Ciclo di Seminari
AIDIPSaM
Giugno-Dicembre 2025

NUOVE FRONTIERE PER GLI INTERVENTI PSICOEDUCATIVI

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Webinar AIDIPSaM

Giugno – Dicembre 2025

Nuove Frontiere per gli Interventi psicoeducativi

- Aspetti Nutrizionali della Persona con Disturbo Mentale grave, a cura della Prof.ssa Rita Roncone
- Cambiamento Climatico, Inquinamento atmosferico e salute mentale, a cura del Prof. Alfonso Tortorella
- Fenomeni migratori, a cura del Prof Massimo Clerici
- Interventi Psicoedecativi e Relazione Terapeutica, a cura del Prof Massimo Biondi
- Minority Stress a LGBQTi+, a cura dei Prof.i Gian Maria Galeazzi e Antonio Ventriglio
- Ritiro Sociale, a cura dei Prof Laura Orsolini e Umberto Volpe
- Shared Decision Making, a cura del Prof Mario Luciamo

Cosa è la Psicoeducativa.

A cura del Consiglio Direttivo AIDIPSaM-APS

1. PSICOEDUCAZIONE=INFORMAZIONE?

L'approccio psicoeducativo viene proposto agli inizi degli anni '70 come "insegnamento di abilità e modalità comportamentali personali e interpersonali che un individuo può applicare per risolvere problemi di natura psicologica e per migliorare la propria soddisfazione esistenziale" (Guerney et al. 1971). Nasce come modello alternativo al tradizionale approccio psicoterapico, proponendosi come una modalità pratica di insegnamento di abilità per le persone con disturbi mentali gravi, che non richiedeva lunghi tempi di formazione e che potesse essere somministrato da diverse figure professionali, con background eterogenei. Il modello psicoeducativo si è molto evoluto negli anni '80 grazie ai contributi delle scuole anglosassoni e americane attraverso il coinvolgimento delle famiglie, anche se con modalità diverse, e dei pazienti ospedalizzati con attività di gruppo. I primi studi di efficacy ed effectiveness sono comparsi infatti proprio a partire dagli anni '80 e hanno messo in evidenza i benefici terapeutici di questi interventi in termini di miglioramento dell'aderenza ai trattamenti farmacologici, riduzione delle ricadute e delle ospedalizzazioni, miglioramento del clima familiare, riduzione del carico dei *caregivers* e miglioramento della qualità di vita dell'intero nucleo familiare.

Nel corso del tempo, sono state fornite definizioni di psicoeducazione che ne racchiudessero tutti gli elementi fondamentali. La definizione che proponiamo è la seguente "***un approccio strutturato che integra aspetti delle teorie cognitivo-comportamentali con quelli educazionali e motivazionali con lo scopo di migliorare le abilità personali, sociali e di fronteggiamento dei problemi***".

Gli interventi psicoeducativi sin dalle origini non hanno preso in considerazione solo la componente informativa per aumentare la conoscenza della persona circa il disturbo di cui soffre. Essi hanno anche considerato la comprensione e gestione dello stress, l'identificazione dei segni precoci di crisi, il miglioramento delle abilità di comunicazione, il funzionamento personale e sociale, la comprensione delle emozioni; in tempi recenti in alcuni programmi anche la comprensione delle emozioni altrui.

2. CHE COSA È LA PSICOEDUCAZIONE?

La psicoeducazione, come da sua etimologia, dal latino educĕre «trarre fuori, allevare», si basa sullo scambio informativo, interattivo e partecipato, tra la persona che soffre del disturbo con le sue conoscenze e il suo vissuto, e il professionista esperto di quel disturbo. Non avviene quindi con modalità didattica "professorale" ex-cattedra. È importante considerare dapprima i livelli di conoscenza che la persona ha del disturbo di cui soffre, le risorse personali, le relative compromissioni, così come gli aspetti emotivi, cognitivi e psicopatologici. Il fondamento è senza dubbio l'insegnamento che deve svolgersi come se fosse un auto-apprendimento. Nel sottolineare ancora l'origine etimologica del termine, di educĕre, di «trarre fuori, allevare», diventa implicito il significato di promozione; di promuovere una migliore gestione degli aspetti problematici del disturbo e di valorizzare le risorse personali e ambientali.

Un'altra caratteristica di tale approccio è la flessibilità, pur rimanendo un intervento strutturato. Infatti, questi interventi possono essere svolti in diversi ambiti assistenziali quali: ambulatori territoriali e ospedalieri, domicilio, centri diurni, strutture residenziali (comunità protette a bassa, media ed alta assistenza), reparti ospedalieri.

2.1 Figure professionali coinvolte

Gli interventi possono essere condotti da diverse figure professionali che ruotano attorno ai servizi e centri per la salute mentale: psichiatri, psicologi, tecnici della riabilitazione psichiatrica, educatori, infermieri. Il comune denominatore essenziale per ciascun conduttore di un percorso psicoeducativo è una adeguata formazione relativa all'intervento specifico che si intende proporre. È preferibile che le persone abbiano comunque una specifica pregressa formazione specialistica nel campo della psichiatria e che ricevano un approfondito training di psicoeducativa poiché le conoscenze in questo campo sono in continua evoluzione.

2.2 I luoghi degli interventi

Gli interventi infatti si prestano ad essere adattati a diversi setting, in base alle esigenze cliniche e di contesto della persona con disturbo mentale. Il **setting individuale** è indirizzato principalmente alla persona con disturbo e prevede la sua partecipazione insieme a quella del professionista che conduce l'intervento. In alcuni casi potrebbe verificarsi anche la necessità di svolgere incontri psicoeducativi individuali rivolti a un familiare (magari l'unico di riferimento). Il **setting monofamiliare** invece è rivolto all'intero nucleo familiare: generalmente prevede la presenza della persona con disturbo (almeno nella maggior parte degli incontri) e di tutti i membri disponibili, in particolare i principali *caregivers*, insieme a uno o due professionisti conduttori. Infine, è presente il **setting di gruppo**, che riveste sicuramente un ruolo chiave tra gli interventi psicoeducativi, sia per le sue caratteristiche di ottimizzazione del rapporto costi-benefici, sia per il valore aggiunto dei fattori terapeutici intrinseci al gruppo. Tra questi l'elemento di condivisione nel gruppo che favorisce la percezione di supporto e 'normalizzazione', alleviando lo stigma e il senso di solitudine. Inoltre il gruppo diventa catalizzatore di alcuni processi di elaborazione, comprensione e accettazione di diversi aspetti della malattia, attraverso il rispecchiamento con gli altri membri. La condivisione dei diversi vissuti, infatti, elicita somiglianze o differenze, che possono rimandare alla propria storia. Questo costituisce, nella stragrande maggioranza dei casi, un canale preferenziale e di facilitazione di accesso dei contenuti condivisi all'interno del gruppo, sia da un punto di vista cognitivo sia emotivo. Il setting di gruppo (che può prevedere un numero variabile di partecipanti, solitamente tra i 6 e i 12) può essere rivolto ai soli pazienti, ai soli familiari, o a nuclei familiari (in questo ultimo caso si parla di interventi 'multifamiliari'). Nei protocolli d'intervento di gruppo è sempre consigliata la presenza di due conduttori, i quali ricoprono 2 ruoli ben distinti (che possono essere fissi o interscambiabili): il conduttore principale ha il compito di presentare i contenuti della seduta, mentre il co-conduttore quello di monitorare il clima emotivo del gruppo e di rispondere ad eventuali esigenze dei singoli partecipanti.

2.3 La diffusione nel nostro paese e manuali disponibili in italiano

Considerato che la psicoeducativa è un approccio strutturato è importante l'uso del manuale specifico per il tipo di intervento che si effettua. Oggi vi è ampia disponibilità di manuali.

A partire dagli anni '80 gli interventi psicoeducativi si sono diffusi in tutto il mondo, anche in Italia, soprattutto grazie al lavoro di Ian Falloon, ideatore dell'approccio psicoeducativo familiare per pazienti con schizofrenia. Nonostante l'opera di Falloon e i numerosi corsi di formazione condotti con gli operatori della salute mentale, in numerosi centri di salute mentale, la disponibilità di questi interventi in condizioni di routine non è stata adeguata ai bisogni e a quanto previsto da Raccomandazioni e Linee-Guida. "**L'Intervento psicoeducativo integrato in psichiatria**" di I. Falloon, seppur datato e quindi da usare con qualche adattamento, è un concentrato di elementi essenziali e sempre attuali per trattare con le famiglie. Tale intervento fu integrato alle origini dal manuale illustrato con vignette "**Che cos'è la schizofrenia**" di Casacchia e Roncone per facilitare l'apprendimento delle conoscenze del disturbo. L'intervento di Falloon è stato recentemente adattato ai pazienti con depressione maggiore e disturbo bipolare dal gruppo guidato dal Prof. Fiorillo, dell'Università degli Studi della Campania "Luigi Vanvitelli"; il manuale originario di Ian Falloon è stato aggiornato ad un contesto familiare mutato e ampliato di numerose sezioni, dallo stesso gruppo di ricerca. Un' evoluzione dell'approccio per le famiglie è stato quello multifamiliare promosso da Roncone, Casacchia e Falloon che poi ha visto la proposta di un manuale strutturato "**Intervento Psicoeducativo Multifamilare basato sul Problem Solving**" di Veltro et al., che incorpora le strategie di Problem Solving sulla base del lavoro svolto sia dal gruppo di Falloon, Roncone, Casacchia e Morosini, sia di quello di Barbieri, La Monaca e Boggian con il manuale **"Problem Solving nella riabilitazione Psichiatrica"**.

3. LE PROMETTENTI INNOVAZIONI IN AMBITO PSICOEDUCATIVO

Più recentemente tra gli interventi psicoeducativi vi è il **programma INTE.G.R.O.** di Veltro e al. (Intervento psicoeducativo di gruppo per il raggiungimento degli obiettivi) che prevede un percorso psicoeducativo strutturato che contiene principi di salutogenesi per sostenere il processo di recovery delle persone con disturbo mentale. Ancora, è stato messo a punto un **Intervento cognitivo-comportamentale di gruppo nel Servizio di Diagnosi e Cura**, a cura di Vendittelli, Veltro, Oricchio, Cappuccini, Simonato e Roncone et al. che guida gli operatori di reparto ad effettuare una psicoeducazione "tagliata su misura" per i pazienti in regime di ricovero e quindi in stato di acuzia.

Di origine anglosassone ma disponibile in italiano si ricorda l'"**Illness Management and Recovery**" (E-IMR) di Mueser e Gingerich, programma corposo che incorpora al suo interno in modo trasversale strategie psicoeducative per fare in modo che l'utente conosca e gestisca il proprio disturbo mentale e le conseguenze che questo comporta, per dedicare più tempo ai propri progetti di vita. Ci sono poi manuali specifici per alcune tipologie di disturbi, come il "**Manuale di psicoeducazione per il disturbo bipolare**" di Colom e Vieta, l'adattamento di Luciano et al dell'intervento di Falloon per lo stesso disturbo, il "**Manuale di psicoeducazione per i disturbi dell'alimentazione**" a cura di Salvo, il manuale per "**L'intervento psicoeducativo telefonico per la gestione delle problematiche stress-correlate**" di Veltro et al., il manuale "**Diamanti Grezzi: manuale psicoeducativo del trattamento del disturbo di personalità Borderline. Programma strutturato per i professionisti**" a cura di Mosquera. Un altro approccio che viene proposto come psicoeducativo è quello di Gunderson con il "**Good Psychiatric Management nel trattamento del Disturbo Borderline**" tradotto da Maffei e Smeraldi. Recentemente è stato anche pubblicato il manuale "**Psicoeducazione di gruppo per il paziente grave**" di Popolo e Poliseno.

4. AMBITI DI APPLICAZIONE

4.1 Disturbi psichici

Attualmente, come abbiamo visto l'approccio psicoeducativo viene utilizzato per il trattamento integrato di numerose condizioni patologiche.

Gli approcci psicoeducativi sono utilizzati anche per la promozione della salute fisica dei pazienti con disturbi mentali, attraverso il miglioramento degli stili di vita, inclusa la promozione di un'alimentazione sana, di attività fisica regolare, la riduzione della sedentarietà e dell'abitudine tabagica e dell'uso di alcool e droghe, che nei pazienti con disturbi mentali gravi è significativamente maggiore, rispetto alla popolazione generale.

4.2 Promozione della salute mentale

Un altro campo di applicazione è quello della Promozione della Salute Mentale. In Italia vi è ampia e documentata esperienza con manuali specifici tra i quali quello della "**Promozione del benessere psicologico e dell'intelligenza emotiva a scuola: un manuale per definire obiettivi e risolvere problemi**" di Gigantesco e Morosini, che l'Associazione fornisce gratuitamente ai soci.

5. BARRIERE NELLA DIFFUSIONE

L'approccio psicoeducativo ha dimostrato anche in Italia di essere particolarmente efficace nella maggior parte dei contesti in cui è stato utilizzato. Esiste ampia letteratura di cui Aidipsam-Aps si impegna a favorire la diffusione.

Diversi fattori, però, hanno limitato la diffusione di questi interventi nonostante i numerosi sforzi effettuati per rendere questo approccio, evidence-based, accessibile alla maggior parte dei pazienti con disturbi mentali. Tra questi vanno elencati: 1) problemi di natura organizzativa dei servizi di salute mentale italiani; 2) presenza di resistenze da parte dei responsabili dei servizi che valutano particolarmente gravoso in termini di tempo l'applicazione di questi interventi la cui applicazione però è efficiente nel medio-lungo periodo; 3)"resistenza culturale" verso i principi di linee-guida e raccomandazioni nazionali e internazionali, che affonda le radici nel concetto per cui la cura dei disturbi mentali si esaurisce con la sola prescrizione di terapie farmacologiche; 3) resistenza dei professionisti che tendono a sottovalutare gli effetti positivi a breve e a lungo termine di questi interventi; 3) riduzione dei budget dedicati alla formazione degli operatori, che quindi non hanno molte possibilità di partecipare a corsi di formazione adeguati; 4) elevato turnover degli operatori di salute mentale, che quindi hanno poco tempo per conoscere il contesto di riferimento dei pazienti e dei loro familiari e di strutturare gli interventi; 5) mancanza di figure professionali ad hoc, come i tecnici della riabilitazione psichiatrica, che potrebbero dedicarsi alla conduzione di questi interventi in condizioni di routine.

6. L'IMPEGNO DELLA NOSTRA ASSOCIAZIONE

AIDIPSaM-APS si impegna anche per contribuire al superamento di questi ostacoli affinché in Italia soprattutto le persone con disturbi mentali e i familiari nei contesti di cura, oltre a persone della popolazione generale nell'ottica di promozione della salute (nonché prevenzione di stati di disagio psichico) come gli studenti a scuola, possano beneficiare di questi interventi di consolidata efficacia ed efficienza. L'impegno di AIDIPSaM-APS è reso esplicito nello statuto costitutivo dell'Associazione.

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Twelve-month outcomes in overweight/obese users with mental disorders following a multi-element treatment including diet, physical activity, and positive thinking: The real-world "An Apple a Day" controlled trial

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The present study aimed to evaluate the 12-month effectiveness of a real-world weight loss transdiagnostic intervention in overweight/obese participants affected by mental disorders under psychopharmacological treatment. We conducted a real-world, controlled, pragmatic outpatient trial. We allocated 58 overweight/obese adults under psychopharmacological treatment from a mental health outpatient unit and 48 overweight/obese adults from a cardiovascular prevention outpatient unit, and assigned them to an intervention or treatment usual as condition (TAU) enriched by life-style advice. Participants in both intervention groups took part in a diet programme (the modified OMNIHeart dietary protocol) and monitoring of regular aerobic activity. A brief group programme ("An Apple a Day" Metacognitive Training, Apple-MCT) was added in the intervention group of participants affected by mental disorders. The primary outcome was weight loss. Secondary outcomes included anthropometric, clinical, and metabolic variables. Psychopathology and health-related quality of life were also evaluated in the psychiatric sample. At 12 months, both intervention groups showed a more marked mean decrease in weight (6.7 kg, SD: 3.57) than the TAU group (0.32 kg, SD: 1.96), and a statistically significant improvement in metabolic variables compared with the control groups. Furthermore, the participants affected by mental disorders included in the intervention group reported improved health-related quality of life. Our findings suggest the need to implement integrated interventions based on a dietary protocol, physical activity, and modification of cognitive style in overweight/obese users with mental disorders.

KEYWORDS

diet protocol, physical activity, metacognitive group intervention, cardiovascular risk, mental disorders, obesity, metabolic syndrome, psychopharmacological treatment

Introduction

Individuals with severe mental disorders (SMDs) die, on average, 15–20 years earlier than the general population. This pre-mature mortality is mainly due to metabolic and cardiovascular diseases that occur more frequently, are not prevented, and are inadequately identified in this population (1, 2).

Cardiovascular risk factors in individuals with several SMDs—such as schizophrenia spectrum disorder, bipolar disorder, and major depression—include not only common factors, such as "unhealthy" dietary patterns, smoking habits, low levels of physical activity, obesity, hypertension, diabetes, and dyslipidaemia, but also drug-related factors, therapeutic inertia, and poor adherence to prescribed medication (3–7).

The assumption of consuming psychotropic drugs such as antipsychotics, antidepressants, and mood stabilizers seems to be associated with metabolic and clinical disorders, including weight gain, diabetes, dyslipidaemia, and hypertension (4, 8–10). There is a well-documented relationship between clinical/metabolic complications and second-generation antipsychotics, including olanzapine and clozapine, since they are used in the early stages of mental illness (11–19).

The problem of weight gain induced by psychotropic drugs is underestimated in terms of its consequences (8). It can compromise long-term treatment adherence (20) and increase relapse risk (21). Because of the associated metabolic complications, weight gain can negatively impact one's overall quality of life (22, 23) as well as social stigmas associated with mental disorders (24), life expectancy (25), self-esteem, and poorer psychosocial adaptation (26).

Patients in the early phases of schizophrenia and bipolar disorder are at extremely high risk for developing cardiovascular comorbidity; moreover, their metabolic profile worsens quickly (27, 28). Individuals with schizoaffective disorder are more likely to suffer from metabolic syndrome comorbidity than individuals with schizophrenia or other non-affective psychoses (29).

Not only do those affected by psychotic disorders display metabolic problems, but persons affected by depression (compared to non-depressed people) have a significantly greater risk for developing obesity, especially adolescent women (30), in light of the comorbidity of depression with metabolic ailments (31). The link between depression and cardiovascular disease is complex. Major depressive disorder and self-reported depressive symptoms are associated with elevated visceral adipose tissue and subcutaneous adipose tissue (32).

A very recent review (33) investigating the relationship among adipose tissue compartments, inflammation, and cardiovascular risk in depressive disorder emphasized the significant association of depressive symptoms with severe body composition changes starting in early adulthood. Stapel et al. (33) suggested that this group of patients could be predisposed to common physical disorders, such as diabetes mellitus type 2 and cardiovascular diseases. Increased activity of the HPA axis, physical inactivity, poor nourishment, poor adherence to treatment recommendations, and low-grade inflammation might directly or indirectly worsen this vicious cycle, resulting in higher morbidity and mortality rates due to cardiometabolic disorders (33). The same anxiety disorders were observed in frequent co-occurrence with various medical illnesses, with percentages of up to 30% in participants with cardiovascular diseases, 47.0% in those with diabetes mellitus, and vice versa. High rates of medical conditions were reported in samples of participants with anxiety disorders, and greater severity of both anxiety disorders and medical diseases are observed when they coexist (34).

Compared to the general population, individuals suffering from severe psychiatric disorders, especially schizophrenia, tend to engage in a low level of physical activity (35–37), are more inclined to smoke, and exhibit a greater preference for a high-calorie diet (38). This unhealthy lifestyle and non-adherence to treatment over time could be ascribed to a low level of self-regulatory behaviors (39), cognitive flexibility (40, 41), and low levels of self-esteem (42). In recent years, both national and international groups have developed cost-effective screening and monitoring guidelines (17, 43–46), although they are not being implemented in the clinical care of users (47, 48). Based on a review of the evidence that users with serious mental illness (SMI) are at increased risk of CVD and diabetes, the European Psychiatric Association (EPA), supported by the European Association for the Study of Diabetes (EASD) and the European Society of Cardiology (ESC), published a statement regarding the guidelines of ESC and EASD Fourth Joint Task Force of the European Society of Cardiology and Other Societies on

Cardiovascular Disease Prevention in Clinical Practice (49). The initiative was aimed at improving the care of users suffering from SMI, initiating cooperation and shared care between different health care professionals to raise the awareness of psychiatrists and primary care physicians who care for patients with SMI for screening and treatment of cardiovascular risk factors and diabetes (50). More recently, a meta-analysis of physical activity interventions and their impact on health outcomes for people with SMI, including schizophrenia-spectrum disorders, major depressive disorder (MDD) and bipolar disorder (51), showed that PA can improve cardiorespiratory fitness, quality of life and depressive symptoms, with effects on depressive symptoms comparable to those of antidepressants and psychotherapy. For schizophrenia-spectrum disorders, much evidence indicates that aerobic physical activity can reduce psychiatric symptoms and improve cognition in various subdomains and cardiorespiratory fitness. In contrast, evidence for the impact on anthropometric measures was inconsistent. Lastly, there was a lack of studies investigating physical activity in bipolar disorder, precluding any definitive recommendations.

Among effective diet programs in clinical populations not affected by psychiatric disorders, some studies used a redistribution of dietary macroelements, from cholesterol and saturated fats to carbohydrates, at a low glycaemic index, based on results obtained from the Optimal Macronutrient Intake Trial, to prevent heart disease (OMNIHeart) (52). Moreover, diet and physical activity modification protocols are widely applied in populations affected by hypertension (53, 54).

At present, most studies on weight management during psychopharmacological treatment include behavioral advice, diet programmes, physical exercise (55), and tailored educational programmes (56). Many studies have used pharmacological or cognitive-behavioral approaches (57) rooted in programmes to change lifestyles to reduce weight gain in individuals with mental illness (58–63).

Our primary aim was to evaluate the effectiveness of a dietary protocol and regular aerobic activity on weight, laboratory, and clinical parameters in participants with and without mental disorders compared to an intervention based on correct lifestyle advice. Additionally, we aimed to evaluate the "add-on" results of a brief metacognitive group programme to enhance the intervention's effectiveness in the sample of overweight/obese users with mental disorders undergoing psychopharmacological treatment.

We hypothesized that (1) the dietary protocol and monitoring of regular aerobic activity would have beneficial effects in participants with and without mental disorders on weight, laboratory, and clinical parameters and would produce outcomes that are superior to advice to improve one's self-regulation of food intake and to engage in more physical activity; (2) integrating a brief, structured group metacognitive intervention could further improve the adhesion of participants affected by mental disorders to maintain metabolic and clinical improvements over time, thereby contributing to better mental health.

Materials and methods

Design

The design was a real-world, controlled, pragmatic trial comparing four parallel groups of consecutively allocated participants: those affected by mental disorders undergoing an intervention including a diet protocol, monitoring of regular aerobic activity, and the "An Apple a Day" group Metacognitive Training (Apple-MCT) (G1); participants affected by mental disorders, receiving TAU and advice on a better life-style and bimonthly clinical consultations (G2); participants affected by hypertensive disease undergoing an intervention including a diet protocol and monitoring of regular aerobic activity (G3); and participants affected by hypertensive disease receiving TAU and advice on a better life-style and bimonthly clinical consultations (G4) (Figure 1).

For the psychiatric sample, their assignment was adapted to users' preferences and logistic factors (home distance from the unit, work rotations, difficulty in reaching the unit *via* public transit, etc.). We considered the problems they expressed, mainly when they were offered inclusion in the group intervention and were estimated to attend group sessions.

The inclusion in the protocol did not involve additional fees for the participants.

We carried out the study in compliance with the ethical principles of the Declaration of Helsinki; it was approved by the Ethical Committee of the University of L'Aquila (approval date: 14 October 2014).

Participants and procedures

All participants were recruited over a 12-month period between January and December 2015 from the TRIP service (Psychosocial Rehabilitation Treatment, Early Interventions in Mental Health Unit) and from the Hypertension and Cardiovascular Prevention Outpatient Unit, both at the University of L'Aquila (Italy).

The participants (aged at least 18) were included according to the presence of at least two of the following:

1) body mass index (BMI) (kg/m^2) >26;
2) waist circumference (men >102 cm, women >88 cm);
3) hypertriglyceridaemia (≥ 150 mg/dl);
4) high-density lipoprotein cholesterol (HDLc) (men: <40 mg/dl, women: <50 mg/dl);
5) systolic/diastolic blood pressure levels ($\geq 130/85$ mmHg) or diagnosed hypertension;

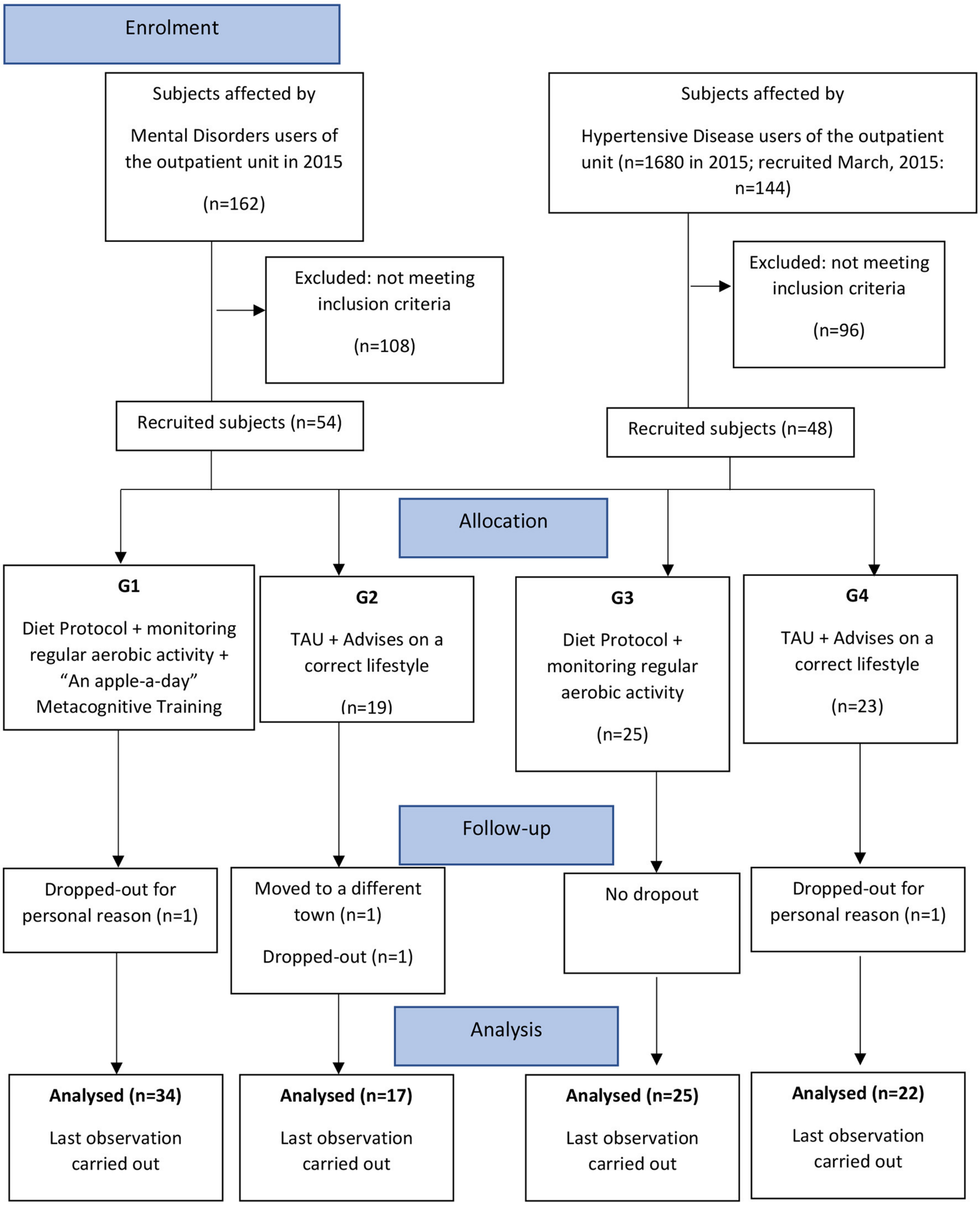

FIGURE 1
Flow of subjects through the 4-arm study.

6) fasting hyperglycaemia (≥100 mg/dl).

The presence of 3 or more of the abovementioned latter elements characterizes metabolic syndrome (MS) (64). MS represents a clustering of factors (hypertension, dyslipidaemia, abdominal obesity, impaired glucose tolerance) predicting an increased risk of cardiovascular disease and stroke (65).

The exclusion criteria for both groups were as follows:

1) severe neurological disorder or intellectual disability or developmental abnormalities or previous head injury;
2) diabetes mellitus, cancer or chronic ailments, prior cardiovascular disease, serum total cholesterol (TC) concentrations >310 mg/dl, triglyceride (TRG) concentrations >350 mg/dl, renal and/or liver insufficiency and any concomitant disease.

All participants included in the psychiatric sample (G1 and G2) received pharmacological treatment: selective serotonin reuptake inhibitor (SSRI) and noradrenergic and specific serotonergic antidepressants (NaSSAs); second-generation antipsychotics; anxiolytics; mood stabilizers; and first-generation antipsychotics (Table 1).

Waist circumference, height, weight, and blood pressure were measured by trained clinical staff during clinic visits, while fasting plasma lipid levels (triglycerides and low density lipoproteins) and fasting blood glucose levels were measured using regular hospital laboratories. Regarding the metabolic measures, serum low-density lipoprotein cholesterol (LDLc) levels were calculated according to the Friedewald formula (LDLc=TC-(HDL + TRG/5). All analyses were validated by the ISO 9001: 2000 EA: 38 CISQ n. 9122. ASL-IQNET n. IT-65188 quality system. Waist circumference was measured to the nearest 0.1 cm using a standard, inelastic tape maintained on a horizontal plane, with the participant standing with his/her weight distributed evenly on both feet. Height was measured to the nearest 0.1 cm using a wall-mounted stadiometer (without shoes). Weight was measured to the nearest 0.1 kg using standard electronic scales (light clothing without shoes). Blood pressure (BP) was monitored through an OMRON healthcare M2 device while the participant was comfortably seated. Two measurements for SBP/DBP were recorded, and an average was computed.

In this study, BP (i.e., systolic and diastolic BP, SBP/DBP levels) was reported only for participants included in G1 and G2 every 3 months. Those in G3 and G4 consumed anti-hypertensive drugs and were stabilized based on this clinical parameter.

All participants were evaluated at baseline and at the end of treatment (12 months) through a complete electrochemical check.

Dietary monitoring was conducted "face-to-face" by the clinical nutritionist (AnnalisaA.) through meetings every 15 days to check adherence to the dietary protocol and physical activity. The participants included in G1 and G3 were asked to record their weekly physical activity on a form ("My physical activity diary") about their weekly activity, recorded in hours.

Our study design would investigate psychopathological and psychosocial dimensions only in the group of psychiatric subjects. The cardiovascular prevention outpatient unit clinicians considered that the psychopathological assessment would have taken longer, which is not consistent with the time-sparing organizational goals of the operating outpatient unit. Moreover, they wanted to avoid "psychiatrizing" their users.

Measures for participants included in the psychiatric groups

Participants affected by mental disorders (G1 and G2) were also evaluated through assessments of psychopathology, health-related quality of life, and personal resources.

The severity of psychopathology was assessed using the Brief Psychiatric Rating Scale-24, BPRS (66) in its Italian version (67). Each symptom on the 24-item scale was rated from 1 to 7 (1 = absence of symptoms; 7 = very severe symptoms). The key score was composed of the total item score.

Health-related quality of life was assessed by the SF-36 Health Survey (68). It is a short-form health survey with only 36 questions. The SF-36 contains eight scaled scores, which are the weighted sums of the questions in their section. Each scale is directly transformed into a 0–100 scale, assuming that each question carries equal weight. The lower the score, the more severe the disability. The higher the score, the less severe the disability; i.e., a score of zero is equivalent to a maximum disability, and a score of 100 is equal to no disability. The eight sections are (1) vitality, (2) physical functioning, (3) bodily pain, (4) general health, (5) physical role functioning, (6) emotional role functioning, (7) social role functioning, and (8) mental health. In the present study, we only considered the "general health" domain.

Self-esteem was assessed by the Self-esteem Rating Scale (SERS) (69). The SERS consists of 40 items rated on a 7-point Likert scale, 20 scored positively and 20 scored negatively, with total scores ranging from −120 to +120. The SERS taps into multiple aspects of self-evaluation, such as overall self-worth, social competence, problem-solving ability, intellectual ability, self-competence, and worth compared to others. Positive scores are indicative of higher self-esteem. The instrument shows a high level of internal consistency ($\alpha = 0.97$) and good content and factorial validity.

Interventions

Diet protocol

The diet protocol consisted of the modified OMNI-heart programme diet, an individualized, moderately hypocaloric diet based on personal and daily caloric needs; it includes the following:

1) a reduction of 500 kcal/day;
2) daily carbohydrate energy intake of 45%, 50% from whole wheat, and 50% from fruits and vegetables, characterized

TABLE 1 The demographic and clinical characteristics of the 98 users participating in the study were divided into four groups.

	Participants affected by mental disorders ($n = 51$)		Participants affected by hypertensive disease ($n = 47$)	
	G1 ($n = 34$)	**G2 ($n = 1\ 7$)**	**G3 ($n = 25$)**	**G4 ($n = 22$)**
Gender, *n* (%)				
Male	11 (32.4)	3 (17.6)	10 (40)	10 (45.5)
Female	23 (67.6)	14 (82.4)	15 (60)	12 (54.5)
Age, mean (SD)	41.3 (13.4)	43.5 (15.8)	49.1 (12.0)	49.3 (13.8)
Education, years, mean (SD)	13.2 (3.4)	13.4 (3.8)	14.7 (3.1)	13.4 (2.6)
Marital status *n* (%)				
Unmarried/single	23 (67.6)	9 (52.9)	9 (36)	8 (36.5)
Married	10 (29.4)	6 (35.2)	14 (56)	12 (54.5)
Divorced	–	1 (5.9)	2 (8)	1 (4.5)
Widower	1 (3)	1 (5.9)	–	1 (4.5)
Work status, *n* (%)				
Employed	24 (70.6)	13 (76.4)	19 (76)	18 (81.8)
Unemployed	7 (20.6)	2 (11.8)	5 (20)	3 (13.7)
Student	3 (8.8)	2 (11.8)	2 (4.3)	1 (4.5)
BMI overweight range (25–<30)%	20 (58.8)	5 (29.4)	12 (48)	9 (40.9)
BMI obesity range ($\geq$30)%	14 (41.2)	12 (70.6)	13 (52)	13 (59.1)
Diagnosis (DSM-5) (%)				
Anxiety disorders	16 (47.1)	11 (64.7)		
Depressive disorder	10 (29.4)	4 (23.5)		
Psychotic non-affective disorder	6 (17.6)	2 (11.8)		
Bipolar disorder	2 (5.9)	–		
Length of illness, years, mean (SD)	4.9 (5.1)	3.1 (2.5)		
Medication (%)				
SSRI-NaSSAs antidepressants	23 (67.6)	14 (82.3)		
Second generation antipsychotics	5 (14.7)	2 (11.8)		
Anxiolytics	3 (8.8)	1 (5.9)		
Mood stabilizers	2 (5.9)	–		
First-generation antipsychotics	1 (3)			
Polidrug therapy (%)	6 (17.6)			

by a low glycaemic index with a predominance of fructose and sucrose compared to glucose;

3) daily protein energy intake of 25%: 60% from a vegetable source (soy, seitan, beans) and 40% from an animal source (white meat, fish, cheese, milk, and eggs);
4) daily fat energy intake of 30%: 10% Kcal saturated (70), 6% Kcal polyunsaturated fatty acids (omega 3–6), 14% Kcal monounsaturated (extra virgin olive oil);
5) vegetable fiber $\geq$20 g/die;
6) sodium intake <100 mmol/day, corresponding to a daily intake of 2.4 g;
7) potassium intake >150 mmol/day, corresponding to a daily intake of at least 5 servings of raw fruits and vegetables.

In the present study, the clinical nutritionist (A.A.) applied slight modifications to the basic OMNIHeart dietary protocol, with a carbohydrate decrease and a moderate increase in monounsaturated fatty acids (45% carbohydrates, 25% proteins, and 30% fats in the modified OMNIHeart dietary group and 50% carbohydrates, 25% proteins, and 25% fats in the basic OMNIHeart dietary group). The rationale of this OMNIHeart diet modification was justified by the high rate consumption of carbohydrates in the form of pasta, bread, and sweets (honey and jellies) in the population of L'Aquila in the Abruzzo region. At the same time, there was a relatively low consumption of fats in the form of extra virgin olive oil, which is useful for preventing cardiovascular risk factors. In addition, the increase in monounsaturated fatty acids makes food more palatable to ensure high adherence to the diet programme.

Physical activity protocol

Current physical activity levels were assessed by asking the participants about their weekly activity levels as measured using the Metabolic Equivalent of Task (MET) (71). The intensity of physical activity recommended was three METs, equal to a moderate degree (walking) for 3 h per week at 700 METs in accordance with the indications of the World Health Organization (WHO). The MET is a physiological measure expressing the energy cost of physical activities. It is defined as the ratio of metabolic rate (and therefore the rate of energy consumption) during a specific physical activity to a reference metabolic rate, set by convention to 3.5 ml $O2$/kg/min or 1 kcal/kg/hour.

APPLE-MCT

Apple-MCT was a brief, positive, group health-based intervention, followed only by G1, including two modules from the metacognitive training portion (72), (73) using "drill and practice" tasks. The interventions were conducted by a clinical psychologist (L. G.) and a psychiatric rehabilitation technician (A. S.). According to the study protocol, each group was comprised of three to five participants. The Apple-MCT was introduced by a psychoeducational module, including crucial topics for mental and physical health such as sleep–wake cycle regulation, regular physical activity, the timing of meals and meal preparation, good management of comfort eating, and the identification of strengths, new hobbies, and interests, reflecting on what brings happiness. The Apple-MCT included four bimonthly sessions lasting 45–60 min and focused on two specific modules/kinds of content, each alternatively presented in two versions, including different exercises and tasks.

(1) Module 3 "Changing beliefs" with the target domain "bias against disconfirmatory evidence" aimed at reducing cognitive inflexibility and the tendency toward overconfidence. In Module 3 (versions A and B), it is explained to the user that it is important to withstand the normal tendency to stick to first impressions, as this response bias can lead to faulty decisions. It is therefore desirable to maintain an open mind. Some negative and dysfunctional beliefs represent severe obstacles to starting and adhering to a diet programme (i.e., "*I am a fickle person and I easily lose motivation,*" "*I do not have the time to stick to a diet and exercise,*" "*I'm destined to stay fat*").

(2) Module 8 Self-esteem and mood with the target domains "negative cognitive schemata" and "low self-esteem" (versions A and B) aimed at modifying dysfunctional thinking styles, which may contribute to the formation and maintenance of depression and low self-esteem; these are especially correlated with weight control and physical appearance, and lead to difficulty in changing one's eating habits, with an excessive focus on body image or body shape (i.e., "*I am fat and will never be successful in life,*" "*No one will ever love me because of my body and my problems,*" and "*It is all my fault because I neglected my health condition*").

The psychiatric and hypertension treatment as usual group

In the TAU groups, G2 and G4, the participants continued to receive the usual treatment, including regular outpatient assessments, pharmacological treatment, and managing the side effects of medication. Additionally, they were given non-structured information about weight gain and encouraged to limit their food intake and increase the degree to which they exercised.

Statistical analysis

Descriptive analyses were used to characterize our sample concerning sociodemographic and clinical details. Continuous variables are reported as means (standard deviations), and categorical variables are reported as frequencies (percentages). Baseline comparisons [chi-square, *t*-tests, and one-way analysis of variance (ANOVA)] were performed to assess differences between the psychiatric and medical samples and the four groups. Bonferroni *post-hoc* correction was calculated.

We developed general linear models for repeated measures analyses with a between-subjects factor (G1, G2, G3, G4) and a within-subjects factor (pre-treatment–T0 vs. post-treatment–T1) for physical and metabolic variables. For the variables not fitting the normal distribution, to test the intergroup differences for anthropometric and metabolic variables in the study arms, we used the Kruskal–Wallis test and then made paired comparisons with the *post-hoc* Bonferroni's correction test.

In the psychiatric sample, we employed a general linear model for repeated measures with a between-subjects factor (G1, G2) and a within-subjects factor (pre-treatment–T0 vs. post-treatment–T1) for psychopathological and health-related quality of life variables. Statistical analyses were performed using SPSS 27.0 (SPSS Inc., Chicago, IL, USA). All tests were two-tailed, and $P < 0.05$ was considered significant.

Results

We recruited a total of 102 people: 54 stabilized participants affected by anxiety disorders, mood, and psychotic disorders according to DSM-5 criteria (74), and 48 participants affected by hypertensive disease.

All participants signed informed written consent forms.

Table 1 describes the final analyzed sample's main demographic and clinical characteristics of 98 subjects.

In the entire sample, the mean age was 45.2 (SD: 13.9) (range: 18–75). The majority of the participants were women (65.3%). There were no statistically significant differences between the two groups (psychiatric and medical participants) concerning sociodemographic variables such as sex, education level, and employment status (Table 1). The medical participants in G3 and G4 were older than those in the psychiatric groups, G1 and G2 [49.23 (SD 12.8) vs. 42.10 (SD 14.10); *t*-test −2.613; $p = 0.010$], the latter showing a higher statistically significant proportion of singletons (62.7 vs. 36.2%; chi-square: 8–156; $p = 0.043$).

No statistically significant differences were found in the proportion of overweight/obese participants included in the four groups (chi-square: 4.357; d.f. 3; $p = 0.225$).

The majority of the participants included in the psychiatric sample were affected by anxiety and depressive disorders (80.4%). According to diagnosis and psychopathological severity, all participants affected by mental disorders were taking psychopharmacological treatments with differences in type and dosage. Regarding G1 and G2, there were no statistically significant differences for the diagnoses and psychopharmacological treatments (Table 1). The participants affected by hypertensive disease were administered hypertensive pharmacological therapies.

Anthropometric and metabolic variables

At baseline (T0), no statistically significant differences were found among the four groups concerning weight, BMI, and waist circumference.

After 12 months (T1), significant differences over time—but not among the four groups—were found in all measured physical and metabolic variables (Table 2). The significant effects of the interaction time × group ($p < 0.001$) for all the considered variables indicate the intervention's benefit over time, without highlighting differences in the four arms of the study.

Changes in anthropometric and metabolic variables at the 12-month follow-up (T1) compared to the time of entry into the study (T0) were analyzed.

At 12 months, both intervention groups showed a more marked mean decrease in weight at −6.7 kg (SD: 3.57) than the TAU groups at −0.32 kg (SD: 1.96) (Table 3).

A Kruskal–Wallis test and post hoc analysis provided strong evidence of differences between the mean ranks of the two groups (G1 and G3) compared to G2 and G4 at T1 concerning weight [H(3) = 59.811; $p = 0.00$], BMI [H(3) = 50.868; $p = 0.00$], and waist circumference [H(3) = 49.235; $p = 0.00$] reduction (Figures 2A–C). No differences in weight reduction, BMI, or waist circumference were noted between G1 and G3 or between G2 and G4. These results suggest that G1 and G3 exhibited a larger statistically significant improvement than G2 and G4 regarding anthropometric parameters, body weight, waist circumference, and BMI.

Figure 3 displays the percentages of participants meeting certain weight-loss thresholds at 12 months in the four groups, showing a significantly different proportion of subjects losing more weight (chi-square: 67.041; d.f. 6; $p = 0.000$). Briefly, the intervention groups G1 and G3 revealed a statistically significant difference in the proportion of participants who lost 5% (59.3%) or 10% (25.4%) of their baseline weight compared to participants included in G2 and G4 who lost 5% (7.7%) or 10% of their baseline weight (0%). Both control groups indicated that 92.3% of the participants recorded a <5% weight loss compared to the intervention groups (15.3%) (chi-square = 56.415; d.f. 2; $p = 0.000$).

A Kruskal–Wallis test and *post-hoc* analysis provided strong evidence of differences between the mean ranks of two groups (G1 and G3) compared to G2 and G4 at T1 concerning reduction of total cholesterol (mg/dl) [H(3) = 46.584; $p = 0.00$], LDLc (mg/dl) [H(3) = 55.415; $p = 0.00$], TRG (mg/dl) [H(3) = 46.954; $p = 0.00$], glucose (mg/dl) [H(3) = 50.198; $p = 0.00$] and an increase in HDLc (mg/dl) [H(3) = 54.172; $p = 0.00$; Figures 4A–E. No difference in such metabolic variables was observed between G1 and G3 or between G2 and G4. These results imply that G1 and G3 experienced a larger statistically significant improvement than G2 and G4 in terms of the metabolic variables.

Clinical measures

Blood pressure in the psychiatric sample

At baseline, T0, no significant differences were found among the psychiatric groups concerning SBP [G1 133.24 (SD 7.6) vs. G2 131.1 (9.1); *t*-test for paired samples: $t = 0.848$; $p = 0.400$] and DBP [G1 88.4 (SD 3.9) vs. G2 89.1 (4.4); *t*-test for paired samples: $t = -0.551$; $p = 0.584$].

After 12 months (T1), significant differences over time—but not between groups—were found for SBP (Figure 5A). At the end of the intervention, for DBP, a change over time with a significant *group for time interaction* ($F = 13.999$; $p = 0.001$; $\eta^2 = 0.221$) was found between the two groups ($F = 8.611$; $p = 0.005$; $\eta^2 = 0.149$), indicating a greater reduction in G1 compared to G2 (Figure 5B).

Life-Style

The main life-style behavior information (physical activity and smoking) upon entry is outlined in Table 4.

Regarding physical exercise, all participants practiced low physical activity (average of 2 h weekly < 3 MET). The majority of the participants (80.6%) did not engage in any physical activity, except the participants included in

TABLE 2 Anthropometric and metabolic variables upon entry into the study (T0) and at the 12-month follow-up (T1).

Characteristics	Participants affected by mental disorders ($n = 51$)				Participants affected by hypertensive disease ($n = 47$)				F (group × time interaction)	N_2p (estimated effect size)
	G1 ($n = 34$)		G2 ($n = 17$)		G3 ($n = 25$)		G4 ($n = 22$)			
	T0	T1	T0	T1	T0	T1	T0	T1		
Anthropometric variables, mean (SD)										
Weight, kg	81.3 (15.89)	74.2 (14.7)	85.7 (12.7)	85.0 (13.2)	85.30 (14.9)	79 (14.8)	84.9 (12.4)	84.9 (12.0)	Time: 122.281** Group: 1.651 Interaction: 35.016**	0.528
BMI, kg/m^2	30.7 (5.3)	28.0 (5)	32.4 (3.6)	31.8 (3.8)	31 (3.6)	28.7 (3.4)	30.9 (2.4)	30.9 (2.4)	Time: 81.606** Group: 2.045 Interaction: 20.923**	0.400
Waist circumference, cm	100.3 (10.7)	94.5 (9.3)	102 (7.3)	101.0 (8)	103 (6.1)	96.5 (6.3)	103.3 (8.6)	102.6 (9.6)	Time: 137.224** Group: 2.107 Interaction: 27.412**	0.467
Lipids, mean (SD)										
Total cholesterol, mg/dl	229.09 (35.0)	207.7 (27.2)	226.4 (29.3)	223.2 (33.6)	228.44 (23.4)	212 (21.2)	224.95 (23.6)	224.23 (24)	Time: 67.615** Group: 0.348 Interaction: 17.042**	0.352
LDLc, mg/dl	140.4 (26.4)	120.97 (17.9)	137.5 (32.6)	137.2 (32.4)	144.96 (22.2)	130.5 (17.4)	147.05 (25.5)	146.6 (25.08)	Time: 38.304** Group: 2.078 Interaction:13.129**	0.295
HDLc, mg/dl	43.12 (12.1)	47.03 (11.2)	44.8 (11.0)	44.7 (10.6)	44.7 (9.5)	47.8 (10.3)	40.1 (7.9)	39.3 (8.05)	Time: 32.666** Group: 1.827 Interaction: 20.083**	0.391
TRG, mg/dl	176.7 (71.5)	135.8 (46.5)	160.0 (68.1)	154.2 (68.1)	177.8 (65.4)	142.9 (35.0)	169.9 (35.3)	168.8 (34.8)	Time: 28.143** Group: 0.313 Interaction: 7.117**	0.185
Fasting glucose, mean (SD)										
GLU, mg/dl	97.6 (10)	87.09 (6.9)	93.3 (9)	92.8 (8.6)	97.2 (8.08)	89.5 (5.9)	96.3 (8.7)	96.0 (8.5)	Time: 69.701** Group: 1.114 Interaction: 23.637**	0.419

**$p = 0.01$.

TABLE 3 Mean differences (SD) in anthropometric and metabolic variable changes at the 12-month follow-up (T1) compared to entry into the study (T0).

Variables	Change G1 (T1–T0)	Change G2 (T1–T0)	Change G3 (T0–T1)	Change G4 (T0–T1)
Physical, mean (SD)				
Weight, kg	−7.06 (4.21)	−0.76 (2.27)	−6.24 (2.47)	0.022 (1.67)
BMI, kg/m^2	−2.65 (1.97)	−0.53 (1.43)	−2.27 (1.04)	0.059 (0.57)
Waist circumference, cm	−5.88 (3.19)	−1.00 (3.18)	−6.48 (2.46)	−0.63 (2.46)
Lipids, mean (SD)				
Total cholesterol, mg/dl	−21.32 (16.70)	−3.17 (12.51)	−16.44 (8.82)	−0.72 (3.89)
LDLc, mg/dl	−19.44 (21.06)	−0.35 (2.66)	−14.40 (8.85)	−0.40 (3.63)
HDLc, mg/dl	+3.91 (3.75)	−0.05 (2.46)	+3.12 (1.48)	−0.81 (0.79)
TRG, mg/dl	−40.82 (50.39)	−5.76 (14.45)	−34.88 (42.51)	−1.09 (5.15)
Fasting glucose, mean (SD)				
GLU, mg/dl	−10.58 (7.28)	−0.47 (2.62)	−7.64 (5.62)	−0.27 (2.86)

G1, who showed significantly higher activity (chi-square: 18.955; df 6; $p = 0.004$). The four groups did not exhibit statistically significant differences in the proportion of smokers compared to non-smokers (chi-square: 0.556; df 3; $p = 0.906$).

Regarding eating habits, no statistically significant differences were found among the four groups at the time of entry into the study. All participants reported irregular eating habits (low consumption of fruits, vegetables, and olive oil; high consumption of sugar, alcohol, and saturated fats).

At the end of the intervention, concerning physical activity, a significant change over time (group for time interaction $F = 26.901$; $p = 0.000$; $\eta^2 = 0.467$) was observed in the four groups (Figure 6).

At the end of the study, significant differences were found between G1 and G2 (95% CI: 0.52, 1.50; $p = 0.000$), G1 and G4 (95% CI: 0.43, 1.44; $p = 0.000$), G2 and G3 (95% CI: −1.5, −0.37; $p = 0.000$), and G3 and G4 (95% CI: 0.27, 1.35; $p = 0.001$), showing a statistically significant increase in physical activity for both G1 and G3 compared to G2 and G4 (Figure 6).

No statistically significant differences were observed in smoking habits at T1 compared to T0.

Concerning eating habits, diet improvements can be mainly inferred from weight changes at T1.

Psychopathology

At baseline, no statistically significant differences were found between the G1 and G2 groups for BPRS total scores. There was a psychopathological improvement at the end of treatment with a significant *group for time interaction* and a decrease in the BPRS total score for both groups (Table 5).

Health-related quality of life

At baseline, no significant differences were found between the G1 and G2 groups concerning health-related quality of life, evaluated through the SF-36. At the end of the intervention, health-related quality of life scores changed for the two groups with a significant *group for time interaction*. Participants in G1 experienced better improvements in their health-related quality of life SF-36 scores than participants included in G2 (Figure 7).

Self-esteem

At baseline, low values of self-esteem, evaluated by the SERS, were reported by all participants included in G1 and G2, without significant differences between the two groups. At the end of the intervention, participants in both groups revealed increased SERS scores regarding self-esteem levels without a significant change over time and between the two groups (Table 5).

Discussion

To the best of our knowledge, the present study is the first Italian real-world pragmatic controlled study to assess the effectiveness of a multi-component intervention based on a modified OMNI-heart programme diet and physical activity, including a group metacognitive programme, in a sample of overweight/obese users of a psychiatric outpatient service.

The study showed the same effectiveness for overweight/obese participants affected by hypertension

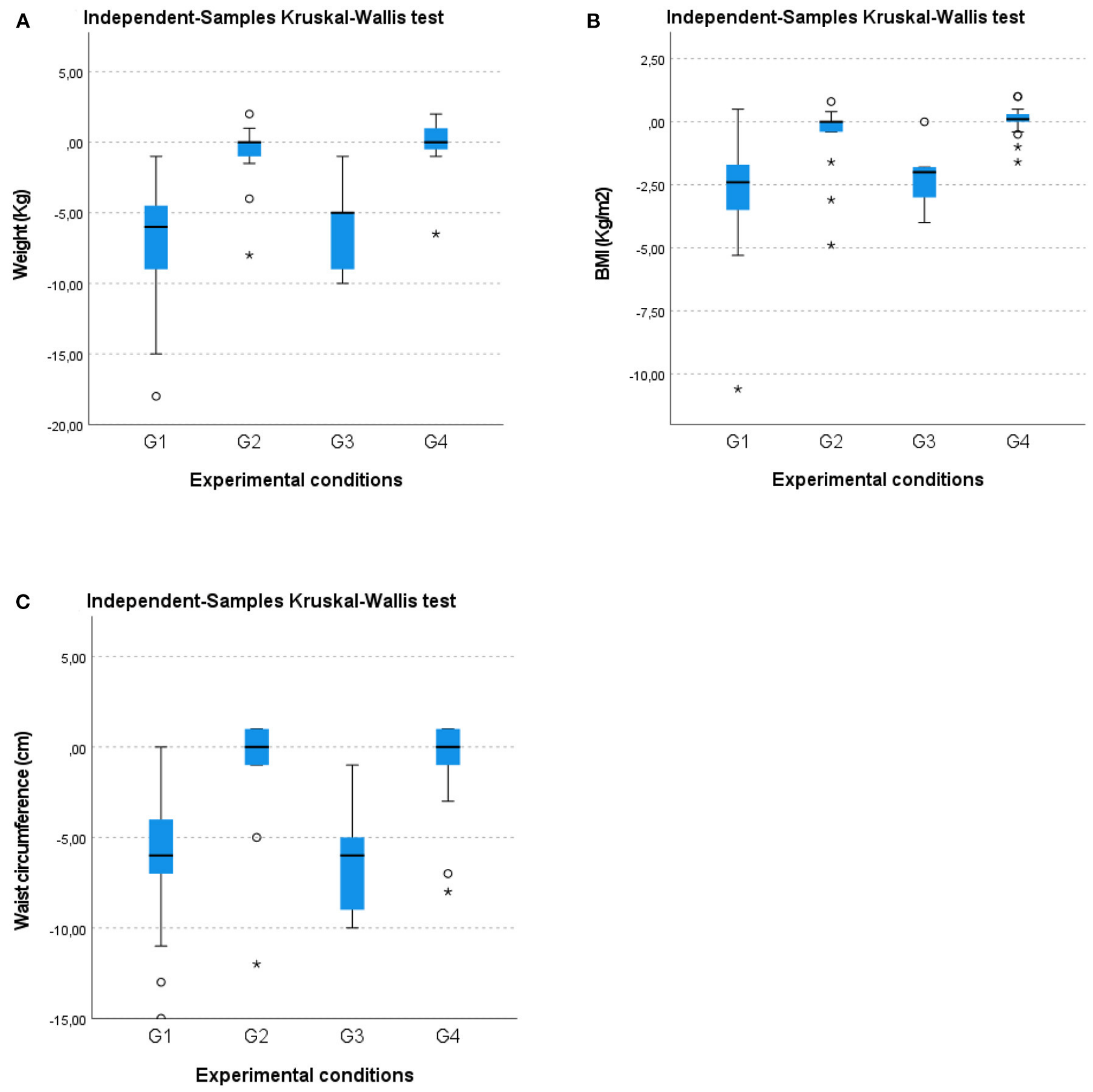

FIGURE 2
Box-whisker plots showing **(A)** weight (kg), **(B)** BMI (kg/m^2), and **(C)** waist circumference (cm) changes in the four groups at the 12-month follow-up (T1). O, Outliers; *, Extremes.

and overweight/obese participants affected by mental illness undergoing psychopharmacological treatment, with an added transdiagnostic brief metacognitive group programme, compared to an intervention limited to recommendations on how to live a better life-style. Moreover, at the 12-month follow-up, participants in this intervention group exhibited increased health-related quality of life compared to participants receiving only recommendations on a healthy life-style.

Our findings align with previous results about reducing body weight, modifying metabolic parameters, and life-style in both populations of psychiatric and hypertensive individuals using a multi-component intervention (53–55). Our overall cardiovascular risk reduction is comparable to prior multi-component studies in the psychiatric (61, 75) and general populations (76). The effects of the macro-element redistribution were investigated, which concerned almost all the other cardiovascular risk factors including TC, LDLc, HDLc, TRG, and fasting GLU; these are probably more reliable and robust, albeit with substantially quantitative differences. In particular, the impressive reduction of serum TRG levels in both intervention groups could be due to an array of independent factors such as the reduction of carbohydrate energy, concomitant increases in protein, and perhaps to a greater extent in unsaturated fats (77, 78). The observed

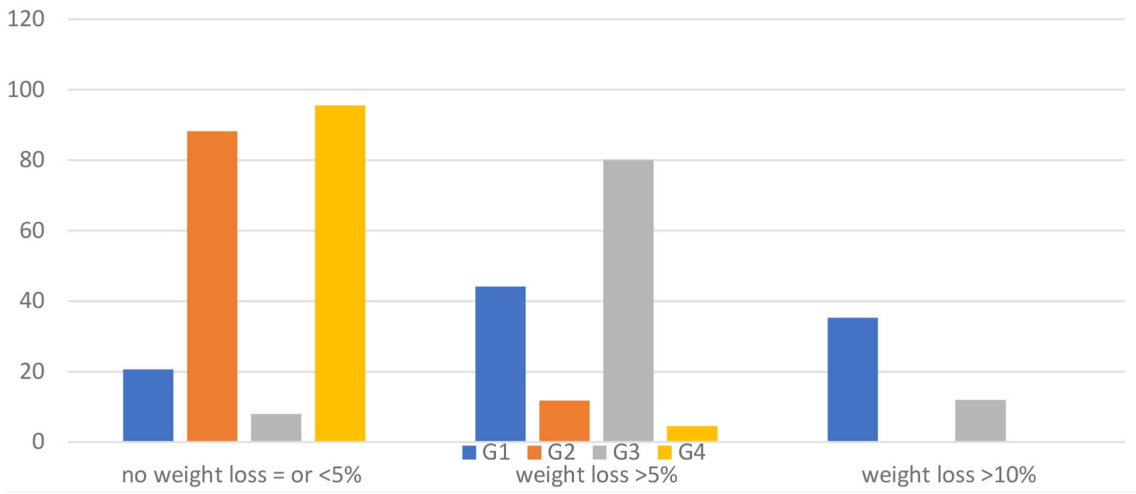

FIGURE 3
Percentage of weight change at the 12-month follow-up (T1) in the four groups compared to entry in the study (T0).

reduction in fasting glycaemia levels may also be due to the combination of low carbohydrates, high protein, and high-unsaturated fats in association with the moderately hypocaloric diet plus physical exercise.

Our results are encouraging and identify a new "target" of life-style interventions, not only for persons affected by severe mental illness, but also for a transdiagnostic group receiving mental health care, as proposed in a recent protocol for young people (79). Reduced weight loss in the range of 2% (80) to 4.2% (81) was reported in adults with severe mental illness, while we observed a mean weight loss of −8.6% for our psychiatric intervention group. Compared to studies including only psychotic populations, our findings seem to show a more marked net weight loss in the intervention group, presumably justified by a larger share of participants affected by anxiety and depressive disorders.

The length, the multi-component nature of our study, and the strict monitoring at 12 months could justify our results as better compared to the findings of a shorter 3 month intervention based only on an educational programme that demonstrated effectiveness only in increasing physical activity, but not for clinical and laboratory parameters (82). The critical aspect of the duration of life-style interventions of 12 months or more for treating overweight and obese people with serious mental illness was already stressed (83, 84), and their systematic reviews and meta-analyses reported that these interventions achieve more consistent outcomes.

Length does not seem to be the only critical variable in the effectiveness of life-style interventions. Our "face-to-face" intervention seems more promising than a multimodal web-based intervention administered by nurses to manage life-style changes in participants affected by severe mental illness (85). Using a web tool in the multi-modal, patient-centered life-style intervention did not seem to improve waist circumference and metabolic health after 12 months in a Dutch sample (85).

In a multi-component intervention, the "active ingredients" are difficult to identify. The added intervention for the psychiatric intervention group, including a group metacognitive programme, could have contributed to the intervention's effectiveness in the psychiatric group. We can hypothesize that the "An Apple a Day" metacognitive group intervention could have contributed to the outcomes, improving cognitive flexibility, a crucial variable specifically influencing self-regulatory behavior associated with healthier eating (86). Self-regulatory skills applied to controlled eating may be a far more critical factor than knowledge of appropriate nutrition principles in the behavioral treatment of obesity (87, 88). Additionally, the increased physical activity per week of the intervention group, favored by frequent checks leading to high user compliance (89), could have contributed to the outcomes. The health benefits of physical activity include the impact of exercise on cognitive functioning in general (90) and psychiatric populations (91).

At the 12-month follow-up, all participants affected by mental disorders improved their psychopathological conditions and self-esteem since they adhered to their pharmacological treatment and were compliant with the monthly consultations. Our intervention in the psychiatric group did not show specific symptomatologic benefits. Regarding psychopathology, our results are partially similar to those of a previous study on individuals with severe mental illness (81). The

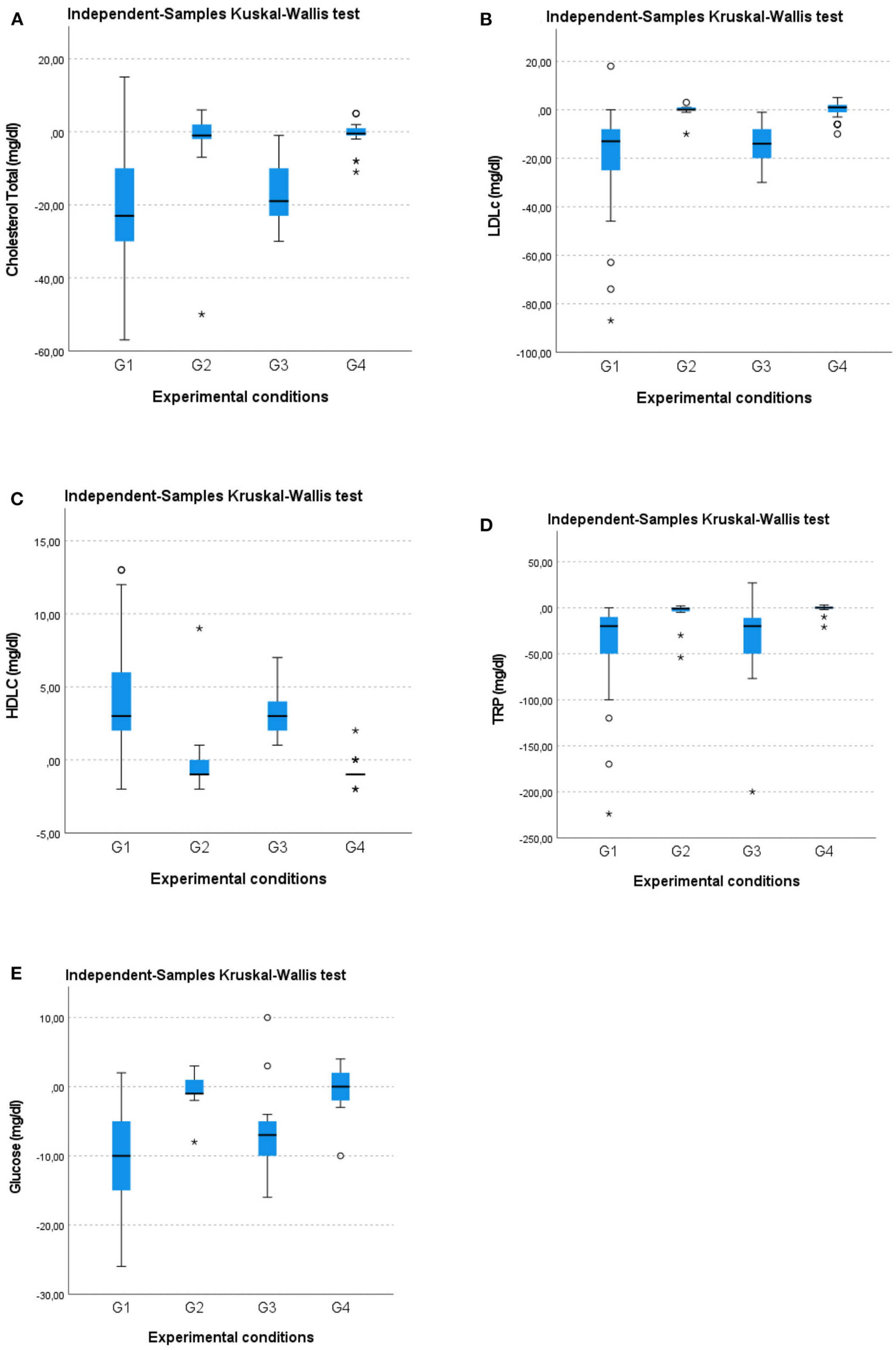

FIGURE 4
Box-whisker plots showing **(A)** total cholesterol (mg/dl), **(B)** low-density lipoprotein cholesterol, LDLc (mg/dl), **(C)** high-density lipoprotein cholesterol, HDLc (mg/dl), **(D)** triglycerides, TRG (mg/dl), and **(E)** glucose (mg/dl) changes in the four groups at the 12-month follow-up (T1). O, Outliers; *, Extremes.

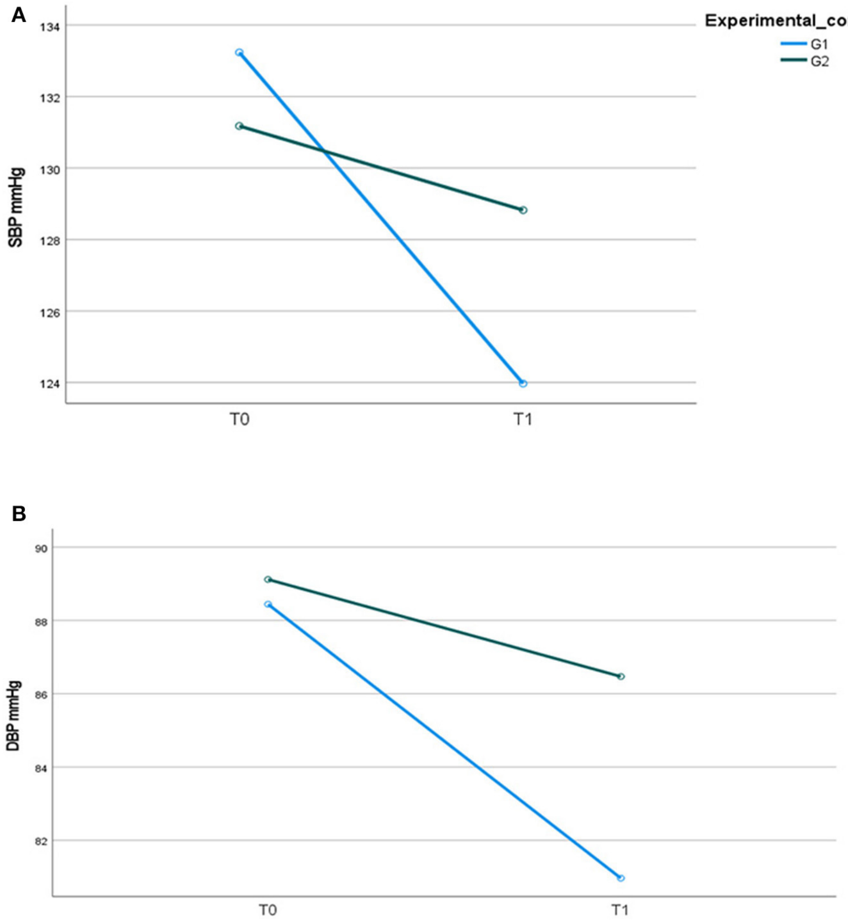

FIGURE 5
(A) Systolic blood pressure, SBP mmHg; **(B)** diastolic blood pressure, DBP mmHg, in the two psychiatric samples at T0 and T1.

TABLE 4 Physical activity and smoking habits of the participants included in the sample at the time of entry into the study.

	Participants affected by mental disorders ($n = 51$)		Participants affected by hypertensive disease ($n = 47$)	
Variables	**G1 ($n = 34$)**	**G2 ($n = 17$)**	**G3 ($n = 25$)**	**G4 ($n = 22$)**
Physical activity (hours/week) T0 (%)				
No physical activity	22 (64.7)	16 (94)	23 (92)	18 (81.8)
1 h	1 (2.9)	1 (6)	–	3 (13.6)
2 h	11 (32.4)	–	2 (8)	1 (4.6)
Smoking habits T0 (%)				
No smoking habits	18 (53)	8 (47)	11 (44)	10 (45.5)
1/2 cigarettes daily	2 (6)	2 (11.8)	–	3 (13.6)
5 cigarettes daily	6 (17.6)	1 (6)	3 (12)	2 (9.1)
10 cigarettes daily	3 (8.8)	3 (17.6)	8 (32)	3 (13.6)
20 cigarettes daily	5 (14.6)	3 (17.6)	3 (12)	4 (18.2)

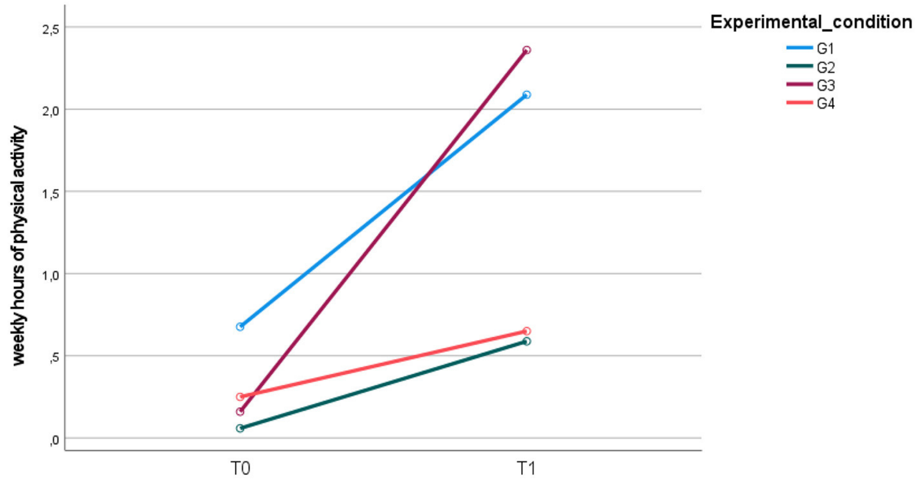

FIGURE 6
Mean weekly hours of physical activity upon entry into the study (T0) and at the 12-month follow-up (T1).

TABLE 5 Psychopathological, health-related quality of life, and personal resources in G1 and G2 at T0 and T1.

	Participants affected by mental disorders					
	G1 ($n = 34$)		G2 ($n = 17$)		***F*-value**	**η^2p**
	T0	**T1**	**T0**	**T1**		
Psychopathology, mean (SD)						
Brief psychiatric rating scale-24, BPRS, total score	59.9 (5.8)	51.5 (4.7)	57.5 (4.8)	51.8 (5.5)	Time 138.568** Group 0.508 Interaction 5.359*	0.099
Health-Related quality of Life, mean (SD)						
Health-related quality of life, SF-36 self-perception general health	46.2 (10.2)	59.8 (8.6)	44.7 (9.9)	48.2 (11.5)	Time 134.427** Group 5.237* Interaction 46.419**	0.486
Personal resources variable, mean (SD)						
Self-Esteem rating scale, SERS	25.0 (30.6)	41.3 (26.4)	17.3 (26.4)	35.2 (21.6)	Time 66.966** Group 0.134 Interaction 0.781	0.003

*$p \leq 0.05$.
**$p \leq 0.01$.

study revealed significant improvement in total activity, weight, abdominal girth, systolic blood pressure, and HDL cholesterol following the Multidisciplinary Life-style enhancing Treatment for Inpatients (MULTI) compared to treatment as usual (TAU). Despite such improvement, the participants included in MULTI did not display psychopathological progress after 18 months (81). In addition, similar results were reported by Kahl et al. (92) in a randomized pilot study: they showed the favorable additional effect of a 6-week structured, supervised exercise program on visceral, in particular epicardial and subcutaneous, adipose tissue in users with MDD undergoing cognitive behavioral therapy, with significant improvement of factors constituting the metabolic syndrome.

A reduction in symptom severity was reported in physical activity interventions (35, 51, 93), which is not in line with our findings. A systematic review and meta-analysis of the future risk of mental illness indicated that the incidence of mental disorders and suicidality was inversely related to fitness (94).

Our psychiatric intervention sample showed significantly improved health-related quality of life compared to the controls,

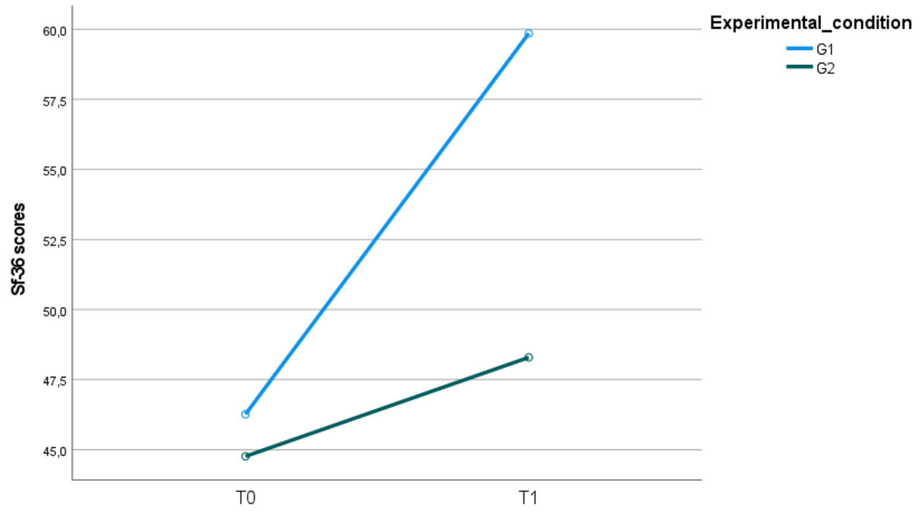

FIGURE 7
Health-related quality of life (SF-36) scores in the two psychiatric samples (G1, G2) at T0 and T1.

confirming recent findings (75, 88, 95). Improvements in body image and health-related quality of life seem closely linked to changes in weight (89).

However, our findings did not confirm increased psychological wellbeing in terms of self-esteem in our intervention group as an outcome frequently reported in life-style interventions (75, 96). Surprisingly, the participants in our psychiatric group did not display improved self-esteem, which was found to be inversely correlated with weight gain and good psychosocial adaptation (26).

The weight control issue is overwhelmingly salient in society and of great relevance and concern, also following the COVID-19 pandemic (97, 98). A general population study demonstrated that 22% of American adults gained weight during the COVID-19 pandemic. Lack of sleep, decreased physical activity, snacking after dinner, and eating in response to stress seemed to be behaviors tied to weight gain during self-quarantine (97). During the Italian COVID-19 lockdown, the perception of weight gain was observed in 48.6% of the general Italian population (99). More than 40% reported that they have gained weight to a slight extent, while 8.3% of the studied population said they have gained weight to a high extent. Prevention and management of obesity require consumption of a healthy and energy-balanced diet and adequate physical activity levels (100, 101).

As a pandemic-related physical health change, weight gain was also registered in psychiatric samples, with a greater impact than on the general population (102).

Strengths and limitations

To the best of our knowledge, no intervention studies have been conducted in psychiatric populations using an integrated intervention based on diet and physical activity programmes and metacognitive modules. The only experience reported was related to cardiac rehabilitation participants included in group metacognitive therapy (six sessions). The intervention successfully improved depression and anxiety compared with usual care, leading to more significant reductions in unhelpful metacognition and repetitive negative thinking (103).

Second, the strength of our study was based on the multi-component and transdiagnostic structure of our intervention, which was well-accepted by our participants. Beyond the diagnosis, from a comprehensive early intervention perspective, the protocol aimed to reduce weight and cardiovascular risk factors such as hyperglycaemia, dyslipidaemia, hypertension, and poor physical activity, all the more reason given the overweight/obese individuals already present and a source of concern for the users. All participants showed good adherence to treatment and reported being very glad to be offered an “extra service” to improve their physical health without any cost.

Our study has several main methodological limitations.

First, our study was a real-world pragmatic trial taking into account psychiatric users’ needs and logistic factors. During the informed consent process, the clinicians informed the participants affected by mental disorders that they would have to take part in weekly group sessions. Working or living far away from the site of our service seemed very difficult for some participants. Therefore, they were allocated to the "control" group.

Second, we used an exclusive univariate analytical approach without calculating the power and sample size due to the study's exploratory nature.

Third, the psychiatric sample, including psychopathologically stable participants, had different diagnoses and received different psychopharmacological treatments. Most of them (∼80%) were affected by depression and anxiety disorders and treated with SSRIs. The remaining 20%, affected by psychotic disorders, were treated with atypical antipsychotics. Although with varying degrees of severity, the impact of antidepressants and antipsychotics on weight seems sufficiently homogeneous, with an increase in body weight while taking these drugs (8, 104).

The weekly self-report of dietary and physical activity constituted a further limitation for participants in the intervention groups; every 15 days, during the clinical check-up, the clinical nutritionist (A. A.) weighed the participants based on the interventions. However, adherence to the physical activity protocol relied upon the users' statements only.

Conclusions

The study showed significant benefits of our intervention, including a modified OMNIHeart dietary protocol, in terms of percentage of weight reduction, improvement of metabolic parameters, as recently stressed by Volpe et al. (105), and increased physical activity for both our users and psychiatric and medical subjects. For the psychiatric intervention group, which experienced better health-related quality of life, these differences were found irrespective of medication in an overweight/obese population already presenting with a consistent cardiovascular risk. Life-style interventions can help to manage the physical and mental health symptoms of people affected by psychiatric disorders (106). Alongside medication, a range of psychosocial interventions and behavioral weight management needs to be included to achieve a full and sustained recovery for persons impacted by mental illnesses.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Ethical Committee of the University of L'Aquila (approval date: 14 October 2014). The patients/participants provided their written informed consent to participate in this study.

Author contributions

LG, RR, and MC contributed to the design. VB, SM, and AS contributed to data acquisition. LG, RR, MC, CF, and SN participated in the analysis and interpretation. AAg carried out nutritional consultations for all patients involved in the study. CF and AAl contributed to the collection of clinical and metabolic data of hypertensive patients from the division of internal medicine and nephrology. All authors contributed to the manuscript, revised the work, agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved, read, and approved the manuscript.

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Conflict of interest

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

Publisher's note

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Review

The Influence of the Urban Environment on Mental Health during the COVID-19 Pandemic: Focus on Air Pollution and Migration—A Narrative Review

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Abstract: The coronavirus disease 2019 (COVID-19) pandemic caused a crisis worldwide, due to both its public health impact and socio-economic consequences. Mental health was consistently affected by the pandemic, with the emergence of newly diagnosed psychiatric disorders and the exacerbation of pre-existing ones. Urban areas were particularly affected by the virus spread. In this review, we analyze how the urban environment may influence mental health during the COVID-19 pandemic, considering two factors that profoundly characterize urbanization: air pollution and migration. Air pollution serves as a possibly risk factor for higher viral spread and infection severity in the context of urban areas and it has also been demonstrated to play a role in the development of serious mental illnesses and their relapses. The urban environment also represents a complex social context where minorities such as migrants may live in poor hygienic conditions and lack access to adequate mental health care. A global rethinking of the urban environment is thus required to reduce the impact of these factors on mental health. This should include actions aimed at reducing air pollution and combating climate change, promoting at the same time a more inclusive society in a sustainable development perspective.

Keywords: COVID-19; SARS-CoV-2; mental health; social determinants; air pollution; climate change; migration; refugees; urban environment; urbanization

1. Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, resulting in the coronavirus disease 2019 (COVID-19) pandemic, caused a public health emergency not only due to the possible serious consequences of the infection itself, but also in consideration of the subsequent socio-economic crisis [1]. The pandemic also determined a high risk for developing negative emotions among the general population resulting from different factors, such as fear of the contagion, economic burden, and social isolation [2]. In fact, the global situation contributes to creating an environment of disruption and trauma, as it was already demonstrated during previous pandemics [3]. A higher stress perception during pandemics and disasters can thus impair the overall wellbeing of subjects, with effects on sleep, concentration, cognitive function, and behaviors [4]. Specific populations, including subjects affected by COVID-19 or having their relatives affected, health professionals and subjects with pre-existing mental disorders, have been defined as presenting higher risk for developing psychiatric manifestations during the pandemic [5–8]. The mental health effects of the present pandemic also arose from the implementation of countermeasures such as lockdown and home quarantine. Concerning these, psychiatric manifestations that have been described in the context of lockdown measures mainly belong to the diagnostic categories of depression, anxiety, and psychosomatic disorders [2,9]. In consideration of what stated above and of the high prevalence that mental health consequences of the virus spread demonstrated, mental health needs were pointed out as a priority in the context of the response to the global crisis [10,11]. In addition, SARS-CoV-2 was also demonstrated to exert a direct effect on the central nervous system (CNS), possibly contributing to the occurrence of several neurological manifestations, among which the most frequently reported are hypo/anosmia, dysgeusia or ageusia, dizziness, headache, paresthesia, dysphonia [12]. The neurotropism of COVID-19 may also be directly responsible for behavioral disturbances and mood changes, such as depressive and anxiety symptoms [13].

In this already complex scenario, it is to note that the countermeasures that were established by countries and local governments to control the virus dissemination determined the loss of financial resources for many workers from different sectors [14], seriously affecting employment possibilities [15]. Despite this crisis spread worldwide, the economic consequences of the pandemic are more severe in low-income countries, confirming inequalities among different health systems and resources [16,17]. Furthermore, residents that appear to be more seriously affected by such consequences are the vulnerable ones, frequently presenting scarce economic resources and high rates of unemployment, together with lack of access to health care and poor education about preventive measures [15]. Additionally, urban areas, namely densely populated areas where at least 50% of the inhabitants live in high-density clusters [18], were particularly affected by the virus dissemination, although several factors associated with COVID-19 vulnerability were also reported for rural areas [19,20]. To note, living in urban centers was also found to be associated with the development of psychiatric symptoms among different populations during the pandemic [21,22]. This could be connected with the fact that urbanicity (being born or raised in cities) represents a possible risk factor for the development of serious mental illnesses, such as schizophrenia spectrum disorders and other psychotic disorders [23,24]. Different explanations were sought for this association, including not only social stressors such as inequalities and low social cohesion [25,26], but also possible influences of urbanicity on brain structure [27] and coping styles [28]. The lack of green spaces was also hypothesized to be involved in this relationship, suggesting a higher exposure to pollution and toxins, as confirmed by the evidence that contact with green spaces during the childhood may protect from the later development of psychiatric disorders [29].

In the context of the pandemic, urban environment was hypothesized to be extremely affected by the virus dissemination because of higher population density, higher concentration of air pollutants and specific risks associated with lifestyle [21]. Furthermore, the mortality from COVID-19 was significantly higher in metropolitan areas where poorer general health was associated with lower socio-economic and educational status [15]. Among social factors that may significantly influence the response to the pandemic in urban areas, the presence of ethnic minorities and higher international migration rates were listed among relevant factors, possibly being connected with inequalities in access to health care and relevant socio-economic load [19]. Migration itself is as well connected to mental health problems, since it has been demonstrated that different phases of the migration process may cause a higher risk for developing serious psychiatric disorders, particularly psychosis [30]. The above-mentioned social determinants also influence the emergence of mental health problems, acting as mediators of the COVID-19 psychological impact [31]. Furthermore, social determinants themselves are also expected to be seriously influenced by the pandemic [32], with the risk of implementing a vicious cycle possible leading to even more severe consequences of the present situation on mental health.

In this narrative review, we analyze the role of urban environment as a possible mediator of the effect that COVID-19 may exert on mental health. In particular, the present review will be focused on air pollution and migration. These two apparently different factors were chosen in consideration of the significant association that they already demonstrated with mental health, as both were considered to present a causal relationship with psychiatric disorders. Furthermore, air pollution and urbanicity are among the factors that most represent the complexity of urban environment under different perspectives. Indeed, the first is connected with anthropogenic activities that are typical of the urban environment, i.e., industries, whilst the second profoundly affects the social texture of urban societies and mirrors social inequalities in this context. We hypothesized that the analyzed literature may support a stronger association between COVID-19 and mental health in urban contexts as possibly mediated by these two phenomena, confirming their importance as social and environmental determinants of mental health.

2. Methods

A comprehensive literature search was performed in the research databases PubMed/Index Medicus/MEDLINE, Scopus and Web of Science, by variously combining the words "COVID-19", "SARS-CoV-2", "mental health", "urban*", "air pollution", "pollutant*", "migrant*", "migration", "refugee*", "asylum seeker*" until 31 December 2020. We included papers in English, French, Italian and Spanish that reported data concerning the impact of the pandemic on mental health with particular attention to the considered determinants related to the urban environment, namely air pollution and migration. In consideration of the relatively recent emergence of the pandemic, papers that considered the possible role of the above-mentioned factors in the occurrence and spread of the pandemic itself were also included. Furthermore, due to the possible communication of preliminary data concerning the considered aspects, we did not limit to the inclusion of full-length original articles, but also included reviews, commentaries and letters to the editor. We excluded papers that did not provide sufficient information concerning possible causal relationships between air pollution and related phenomena, mental health, and COVID-19, as well as papers providing only a theory or hypothesis not supported by sufficient data.

3. Results

The literature search yielded 663 records (226 PubMed/Index Medicus/MEDLINE, 278 Scopus, 159 Web of Science). After the whole screening process, including hand-screening of references, was completed, 33 papers were included in this review. Among these, 14 focused on air pollution and related phenomena, whilst 19 focused on migration. For a list of the included papers concerning the two main topics of this review see Appendix A.

3.1. Urban Environment and Mental Health: The Role of Air Pollution

Air pollution has already been listed among the factors associated with higher viral transmission and COVID-19 severity. This could be due to the proven role of atmospheric particulate matter (PM) in creating an environment where the virus survival is facilitated for hours, causing the widespread via airflows over large distances [33]. Additionally, air pollutants such as nitrogen dioxide and carbon dioxide can contribute to the development of a serious inflammatory response that mainly concerns the respiratory system, which represents a possible reason for the higher severity of COVID-19 observed in highly polluted regions in China and Northern Italy [34,35]. Noteworthy, high levels of air pollution could also act synergistically with the virus in its already mentioned neurotrophic mechanism [15]. Furthermore, air pollutants contribute to the phenomenon of global warming, which seriously affects climate change. Modifications in meteorological parameters, such as temperature, are also connected with climate change and were demonstrated to facilitate the infection spread. Indeed, both higher and lower temperatures appeared to be beneficial in decreasing COVID-19 transmission, whilst average temperatures were linked to higher possibility of viral spread [36,37]. Nanoparticles that contribute to air pollution can reach the CNS via the olfactory-neural tract, activating several pathophysiological pathways that include cerebrovascular dysfunction, oxidative stress, inflammatory processes, activation of the immune system, damage to blood vessels, alterations in neurotransmitter concentrations, and alterations in the blood-brain barrier [38,39], possibly playing a role in the pathophysiology of neuropsychiatric symptoms that are strictly connected with the infection. Recently increasing literature is investigating negative impacts of air pollution exposure on mental health. In particular, air pollutants exposure seems to be associated with a higher risk of severe mental disorders [40–42], as well as with a higher number of hospital admissions for psychiatric reasons [43,44]. Further phenomena that were linked to air pollution are represented by suicidal ideation and suicidal behaviors [45–47]. To note, urbanicity has been commonly described as one of the risk factors for the onset of schizophrenia spectrum disorders, and air pollution exposure could be considered as a potential mediator of the association between urbanicity and the risk of both psychotic disorders and viral epidemics or pandemics [48–50]. Moreover, air pollution indirectly affects mental health by causing climate change, that can be responsible for natural disasters and extreme events, leading to mental distress and to psychiatric disorders such as post-traumatic stress disorder (PTSD) [51,52]. Furthermore, gradual climate changes could play and indirect role in the emergence of psychiatric symptoms, i.e., contributing to social changes and migration phenomena, but also inducing negative emotional responses such as anxiety and sense of guilt for the ongoing situation [53]. The association of both air pollution and COVID-19 with mental health problems led to the hypothesis that these phenomena may to some extent be all linked [48].

It has also been demonstrated that urbanicity could represent a possible risk factor for the spillover phenomenon, facilitating the virus transition from animals to humans via intermediate hosts. Particularly, deforestation policies may facilitate this process, resulting in the destruction of natural habitats of numerous species and reduction of biodiversity, as well as in greater interaction between wildlife and human activity [54]. At the same time, during the COVID-19 pandemic, deforestation registered an increasing trend, probably due to socio-economic reasons that were exacerbated by the global situation [55]. This is expected to facilitate the interaction between humans and wild animals, leading to a vicious circle that may cause the emerge of new diseases. Furthermore, airborne particles may result from forest fires, increasing pollutants level in surrounding areas, which suggests that the current situation could also potentially increase the burden of pollution-related medical conditions [33,56].

Anyway, the relationship between air pollution and COVID-19 presents a multi-facet nature. In fact, the countermeasures adopted for containing the viral spread, such as social distancing and home quarantine, led to several environmental changes, above all the reduction of toxic emissions produced by industries and other anthropogenic activities [17,57]. On the other side, higher levels of household air pollution might be associated with quarantine measures since indoor anthropological activities significantly increased during this timeframe [58]. Noteworthy, depressive symptoms were associated with living in small apartments characterized by poor housing, such as scarce air and lighting quality [59]. Higher risk for developing depression in the middle-aged and older population was found to be associated with indoor air pollution caused by solid fuels (i.e., coal) when compared to “clean” sustainable fuels (i.e., natural gas) [60]. Above all, being subjected to lockdown measures was demonstrated to facilitate the emergence of psychiatric symptoms, that significantly increased with the persistence of such measures [11]. To this end, future studies are expected to clarify to which extent these symptoms may be mediated by indoor pollution. Additionally, the presence of green spaces in living environments demonstrated a link with a reduction of perceived stress. This could be in part confirmed by the evidence that interventions based on video-audio stimuli reduced anxiety levels in subjects undergoing lockdown and quarantine measures, with a higher efficacy when forest environments were displayed [61]. In addition, the access to green spaces was reported as a crucial need during the pandemic, also connected with the possibility for physical exercise and relaxation. At this regard, citizens who underwent quarantine measures also suggested to improve urban plans to project wider big areas in metropolitan centers, which was hypothesized to determine an improved quality of life [62].

The sensibilization about green policies could also allow a better perception of actions required for contrasting climate change [63]. This represents a relevant issue, especially in countries where climate-induced natural disasters frequently occur, since food deficiency and lack of medical assistance during such events is expected to be even more critical in consideration of the ongoing pandemic situation [14]. Indeed, climate-related calamities, i.e., heat waves, hurricanes, cyclones, still represent a global threat for under-resourced health systems, that may not be able to guarantee an adequate response [64]. This could particularly affect overloaded mental health professionals, which would be conversely expected to implement different actions in order to face these disasters, providing psychosocial treatments and improving technology-based interventions that could be spread on large scale [65].

3.2. Urban Environment and Mental Health: Focus on Migrant Populations Mental Health during the COVID-19 Pandemic

The public health needs of minorities such as migrants generally represent a relevant issue in modern societies, which should be afforded by means of culturally competent services. As stated above, the pandemic situation represents a factor which may potentially increase the vulnerability of this population, since anxiety related to COVID-19 could overlap with worries concerning the precariousness of their condition and the lack of a regular working status [66].

In this context, undocumented migrants, asylum seekers, refugees and those living in camps and detention centers may be subjected to a dramatic situation due to difficulties in adhering to public health directives and to specific environmental conditions that may result in higher risk for contracting the infection [67]. As for refugee camps, these were particularly affected by the viral spread, as demonstrated by specific cases of COVID-19 outbreaks, i.e., in European countries such as Greece [68] and Malta [69]. In these settings both direct and indirect pathways of transmission should be considered. Indeed, overcrowding is frequent and may hinder the implementation of social distancing measures [70]. At the same time, adequate facilities for hygiene measures such as handwashing may not always be available. Additionally, in settings with a heavy viral contamination, the contagion could spread by fingertip contact with infected surfaces and it has also been hypothesized that the transmission could be mediated by food [71].

Refugee camps do not represent the only cause due to which these populations may be exposed to high infectious risk. For example, asylum seekers whose request of international protection has been rejected do not own regular documents and are most frequently homeless, living in conditions of poverty due to lack of work [1]. In such cases, the COVID-19 spread could also cause changes in the humanitarian corridors and asylum seekers may be returned to their countries of origins, where they are at risk of being persecuted [72]. For similar reasons, in some countries asylum seekers and undocumented migrants can avoid seeking help for health matters due to fear of being repatriated [73,74]. Rescue operations in the Mediterranean Sea were suspended as well due to logistic reasons, whilst the few that were carried led to quarantine measures in refugee camps with subsequent organizational concerns [72]. Furthermore, shortage of food and medicines that already affected refugee camps in several parts of the world could be exacerbated during the pandemic, adding further concerns to administrative, socio-economic, legal and language barriers in accessing health care [72,75]. These conditions can foster feelings of uncertainty and loneliness that often prelude to the onset of anxiety and depressive symptoms. Additionally, pre-existing mental disorders that are particularly prevalent among this population may be exacerbated during the pandemic, also representing an obstacle to the recognition of specific symptoms and determining a higher risk for the infection spread [67].

Indeed, migrants and especially asylum seekers represent a vulnerable group of individuals, facing traumatic events during different phases of the migration process, i.e., childhood abuse, armed violence, detention, and isolation [76], often leading to the development of PTSD, adjustment disorders and depressive symptoms [1]. Such symptoms may also be influenced by difficulties in adaptation to the culture of the host country, poverty, and racism [77]. The pandemic can act as a trigger for the recall of traumatic experiences, as demonstrated by a study conducted in a refugee camp in Iraq where different PTSD symptoms measured by the Impact of Event Scale-Revised (IES-R) were more severe after the COVID-19 outbreak than they were before [78]. Not only did fear of illness and death, as well as concerns for safety of the loved ones cause symptom exacerbation, but also social distancing might have contributed to more serious psychopathology by hindering the creation of social networks that could help refugees to connect with the host culture and society [79]. This could further be exacerbated by quarantine measure, which cause anger and confusion and could evoke memories of restricted freedom to those who experienced imprisonment in their past. Moreover, refugees often escaped oppressive regimens during and can perceive the reinforcement of police and military presence to help respecting restrictions as a threat to personal security [79]. Symptom exacerbation during the pandemic, together with limited access to mental health care and lack of adequate psychological support, can lead to serious consequences and to a higher suicide risk [80]. Results from a population of individuals in low socio-economic conditions, including migrants, detected a significantly lower percentage of users after the adoption of lockdown measures, with fewer subjects attending follow-up visits during the next months [1], demonstrating the need for a reorganization of mental health services that are addressed to this population. Tailored psychological aid programs for refugees were implemented, based on informative materials about the virus spread and on mental health condition monitoring by means of phone and, when possible, using telemedicine [81]. This latter resource, despite limitations due to scarce internet access and setting variation, allowed in some cases to continue treatment programs especially in young subjects [81].

Another population that may suffer from mental health problems related to the CoV-Sars-2 spread is represented by international migrant workers [82], 95% of which are living in regions affected by the pandemic [83]. Migrant workers, especially in urban areas, often engage in occupations characterized by low wages and experiment a condition of global uncertainty, facing social and cultural barriers [84]. Furthermore, these individuals are prone to the development of psychiatric disorders [85–87] and are frequently affected by comorbid medical illnesses, also due to poor hygienic conditions and chronic malnutrition [82]. Factors that contribute to the development of mental health problems in this population are loneliness, lack of familiar support [88], social exclusion [89], and difficulties in accessing psychiatric care [82]. Due to the pandemic situation, these individuals are expected to cope with serious economic load due to job loss in the next future, as already demonstrated in some areas of the world [87], and could be subject to an inverse migration phenomenon, thus returning to their native villages [90], which was also demonstrated to be a risk factor for suicide [72]. Language barriers create further limitations to the acquisition of adequate information about the public health situation and personal protection [83], with the latter becoming even more difficult to address for migrant workers living in shelter and camps [84]. These issues, together with perceived and internalized stigma and low education level, hinder the access of this population to specific psychological aid services that were settled in some countries during the pandemic [87,91–93]. To note, the stigmatization of minorities underpins a process through a specific human characteristic is labeled as socially salient and is usually considered under a discrediting point of view [94]. This phenomenon, that has historically been associated with psychiatric illness in modern societies, gains further relevance when considering mental health among minorities.

We should also consider that international migrant workers are also affected by worries for their families of origin living in countries that are highly affected by the COVID-19 pandemic [95], expressing their struggle to travel to native countries and meet the loved ones, despite adjunctive quarantine measures that they usually have to undergo [84,87]. This could further facilitate the virus transmission towards native villages and countries which could initially be less affected by the pandemic, since migrations was listed among the main reasons for the long-distance viral spread [96].

In a cross-sectional study based on self-reports and interviews, migrant workers reported a high rate of negative emotions including frustration, fear, and irritability [96]. In the same population, 75% of migrants screened positive for anxiety or depression, with the first being more frequent than the latter [97]. In a research focusing on Italian foreign workers, PTSD was detected among about 22% of them and was significantly predicted by the development of anxiety and depression [95]. Another study where migrant workers living in camps and shelters were interviewed, a high burden of substance abuse emerged, determining further issues during the pandemic due to withdrawal symptoms and craving for substances that could not be easily accessed [84].

4. Conclusions

In this narrative review, we underlined how different aspects that characterize the urban environment can contribute to the SARS-CoV-2 spread and increase the COVID-19 pandemic complexity. Indeed, the current situation seriously affects public health, but it also presents relevant implications under a socio-economic point of view. The overall severity of the emergency was demonstrated to present relevant implications for mental health as well. Noteworthy, several factors connected with the urbanization process are associated with such implications. Among these, air pollution represents a potential link between COVID-19 and mental health, since it was proved to be a risk factor for the development of both conditions. Furthermore, this phenomenon is also connected with major issues that have relevant societal consequences and particularly, but not only, climate change. Additionally, the urban environment presents a social structure that often leads to inequalities and hampers the access to adequate health care for specific populations.

This was particularly demonstrated for minorities such as refugees, asylum seekers and migrant workers, that can be subjected to major issues concerning the maintenance of adequate hygienic conditions, determining a higher risk of contagion in the pandemic era. Additionally, during the pandemic access to health facilities may be even more difficult, with relevant influence on general health and particularly on mental health. Several factors connected with the migrant condition, as well as the high prevalence of pre-existing psychiatric disorders, contribute to the significant burden that mental health issues cause in this population during the COVID-19 pandemic. Possible causal relationships between COVID-19, mental health, and urbanization are described in Figure 1.

Although we considered only some among the possible determinants of mental health, the evidence we summarized suggests the need for a comprehensive rethinking of the urban environment. This represents a crucial topic since fifty per cent of the world population lives in densely populated urban areas and further urbanization is expected during the next decades. The promotion of human behaviors aimed at reducing air pollution and contrasting climate change, together with a more sustainable exploitation of natural resources in populated areas, represent unique possibilities to improve human health, with significant influence on mental health as well. Specific initiatives focused on the maintenance of biodiversity, the improvement of urban green cover and the promotion of agriculture activities in adjacent areas may help reaching these goals. Greater attention should also be dedicated to indoor environments, as suggested by some of the reported literature.

Noteworthily, the COVID-19 pandemic led to a global change concerning the possibility for long-distance working, as well as to a redefinition of activities that may be held in the context of households. Furthermore, the reduction of inequalities that could be exacerbated in urban environments should also be considered as a priority. Migration phenomena are not expected to decrease in the next decades, and most of the global population will be living in urban areas. In this context, policies aimed at social and economic inclusion could significantly affect the burden of mental health problems related with a distressing marginalization condition. The promotion of access to health care, with particular attention to mental health care, should be strongly implemented among minorities.

Noteworthy, mental health and well-being were also included in the United Nations Sustainable Development Goals, together with the implementation of sustainable cities and communities, inequalities reduction and climate change-related issues, suggesting that these are all aspects of a multi-facet global change program. In order to address these goals, a multidisciplinary approach is required, involving the participations of professionals working in public health and specialists in different medical fields, as well as experts in sociology, engineering, architecture, and environmental sciences.

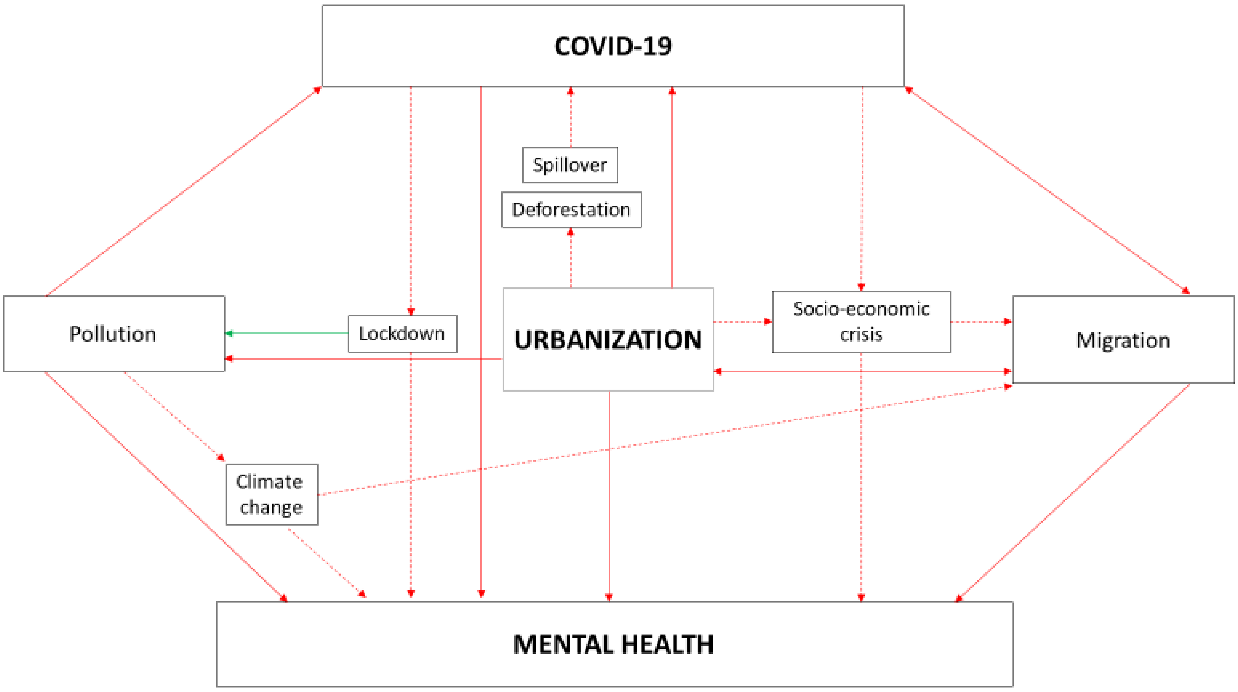

Figure 1. Possible causal relationships between COVID-19, mental health and urbanization.

Despite the lack of a systematic approach that might have led to the inclusion of heterogeneous literature, i.e., not defining urban areas clearly, the present review presents among its strength the consideration of mental health under a comprehensive approach, taking into account general health and socio-economic determinants. Future prospective studies targeting mental health in urban areas in the COVID-19 era may better address the issues raised in this paper.

In conclusion, the COVID-19 pandemic and the related mental health problems raise several issues that lay the foundations for future strategies oriented towards a more sustainable and inclusive planning of urban environments. This also depends on higher awareness concerning social determinants of mental health, as well as an overall reduction of social stigma that affects both mental health and minorities.

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Appendix A

Table A1. Papers evaluating the relationship between air pollution and related phenomena, the COVID-19 pandemic and mental health.

Author (Year) [Reference]	Article Type	Study Design (for Studies with Human Sample)
Bodrud-Doza et al. (2020) [14] (pp. 2, 6)	Original research	Cross-sectional survey
Chakraborty et al. (2020) [17] (pp. 2, 5)	Review	Not applicable
Wu et al. (2020) [34] (p. 4)	Original research	Cross-sectional study
Conticini et al. (2020) [35] (p. 4)	Commentary	Not applicable
Tosepu et al. (2020) [36] (p. 5)	Original research	Retrospective study
Li et al. (2021) [37] (p. 4)	Original research	Not applicable (no human sample)
Marazziti et al. (2021) [48] (p. 5)	Review	Not applicable
Brancalion et al. (2020) [55] (p. 5)	Policy Forum	Not applicable
Venter et al. (2020) [57] (p. 5)	Original study	Not applicable (no human sample)
Sharma et al. (2020) [58] (p. 5)	Letter to the editor	Not applicable
Amerio et al. (2020) [59] (p. 6)	Original research	Cross-sectional survey
Zabini et al. (2020) [61] (p. 6)	Original research	Interventional study
Ugolini et al. (2020) [62] (p. 6)	Original research	Cross-sectional survey
Barouki et al. (2020) [64] (p. 6)	Review	Not applicable

Table A2. Papers evaluating the relationship between migration, the COVID-19 pandemic and mental health.

Author (Year) [Reference]	Article Type	Study Design (for Studies with Human Sample)
Aragona et al. (2020) [1] (pp. 1, 6, 7)	Research article	Naturalistic study
Liu et al. (2020) [60] (p. 5)	Commentary	Not applicable
Bhopal et al. (2020) [66] (p. 6)	Letter to the editor	Not applicable
Ralli et al. (2020) [67] (pp. 6, 7)	Review	Not applicable
Kluge et al. (2020) [72] (pp. 6, 7)	Letter to the editor	Not applicable
Mukumbang et al. (2020) [73] (p. 6)	Review	Not applicable
Page et al. (2020) [74] (p. 6)	Commentary	Not applicable
Dalexis and Cenat (2020) [76] (p. 7)	Letter to the editor	Not applicable
Kizilhan and Noll-Hussong [78] (2020) (p. 7)	Letter to the editor	Naturalistic study
Rees et al. (2020) [79] (p. 7)	Review	Not applicable
Endale et al. (2020) [81] (p. 7)	Experiential account	Experiential account
Choudhari (2020) [82] (p. 7)	Review	Not applicable
Liem et al. (2020) [83] (p. 7)	Letter to the editor	Not applicable
Chander et al. (2020) [84] (pp. 7, 8)	Experiential account	Experiential account
Espinel et al. (2020) [90] (p. 7)	Commentary	Not applicable
Chan and Kuan (2020) [93] (p. 7)	Research article	Naturalistic study
Barbato and Thomas (2020) [95] (pp. 7, 8)	Letter to the editor	Cross-sectional survey
Fan et al. (2020) [96] (p. 8)	Research article	Retrospective study
Kumar et al. (2020) [97] (p. 8)	Letter to the editor	Cross-sectional survey

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Effectiveness of a stepped-care programme of WHO psychological interventions in a population of migrants: results from the RESPOND randomized controlled trial

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Migrant populations – including labour migrants, undocumented migrants, asylum seekers, refugees, internationally displaced persons, and other populations on the move – are exposed to a variety of stressors that affect their mental health. We designed and tested the effectiveness of a stepped-care programme consisting of two scalable psychological interventions developed by the World Health Organization (WHO) and locally adapted for migrant populations. A parallel-group randomized controlled trial was conducted in Italy. We recruited migrant adults (≥18 years) with psychological distress (score of at least 16 on the Kessler Psychological Distress Scale, K10). The experimental arm received psychological first aid (PFA) and a stepped-care programme consisting of two WHO interventions adapted for this population group: first, Doing What Matters in Times of Stress (DWM) and, for participants who still reported significant levels of psychological distress after DWM, Problem Management Plus (PM+). Each intervention lasted 5-6 weeks and was delivered remotely by lay facilitators. The control arm received PFA and care as usual (CAU). The primary outcome was the change in symptoms of depression and anxiety from baseline to week 21 after randomization, measured by the Patient Health Questionnaire Anxiety and Depression Scale (PHQ-ADS). Between December 14, 2021 and April 18, 2023, 108 migrants were randomized to the stepped-care intervention and 109 to CAU. Analysis of the primary outcome revealed that participants receiving the stepped-care programme showed a greater reduction in anxiety and depression symptoms compared to those receiving CAU (coefficient: –3.460, standard error, SE: 1.050, $p=0.001$) at week 21. The same difference was observed at week 7 (coefficient: –3.742, SE=1.008, $p<0.001$) and week 14 (coefficient: –6.381, SE=1.039, $p<0.001$). The stepped-care programme was also associated with a greater improvement of depression and anxiety symptoms assessed separately at all timepoints, of post-traumatic stress disorder symptoms at weeks 14 and 21, and of self-assessed problems, function and well-being at all timepoints. No serious adverse events occurred. This study provides evidence supporting the stepped-care delivery of DWM and PM+ for migrant population groups with elevated distress. As these interventions are low-intensity, transdiagnostic and task-shifting, they are highly scalable. Existing evidence-based guidelines and implementation packages should be updated accordingly.

Key words: Migrants, psychological distress, WHO psychosocial interventions, Problem Management Plus, anxiety, depression, stepped-care model

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Migration has been a common phenomenon for centuries. The term "migrant" typically encompasses many different groups: labour migrants, undocumented migrants, asylum seekers, refugees, internally displaced individuals, and other populations on the move[1].

According to the International Organization for Migration, there were about 281 million international migrants worldwide in 2021, marking a 27% increase compared to the 221 million migrants in 2010. Migrants represent a total of 3.6% of the world's population. Many migrants arrive in Europe through Italy, with 34,000 new arrivals in 2020 and almost 60,000 in 2021[2].

Migrant population groups are exposed to various risk factors for mental health conditions. These include discrepancies between expectations and actual achievements, inadequate support systems, challenges in adaptation and acculturation processes, along with financial, administrative and legal hurdles throughout and after the migration trajectory[3]. Among migrants, forcibly displaced people – such as refugees and asylum seekers – face additional severe stressors, including the loss of their homes and possessions, and other traumatic events such as bombings, threats, imprisonment and torture.

In recent years, there has been a growing number of randomized controlled trials (RCTs) exploring the benefits of psychosocial interventions targeting psychological symptoms in migrant populations[4]. A systematic review of 52 studies (including 26 RCTs) identified a significant effect of psychological interventions in reducing depression, anxiety and somatization symptoms[5]. These results align with those of a scoping review of mixed-methods studies, which indicated a positive effect of psychosocial interventions on participants' mental health, mainly through a reduction in depressive symptoms and an improvement in social functioning[6].

However, implementing the above interventions necessitates extensive training, a significant time for delivery, staff members with a background in mental health, and a robust monitoring and supervision framework. Moreover, it involves face-to-face individual delivery in most instances. As these characteristics are barriers to implementation, the World Health Organization (WHO) has developed a stress management intervention named Self Help Plus (SH+)[7], and a brief intervention based on cognitive-behavioral and problem-solving strategies called Problem Management Plus (PM+)[8]. A guided self-help programme based on the SH+ course, called Doing What Matters in Times of Stress (DWM), is also available and has been adapted to be delivered as a mobile-supported website[9].

SH+, PM+ and DWM are designed to be scalable, transdiagnostic and task-shifting. They have been tested as stand-alone interventions in diverse populations, including health care staff, asylum seekers, refugees, international migrants, involuntarily displaced people, and individuals exposed to armed conflicts, natural disasters, and health stressors such as the COVID-19 pandemic[10-14]. Studies have generally found benefits in mental health outcomes, though the effectiveness of interventions may diminish over time[15]. One study conducted among health care staff with COVID-19-related distress combined DWM and PM+ into a stepped-care programme compatible with fully remote training, delivery and supervision[16]. The stepped-care programme was found to be feasible. It resulted in clinically significant reductions in symptoms of anxiety, depression and post-traumatic stress disorder (PTSD)[17], suggesting that it may be potentially beneficial in other populations exposed to adversity.

Against this background, the present study examined the efficacy of DWM and PM+ delivered as a stepped-care programme in reducing anxiety and depression symptoms in a sample of migrants with elevated psychological distress.

METHODS

Study design

We conducted a parallel-group RCT in Italy. The trial protocol was published and registered in clinicaltrials.gov (NCT04993534)[18]. No changes were made to the design after the trial started. The Ethics Committee of the University of Verona approved the project. Written informed consent was mandatory for all participants. In accordance with the Declaration of Helsinki, participants' confidentiality was preserved, and the contents of the recruitment and follow-up forms were not disclosed to any third party.

An Ethics and Data Advisory Board monitored the study and provided expert advice on data management and all ethical, legal and societal issues related to the project. The Consolidated Standards of Reporting Social and Psychological intervention Trials (CONSORT-SPI) statement was followed in reporting trial results[19]. Participant recruitment occurred from December 14, 2021 to April 18, 2023.

Participants were adult migrants recruited through: a) key stakeholders such as non-governmental organizations (NGOs) located in Italy; b) other community-based organizations offering legal and/or social and/or psychosocial support to this vulnerable group; or c) social media and "word of mouth" (i.e., investigators proactively approached local organizations providing social, health and/or legal support to migrant populations, including refugees and asylum seekers, to identify potentially eligible participants).

Interested individuals were informed (in English, Italian or French), using an easily accessible terminology, about the nature and scope of the study. A research assistant explained details of the study and provided study materials. Participants meeting the inclusion criteria were randomized to receive psychological first aid (PFA) combined with the adapted stepped-care DWM/PM+ intervention, or to receive PFA and care as usual (CAU) alone. After the screening at T0, participants were assessed at baseline before random allocation (T1) (one week after the screening), and after randomization at week 7 (T2), week 14 (T3), and week 21 (T4) (primary endpoint).

Inclusion and exclusion criteria

Participants were included if they met the following criteria: a) aged 18 years or older; b) being a migrant resettled in Italy temporarily or permanently (including labour migrants, undocumented migrants, asylum seekers, refugees, internationally displaced persons, or other persons on the move); c) having elevated levels of psychological distress (score of at least 16 on Kessler Psychological Distress Scale, K10[20]); d) sufficient mastery of English, Italian or French (written and spoken); e) oral and written informed consent before entering the study.

Individuals who met the inclusion criteria were excluded from participation if they met any of the following criteria: a) acute medical conditions requiring hospitalization; b) imminent suicide risk or expressed acute needs or safeguarding risks that required immediate follow-up; c) severe mental disorder (e.g., psychotic disorder); d) severe cognitive impairment (e.g., severe learning difficulties or dementia); e) initiated, stopped or significantly modified psychiatric drug treatment over the previous two months; f) receiving specialized psychological treatment at enrolment (e.g., cognitive-behavioral therapy, eye movement desensitization and reprocessing); g) planning to permanently move back to their home country before the last quantitative follow-up assessment (T4).

Randomization and masking

Randomization was coordinated by the WHO Collaborating Centre at the University of Verona. The electronic software Castor Electronic Data Capture (EDC) generated the randomization schedule, employing a variable block randomization method[21]. Research team members involved in recruitment could access the web-based software to randomize each newly enrolled participant, but were not able to access the randomization list and were not aware of the block size. The Castor EDC software allowed random allocation only after the main information on the enrolled participant was entered, upon verification of the inclusion criteria. After random allocation, the software produced a unique identification number for each participant.

Masking participants and research staff was not feasible, due to the nature of the intervention programme. However, the statistician performing the analyses was masked to participant allocation status through pseudo-blinding using coded groups. The trial statistician was not involved in determining participants' eligibility, administering the intervention, measuring the outcomes, or entering data.

Experimental and control intervention

All participants initially received a phone call of up to 15-20 min where intervention helpers provided information on which group they were allocated to, as well as on specific resources and supports they could access following the principles of PFA.

PFA is a WHO-developed support strategy that involves human, supportive and practical help for individuals who have been affected by humanitarian crises[22]. It consists of a conversation during which the helper provides non-intrusive practical care and support, assesses needs and concerns, helps people to address basic needs (e.g., information), listens to people without pressuring them to talk, comforts them and helps them calm down; and helps them to connect to information, services and social support[22,23].

Participants allocated to the control arm received PFA and CAU, which could include community care, social/legal support, and psychoeducation on general distress and personal and community resources.

Participants allocated to the intervention arm received PFA, CAU and the stepped-care program, which included DWM and – for participants who reported significant levels of psychological distress after DWM (score of at least 16 on the K10 scale) – PM+.

After allocation, participants in the intervention arm were assigned to a helper who provided ongoing support over the phone, assisting with practical exercises and explaining key concepts of DWM. After an initial welcome call, participants received a message with login details to access the DWM course. As a result of the local adaptation process, reported elsewhere[24], we transformed DWM into a mobile-friendly website and adapted some content to reflect barriers or stress triggers that might affect migrant populations in Italy.

The DWM course was delivered over a period of 5-6 weeks, with new modules released every week. Helpers scheduled weekly support calls lasting approximately 15 min each, and provided motivation and support in using DWM. Participants who did not want to receive phone calls could contact their helpers using the messaging system available on the website. The DWM course is based on acceptance and commitment therapy techniques (e.g., acting on values, making room for difficult thoughts and feelings, keeping attention and curiosity), along with audio recordings to support practice[24]. Participants were reminded of the sessions through text messages, in accordance with the WHO manual for delivery of the intervention.

After 5-7 days from DWM completion (T2), an assessment was made of the criterion for stepping up to PM+, i.e. significant levels of psychological distress as measured by the K10 scale (score of at least 16). The PM+ intervention, culturally and contextually adapted according to WHO protocols, was administered by trained helpers without a formal background in mental health[25], over a period of 5-6 weeks.

The PM+ protocol provides five different behavioral strategies: stress management, problem-solving techniques, behavioral activation, promoting social support, and maintaining the effects. The cultural adaptation of the intervention was conducted through ten online meetings over a 6-month period between the staff of the University of Verona, WHO officers, and representatives of other sites of the RESPOND Consortium.

Both DWM and PM+ interventions had an online format and were delivered in Italian, English or French. The intervention manuals are available on the WHO website (www.who.int). A detailed description of the interventions delivered during the trial (PFA, CAU, DWM and PM+) is provided in the supplementary information.

Helpers were bilingual (Italian/English or Italian/French) and received training in Italian on PFA, DWM and PM+ according to WHO protocols and manuals[26]. The training was conducted by master trainers based at the University of Verona (clinical psychologists trained by WHO officers and/or experts with long experience in delivering WHO interventions). Details on the training activities are provided in the supplementary information. Intervention supervision was provided for DWM and PM+ helpers by clinical psychologists, who were available to address questions, as well as to provide debriefing after sessions. If necessary, additional training and consultation were available. Fidelity was checked by the intervention supervisor, who was not involved in the delivery of interventions, observed at least 10% of DWM sessions, and listened to at least 10% of recorded PM+ sessions.

Participants in both arms received: a) baseline and follow-up assessments according to the study schedule, b) information about freely available health and social services, and c) links to community networks providing support for migrant populations.

Measures

Participants completed online questionnaires, using the Castor EDC software[21], at T0 (screening for eligibility); T1 (baseline assessment, before random allocation); T2 (week 7 after randomization); T3 (week 14 after randomization); and T4 (week 21 after randomization).

Screening for eligibility was conducted using the K10. This is a ten-item self-report questionnaire to screen broadly for psychological distress experienced in the past 30 days[20]. Each item is scored from 1 ("none of the time") to 5 ("all of the time"). Scores of the ten items are then summed, yielding a minimum score of 10 and a maximum score of 50. The K10 has robust psychometric properties and strong discriminatory power to distinguish DSM-IV cases from non-cases[20]. Suicidality was explored by the "Assessment of suicidal thoughts" risk tool from PM+. The possible presence of a severe mental disorder or cognitive impairment was assessed using the PM+ tool "Impairments possibly due to severe mental, neurological or substance use disorders".

The primary study outcome was the change in symptoms of depression and anxiety from baseline to week 21 after randomization (T4), measured through the combined sum score of the Patient Health Questionnaire-9 (PHQ-9)[27] and the Generalized Anxiety Disorder-7 (GAD-7)[28], previously validated as the Patient Health Questionnaire Anxiety and Depression Scale (PHQ-ADS)[29]. The scale scores range from 0 to 48, with higher scores indicating higher levels of depression and anxiety symptoms.

Secondary measures included the changes in symptoms of anxiety, depression and PTSD, and self-assessed problems, function and well-being, evaluated at all timepoints (T1, T2, T3 and T4). Depression and anxiety symptoms were measured using PHQ-9 and GAD-7, respectively. PTSD symptoms were assessed using the eight-item version of the PTSD Checklist for DSM-5 (PCL-5)[30], which provides scores ranging from 0 to 32, with higher scores indicating higher levels of PTSD symptoms. The instrument is based on the PTSD Checklist - Civilian Version (PCL-C), a DSM-IV-based checklist[31].

Self-assessed problems, function and well-being were measured using the Psychological Outcomes Profiles (PSYCHLOPS)[32], a patient-generated tool consisting of four questions (two for problems, one for function, and one for well-being). Participants are asked to give free text responses to the questions. Responses are scored on an ordinal six-point scale ranging from 0 to 5, producing a maximum score of 20. If both problem questions have been responded, the total score is the sum of the four items. If only the first problem question has been responded, the score of the first question is doubled.

Assessments were completed remotely via secure online links to Castor EDC. Adverse events reported spontaneously by the participants or observed by the research staff were recorded, and any serious adverse events were reported to the Ethics and Data Advisory Board.

Statistical analysis

Based on prior studies on PM+[33,34], we aimed to detect a medium effect size (defined as the square root of the ratio of the variance of the tested effect to its error variance) of 0.3 in the PM+ group at T4, based on the primary composite outcome PHQ-ADS. A power calculation for a repeated measurement design suggested a minimum sample size of N=74 per group (power = 0.95, alpha = 0.05, two-sided) in order to identify an effect at the time of interest. Assuming an attrition rate of 30%, we aimed to include 212 participants (106 in the DWM/PM+ intervention group and 106 in the control group).

All primary and secondary analyses were performed on an intention-to-treat (ITT) basis. The ITT population consisted of all participants randomly assigned to one of the two groups and with data available on at least the baseline assessment. In order to check the robustness of results, all outcomes were additionally analyzed using a per-protocol (PP) approach that included only DWM participants clicking through all the contents of at least three modules and PM+ participants attending at least four sessions.

We calculated the descriptive statistics (mean with SD for interval-level variables, number and percentage for categorical variables) at baseline and for the two intervention arms separately. Arms were compared using standardized mean differences (SMDs).

The primary analysis assessed the intervention effect on the average PHQ-ADS score at each timepoint in the ITT population. To estimate the intervention effect for the timepoints T2, T3 and T4, we employed a linear mixed model for the analysis of PHQ-ADS, which had time as a fixed effect, baseline measurement of PHQ-ADS as a covariate, and subject as a random effect. The model was re-parametrized by constraining the intervention fixed-effect to be 0, and by including a time-intervention interaction at T2 as well. In this way, at each timepoint, the intervention effect was measured as the interaction between time (as a categorical variable) and intervention, with its value at T4 being our outcome of interest.

The interaction effects and confidence intervals (CIs) represent the average difference between the two study arms at each timepoint. We used the mean of the values predicted from the model to calculate the estimated average values for the two study arms in case all participants were assigned to the intervention versus the control arm. In addition, a covariate-adjusted mixed model of the primary outcome was performed by adding covariates showing imbalance at baseline (as measured by a SMD above 0.1 in absolute value). Robust standard errors (SEs) were used in all models.

A secondary analysis of the effect of the intervention on the outcomes was conducted in the PP population, using the same approach as reported above. In addition, a covariate-adjusted mixed model of primary outcome was performed using this population by adding pre-specified covariates at baseline (gender, age, whether the person had at least secondary education; prior trauma expressed as replying "Yes" to at least one item from the Brief Trauma Questionnaire[35]; whether the person had been infected by COVID-19; and the stressor exposure as measured by the Mainz Inventory of Microstressors[36]).

No imputations of missing values at the scale level were made, as multilevel models can deal with missing data in case the missing at random assumption holds[37]. If only some items were missing for a particular scale, we used the corrected item mean substitution method (i.e., the item mean across participants weighted by the subject's mean of completed items)[38], using information from subjects belonging to the same intervention arm for the same follow-up time (estimated values above the maximum or below the minimum admissible value were set to maximum/minimum). As a sensitivity analysis, the analyses for outcomes with partially imputed scales were repeated by excluding such imputed values. To avoid missing values among categorical predictors, a category "missing value" was included.

A linear mixed model with robust SEs, as mentioned for the primary analysis, was carried out to analyze the following secondary outcomes: changes in depressive symptoms (PHQ-9), generalized anxiety symptoms (GAD-7), PTSD symptoms (PCL-5), self-assessed problems, function and well-being (PSYCHLOPS).

Possible interactions between the intervention and specific variables (baseline score on the primary outcome, age, gender, legal status, time since resettlement; whether the person had at least secondary education, was receiving an income, and had ever consulted a mental health professional) were evaluated, by excluding categories with data from less than ten participants. A global test on each variable was implemented and, in case of statistical significance after applying the Benjamini-Hochberg correction[39], statistical significance at each timepoint was evaluated for that variable.

Finally, the loss-to-follow-up rate was compared between the two groups using a chi-square or a Fisher exact test, as appropriate. All analyses were performed using Stata/SE, Release 17.0[40].

RESULTS

After screening 238 potentially eligible participants, 21 were excluded (19 of them had a level of distress lower than the established cut-off; one was on an unstable dose of psychotropic medication; and one refused to participate) (see Figure 1). This left 217 individuals who met the inclusion criteria, consented to be randomized by signing a written informed consent form, and were allocated to either the stepped-care programme (N=108) or CAU (N=109). Only 16.6% of randomized participants were lost to follow-up. The distribution of participants lost to follow-up did not differ between the study groups at any timepoint (see supplementary information).

Selected socio-demographic characteristics of the included participants are shown in Table 1 (see supplementary information for other variables). More than one third of participants were male; the average age was about 36 years in both groups. The majority of participants had at least a secondary education, with almost 40% having an academic education. The country of origin was in Asia/Pacific for 14.8% of them; in Europe or Central Asia for 34.0%; in the Americas or the Caribbean for 26.8%; and in the Middle East or Africa for 24.4%. Most participants were permanent residents in Italy (59.7%), 22.4% had a temporary permit to stay, and 17.9% were refugees or asylum seekers. The reported travel duration to reach Italy was over six months for 16.3% of participants (see Table 1).

Assessment of more than 10% of DWM and PM+ sessions indicated near-perfect fidelity. Only in a few cases (<10) DWM calls were longer than the established duration (i.e., 30 min). We identified minor deviations from the PM+ protocol, due to adaptations for cultural aspects, or specific content that did not totally apply to the problems reported by participants. The total supervision time required for all sessions of DWM and PM+ was 3 hours per helper on average (approximately 12 hours in total).

At T2 (week 7), 32.4% (35/108) of participants allocated to the intervention arm versus 21.1% (23/109) allocated to the control condition reported a clinically significant improvement in distress, as shown by a score below the cutoff of 16 at the K10. In the experimental arm, therefore, 35 participants did not step into PM+. The mean K10 value at T2 was 19.49 (SD=5.91) in the intervention arm and 22.94 (SD=8.13) in the control condition. During the study period, apart from the experimental or control intervention, the mental and physical health care received did not differ between the two groups (see supplementary information).

Differences between study conditions on primary and secondary outcome measures are reported in Table 2. The stepped-care programme led to a significant reduction of anxiety and depression symptoms compared to CAU, as measured by the PHQ-ADS at T4 (coefficient: –3.460, SE=1.050, p=0.001) (primary outcome). The same was observed at the other timepoints (coefficient:

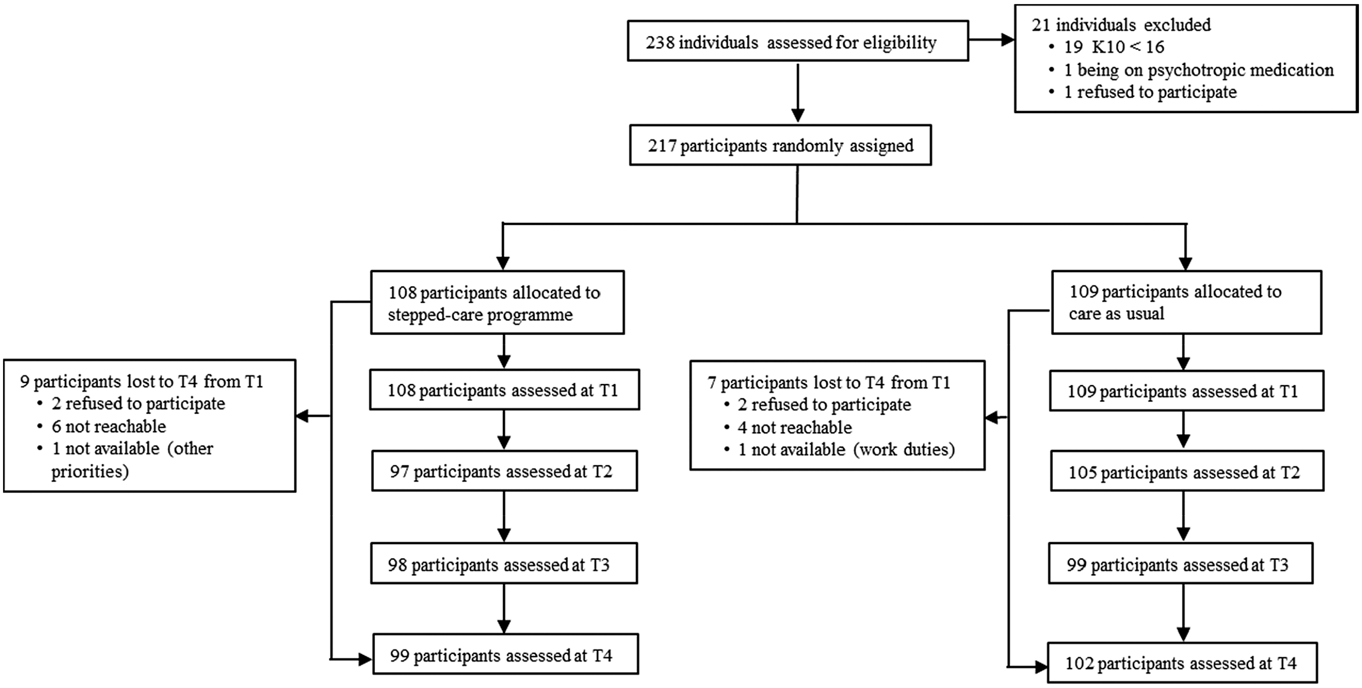

Figure 1 CONSORT-SPI flow diagram. K10 – Kessler Psychological Distress Scale

Table 1 Socio-demographic and clinical characteristics of study participants by treatment allocation

	All participants	Intervention group	Control group	Difference (SE)	SMD
Age (years), mean±SD	35.7±12.5	35.5±13.1	35.9±11.9	–0.414 (1.735)	0.033
Gender (%)					
Female	62.7	68.5	56.9	0.116 (0.065)	**0.241**
Male	36.4	31.5	41.3	–0.098 (0.065)	**0.204**
Other	0.9	0	1.8	–0.018 (0.013)	**0.192**
Education level (%)					
Up to primary school	12.2	8.3	16.0	–0.077 (0.047)	**0.235**
Secondary school	48.5	50.0	47.0	0.030 (0.072)	0.060
University	39.3	41.7	37.0	0.047 (0.070)	0.095
Country of origin (%)					
Asia/Pacific	14.8	17.5	12.3	0.052 (0.049)	**0.146**
Europe or Central Asia	34.0	35.9	32.1	0.038 (0.066)	0.081
America or Caribbean	26.8	23.3	30.2	–0.069 (0.061)	**0.155**
Middle East or Africa	24.4	23.3	25.5	–0.022 (0.060)	0.050
Legal status (%)					
Temporary permit	22.4	22.9	22.0	0.009 (0.060)	0.022
Permanent resident	59.7	64.6	55.0	0.096 (0.070)	**0.195**
Refugee or asylum seeker	17.9	12.5	23.0	–0.105 (0.054)	**0.276**
Travel duration (%)					
Up to six months	83.7	85.4	82.0	0.034 (0.053)	0.092
Over six months	16.3	14.6	18.0	–0.034 (0.053)	
Ever consulted a mental health professional (%)					
Yes	41.5	38.9	44.0	–0.051 (0.071)	**0.102**
No	58.5	61.1	56.0	0.051 (0.071)	
Having an income (%)					
Yes	56.5	60.2	53.1	0.072 (0.072)	**0.144**
No	43.5	39.8	46.9	–0.072 (0.072)	
Measures at baseline, mean±SD					
PHQ-ADS score	19.08±8.69	19.14±8.56	19.02±8.89	–0.119 (1.185)	0.014
PHQ-9 score	10.05±4.93	9.87±4.82	10.22±5.07	–0.350 (0.672)	0.071
GAD-7 score	9.03±4.52	9.15±4.65	8.92±4.43	0.231 (0.616)	0.051
PCL-5 score	11.77±7.23	12.05±7.36	11.49±7.14	0.562 (0.989)	0.075
PSYCHLOPS score	13.304±4.079	13.343±4.276	13.264±3.890	0.079 (0.566)	0.019

SMD – standardized mean difference, SE – standard error, PHQ-ADS – Patient Health Questionnaire Anxiety and Depression Scale, PHQ-9– Patient Health Questionnaire-9, GAD-7 – Generalized Anxiety Disorder-7, PCL-5 – PTSD Checklist for DSM-5, PSYCHLOPS – Psychological Outcomes Profiles. SMD values in bold prints are those above the threshold for imbalance.

–3.742, SE=1.008, p<0.001 at T2; coefficient: –6.381, SE=1.039, p<0.001 at T3). Figure 2 shows the trend over time in the average values of symptoms of depression and anxiety measured by the PHQ-ADS in each of the two groups, with their CIs.

A significant difference was also observed considering depression and anxiety symptoms separately at all timepoints (see Table 2). The stepped-care programme, compared with CAU, was also associated with larger improvements for PTSD symptoms at T3 (coefficient: –3.513, SE=0.827, p<0.001) and T4 (coefficient: –2.523, SE=0.763, p=0.001), and for self-assessed problems, function and well-being at all timepoints (see Table 2).

The results of the ITT analysis were confirmed by the PP analysis (see Table 3). Secondary analyses conducted without any imputations of missing values did not identify any relevant difference with respect to the main analyses (see supplementary information). As the two groups differed on some socio-demographic vari-

Table 2 Results for primary and secondary outcomes at each timepoint (intention-to-treat analysis)

	Intervention Estimated average value (SE)	Control Estimated average value (SE)	Coefficient (SE)	p	Standardized coefficient (SE)
PHQ-ADS score					
T2	12.303 (0.696)	16.045 (0.728)	–3.742 (1.008)	**<0.001**	–0.414 (0.111)
T3	9.112 (0.631)	15.493 (0.825)	–6.381 (1.039)	**<0.001**	–0.705 (0.115)
T4 (primary outcome)	10.625 (0.730)	14.085 (0.755)	–3.460 (1.050)	**0.001**	–0.382 (0.116)
PHQ-9 score					
T2	6.769 (0.390)	8.414 (0.400)	–1.645 (0.560)	**0.003**	–0.324 (0.110)
T3	5.123 (0.368)	8.300 (0.502)	–3.177 (0.623)	**<0.001**	–0.625 (0.123)
T4	5.978 (0.418)	7.292 (0.420)	–1.314 (0.593)	**0.027**	–0.258 (0.117)
GAD-7 score					
T2	5.537 (0.336)	7.621 (0.391)	–2.085 (0.516)	**<0.001**	–0.471 (0.117)
T3	3.995 (0.308)	7.193 (‘0.423)	–3.198 (0.523)	**<0.001**	–0.723 (0.118)
T4	4.652 (0.348)	6.783 (0.400)	–2.131 (0.531)	**<0.001**	–0.482 (0.120)
PCL-5 score					
T2	8.422 (0.630)	10.056 (0.568)	–1.633 (0.849)	0.054	–0.235 (0.122)
T3	6.079 (0.540)	9.592 (0.625)	–3.513 (0.827)	**<0.001**	–0.506 (0.119)
T4	5.994. (0540)	8.517 (0.538)	–2.523 (0.763)	**0.001**	–0.363 (0.110)
PSYCHLOPS score					
T2	8.085 (0.506)	10.234 (0.529)	–2.149 (0.732)	**0.003**	0.392 (0.134)
T3	6.379 (0.520)	9.907 (0.572)	–3.528 (0.773)	**<0.001**	–0.644 (0.141)
T4	5.427 (0.479)	8.995 (0.533)	–3.567 (0.717)	**<0.001**	–0.651 (0.131)

SE – standard error, PHQ-ADS – Patient Health Questionnaire Anxiety and Depression Scale, PHQ-9 – Patient Health Questionnaire-9, GAD-7 – Generalized Anxiety Disorder-7, PCL-5 – PTSD Checklist for DSM-5, PSYCHLOPS – Psychological Outcomes Profiles. Bold prints indicate statistically significant differences.

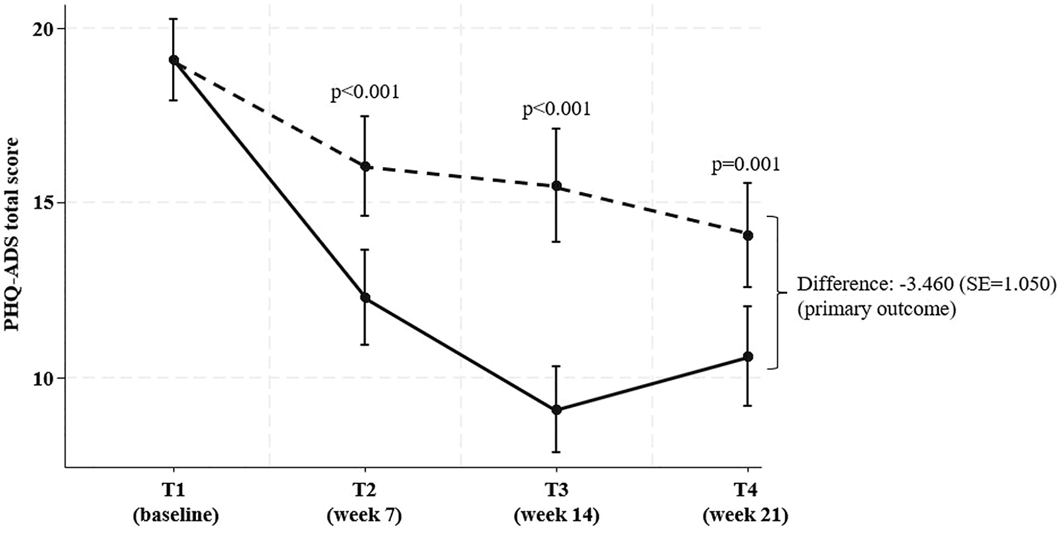

Figure 2 Average PHQ-ADS (Patient Health Questionnaire Anxiety and Depression Scale) total score at different timepoints, with confidence intervals, in intervention (solid line) and control (dotted line) arms (intention-to-treat population). SE – standard error.

ables at baseline, we included these variables in planned regression analyses of the primary outcome, without finding relevant differences in relation to our main analyses (see supplementary information).

We also tested, as planned, for interactions between intervention allocation and potential moderators (baseline score on the

Table 3 Coefficients for primary and secondary outcomes at each timepoint (per-protocol analysis)

	Coefficient (SE)	p
PHQ-ADS score		
T2	–4.215 (1.039)	**<0.001**
T3	–6.982 (1.043)	**<0.001**
T4 (primary outcome)	–4.208 (1.068)	**<0.001**
PHQ-9 score		
T2	–1.948 (0.609)	**0.001**
T3	–3.493 (0.612)	**<0.001**
T4	–1.696 (0.612)	**0.006**
GAD-7 score		
T2	–2.256 (0.542)	**<0.001**
T3	–3.491 (0.545)	**<0.001**
T4	–2.504 (0.545)	**<0.001**
PCL-5 score		
T2	–1.831 (0.828)	**0.027**
T3	–4.088 (0.826)	**<0.001**
T4	–2.930 (0.830)	**<0.001**
PSYCHLOPS score		
T2	–2.606 (0.739)	**<0.001**
T3	–3.796 (0.776)	**<0.001**
T4	–4.044 (0.729)	**<0.001**

SE – standard error, PHQ-ADS – Patient Health Questionnaire Anxiety and Depression Scale, PHQ-9 – Patient Health Questionnaire-9, GAD-7 – Generalized Anxiety Disorder-7, PCL-5 – PTSD Checklist for DSM-5, PSYCHLOPS – Psychological Outcomes Profiles. Bold prints indicate statistically significant values.

primary outcome, age, gender, legal status, time since resettlement; whether the person had at least secondary education, was receiving an income, and had ever consulted a mental health professional). In mixed models built on our main model, by adding such variables and their interaction with intervention allocation as regressors, only the baseline value of the primary outcome measure was statistically significant, and remained so after the Benjamini-Hochberg correction (p=0.006, see Table 4). The effect of the intervention on reducing PHQ-ADS scores was stronger for participants with higher scores at baseline (see supplementary information).

Table 4 Test for interactions of potential moderators with treatment

	Chi-square	p	Adjusted p
Baseline score on the primary outcome	17.17	**0.0007**	**0.006**
Gender	0.71	0.872	0.885
Age	4.48	0.214	0.506
At least secondary education	7.32	0.292	0.506
Legal status	7.06	0.316	0.506
Time since resettlement	3.65	0.302	0.506
Income	1.85	0.605	0.807
Ever consulted a mental health professional	0.65	0.885	0.885

The reported adjusted p values are those following Benjamini-Hochberg correction. Bold prints indicate statistically significant values.

We did not identify any serious adverse event. Six adverse events were identified, all of them regarded as unrelated to study participation (one accidental fall, one suicidal thought, two hospitalizations for a medical condition, two bereavement conditions).

DISCUSSION

In a migrant population with elevated psychological distress, a stepped-care programme combining DWM and PM+ (two WHO-developed, low-intensity, task-shifting psychological interventions) was effective in alleviating anxiety and depressive symptoms.

Efficacy was consistently observed at different timepoints, with coefficients indicating a substantial impact. Improvements were noted in depression and anxiety symptoms separately across all timepoints. Furthermore, the stepped-care programme showed positive effects on PTSD symptoms and self-assessed problems, function and well-being.

Exploratory analyses for heterogeneity did not detect significant interactions between the intervention and potential moderators, except for baseline values of the primary outcome measure. Notably, the intervention effect was more pronounced in participants with higher baseline levels of anxiety and depression, which can be seen as further evidence of its impact. The same finding was reported in a trial of PM+ for Syrian refugees[41] and in a trial testing stepped-care DWM/PM+ in health care workers in Spain[17]. In terms of acceptability, no serious adverse events were detected and very few participants were lost at follow-up. These findings support the programme's effectiveness and suggest its applicability to migrant populations.

The beneficial effects of the stepped-care programme may be related to various factors. DWM, based on acceptance and commitment therapy, aims to increase psychological flexibility and improve coping strategies to deal with adversity. As it is self-administered and only facilitated by trained helpers, it offers the opportunity to practice exercises through an online web/app, and to learn ways of recognizing and managing emotional states[9,42,43]. DWM might have encouraged participants to better adapt to fluctuating situational demands, by helping them to find ways of acting in accordance with their values, even in the face of external difficulties and migration-related stressors[43]. Participants may have acquired and consolidated skills to accommodate and "unhook" from difficult thoughts and feelings, through the integration of mindfulness techniques practiced regularly.

The possibility to move to PM+ for those still experiencing distress after DWM was a practical source of help in identifying and managing problems. PM+ helps people to improve the management of practical (e.g., unemployment, interpersonal conflict, poverty) and psychological (e.g., depression, anxiety, grief, fear, feelings of helplessness) problems. Additionally, PM+ ingredients such as behavioral activation and use/strengthening of social support may have contributed to lowering symptoms of common mental disorders. Psychotherapy research indicates that guided Internet-based psychological interventions are influenced by social support to a greater extent than in-person therapy[44,45]. This is attributed to the fact that online interventions heavily depend on self-motivation and the completion of activities even in the absence of direct or long therapist interaction[44,46].

Moreover, the interpersonal dynamics with helpers may have exerted a direct and positive impact on outcomes[47]. These dynamics are particularly important for migrants, because of the potential lack of robust social support and networks in the country of resettlement. A systematic review of 35 RCTs, which examined 33 mental health interventions delivered through a digital format, found that the effects were larger when interventions were complemented with clinical assistance[48]. This underscores the key role of helpers in our trial, especially for PM+.

In addition, the digital format of DWM and PM+ is more flexible than in-person delivery, and could have contributed to increasing attendance, as highlighted by the low number of participants who did not complete the sessions. This, in turn, could have reinforced the effect of the intervention. In previous RCTs testing SH+ delivered in person and in groups to asylum seekers and refugees, we identified high proportions who did not attend the sessions[12,13]. This may reflect the fact that migrants have many competing priorities other than attending mental health-focused interventions, such as meeting basic needs, securing housing, navigating legal procedures, finding a job, and learning a new language[24].

We note some limitations of our study. First, we were inclusive in the definition of migrant participants, with the advantage of identifying a large group of distressed people, including asylum seekers, refugees and people in unstable living conditions. However, factors such as the type and number of stressors, barriers in the host country, availability of social support and sheltering centres, and time since resettlement, might have generated heterogeneity in the sample, with potential impact on the intervention's effect[49]. Nonetheless, when we tested for interactions between intervention allocation and age, gender, education level, time since resettlement, legal status and receiving an income, we found no signal that the effect of the stepped-care programme might differ with respect to these factors. Additionally, the main socio-demographic characteristics of the population group of our trial are aligned with those reported by the International Organization for Migration in relation to international migration flows and migrants resettled in Italy[1]. All this suggests that the stepped-care programme has a potential of uptake across migrant populations beyond this trial.

A second limitation is that a double-blind design was not feasible, and outcome measures were not assessed by masked assessors, but were self-reported. The use of self-reports can introduce variability and reduce the reliability of data, and the participants' overall perception of the intervention may influence how they report outcomes, leading to wrong estimates of effects. In the present study, however, this risk was mitigated by a design in which all participants received a supportive intervention, i.e. PFA. It is therefore likely that participants in both arms had similar perceptions of care. The finding that losses to follow-up were minimal and similarly distributed in the two intervention arms appears to support this consideration. We also observed that the use of social and health care services was similar in the two groups during the study, highlighting a low risk of performance bias.

Third, the study had a relatively short follow-up period. Therefore, we cannot exclude that the positive effects that we observed would diminish over longer follow-up periods. Moreover, our study was not specifically designed to test a stepped-care model against a single intervention. Future studies could usefully examine the stepped-care model versus PM+ or DWM as stand-alone interventions.

Overall, these results significantly expand the existing knowledge on the efficacy of psychological interventions in migrant populations, by showing for the first time that low-intensity, task-shifting interventions with freely accessible manuals may be implemented as a stepped-care programme to alleviate anxiety and depression in migrants with elevated distress. Due to these characteristics, these interventions are uniquely suited for implementation in low-resource settings. Considering that even countries classified as middle- or high-income, such as Italy, may experience significant resource constraints in certain sectors, regions, or for certain populations such as migrants, these interventions may be appropriate for countries at any level of economic development.

Regarding implications for policy makers aiming to scale up these interventions, local adaptation may be a key factor[26,50,51]. It is important to tailor the stepped-care programme to the specific needs and characteristics of the target population. The demographics, cultural norms and unique challenges of the community or group for whom the intervention is intended should be carefully assessed[52-54]. Adaptation may involve translating materials into local languages, considering cultural sensitivities, and incorporating feedback from local stakeholders, to make the intervention accurate, understandable and acceptable.

A second consideration is that the stepped-care programme may be scaled up in parallel or in series with existing services. In the parallel approach, it is introduced alongside the existing services, creating a parallel track for addressing vulnerability to mental health challenges. By introducing parallel interventions, it may be possible to reach more migrant groups, outside the health care sector, ensuring that a broader spectrum of people can access the support that they require. However, there are some challenges associated with parallel implementation: in particular, it can strain resources, as it necessitates separate funding, staffing and infrastructure. This can lead to inefficiencies or duplication of efforts.

In contrast, the series approach involves introducing the stepped-care programme sequentially, for example before or after migrants have received the existing social services. One key advantage of implementing in series is resource efficiency. It maximizes the use of existing infrastructure and personnel before introducing new elements, minimizing duplication of resources. However, the series approach may be less adaptable to evolving needs or changing circumstances, and it may not accommodate specific, targeted interventions as effectively as the parallel approach.

The scale-up of the stepped-care programme, either in parallel or in series with existing services, needs to be studied using quantitative or mixed approaches, aiming to identify the most cost-effective implementation strategies.

In conclusion, this study provides evidence supporting the effectiveness of the stepped-care delivery of DWM and PM+ in migrant population groups with elevated distress. Existing evidence-based guidelines and implementation packages should be updated accordingly, and applied by various social and health care organizations, to ensure that migrant groups have equitable access to high-quality mental health care.

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ORIGINAL ARTICLE

Clinical decision making and outcome in the routine care of people with severe mental illness across Europe (CEDAR)

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Aims. Shared decision making has been advocated as a means to improve patient-orientation and quality of health care. There is a lack of knowledge on clinical decision making and its relation to outcome in the routine treatment of people with severe mental illness. This study examined preferred and experienced clinical decision making from the perspectives of patients and staff, and how these affect treatment outcome.

Methods. "Clinical Decision Making and Outcome in Routine Care for People with Severe Mental Illness" (CEDAR; ISRCTN75841675) is a naturalistic prospective observational study with bimonthly assessments during a 12-month observation period. Between November 2009 and December 2010, adults with severe mental illness were consecutively recruited from caseloads of community mental health services at the six study sites (Ulm, Germany; London, UK; Naples, Italy; Debrecen, Hungary; Aalborg, Denmark; and Zurich, Switzerland). Clinical decision making was assessed using two instruments which both have parallel patient and staff versions: (a) The Clinical Decision Making Style Scale (CDMS) measured preferences for decision making at baseline; and (b) the Clinical Decision Making Involvement and Satisfaction Scale (CDIS) measured involvement and satisfaction with a specific decision at all time points. Primary outcome was patient-rated unmet needs measured with the Camberwell Assessment of Need Short Appraisal Schedule (CANSAS). Mixed-effects multinomial regression was used to examine differences and course over time in involvement in and satisfaction with actual decision making. The effect of clinical decision making on the primary outcome was examined using hierarchical linear modelling controlling for covariates (study centre, patient age, duration of illness, and diagnosis). Analysis were also controlled for nesting of patients within staff.

Results. Of 708 individuals approached, 588 adults with severe mental illness (52% female, mean age = 41.7) gave informed consent. Paired staff participants ($N = 213$) were 61.8% female and 46.0 years old on average. Shared decision making was preferred by patients ($\chi^2 = 135.08$; $p < 0.001$) and staff ($\chi^2 = 368.17$; $p < 0.001$). Decision making style of staff significantly affected unmet needs over time, with unmet needs decreasing more in patients whose clinicians preferred active to passive (−0.406 unmet needs per two months, $p = 0.007$) or shared (−0.303 unmet needs per two months, $p = 0.015$) decision making.

Conclusions. Decision making style of staff is a prime candidate for the development of targeted intervention. If proven effective in future trials, this would pave the ground for a shift from shared to active involvement of patients including changes to professional socialization through training in principles of active decision making.

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Introduction

The implementation of effective interventions hinges upon clinical decisions made between patients and mental health professionals. Clinical decision making

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in persistent conditions differs from well-defined acute care situations in many ways. Clinical decision-making in the treatment of severe mental illness (SMI) is characterised by a focus on long-term disease management, with patients being highly knowledgeable about their illness. A high number of decisions have to be made frequently, often involving more than one service provider or informal carer (Watt, 2000). The defining features of decision making include context (direct and indirect background variables, such as information and preferences), the actual process of decision making and its evaluation, and outcome (Entwistle & Watt, 2006; Puschner *et al.* 2010; Wills & Holmes-Rovner, 2006).

Three of decision making styles have been proposed to characterise the degree of patient involvement in decision making: passive or paternalistic (decision is made by the staff, patient consents), shared (information is shared and decision jointly made) and active (staff informs, patient decides) (Charles *et al.* 1997; Coulter, 2003). Over the past 20 years, shared decision making has been recommended as the optimal style to improve patient-orientation and quality of health care (The Lancet, 2011; Del Piccolo & Goss, 2012). Although it has been shown that people with mental illness want to be informed about and have a say in their care (Hamann *et al.* 2005; Hill & Laugharne, 2006), practitioners have largely failed to adopt principles of shared decision making in their daily routine (Goss *et al.* 2008; Karnieli-Miller & Eisikovits, 2009; Légaré *et al.* 2010; de las Cuevas *et al.* 2012; Storm & Edwards, 2013). Furthermore, the evidence base for the impact of shared decision making on health status is limited (Joosten *et al.* 2008), especially in mental health care (Duncan *et al.* 2010). This is a clinically important knowledge gap. Staff decision-making style can be changed, so if it impacts on patient outcome then it provides a target for potential intervention. Longitudinal studies are necessary to provide empirical data about these important clinical issues (Hölzel *et al.* 2013).

In summary, there is a lack of knowledge on clinical decision making and its relation to outcome in the routine treatment of people with SMI. Specifically, the process of decision-making in real-time encounters has been under-researched (Karnieli-Miller & Eisikovits, 2009; Kon, 2010). This paper addresses these knowledge gaps by examining the following research questions:

(a) Which clinical decision making style is preferred by patients and staff?
(b) What are the levels of involvement and satisfaction with clinical decisions from patient and staff perspectives, and how do these change over time?
(c) How are these aspects of clinical decision making related to outcome?

Methods

'Clinical Decision Making and Outcome in Routine Care for People with Severe Mental Illness' (CEDAR) is a naturalistic prospective longitudinal observational study with bimonthly assessments during a 12-month observation period (T0–T6). The study has been registered (ISRCTN75841675) and is reported in line with the STROBE statement (von Elm *et al.* 2007). The six study sites reflect the diversity across Europe in the organisation of mental health services.

Ulm, Germany (coordinating centre): The Department is responsible for the provision of mental health care in a large catchment area in rural Bavaria (population 671 000). Multidisciplinary teams (psychiatrists, psychologists, social workers, nurses and occupational therapists) offer the full range of pharmacological and psychosocial interventions in inpatient, outpatient and day care clinics. The Department collaborates closely with office-based psychiatrists and psychotherapists in the area. *London, UK*: The site comprised three specialist community teams: early psychosis, assertive outreach and Rehabilitation and Recovery. All teams are multidisciplinary ($n = 10–15$), comprising clinical psychology, nursing, occupational therapy, psychiatry and social work professionals, as well as support workers and administrative staff. These teams provide a service across the London Borough of Croydon (population 330 000) as part of a range of services for adults aged 18–65, including three community mental health teams, home treatment team, community forensic team and in-patient beds. *Naples, Italy*: The Department includes inpatient and outpatient units and 1 day hospital. The outpatient units include specialist clinical teams for the management and treatment of psychotic disorders, mood disorders, eating disorders and obsessive–compulsive disorders. Specialist teams for early detection and management of psychoses and for cognitive and psychosocial rehabilitation are available. *Debrecen, Hungary*: The Department provides in- and outpatient mental health care for the city of Debrecen (population 200 000). The team is completed by an occupational therapist and a social worker professional who keeps contact with the regional rehabilitation institutions and mental homes. *Aalborg, Denmark*: The Psychiatry Region North includes various treatment centres, including inpatient treatment, outpatient teams and early psychosis teams. The collaborating centres in the CEDAR study were organised within Universities of Aarhus, Aalborg, Copenhagen and Southern Denmark. Others were provincial hospitals with associations to Aarhus University. Furthermore, CEDAR collaborated with office-based psychiatrist. *Zurich, Switzerland*: The Department takes responsibility for a defined catchment area in Zurich City of about 390 000 inhabitants. It comprises 488 beds and additionally offers specialised care in a crisis centre and centre for psychiatric rehabilitation.

Participants

The study was approved by the ethical review boards at each study site. Participants were recruited from caseloads of outpatient/community mental health services. Inclusion criteria were: adult age (18–60 years, chosen to match the age range seen by adult mental health services across the participating sites) at intake, mental disorder of any kind as main diagnosis established by case notes or staff communication using SCID criteria (First *et al.* 1997); presence of SMI (Threshold Assessment Grid ≥5 points (Slade *et al.* 2003) and illness duration ≥2 years); expected contact with mental health services (excluding inpatient services) during the time of study participation; sufficient command of the host country's language; and capability of giving informed consent. Exclusion criteria were: primary clinical diagnosis of mental retardation, dementia, substance use or organic brain disorder; cognitive impairment severe enough to make it impossible to give meaningful information on study instruments; and treatment by forensic mental health services. A paired member of staff was identified by the service user. Data were collected via questionnaires (filled in by the patient and their key worker) or via interviews conducted by the *CEDAR* study workers every 2 months for 1 year. Data entry modes were via computer or paper-pencil forms. Figure 1 shows the flow of participants through the phases of the study. Between November 2009 and December 2010, 708 patients were screened for inclusion of which 588 were included after having given written informed consent.

Measures

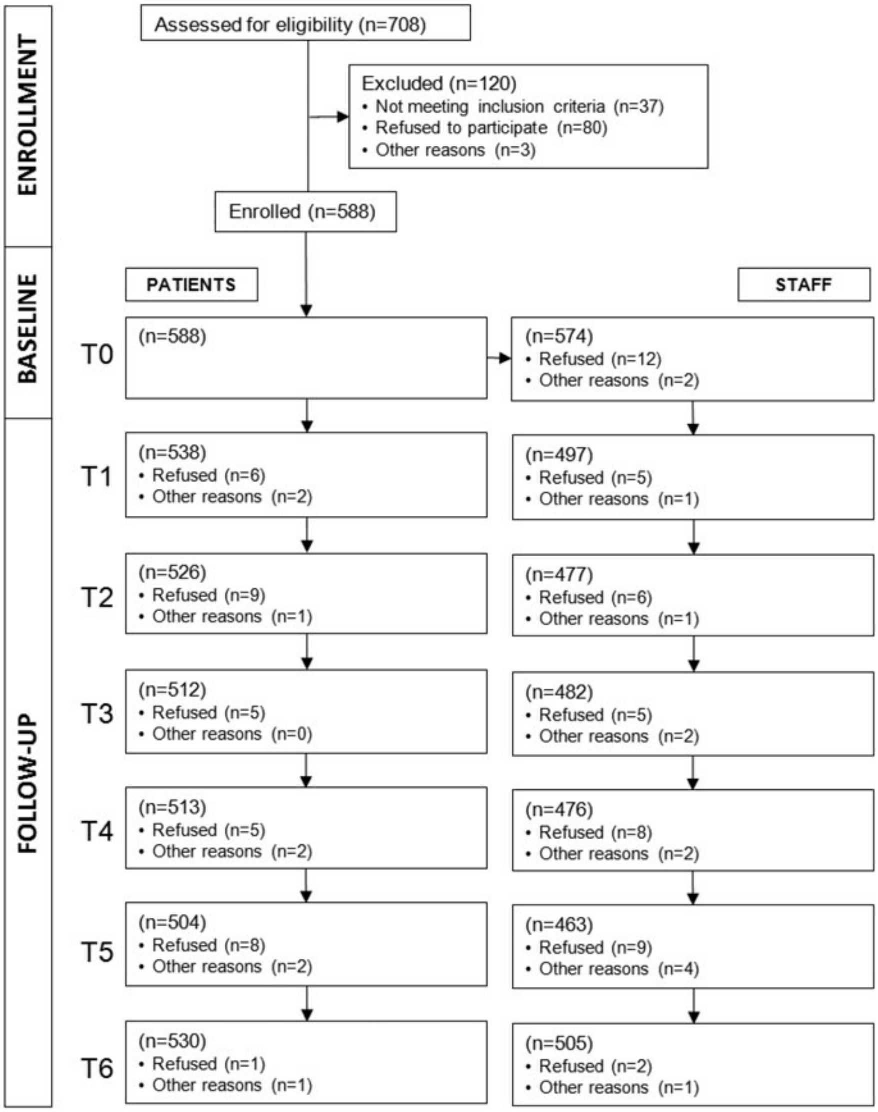
The *Clinical Decision Making Style Scale* (CDMS; Puschner *et al.* 2013) measured preferences for decision making at baseline. Parallel patient (CDMS-P) and staff (CDMS-S) versions both have 20 items rated on a five-point Likert scale in three sections: (A) six items referring to general preferences regarding patient autonomy in decisions; (B) nine items referring to decision making preferences in three scenarios; and (C) five items referring to desire for information. CDMS sub-scales are Participation in Decision Making (PD) which consists of the mean of items in sections A and B (with a higher score indicating a higher desire by the service user to be an active participant in decision making), and Information (IN) consisting of the mean of items in sections C (ranging 0–4, 0 with a higher score indicating a higher desire by the service user to be provided with information). Categorical sum scores were formulated on the basis of utility where an emphasis was placed on separating categories according to clinical meaningfulness. Categories for the PD sub-scale were 'passive' (<1.5), 'shared' (1.5–2.5) and 'active' (>2.5), and for the IN sub-scale were 'low' (<2.0), 'moderate' (2.0–3.0) and 'high' (>3.0).

The *Clinical Decision Making Involvement and Satisfaction Scale* (CDIS; Slade *et al.* 2014) measured involvement and satisfaction with a specific decision at all time points. In order to have a common unit of analysis, patient and staff rated the decision identified by the patient as being the most important made at the latest treatment session. The scale has parallel patient (CDIS-P) and staff versions (CDIS-S). Each of the six items of the Satisfaction sub-scale is rated on a five-point Likert scale from 'strongly disagree' (1) to 'strongly agree' (5), yielding a total score of the mean of all items, ranging from 1 (low satisfaction) to 5 (high satisfaction). Clinical utility categories for the Satisfaction sub-scale were 'low' (<3.0), 'moderate' (3.0–4.0) and 'high' (>4.0). The Involvement sub-scale comprises one item about level of involvement experienced, which uses five categories which were collapsed into three ('active', 'shared' and 'passive' involvement). The CDMS and CDIS in all five study languages can be downloaded at http://www.cedar-net.eu/instruments.

Needs were assessed at all time points by the patient-rated version of the *Camberwell Assessment of Need Short Appraisal Schedule* (CANSAS-P; Trauer *et al.* 2008) which measures the presence of a met or unmet need in 22 domains, yielding a total score indicating number of unmet needs ranging from 0 (low) to 22. Further measures included the *Global Assessment of Functioning Scale* (GAF; Jones *et al.* 1995) which is a staff-rated one-item global measure of symptomatology and social functioning, ranging from 1 (worst) to 100, and the *Client Sociodemographic and Service Receipt Inventory* (CSSRI-EU; Chisholm *et al.* 2000) which is a standardised method for collating information on socio-economic status and service use. Participants were assessed by trained researchers not involved in the care process.

Sample size

Sample size calculation for the analyses of the primary outcome (effect of decision making on unmet needs over 1 year) via hierarchical linear modelling taking



Numbers given for staff indicate observations per patient, not number of staff.

Fig. 1. Study participant flow.

into account the centre-effect yielded a needed sample size of $N = 561$ (94 per centre). See study protocol for details (Puschner *et al.* 2010).

Statistical analysis

Chi-square tests were used to compare proportions of the four nominal CDMS subscales. Baseline differences and change over time of the nominal CDIS subscales were examined by four mixed-effects multinomial regression models with time as fixed effect (Hedeker, 2003). Based on concepts of causality (Bollen, 1989) and modelling change (Singer & Willett, 2003), it was specifically tested for the 1-year observation period whether time-invariant (CDMS at baseline and covariates) and time-varying (CDIS at T0–T5) predictors affected subsequent unmet needs 2 months thereafter (T1–T6). This was done using of hierarchical linear modelling (Raudenbush & Bryk, 2002) with the time variable months (0, 2, 4, 6, 8, 10 and 12). Fixed effects were time, clinical decision making variables, and covariates to control for confounding (study centre, patient age, duration of illness and diagnosis). Clustering of data (patients nested in key workers) was taken into account by specifying participants and staff as random effects.

Double-sided critical levels for significance tests were used. Prorating was used to deal with missing items in the computation of subscales for each

Table 1. Characteristics of patients ($n = 588$) and staff ($n = 213$)

Patients	
Study centre: Ulm, *n* (%)	112 (19.05)
London, *n* (%)	85 (14.46)
Naples, *n* (%)	101 (17.18)
Debrecen, *n* (%)	97 (16.49)
Aalborg, *n* (%)	98 (16.67)
Zurich, *n* (%)	95 (16.16)
Gender; female, *n* (%)	307 (52.21)
Age; years, mean (s.d.)	41.69 (10.74)
Married; *n* (%)	149 (25.38)
Ethnic group; Caucasian; *n* (%)	552 (94.04)
Years in school; mean (s.d.)	10.43 (1.88)
Living alone; *n* (%)	231 (39.55)
Paid or self employed; *n* (%)	110 (18.74)
Receiving state benefits; *n* (%)	425 (72.40)
Illness duration; years, mean (s.d.)	12.51 (9.27)
Diagnosis: psychotic disorder, *n* (%)	269 (45.75)
Mood disorder, *n* (%)	200 (34.01)
Other, *n* (%)	119 (20.24)
TAG; mean (s.d.)	7.54 (2.24)
GAF; mean (s.d.)	49.03 (10.96)
Staff	
Study centre: Ulm, *n* (%)	48 (22.54)
London, *n* (%)	38 (17.84)
Naples, *n* (%)	17 (7.98)
Debrecen, *n* (%)	8 (3.79)
Aalborg, *n* (%)	59 (27.69)
Zurich, *n* (%)	43 (20.19)
Gender; female, *n* (%)	128 (61.84)
Age; years, mean (s.d.)	46.03 (10.47)
Profession: psychiatrist, *n* (%)	75 (36.41)
Psychologist, *n* (%)	19 (9.22)
Social worker, *n* (%)	11 (5.34)
Other, *n* (%)	101 (49.03)
Working in outpatient mental health services; years, mean (s.d.)	9.41 (8.44)
Working in mental health services; years, mean (s.d.)	14.99 (9.66)
Number of patients in study; mean (s.d.)	2.76 (4.46)

Missing values patients: $n = 1$ (married, ethnic group, work and benefits), $n = 4$ (living), $n = 11$ (school), $n = 29$ (GAF). Missing values staff: $n = 6$ (gender), $n = 7$ (profession), $n = 54$ (working outpatient), $n = 41$ (working mental health).

participant, so long as there were fewer than 20% missing items for that participant, or else the scale was set to missing. Scales with specific instructions were exempted from this rule (as in the case of the CANSAS). Otherwise, there was no imputation of missing values. EpiData and SPSS versions 19–21 were used for data acquisition and checking, SuperMix 1 for the mixed-effects multinomial regression models and S-PLUS (version 6.2) for the hierarchical linear models.

Results

Sample

Table 1 gives an overview of sample characteristics. GAF score indicates serious symptomatology and social disability, indicating that the TAG threshold had successfully resulted in a sample of participants who can be characterised as having SMI. The 'other' category for professions included nurses, district nurses, support time and recovery workers, and psychiatric trainees.

Preferred and experienced clinical decision making

Differences in proportions were significant for all four CDMS subscales. Both patients and staff indicated 'shared' as their preferred style of participation in decision making, with staff showing a stronger preference than patients. Desire for information was predominantly high in patient report, and mostly moderate in the view of staff (Table 2).

For the CDIS it was found that at baseline involvement in the last decision made was predominantly rated as 'shared' by both patients and staff (see intercepts in upper part of Table 3 and starting levels in Figure 2). Furthermore, patient ratings of 'shared' involvement significantly increased over time, accompanied by a decrease in rating of 'active' and 'passive'. A similar trend of involvement ratings was found for staff (see month 2–month 12 in upper part of Table 3).

Furthermore, the majority of the patients rated high the satisfaction with the way the last decision was made, a considerable proportion were moderately satisfied, and hardly any indicated low satisfaction. In comparison, staff satisfaction ratings were mostly moderate, closely followed by high and hardly ever low (see intercepts in lower part of Table 3 and starting levels in Figure 3). With only minimal changes, satisfaction ratings by both patients and staff were rather stable over time (Table 3).

Clinical decision making and outcome

As shown in Table 2, there was a decrease in number of unmet needs over time. An unconditional hierarchical linear model showed that at baseline, starting level (intercept) was 3.30 unmet needs which significantly declined over time by −0.16 points per 2 months (slope; $t = -9.06$; $p < 0.001$; 3640 observations of 586 participants). To control for effects of study drop-out, this analysis was repeated for participants for whom number of unmet needs were available at all seven measurement points ($N = 378$), resulting in a similar pattern with intercept = 3.05 unmet needs and slope = −0.18 ($t = -9.41$; $p < 0.001$; 2646 observations).

As shown Table 4, a conditional hierarchical linear model yielded that slope constant was no longer

Table 2. *Preferred clinical decision making style (participation and information) at baseline, and unmet needs over time*

		N	Difference
CDMS-P participation			
Passive, *n* (%)	175 (29.9)	586	$\chi^2 = 135.08$; $p < 0.001$
Shared, *n* (%)	319 (54.4)		
Active, *n* (%)	92 (15.7)		
CDMS-P information			
Low, *n* (%)	21 (3.6)	587	$\chi^2 = 292.02$; $p < 0.001$
Moderate, *n* (%)	207 (35.3)		
High, *n* (%)	359 (61.2)		
CDMS-S participation			
Passive, *n* (%)	124 (22.0)	563	$\chi^2 = 368.17$; $p < 0.001$
Shared, *n* (%)	397 (70.5)		
Active, *n* (%)	42 (7.5)		
CDMS-S information			
Low, *n* (%)	45 (7.9)	570	$\chi^2 = 205.80$; $p < 0.001$
Moderate, *n* (%)	324 (56.8)		
High, *n* (%)	201 (35.3)		
CANSAS-P unmet needs			
Baseline, mean (S.D.)	3.45 (3.09)	574	
Month 2, mean (S.D.)	3.15 (2.99)	526	
Month 4, mean (S.D.)	2.81 (2.86)	514	
Month 6, mean (S.D.)	2.43 (2.67)	501	
Month 8, mean (S.D.)	2.33 (2.81)	510	
Month 10, mean (S.D.)	2.41 (2.76)	497	
Month 12, mean (S.D.)	2.66 (2.82)	518	

CDMS, Clinical Decision Making Style Scale; CANSAS, Camberwell Assessment of Need Short Appraisal Schedule.

significant in the model indicating that the included predictors substantially contributed to explaining variance of the rate of change of unmet needs (Singer & Willett, 2003). Slope was affected by CDMS-S Participation, indicating that reduction of unmet needs over time was significantly higher in patients whose key workers rated their decision making style as active at T0 (*v.* passive). No effects were found for the other variables in the model. When recoding the reference category to shared, the effect of CDMS-S participation on slope remained (active: $\beta = -0.303$, $t = -2.417$, $p = 0.015$).

Discussion

This observational study on clinical decision making in routine care for people with SMI analysed the relationships between decision making style, involvement and satisfaction with decision making, and patient outcome. Both patient and staff perspectives were considered. The study design was longitudinal with seven assessment points.

In line with previous evidence (Hamann *et al.* 2005; Hill & Laugharne, 2006), people with SMI and their key workers predominantly stated a preference for a shared (rather than passive or active) decision making style. Both patients and staff indicated that involvement in decision making during their last treatment session was mainly shared. This trend increased over time, with about 10% more patients and key workers indicating that decision making 1 year later was shared. Furthermore, satisfaction with the decision made at the last treatment session was mostly high in patients and moderate in staff, with very little change over time. This finding corresponds with high and rather stable patient satisfaction with mental health service provision (Ruggeri *et al.* 2006).

Patient-rated unmet needs significantly decreased over time. This pattern was found even when restricting the analysis to participants who had completed all seven measurement points, indicating that the decrease in unmet needs is not due to selective attrition. A comprehensive hierarchical linear model controlling for confounding effects showed that a staff-rated active decision making style was causally related to a significant reduction in patient-rated unmet needs. After 1 year, reduction of unmet needs in patients whose clinicians indicated a preference for an active decision

Table 3. *Experienced clinical decision making (involvement and satisfaction) over time*

	CDIS-P involvement[a]								CDIS-S involvement[b]							
	Shared *v.* passive				Active *v.* passive				Shared *v.* passive				Active *v.* passive			
Parameter	Est.	S.E.	*z*	*p*	Est.	S.E.	*z*	*p*	Est.	S.E.	*z*	*p*	Est.	S.E.	*z*	*p*
Intercept	1.15	0.18	6.49	<0.001	0.32	0.20	1.62	0.106	0.79	0.17	4.53	<0.001	−1.03	0.28	−3.75	<0.001
Month 2	0.47	0.23	2.08	0.038	0.72	0.25	2.92	0.004	0.31	0.22	1.41	0.159	0.59	0.28	2.06	0.039
Month 4	0.50	0.23	2.15	0.031	0.37	0.26	1.44	0.150	0.48	0.24	2.05	0.040	0.80	0.30	2.67	0.008
Month 6	0.62	0.24	2.63	0.009	0.41	0.27	1.56	0.120	0.62	0.24	2.58	0.010	0.71	0.31	2.31	0.021
Month 8	0.67	0.24	2.83	0.005	0.35	0.27	1.29	0.196	0.78	0.24	3.26	0.001	0.03	0.33	0.08	0.934
Month 10	0.78	0.24	3.20	0.001	0.30	0.28	1.06	0.289	0.39	0.26	1.49	0.137	0.07	0.34	0.20	0.845
Month 12	1.13	0.24	4.74	<0.001	0.70	0.27	2.59	0.010	0.75	0.24	3.12	0.002	0.21	0.31	0.67	0.505

	CDIS-P satisfaction[c]								CDIS-S satisfaction[d]							
	Moderate *v.* low				High *v.* low				Moderate *v.* low				High *v.* low			
Parameter	Est.	S.E.	*z*	*p*	Est.	S.E.	*z*	*p*	Est.	S.E.	*z*	*p*	Est.	S.E.	*z*	*p*
Intercept	2.73	0.35	7.90	<0.001	3.05	0.35	8.72	<0.001	3.29	0.41	8.09	<0.001	3.13	0.41	7.56	<0.001
Month 2	1.12	0.40	2.77	0.006	0.58	0.41	1.40	0.162	0.03	0.39	0.08	0.939	−0.54	0.40	−1.35	0.178
Month 4	0.16	0.35	0.47	0.640	−0.33	0.36	−0.93	0.353	−0.25	0.39	−0.63	0.528	−0.93	0.41	−2.29	0.022
Month 6	0.80	0.40	2.00	0.046	0.45	0.41	1.10	0.272	−0.03	0.41	−0.08	0.936	−0.52	0.42	−1.23	0.219
Month 8	0.40	0.38	1.06	0.290	0.19	0.38	0.48	0.629	0.52	0.49	1.06	0.291	0.39	0.50	0.79	0.431
Month 10	0.14	0.37	0.37	0.709	0.18	0.37	0.47	0.637	0.73	0.60	1.23	0.219	0.84	0.60	1.40	0.163
Month 12	0.88	0.40	2.22	0.026	0.63	0.41	1.56	0.119	0.85	0.51	1.66	0.096	0.51	0.52	0.97	0.330

CDIS-P/S, Clinical Decision Involvement and Satisfaction Scale Patient or Staff version; Est., estimate; S.E., standard error

[a] 2444 observations of 651 patients; AIC = 4456.06;

[b] 2223 observations for 621 patients; AIC = 3800.63;

[c] 2447 observations of 650 patients; AIC = 3947.11;

[d] 2227 observations for 621 patients; AIC = 3375.79.

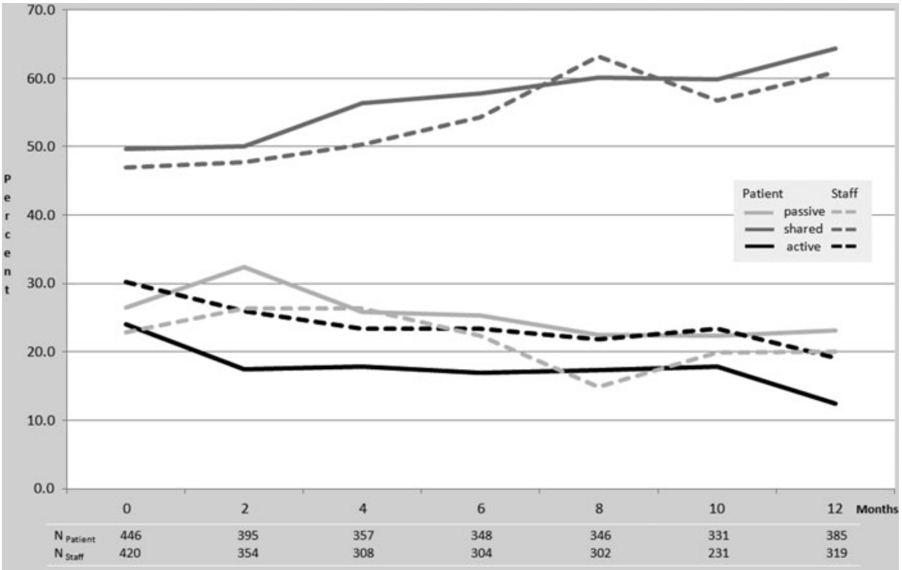


Fig. 2. CDIS involvement over time from patient and staff perspectives.

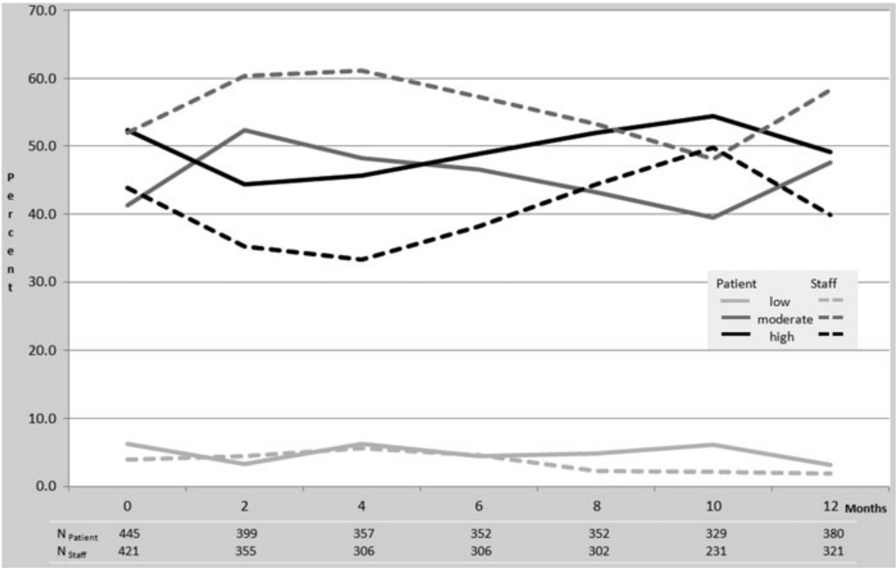


Fig. 3. CDIS satisfaction over time from patient and staff perspectives. Numbers given for staff indicate observations per patient, not number of staff.

making style was 2.44 (0.406 × 6, cf. Table 4) compared to passive, and 1.81 compared to shared. This effect is important because patient-rated unmet needs are associated with important outcome and process variables such as quality of life (Slade *et al.* 2005) and the therapeutic alliance (Junghan *et al.* 2007).

Unmet needs decreased over time, and patient and staff ratings of experienced shared involvement in decisions increased. CEDAR neither delivered an intervention nor encouraged a specific decision making approach, to the finding of decreased unmet needs might indicate the general effectiveness of specialist community treatment over 1 year. However, this result is inconsistent with other research showing relative stability in unmet needs in people with SMI over time at both 4-year (Lasalvia *et al.* 2007) and 10-year follow-up (Arvidsson, 2008). Changes in experienced involvement may be due to social desirability bias, although it is unclear why such bias should increase over time. It is also possible that the increase over time was solely due to study participation, perhaps associated with increased self-monitoring or an

Table 4. *Effect of clinical decision making on unmet needs*

		β	S.E.	CI 95% lower	CI 95% upper	*t*	*p*
Slope constant		−0.290	0.329	−0.935	0.355	−0.88	0.377
CDMS-P	Shared	−0.049	0.067	−0.180	0.082	−0.74	0.461
Participation	Active	−0.128	0.111	−0.346	0.089	−1.16	0.248
CDMS-P	Moderate	0.080	0.151	−0.216	0.376	0.53	0.596
Information	High	0.109	0.149	−0.183	0.401	0.74	0.462
CDIS-P	Shared	0.032	0.090	−0.145	0.210	0.36	0.720
Involvement	Active	0.005	0.103	−0.198	0.207	0.05	0.964
CDIS-P	Moderate	0.000	0.155	−0.305	0.305	0.00	1.000
Satisfaction	High	−0.026	0.156	−0.331	0.280	−0.16	0.870
CDMS-S	Shared	−0.100	0.088	−0.272	0.072	−1.14	0.253
Participation	Active	−0.406	0.149	−0.698	−0.114	−2.73	0.007
CDMS-S	Moderate	0.170	0.128	−0.082	0.421	1.32	0.186
Information	High	0.175	0.132	−0.084	0.434	1.33	0.184
CDIS-S	Shared	0.058	0.083	−0.106	0.222	0.69	0.488
Involvement	Active	−0.023	0.112	−0.242	0.196	−0.20	0.838
CDIS-S	Moderate	0.069	0.181	−0.285	0.424	0.38	0.702
Satisfaction	High	0.068	0.182	−0.290	0.425	0.37	0.711

β, effect estimate; S.E., standard error; CI, confidence interval; 1726 observations of 499 patients within 189 key workers. Akaike information criterion (AIC) = 7668.6. CDMS-P/S, Clinical Decision Making Style Scale Patient or Staff version; CDIS-P/S, Clinical Decision Involvement and Satisfaction Scale Patient or Staff version. Reference categories: 'passive' for CDMS-P/S participation and CDIS-P/S involvement; 'low' for CDMS-P/S information and CDIS-P/S satisfaction. Results of control variables in the model not reported.

assumption – even though not held by the study team – that shared decision making style was optimal. In other words, participation in the study might have been an important stimulus towards shared involvement, at least for staff. Clinical decision making might also differ within subgroups (e.g. by diagnosis, study cite or staff profession). Further analysis of the CEDAR data will examine these important issues.

Strengths and limitations

Strengths of the study include a large sample size of people with SMI from six European countries, and assessment of clinical decision making from both patient and staff perspectives. While adjusted for a number of variables, analyses could still be affected by confounders not controlled for, e.g. change of service provider of dissatisfied patients. It should also be noted that the instruments used to assess decision making did not measure actual behaviour, but preferences and subjective experiences with decision making. Furthermore, outcomes were patient-reported, so results might differ if staff- or observer-rated outcomes were used, as patient-rated scores might have been affected by study participation. Finally, even though overall dropout rates were low, the sample size varied in the different analyses of this paper, with number of missing values increasing with complexity of analyses.

Conclusions and outlook

This study provides evidence to improve decision making by professionals, and at the same time provides tools (CDMS and CDIS measures) for assessing important aspects of clinical decision making (Légaré *et al.* 2010). For the first time, a staff-based causal influence of clinical decision making on outcome could be demonstrated, with two additional patient needs being met over 1 year being a substantial improvement. In line with emerging evidence that increased involvement leads to higher satisfaction (Clarke *et al.* 2014), this means that decision making style of staff is a prime candidate for the development of targeted interventions building upon shared decision making approaches (Torrey & Drake, 2010). If proven effective in future trials, this would pave the ground for a shift from shared to active involvement of patients including changes to professional socialisation through training in principles of active decision making.

CEDAR study group

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Conflict of Interest

None.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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Post-traumatic stress disorder among LGBTQ people: a systematic review and meta-analysis

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Abstract

Aims. Lesbian, gay, bisexual, transgender and queer people (LGBTQ) are at increased risk of traumatization. This systematic review aimed to summarize data regarding the risk of post-traumatic stress disorder (PTSD) for LGBTQ people and their subgroups.
Methods. Medline, Scopus, PsycINFO and EMBASE were searched until September 2022. Studies reporting a comparative estimation of PTSD among LGBTQ population and the general population (i.e., heterosexual/cisgender), without restrictions on participants' age and setting for the enrolment, were identified. Meta-analyses were based on odds ratio (OR and 95% confidence intervals [CI]), estimated through inverse variance models with random effects.
Results. The review process led to the selection of 27 studies, involving a total of 31,903 LGBTQ people and 273,842 controls, which were included in the quantitative synthesis. Overall, LGBTQ people showed an increased risk of PTSD (OR: 2.20 [95% CI: 1.85; 2.60]), although there was evidence of marked heterogeneity in the estimate ($I^2 = 91\%$). Among LGBTQ subgroups, transgender people showed the highest risk of PTSD (OR: 2.52 [95% CI: 2.22; 2.87]) followed by bisexual people (OR: 2.44 [95% CI: 1.05; 5.66]), although these comparisons are limited by the lack of data for other sexual and gender minorities, such as intersex people. Interestingly, the risk of PTSD for bisexual people was confirmed also considering lesbian and gay as control group (OR: 1.44 [95% CI: 1.07; 1.93]). The quality of the evidence was low.
Conclusions. LGBTQ people are at higher risk of PTSD compared with their cisgender/heterosexual peers. This evidence may contribute to the public awareness on LGBTQ mental health needs and suggest supportive strategies as well as preventive interventions (e.g., supportive programs, counselling, and destigmatizing efforts) as parts of a tailored health-care planning aimed to reduce psychiatric morbidity in this at-risk population.

Introduction

Despite continuing actions put to achieve social recognition and legal rights, in many areas of the world, sexual minorities are still highly exposed to traumatization (International Lesbian, Gay, Bisexual, Trans and Intersex Association, 2015). A growing body of evidence underlined that the lesbian, gay, bisexual, transgender and queer people (LGBTQ) are more exposed to traumatic events in life, including hate crimes, intimate partner violence and sexual assaults (Mongelli *et al.*, 2019; Roberts *et al.*, 2010; Seelman *et al.*, 2017; Trombetta and Rollè, 2022; Walters *et al.*, 2013). Also, a higher prevalence of childhood abuse was found among sexual minority children, which accounted for up to half of mental health disparities by sexual orientation, especially for post-traumatic stress disorder (PTSD) (Roberts *et al.*, 2012). According to the diagnostic criteria, PTSD is developed in response to events that overpower the adaptative ability of the person, and the listed traumatic experiences entail being directly exposed to death, threatened death or severe personal damage, including physical or sexual assault (Long *et al.*, 2008). The core clinical features of PTSD are that people tend to re-experience the traumatic event intrusively, with detrimental consequences on personal functioning and high psychological suffering (Pai *et al.*, 2017; Sareen, 2014). In addition, PTSD revealed as a multidimensional disorder, with different neurobiological underpinnings, including alterations of the sympathetic nervous system (De Berardis *et al.*, 2015, 2020). Over the years, the literature identified as traumatic also less intense situations, but for which the traumatic potential consists in the systematic repetition of the experience, such as being persecuted and discriminated against, especially for invariable personal characteristics such as race, religious beliefs, gender and sexual orientation

(Alessi *et al.*, 2013; Auxéméry, 2018; Keating and Muller, 2020; Livingston *et al.*, 2022; Solomon *et al.*, 2021). The Minority Stress Model proposed by Meyer (2003), provides a theoretical framework for understanding the ways in which repeated traumas can lead to an increased prevalence of mental disorders among sexual minorities. Research showed that sexual minorities' minority stress can lead to emotional dysregulation, social and interpersonal conflicts and negative cognition that can mediate the association with poor mental health outcomes (Hatzenbuehler, 2009; Marchi *et al.*, 2022a; Mongelli *et al.*, 2019). Moreover, internalized homophobia has been shown to predict PTSD symptom severity in sexual minorities with a history of trauma (Gold *et al.*, 2011). LGBTQ groups are also at increased risk of suicidal behaviours, and that has been hypothesized to be a consequence of the experience of repeated discrimination (Livingston *et al.*, 2022; Marchi *et al.*, 2022a). Therefore, recognizing and addressing PTSD may have an impact on psychopathology translationally.

Our study aimed to explore the risk of PTSD in the LGBTQ population compared with non-LGBTQ individuals, independent of the type or intensity of the trauma to which individuals may have been exposed. The secondary goal was to detail the risk of PTSD among different subgroups such as gay, lesbian, bisexual, transgender, intersex and queer individuals, compared with cisgender heterosexual ones.

Methods

This systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page *et al.*, 2021). The protocol of this study was registered with PROSPERO (CRD42022354616).

Data sources and search strategy

We searched the PubMed (Medline), Scopus, PsycINFO and EMBASE databases until September 30, 2022, using the strategy outlined in the Supplementary Table S1 of the Appendix. With the aim to maximize the number of studies included, no restrictions regarding the language of publication or publication date were set.

Eligibility criteria

We included observational studies reporting a comparative estimation of rate of PTSD among the LGBTQ population vs. the general population (i.e., heterosexual cisgender—controls), without any restriction on participants' age or setting of the enrolment.

We excluded reviews, case reports, case series and studies that did not report data for the measurements of the outcome in the targeted population. We only included studies published in peer-reviewed journals, excluding conference abstracts and dissertations. If data from the same sample were published in multiple works, we considered only that study reporting more exhaustive information. Sample overlap was ruled out through a careful check of the registration codes as well as the place and year(s) of sampling.

Terms and definitions

LGBTQ status was defined as self-reported. PTSD diagnosis had to be defined according to standard operational diagnostic criteria (i.e., according to the Diagnostic and Statistical Manual of Mental Disorders [DSM] (American Psychiatric Association, 2013) or the International Classification of Diseases [ICD] (World Health Organization, 2018)). We also included studies where PTSD diagnosis was made according to the score on validated psychometric tools, operationalized to ICD or DSM definition.

Data collection and extraction

Four authors (MM, DU, EDM and AT) preliminarily reviewed titles and abstracts of retrieved articles. The initial screening was followed by the analysis of full texts to check compliance with inclusion/exclusion criteria. A standardized form was used for data extraction. Information concerning the year of publication, country, setting, name of the study/cohort, characteristics of study participants (sample size, age, percentages of men and women), LGBTQ status and PTSD rates among the LGBTQ groups and the controls were collected by two authors (MM and PG) independently. Extraction sheets for each study were cross-checked for consistency, and any disagreement was resolved by discussion within the research group.

Statistical analyses

The meta-analysis was performed by comparing PTSD rates between controls vs. overall LGBTQ people and controls vs. each LGBTQ subgroup. Pooled odds ratios (ORs) with 95% confidence intervals (95% CIs) were generated using inverse variance models with random effects (DerSimonian and Laird, 1986). The results were summarized using forest plots. Standard Q tests and the I^2 statistic (i.e., the percentage of variability in prevalence estimates attributable to heterogeneity rather than sampling error or chance, with values of $I^2 \geq 75\%$ indicating high heterogeneity) were used to assess between-study heterogeneity (Higgins and Thompson, 2002). Leave-one-out analysis and meta-regression were performed to examine sources of between-study heterogeneity.

If the meta-analysis included more than 10 studies (Sterne *et al.*, 2011), funnel plot analysis and the Egger test were performed to test for publication bias. The Egger test quantifies bias captured in the funnel plot analysis using the value of effect sizes and their precision (i.e., the standard errors) and assumes that the quality of study conduct is independent of study size. If analyses showed a significant risk of publication bias, the 'trim and fill' method was employed to estimate the number of missing studies and the adjusted effect size (Duval and Tweedie, 2000; Sterne *et al.*, 2008; Sutton, 2000; Terrin *et al.*, 2003). All the analyses were performed in R (RStudio Team, 2021) using *meta* and *metafor* packages (Balduzzi *et al.*, 2019; Viechtbauer, 2010). Statistical tests were two-sided and used a significance threshold of p-value < 0.05.

Risk of bias assessment and the GRADE

Bias risk in the included studies was independently assessed by five reviewers (AT, DU, EDM, PG and EA), using the Cochrane risk of bias tool (Higgins *et al.*, 2011). Each item on the risk of bias assessment was scored as high, low or unclear, and the GRADE tool was used to assess the overall certainty of evidence (Schünemann *et al.*, 2013). Further information is available in the Supplementary Appendix.

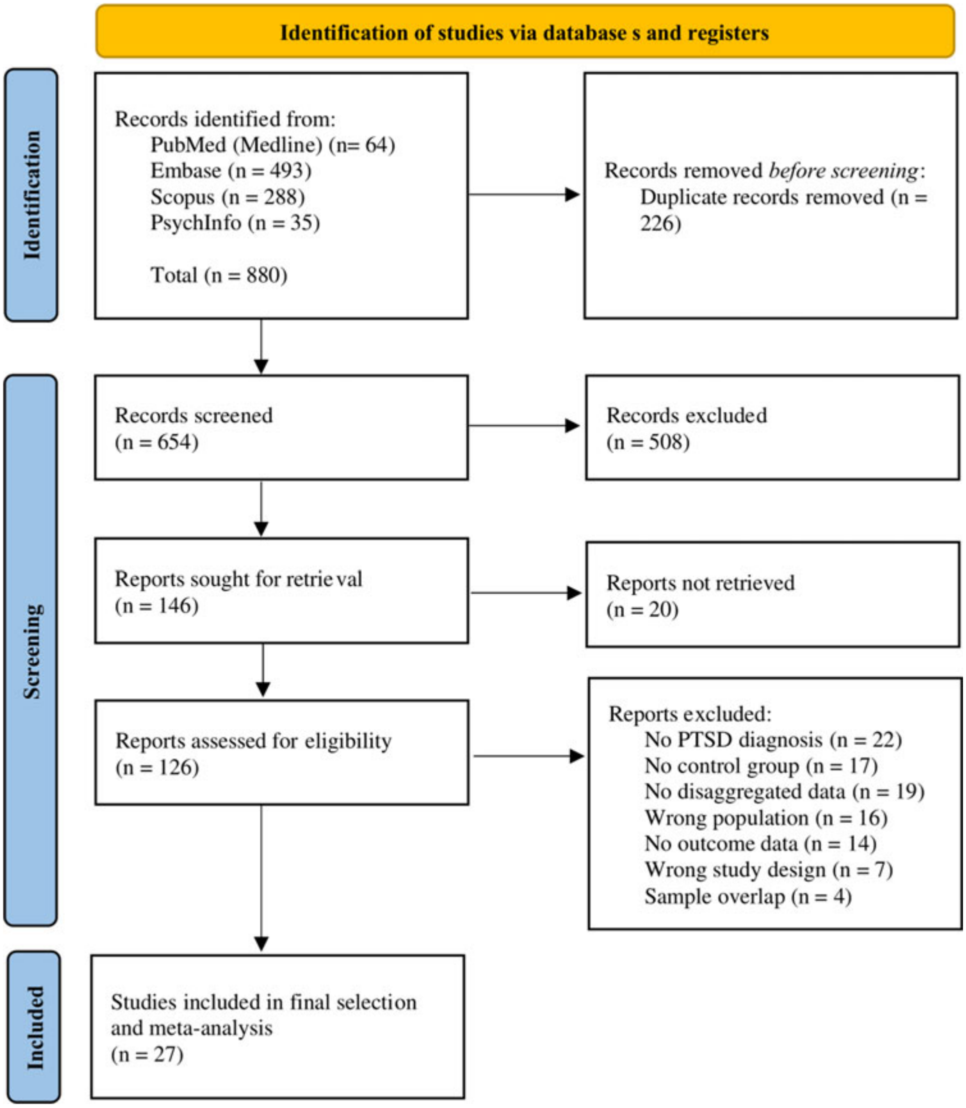


Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram.

Results

Study characteristics

Figure 1 summarizes the paper selection process: from 654 records screened on title and abstract, 126 full texts were analysed. The review process led to the selection of 27 studies (Alba *et al.*, 2022; Bettis *et al.*, 2020; Brewerton *et al.*, 2022; Brown and Jones, 2016; Burns *et al.*, 2015; Caceres *et al.*, 2019; Carey *et al.*, 2022; Evans-Polce *et al.*, 2020; Flentje *et al.*, 2016; Hao *et al.*, 2021; Harper *et al.*, 2021; Hatzenbuehler *et al.*, 2009; Holloway *et al.*, 2021; Jeffery *et al.*, 2021; Lehavot and Simpson, 2014; Livingston *et al.*, 2022; Lucas *et al.*, 2018; McDonald *et al.*, 2020; Mustanski *et al.*, 2010; Roberts *et al.*, 2012; Rodriguez-Seijas *et al.*, 2019; Schefter *et al.*, 2022; Terra *et al.*, 2022; Walukevich-Dienst *et al.*, 2019; Wang *et al.*, 2021; Weiss *et al.*, 2015; Whitbeck *et al.*, 2004), referring to 27 different samples, leading to a total of 273,842 controls (i.e., heterosexual or cisgender) and 31,903 LGBTQ people, which were included in the quantitative synthesis.

On average across the studies, the assigned sex at birth was female for 53.5% of participants (range: from 0% to 100%). The mean age of participants across the studies ranged from 14.7 to 60 years old (median age across the studies was 26.4). The selected studies were conducted in four countries: US ($n = 24$; 88.9%), Australia, Brazil and Kenya ($n = 1$ each; 3.7%). All the studies included were published in the last 20 years. Data collection begun after 2000 for most of the studies ($n = 20$; 74.1%), before 2000 for three studies (11.1%), and not reported in four studies (14.8%). PTSD was defined according to DSM ($n = 16$; 59.3%), ICD ($n = 3$; 11.1%), self-reported ($n = 3$; 11.1%) and validated psychometric scales ($n = 5$; 18.5%). Sample weights ranged from 6.3% to 1.3%.

All study characteristics are summarized in Table 1.

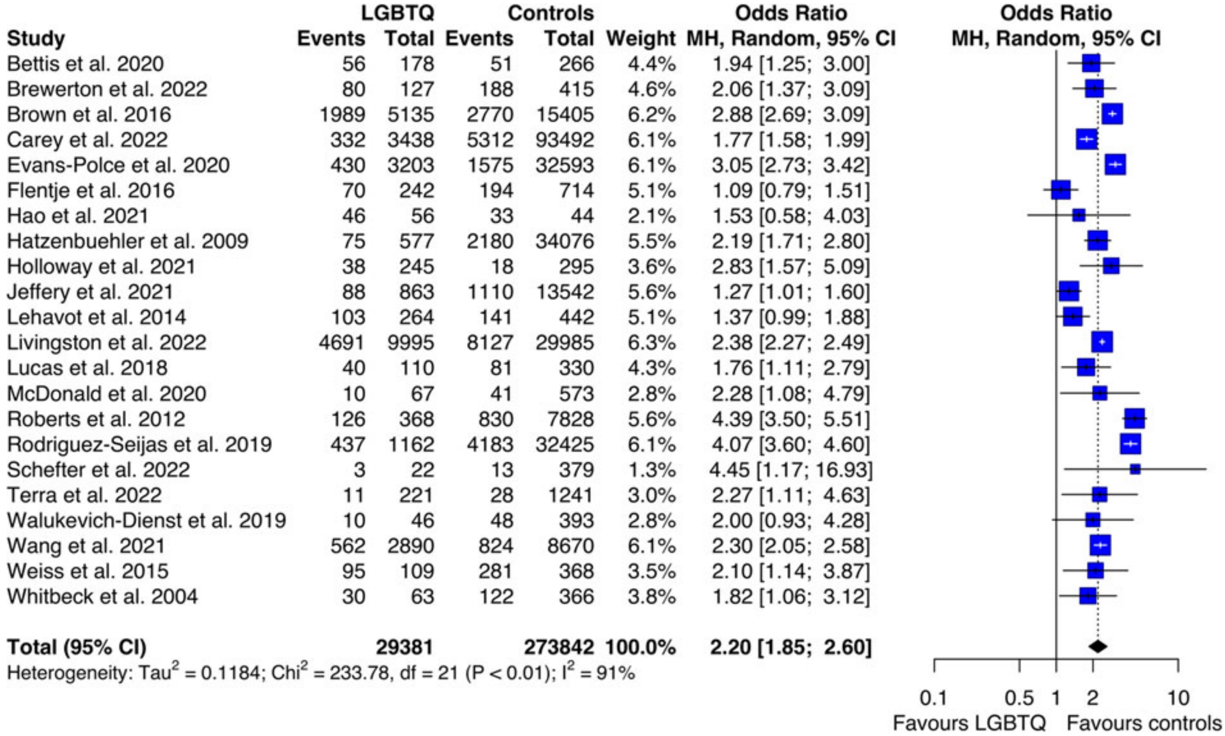
Narrative synthesis of the type of trauma reported across the studies

Besides PTSD diagnosis, 16 (59.3%) studies also collected information about the type of trauma experienced by participants. However, it is worth noting that the studies investigated traumatic experiences without necessarily establishing a temporal or

Table 1. Characteristics of the included studies

Author, year	Country	Date	Study design	*N* LG (% females)	*N* B (% females)	*N* T (% females)	*N* other SM (% females)	*N* LGBTQ+ (% females)	*N* controls (% females)	Females (%)	Age, mean (range)
Alba *et al.*, 2022	Australia	2017	Cross-sectional	756 (32.1)	NR	NR	NR	756 (32.1)	NR	NR	NR (NR)
Bettis *et al.*, 2020	USA	2017–2019	Cross-sectional	38	125	NR	15	178	266	57.5	14.7 (NR)
Brewerton *et al.*, 2022	USA	2017–2019	Cross-sectional	29	69	NR	29	127	415	96.7	25.0 (NR)
Brown *et al.* 2016	USA	1996–2013	Cohort	NR	NR	5135	NR	5135	15,405	30	55.8 (NR)
Burns *et al.*, 2015	USA	2009–2013	Longitudinal Cohort	329	96	NR	24	449	NR	0	18.9 (NR)
Caceres *et al.*, 2019	USA	2010–2012	Longitudinal Cohort	323	137	NR	87	547	0	100	NR (18–75)
Carey *et al.*, 2022	USA	2014–2016	Cross-sectional	1824 (64)	1614 (59.6)	NR	NR	3438 (61.9)	93,492 (28)	29.2	40 (NR)
Evans-Polce *et al.*, 2020	USA	2012–2013	Cross-sectional	NR	NR	NR	NR	3203	32,593	NR	NR (≥18)
Flentje *et al.*, 2016	USA	2015	Cross-sectional	100 (56)	88 (75)	49 (67.3)	54 (38.9)	242 (59.1)	714 (27)	35.1	41.8 (NR)
Hao *et al.*, 2021	USA	2017–2018	Cross-sectional	26	25	3	2	56	44	28	21.7 (NR)
Harper *et al.*, 2021	Kenya	NR	Cross-sectional	196	250	62	16	524	NR	NR	NR (≥18)
Hatzenbuehler *et al.*, 2009	USA	2004–2005	Retrospective Cohort	NR	NR	NR	NR	577 (51.3)	34,076 (52.1)	NR	NR (≥25)
Holloway *et al.*, 2021	USA	2017–2018	Cross-sectional	NR	NR	58	187	245	295	29.8	27.7 (NR)
Jeffery *et al.*, 2021	USA	2015	Cross-sectional	424 (73.6)	439 (71.7)	NR	NR	863	13,542 (35.3)	37.6	NR (NR)
Lehavot *et al.* 2014	USA	2013	Cross-sectional	209	55	NR	NR	264	442	100	49.8 (NR)
Livingston *et al.*, 2022	USA	1999–2021	Cohort	NR	NR	9995	NR	9995	29,985	35.5	NR (NR)
Lucas *et al.*, 2018	USA	2014–2015	Cross-sectional	NR	NR	NR	NR	110	330	39.1	NR (≥18)
McDonald *et al.*, 2020	USA	2016	Cross-sectional	NR	NR	NR	NR	67 (56.7)	573 (23.1)	26.6	NR (≥18)
Mustanski *et al.*, 2010	USA	2007–2008	Cross-sectional	152	70	20	NR	246	NR	50.8	18.3 (NR)
Roberts *et al.*, 2012	USA	2007	Longitudinal Cohort	196	172	NR	NR	368	7828	62.8	NR (19–27)
Rodriguez-Seijas *et al.*, 2019	USA	2012–2013	Cross-sectional	581	581	NR	NR	1162	32,425	56.3	NR (18–90)
Schefter *et al.*, 2022	USA	2017–2020	Cross-sectional	14	8	1	NR	22	379	100	60 (NR)
Terra *et al.*, 2022	Brazil	NR	Cross-sectional	60	151	9	1	221	1241	47.8	NR (NR)
Walukevich-Dienst *et al.*, 2019	USA	NR	Cross-sectional	13	31	NR	2	46	393	100	20.7 (NR)
Wang *et al.*, 2021	USA	2000–2012	Cohort	NR	NR	2890 (30.9)	NR	2890 (30.9)	8670 (6.3)	12.4	NR (≥18)
Weiss *et al.*, 2015	USA	1995–2007	Cross-sectional	38	57	NR	14	109	368	100	36.1 (NR)
Whitbeck *et al.*, 2004	USA	NR	Longitudinal Cohort	NR	NR	NR	NR	63	366	56.3	17.4 (NR)

Abbreviations: LG: lesbian and gay; B: bisexual; T: transgender; SM: other sexual minorities; USA: United States of America; NR: not reported.



Study	LGBTQ Events	LGBTQ Total	Controls Events	Controls Total	Weight	Odds Ratio MH, Random, 95% CI
Bettis et al. 2020	56	178	51	266	4.4%	1.94 [1.25; 3.00]
Brewerton et al. 2022	80	127	188	415	4.6%	2.06 [1.37; 3.09]
Brown et al. 2016	1989	5135	2770	15405	6.2%	2.88 [2.69; 3.09]
Carey et al. 2022	332	3438	5312	93492	6.1%	1.77 [1.58; 1.99]
Evans-Polce et al. 2020	430	3203	1575	32593	6.1%	3.05 [2.73; 3.42]
Flentje et al. 2016	70	242	194	714	5.1%	1.09 [0.79; 1.51]
Hao et al. 2021	46	56	33	44	2.1%	1.53 [0.58; 4.03]
Hatzenbuehler et al. 2009	75	577	2180	34076	5.5%	2.19 [1.71; 2.80]
Holloway et al. 2021	38	245	18	295	3.6%	2.83 [1.57; 5.09]
Jeffery et al. 2021	88	863	1110	13542	5.6%	1.27 [1.01; 1.60]
Lehavot et al. 2014	103	264	141	442	5.1%	1.37 [0.99; 1.88]
Livingston et al. 2022	4691	9995	8127	29985	6.3%	2.38 [2.27; 2.49]
Lucas et al. 2018	40	110	81	330	4.3%	1.76 [1.11; 2.79]
McDonald et al. 2020	10	67	41	573	2.8%	2.28 [1.08; 4.79]
Roberts et al. 2012	126	368	830	7828	5.6%	4.39 [3.50; 5.51]
Rodriguez-Seijas et al. 2019	437	1162	4183	32425	6.1%	4.07 [3.60; 4.60]
Schefter et al. 2022	3	22	13	379	1.3%	4.45 [1.17; 16.93]
Terra et al. 2022	11	221	28	1241	3.0%	2.27 [1.11; 4.63]
Walukevich-Dienst et al. 2019	10	46	48	393	2.8%	2.00 [0.93; 4.28]
Wang et al. 2021	562	2890	824	8670	6.1%	2.30 [2.05; 2.58]
Weiss et al. 2015	95	109	281	368	3.5%	2.10 [1.14; 3.87]
Whitbeck et al. 2004	30	63	122	366	3.8%	1.82 [1.06; 3.12]
Total (95% CI)		**29381**		**273842**	**100.0%**	**2.20 [1.85; 2.60]**

Heterogeneity: $Tau^2 = 0.1184$; $Chi^2 = 233.78$, df = 21 ($P < 0.01$); $I^2 = 91\%$

Figure 2. Forest plot of PTSD among LGBTQ people compared with controls (heterosexual or cisgender).

etiological association with the current PTSD status; rather they often reported that information seemingly for descriptive purposes. The reported type of trauma consisted of childhood maltreatment or adverse childhood experiences in three studies, sexual abuse in five studies, interpersonal violence and sexual and violence related to gender minorities in three studies and a cancer diagnosis in one study. Two studies examined violence experienced during both childhood and adulthood, while two veteran studies did not specify the type of traumatic experience, although it is reasonable to assume exposure to military and war-related trauma in these cases. For a more comprehensive overview of the exposure to traumatic experiences across the studies, see Supplementary Table S2.

Analysis of PTSD rate among LGBTQ and controls

Twenty-two studies (81.5%) reported outcome data about PTSD among LGBTQ and controls. As displayed in Fig. 2, LGBTQ people showed an increased risk of PTSD compared with matched non-LGBTQ controls, though with significant evidence of between-study heterogeneity (pooled OR: 2.20 [95%CI: 1.85; 2.60]; $I^2 = 91\%$; $p < 0.001$).

Analysis of PTSD rate among lesbian and gay and controls

Four (14.8%) studies detailed data on PTSD for the lesbian and gay subgroups. Meta-analyses indicated that lesbian and gay people displayed increased risk of PTSD (pooled OR: 1.96 [95% CI: 1.13; 3.39]), though the estimate was affected by significant between-study heterogeneity ($I^2 = 93\%$; $p < 0.001$). The results are displayed in Fig. 3.

Furthermore, two studies (7.4%) compared the risk of PTSD among lesbian and gay: one study detected significant increased risk for lesbian, the other did not find significant differences between the two groups. The pooled estimate was indicating increased risk for lesbian than gay, but the CIs crossed zero (pooled OR: 1.79 [95% CI: 0.74; 4.33]), and there was evidence of high between-study heterogeneity ($I^2 = 89\%$; $p < 0.001$). The results are displayed in the Supplementary Figure S1.

Analysis of PTSD rate among bisexual and controls

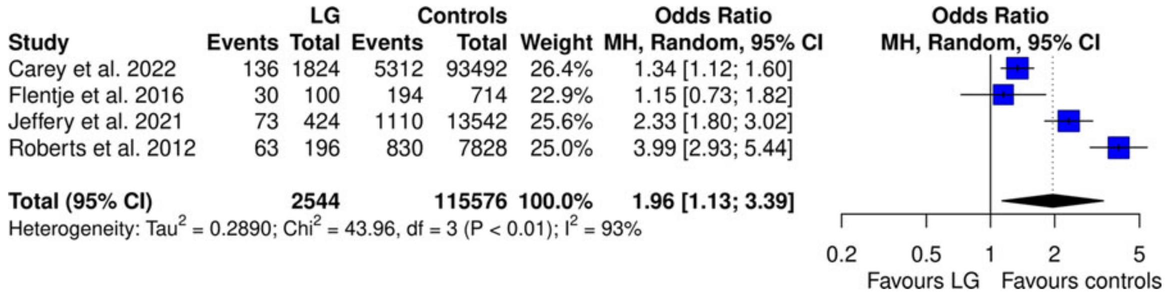
Four studies (14.8%) detailed data on PTSD for the bisexual subgroup. Meta-analyses showed that bisexual people displayed increased risk of PTSD (pooled OR: 2.44 [95% CI: 1.05; 5.66]), with significant between-study heterogeneity affecting the estimate ($I^2 = 95\%$; $p < 0.001$). The results are displayed in Fig. 4.

Analysis of PTSD rate among lesbian and gay and bisexual

Seven studies (25.9%) provided data on PTSD rate among lesbian, gay and bisexual. Meta-analysis of the comparison of the PTSD risk among the two groups showed increased risk for bisexual than lesbian and gay (pooled OR: 1.44 [95% CI: 1.07; 1.93]). The between-study heterogeneity was moderate, though statistically significant ($I^2 = 61\%$; $p = 0.02$). The results are displayed in Supplementary Figure S2.

Analysis of PTSD rate among transgender and controls

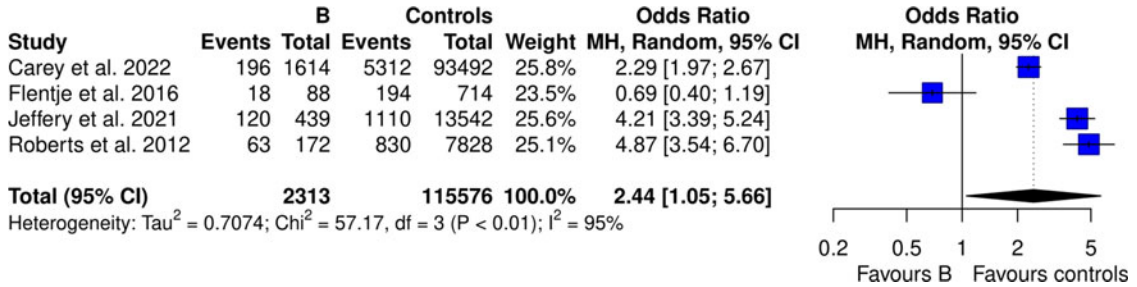
Seven studies (25.9%) reported outcome data about PTSD among transgender and cisgender controls. As displayed in Fig. 5, transgender people showed an increased risk of PTSD compared with matched cisgender controls, though with significant evidence of between-study heterogeneity (pooled OR: 2.52 [95% CI: 2.22; 2.87]; $I^2 = 79\%$; $p < 0.001$).



Study	LG Events	LG Total	Controls Events	Controls Total	Weight	Odds Ratio MH, Random, 95% CI
Carey et al. 2022	136	1824	5312	93492	26.4%	1.34 [1.12; 1.60]
Flentje et al. 2016	30	100	194	714	22.9%	1.15 [0.73; 1.82]
Jeffery et al. 2021	73	424	1110	13542	25.6%	2.33 [1.80; 3.02]
Roberts et al. 2012	63	196	830	7828	25.0%	3.99 [2.93; 5.44]
Total (95% CI)		**2544**		**115576**	**100.0%**	**1.96 [1.13; 3.39]**

Heterogeneity: $Tau^2 = 0.2890$; $Chi^2 = 43.96$, df = 3 ($P < 0.01$); $I^2 = 93\%$

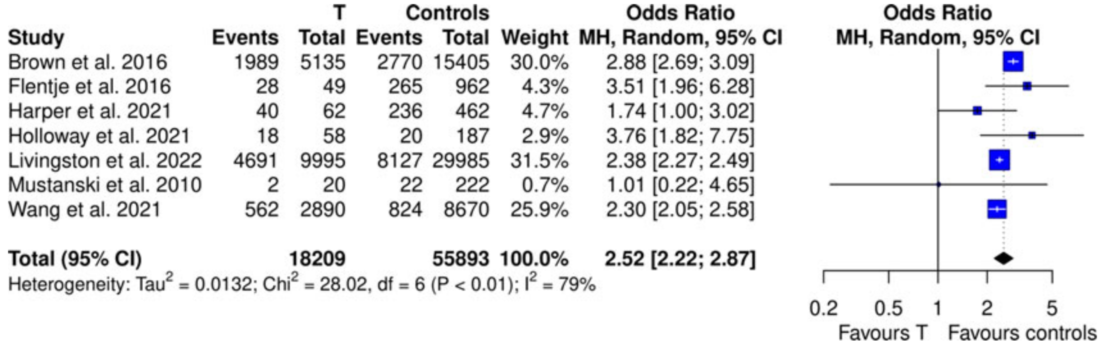
Figure 3. Forest plot of PTSD among LG people compared with controls (heterosexual or cisgender).



Study	B Events	B Total	Controls Events	Controls Total	Weight	Odds Ratio MH, Random, 95% CI
Carey et al. 2022	196	1614	5312	93492	25.8%	2.29 [1.97; 2.67]
Flentje et al. 2016	18	88	194	714	23.5%	0.69 [0.40; 1.19]
Jeffery et al. 2021	120	439	1110	13542	25.6%	4.21 [3.39; 5.24]
Roberts et al. 2012	63	172	830	7828	25.1%	4.87 [3.54; 6.70]
Total (95% CI)		**2313**		**115576**	**100.0%**	**2.44 [1.05; 5.66]**

Heterogeneity: $Tau^2 = 0.7074$; $Chi^2 = 57.17$, df = 3 ($P < 0.01$); $I^2 = 95\%$

Figure 4. Forest plot of PTSD among B people compared with controls (heterosexual or cisgender).



Study	T Events	T Total	Controls Events	Controls Total	Weight	Odds Ratio MH, Random, 95% CI
Brown et al. 2016	1989	5135	2770	15405	30.0%	2.88 [2.69; 3.09]
Flentje et al. 2016	28	49	265	962	4.3%	3.51 [1.96; 6.28]
Harper et al. 2021	40	62	236	462	4.7%	1.74 [1.00; 3.02]
Holloway et al. 2021	18	58	20	187	2.9%	3.76 [1.82; 7.75]
Livingston et al. 2022	4691	9995	8127	29985	31.5%	2.38 [2.27; 2.49]
Mustanski et al. 2010	2	20	22	222	0.7%	1.01 [0.22; 4.65]
Wang et al. 2021	562	2890	824	8670	25.9%	2.30 [2.05; 2.58]
Total (95% CI)		**18209**		**55893**	**100.0%**	**2.52 [2.22; 2.87]**

Heterogeneity: $Tau^2 = 0.0132$; $Chi^2 = 28.02$, df = 6 ($P < 0.01$); $I^2 = 79\%$

Figure 5. Forest plot of PTSD among T people compared with heterosexual controls.

Analysis of PTSD rate among queer and controls

Since only one study (3.7%) provided outcome data about queer and controls, meta-analysis was not performed on that outcome, even though the study reported an increased risk for the queer group (OR: 1.84 [95% CI: 1.04; 3.25]).

Publication bias and meta-regression

There was no evidence of publication bias in the primary estimate as shown by Egger's test p-value > 0.05 and by the funnel plots displayed in the Supplementary Figure S3.

Leave-one-out analysis, in which the meta-analysis of PTSD among LGBTQ and controls was serially repeated after the exclusion of each study, showed that irrelevant changes in the pooled estimate were obtained by excluding each one study. When the study from Flentje et al. (Flentje *et al.*, 2016) was excluded from the analysis, there was a decrease in the amount of heterogeneity, which, however, was not statistically significant because the value of $I^2 = 76\%$ still indicated high between-study heterogeneity. Therefore, there was no evidence of significant outlier effect played by any of the study (leave-one-out data available in Supplementary Table S3).

Meta-regression analyses were performed on the following variables, potentially associated with heterogeneity: (1) the percentage of females in the total sample; (2) the mean age of participants; (3) the country where the study was conducted; (4) assessment of PTSD applied; and (5) the year of publication. In the univariable meta-regression model the variables that resulted significantly correlated with the variance in the risk of PTSD were the country where the study was performed (USA, B: 0.786 [95% CI: 0.611; 0.960]) and the PTSD assessment applied (DSM or ICD, B: 0.996 [95% CI: 0.779; 1.21]; validated psychometric scale, B: –0.402 [95% CI: –0.721; –0.084]). Univariable meta-regression results are displayed in Supplementary Table S4.

GRADE of the evidence

A summary on the risk of bias in all 27 trials is reported in the Supplementary Figures S4 and S5, along with an assessment of the quality of the evidence (Supplementary Table S5). In the GRADE system, the evidence from observational studies is initially set to low, there are then criteria that can be used either to downgrade or upgrade (see further information in the Supplementary Material). The quality of the evidence was rated low for the main analysis of LGBTQ vs. controls. For the secondary analyses, the evidence was rated from low to very low.

Discussion

This systematic review and meta-analysis aimed to describe the risk of PTSD among LGBTQ people. Our results indicate that LGBTQ people are at increased risk of PTSD compared to matched non-LGBTQ controls. These findings confirm the relationship between sexual variant status and exposure to trauma (International Lesbian, Gay, Bisexual, Trans and Intersex Association, 2015; Livingston *et al.*, 2022; Marchi *et al.*, 2022a; Walters *et al.*, 2013). For example, violence provoked by the same partner and sexual assault in adulthood are disproportionately more prevalent among minorities of sexual orientation (Trombetta and Rollè, 2022), and individuals with minority sexual orientation reported a high frequency, severity and persistence of physical and sexual abuses during childhood (Roberts *et al.*, 2012). Interestingly, research evidence on the psychological consequences of the exposure to trauma, including adverse childhood experience, are not limited to PTSD (Elkrief *et al.*, 2021; Marchi *et al.*, 2022b, 2020). In this perspective, the association between the sexual variant status and experiences of traumatization may be relevant also for other forms of psychopathology. Intersectionality may be another appropriate model for understanding the different impact of trauma on LGBTQ people. In our review, we included six studies conducted on samples of veterans (Brown and Jones, 2016; Carey *et al.*, 2022; Holloway *et al.*, 2021; Jeffery *et al.*, 2021; Livingston *et al.*, 2022; McDonald *et al.*, 2020), all showing that LGBTQ veterans are at increased risk of PTSD compared to their non-LGBTQ peers, independent of the experience of traumatization to which they may have been exposed. Such higher risk of PTSD has been observed also in other LGBTQ people belonging to vulnerable populations, such as with HIV or part of racial and ethnic minorities (Glynn *et al.*, 2021). For these populations, treatment seeking and adherence are still a challenge, and suffering from mental health problems, such as PTSD, may be playing as a mediator (Marchi *et al.*, 2022c; Oni *et al.*, 2019).

Although the comparison of the PTSD risk between the sexual and gender minority groups was limited by the lack of data from some less studied populations, such as intersex, our data suggest that among LGBTQ groups, the highest risk of PTSD was found for transgender people, followed by bisexuals. This is consistent with previous evidence estimating increased risk of interpersonal violence for transgender people, as well as higher risk of depression, anxiety, substance use and suicidality (Valentine and Shipherd, 2018). Research on bisexual individuals, instead, suggested that they may be potentially excluded from LGBTQ community initiatives, due to the stereotypes according to which bisexuals are promiscuous or that bisexuality is 'just a phase'. Indeed, from a social perspective, bisexuality—and to some extent also intersexuality—challenges binary thinking and normative assumptions. Invisibility and lack of community support could explain the higher incidence of mental health problems, including PTSD (Baams *et al.*, 2015). Embracing an ethical perspective able to account for fluidity and multiplicity, such as queer ethics, might create a more inclusive framework that accounts for the experiences of all members of the LGBTQ communities (Däumer, 1992).

By looking at the contribution of each study in the analyses, it is possible to observe that the studies from Flentje et al. (Flentje *et al.*, 2016) and Mustanski et al. (Mustanski *et al.*, 2010) provided estimates that were less coherent with the others. This can be due to the sampling strategies implemented: Mustanski et al. enrolled a sample made only of sexual minority individuals and observed a small number of cases of PTSD; Flentje et al. made comparison of PTSD rates by sexual orientation or by gender identity; therefore, the comparison of PTSD risk by sexual orientation could include also transgender individuals. This intuition is supported by the fact that the comparison between transgender and cisgender provided by Flentje et al. was coherent with the others. In addition, the sample by Flentje et al. was made of homeless people, which is already a population with relevant vulnerabilities for mental health. This is supported also by the results of another study included in this review and conducted on a sample of homeless people (Hao *et al.*, 2021) providing estimates with CI crossing 1. Consequently, the estimate of higher risk of PTSD for transgender homeless compared to cisgender homeless people provided by Flentje et al. is consistent with the intersectionality model proposed above in this section. The analysis of the forest plot of the primary comparison showed substantial between-study heterogeneity. Despite this, leave-one-out analysis did not detect significant outlier effects. Univariable meta-regression found that the pooled estimate of PTSD risk was affected by the country, although with much imbalance in the distribution of the classes (i.e., 21 out of 22 studies were conducted in USA) and the assessment of PTSD applied. Specifically, studies assessing PTSD by applying diagnostic manuals criteria (i.e., DSM or ICD) could provide lower effect size for the pooled odds of PTSD among LGBTQ. This is consistent with previous evidence of only moderate diagnostic agreement between the systems used, with likely stricter definition of PTSD applied in the diagnostic manuals (Elmose Andersen *et al.*, 2022; Murphy *et al.*, 2017). Nevertheless, the high heterogeneity detected would not seem to be a limitation but a possible indicator of the trend of PTSD in LGBTQ people through time and in its possible declination across different samples. The low detection of publication bias seems to support this interpretation.

Limitations

The present study yielded robust findings; however, it should be interpreted considering some limitations. First, the heterogeneity on the PTSD assessment used in the studies. Most of the studies considered DSM and ICD definitions of PTSD, which consisted, respectively, in the presence of a traumatic event involving exposure to real or threatened death, serious injury or sexual violence (criterion A of DSM) or a protracted response to a stressful event or situation of an exceptionally threatening or catastrophic nature, which is likely to cause distress to almost anybody (ICD). Evaluations tailored on specific stress experienced by LGBTQ people (e.g., consistent with the Minority Stress Model) are lacking. These could lead to more accurate understanding of the risk of post-traumatic stress to which this population is exposed. Second, some studies included in the final selection did not provide all information about the sample composition (i.e., four studies did not report participants age and two studies did not report the sex assigned at birth of participants). This lack of information might have affected the results of meta-regression. Third, although the Egger test did not detect publication bias in any of the analyses, the funnel plot of the primary comparison seems to suggest that publication bias might be present. That may be due to between-study heterogeneity, which can give that plotting especially for those studies with large standard error. In addition, the number of the studies included in the subgroups meta-analyses was <10, which was not enough to inform about publication bias (Sterne *et al.*, 2011). Finally, we could not achieve our initial aim to detail PTSD risk for each LGBTQ group (i.e., lesbian, gay, bisexual, transgender and queer) because many studies did not consider these separated groups. In addition, there is limited research with enough participants that could be used to validate these findings for other sexual and gender minority groups, such as intersex people. There is an important need for international research to explore this area further.

Implications for research and practice

Traumatization and post-traumatic stress among sexual minorities are unaddressed issues. Critically, the concept of trauma should be investigated also beyond that considered by the diagnostic systems, especially for minority populations, such as LGBTQ. For instance, the literature is highlighting the negative effect of repeated interpersonal microaggressions. These are verbal expressions, attitudes and behaviours, which, intentionally or unintentionally, communicate hostile, derogatory, negative, prejudicial and offensive messages towards members of minority groups (Johnston and Nadal, 2010; Nadal *et al.*, 2016). The prefix micro does not describe the quality or the impact of these aggressions but rather the subtle way in which this type of discrimination occurs, making microaggressions very difficult to recognize, study and demonstrate, eluding the available diagnostic criteria. Microaggression may be considered benign or harmless by the perpetrator, with the risk to become pervasive and automatic in daily interactions. Research has shown that experiencing microaggressions can damage people's mental health and lead to chronic stress, depression, anxiety and low self-esteem (Flentje *et al.*, 2020; Nicholson *et al.*, 2022).

On a primary prevention level, programs and guidelines should be developed and employed in violence prevention to strengthen protective factors and foster resilience. Such efforts should be intensified for LGBTQ people with the aim of reducing minority stress and the barriers to disclosure and seeking help among the victims. For example, psychoeducation campaigns aimed at reducing victim-blaming and promoting intervening behaviours by bystanders has shown to be an effective mean of preventing interpersonal violence in societal settings (Fischer *et al.*, 2011; Wijaya *et al.*, 2022). Also, awareness and education campaigns, associated with severe sentences for sexual minority-related crimes, could be valid responses to reduce the risk of violence and increase the security of LGBTQ people. Arguably, intersectional analysis would make it possible to give a modern reading of social discrimination phenomena. Embracing this would allow better understanding of systemic, institutional and social disparities contributing to the experiences of discrimination of the LGBTQ communities (Bendl *et al.*, 2015).

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S2045796023000586

Availability of data and materials. The codes for reproducing the analyses can be accessed here: https://github.com/MattiaMarchi/Meta-Analysis–PTSD-Among-LGBTIQ-people.

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Competing interests. None

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Homophobia and mental health: a scourge of modern era

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Editorial

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Abstract

Homophobia is still a scourge in the modern era. Despite a greater acceptance of sexual variations and same-sex marriage in many countries, homophobia is widely sustained by religious, political and cultural values and beliefs at individual and social level. Most of homophobic attitudes are based on the principle of heteronormativity according to which heterosexuality is the standard for legitimating social and sexual relationships and homosexuality is considered as an abnormal variant. Homophobia may be also recognised at institutional level (state-sponsored homophobia, social homophobia) and supported by laws or religious beliefs. Moreover, internalised homophobia (IH) is defined as the inward direction of societal homophobic behaviours at individual level and refers to the subjective psychological impact of these negative attitudes. In fact, IH is significantly associated with a high prevalence of internalising mental disorders such as depression, anxiety, stress/trauma-related disorders, etc. We believe that a set of immediate actions are needed in order to contrast homophobia and its impact on mental health, in particular political initiatives, educational trainings and scientific research should be promoted with a specific focus on mental health needs of people target of homophobia.

Homophobia

Despite an increasing acceptance of homosexuality and sexual variations in the last decades with greater recognition of same-sex marriage and humans rights, also sustained by LGBTQI (Lesbian, Gay, Bisexual, Transgender, Queer, Intersexual) activism and socio-political changes, homophobia is still a scourge in the modern era and the fight against this social and cultural phenomenon ought to be an immediate priority (Poushter and Kent, 2020). In fact, attitudes of acceptance may vary around the globe with a higher level in the American and Western European countries, and lower in Eastern Europe, the Middle East, Russia and part of Africa.

Homophobia is defined as a range of behaviours, feelings, negative attitudes towards sexual variations and people identified or perceived as LGBTQI (Renzetti and Edleson, 2008). The origin of the term is traced back to Weinberg, a Jewish-American psychologist of the 1960s (Grimes, 2017), and refers to a composite term deriving from the words *homo-sexuality* and *phobia*, which is a Greek term (φόβος) meaning 'fear' or 'aversion' or 'dread'. This term has appeared in the printed media in the following years: *homophobic panic* on *Time* (US) magazine in 1969, *homophobia* on *The Times* (London, UK) in 1981 until it became of common use globally (Longley, 1981). In 1972, Weinberg published his book entitled *Society and the Healthy Homosexual* with a broader analysis on homophobia and its consequences on health. It is of interest that one year later, in 1973, the category homosexuality has been removed from the upcoming version of Diagnostic and Statistical Manual of Mental Disorders (DSM-III edition; 1980): the task force coordinated by Professor Robert Spitzer reformulated the concept of homosexuality and sexual orientation disturbance proposing the differentiation between the normal sexual variant from other same-sex attractions characterised by experienced distress or psychological disturbance.

Some other authors have also disputed that homophobia is not consistent with the definition of *phobia* that should be intended as an 'intense, somewhat illogical, or abnormal fear of a specific thing or situation': homophobia is sustained by negative attitudes, emotions as well as religious, political and cultural values and beliefs (Plummer, 2016). In fact, many factors may lead to homophobia: prejudice, ignorance, fear, hate, mistrust, discomfort. Undoubtedly, homophobia relies on religious, political and cultural values and beliefs, as well as, generally, negative attitudes towards homosexuality are inspired by the concept of heteronormativity. *Heteronormativity* is a principle according to which heterosexuality is the standard for

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legitimating social and sexual relationships whereas homosexuality is a variant and may be seen as an abnormality (Berlant and Warner, 1998). Homophobia may be named as *lesbophobia* (directed against lesbians), *biphobia* (against bisexuals), *transophobia* (against transsexuals). Intolerance against any diversity (sexual variation, race, political and religious minorities, etc.) may be individual or affecting the community or institutions. It has been proposed that at an individual level, homophobia as well as other aversions against minority may be linked to a psychopathological construct such as the *intolerant personality disorder* (Guindon *et al.*, 2003) with the following characteristics: (a) a rigid set of beliefs and values based on the superiority of race or religion, culture, sexual orientation, etc.; (b) lack of empathy; (c) antagonism and hostility against a specific target population; (d) aversion and efforts to block, contrast, impede people considered to be inferior; (e) use of power to contrast the intolerable people or ideas; (f) a sense of entitlement based on the sense of being part of a superior group; (g) disregard for human rights; (h) lack of remorse.

At societal level, many categories and definitions of homophobia have been proposed as: *institutionalised* homophobia, *state-sponsored* homophobia, *social* homophobia and *internalised* homophobia (IH) (Frost and Meyer, 2009).

Institutionalised homophobia: institutions may be strongly based or oriented on specific cultural, religious as well as prevalent ideologies. All these factors may consequently affect social attitudes towards minorities or part of population. Religions in the world may show a variable approach to the theme of sexual variations with a range of degrees of acceptance. Catholic religion has modulated teachings and positions towards homosexuality over time. An implicit condemn of same-sex attractions might be found in the Old and New Testaments of The Bible (e.g. Leviticus 18:22; the story of the judgment of Sodom and Gomorrah; King, 1976); the Catechism of Catholic Church also disapproved homosexuality and same-sex acts stating they may be considered as contrary the natural law (The Vatican, 2020). Pope Francis, after his election in 2013, opened to homosexuality and stated that Catholic Church should love people regardless of their sexual orientation: in 2019, he specified that homosexual orientations are not considered as a sin by the Catholic teaching even if homosexual acts are a sin; later in 2020, in a documentary named *Francesco*, he stated that homosexuals have the right to be part of the family and are God's children; he also opened to civil unions among same-sex lovers (San Martín, 2019; Horowitz, 2020).

Homosexuality is forbidden by Islam and is considered a crime under Sharia Law: in Afghanistan, same-sex acts are punished with the death penalty under the Taliban as well as gay people have been persecuted by Islamist forces in Iraq or Syria (Mc Claughlin, 2016). The International Lesbian and Gay Association (ILGA) reported that about 80 countries around the world continue to consider homosexuality as illegal (2009). Penalisation as well as criminalisation of homosexuality in these countries, including also persecution of LGBT, is also considered state-sponsored homophobia (Bruce-Jones and Lucas Paoli, 2011). Many examples of state-sponsored discrimination may be described in the history: the Medieval Inquisition, the Republic of China (under the Qing Dynasty), Soviet Union (under Lenin), Nazi Germany, North Korea, Zimbabwe, etc.

In communities based on homophobia, the fear of being identified as gay is higher and may be recognised as a social-homophobia: this may lead to an exhibition of heterosexual behaviours, congruent with the heteronormative culture, with a distancing from gay people in order to reaffirm a conventional social role and gain social validation (Eguchi, 2006).

Internalised homophobia (IH): may be defined as the inward direction of societal homophobic attitudes at individual level. It is a psychological construct including the internalisation of negative attitudes conflicting with the self-regard and leading to a self-denigration or identification with the heterosexual beliefs as theorised by Allport (1954). This process may cause discomfort with the own sexual orientation seen as ego-dystonic: personal desires and attractions are seen odds with the individual self-image and may cause extreme stress, repression and discordance (Newcomb and Mustanski, 2010). As further discussed, IH may lead to repression of the own desires, internalising mental health problems, clinical depression and a higher risk of suicide (Newcomb and Mustanski, 2010).

Homophobia and mental health

We argue that the impact of homophobia on mental health is understated and undetected in the clinical setting as well as poorly described in the literature.

In 2010, a meta-analytic review of literature conducted on the relationship between IH and mental health among LGBTQIs concluded that IH is significantly associated with internalising mental disorders (e.g. depression, anxiety, stress/trauma-related disorders, obsessive-compulsive disorder, eating and dissociative disorders) (Newcomb and Mustanski, 2010).

Several authors include the homophobic experience into the framework of '*minority stress model*': minority stress derives from the conflict between being a minority and dominant social and cultural values, and may be based on homophobic experiences, harassment, maltreatment, discrimination and victimisation, all affecting individuals' physical and mental health outcomes (Meyer, 1995).

Newcomb and Mustanski (2010) meta-analysed 31 articles on the association between IH and mental health covering a total sample of 5831 LGBTQI individuals and reported that homophobic experiences were associated with high rates of internalising mental disorders, mostly described in older individuals and based on prevalent depressive symptomatology. Interestingly, Van Beusekom *et al.* (2018), after assessing 724 LGB individuals, proposed that homophobic stigmatisation and IH are significant *mediators* of the association between gender non-conformity and the onset of mental health issues: subjects reporting less homophobic experiences have shown lower mental health morbidity. Lorenzi *et al.* (2015), assessing LGB subjects in Belgium and Italy, found that social support is a protective mediator between IH and anxiety as well as depressive symptoms in their path-analysis model. Also, higher levels of IH and social heteronormativity have been associated with a significant increase of sexual risk behaviours and increased incidence of sexually transmitted diseases among LGBs (Perez-Brumer *et al.*, 2019).

IH also affects the quality of life and life satisfaction: as reported by Wen and Zheng (2019), there is a significant association between homophobic experiences and lower life satisfaction among LGB individuals ($N = 528$), as well as their mental health status was reported as a statistically significant mediator. These findings confirm what is reported by a recent high-quality review on suicidal behaviours among sexual minorities: authors listed homophobia and micro-aggressions as recognised *specific* risk factors for suicide among LGBTs (Poštuvan *et al.*, 2019).

Alongside the impact of homophobia on mental health, it is of note that high homophobic and discriminatory attitudes have been found among health care professionals with potential negative effects on the quality of care and therapeutic relationship towards LGBT patients (Taskiran Eskici *et al*., 2021).

What's next

We argue that a set of immediate actions are needed in order to fight homophobia and reduce the impact of social pressure on LGBTs' mental health: (a) a synergy between governments, LGBT-rights organisations, mental health associations in order to promote campaigns against homophobia and raise awareness on the impact of discrimination and non-acceptance on mental health; (b) educational trainings on homophobia for secondary schools and universities; (c) specific courses on health and mental health of LGBTQIs and related issues among health care professionals, to be added in their core curriculum; (d) promotion of the detection and measurement of homophobia in the clinical setting (including mental health services); (e) training on specific instruments of measurement (e.g. Short Internalised Homonegativity Scale, Nungesser Homosexual Attitudes Instrument, Internalised Homonegativity Inventory) and development of more specific tools, (f) promotion of more research on LGBTQIs mental health and their health unmet needs.

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PCN Psychiatry and Clinical Neurosciences

LETTER TO THE EDITOR

Hikikomori-like social withdrawal: An Italian case report

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The term Hikikomori refers to an individual's deliberate social withdrawal lasting at minimum 6 months.[1] It is a culture/Japan-bound syndrome, recently described also in Italy.[2–6] Early assessment, diagnosis and intervention are often missing in Western countries, due to the lack of knowledge and expertise.[1] Hereby, we describe the clinical history of a young Italian inpatient with a delayed Hikikomori diagnosis. The patient gave informed consent, and his anonymity was preserved.

A 21-year-old male with a self-isolation period in his room of approximately 4 years was hospitalized due to severe physical health impairment, apathy, anhedonia and depression. He avoided every daily social contact, including his family. He was used to leaving his room only when his relatives were not at home. He also removed the door handle to prevent contact with them. At the first psychiatric evaluation, he was hypomimic, with severe psychomotor retardation, altered prosody with monotony and affective flattening. He was initially unavailable for a deepened clinical interview, refusing any communication. He displayed sleep–wake inversion, poor appetite with food restriction, low self-esteem, and feelings of helplessness with unstructured death ideation. A positive psychiatric family history for mood disorders was reported. During childhood, a separation anxiety disorder was referred which did not allow him to join kindergarten. During primary school, he established good relationships with other children, even playing soccer. His psychopathological onset was during middle school, due to educational difficulties and a reactive depressive state. Due to a progressive social isolation, the patient underwent a neuropsychiatric evaluation at the age of 11 in which he was diagnosed with a mood and behavioral disorder with a learning disability [F81.9].[7] When he was 12 years old, he underwent a neuropsychiatric evaluation in hospital, in which he was diagnosed mild cognitive disability, learning disorder [F81.9], language disorder [F80.9], and depressive disorder [F34.9] with oppositional-defiant behavioral expressiveness [F91.3].[7] Psychopharmacological therapy was recommended, despite the patient's refusal. At the age of 14, his parents divorced, and he was transferred to his mother's house. Following several conflictual dynamics, the patient moved to his maternal grandparents' house for about one and a half years and later he went to live with his father. He definitively dropped out of school at 15 years old. A further neuropsychiatric evaluation reported a worsened depressive symptomatology, associated with a physical, affective and sexual development retardation. He manifested a clinically relevant dysphoric mood, and provocative/oppositional behaviors towards his mother. Sertraline 50 mg/day and family psychotherapy was recommended. His father reported a good clinical response and a subsequent treatment discontinuation following medical advice. A further psychopathological worsening emerged, which led the patient to send a text message to his father asking for help ("get me out of this hellhole"), when he was 20 years old. Aripiprazole 15 mg/day was prescribed. At the age of 21, his father decided to move him from their small peripheral village to a more urbanized and bigger city to help him to escape from what the patient called "the hellhole", but nothing really changed.

Following a further psychopathological worsening, he was hospitalized at our Transitional Psychiatric ward, in Ancona, during which he was assessed with a set of general psychopathology and Hikikomori specific psychometric tools (Supplementary Table S1). A psychotic disorder and autism spectrum disorder were excluded. An in-person structured clinical interview was also performed by Professor Kato who confirmed Hikikomori syndrome. He was discharged with a diagnosis of moderate depressive episode [F32.1] with schizoid personality disorder [F60.1][7] and he was prescribed aripiprazole 20 mg/day and bupropion 300 mg/day. At discharge, the patient was more cooperative, with reduced depressive levels and more social proneness, without any emotional/behavioral dysfunction. Self-injurious/suicidal ideation was absent. Hypno-alimentary pattern improved. A cross-culturally adapted psychoeducational family-based program[8] was administered, with the significant improvement of family communication and in-person interaction with the patient and indirectly with enhancement of the individual's psychopathological load. This case vignette demonstrated how it is essential to identify at-risk individuals for severe social withdrawal through structured and validated assessment tools as well as provide early integrated therapeutic approaches, involving family, peer-group, and the individual, at very early treatment stages. Trans-culturally adapted assessment tools and interventions for youth social withdrawal could significantly reduce individual social isolation, improving interpersonal relationships, general functioning, and associated psychopathology.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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RESEARCH **Open Access**

Predominant affective temperaments in depressive patients with severe social withdrawal

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Abstract

Background Hikikomori (HK) is characterized by self-isolation and social refusal, being more likely also associated with affective disorders, including depression. This case–control study primarily aimed at identifying (if any) predominant affective temperaments are associated with HK in depressed versus not-depressed individuals. Secondary objectives comprise assessing which other psychopathological dimensions (e.g., boredom, anxiety) are associated with the HK specifier in depressed individuals.

Methods From the larger SWATCH study, 687 Italian young people were screened for depression, as measured by 9 items-Patient Health Questionnaire (PHQ-9) and HK-like social withdrawal, through the Hikikomori Questionnaire-25 (HQ-25). All subjects were administered a brief-Temperament Evaluation of Memphis, Pisa, Paris and San Diego (TEMPS-M), the 7 items-Generalized Anxiety Disorder (GAD-7) and the Multidimensional State Boredom Scale (MSBS).

Results Males reported significantly higher scores at HQ-25 total score than females ($p = 0.026$). In the total sample, HK social withdrawal is positively predicted by MSBS low arousal, disengagement, depressive levels, depressive and irritable affective temperaments, while negatively by anxiety ($F(6, 680) = 82.336$, $p < 0.001$, $R^2 = 0.421$). By selecting only depressed sample, HQ-25 is positively predicted by MSBS total score, low arousal and depressive affective temperament, while negatively by MSBS high arousal ($F(4, 383) = 48.544$, $p < 0.001$, $R^2 = 0.336$). The logistic regression model found that the likelihood of developing depression with the HK specifier is significantly predicted by depressive and cyclothymic affective temperaments.

Conclusions These preliminary findings could help in clinically characterizing the relationship between specific affective temperamental profiles among individuals with depression with/without HK specifier, in order to provide a more tailored and personalized therapeutic approach. Our Italian study should be extensively replicated in larger, longitudinal and multicentric pan-European studies, by specifically assessing the impact of these findings on depression clinical course, prognosis and treatment outcomes.

Keywords Affective temperament, Hikikomori, Social withdrawal, Temperaments, Youth, Youth mental health

Background

During the last years, there has been an increasing interest in investigating and clinically characterizing certain newly described psychopathological entities in Western Countries, originally described only in oriental ones, such as in Japan [1, 2]. The Hikikomori syndrome (引き籠もり) was described for the first time in Japan and it has been considered for long time as a culture/Japan-bound

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syndrome [3, 4], even though nowadays evidence confirmed its spread as diagnostic entity in Western countries, including Italy [5–8]. Hikikomori, firstly described by the psychiatrist T. Saito in 1998 [9], refers to any individual who intentionally withdraws him/herself into his/her home or room for at least 6 months, refusing any social situation and interaction with all people in-person, including friends and/or relatives [4]. Etymologically, it derives from the Japanese composed verb, formed by "*hiku*" (i.e., "*to pull back*") and "*komoru*" (i.e., "*seclude oneself*") [4]. Hikikomori syndrome could be classified as a primary (or idiopathic) or secondary. The primary form is not associated with other diseases. While secondary form is associated with other (psychiatric or not) illnesses [4]. Diagnostic criteria for Hikikomori are described in Fig. 1.

Indeed, social withdrawal has been identified to be associated with several psychiatric conditions such as psychotic disorders, personality disorders and affective disorders (mainly major depression) [10, 11]. Furthermore, despite Hikikomori has been described in Japan for more than 20 years, there are few studies specifically investigating psychopathological, personality and temperamental characteristics of individuals with Hikikomori-like social withdrawal [2, 12–15]. Pioneering studies are focusing on various psychological factors frequently reported among hikikomori subjects such as the lack of functional coping strategies, interpersonal difficulties, low self-esteem levels, poor autonomy capacity, tendency to experience anxious-depressive states, environmental sensitivity, and insecure/anxious attachment pattern [13, 16–18]. Indeed, determining which are the typical/predominant/predisposing hikikomori temperamental patterns, also considering sex-based differences, would be important not only to allow an early and precise clinical characterization of the phenomenon also in Italy, but also to predict potentially risky psychopathological trajectories such as suicidal behaviours as well as personalizing more tailored interventions [1, 15, 19]. However, currently there are no studies specifically conducted to explore the role of predominant affective temperaments in the onset and maintenance of Hikikomori-like social withdrawal symptomatology.

The concept of affective temperament refers to the emotional domain of personality, which is related to the subject's predisposition to the development of mood disorders [20] and, potentially, also to those depressive pictures associated with Hikikomori-like social withdrawal symptomatology. Temperament is defined as a stable personality trait and refers to the activity levels, social and biological rhythms, mood and daily variability of patients [21]. According to Akiskal, all mental disorders, including both affective and psychotic conditions, have been supposed to represent abnormal forms of normal temperamental traits [22]. Indeed, Kraepelin was the first to identify affective temperaments, recognising the depressive, irritable, manic, and cyclothymic temperamental dispositions [22]. While Kretschmer identified the cyclothymic temperament (which combines all those affective temperaments previously theorized by Kraepelin) and its opposite schizotymic affective temperament [22]. Akiskal was indeed the first to clearly characterize and define five affective temperaments (i.e., cyclothymic, depressive, hyperthymic, irritable, and anxious) and to investigate the associations between specific predominant affective temperaments with the variable clinical characterization of mood disorders [21].

Overall, due to the extremely need to clinically characterize Hikikomori individuals, and, particularly, in stratifying depressed individuals with or without Hikikomori as diagnostic specifier, by investigating the potential association with specific predominant affective temperaments, according to the Akiskal's classification, we carried out a sub-analysis within the larger SWATCH (Social Withdrawal And TeCno-mediated mental Health issues) study. Specifically, our main hypothesis to be tested consisted in assessing whether it is possible to identify (if any) specific predominant affective temperaments are more likely associated with the presence versus absence of the Hikikomori specifier to depression in order to provide a diagnostic subtyping of young depressed individuals useful for considerations regarding a more tailored and personalized therapeutic approach. Therefore, the primary objective of the present study aimed at investigating which predominant affective temperamental profiles are prevalent within a sample of Italian young people stratified according to the presence/absence of clinically significant depressive symptomatology with or without the Hikikomori diagnostic specifier. Secondary objectives comprise assessing whether there sex-based differences and whether other variables could be variably associated with the presence of the Hikikomori specifier among depressed individuals and a set of supposed more predominant associated affective temperaments, such as the boredom dimension and the associated anxiety symptomatology.

Methods

Study design and recruitment strategies

The study was carried out by recruiting a sub-sample of Italian young people (aged 18–35) during the timeframe March-October, 2022, within the larger SWATCH study aimed at investigating the main psychopathological determinants of the severe youth social withdrawal condition (hikikomori-like) and web-based psychopathologies in Italian adolescents/young adults. From

Hikikomori is a form of pathological social withdrawal or social isolation whose essential feature is physical isolation in one's home.

The person must meet the following criteria:

1. Marked social isolation in one's home.
2. Duration of continuous social isolation for at least 6 months.
3. Significant functional impairment or distress associated with social isolation.

Individuals who occasionally leave their home (2–3 days/week), rarely leave their home (1 day/week or less), and rarely leave a single room may be characterized as mild, moderate, and severe, respectively. Individuals who leave their home frequently (4 or more days/week), by definition, do not meet criteria for hikikomori. The estimated continuous duration of social withdrawal should be noted (e.g., 8 months). Individuals with a duration of continuous social withdrawal of at least 3 (but not 6) months should be noted as pre-hikikomori. The age at onset is typically during adolescence or early adulthood. However, onset after the third decade is not rare, and homemakers and elderly who meet the above criteria can also be considered.

The following specifiers are not mandatory criteria; however, they may be useful for additional characterization of hikikomori:

A. With lack of social participation. The individual occasionally (2–3 days/week) or rarely (1 day/week or less) participates in activities, such as attending school, going to a workplace, or going to medical appointments. This specifier would likely apply to hikikomori who are also not in education, employment, or training (i.e., 'NEET').
B. With lack of in-person social interaction. The individual occasionally (2–3 days/week) or rarely (1 day/week or less) has meaningful in-person social interactions (conversations) with people outside home. In severe cases, the individual rarely has in-person social interaction even with cohabitating people, such as family members. This specifier would likely apply to individuals with hikikomori who have social interactions that primarily occur via digital communication technologies (e.g., social media, online gaming).
C. Indirect communication. Due to the proliferation of the Internet in modern society, 'indirect' communication via web-based or other technologies is increasingly common. Thus, such indirect communication should be assessed in accordance with direct communication. Some cases have daily bidirectional indirect communication via online tools such as social networking services and/or online games.
D. With loneliness. The individual endorses feeling lonely. The presence of loneliness tends to be more common as the length of hikikomori increases.
E. With a co-occurring condition. Hikikomori may co-occur with numerous psychiatric disorders, such as avoidant personality disorder (e.g., isolation due to fears of criticism or rejection), social anxiety disorder (e.g., avoidance of social situations because of fear of embarrassment), major depressive disorder (e.g., avoidance of social situations as a reflection of neurovegetative symptoms), autism spectrum disorder (deficits in social interactions and communication), or schizophrenia (e.g., isolation due to positive and negative symptoms of psychosis).
F. Age at onset. In many cases, the age at onset is adolescence and early adulthood; however, cases with onset after the third decade are not rare.
G. Family pattern and dynamics. Socioeconomic status and parenting styles may influence the development of hikikomori. For instance, overprotective parenting and/or absence of paternal involvement are suggested to be linked to the occurrence of this phenomenon.
H. Cultural background. Pathological social withdrawal was originally characterized and described in Japan and more recently has been identified in other countries, especially in East Asia and Europe. Sociocultural situations may influence this condition.
I. Intervention. Even though no evidence-based interventions have been established, pharmacotherapy (if the individuals are comorbid with psychiatric disorders), a variety of psychotherapy, social work, and family approach have been provided. Precision (individualized) approach is recommended based on the above assessments.

Fig. 1 Diagnostic criteria for Hikikomori Syndrome (from Kato et al. [4]

the SWATCH dataset, the following inclusion criteria were considered: (a) age ranging from 18 to 35 years-old; (b) written informed consent to participate in the current study. All participants who did not agree to provide a written informed consent and those who did not fully complete all questionnaires were properly excluded by the analysis. The final sample was stratified in two groups: subjects with clinically relevant depressive symptomatology (DEP+) and subjects without clinically relevant depressive symptomatology (DEP-), by using the 9-item Patient Health Questionnaire (PHQ-9) cut-off of 10 or above [23]. Both groups were homogeneous according to the sex and age. Sample size was calculated using the Statistical Software G*Power version 3.1. (Franz, Universitat Kiel, Germany), by keeping the values of confidence level as 99%, anticipated population proportion 0.5, an α error of 0.05, a power of 80%, and taking into consideration all variables to be entered in the multivariable analysis, in order to obtain at least an effect size of > 0.3. A minimum total sample size of 278 was established to be reached for the present study, divided in two groups (DEP+and DEP-) constituted by at least 139 participants each one. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and according to the guidelines for Good Clinical Practice (GCP) (WHO, 2013), following the approval by the local Institutional Review Board. All participants gave informed consent to take part in the study.

Measurements

A case report form (CRF) was developed to collect a set of socio-demographic and clinical characteristics, including participants' age, sex, occupational and marital status, living condition, parents' marital status, and previous psychiatric history. All participants were administered at baseline the following self-administered questionnaires, as described below.

The PHQ-9 is a 9-items tool designed to screen for depression in primary care and specialty medical settings [23]. The standard cutoff score to identify possible major depression is 10 or above, with a sensitivity of 88% and a specificity of 88% for major depression [23]. The PHQ-9 total score obtained by summing all 9 items, allows clinicians to discriminate between mild (PHQ-9 ranging 10–14), moderate (PHQ-9 ranging 15–19) and severe (PHQ-9 ≥ 20) depression [24]. The instrument has a good reliability in identifying clinically relevant depressive symptomatology also in the Italian sample [25]. In our study, Cronbach's α of the PHQ-9 showed a satisfactory internal reliability (α = 0.849).

The Generalized Anxiety Disorder-7 (GAD-7) is a 7-items questionnaire primarily identified for screening of GAD suitable to individuation of anxious patterns of symptoms [26]. The standard score to identify clinically significant anxiety indicative of a generalized anxiety disorder is 10 or above, with a sensitivity of 89% and a specificity of 82%, while the cut-off of 5 or above was established to identify significant clinically relevant anxiety symptomatology [26]. The GAD-7 total score obtained by summing all 7 items, allows clinicians to discriminate between mild (GAD-7 ranging 5–9), moderate (GAD-7 ranging 10–14) and severe (GAD-7 ≥ 15) anxiety [26]. In our study, Cronbach's α of the GAD-7 showed satisfactory internal reliability (α = 0.887).

The 25-item Hikikomori Questionnaire (HQ-25) is a 25-item self-report scale measuring symptoms of Hikikomori-like social withdrawal over the past 6 months. For each item, response options range from 0 "strongly disagree" to 4 "strongly agree" [27]. The HQ-25 provides a three-factor theoretical model of Hikikomori construct, namely socialization, isolation and emotional support. A total HQ-25 score was obtained by summing up individual items' scores. In the original and Italian study, the standard cutoff score to discriminate between individuals at risk for Hikikomori and those not at risk is 42 or above, with a sensitivity of 94% and a specificity of 61% [27, 28]. HQ-25 showed a good internal consistency, with Cronbach's α values ranging 0.88 to 0.96 for the total scale, while 0.94, 0.91 and 0.88, respectively, for the three abovementioned subscales [27]. Reliability and validity of this instrument has been tested also in Italian samples and reported good results, by confirming that the originally proposed Japanese three-factor measurement model structure of the HQ-25 and total score could be adapted in the Italian context as well [28]. In our study, Cronbach's α of the HQ-25 showed a satisfactory internal reliability (α = 0.813).

The brief version of the Munster Temperament Evaluation of Memphis, Pisa, Paris and San Diego (TEMPS-M) [29] is a 35-items self-report questionnaire used to assess affective temperaments described by Akiskal [30, 31], i.e. depressive, anxious, hyperthymic, cyclothymic and irritable, using a dimensional approach with a 5-point Likert scale ranging from 1 ("not at all") to 5 ("very much") [29]. TEMPS-M has been developed in different clinical and research settings [32]. In our study, Cronbach's α of the TEMPS-M total score and depressive, cyclothymic, hyperthymic, irritable and anxious showed satisfactory internal reliability (respectively, α = 0.898, α = 0.884, α = 0.903, α = 0.841, α = 0.853, α = 0.803).

The Multidimensional State Boredom Scale (MSBS) consists of 29 items with answers on a seven-point Likert scale, from 1 ("strongly disagree") to 7 ("strongly agree") [33]. The items are divided into five factors/subscales: (a) time perception (TP), which describes the slow passage of time; (b) disengagement (DIS), regarding a lack of involvement; (c) inattention (INA), or difficulty focusing attention on events; (d) high arousal (HA), which concerns the negative effects of an excessively high arousal; and (e) low arousal (LA), which covers the experiences and behavior attributable to an excessively low arousal. Scores obtained for these five factors are combined to obtain an overall boredom score. The instrument has been also validated in Italian samples [33], by showing good psychometric properties, including an excellent internal consistency. In our study, Cronbach's α of the MSBS also showed an excellent internal reliability (α = 0.965).

Statistical analyses

All analyses were performed using the software Statistical Package for Social Science (SPSS) per MacOS version 28.0 (IBM SPSS Statistics, Chicago, IL, United States). For all analyses, the level of statistical significance was set at $p < 0.05$, two-tailed. Descriptive statistics were performed in order to describe the socio-demographic and clinical characteristics of the sample. Categorical variables are summarized as frequency (n) and percentage (%) whilst continuous variables as means [standard deviation (SD)]. The normality of the distribution of all continuous variables were verified by using skewness, kurtosis and the Kolmogorov–Smirnov test, and the equality of variances by Levene test. The total sample was initially divided into two groups: DEP + and DEP-. Then, the sample was also stratified into four groups, depending on the presence or absence of clinically significant depression (as measured through PHQ) and the presence or absence of specifier Hikikomori (as measured through HQ-25): group 1 (DEP + /HK +), group 2 (DEP + /HK-), group 3 (DEP-/HK +) and group 4 (DEP-/HK-). To compare all socio-demographic and categorical variables in each group, the χ^2 Test was used. While Student's t-test and two-way tailored analysis of variance (ANOVA) were performed, respectively, to compare all continuous variables between DEP + versus DEP- groups and between four groups (DEP + /HK +; DEP + /HK-; DEP-/HK +; DEP-/HK-), after verifying the normality of quantitative variables. Primary outcome was evaluating which predominant Akiskal's affective temperament is more likely associated with Hikikomori-like social withdrawal specifier (as measured by HQ-25) in the total sample and within the depressive versus not-depressed subsample. Bivariate Person's correlations have been used to investigate potential associations between the primary outcome and other variables, particularly TEMPS-M, MSBS, GAD-7 and PHQ-9. Multivariate linear regression models have been assessed to investigate variables associated with the severity of Hikikomori-like social withdrawal symptomatology, including as independent variables depressive symptomatology (as measured by PHQ-9), anxiety symptomatology (as measured by GAD-7), Akiskal's affective temperaments (as measured by TEMPS-M), boredom dimension (as measured by MSBS and its subscales). Multivariate linear regression models have been performed in the total sample, with also a sub-analysis across both sexes (males versus males), in order to investigating potentially sex-based differences in the findings, and within the depressed sample only, in order to investigate whether (if any) differences were found considering the presence of depressive symptomatology. Then, a binary logistic regression analysis was run within the sample of individuals with depression, to evaluate which predominant affective temperament are associated with a concomitant Hikikomori-like social withdrawal symptomatology. The odds ratios (OR), corresponding to 95% of confidence intervals (CI), standardized coefficient β values were generated for each variable.

Results

Socio-demographic characteristics of the sample

A sample of 687 outpatients young adults was included in the study (Table 1). Participants' mean age was 24.1 (SD = 3.2), without sex-based differences (p = 0.671). Around two-third of the sample is represented by females (N = 523; 76.1%). Most participants declared to have a stable affective relationship (N = 637; 92.8%) and to live with his/her family members (N = 372; 54.1%). Most of the sample declared that their parents are not separated and/or divorced (N = 537; 78.2%). Most of the sample declared a previous positive psychiatric history (N = 524; 76.3%). The mean education level (in years) was 17.6 (SD = 2.5), without sex-based differences (p = 0.546).

Psychopathological characteristics of the sample

The mean score at PHQ-9 was 11.0 (SD = 5.8), without sex-based differences (p = 0.221). Regarding depressive symptomatology, the sample is slightly mainly represented by individuals with clinically relevant depressive symptomatology (N = 388; 56.5%), based on the stratification of the sample by using the PHQ-9 cutoff ≥ 10 (Table 2).

The mean score at GAD-7 was 10.3 (SD = 5.4), with females who reported significantly higher anxiety scores, compared to males (p = 0.003). Regarding the anxiety symptomatology, the sample is highly represented by individuals who reported clinically relevant anxiety symptomatology (N = 569; 82.8%), based on stratification of the sample by using the GAD-7 cutoff ≥ 5 (Table 2).

The mean score at HQ-25 was 42.1 (SD = 13.6), with males who reported significantly higher scores at HQ-25 total score, compared to females (p = 0.026). The mean score at HQ-25 socialization subscale was 18.5 (SD = 6.4),

Table 1 Socio-demographic characteristics of the sample

	Total sample	DepHK	DepHK-	noDepHK +	noDepHK-	p-value
Sex						
Males	164 (23.9%)	62 (25.4%)	26 (18.1%)	31 (34.8%)	45 (21.4%)	$\chi^2 = 9.570$
Females	523 (76.1%)	182 (74.6%)	118 (22.6%)	58 (65.2%)	165 78.6%)	**p = 0.023**
Age (years)						
M (SD)	24.1 (3.2)	24.1 (3.2)	24.2 (3.4)	26.6 (3.1)	24.2 (3.2)	p = 0.625
Educational level (years)						
M (SD)	17.6 (2.5)	17.7 (2.4)	17.6 (2.7)	17.9 (2.6)	17.5 (2.2)	p = 0.521
Living condition						
With their nuclear family	372 (54.1%)	122 (50%)	72 (50%)	52 (58.4%)	126 (60%)	$\chi^2 = 26.440$
With one their parents	63 (9.2%)	26 (10.7%)	17 (11.8%)	2 (2.2%)	18 (8.6%)	p = 0.190
With other relatives (not parents)	11 (1.6%)	4 (1.6%)	3 (2.1%)	1 (1.1%)	3 (1.4%)	
Alone	35 (5.1%)	13 (5.3%)	10 (6.9%)	6 (6.7%)	6 (2.9%)	
In a university hostel/boarding school	19 (2.8%)	9 (3.7%)	4 (2.8%)	5 (5.6%)	1 (0.5%)	
Together with friends	72 (10.5%)	31 (12.7%)	13 (9%)	9 (10.1%)	19 (9%)	
With their partner	76 (11.1%)	26 (10.7%)	20 (13.9%)	9 (10.1%)	21 (10%)	
Other	39 (5.7%)	13 (5.3%)	5 (3.5%)	5 (5.6%)	16 (7.6%)	
Psychological problem history						
None	163 (23.7%)					$\chi^2 = 25.207$
Yes	524 (76.3%)					**p < 0.001**
Siblings						
Yes	568 (82.7%)	47 (19.3%)	25 (17.4%)	10 (11.2%)	37 (17.6%)	$\chi^2 = 2.956$
No	119 (17.3%)	197 (80.7%)	119 (82.6%)	79 (88.8%)	173 (82.4%)	p = 0.401
Relationship status						
Single	12 (1.7%)	2 (1%)	2 (1.4%)	2 (2.3%)	6 (2.9%)	$\chi^2 = 11.620$
In a stable relationship	370 (53.9%)	122 (50%)	80 (55.6%)	43 (48.3%)	125 (59.5%)	p = 0.236
In a unstable relationship	38 (5.5%)	14 (5.7%)	11 (7.6%)	4 (4.5%)	9 (4.3%)	
Married	267 (38.9%)	106 (43.3%)	51 (35.4%)	40 (44.9%)	70 (33.3%)	

In bold significant p-values

without sex-based differences ($p = 0.097$). The mean score at HQ-25 isolation subscale was 11.8 (SD = 6.4), with slightly significantly higher scores among males ($p = 0.042$). The mean score at HQ-25 emotional support subscale was 11.9 (SD = 2.9), with significantly higher scores among males ($p = 0.034$) (Table 2).

The mean score at MSBS was 104.3 (SD = 41.4), without sex-based differences ($p = 0.975$). The mean score at MSBS Disengagement subscale was 38.9 (SD = 16.4), without sex-based differences ($p = 0.290$). The mean score at MSBS High Arousal subscale was 17.7 (SD = 8.1), without sex-based differences ($p = 0.061$). The mean score at MSBS Inattention subscale was 17.6 (SD = 7.3), without sex-based differences ($p = 0.874$). The mean score at MSBS Low Arousal subscale was 19.2 (SD = 9.3), without sex-based differences ($p = 0.976$). The mean score at MSBS Time Perception was 11.1 (SD = 7.0), without sex-based differences ($p = 0.743$) (Table 2).

The mean score at depressive temperament subscale at TEMPS-M was 20.9 (SD = 7.4), without significant sex-based differences ($p = 0.191$). The mean score at cyclothymic temperament subscale at TEMPS-M was 20.1 (SD = 8.0), without sex-based differences ($p = 0.161$). The mean score at hyperthymic temperament subscale at TEMPS-M was 19.0 (SD = 6.0), with males who reported significantly higher scores ($p = 0.002$). The mean score at irritable temperament subscale at TEMPS-M was 14.9 (SD = 6.1), without sex-based differences ($p = 0.735$) (Table 2). The mean score at anxious temperament subscale at TEMPS-M was 19.5 (SD = 7.0), with significantly higher scores among females ($p \leq 0.001$).

Variables associated with Hikikomori-like social withdrawal specifier within the depressed versus not-depressed sample

Considering all the total sample without distinguishing between depressive versus not-depressed individuals, according to the multivariate regression model, HQ-25 levels were positively predicted by MSBS low arousal levels (Beta coefficient, B = 0.428; 95%Confidence Interval,

Table 2 Psychopathological features of the sample

Scale, M (SD)	Total sample	DepHK	DepHK-	noDepHK+	noDepHK-	p-value
PHQ-9 total score	11.0 (5.8)	16.1 (4.3)	13.4 (3.1)	6.4 (2.1)	5.5 (2.3)	$F_{(3,683)}=486.263$ **$p<0.001$***
GAD-7 total score	10.3 (5.4)	13.9 (4.3)	12.2 (3.9)	5.9 (3.9)	7.2 (3.9)	$F_{(3,683)}=176.712$ **$p<0.001$***
HQ-25 total score	42.1 (13.6)	55.1 (8.6)	32.7 (6.1)	49.9 (6.7)	30.2 (6.8)	$F_{(3,683)}=547.499$ **$p<0.001$***
HQ-25 Socialization	18.5 (6.4)	24.4 (4.5)	14.4 (3.4)	21.4 (4.3)	13.1 (3.5)	$F_{(3,683)}=373.610$ **$p<0.001$***
HQ-25 Isolation	11.8 (6.4)	17.4 (4.7)	7.6 (3.0)	15.6 (4.1)	6.4 (3.1)	$F_{(3,683)}=392.189$ **$p<0.001$***
HQ-25 emotional support	11.9 (2.9)	13.3 (2.6)	10.7 (2.7)	12.9 (2.1)	10.7 (2.8)	$F_{(3,683)}=50.432$ **$p<0.001$***
TEMPS-M depressive	20.9 (7.4)	25.7 (6.6)	21.8 (5.9)	19.2 (6.3)	15.6 (5.8)	$F_{(3,683)}=103.307$ **$p<0.001$****
TEMPS-Mcyclothymic	20.1 (8.0)	25.0 (6.9)	22.0 (7.2)	17.4 (6.6)	14.1 (5.7)	$F_{(3,683)}=112.067$ **$p<0.001$***
TEMPS-M hyperthymic	19.0 (6.0)	17.9 (6.2)	18.9 (5.4)	18.9 (6.0)	20.4 (6.0)	$F_{(3,683)}=6.832$ **$p<0.001$****
TEMPS-M Irritable	14.9 (6.1)	17.3 (6.7)	15.2 (5.6)	14.1 (5.4)	12.5 (4.8)	$F_{(3,683)}=27.071$ **$p<0.001$***
TEMPS-M anxious	19.5 (7.0)	22.7 (6.7)	20.5 (6.4)	18.0 (6.6)	15.7 (5.8)	$F_{(3,683)}=48.300$ **$p<0.001$***
MSBS total score	104.2 (41.4)	136.8 (29.5)	102.0 (34.1)	96.1 (33.8)	71.7 (31.6)	$F_{(3,683)}=161.565$ **$p<0.001$***
MSBS Disengagement	38.9 (16.4)	51.5 (11.6)	37.4 (13.9)	35.9 (13.9)	26.6 (13.1)	$F_{(3,683)}=143.205$ **$p<0.001$***
MSBS high arousal	17.7 (8.1)	23.5 (6.7)	18.3 (7.0)	15.7 (6.3)	11.5 (5.9)	$F_{(3,683)}=132.424$ **$p<0.001$***
MSBS inattention	17.6 (7.3)	22.0 (5.6)	17.9 (6.9)	16.2 (6.9)	12.7 (6.4)	$F_{(3,683)}=83.919$ **$p<0.001$**
MSBS low arousal	19.2 (9.3)	26.6 (6.9)	17.9 (7.6)	17.7 (8.0)	11.9 (6.6)	$F_{(3,683)}=166.017$ **$p<0.001$**
MSBS time perception	11.1 (7.0)	13.2 (8.4)	10.5 (6.3)	10.6 (5.8)	9.1 (5.5)	$F_{(3,683)}=14.586$ **$p<0.001$**

HQ-25 hikikomori questionnaire-25 items, *PHQ-9* Patient health Questionnaire-9, *MSBS* multidimensional state boredom scale, *TEMPS-M* munster temperament evaluation of memphis, Pisa, Paris and San Diego; *GAD-7* generalized anxiety disorder-7

* Bonferroni

** T2 Tamhane

In bold significant p-values

CI = (0.272)—(0.585); $p < 0.001$], MSBS disengagement (B = 0.145; 95%CI = (0.058)–(0.232); $p = 0.001$], depressive levels, as measured by PH9 total score (B = 0.482; 95%CI = (0.264)–(0.700); $p < 0.001$] and by irritable affective temperament (B = 0.215; 95%CI = (0.0075)–(0.325); $p = 0.003$] and depressive affective temperaments (B = 0.190; 95%CI = (0.043)–(0.338); $p = 0.011$]. While HQ-25 levels were negatively predicted by GAD-7 total score [B = − 0.252; 95%CI = (− 0.484)–(− 0.020); $p = 0.033$]. These variables statistically significantly predicted Hikikomori-like social withdrawal symptomatology (F(6, 680) = 82.336, $p < 0.001$, $R^2 = 0.421$) (Table 3). Furthermore, we explored sex-based differences in Hikikomori-like social withdrawal symptomatology within the total sample, by splitting the multivariate regression linear model according to the sex (males versus females).

According to the multivariate regression model, among males, HQ-25 levels were positively predicted by only MSBS total scores [B = 0.147; 95%CI = (0.092)–(0.202); $p < 0.001$] and depressive symptomatology, as measured by PHQ-9 [B = 0.564; 95%CI = (0.186)–(0.943); $p = 0.004$]. While, HQ-25 levels were negatively predicted by hyperthymic affective temperament [B = -0.266; 95%CI = (− 0.529)–(− 0.004); $p = 0.047$]. These variables statistically significantly predicted Hikikomori-like social withdrawal symptomatology (F(3, 160) = 37.520, $p < 0.001$, $R^2 = 0.413$) (Table 4)(Fig. 2).

Table 3 Multiple linear regression with HQ-25 total score (as dependent variable)—total sample

	B	SE	β	t	p-value	95%IC lower limit	95%IC upper limit	Tolerance	VIF
MSBS Low Arousal	0.428	0.080	0.295	5.368	**< 0.001**	0.272	0.585	0.282	3.552
PHQ-9 total score	0.482	0.111	0.205	4.346	**< 0.001**	0.264	0.700	0.382	2.619
MSBS Disengagement	0.145	0.044	0.175	3.260	**0.001**	0.058	0.232	0.294	3.398
TEMPS-M Irritable	0.215	0.071	0.096	3.026	**0.003**	0.075	0.325	0.839	1.192
TEMPS-M Depressive	0.190	0.075	0.104	2.536	**0.011**	0.043	0.338	0.502	1.992
GAD-7 total score	− 0.252	0.118	− 0.100	− 2.137	**0.033**	− 0.484	− 0.020	0.387	2.581

SE standard error, *HQ-25* hikikomori questionnaire-25 items, *PHQ-9* patient health questionnaire-9, *MSBS* Multidimensional state boredom scale, *TEMPS-M* munster temperament evaluation of memphis, Pisa, Paris and San Diego; GAD-7: generalized anxiety disorder-7

In bold significant p-values

Table 4 Multiple Linear Regression with HQ-25 total score (as dependent variable)

Only sample of males

	B	SE	β	t	p-value	95%IC Lower Limit	95%IC Upper Limit	Tolerance	VIF
MSBS total score	0.147	0.028	0.428	5.293	**< 0.001**	0.092	0.202	0.562	1.779
PHQ-9 total score	0.564	0.192	0.237	2.944	**0.004**	0.186	0.943	0.567	1.763
TEMPS-M Hyperthymic	− 0.266	0.133	− 0.123	− 2.003	**0.047**	− 0.529	− 0.004	0.971	1.030

Only sample of females

	B	SE	β	t	p-value	95%IC lower limit	95%IC upper limit	Tolerance	VIF
MSBS Low Arousal	0.475	0.088	0.332	5.365	**< 0.001**	0.301	0.649	0.285	3.512
MSBS Disengagement	0.107	0.050	0.130	2.125	**0.034**	0.008	0.206	0.289	3.461
PHQ-9 total score	0.502	0.126	0.215	3.971	**< 0.001**	0.254	0.750	0.371	2.697
GAD-7 total score	− 0.354	0.138	− 0.140	− 2.559	**0.011**	− 0.625	− 0.082	0.363	2.755
TEMPS-M Irritable	0.206	0.081	0.094	2.543	**0.011**	0.047	0.365	0.801	1.248
TEMPS-M Anxious	0.168	0.077	0.087	2.166	**0.031**	0.016	0.320	0.675	1.482
TEMPS-M Depressive	0.176	0.084	0.098	2.102	**0.036**	0.012	0.340	0.498	2.010

SE standard error, *HQ-25* hikikomori questionnaire-25 items, *PHQ-9* patient health questionnaire-9, *MSBS* multidimensional state boredom scale, *TEMPS-M* munster temperament evaluation of memphis, Pisa, Paris and San Diego

In bold significant p-values

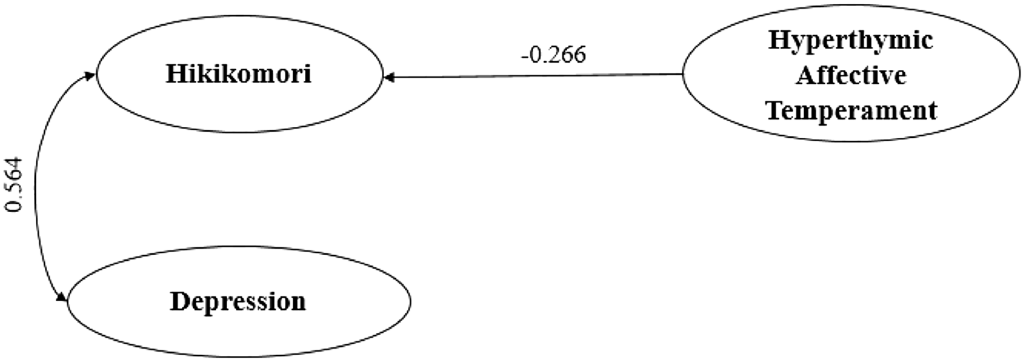

Fig. 2 Graphical representation of relationships between Hikikomori, depression and affective temperaments (males)

Conversely, according to the multivariate regression model, among females, HQ-25 levels were positively predicted MSBS low arousal levels [B = 0.475; 95%CI = (0.301)–(0.649); p < 0.001], MSBS disengagement [B = 0.107; 95%CI = (0.008)–(0.206); p = 0.034], depressive levels, as measured by PH9 total score [B = 0.502;

95%CI = (0.254)–(0.750); p < 0.001]; and by irritable affective temperament [B = 0.206; 95%CI = (0.047)–(0.365); p = 0.011], anxious affective temperament [B = 0.168; 95%CI = (0.016)–(0.320); p = 0.031] and depressive affective temperament (B = 0.176; 95%CI = (0.012)–(0.340); p = 0.036]. While HQ-25 levels were negatively predicted by GAD-7 total score [B = -0.354; 95%CI = (– 0.626)–(– 0.082); p = 0.011]. These variables statistically significantly predicted Hikikomori-like social withdrawal symptomatology (F(7, 515) = 57.605, p < 0.001, R^2 = 0.439) (Table 4)(Fig. 3).

When the multivariate linear regression model was run, by selecting only depressed individuals, HQ–25 levels were positively predicted by MSBS total score levels (B = 0.172; 95%CI = (0.098)–(0.245); p < 0.001], MSBS low arousal levels (B = 0.358; 95%CI = (0.114)–(0.602); p < 0.001], and by depressive affective temperament (B = 0.277; 95%CI = (0.094)–(0.459); p = 0.003]. While HQ-25 levels were negatively predicted by MSBS High Arousal levels [B = – 0.347; 95%CI = (– 0.620)–(– 0.074); p = 0.013]. These variables statistically significantly predicted Hikikomori-like social withdrawal symptomatology (F(4, 383) = 48.544, p < 0.001, R^2 = 0.336) (Table 5).

A logistic regression analysis was performed to ascertain the effects of all types of five affective temperaments (as measured by TEMPS-M), on the likelihood of developing depression with Hikikomori-like social withdrawal symptomatology. The logistic regression model was statistically significant, $\chi2(1) = 4.423$, $p = 0.035$. The model explained 12.3% (Nagelkerke $R2$) of the variance in depression with Hikikomori-like social withdrawal symptomatology and correctly classified 65.5% of cases. According to the logistic regression model, depression with Hikikomori-like social withdrawal symptomatology was significantly predicted by higher levels at TEMPS-M subscales which measures depressive and cyclothymic affective temperaments. Other affective temperaments did not show to be predictive of the onset of a depression with Hikikomori-like social withdrawal symptomatology (Table 6).

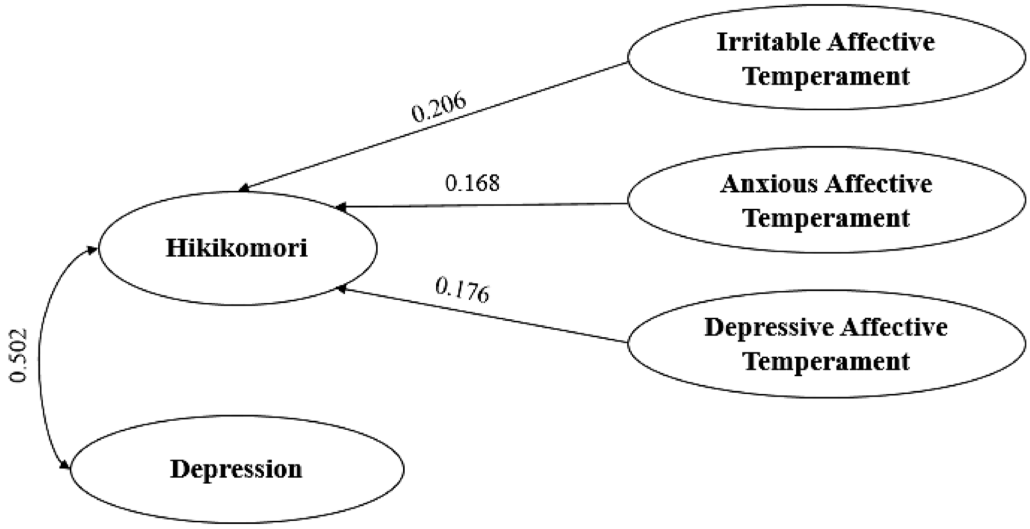

Fig. 3 Graphical representation of relationships between Hikikomori, depression and affective temperaments (females)

Table 5 Multiple linear regression with HQ-25 total score (as dependent variable)—only sample of depressed individuals (PHQ ≥ 10)

	B	SE	β	t	p-value	95%IC lower limit	95%IC upper limit	Tolerance	VIF
MSBS Low Arousal	0.358	0.124	0.224	2.886	**0.004**	0.114	0.602	0.289	3.464
MSBS total score	0.172	0.038	0.457	4.565	**< 0.001**	0.098	0.245	0.173	5.796
MSBS High Arousal	– 0.347	0.139	– 0.188	– 2.500	**0.013**	– 0.620	– 0.074	0.305	3.279
TEMPS-M Depressive	0.277	0.093	0.138	2.983	**0.003**	0.094	0.459	0.813	1.230

SE standard error, *HQ-25* hikikomori questionnaire-25 items, *PHQ-9* patient health questionnaire-9, *MSBS* multidimensional state boredom scale, *TEMPS-M* munster temperament evaluation of Memphis, Pisa, Paris and San Diego

In bold significant p-values

Table 6 Logistic Binary Regression within depressive sample with HK (presence/absence as dichotomous dependent variable)

	B	SE	Wald	Exp (B)	p-value	95%IC lower limit	95%IC upper limit
TEMPS-M Depressive	0.080	0.018	19.385	1.083	**< 0.001**	1.045	1.122
TEMPS-M Cyclothymic	0.035	0.017	4.407	1.033	**0.036**	1.002	1.069

SE standard error, *HQ-25* Hikikomori questionnaire-25 items, *TEMPS-M* munster temperament evaluation of memphis, Pisa, Paris and San Diego

In bold significant p-values

Discussion

To the best of our knowledge, this is the first study investigating the relationship between affective temperaments and Hikikomori-like social withdrawal symptomatology in a cohort of young adults, by comparing clinically significant depressed versus not-depressed individuals and exploring differences between sexes. In particular, following more recent research directions which suggested to explore Hikikomori-like social withdrawal as a transdiagnostic specifier, particularly within the sample of individuals with depressive symptomatology [6, 34], our study specifically explored the association between Hikikomori as diagnostic specifier associated with depression and the identification of specific predominant associated affective temperaments. Overall, our findings found that, within the total recruited sample, HQ-25 mean total scores are overly higher compared to previous published studies carried out within an Italian sample [28, 35, 36], probably due to the younger age of our sample and the recruitment period which was after the COVID-19 pandemic. Comparable with previous studies [28, 35, 36], in our sample, males reported significantly higher HQ-25 scores, particularly in the subscales 'isolation' and 'emotional support', compared to females. In the total sample, Hikikomori-like social withdrawal symptomatology was found to be significantly predicted by higher levels of low arousal boredom (i.e., by manifesting dysphoria, feelings of emptiness and fatigue) and feelings of disengagement from meaningful and interesting life activities (as measured by MSBS). Moreover, Hikikomori-like social withdrawal has been significantly predicted by higher depressive levels, lower anxiety levels and by higher levels at irritable and depressive affective temperaments (as measured by TEMPS-M). Indeed, despite some studies having been carried out by exploring some child temperamental features and social isolation, there are no published studies specifically addressed to young adults [37, 38]. These studies found an association between child social isolation and the presence of the so-called behavioral inhibition temperament, i.e. the tendency to react following exposure to unfamiliar stimuli by developing anxiety and avoidance behavior [37, 38]. Akiskal already identified a possible association between social isolation and specific affective temperaments, such as cyclothymic (particularly in transient social isolation episodes), and depressive affective temperaments (more associated with the tendency to develop a social withdrawal) [39, 40]. Subjects with depressive affective temperaments tend to be sensitive to suffering, self-denying and devote themselves to others [40]. Their optimal balance is achieved when they are in harmony with others, adhering to social norms and roles [40]. According to this perspective, social isolation could be a maladaptive mechanism to escape suffering or the inability to find harmony with the world around them. In addition, such subjects are characterized by harm avoidance and low novelty seeking, which often leads the subject to a boring life and, hence, could result in a progressive isolation [40]. On the other hand, subjects with an irritable affective temperament, are characterized by the presence of irritable-lunatic mood with 'ill-humored joking' [30]. Such traits could result in disagreements with peers and social impairment leading to progressive social withdrawal both as distanced from others and as a maladaptive defense mechanism (such a person might feel not understood by others) [30]. This could be reinforced by the fact that such individuals have a tendency to brood and great impulsivity [30]. Disengagement in the process leading to boredom is characterized by a difficulty in the process of orienting and attributing attention to the environment resulting in a mismatch between fully experiencing an activity and paying attention to it [41, 42]. This process may explain why this dimension is related to social withdrawal. Indeed, the lack of attention to the environment results in a disinterest in what we find in the environment, with a progressive isolation. Finally, low arousal is connected with the proneness to boredom. In particular, subjects with a low arousal try to find some activities to enhance their arousal [43]. If this process is maladaptive, we can hypothesize that persistent low activation could lead to isolation through feelings of emptiness and fatigue, despite we should integrate these findings by using longitudinal cohort studies to demonstrate whether there is a causal relationship between boredom dimension and the onset of a HK-like social withdrawal within the depressed individuals.

Moreover, considering that our sample is mainly represented by females, we also carried out a sub-analysis assessing potentially sex-based differences in the clinical and predisposition to the development of a depression with or without a Hikikomori diagnostic specifier. In particular, according to our findings, within the male sample, Hikikomori-like social withdrawal conditions seemed to be significantly predicted by general higher boredom levels and the level of depressive severity. While only the presence of a predominant hyperthymic temperament seemed to be negatively associated with the presence of a Hikikomori-like social withdrawal, by suggesting a potential protective role, which should be further investigated and confirmed in larger longitudinal studies evaluating both depressed and not-depressed HK individuals and considering sex-based differences between both samples. Indeed, there are no published studies which allow us to confirm these findings, despite Akiskal previously suggested a possible association of transient social isolation episodes (not Hikikomori-like) and a predominant hyperthymic temperament, mainly occurring as a reaction to the social and seldom maladaptive consequences of their temperaments and the subsequent need to self-isolate in order to have not been exposed to a negative judgment from others [40]. However, social isolation among hyperthymic individuals, may indeed represent a transient reaction which rarely meets Hikikomori diagnostic criteria [6]. Furthermore, our findings reported that, among females, Hikikomori-like social withdrawal seemed to be significantly associated with low arousal and disengagement boredom levels, by depression severity and by irritable, anxious and depressive affective temperaments. Indeed, previous literature already documented that, among females, the most predominant affective temperaments are generally represented by anxious and depressive affective temperaments [20] by, hence, suggesting that probably the irritable affective temperament could indeed more likely be associated to the psychopathological trajectory leading to HK-like social withdrawal symptomatology [30]. However, also these preliminary findings should also be extensively confirmed and replicated in more larger sex-based cohort longitudinal studies, as there is no still published literature on the topic, either in depressed versus not depressed young adults.

Furthermore, after stratifying the entire sample according to the presence versus absence of a depressive symptomatology, according to our findings, depression associated with Hikikomori specifier seemed to be positively associated with higher general boredom levels, particularly low arousal boredom levels. Therefore, within the depressed sample, Hikikomori seemed to not be predicted by disengagement boredom levels as observed in the total sample. This could be explained by the fact that individuals in whom there is a greater component of the disengagement dimension, could display some difficulty in recognizing internal information (e.g., thoughts and emotions) [41]. On the other hand, this ability is often present in those suffering from depression, and this would result in the ability to direct attention to specific environmental elements, more likely responsible for the development of the depressive symptomatology. Moreover, the likelihood of developing Hikikomori-like social withdrawal symptomatology within the context of a depression seemed to be positively predicted by the presence of predominant depressive and cyclothymic affective temperaments, confirming data already observed by Akiskal [21, 30]. Generally, major depressive disorder (MDD) is associated with depressive and anxious temperament [20, 44]. Cyclothymic temperament is associated with the development of Bipolar Disorder (BD), in particular to type II [20, 44]. However, this temperament is also associated with forms of MDD lately evolving into BD, in those individuals who develop MDD but with a positive family history for BD and in atypical forms of MDD [20, 44]. Therefore, cyclothymic temperament could be associated with those clinical phenotypic depressive forms which could be different from the classic MDD clinical picture. Cyclothymic could evolve into depression associated with Hikikomori-like social withdrawal as a diagnostic specifier, manifested by mood swings, which could lead to increasingly frequent depressive episodes over time and, hence, resulting in the potential development of a progressive social and emotional isolation.

Therefore, based on our preliminary findings, one could argue that depression associated with Hikikomori-like social withdrawal symptomatology could represent a distinct type of depression which should be adequately investigated and clinically characterized from a diagnostic and therapeutic perspective, in order to build a personalized and tailored-based intervention. The association with specific affective temperamental profiles could also help clinicians in early identifying those depressed individuals at-risk to develop a clinical picture associated with Hikikomori specifier which, indeed, could potentially modify clinical course, outcomes and treatment strategies.

However, despite these preliminary and promising findings, our study has several limitations which should be adequately addressed and discussed before generalizing our results. Firstly, findings coming from the total sample could be influenced by sex unbalance, being our total sample mainly represented by females. Secondly, our sample could be influenced by the highly age-based selection, mainly represented by young adults (aged

18–35). Therefore, further studies should be carried out by including a more representative sample of individuals (independently by the presence of comorbid depressive symptomatology), in order to clearly confirm these findings only in primary Hikikomori and according to different age ranges. Conversely, when comparing both groups (depressed versus not-depressed), both samples are sex- and age-based homogeneously represented. Therefore, one could argue that findings coming from sub-analysis could be more easily generalizable to the sample of individuals affected by Hikikomori secondary to depression. Thirdly, the cross-sectional nature of our study does not allow us to draw up definitive conclusions regarding the relationship between depression and Hikikomori-like social withdrawal (i.e., identifying whether an individual is affected by a primary depression with Hikikomori or a depression secondary to Hikikomori). Fourthly, being our total sample mainly represented by females, our findings regarding the association between specific affective temperaments and Hikikomori-like social withdrawal symptomatology could be biased by the female-effect in temperamental profiles. Fifthly, our study is a nationwide population-based study and, hence, our findings could be influenced by selection bias, by the fact that our sample is a nonclinical one. Therefore, further larger longitudinal, multicentric and pan-European based studies should be conducted in order to replicate our preliminary findings as well as longitudinally identifying specific sex-based predictors influencing the clinical course, manifestation, treatment outcomes and prognosis of individuals affected by depression depending on the presence of Hikikomori diagnostic specifier. Furthermore, despite our preliminary findings also investigated as secondary exploratory outcomes, boredom dimensions and anxiety symptomatology, the cross-sectional nature of the study did not allow to draw uo definitive conclusions regarding the potential causal relationship between boredom dimension and subdimensions and the increased/decreased chance to develop Hikikomori-like social withdrawal both in depressed versus not depressed individuals, despite our findings could suggest also a potential association and role depending on the type of predominant affective temperament.

Overall, our preliminary findings could significantly help clinicians working with young adults manifesting depressive symptomatology by potentially shedding the light on the possible association between specific predominant affective temperamental profiles and the increased chance to develop a depression associated with the Hikikomori diagnostic specifier. However, our findings coming from a nationwide, Italy-based, nonclinical population-based study specifically recruiting young adults aged 18–35 which could indeed help in providing a current snapshot of the Italian situation regarding youth depression with/without Hikikomori, despite our findings should be extensively replicated in longitudinal clinical studies recruiting both primary and secondary Hikikomori subjects. An interesting result comes from our sex-based stratified sub-analysis, which suggested a potential different clinical phenotypization depending on the sex and also influenced by predominant affective temperament, which should also be confirmed and verified in larger longitudinal clinical studies. In particular, there is the need to confirm which affective temperaments could be protective (or risky) for the development of a Hikikomori-like social withdrawal symptomatology in depressed individuals. Early identification of affective temperament in patients with depression could help in predicting which will be the potential developing psychopathological trajectory leading to the onset of a Hikikomori-like social withdrawal associated with depressive symptomatology and which should be the tailored and personalized treatment to be adapted accordingly. Meanwhile, a comprehensive personological characterization of individuals who develop Hikikomori-like social withdrawal, considering both depressed versus not depressed individuals would be useful to better clinically characterize from a diagnostic and therapeutic perspectives these subjects, also investigating the (potential) mediatory role of the boredom dimensions as well as attachment style profiles and anxiety trait and state. Finally, following suggestions and research hypotheses of previous researchers [1, 2, 4, 10], it would be appropriate to clinically characterize depression associated with Hikikomori by identifying similarities and differences (if any) with the psychopathological construct of the Modern-Type Depression.

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Author contributions
L.O. and G.L. conceived and conceptualized the study. G.L. and S.B. contributed to data collection. L.O. performed formal data analysis. A preliminary draft was written by G.L. and L.O. L.O. wrote the final draft. U.V. revised and edited all drafts and the final draft. T.A.K. and U.V. supervised the work and provided the final feedback to the manuscript. All authors have read and agreed to the published version of the manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the local Institutional Review Board of the Department of Experimental and Clinical Neurosciences/DIMSC, Polytechnic

University of Marche (protocol code ACPS-D-21-00347, 28th September, 2021) and it complies with the Declaration of Helsinki. All participants provided their written informed consent to participate in the study.

Consent for publication

All participants provided their consent for publication of the present findings.

Competing interests

The authors declare that they have no competing interests. All authors declared that the research was conducted in the absence of any commercial or financial relationships that could be constructed as a potential conflict of interest.

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Recovery and decision-making involvement in people with severe mental illness from six countries: a prospective observational study

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Abstract

Background: Clinical decision-making is the vehicle of health care provision, and level of involvement predicts implementation and satisfaction. The aim of this study was to investigate the impact of decision-making experience on recovery.

Methods: Data derived from an observational cohort study "Clinical decision making and outcome in routine care for people with severe mental illness" (CEDAR). Adults (aged 18–60) meeting standardised criteria for severe mental illness were recruited from caseloads of outpatient and community mental health services in six European countries. After consenting, they were assessed using standardised measures of decision-making, clinical outcome and stage of recovery at baseline and 1 year later. Latent class analysis was used to identify course of recovery, and proportional odds models to investigate predictors of recovery stage and change.

Results: Participants ($n = 581$) clustered into three stages of recovery at baseline: Moratorium ($N = 115$; 19.8%), Awareness/Preparation ($N = 145$; 25.0%) and Rebuilding/Growth ($N = 321$; 55.2%). Higher stage was cross-sectionally associated with being male, married, living alone or with parents, and having better patient-rated therapeutic alliance and fewer symptoms. The model accounted for 40% of the variance in stage of recovery. An increased chance of worse outcome (change over 1 year to lower stage of recovery) was found for patients with active involvement compared with either shared (OR = 1.84, 95% CI 1.15–2.94) or passive (OR = 1.71, 95% CI = 1.00–2.95) involvement. Overall, both process (therapeutic relationship) and outcome (symptomatology) are cross-sectionally associated with stage of recovery.

Conclusions: Patient-rated decision-making involvement and change in stage of recovery are associated. Joint consideration of decision practise within the recovery process between patient and clinician is supposed to be a useful strategy to improve clinical practice (ISRCTN registry: ISRCTN75841675. Retrospectively registered 15 September 2010).

Keywords: Clinical decision making, Patient involvement, Recovery, Severe mental illness (SMI), Routine mental health services, Multinational health service research

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Background

A policy consensus has emerged internationally supporting a mental health system orientation around recovery [1]. Converting this policy rhetoric into clinical practice has proved challenging, partly because the policy is not yet matched by a strong evidence base [2]. Syntheses are now beginning to be published addressing the concept of personal recovery [3] and its relation to outcome e.g. quality of life [4], specific pro-recovery interventions such as peer support [5], and implications for services [6]. However, wide variation is evident in emerging practices across different national and regional mental health systems [7]. The disparate commentaries on a recent overview [8] highlights the challenges of identifying best practice in supporting recovery.

More and different research is needed. Why different? Best available evidence indicates the key processes involved in recovery which are Connectedness ("community integration" in North America, "social inclusion" in the UK, continental Europe and Australia), Hope and optimism about the future, a positive non-stigmatised Identity, Meaning in life, and Empowerment—the CHIME Framework [3]. This framework has been validated internationally [9] and in current mental health service users [10], and the five processes are all potential target outcome domains for mental health services, yet the current evidence base and practice does not support this orientation. To illustrate this point, in England the National Institute for Health and Clinical Excellence (NICE) produces clinical guidelines for a range of disorders, including the schizophrenia guideline updated in 2014 [11]. No clinical trial evidence with primary clinical end-points involving any of the CHIME processes was cited in the evidence summary. Evidence about the relationship between clinical practice and recovery support is needed.

The necessary scientific building blocks are becoming available. Recovery measures have been developed [12, 13], and trials with recovery outcomes as primary clinical end-points are being published [14, 15]. However, an evidence gap remains about the relationship between clinical processes and recovery. Specifically, there is an absence of empirical evidence about recovery and clinical decision-making—the important process of treatment planning jointly between clinician and patient.

Clinical decision-making is the primary vehicle of mental health service delivery. Three levels of patient involvement in decision-making have been described: informed, shared and passive [16]. Passive decision-making occurs when the clinician makes the decision for the patient. Informed (or active) decision-making occurs when the patient makes the decision, having received information from the clinician. Shared decision-making (SDM) is collaborative decision-making involving the sharing of information and expertise by both participants.

Shared decision-making in mental health is widely recommended [11], despite being under-researched. A recent systematic review identified only two randomised controlled trials investigating shared decision-making [17], and a Cochrane review identified that *'further research is urgently needed'* [18]. Despite the limited research base, it is recommended that *'a shared decision making approach should be facilitated'* in adult mental health services [11].

In this study, the determinants of stage of recovery were investigated, with a particular focus on the experience of involvement in clinical decision-making. The aims are to identify (1) the course of change in stage of recovery, (2) cross-sectional predictors of stage of recovery, and (3) predictors of 1-year change in the stage of recovery.

Methods

Design

The CEDAR Study is a naturalistic prospective longitudinal observational study with bimonthly assessments during a 12-month observation period [19]. The overall aim of the CEDAR Study is to assess the scope and quality of clinical decisions in the treatment of people with severe mental illness, and the impact of clinical decision making in routine care on patient outcome.

Participants and procedure

A total of 588 participants were recruited from caseloads of outpatient and community mental health services at six centres throughout Europe: Aalborg (Denmark), Debrecen (Hungary), London (England), Naples (Italy), Ulm (Germany) and Zurich (Switzerland). Inclusion criteria: aged 18–60 years at intake; mental disorder of any kind as main diagnosis established by case notes or staff communication using SCID criteria; presence of severe mental illness (defined as Threshold Assessment Grid (TAG) [20] score of > =5 and illness duration > = 2 years); expected contact with mental health services (excluding inpatient services) during the time of study participation; sufficient command of the host country's language; capable of giving informed consent. Exclusion criteria: main diagnosis of mental retardation, dementia, substance use or organic brain disorder; cognitive impairment severe enough to make it impossible to give meaningful information on study instruments; treatment by forensic psychiatric services. After complete description of the study to the subjects, written informed consent was obtained.

Clinical staff rated TAG to identify presence of severe mental illness, and eligible patients were approached to give informed consent. At baseline, patients nominated a clinician closely involved in their treatment, and both completed baseline measures. At 1-year follow-up, patients and staff completed all baseline measures again. Bi-monthly, patients and staff were asked independently about context, content and implementation of clinical decision making. They wrote down the most important decision made at their last meeting, A list of predefined topics with three possible responses (“not discussed”, “discussed, no decision made” and “discussed, decision made”) was presented to indicated what was discussed in general in the selected meeting. Patients most frequently indicated having discussed “medication”, whereas staff reported “symptoms” most frequently, the third most frequent topic was “family” for both.

Ethical committee approval was obtained in all sites. Quality assurance in data collection was maximised by thorough training sessions for all study workers conducted by experts prior to the start of data collection, with biannual booster trainings for study workers during the data collection period. The characteristics of the sample are shown in Table 1.

Measures

All measures were used in the local language. Existing translations were used when available, otherwise the measure was translated using intensive forward and backward translation by experienced bilingual clinical researchers following common standards [21]. All total scores except for Clinical Decision-Making Involvement and Satisfaction (CDIS) and Camberwell Assessment of Need Short Appraisal Scale (CANSAS) were pro-rated where 80% of items were completed.

Table 1 Sociodemographic and clinical characteristics of patient participants (*N* = 581)

Study centre *(n, %)*		
Ulm	111	19.1
London	80	13.8
Naples	101	17.4
Debrecen	97	16.7
Aalborg	97	16.7
Zurich	95	16.4
Gender (female) *(n, %)*	306	52.7
Age (years) *(M, SD)*	41.7	10.8
Married *(n, %)*	145	25.5
Ethnic group (White) *(n, %)*	549	94.5
Years in school *(M, SD)*	10.4	1.9
Living alone *(n, %)*	230	39.6
Paid or self-employed *(n, %)*	109	18.8
Receiving state benefits *(n, %)*	419	72.2
Illness duration (years) *(M, SD)*	12.5	9.3
Diagnosis *(n, %)*		
Psychotic disorder	264	45.4
Mood disorder	198	34.1
Other	119	20.5
TAG *(M, SD)*	7.5	2.2
GAF *(M, SD)*	49.2	10.9

Abbreviations: *M* mean, *SD* standard deviation, *TAG* Threshold Assessment Grid, *GAF* Global Assessment of Functioning

Diagnosis was established at baseline from casenotes by researcher-assessed Structured Clinical Interview for DSM-IV Axis I Disorders—Clinical Version (SCID) [22].

Three patient-rated measures: *1. Stages of Recovery Inventory (STORI)* is a 30-item assessment resulting in allocation to one of five stages of recovery [23]. Because the original study and three replication studies [24–26] found a 3-cluster solution better fitted the data, a summary score comprising three stages was used: a) Moratorium (withdrawal characterized by a profound sense of loss and hopelessness), b) Awakening/Preparation (emergence of hope and taking first steps to work on recovery skills), c) Rebuilding/Growth (from actively working towards a positive identity and goals to a full and meaningful life). *2. Outcome Questionnaire-45 (OQ-45.2)* is a 45-item measure which provides an index of mental health functioning, ranging from 0 (good outcome) to 180 [27]. Sub-scales are symptom distress (range 0 to 100), interpersonal relations (0 to 44) and social role (0 to 36). Psychometric properties are confirmed in many studies with high internal consistency (.90) and test-re-test reliability (.84 over 3-weeks [28]). *3. Manchester Short Assessment of Quality of Life (MANSA)* is a 16-item assessment of quality of life ranging from 1 (low quality of life) to 7 [29]. Correlations between subjective quality of life scores on MANSA and Lancashire Quality of Life Profile were 0.83 or higher, Cronbach’s alpha for satisfaction ratings was 0.74.

Three staff-rated measures: *1. Global Assessment of Functioning (GAF)* is a staff-rated one-item global measure of symptomatology and social functioning, ranging from 1 (worst) to 100 (best) [30]. *2. Health of the Nation Outcome Scale (HoNOS)* is a staff-rated 12-item assessment of social disability ranging from 48 (worst) to 0 (best) [31]. *3. Threshold Assessment Grid (TAG)* is a staff-rated seven-item measure of severity (comprising Safety, Risk and Needs/Disabilities) of mental illness ranging from 0 (low severity) to 24 (20), and a score of 5 or more indicates severity [20].

Four measures rated by staff and patients: *1. Clinical Decision-Making Involvement and Satisfaction (CDIS)* scale measures involvement and satisfaction experienced with a specific decision, with versions rated by the service user (CDIS-P) and staff (CDIS-S) [32]. The Satisfaction sub-scale ranges from 1 (low satisfaction) to 5, and the Involvement sub-scale has three categories: Active (patient made the decision), Shared (decision jointly made by staff and patient) and Passive (staff made the decision). Note therefore that staff-rated passive involvement indicates passive involvement by the service user, i.e. active staff involvement. *2. The Clinical Decision Making Style Scale (CDMS)* [33] measured preferences for decision making. Parallel patient (CDMS-P) and staff (CDMS-S) versions rated on a five-point Likert scale.

CDMS sub-scales are: Participation in Decision Making (PD), and Information (IN). *3. Helping Alliance Scale (HAS)* measures therapeutic alliance, with versions rated by staff (HAS-S, five items) and patients (HAS-P, six items) both ranging from 0 (low therapeutic alliance) to 10 [34]. *4. Camberwell Assessment of Need Short Appraisal Scale (CANSAS)* measures the presence of a met or unmet need in 22 domains, with versions rated by staff (CANSAS-S) [35] and patients (CANSAS-P) [35, 36]. Three summary scores are produced: unmet need, met need and no need, each ranging from 0 (low) to 22.

Data analysis

To meet aim 1 (Stages of recovery), baseline STORI data were analysed using latent class analysis (LCA) [37] to identify adequate number of courses of recovery. In LCA, the observed variation in the indicator variable (stage of recovery) is ascribed to unobserved variation in the sample. Inter-individual differences concerning item response are explained by the existence of sub-groups with distinct response patterns. To keep the number of estimated parameters of the model within a reasonable range, we pooled the six response categories of the 30 items of the original measure into two categories ("not true now" and "true now"). Initial modelling involved the estimation of a single latent growth curve model, followed by the addition of a series of unconditional models. Models are viewed and compared based on practical considerations and information criteria to determine the adequate number of latent classes. In this study the models were compared using Bayesian Information Criterion (BIC). Better fitting models show a small BIC.

To meet aims 2 (Predictors of recovery stage) and 3 (Predictors of change in recovery stage), proportional odds models [38] were used. This approach is an extension of logistic regression, and was used because of the ordinal structure of the dependent variable. A latent continuum is divided into sections, and thresholds indicate to which observed category of the dependent variable the latent value relates (one threshold less than categories). The dependent variable was coded as 1 = Moratorium, 2 = Awareness/Preparation, 3 = Rebuilding/Growth.

For aim 3, generalized estimating equations (GENMOD procedure in SAS) were used to estimate the association between 1-year change in recovery stage (1 = improved (by one or two stages), 2 = no change, 3 = deteriorated (by one or two stages)) and baseline recovery stage, baseline and 1-year follow-up clinical measures and sociodemographic predictor variables. Several models were fitted, and the 'Quasi-likelihood under the Independence model Criterion' (QIC) statistic was used to compare models, with smaller QIC indicating better fit [39]. Analyses were conducted using Mplus software package 6.1, SPSS 21 and SAS 9.2.

Results

A total of 581 participants self-rated stage of recovery at baseline: 115 (19.8%) Moratorium, 145 (25.0%) Awareness and preparation, 321 (55.2%) Rebuilding and growth. At 1-year follow-up, 512 (88.1%) of the 581 re-rated stage of recovery: 50 (9.8%), 153 (29.9%) and 309 (60.4%) respectively.

Completers of both measurement points did not differ from non-completers (with only one completed measure) with respect to sex, age, ethnicity, years in school, duration of illness, TAG and OQ-45 at T0. Completers had a significantly higher functioning (GAF mean = 49.40 (SD = 10.49) vs. 46.68 (SD = 13.57); $t = -9.97(556)$, $p = 0.002$).

Stages of recovery

We investigated the adequate number of courses of recovery by means of the number of classes representing a certain stage of recovery. Each stage of recovery maps toa certain response pattern of STORI items (e. g. being on a low recovery stage means high values in Moratorium items and lower values in other items). The latent class analysis of STORI data is shown in Fig. 1.

The three-stage model best fitted the data (compared to the five-class solution for recovery suggested by the original publication). This indicates that participants answers in the measure clearly cluster only into one of three stages of recovery, not in five (BIC = 21017.699). Class 1: medium stage of recovery, Class 2: lower stage of recovery, and Class 3: higher stage of recovery. The average probability for allocation into one distinctclass was 0.95 for class 1, 0.98 for class 2 and 0.97 for class 3.

Predictors of recovery stage

The cross-sectional predictors of stage of recovery are shown in Table 2.

Higher stage of recovery was associated with being male, married, living alone / with parents (versus with others), not living in the Italian site (compared to those living in the Switzerland site), and having better patient-rated therapeutic alliance and fewer symptoms. The model accounted for 40% of the variance in stage of recovery.

Predictors of change

At 1 year follow-up, 80 participants (15.8%) had deteriorated (changed to a lower STORI stage), 296 (58.5%) had no change, and 130 (25.7%) had improved (changed to a higher STORI stage). The best model (QIC fit index 1289.2; other models not shown) of predictors of change in stage of recovery is shown in Table 3.

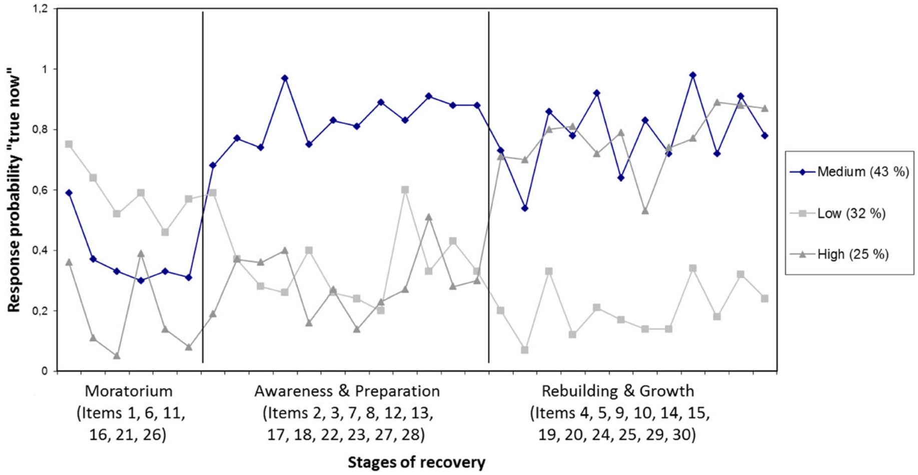

Fig. 1 Latent class profiles for the three-class solution

Table 2 Baseline predictors of stage of recovery ($n = 397$)

		B	SE	Wald	Sig.
Threshold					
STORI T0 = 1		−2.75	1.02	7.32	.01
STORI T0 = 2		−1.59	1.01	2.49	.12
Coefficients					
Centre (vs Zurich)	Ulm	.24	.29	.68	.41
	London	.21	.48	.19	.67
	Naples	−1.03	.37	7.80	**.01**
	Debrecen	−.23	.35	.45	.50
	Aalborg	.13	.34	.14	.71
Age		.01	.01	.82	.37
Gender (female vs. male)		−.42	.18	5.56	**.02**
Ethnicity (white vs. not)		−.49	.53	.86	.35
Years in school		.08	.04	3.76	.05
Married (yes vs. no)		.68	.29	5.56	**.02**
Living situation (alone vs other)		.68	.27	6.50	**.01**
Living situation (with parents vs other)		.86	.32	7.27	**.01**
Work status (employed vs not)		.31	.25	1.63	.20
State benefits (no vs. yes)		−.42	.27	2.46	.12
Duration of Illness		.00	.01	.07	.79
GAF		.01	.01	1.61	.21
HAS-P total		.10	.04	5.25	**.02**
OQ-45	Interpersonal relations	−.10	.02	37.65	**.00**
	Social role	−.08	.02	14.74	**.00**
CDMS	Participation	−.14	.15	1.41	.24
	Information	.02	.13	.02	.90
CDIS-P (vs Passive)	Shared	.13	.19	.44	.51
	Active	.41	.25	2.61	.11

Pseudo $R^2 = 0.40$

Abbreviations: *STORI* stages of recovery inventory, *GAF* Global Assessment of Functioning, *HAS* Helping Alliance Scale, *OQ-45* outcome questionnaire, *CDMS* Clinical Decision Making Style Scale, *CDIS* Clinical Decision-Making Involvement and Satisfaction

Bold = $p < 0.05$

Table 3 Generalized estimating equation for change in stage of recovery ($n = 587$)

	Odds ratio (95% Confidence interval)	*p*
Gender	0.77 (0.51–1.14)	.19
Ethnicity (White vs. nonWhite)	0.86 (0.25–2.97)	.82
Age	1.01 (0.99–1.03)	.48
Years in school	1.01 (0.90–1.13)	.88
Marital status (Married vs. not)	0.71 (0.44–1.12)	.16
Work status (Employed vs. not)	1.39 (0.85–2.24)	.19
OQ-total	0.99 (0.98–1.01)	.43
CANSAS-P unmet needs	1.01 (0.94–1.09)	.76
CDMS-P Participation	0.79–(0.60–1.04)	.10
CDMS-P Information	1.08 (0.82–1.44)	.58
CDIS-P Involvement (0 = active, 1 = shared)	1.84 (1.15–2.94)	**.01**
CDIS-P Involvement (0 = active, 1 = passive)	1.71 (1.00–2.95)	.05
CDIS-P Involvement (0 = shared, 1 = passive)	0.93 (0.65–1.34)	.69
MANSA	1.06 (0.82–1.29)	.77
HAS-P	0.99 (0.86–1.14)	.90
GAF	1.01 (0.99–1.03)	.19
HONOS	0.98 (0.95–1.01)	.25
Time (Baseline vs. 1 year)	1.19 (0.98–1.45	.08

Effects adjusted for all other appropriate effects in the model

Abbreviations: *OQ-45* outcome questionnaire, *CANSAS* Camberwell Assessment of Need Short Appraisal Scale, *CDMS* Clinical Decision Making Style Scale, *CDIS* Clinical Decision-Making Involvement and Satisfaction, *MANSA* Manchester Short Assessment of Quality of Life, *HAS* Helping Alliance Scale, *GAF* Global Assessment of Functioning, *HONOS* Health of the Nation Outcome Scale

Bold = $p < 0.05$

Only time-adjusted patient-rated decision involvement was significantly associated with a change in stage of recovery over 1 year. We found an increased chance for worse outcome (change to lower stage of recovery) for patients with active involvement compared with either shared or passive involvement. Patients who experienced active involvement compared to those with shared involvement had a 1.84-fold increased risk for worse outcome ($p = .01$), and compared to those with passive involvement had a 1.71-fold increased risk for worse outcome ($p = .05$). No significant interaction between time and involvement was found.

Discussion

This multinational study on stages, predictors and change in recovery has three findings. First, empirical data distinguish between three distinct stages of recovery, which can be labelled as Moratorium (=cognitive, volitional and behavioral disengagement), Awareness/Preparation (=partial subjective engagement) and Rebuilding/Growth (=full behavioral engagement). The instrument STORI was originally based on a 5-category framework [36], and our study is consistent with three cluster-analytic studies [24–26] in identifying three distinct and interpretable stages. This indicates the need to develop treatment protocols which are organised by these stages of recovery.

Second, specific clinical, sociodemographic and geographic variables have cross-sectional association with stage of recovery. This adds more clarity to a comprehensive and multi-level evidence base for personal recovery. Compared to research into clinical recovery—the traditional understanding of recovery, involving sustained symptom amelioration and restoration of functioning—we already find a development of a comprehensive evidence base, including global epidemiological prevalence studies [36] and randomised controlled trial evidence investigating biological, psychological and social intervention.

Third, patients rating active involvement (compared with either passive or shared involvement in decision-making) at baseline were more likely to have changed to a lower stage of recovery 1 year later. This is a counter-intuitive result at first glance. Experience by the patient of active involvement is influenced by role expectations, treatment context, information, and clinician behavior. There is emerging evidence that more active decision-making (even than initially preferred by the patient) is associated with increased satisfaction and subsequent decision implementation [40] and poorer involvement and satisfaction in regard to treatment-related decisions, compared with social and financial decisions [41]. Furthermore, a preference by clinicians for active rather than shared or passive patient involvement in decision-making is associated with reductions in patient-rated unmet need 1 year later [42].

One possible explanation would be that in the short term, active involvement is experienced as positive and empowering, whereas in the longer term (as in the current study) active involvement is a marker of staff-patient relationships which are insufficiently partnership-based. However, our therapeutic alliance measure (HAS) was not a significant predictor of change in stage of recovery. Therapeutic alliance was though a cross-sectional predictor of recovery, consistent with other empirical studies in which working alliance was a mediator of recovery [43].

The main strengths of the study are the large, varied, multisite sample recruited within routine mental health services. All patients were screened for severe mental illness, enhancing generalizability to other mental health systems. Multi-perspective assessments of decision-making by both staff and patients were used. In this naturalistic study, patients rated any type of decision they made with their clinician [41, 44], rather than the approach taken in some reviews [17] of restricting consideration to medical treatment decisions.

Several limitations apply. The use of a convenience rather than cohort sample in each site reduces representativeness, due to factors such as clinician bias in referral. More generally, optimal involvement in clinical decision-making may also differ between people with long-term mental health problems (as investigated here) and acute medical contexts. Measures used were patient and clinician self-report and did not include independent observer ratings of involvement style. The choice of predictors was a selective process and we cannot rule out that further variables might also influence the course of recovery.

Conclusions

This study indicates that the relationship between involvement in decision-making and subsequent recovery is complex. The research implication of our study is that decision-making involvement and recovery are associated, so merit longitudinal investigation using standardised assessments to understand the direction of any causal relationship. It is plausible that the optimal level of involvement varies with stage of recovery. Therefore, clinical implication arising from this study to adapt patient involvement to changes in recovery process and preferences.

Abbreviations

BIC: Bayesian Information Criterion; CANSAS: Camberwell Assessment of Need Short Appraisal Scale; CDIS: Clinical Decision-Making Involvement and Satisfaction; CDM: Clinical decision making; CDMS: The Clinical Decision Making Style Scale; CEDAR: Clinical decision making and outcome in routine care for people with severe mental illness; CHIME: Framework: connectedness; hope and optimism about the future; identity; meaning in life; and empowerment; GAF: Global Assessment of Functioning; GEE: Generalized estimating equations; HAS: Helping Alliance Scale; HoNOS: Health of the Nation Outcome Scale; LCA: Latent class analysis; MANSA: Manchester Short Assessment of Quality of Life; NICE: National Institute for Health and Clinical Excellence; OG-45: Outcome questionnaire-45; QIC: Quasi-likelihood under the Independence model Criterion;

SCID: Structured Clinical Interview for DSM; SMI: Severe mental illness; STORI: Stages of recovery inventory; TAG: Threshold Assessment Grid

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Authors' contributions
SL, MS and BP designed research questions, conducted the data analysis and interpretation, and BM conducted part of data analysis and interpretation. The manuscript was written by SL and MS, and was critically revised for important intellectual content by all authors (EC, HJ, AF, ML, TI, EM, MKB, HØS, WR, WK, BM, and BP) who also gave final approval of the version to be published.

Competing interests
The authors declare that they have no competing interests.

Consent for publication
Not applicable.

Ethics approval and consent to participate
The study was approved by the clinical research ethics committees of the respective study centers: Ulm University Ethics Commission; Joint South London and Maudsley and Institute of Psychiatry Research Ethics Committee; Ethical Committee of the Second University of Naples, Naples; National Committee on Health Research Ethics, North Denmark Region; Regional and Institutional Ethics Committee, University of Debrecen Medical and Health Science Center; Kantonale Ethikkommission Zürich. An informed consent was obtained from all patients prior to their participation in the study.

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SPECIAL ARTICLE

Social connection as a critical factor for mental and physical health: evidence, trends, challenges, and future implications

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Rising concerns about social isolation and loneliness globally have highlighted the need for a greater understanding of their mental and physical health implications. Robust evidence documents social connection factors as independent predictors of mental and physical health, with some of the strongest evidence on mortality. Although most data are observational, evidence points to directionality of effects, plausible pathways, and in some cases a causal link between social connection and later health outcomes. Societal trends across several indicators reveal increasing rates of those who lack social connection, and a significant portion of the population reporting loneliness. The scientific study on social isolation and loneliness has substantially extended over the past two decades, particularly since 2020; however, its relevance to health and mortality remains underappreciated by the public. Despite the breadth of evidence, several challenges remain, including the need for a common language to reconcile the diverse relevant terms across scientific disciplines, consistent multi-factorial measurement to assess risk, and effective solutions to prevent and mitigate risk. The urgency for future health is underscored by the potentially longer-term consequences of the COVID-19 pandemic, and the role of digital technologies in societal shifts, that could contribute to further declines in social, mental and physical health. To reverse these trends and meet these challenges, recommendations are offered to more comprehensively address gaps in our understanding, and to foster social connection and address social isolation and loneliness.

Key words: Social connection, social isolation, loneliness, mental health, physical health, mortality, public health

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In a joint statement published in January 2024, the governments of the US, Japan, Morocco, Sweden, Kenya and Chile highlighted "the importance of social connection to the health and well-being of individuals, communities and societies"[1]. This came at the heels of the COVID-19 pandemic, a more than three-year period in which the global population had to isolate, practice "social distancing" and, in many cases, was homebound, all factors contributing to reduced social contact. However, while that global health crisis helped raise awareness of the importance of this issue, scientific evidence was already documenting the significant mental and physical health implications of declining social connection.

Social connection is widely acknowledged to be a fundamental human need[2,3], linked to higher well-being, safety, resilience and prosperity, and to longer lifespan[4]. Across social species, research demonstrates that social connection is one of the strongest predictors of survival, both early and later in life, through adaptive behavioral and biological mechanisms[5,6]. The availability and diversity of social relationships, interactions and networks are critical for health and well-being[4,7,8]. Therefore, it is imperative to understand how new trends involving social connection relate to shifts in important societal outcomes such as mental disorders and physical diseases.

Rising global concerns about a "loneliness epidemic" in public discourse have been accompanied by increased academic research and heightened engagement among communities, institutions and governments. These concerns are being reflected in national and international responses to this "epidemic". In 2018, the UK appointed a Minister of Loneliness[9], establishing a national strategy and awareness campaign. Japan followed by appointing a Minister of Loneliness in 2021[10]. Beginning in 2018, the European Union has produced several reports on loneliness[11]. In 2023, the US Surgeon General issued an Advisory and a framework for a national strategy on "our epidemic of loneliness and isolation"[4]. In the same year, the South Korean government took a tangible step, offering monthly stipends to encourage young socially isolated individuals to reintegrate into society[12]. Outside governments, the World Health Organization (WHO) launched in 2023 a Commission on Social Connection, a three-year effort to raise global awareness and mobilize support in this area[13].

These efforts have been prompted by data documenting recent increases in social isolation and loneliness, and decreases in social connection globally[4]. Factors including modernization in society, economic disparities, the introduction of digital technologies, shifts in civic engagement, growing political divides and radicalization, and others, have been examined as potential contributors to this decline in social connection. Whether this is a social recession, a loneliness epidemic, or a public health crisis, it is clearly a pressing issue.

This is a critical moment to act and bridge the gaps in our collective knowledge to mitigate adverse outcomes. However, there are several challenges to be addressed. Over the years, the relevance of social connection to our health has emerged in various disciplines, leading to a complex and potentially confusing evidence base. This calls for a common language to be established. However, in the process, we risk oversimplifying the issue and falling short of an adequate response. With increasing public and governmental attention, this is a critical time to take stock of the strengths and gaps in the existing evidence, the challenges to be faced, and the implications for the future.

SOCIAL CONNECTION AND MENTAL HEALTH

There is a robust evidence base linking social connection to mental health outcomes. Social connection plays a vital role in preventing mental health problems, maintaining good mental health, and aiding in the recovery from both moderate and severe mental health conditions, while isolation and loneliness have been associated with poorer mental health. Most of this evidence regards depression, with fewer studies considering other mental disorders.

Although most available data are observational and cannot demonstrate causality, there are longitudinal studies that provide more robust evidence to indicate directionality, and recent evidence using Mendelian randomization to establish causal relationships[14]. In some cases, associations appear to be bidirectional, meaning that there is evidence to suggest that social isolation and loneliness increase the risk for poorer mental health, as well as evidence that poorer mental health increases the risk for isolation and loneliness[15].

Depression

There is a strong positive association of social isolation and loneliness with depression from youth to older adulthood. Further, higher social connectedness is protective towards depressive symptoms and disorders[16].

When looking at adults of all ages, 18 years and older, data from the US National Health Interview Survey examined the impact of living alone and the availability of social and emotional support on depression[17]. Adults living alone reported significantly higher depression than those living with others, and this difference held across several sociodemographic factors. Adults never or rarely receiving social and emotional support were twice as likely to report depression, but adults living alone were still more likely to report depression even compared to adults living with others who did not receive social and emotional support[17].

Importantly, longitudinal evidence suggests that social isolation and loneliness likely cause or worsen depression over time. For example, a systematic review of 32 longitudinal studies from the general population examined whether subjective feelings of loneliness predicted the onset of a new diagnosis of depression[18]. Studies followed participants from six months to 16 years, with an average follow-up of 3.5 years. The odds of developing new depression in adults were more than double among those who reported often feeling lonely compared to those rarely or never feeling lonely. While there were more studies among older adults, the findings were consistent among younger age groups, including university students and new mothers.

Using two large datasets – the Psychiatric Genomics Consortium meta-analysis of major depression (N=142,646)[19], and the Million Veteran Program (N=250,215)[20] – to apply a two-sample Mendelian randomization design, loneliness appeared to cause incident major depression and depressive symptoms[14]. These analyses were then reversed using loneliness outcome data from the UK biobank. Remarkably, data demonstrated that loneliness causally predicts major depression, but the reverse is also true, with major depression causally predicting loneliness[14]. This suggests that loneliness is both a cause and a consequence of major depression; thus, public health strategies to reduce loneliness may potentially be effective in preventing the onset of depression and reducing depressive symptoms, and better treatments for depression are likely to reduce loneliness.

The link between social connection and depression has also been examined among patients in medical settings, suggesting potential spillover effects on other clinical conditions. For example, low social support had a significant positive association with antenatal depression, which contributes significantly to maternal physical health[21]. In a review, 83% of studies found that pregnant women with low social support had greater depressive symptoms[16].

The links between social connection and mental health are also relevant within occupational settings. The strain on employees across sectors, particularly those hit hardest during the COVID-19 pandemic – such as health care providers, educators, and other “essential employees” – has brought greater attention to burnout and other mental health concerns. A meta-analysis of studies in health care workers found that a lack of social support significantly contributed to higher risk for acute stress disorder, burnout, anxiety, depression, and post-traumatic stress disorder[22].

Cognitive health

Several meta-analyses consistently show that stronger social connection – including social networks (e.g., number of social contacts, frequency of interaction, marital status, living arrangement) and social engagement (e.g., attending social groups; visiting family, friends and neighbors; engaging in voluntary or paid work, participation in cultural or leisure activities) – is associated with better cognitive function, but the evidence is less consistent for perceptions of loneliness.

For example, a meta-analysis including over 2.3 million participants showed that living alone, having a smaller social network, having a low frequency of social contact, and having poor social support were risk factors for dementia, while loneliness was not[23]. However, other meta-analyses did find that greater loneliness was significantly associated with incident dementia[24,25]. Conversely, greater social engagement, including a greater number of social memberships, number of social contacts, and more social participation, may be protective, as these were associated with lower dementia risk[23,26].

SOCIAL CONNECTION AND PHYSICAL HEALTH

Robust evidence links social connection, isolation and loneliness to an increased incidence of several physical diseases and to earlier death. The strength of this evidence has been acknowledged in multiple National Academy of Science, Engineering, and Medicine (NASEM) consensus study reports[15,27], scientific statements by professional associations such as the American Heart Association[28], and the US Surgeon General Advisory issued in 2023[4]. The evidence can be found in several meta-analyses and systematic reviews that document the overall effects on physical morbidity[29-31], and on disease-related as well as all-cause mortality[32-43]. There are also meta-analyses on clinical outcomes such as response to vaccine[44].

This body of evidence led a NASEM consensus study report to conclude that "social isolation is a major public health concern"[15]. This is noteworthy, since the report was published before the COVID-19 pandemic and there has been a significant volume of research on this topic from 2020 onward.

Physical morbidity

There is a rich and growing body of evidence across a variety of physical health outcomes, including major health indicators such as cardiovascular diseases, stroke and diabetes mellitus.

Cardiovascular diseases are the leading cause of death globally, accounting for roughly one third of all deaths; therefore, factors that increase or decrease this risk can have a major global health impact[45]. Dozens of studies have found that social isolation and loneliness significantly influence the risk of cardiovascular and cerebrovascular morbidities[15,29].

The culmination of this evidence resulted in a statement published by the American Heart Association in 2022, acknowledging this risk from objective and perceived social isolation[28]. According to this review of the evidence, there is a clear link of social isolation and loneliness with risk for coronary heart disease and stroke. Among the evidence, a synthesis of data across 16 independent longitudinal studies demonstrates that poor social relationships (social isolation, poor social support, loneliness) were associated with a 29% increase in the risk of incident coronary heart disease and a 32% increase in the risk of stroke[29]. These findings were consistent across genders.

Low social connection and loneliness have also been associated with a greater risk for hypertension. Indeed, data from the National Social Life, Health and Aging Project suggest that the impact of social isolation on risk for hypertension exceeds that of clinical factors such as diabetes mellitus, pointing to a "causal role of social connections in reducing hypertension" in older age[46].

Diabetes mellitus is a leading source of disability, lost productivity, mortality, and lower quality of life, affecting nearly half a billion people worldwide, with a significant global economic burden on individuals, health care systems, and countries[47]. Studies have repeatedly shown that social connection (e.g., family support and involvement) can positively influence the management and overall health of individuals with type 1 and 2 diabetes. Large population studies also demonstrate the influence of social connection on the incidence of type 2 diabetes. For example, people with smaller social networks were more likely to have been recently diagnosed with type 2 diabetes, to have previously been diagnosed with this condition, and to have diabetic complications[48,49].

However, gender differences have been found along different indicators of social connection. Low social participation was linked to pre-diabetes and complications among women but not men, while living alone increased the likelihood of previously diagnosed type 2 diabetes and its complications in men but not in women[48,49]. These findings were independent of glycemic control, quality of life, and cardiac risk factors.

Diabetic outcomes may be due to better self-care among those who are more socially connected. For example, in a meta-analysis of 28 studies, social support was significantly associated with better self-care, particularly glucose monitoring, and was stronger among those with type 2 than type 1 diabetes[50]. Improving diabetic outcomes via social connection can have cascading public health implications, given that diabetes mellitus often leads to other health outcomes, including heart disease, kidney failure, blindness, amputation and dementia.

There is also evidence to suggest that poor social connection is associated with worse outcomes among those who are already ill. For example, heart failure patients who self-reported high levels of loneliness had a 68% increased risk of hospitalization, a 57% higher risk of emergency hospital visits, and a 26% increased risk of outpatient visits compared with patients reporting low loneliness[51]. In a meta-analysis of 13 studies on heart failure patients, poor social connection was associated with a 55% greater risk of hospital readmission[52]. This was consistent across both objective and perceived social isolation, living alone, lack of social support, and poor social network. These data suggest that improving social connection among those who are sick can improve medical outcomes.

Mortality

Several reviews of the evidence, including a NASEM scientific consensus study, have concluded that some of the strongest evidence linking social connection, isolation and loneliness to health-relevant outcomes is that concerning mortality[15]. Large population-based epidemiological studies have tracked initially healthy populations over time, for years and often decades, documenting that those who are more socially connected live longer[35,38,41,42], while those who experience social deficits (isolation, loneliness, living alone, poor-quality relationships) are more likely to die earlier, regardless of the cause of death[33,36,37,39,40,43]. Although social isolation has been implicated as a risk factor for death by suicide[53], most meta-analyses on mortality exclude suicide as a cause of death.

Based on meta-analytic data, one estimate suggests that the association between social connection and survival may be as high as 50%[42], while isolation is associated with 32% and loneliness with 14% increased risk for earlier death[33]. While estimates vary to some extent, they may be conservative, given that many reviews and meta-analyses often exclude studies that focus specifically on deaths due to unnatural causes such as unintended injuries, violence or suicide. While there are more studies and stronger effects on cardiovascular-related deaths (e.g., myocardial infarction, stroke) and cancer-related deaths (e.g., leukemia, lymphomas, breast cancer)[41], more research is still needed on these, in addition to other disease-related causes of death.

Over the years, the number of studies, the rigor of methodology, and the size of samples have all increased substantially, replicating the finding that social connection decreases the risk of premature mortality and providing stronger confidence in this evidence. For example, longitudinal data from the UK Biobank regard nearly half a million people, reducing the likelihood of random error[54]. These data demonstrate that social isolation significantly increases risk for earlier all-cause mortality, overall and consistently across subgroups (i.e., males and females, young and older, health and unhealthy, various ethnicities), even after adjusting for a robust set of lifestyle, socioeconomic, biological, and health risk factors[55].

Several meta-analyses and systematic reviews have documented similar findings across different ways of examining the issue, including social relationships broadly, social networks, social contact frequency, marital/partnership status, marriage dissolution, social isolation, loneliness, and living alone[32,43]. While the magnitude of the effect varies to some extent across studies and depending on which aspect of social connection is being examined, the evidence points to the same general conclusion: indicators of greater social connection are associated with reduced risk, while indicators of social deficits are associated with greater risk for premature mortality.

THE RELATIVE INFLUENCE OF ISOLATION AND LONELINESS

When predicting the risk of future disease, does the subjective (loneliness) or the objective (isolation) aspect matter most? The English Longitudinal Study of Ageing, conducted in nearly 5,400 adults over the age of 50, followed for an average of 5.4 years, found that loneliness was associated with an increased risk for cardiovascular disease (coronary heart disease and stroke), but did not find the same outcomes for social isolation[56]. On the other hand, the UK Biobank, a large-scale research effort collecting data on nearly half a million people, followed for an average of 7.1 years, found that both isolation and loneliness were associated with an increased risk of acute myocardial infarction and stroke[57]. However, the impact of social isolation remained significant after adjusting for other risk factors, while the effect of loneliness was attenuated. Both isolation and loneliness were significant predictors of cardiovascular outcomes; however, the relative importance seemed to be stronger for objective isolation.

Research is increasingly looking at the relative importance of isolation and loneliness, and considering multiple outcomes simultaneously. Growing evidence suggests that loneliness has a stronger impact on mental health outcomes, while isolation has a stronger impact on physical health outcomes[31,58]. For example, a large national prospective study, examining the effects of social isolation and loneliness on 32 physical, behavioral and mental health outcomes, demonstrated that both were independent predictors, but isolation had a stronger effect on mortality while lone-

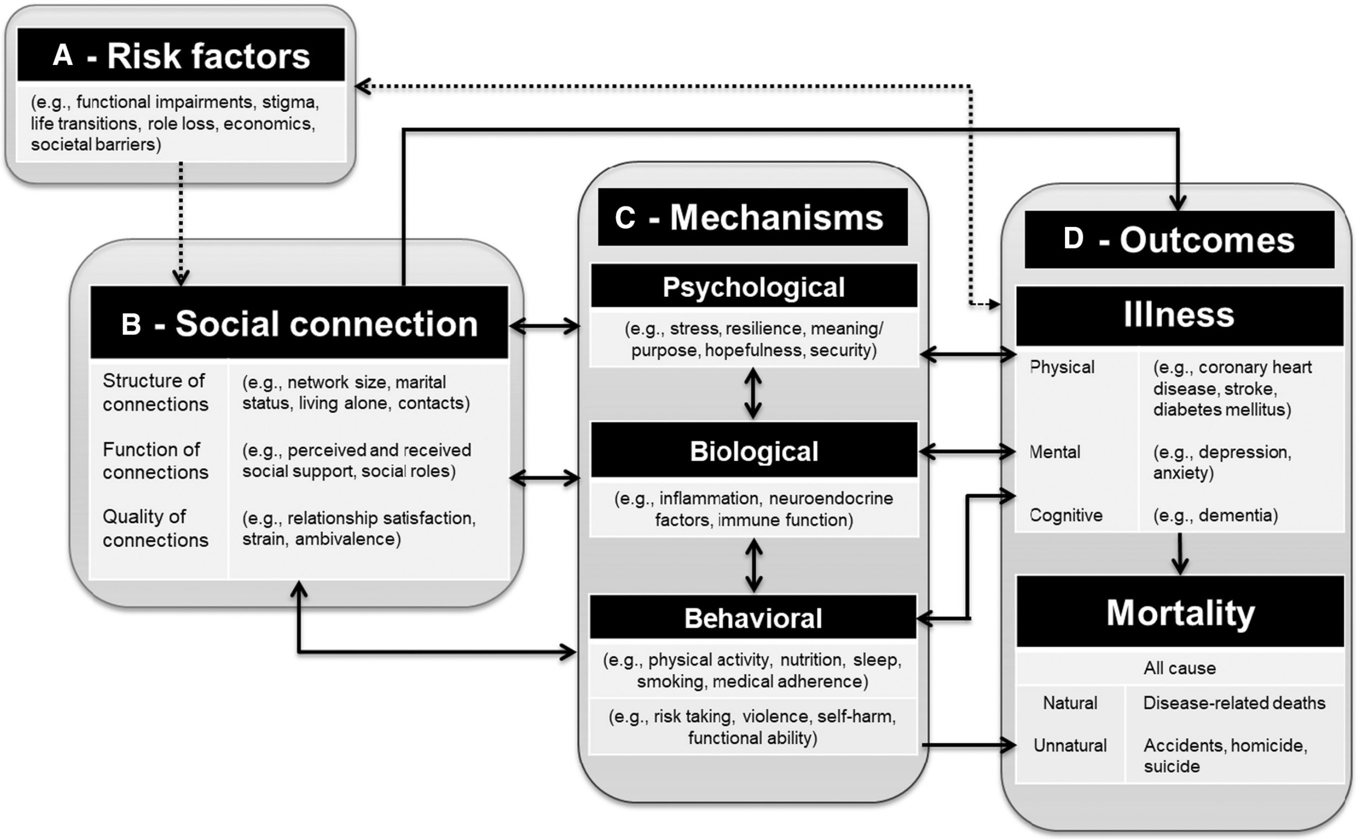

Figure 1 Simplified model of possible direct and indirect, directional and bidirectional, and potentially cyclical pathways by which social connection is associated with morbidity and mortality

liness had a stronger effect on mental health outcomes[58].

PATHWAYS AMONG SOCIAL AND HEALTH FACTORS

The evidence on the protective effects of being socially connected and the risk associated with social disconnection is often studied and discussed separately. However, these conditions intersect in meaningful ways. This includes direct and indirect, bidirectional and cyclical, as well as additive and multiplicative effects. Much of the evidence to date has focused on establishing the direct and indirect effects. A simplified model of these pathways is illustrated in Figure 1.

Among the growing body of literature on social connection and health, studies often focus on establishing a directional influence of some aspects of social connection (represented as B in the figure) on various health or mortality outcomes (represented as D). Further work has examined the mechanisms (represented as C) that provide plausible psychological, biological and behavioral explanations for these effects[59-64].

Several reviews and meta-analyses document the evidence pointing to psychological pathways such as perceived stress[60,65]; behavioral pathways such as sleep[66], physical activity and smoking[67]; and biological factors such as inflammation[68]. Studies further examine the risk factors (represented as A in the figure) that can potentially compromise one's social connection.

The associations of primary interest in research have been between B and D, with B treated as the predictor variable and D as the outcome variable. Subsequent research has treated C as mediator variables and A as risk factors. However, associations are likely far more complex.

Many factors examined as plausible pathways (represented as C in Figure 1) are also notable outcomes, often treated as clinical endpoints. For example, social isolation and loneliness have been linked to poorer nutritional/eating behaviors considered harmful to health, including low fruit and vegetable intake, and poorer overall diet quality[69]. There is also evidence that those who are socially isolated are less likely to get preventive screenings, such as a mammogram[70].

A synthesis of 122 empirical studies examined the effects of differences in social connection on medical adherence[71]. Higher social connectedness, particularly social support, has been linked to better medical adherence across several physical diseases, especially hypertension[72,73] and type 2 diabetes mellitus[74,75]. Similarly, other factors such as stress can be both an endpoint and a mechanism by which social connection influences morbidity and mortality.

The directionality, or bidirectionality, of these associations may be relevant. While those linked to mortality are unidirectional (i.e., end-of-life stops any further influence), nearly all other pathways may be bidirectional. While there is robust evidence of directional effects (i.e., those less socially connected are more likely to develop poorer health conditions), the reverse can also be true (i.e., poorer health also predicts a greater risk for social isolation and loneliness). The relevant mechanisms are both plausible and supported by evidence. Poorer physical health can also contribute to both greater isolation or loneliness and poorer mental health, creating complex bidirectional associations.

These associations may also be cyclical. Poor social connection can dysregulate our physiology and behavior in ways that put us at risk of developing poorer health. Poorer health may reduce people's willingness, ability or access to connect socially, resulting in greater isolation, which in turn impedes their ability to manage their illness, leading to worse prognoses.

We also need to understand the complexity of the factors contained within the model and how that can potentially result in additive and multiplicative effects. For example, co-occurring deficits of social connection (e.g., living alone, small social network, low levels of social support, and loneliness) may contribute to biological, psychological and behavioral pathways, potentially magnifying the risk to health. Furthermore, like many behavioral and lifestyle risk factors that can influence multiple chronic health conditions, the evidence similarly points to poor social connectedness leading to greater risk (and greater social connectedness reducing risk) for multiple health conditions. Thus, it is probable that poor social connection can increase the risk of comorbidities among physical, mental and cognitive health conditions. This is consistent with data from the Health and Retirement Study which demonstrate that social isolation was significantly associated with 32 indicators of physical, behavioral and psychological health outcomes[58].

STRENGTHS AND GAPS IN THE EVIDENCE

The scientific evidence base for the health relevance of social connection is robust, with consistent findings emerging over the past few decades, reinforced across several scientific disciplines (e.g., epidemiology, neuroscience, sociology, medicine, psychology), and using a variety of methodological approaches (e.g., longitudinal, cross-sectional, experimental).

Several meta-analyses and systematic reviews document converging evidence linking social connection, isolation and/or loneliness to psychological, cognitive and physical health. Together, these include hundreds of studies with millions of participants. While most data are observational, there is substantial prospective evidence to establish the temporality of effects[42], and evidence to support a gradient or dose-response effect[46].

There is also experimental evidence in humans and animals to support a potential causal association. For example, experimentally housing animals in isolation versus socially leads to poorer outcomes, including the development of tumors, stroke, impaired healing, and death[5]. Animal models have also validated potential molecular, cellular, immunological and behavioral effects for human social disconnection[3]. These experimental studies further map causal associations between social perception, neural activity, immunological function, and health[3].

In humans, randomized controlled trials (RCTs) experimentally test the potential benefits of social interventions. For instance, a meta-analysis of 106 RCTs found that patients who received psychosocial support in addition to treatment as usual had 20% increased odds of survival than those in the control group who received only standard medical treatment[76]. Although there was variability across types of support interventions, the findings were consistent across patients being treated for cardiovascular diseases, cancer and other conditions.

Drawing causal inferences among factors known to influence health is essential to determine etiology and prevention efforts. However, randomization is not always appropriate in the context of understanding isolation, loneliness, and social connection. Furthermore, although the RCT study design is considered the gold standard for causal inference, it is also criticized because RCTs often have homogeneous and small sample sizes due to inclusion/exclusion criteria, limiting generalizability to real-world application. Thus, additional methods are needed to draw causal inferences for public health. While causal inference is challenging and much debate exists, several models that provide promising support for a causal relationship between social connection and health have been applied.

The Bradford Hill guidelines are among the most widely adopted criteria for drawing causal inferences among variables unsuitable for randomization. These guidelines emphasize nine criteria: strength of association, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, and analogy[77]. Reviews of the evidence on social connection and health have found support for nearly all the Bradford Hill criteria[78-80]. The only criterion not met was specificity, indicating that exposure to the potential cause (social connection) is associated with multiple outcomes rather than a particular outcome and no others. However, smoking also would not meet this criterion for causality, since it results in many health outcomes as well (e.g., cardiovascular disease, cancer). Indeed, Bradford Hill and proponents of these guidelines have noted that meeting all criteria is unnecessary; rather, the more evidence to support the criteria, the stronger the likelihood of causality[77,78]. Nonetheless, critiques of the Bradford Hill guidelines point to the need for more sophisticated analyses.

Additional promising evidence exists to support potential causal associations beyond the Bradford Hill criteria. Drawing causal inferences may be appropriate from sophisticated regression analyses of longitudinal observational data[81], applying a data-integration framework[82], and Mendelian randomization[83]. While few studies focusing on indicators of social connection and health have employed these methods, those that do are supportive[14]. Thus, reviews of this evidence have concluded that the cumulative evidence supports the *likelihood* of a causal association between better social connection and better health[5,78,80].

Despite considerable strengths in the evidence, several notable gaps remain in our knowledge. Some gaps became glaringly apparent during the COVID-19 pandemic, when the scientific community struggled to answer basic questions for the broader public, such as: How much socializing is needed for health benefits? How soon do adverse mental and physical health consequences emerge when we lack social connection? Is there equivalence between in-person and remote means of socializing? What can we do to reduce loneliness? Indeed, there are likely many more questions for which we do not have adequate or firm answers at the moment.

While there are many strengths in our current body of evidence, gaps in this evidence may become barriers or limit our ability to translate this evidence into practice. To address these gaps more

Table 1 Strengths of the evidence, challenges posed by gaps, and consequent priority needs in research on social connection

Strengths of evidence	Challenges	Priority needs
Converging evidence across scientific disciplines	Variability in conceptualization and measurement	A multi-factorial approach is needed.
Many validated assessment tools	Variability in assessment tools limits comparisons across time, or different samples. Validated instruments may not be generalizable to other cultures, settings, and contemporary modes of socializing.	Consistency of assessment to establish prevalence rates and track trends. Improve or create new measures that are valid, reliable and acceptable.
Dose-response of social connection across the lifespan	Most research and attention are on extreme risk and older adults.	A focus across the risk trajectory (including prevention) and across ages is needed.
Converging evidence across social connection components	Fewer studies examine multiple components in the same sample.	Further evidence of potential independent, additive and synergistic effects is needed to assess risk more precisely. Further evidence is needed on how each factor may differentially influence different kinds of outcomes.
Evidence on mortality is consistent across causes of death, country of origin, gender, and health status	Fewer studies include or differentiate: comprehensive health outcomes, low- and middle-income countries, marginalized groups, varying modalities of socializing (e.g., in-person, remote, non-human).	Basic research to fill these gaps is needed.
Robust evidence of mortality and objective health consequences	Weaker and mixed evidence on effective strategies to mitigate risk (weaker methodologies were employed; most interventions are individually focused; most interventions are targeted at those most severely affected). Less is known about other non-health outcomes.	Evidence-based solutions: rigorous evaluations allowing for strong inference; interventions across the socio-ecological model; prevention and mitigation of risk earlier on in the risk trajectory. Evidence on more diverse outcomes (e.g., economic, civic engagement, education, incarceration).

comprehensively, Table 1 provides an overview of some of the strengths and challenges currently existing in the evidence base, further pointing to where future efforts may be prioritized.

EXAMINATION OF TRENDS

Examining trends in prevalence rates, awareness and research on social connection, isolation and loneliness offers valuable insights into the trajectory of societal dynamics and the evolving evidence base. Tracking prevalence rates allows us to understand the scale of these phenomena, informing translation to application and practice. Concurrently, heightened or lack of awareness reflects the perceived importance of the significance and motivation to act upon social factors for mental and physical health.

These trends are both shaped by the evolving landscape of research and may reflect an uneven knowledge base. Collectively, they illuminate the evolving intersection between societal shifts, individual experiences, and the scientific understanding of the intricate connections between social dynamics and health outcomes. Staying attuned to these trends is essential for developing targeted interventions and policies that effectively address the challenges posed by social connection, isolation and loneliness in contemporary society.

Trends in society

Societal trends over the past several decades indicate that, as a population, we have become less socially connected and more isolated, and that a high proportion of the population is lonely.

Based on the available data, loneliness has generally shown little improvement over the last few decades, and may be getting worse. For example, a massive synthesis of 345 studies on emerging adults (ages 18-29), who completed the UCLA Loneliness Scale between 1976 and 2019, found that average loneliness levels linearly increased annually across the 43 years[84]. Furthermore, a meta-analysis of data from 113 countries concluded that a substantial proportion of the population in many countries experiences problematic levels of loneliness[85].

According to the Gallup Global State of Connection survey, nearly a quarter (24%) of the global population reports feeling "very lonely" or "fairly lonely", although there was variability across countries[86]. Of the 29 countries where at least one third of the population felt lonely, 22 were in Africa, four were in the Middle East, and three in South Asia. This also demonstrates that loneliness is not just a wealthy Western country issue, and may even be more severe in other areas of the world. However, inconsistent measurement tools and scoring methods have led to vastly different prevalence estimates. Notably, prevalence rates often favor one indicator (e.g., loneliness) over others, yet indicators may interact in meaningful ways. Thus, the prevalence of those who lack social connection in one or more ways may be far larger than any estimate of a single indicator.

Loneliness trends provide an incomplete picture of the state of social connection, and we must look at the other ways in which individuals and communities may lack connection. For example, data from the American Time Use Survey, regarding how Americans spend their day, demonstrate that, over the past two decades, Americans have spent more time in isolation and less time with household and non-household family members, friends, community engagement, and companionship[87]. Although the COVID-19 pandemic exacerbated these trends, social isolation was increasing, and engagement with family, friends and others (co-workers, neighbors, acquaintances) was declining for years prior to the pandemic. This is consistent with other trends, such as those documenting a decline in social capital and participation in religion[88,89], and changes in family structure (e.g., decline of extended families, rise of single-occupancy households)[90] – many of which are seen globally.

Contemporary society in much of the world is evolving rapidly, likely contributing to our current trends and having important implications for the direction of the trends going into the future. Rapid shifts that may be relevant to social and population health include the increasing aging population, widespread adoption of remote working, increased automation, economic strain and inequity[91], migration and mobility, mental health crisis among youth, rise in xenophobia, civil and political unrest, and environmental crises, all of which may potentially exacerbate trends concerning social connection.

These trends of declining social connection, combined with the evidence on the bidirectional associations with mental and physical morbidities, point to an urgent need to take action. Because multiple factors have been contributing to these trends, building over decades, simply returning to pre-pandemic levels of connection or reducing time on social media may only bring limited benefits.

Trends in scholarly attention

There are also striking trends in the scientific study of the topic. The surging interest in social isolation and loneliness is reflected in research, as demonstrated by the substantial increase of studies on this topic over recent years, potentially providing greater understanding and justification for action. Thus, understanding how loneliness and isolation have been studied over time may provide additional insight.

To examine publication trends, we first used the PubMed by Year search tool. Because of the diverse literature on social, mental and physical health outcomes, the search was limited to two social variables (loneliness and social isolation) and two health outcomes (depression and mortality). We further scanned additional scientific databases (including PsycINFO for depression) using the same social and health variables. The searches were limited to articles published in peer-reviewed academic journals between 1972 and 2023. The mortality search terms included "social isolation" OR "loneliness" AND "death and dying" or "mortality" or "mortality rate" or "mortality risk". The depression search terms in-

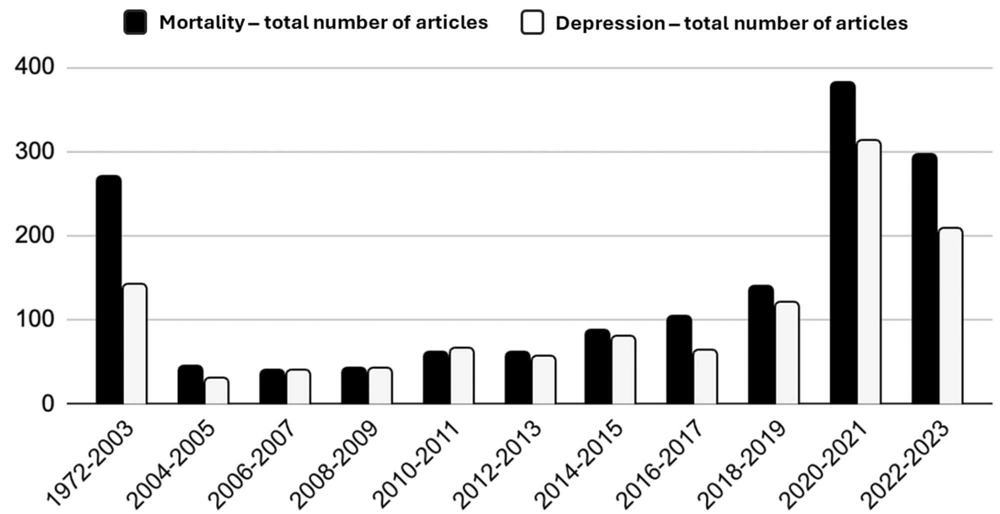

Figure 2 Frequency of loneliness or isolation as search terms in the scientific literature over time. Note that the far-left column refers to 1972-2003, while each of the other columns refers to two years.

cluded "social isolation" OR "loneliness" AND "major depression". PsychINFO also allows narrowing search by methodology: thus, we further used the search parameters "empirical", "quantitative", "longitudinal", "prospective", "retrospective", and "clinical trial".

All studies using those search terms were bracketed into time periods to determine how many articles populated by our search terms were published within each period. Studies published in the past two decades (2004-2023) were demarcated into 2-year periods (2004-2005, 2006-2007, 2008-2009, etc.), while studies published in 1972-2003 were grouped (31 years). Figure 2 graphically presents the number of studies on isolation and loneliness over the years.

Data suggest an exponential increase in the scientific study of social isolation and loneliness. Over the past two decades, the number of relevant articles has grown, with significant increase since 2020. For example, the number of papers published in each subsequent two years since 2020 exceeds the number of studies from 1972 to 2003 combined. However, it is unclear whether scientific interest in other indicators of lacking social connection is similarly surging.

Trends in awareness

Several factors may presumably contribute to greater awareness of the importance of social connection and related aspects of lacking connection (i.e., social isolation and loneliness). These include scientific advancement, social media, government initiatives, the COVID-19 pandemic, and advocacy.

Significant advances in scientific research over the past few decades, especially in the last 5-7 years, may have shed light on the scale of the problem and provided greater confidence in scientific findings. Advancements in social technologies and the widespread use of social media platforms may have played a dual role in awareness. Increased experience of feelings of loneliness associated with that use, and the facilitation of awareness campaigns, discussions and support networks related to health and well-being may occur simultaneously[92].

Government initiatives may have also played a role in greater awareness. Countries have recognized the urgency of the issue and appointed Ministers, formulated policies, and developed strategies to address loneliness and isolation, and highlight social connection as a priority. Awareness efforts have also been undertaken by national and international civil society organizations, coalitions, and networks that have emerged as powerful advocates[7]. These include the UK Campaign to End Loneliness, the Canadian Genwell Project, Australia's Ending Loneliness Together, and the annual Global Loneliness Awareness Week. These collective efforts aim to raise awareness, promote community engagement, and foster a culture of connection.

Unfortunately, trends in public awareness appear to be limited to only certain outcomes. A large survey of US and UK adults published in 2018 found that, when the public was asked to rank various factors contributing to a longer life (e.g., not smoking, exercising, limiting alcohol, maintaining a healthy weight), social connection was amid these factors, but it was rated among the lowest in importance, significantly underestimating its impact relative to effect sizes reported in the scientific literature[93].

Due to a variety of factors occurring since that survey was published – i.e., the COVID-19 pandemic, national awareness campaigns, and increased prevalence within the population – public perception of the health relevance of social connection was expected to increase. However, 2023 data from the UK and a nationally representative sample of US adults demonstrate that there has been essentially no change[94]. Despite increases in public discourse on social isolation and loneliness, the importance of these and other aspects of social connection for health and survival are still underestimated among the public.

Implications from these trends

Overall, these trends point to a large and potentially increasing scale of those lacking social connection, and parallel trends suggest increasing attention within scholarship on the consequent impact on health. Yet, the public perception of risk does not align with either the increasing scale or evidence of the magnitude (effect sizes) for health. This suggests that increased education and awareness of the health relevance is needed.

Discrepancies between the scientific evidence and public perception may have significant implications. First, public perception may significantly influence how resources are allocated and prioritization of various issues within public health agendas[95]. If the public does not perceive social connection and markers of its deficit (e.g., loneliness and social isolation) as relevant to health[93], funding and efforts may not be directed towards addressing them adequately, despite their demonstrated impact on health outcomes[4,15]. Second, public perception influences individual behaviors and societal norms. If social connection is not widely recognized as a protective factor, and loneliness and isolation as serious health risks, individuals may be less likely to change their own behavior or support others experiencing loneliness or isolation[96]. This may perpetuate social disconnection and exacerbate the problem.

Finally, accurate awareness of the health implications among the public may facilitate destigmatizing the issue and promoting help-seeking behavior[97]. When people view loneliness and isolation as a personal rather than a health issue, they may be less inclined to seek support and resources to address these challenges. Aligning public perception with the evidence on the importance of social connection is essential to shaping effective policies, nurturing more connected and supportive communities, and promoting health.

CHALLENGES

The WHO defines health as "a state of complete physical, mental and social well-being, not merely the absence of disease or infirmity"[98]. Considering this definition, social well-being is a critical element of health that has been underappreciated and raises several challenges that we must address.

If physical and mental health are more than the absence of physical or mental illness, we should be taking a similar approach to social health. However, recent attention appears primarily focused on indicators of social deficits, specifically social isolation and loneliness. Yet, our collective and individual capacity as humans to think, feel, engage with others, pursue livelihoods, and experience fulfillment is intrinsically tied to our health – physical health, mental health and social health. The active encouragement, safeguarding and recovery of social health are crucial priorities for individuals, communities and societies globally.

Key challenges include developing a common language, identifying and activating appropriate and effective approaches, and adapting to societal changes. These challenges are also interconnected. Developing a common language is essential to understanding the underlying contributors, predicting outcomes, and measuring changes in risk and protection. Understanding these challenges helps us develop better approaches to preventing and mitigating risk, and adapt these approaches as society evolves.

A common language

Given the array of terms used in the scientific literature, one potential barrier to prioritization within health settings is lack of precision in terminology. It is clear that we need a common language, but the term "loneliness" may fall short. Loneliness is often used as a catch-all term outside academic scientific contexts, but it is defined and measured more narrowly within the scientific literature. While definitions of loneliness vary somewhat, there is broad consensus that it is distinct from social isolation[7,99].

Loneliness is a subjective, unpleasant feeling based on the discrepancy between one's desired and actual level of social connection[100]. It is most often distinguished from social isolation as a separate but related construct[7]. While isolation and loneliness can coexist, they differ in meaningful ways. Social isolation is objectively being alone, having few relationships or infrequent social contact. Thus, social isolation is objective, while loneliness is subjective. Although both social isolation and loneliness can be involuntary, isolation may be chosen[101]. Both are indicators of lacking social connection, but there are many indicators of social connection and, thus, many indicators of social connection deficits[8]. Social disconnection and loneliness are not equivalent[43], and this has implications for measurement and assessment, intervention, policy, and more.

Across scientific disciplines, several constructs have emerged as relevant. Table 2, although not comprehensive, highlights some of the most widely used terms represented in the research and identified in the US Surgeon General Advisory[4]. Pinning down definitions is challenging, given that the same term has been used to refer to different things, while different terms are used to describe the same thing among studies. Some terms, such as social capital, lack a clear consensus on definition[102,103].

Why is this important? These terms refer to related but distinct constructs. Reviews of this evidence find that these measures are not highly correlated empirically[8,104]. Thus, when we only measure one of these, we cannot assume that we are capturing the full scope of how social factors influence health.

We need a common language. "Social connection" has been offered as an umbrella term to encompass these distinct but related terms[4,8,15,105]. From this perspective, the myriad of diverse concepts in the scientific literature can be organized into three key themes or components: structure, function and quality. The first component, *structure*, represents the human need to have others in our life and is often measured by the size and variability

Table 2 Terms commonly found in the scientific literature that are distinct but related (adapted from the US Surgeon General's Advisory[4])

Term	Definition
Loneliness	A subjective distressing experience that results from perceived isolation or inadequate meaningful connections, where inadequate refers to the discrepancy or unmet need between an individual's preferred and actual experience.
Social capital	The resources to which individuals and groups have access through their social connections. The term is often used as an umbrella for both social support and social cohesion.
Social cohesion	The sense of solidarity within groups, marked by strong social connections and high levels of social participation, that generates trust, norms of reciprocity, and a sense of belonging.
Social connectedness	The degree to which any individual or population might fall along the continuum of achieving social connection needs.
Social connection	A continuum of the size and diversity of one's social network and roles, the functions that these relationships serve, and their positive or negative qualities.
Social disconnection	Objective or subjective deficits in social connection, including deficits in relationships and roles, their functions and/or quality.
Social infrastructure	The programs (such as volunteer organizations, sports groups, religious groups, and member associations), policies (such as public transportation, housing and education), and physical elements of a community (such as libraries, parks, green spaces, and playgrounds) that support the development of social connection.
Social isolation	Objectively having few social relationships, social roles, group memberships, and infrequent social interaction.
Social negativity	The presence of harmful interactions or relationships, rather than the absence of desired social interactions or relationships.
Social networks	The individuals and groups a person is connected to and the interconnections among relationships. These "webs of social connections" provide the structure for various social connection functions to potentially operate.
Social norms	The unwritten rules that we follow which serve as a social contract to provide order and predictability in society. The social groups we belong to provide information and expectations, and constraints on what is acceptable and appropriate behavior. Social norms reinforce or discourage health-related and risky behaviors (lifestyle factors, vaccination, substance use).
Social participation	A person's involvement in activities in the community or society that provides interaction with others.
Social support	The perceived or actual availability of informational, tangible and emotional resources from others, commonly one's social network.
Solitude	A state of aloneness by choice that does not involve feeling lonely.

of relationships within a network, being part of groups, and regular social interactions. It is the foundation upon which the other components of social connection are built. The second component, *function*, recognizes that these connections serve essential functions or purposes. Namely, connections can be relied upon for support to meet various needs and goals. Functions are often measured by the interchange of support that is received or perceived to be available, which can be emotional, informational or tangible, and can help us navigate life's challenges. The bulk of the studies within the scientific literature have primarily examined indicators of these structural or functional components. However, a growing body of research is assessing and recognizing the importance of the quality of social relationships, networks and interactions. Thus, the third component, *quality*, refers to our connections' positive and negative aspects. High quality is often measured by the level of satisfaction or intimacy, whereas low quality includes social negativity such as conflict, strain or ambivalence.

While Figure 3 is helpful in identifying these core conceptual themes, individual measurement approaches may overlap to some degree between social connection components. Furthermore, specific assessment tools may appear to align clearly within one component, but contain items that overlap with other components[104]. Generally, high levels of each of these components have been linked to better health and lower levels of poorer health. To more comprehensively understand underlying causes, predict outcomes, and measure risk, we need to consider the distinct contributions of the structure, function and quality of social connection.

Data across multiple scientific disciplines have linked various social connection indicators to health outcomes[8]. Strong structure, function and quality of social connection may be considered optimal for health. On the contrary, when all three are low, this would be associated with high to severe risk. However, there may be unevenness in the extent to which any individual experiences the three components of social connection. The descriptions in Table 3 help illustrate the disaggregation across these components and their relation to various risk profiles. Nonetheless, there is likely further complexity of risk, given that many indicators within each component of social connection are on a continuum and may have synergistic effects. For example, longitudinal data from nearly half a million people, followed for an average of 12.6 years, demonstrated that low levels on both structural and functional indicators of social connection resulted in a significantly higher risk for cardiovascular disease mortality (hazard ratio, HR=1.63), compared to low levels on structural (HR=1.27) or functional (HR=1.17) components alone[54].

Conceptually, loneliness may represent the signal or symptom of unmet social needs. However, loneliness does not represent low levels across all three social connection components. Comparisons demonstrate these distinctions. For example, meta-analyses that establish the effect size for the aggregate measures of social connection on mortality were significantly larger than the effect size for loneliness[43,105]. Thus, loneliness is not the same as lacking

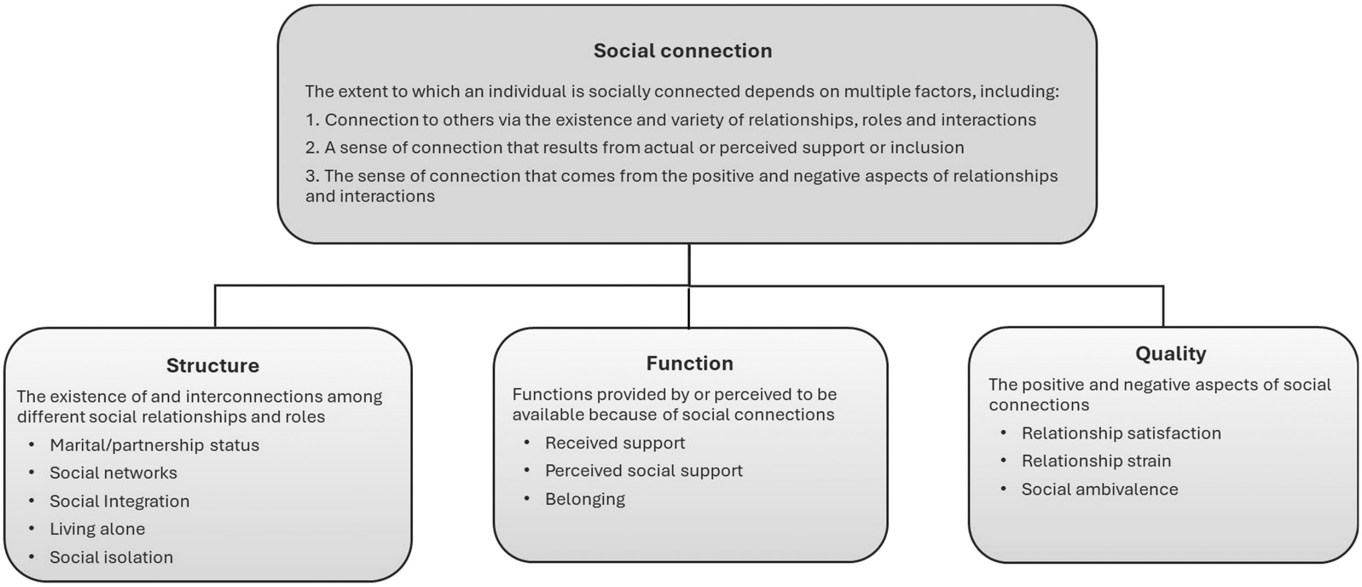

Figure 3 Social connection as a multi-factorial umbrella term encompassing the structural, functional and quality aspects represented in the scientific literature (adapted from Holt-Lunstad[8])

social connection.

Measurement

Another challenge related to the need for a common language is the lack of consensus on measurement[104]. The most widely used measurement tools have helped to build a robust evidence base, but may have limitations when applied to other settings. For instance, most measurement tools were developed in Western countries, prior to the widespread shift to digital and remote means of socializing. Measurement not only needs to be predictive of the outcomes of interest, but must also be feasible to use. Notably, what is feasible may differ in different contexts, such as research, clinical settings, population surveillance, and evaluation of the effectiveness of interventions. Currently there is no measure that is multi-factorial, validated, and feasible or adapted to become feasible across settings.

Given the multi-factorial conceptualization of social connection[7,80], a considerable challenge is developing a feasible multi-factorial measure. Not all social connection components are typically assessed, because this would take too much time. Due to time and space constraints, assessments in medical settings and population surveillance may only assess one indicator; however, this approach will likely result in risk assessment errors. For example, if an individual is assessed on an indicator of the structural component of social connection (e.g., frequency of social contact) and found to have high levels, we may assume that this person is at low risk. However, this assessment may miss low levels on the other two components (e.g., low social support, poor quality relationships), which may put the individual at risk. Similarly, we might assume that this person is at low risk if scores are low on an assessment of loneliness, yet the person may have little or no social contact with others. Furthermore, if an individual is low on one component, we may be missing potential protection associated with high levels on the other components. Thus, one's overall social risk profile may be incomplete because of the limited scope of assessments.

Effective intervention and prevention strategies

The next major challenge is reducing risk through effective intervention and prevention strategies. Social connection is complex, with various factors contributing to its increase or decrease, directly and indirectly[8]. Generally, social connection occurs naturally among individuals and within communities. However, when it does not, intervention becomes necessary to reduce risk. Direct actions, programs or initiatives can be implemented to increase social connection or decrease forms of social disconnection intentionally.

Key challenges include: a) the capacity to develop and evaluate intervention strategies; b) the difficulties to understand what works best for whom in what context; and c) the limited scope of existing strategies, and the need to ensure the full scope of social connection across the socio-ecological model, sectors of society, and life course.

Developing and evaluating interventions

The evidence supporting the positive effects of social connection is far more robust and methodologically rigorous than the evidence supporting the effectiveness of interventions aimed at creating it when it is not occurring naturally, or at reducing social disconnection. However, this challenge (i.e., more substantial evi-

Table 3 Conceptualization of potential risk to mental and physical health according to distribution across the level of social connection components

Risk level	Structure	Function	Quality	Description
Optimal-low risk	High	High	High	Large and varied social network, with regular social contact with people who can be relied upon for support and assistance when needed. These include deep and meaningful relationships characterized by caring and compassionate interactions.
Low-moderate risk	High	High	Low	Large and varied network, with regular contact among people who can be counted upon for support. However, these relationships are strained and/or lack depth, and interactions are void of caring or compassion.
	High	Low	High	Large and varied network, with regular social contact with meaningful and high-quality relationships. However, these are not able or available to provide support or assistance when needed.
	Low	High	High	Small social network and infrequent contact. However, the limited social contact is among those who can be relied upon for support, perhaps strangers or volunteers. Nonetheless, it is caring and compassionate.
Moderate-severe risk	High	Low	Low	Large and varied social network, and regular contact with others. However, they cannot be relied upon for support. These are strained relationships and interactions, with a lack of caring and compassion.
	Low	High	Low	Small social network and limited social contact with others. Support is available and provided by others, perhaps by strangers or volunteers; however, it lacks depth, is accompanied by strain, or lacks caring and compassion.
	Low	Low	High	Small social network and limited social contact with others. It is not possible to rely upon others for support. However, the limited social contact is caring and compassionate.
Severe risk	Low	Low	Low	Small social network and little social contact. There is no one to rely upon. What little social contact does occur is strained or lacks caring and compassion.

dence of health risks compared to treatments to eliminate these risks) is common among many health issues. The National Institutes of Health estimate that therapeutics for *any* condition take, on average, 10-15 years to develop, because 95% of new therapeutics fail[106]. With the increased urgency to address the crisis of social isolation, loneliness and social disconnection, we cannot take a "something is better than nothing" attitude, assuming that all approaches will be helpful.

Rigorous evaluations are needed. However, the resources and capacity to develop and evaluate interventions are limited – particularly for interventions conducted outside academic institutions. Rigorous methodologies are often not utilized, resulting in a low-quality body of evidence[107,108]. To strengthen this evidence, the Multiphase Optimization Strategy (MOST) approach has been utilized for other health issues and could similarly be applied to this area[109]. The MOST framework is an iterative implementation method that uses empirical information about component effects within real-world constraints to develop, evaluate and optimize interventions[110].

Understanding what works for whom in what context

There is a growing body of evidence examining the effectiveness of interventions, including multiple meta-analyses and reviews of the evidence[108,111-116]. Interventions vary in terms of their social connection focus (e.g., loneliness, social isolation, school connectedness, social skills, social support, neighborhood cohesion); setting (e.g., home, clinic, community, school, whole of society policies); delivery (e.g., self-directed, peer group, family or caregiver, professional, volunteer); modality (e.g., in-person, phone, virtually); sub-population group (e.g., older adults, children, disabled, university students, veterans, new parents), and many other characteristics.

Interventions also vary in their timing and duration (e.g., once or repeated, hours to years); their outcomes (e.g., social, health, performance); their target (e.g., general population, high-risk populations); and goals (e.g., prevention, mitigation, treatment). Effectiveness may depend on the specific characteristics of the targeted population, the type and intensity of the intervention, and its length[15]. This variation creates a considerable complexity. We highlight here the interventions with the most promising body of evidence.

Loneliness interventions

There is now a sizable body of research examining interventions focused specifically on reducing loneliness. Systematic reviews and meta-analyses generally find that these interventions are associated with significantly reduced loneliness and improved social support. For example, an umbrella review of 211 studies, including seven different types of interventions, examined their effectiveness in reducing loneliness[116]. They were befriending programs, technological interventions, meditation/mindfulness, animal therapy or robopets, social cognitive training, social skills training, and social support. Of these intervention types, social support, social cognitive training, and meditation/mindfulness significantly decreased loneliness.

Among loneliness interventions designed to target specific age-based sub-populations, there are meta-analyses of evidence for those focused on young people, university students, and older adults. A meta-analysis of 39 studies (including 25 RCTs) focused on loneliness in children and adolescents found that it could be reduced, with no significant differences between various types of interventions[115]. A systematic review of 37 interventions among university students found that bringing students together for an activity or to socialize, in-person or virtually, helped reduce feelings of loneliness[117]. Meditation/mindfulness benefited those who preferred not to join groups. Other reviews identify several effective interventions for reducing loneliness and increasing social connection in older adults, including social support groups, technology-based interventions, and community-based activities[118,119].

Overall, based on the current evidence, no intervention type (e.g., changing maladaptive social cognitions, enhancing social skills, providing psychoeducation, supporting socialization, increasing opportunities for social interaction) seems to be superior to the others. The majority of this evidence has been classified as low to critically-low quality[116].

Interventions in clinical settings

Given the robust evidence of the medical relevance of social connection, addressing isolation and loneliness in clinical settings among patients may improve health outcomes. Early evidence pointed to greater survival among cancer patients who participated in social support groups along with standard treatment compared to standard treatment alone[120]. Since then, various types of programs have been developed to help support patients across different medical conditions, but with mixed outcomes. Nonetheless, when the body of the evidence was examined as a whole via meta-analysis, including 106 RCTs, medical patients randomized to receive some type of psychosocial support intervention in addition to standard medical treatment had a 20% increased survival, and 29% increased survival time compared to patients who only received standard treatment[76].

While there was considerable variability in the effects among the interventions, on average, providing patients with psychosocial support was as effective in increasing survival as many standard medical interventions, including smoking cessation and lifestyle interventions. Thus, not only do high levels of naturally occurring social connection increase one's lifespan, but providing interventions to support patients in medical settings also seems to increase survival. This evidence suggests, consistent with NASEM recommendations, that addressing the social needs of patients by integrating this component into existing treatment within the health care system may be a promising approach[15,121].

Social prescribing

Social prescribing involves referring patients outside the medical setting to community-based services and activities to address social, emotional and practical needs. An integrative review of the evidence found that social prescribing has generally favorable effects in reducing social isolation and loneliness. However, the quality of the evidence was mixed and generally weak methodologically[118]. The interventions were diverse and heterogeneous in design and implementation, relied on self-report, and often lacked adequate controls.

While social prescribing is a promising approach gaining popularity, further research is needed, including RCTs and meta-analyses, as multiple other systematic reviews provide a weak or mixed picture[122-124]. More robust evidence is needed to understand how strong the effects are for individuals, sub-populations and communities regarding loneliness, isolation and social connectedness, and to identify the most effective approaches for different populations.

Technology-based or virtual interventions

Technology-based or virtual interventions – such as online social networking, video conferencing, messaging apps, and virtual companions or pets – are implemented with the aim of reducing social isolation or loneliness among specific populations. Systematic reviews of the evidence found that technology-based interventions were effective in reducing loneliness among older adults and individuals with mental health issues[111,125,126].

The WHO has developed an evidence and gap map for technology-based interventions for reducing social isolation and loneliness among older adults[127]. This includes 200 studies and 97 systematic reviews. Most interventions utilized video conferencing and calls, though assistive robots and virtual pets were also common.

The effectiveness of digital interventions may vary depending on the specific population and the type of technology used. Caution should be used, given that some studies found no effectiveness and, in some cases, negative outcomes. For example, data from the National Social Life, Health and Aging Project found that, despite increases in remote modes of contact with others, individuals still experienced loneliness, depression and decrease in happiness[128].

While some technology-based interventions may be promising, not all effectively reduce social isolation or loneliness. More research is needed to fully understand their effectiveness, for which groups, and how they can be optimally implemented.

School connectedness

There is strong evidence that interventions aimed at increasing school connectedness, or the feeling of belonging and engagement within the school community, can positively impact student outcomes, from academic achievement to reduced suicidality[129-131]. In one review, classroom management approaches were associated with improved school connectedness among students, including teacher caring and support, peer connection and support, student autonomy and empowerment, management of classroom social dynamics, teacher expectations, and behavior management[132].

Research has shown that students who feel more connected to their school are more likely to attend class regularly, have higher grades and test scores, are less likely to engage in risky behaviors (e.g., substance abuse, violence), and have better health[133-136]. Classroom practices that build strong, supportive and trusting relationships help reduce patterns that inappropriately exclude some groups of kids[132].

Policy

There is growing interest in the role of policy as an intervention, with many calls to enact pro-social policies, or policies to address isolation and loneliness[4,137-139]. Policies are explicit guidelines which provide a framework for decision-making; are enforced by groups, organizations or governments; and can directly or indirectly impact social connection. Similar to the Health in All Policy approach that recognizes the health implications across sectors (e.g., education, employment, health, nutrition, housing, transportation)[140], a "Social in All Policy" approach should recognize the social relevance of policies across sectors[80,138].

Policies can directly influence social contact (e.g., policies on visitation or family member involvement in medical care), or can focus on changing other kinds of outcomes (e.g., economic, environmental) that substantially influence social connection (e.g., policies on neighborhood zoning, bussing routes, remote work).

Reviews of existing policies cover social and emotional learning curricula in schools[130,141]; state-level farmer wellness programs[142]; expansion of telehealth services to provide mental health services in schools[143]; and workplace policies that include shorter total work hours and earlier end of the workday, enabling workers to attend to family responsibilities and achieve greater work-life harmony[144]. There is existing US legislation, including the Older Americans Act of 1965, which was amended in 2020, to address social isolation and loneliness.

Many policies are being introduced with the intent to facilitate social connectedness. However, given the scale and magnitude of public health implications, they need to be evaluated for effectiveness like any other intervention.

Targeted vs. broad approaches

Another major challenge is whether to focus solutions on people most severely affected or broadly on the population. When social connection needs are not met, the mental and physical health consequences are broadly found across age and other demographics. However, isolation and loneliness are unequally distributed across the population. Groups that experience marginalization – i.e., lesbian, gay, bisexual, transgender, queer and/or questioning (LGBTQ+) people, racial minorities, migrants, those with disabilities[91] – and life circumstances that may or may not co-occur with aging (e.g., functional or sensory impairments) are disproportionally affected. Thus, a significant challenge is whether to focus efforts more broadly or these groups.

One perspective is that prioritization should be given to the most vulnerable populations and addressing their needs. By focusing on specific populations, such as marginalized or underserved communities, efforts can be directed toward reducing health disparities and ensuring that resources reach those who need them the most[145]. Many sources recommend tailoring interventions to address specific needs, barriers and enablers within these groups, in order to increase the effectiveness of these interventions[15,146]. This approach may be a more efficient use of limited resources, funding and personnel. Moreover, it is easier to measure the impact of targeted approaches, as they are narrowly defined and address a smaller population. However, identifying and targeting people "at-risk" may potentially pathologize and stigmatize such groups further and place the burden of change on the individual. Thus, it has been argued that we should focus on the factors that put people at risk instead of group membership[147].

Another perspective is that we should focus efforts across the population to have larger shifts, rather than just targeting a small portion of the population[77]. Broad approaches can lead to systemic changes in policy, environment, and societal norms, laying the foundation for long-term health improvements. Implementing broad interventions might also benefit from economies of scale, reducing the cost per individual reached compared to targeted interventions.

Both targeted and broad approaches are necessary, starting with broad measures to address general issues, while using targeted interventions to address specific needs within the population. However, targeted approaches should be focused on the factors associated with risk (e.g., marginalization) rather than group membership, to avoid further stigmatization. Universal approaches may help prevent social disconnection, whereas more targeted approaches may be needed for those who are already isolated, lonely, or socially disconnected in other ways for prolonged periods or at severe levels. A hybrid strategy can leverage the strengths of both approaches to maximize public health outcomes.

Limited scope of existing approaches

Despite the growing body of research focused on interventions, the scope of solutions is limited in several ways. The Systemic approach Of Cross-sector Integration and Action across the Lifespan (SOCIAL) framework points to gaps and opportunities in solutions across the socio-ecological model, sectors of society, the life course, and prevention[80].

Evidence points to underlying root causes across the socio-ecological model (e.g., individual, interpersonal, community, institution, society)[8], yet most interventions are being deployed at the individual level[148]. A scoping review of interventions for older adults, including evidence from 30 countries, found that the majority of interventions only measured loneliness, and only three societal-level interventions were found[149].

The health care sector, including both clinical and community health settings, is most often the target of interventions and programs. However, we need to expand our approaches across sectors to engage the whole of society. No one sector of society is likely to be able to address this issue. The "Social in All Policy" approach [138] recognizes the health and social implications across sectors and "systematically takes into account the health implications of decisions, seeks synergies, and avoids harmful health impacts in order to improve population health and health equity"[150].

Social connection is vital at every stage of life, yet most solutions are focused later in life[111,151]. The evidence of a dose-response effect of social connection on biomarkers of health across stages of life[46], and the importance of early social environment[5], highlights the need for efforts to address this issue across life. Social isolation during childhood, for instance, is associated with increased cardiovascular risk factors in adulthood, such as increased blood glucose levels, high blood pressure, and obesity[152].

As is the case with most health issues, primary, secondary and tertiary prevention approaches are needed to address social isolation and loneliness. Unfortunately, few interventions focus on helping the society become more socially connected. Prevention efforts may have many longer-term benefits, such as avoiding costly interventions later, reducing disease burden, and improving quality of life[153].

Efforts to gather and synthesize data, and to identify evidence gaps, are underway. These and similar efforts aim to help create centralized resources to single out evidence-based interventions effective in reducing social isolation and loneliness, or increasing social connectedness. However, without sustained funding, there will be difficulties to evaluate the evidence supporting their effectiveness.

IMPLICATIONS FOR THE FUTURE OF MENTAL AND PHYSICAL HEALTH

The world is beginning to recognize the vital importance of social connection to the health and welfare of countries. Considering the trends that have led to concerns of a public health crisis of social disconnection, we must proactively evaluate the long-term implications if these conditions do not improve or perhaps continue to worsen. Two of the most pressing concerns that have the potential to worsen trends are the unknown long-term consequences of the COVID-19 pandemic and the rapidly evolving technological landscape of society.

Long-term implications of the COVID-19 pandemic

During the COVID-19 pandemic, social developmental processes were significantly disrupted, with potentially critical long-term health implications. Socialization during early life plays a crucial role in shaping a child's development and long-term health[154]. Early socialization provides the foundation for healthy relationships (e.g., learning to communicate, cooperate, negotiate, share), emotional well-being (e.g., learning empathy, expressing emotions), cognitive development (e.g., information processing, critical thinking, problem-solving), self-identity (e.g., self-confidence, self-esteem), ability to navigate cultural norms and values, and overall physical health[155].

Early life experiences with caregivers, peers, schools and communities are all key contributors to the early social environment that ensures longer-term well-being and survival[156-160]. However, the pandemic severely limited socialization for roughly three years, during this critical developmental period, for infants, young children and adolescents. Since it is well documented that early social experiences significantly predict later social, mental and physical health[136,161,162], the long-term health implications of the pandemic may be disproportionately borne for an entire generation.

There may also be longer-term consequences among adults, due to widespread behavioral adaptation that may be sustained over time. The massive adoption and implementation of tools to cope with reduced social contact (e.g., remote work, contactless delivery services, streaming entertainment services, telehealth, automation) came with significant advantages, including increased flexibility, autonomy, convenience, safety, and in some cases cost-effectiveness[163-167].

These advantages have led to preferences that may limit our social contact – particularly with co-workers and weak-ties. Reductions in social contact with both may be critical factors for future health, given the significance of workplace relationships[168,169] and the evidence on the importance of weak-ties[170,171]. While these preferences are obviously not universal, a large portion of the population values such conveniences. Even if they are not preferred, they are often incentivized by lower costs[166]. For example, roughly half of patients preferred in-person visits and half preferred a video visit, but 23.5% switched to a video visit if the cost was lower[172]. What was once initiated or scaled to help us cope with isolation, is now what may be reinforcing isolation, with potential long-term implications for exacerbating existing levels of social disconnection and corresponding health consequences.

The widespread behavioral adaptation to spending more time alone, or not leaving the house, may contribute to a societal shift that normalizes social isolation. This is increasingly being depicted in cultural narratives of a "social-battery" that is drained by socializing, and the benefits of "self-care", "me-time", and solitude. While there is evidence of some benefits of solitude[173], the evidence is quite heterogeneous, and benefits appear limited to short-term bouts of solitude, not chronic time alone[174-175]. There is instead – as we have seen – robust empirical evidence of the harmful effects of social isolation on mental and physical health outcomes, and increased risk for premature mortality. If time spent alone is praised and encouraged, while the risks of social isolation are diminished within public discourse, the consequences to health are likely to be magnified.

The pervasive experience of social isolation and loneliness during the pandemic also fueled self-proclaimed "experts" and influencers who pushed common-sense approaches to wellness, and in some cases misinformation[176-177]. Coupled with a growing distrust in institutions, including science, this may lead to confusion on what is credible. When local community organizations and the general public are skeptical or distrust science, government, and each other, this may increase social disconnection and stifle the development and acceptance of effective interventions and programs to reduce isolation and loneliness.

Technological advancements

The rapid evolution of digital technologies has already demonstrated co-occurring shifts in socializing. Much has been written about the mental and physical health implications of the use of social media[92,178-183]. Similar rapid developments and widespread adoption are occurring with artificial intelligence (AI) and large language models (LLM) tools, that have the potential to similarly result in both benefits and harms, but to an exponentially larger extent.

The long-term consequences of AI are yet unknown, but predictions often fall into either a utopian or dystopian outlook for the future, both of which have implications for social health and policy[184]. From a utopian perspective, AI will be the cure to the “loneliness epidemic”, with 24/7 access to emotional support for all, and increased automation will free up more time for leisure. From a dystopian perspective, AI will replace human interaction, and diminish trust in others due to blurred lines between fact and fantasy. Moreover, several jobs will no longer require humans, resulting in a lack of meaning and purpose in life, and perhaps even the risk of a downfall of humanity altogether[185].

Some of the potential short-term benefits that already have some limited evidence involve AI-powered virtual companions or chatbots that can engage in conversation and provide immediate emotional support[186], and 24/7 access to mental health support as well as increased accessibility among those experiencing barriers (e.g., language, privacy concerns, social anxiety) to in-person therapy. However, increased isolation may occur if there is over-reliance on AI interaction and emotional support and forming attachments to AI companions[187,188]. Generative AI may also magnify our own biases, leading to information echo chambers that further isolate us from others[189,190].

Generative AI is neither inherently good or bad for health and

Table 4 Recommendations for national strategies to foster social connection and address social isolation and loneliness

Policy and strategy	Make social connection a priority in policy agendas of governments and other organizations. Establish a national strategy and leadership at all levels to track, advance and coordinate policies and programs across agencies or units. Assemble an inter-agency, cross-sector coalition to assess and address social implications across all policies and programs. Establish a centralized resource or database for evidence-based interventions and policies.
Integration within the health system	Prioritize social connection in prevention and integration into treatment in clinical settings. Assess and track risk within the electronic medical records. Adequate training, resources and support for health care providers.
Healthy digital environments	Establish greater transparency and cooperation to independently evaluate drivers of connection and disconnection. Increase accessibility (access, affordability, knowledge) to digital tools and environments with demonstrated benefits. Establish safeguards (laws, regulations, guidelines, autonomy) to reduce risk associated with harmful elements.
Evidence, evaluation, measurement	Creation of a global social connection index to allow for comparisons across nations. Establish consistent national measure of social connection, for population surveillance at a national level. Establish a national research and policy center/institute to coordinate cross-sector collaboration in research. Establish Grand Challenges in Social Connection Research, and funding to sustain efforts to address them.
Education and awareness	Establish public-facing national awareness campaigns, ensuring accurate and inclusive messages based on high-quality evidence. Establish National Health Guidelines for Social Connection (similar to dietary guidelines). Include social connection in public-facing health educational resources (websites) of major health organizations. Integrate social connection into formal health education curriculum across all educational settings (primary, secondary, post-secondary, higher education, continuing learning, advanced and continuing education for health professionals). Establish age-appropriate formal education curriculum and practices to foster social connection skills.
Norms and culture	Media, arts and entertainment, local and national leaders, and others in positions of influence, can model positive behaviors that facilitate connection (e.g., respect, openness, responsiveness, kindness, support) Create routines, habits and programs that reinforce regular social connection within formal (workplace, education) and informal (neighborhoods, recreation and leisure) settings. Strengthen norms, incentives and opportunities to create a culture of service. Establish coalitions and networks to coordinate efforts and share best practices.
Infrastructure	Design physical places and spaces to foster socializing (e.g., public, commercial, recreational, religious). Design should consider features of accessibility and inclusiveness across ages, abilities, and economic circumstances. Evaluate existing infrastructure to identify barriers to social connection. Redesign, reduce or eliminate features of infrastructure that are barriers. Create pro-social policies, and evaluate existing policies for barriers relevant to infrastructure (e.g., zoning laws, investing in public transportation, housing and desegregation). Reform policies to allow for the use of existing underutilized public spaces (e.g., schools during nights and weekends, churches on weekdays, commercial buildings during off hours) for community social events and gatherings. Develop programs, services and resources (e.g., recreation, volunteer programs, senior centers, community gardens) to support more connected communities.

humanity. Our current decisions and actions will starkly impact the trajectory of our future, extending across all sectors of society[184].

Recommendations to reverse trends

Several countries are beginning to take steps to promote social connection, and the global COVID-19 pandemic crystalized and accelerated the urgency to act and to coordinate efforts. Table 4 provides a set of recommendations for national strategies to foster social connection and address social isolation and loneliness.

These recommendations align with those made by the National Academy of Sciences, Engineering, and Medicine[15,27,92], expert consensus documents and reports, the US Surgeon General Advisory[4], the WHO[191], the US Centers for Disease Control and Prevention[192], the American Heart Association[28], and national organizations or groups of states (e.g., European Union, UK, Australia, Japan)[193-195].

CONCLUSIONS

In recent decades, we have witnessed a progressive decline in the social connectedness of individuals and communities at the global level. At the same time, scientific evidence has been credibly demonstrating a significant causal effect of lack of social connection on leading physical and mental health indicators, such as cardiovascular disease, stroke, depression and dementia[80]. In some cases, these associations are bidirectional, cyclically reinforcing poorer social connection and worse health. The strongest evidence documents an independent directional influence of social connection indicators on risk for disease-related and all-cause mortality, adjusting for a robust set of demographic, lifestyle, biological, and health relevant factors[15,54,55]. Furthermore, evidence points to several plausible biological, behavioral and psychological mechanisms through which these associations of social connection with morbidity and mortality may occur. The WHO now recognizes social connection as a global public health priority[1,13].

Despite significant strengths, the body of research evidence is complex and uneven, generating several challenges. We need a common language to describe and measure the multiple indicators of social connection and its deficits. Despite the use of "loneliness" as a catch-all term, this construct is distinct from other related ones (e.g., social isolation). There is convergence of evidence of the health relevance across indicators of social connection, or lack thereof. Nonetheless, the relative effect sizes vary in their magnitude. Social isolation appears to be a stronger predictor of physical health outcomes, while loneliness is a stronger predictor of mental health outcomes[58]. Further, the influence of poor social connection across its multiple components appears to be much stronger than that of only one component[42,54]. Explicit recognition of the separate contribution of the structure, function and quality components of social connection is needed in measurement, risk assessment, and health promotion.

Recent surges in the scientific study of social isolation and loneliness have replicated and expanded upon earlier findings, providing larger sample sizes, more rigorous methodologies, and greater confidence. However, studies have also shown that the public underestimates the relevance of social connection for health relative to what has been documented in the scientific literature[93,94]. Since awareness is a critical step to behavior change[96], education efforts should be prioritized as part of health promotion.

There has been a proliferation of interventions with promising results, most often improvements in loneliness. These interventions vary widely in their approaches, foci, modalities and features; yet no one approach appears superior to others[151]. There are also important limitations worth noting. Most interventions are individually focused, and attention to prevention or early intervention is limited[148]. Furthermore, most reviews and meta-analyses of the evidence only examine the effectiveness of interventions on changing social outcomes (e.g., loneliness), with fewer also evaluating the effectiveness on changing health outcomes. Overall, the proposed interventions lack the level of scientific rigor of the evidence that supports their need.

Existing trends in social disconnection and declining health are likely to persist if social factors continue to get relegated as peripheral to health, and interventions are only aimed at people most severely affected. In the presence of growing trends of distrust in institutions, including science, identifying and implementing effective solutions may be challenging. Furthermore, long-term implications from the COVID-19 pandemic and evolving digital technologies point to potential worsening of existing trends in social disconnection.

Looking to the future, the trajectory of social, mental and physical health declines is unknown, but may be accelerated. Global scale reductions in social contact and subsequent behavioral adaptations may reinforce sustaining social isolation or have delayed downstream effects. Among infants, young children and adolescents, the limited social exposure at critical developmental stages may result in longer-term health consequences into adulthood. Across ages, behavioral adaptations through tools and mechanisms meant to cope with isolation (e.g., remote work, streaming entertainment, telehealth, contactless delivery) may instead sustain reduced social contact. Further developments in digital technologies, such as AI, have the potential to both help and exacerbate the problem.

Despite challenges, there is sufficient scientific evidence to prompt action. Importantly, themes have emerged prompting recommendations for individuals, communities and countries. Prioritizing these recommendations will be critical for reversing trends of social isolation and loneliness, and advancing social connection to positively influence the health and well-being of individuals and society at large.

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