treatment.

Fourth, we do not have information about the diagnosis of possible co-morbid disorders of depression. It would have been interesting to know if the treatments were also efficacious in producing changes in other symptomatology such as anxiety. In this way, we could have obtained more information about the role played by the IPPA, which was based on the transdiagnostic perspective.

Fifth, information about the participants' previous history of depression has not been taken into account in this study. These data are important because the possible chronicity or familiarity with treatments (medical or psychological) could have influenced the results (e.g., Görges et al., 2018).

Finally, this study did not use a validated measurement instrument to analyze the cost-effectiveness of the treatments evaluated. It is important that all RCTs include the same or similar instruments in order to analyze their evidence in a more systematic way (e.g., in QALYs).

8. Future directions

In this study, we include some elements related to therapeutic support to increase adherence to the Internet-based intervention. Specifically, there was a face-to-face group session with a therapist to explain the intervention. Moreover, we included weekly text messages and emails to encourage the participants to continue with the program and perform tasks. Future research could explore other types of therapeutic support (e.g., weekly telephone support, use of online therapists) to analyze whether there is greater participation and greater adherence to computerized treatment. Thus far, it has been shown that therapist support is positively associated with greater efficacy and a lower dropout rate from Internet-based interventions (e.g., Johansson & Andersson, 2012; Richards & Richardson, 2012).

Another aspect that would be interesting to analyze in the future is the inclusion of other psychotherapeutic components aimed at NA regulation (e.g., CBT) along with the IPPA, as in other studies (e.g., Díaz et al., 2017). This would allow us to know whether IPPA would be more efficacious for depressive symptomatology and other variables related to positive functioning.

Further studies could include tailored interventions targeted at the characteristics, needs, and preferences of patients with depression and possible comorbid disorders (Batterham, Calear, Farrer, McCallum, & Cheng, 2018). In this way, health professionals (both GPs and psychologists) would more efficaciously treat depression (Johansson et al., 2012).

In addition, hybrid designs are needed to progress in clinical efficacy (to provide evidence-based treatments) and knowledge about implementation (taking into account processes such as planning, educating, financing, restructuring, managing quality, and

policy context) to improve their translation into routine healthcare for the treatment of depression (Powell et al., 2012).

So far, most Internet evidence-based treatments for depression have been delivered through computers. Future studies would also have to take into account other innovative technologies (e.g., smartphone, serious games, avatars and virtual reality) to improve access to these treatments and even their effects (Cuijpers, Kleiboer, Karyotaki & Riper, 2017). A recent meta-analysis shows that smartphone devices are a promising self-management tool for depression (Firth et al., 2017). More studies are needed on the application of these technologies in a PC setting.

9. Conclusions

This is the first study in Spain to analyze the efficacy and cost-effectiveness of a low-intensity Internet-based intervention focused on the transdiagnostic perspective and positive psychology combined with ITAU, and compared to the only-ITAU for the treatment of depression in a PC setting. Moreover, this work provides data on the effect of both interventions over time in relation to the changes achieved after the treatment (6 and 12-month follow-up).

The main findings regarding the objectives of this dissertation are presented in the following points:

- The inclusion of an Internet-based intervention did not substantially improve depression outcomes compared to the only-ITAU. However, our results support the use of low-intensity Internet based-interventions to promote faster improvements in depression along with the ITAU. Its implementation in PC centers would help both the patient (who often does not receive adequate treatment or is on a waiting list) and

the GP (who does not have enough time in consultation to offer adequate treatment) in reducing the gap between the treatment demand and supply.

- Our study did not support the idea that a low-intensity Internet-based intervention along with ITAU was more cost-effective than only-ITAU. Both treatments were equally cost-effective in terms of the quality of the performance of usual or daily life tasks.
- Regarding participants' opinions of the treatment received, the ITAU+IPPA was better valued than the only-ITAU from pre-treatment to post-treatment. This suggests that technologies could be an attractive tool for the treatment of depression in health care.
- The PA was not a mediator variable for the relationship between the condition and the depression severity.
- Some variables of health-related quality of life (physical functioning, role-emotional, social functioning) and mindfulness (observing and describing) were moderator variables associated with a better prognosis in depression severity after the ITAU+IPPA treatment.

It is important to continue to research the role of guided low-intensity Internet-based interventions for the treatment of depression and in the context of PC, taking into account the transdiagnostic perspective, tailored programs, implementation strategies, and other technological devices such as smartphones.

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