NIHR Global Health Research Centre on the Community Management of Long-Term Conditions (NIHR LatAm Centre)

Study Protocol

BOND+ TRIAL

Building on Dynamic DIALOG+ for Non-communicable Diseases: A Hybrid Type I Effectiveness-Implementation trial of Dynamic DIALOG+ (DD+) to Improve Quality of Life Among People with Non-Communicable Diseases in Colombia.

This research was funded by the National Institute for Health Research (NIHR) via its Global Health Research Centre programme. Grant number NIHR203266, using UK aid from the UK Government to support global health research. The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR or the UK Department of Health and Social Care.

Study Title: A Hybrid Type I Effectiveness-Implementation trial of Dynamic DIALOG+ (DD+) to Improve Quality of Life Among People with Non-Communicable Diseases in Colombia.

Chief Investigator:	Professor Vitoria Bird and Dr. Carlos Gómez-Restrepo
Sponsor	Queen Mary University of London & Pontificia Universidad Javeriana
Country Primary Investigator	Adriana Buitrago-López- Pontificia Universidad Javeriana
Investigators:	Carlos Gómez-Restrepo – Pontificia Universidad Javeriana Miguel Uribe Restrepo- Pontificia Universidad Javeriana Sana Sajun- Queen Mary University of London Yazmin Cadena Camargo- Pontificia Universidad Javeriana Esperanza Peña Torres- Pontificia Universidad Javeriana Camilo González- Pontificia Universidad Javeriana Magda Cepeda Gil – Pontificia Universidad Javeriana David Niño-Torres- Pontificia Universidad Javeriana Andrea López González- Pontificia Universidad Javeriana Juan Camilo Marín Urrego- Pontificia Universidad Javeriana
Funder:	This research is funded by the NIHR (National Institute for Health and Care Research) (NIHR203266) using UK aid from the UK government to support global health research.

Conflicts of Interest: Investigators declare no potential conflicts of interest.

Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, the host organisation, and members of the Research Ethics Committee, unless authorised to do so.

TABLE OF CONTENTS

FIGURES

TABLES

1. KEY CONTACTS

Chief Investigators	Colombia: **Dr. Carlos Gómez-Restrepo** cgomez@javeriana.edu.co UK: **Prof. Victoria Bird** v.j.bird@qmul.ac.uk
Principal Country Investigator	Adriana Buitrago-López Buitrago_d@javeriana.edu.co
Participant Institutions	Queen Mary University of London - UK Pontificia Universidad Javeriana Bogotá-Colombia
Funder	This research is funded by the NIHR (National Institute for Health and Care Research) (NIHR203266) using UK aid from the UK government to support global health research.

2. SYNOPSIS

Study Title	Building on Dynamic DIALOG+ for Non-communicable Diseases: A Hybrid Type I Effectiveness-Implementation trial of Dynamic DIALOG+ (DD+) to Improve Quality of Life (QoL) Among People with Non-Communicable Diseases in Colombia.
Funder	National Institute for Health and Care Research. Global Health Research Centres Programme. NIHR203266
Study Design	Hybrid Type I Randomised Controlled Trial
Study Participants	Eligible participants are men and women aged 18 to 65 years who speak, read, and understand Spanish, and hold legal residency in Colombia. They must be receiving outpatient care for either a physical or mental non-communicable disease (NCD) at one of the study sites and report a low quality of life, defined as a MANSA score ≤5. Participants must present with both a long-term physical NCD (diabetes, hypertension, or obesity) and a mental health condition (anxiety, depression, or hazardous alcohol consumption), demonstrated in one of three ways: 1. A diagnosis of a physical NCD and positive screening for a mental health condition; 2. A diagnosis of a mental health condition and positive screening for a physical NCD; or 3. A diagnosis of both a mental health condition and a physical NCD
Sample Size	226 patients 113 Intervention group 113 control comparator group
Intervention	Dynamic DIALOG+ (DD+) is an adaptation of the original DIALOG+ intervention, developed to address limitations identified in the Colombian context. It is a patient-centred, resource-oriented, and technology-assisted approach that supports structured communication between patients and healthcare professionals. The intervention is delivered by trained practitioners during appointments explicitly scheduled for this purpose, at least once per month, over a minimum period of six months. During each session, patients use a tablet/computer to rate their satisfaction across different life domains. Together with the clinician, they identify and prioritise areas to focus on. The conversation is then guided through a structured four-step process: understanding the current

	situation, envisioning a preferred future, exploring available options, and agreeing on concrete actions. This structured dialogue promotes solution-focused care, helps patients draw on personal and external resources, and enables progress to be tracked digitally across sessions. By embedding these features, DD+ aims to enhance patient engagement, improve continuity of care, and address both physical and mental health needs in individuals living with non-communicable diseases (NCDs).		
Comparator/Control	Usual routine care as provided by each healthcare centre.		
Planned Study Period	15 months Recruitment 3 months Intervention Phase: 6 months – monthly intervention Maintenance Phase: 9- and 12-month intervention Follow-up: 6 and 12 months		
Planned Recruitment period	Start date: March 2026 (or if REC/IRB approval is obtained before this date in 2026). End date: July 2027		
	Objectives	Outcome Measures	Timepoints
Primary (Effectiveness)	Evaluate the effectiveness of DD+ intervention for improving QoL of patients with co-existing physical and mental NCDs in Colombia.	Change in QoL at 6 months measured by MANSA.	- Baseline Assessment -6-month follow-up-
Secondary (Implementation)	Analyse the implementation context for DD + intervention for patients with co-existing physical and mental NCD to improve their QoL in local Colombian contexts.	- Barriers and facilitators for implementation through qualitative interviews. - Feasibility measured through qualitative interviews. - Feasibility of Intervention Measure (FIM) - Feasibility measured as completion proportion (participants who agreed to participate, consented to do so, and were allocated to active treatment and completed the intervention as planned in relation to all those who agreed to	- Baseline Assessment -6-month follow-up-

		participate and consented to do so) - Appropriateness measured through qualitative interviews. - Intervention Appropriateness Measure (IAM) - Acceptability measured through qualitative interviews. - Acceptability of Intervention Measure (AIM)	

*Only primary end-points (effectiveness and implementation) are presented in this synopsis.

2.1. Summary of risks and benefits

2.1.1. Risks

We do not foresee any significant ethical, legal or management issues arising from this study. An outline of the potential risks is provided below.

Within the research assessments and qualitative interviews that will take place across both studies, questions will be raised with participants that might trigger feelings of distress or anxiety.

Participants may experience anxiety in trying DD+. Throughout the intervention-testing period, individuals will continue to receive their routine care, including any medication, in addition to the test intervention. The intervention (DD+), which already has evidence for effectiveness in different contexts and populations, can be stopped at any point.

The trial involves screening patients for conditions other than those for which they have already been diagnosed. Therefore, the research team must ensure that patients will receive at least the standard care for any new condition identified.

2.1.2. Benefits

NCD and MH conditions are a cause of high burden for societies with high levels of disability, distress and high costs to affected individuals. This is exacerbated in low and middle-income countries such as Colombia, where there is a lack of human and financial resources for specialised health services in the community. Through the research described in this protocol, we will explore the effectiveness of a low-resource, dynamic digital intervention that helps patients draw on resources available within their relationships with family members, friends, health professionals, and community members. As well as

describing the feasibility and cost-effectiveness of embedding such an intervention into a healthcare program for the screening, diagnosis, and follow-up of patients with NCD and MH conditions.

This study will thus provide evidence on how to include effective and sustainable locally based interventions for community-based NCD control programs. Overall, the study will build both health and research capacity. A potential benefit for all participants involved in the research is that their suggestions and experiences might be incorporated into further adaptations, which will tailor each of the interventions to the needs of patients, carers and clinicians in the context of healthcare systems.

Additionally, the screening phase of the study may support existing efforts to identify previously undiagnosed individuals living with non-communicable diseases, contributing to improved case detection and early intervention.

3. ABBREVIATIONS

CI	Chief Investigator
CRF	Case Report Form
CTRG	Clinical Trials & Research Governance, University of Oxford
GCP	Good Clinical Practice
GP	General Practitioner
HRA	Health Research Authority
ICF	Informed Consent Form
NHS	National Health Service
RES	Research Ethics Service
OXTREC	Oxford Tropical Research Ethics Committee
PI	Principal Investigator
PIL	Participant/ Patient Information Leaflet
R&D	NHS Trust R&D Department
REC	Research Ethics Committee
SOP	Standard Operating Procedure
QoL	Quality of Life
AIM	Acceptability of Intervention Measure
IAM	Intervention Appropriateness Measure
FIM	Feasibility of Intervention Measure
AUDIT	Alcohol Use Disorders Identification Test

AI	Artificial Intelligence
DD+	Dynamic DIALOG+
ISRCTN	International Clinical Trials Registry
CSRI	Client Service Receipt Inventory
SIX	Objective Social Outcomes Index
MANSA	Manchester Short Assessment of Quality of Life
EQ-5D-5L	5-Level EQ-5D version
WHOQOL	World Health Organization Quality of Life Questionnaire

4. DEFINITIONS

Non-communicable diseases (NCD): Long-duration diseases or conditions that are not transmitted from person to person. They result from a combination of genetic, physiological, environmental, and behavioural factors. NCDs include both physical and mental health conditions (1).

Comorbidity: The presence of co-existing or additional diseases with reference to an initial diagnosis or with reference to the index condition that is the subject of study in a research context (different to multimorbidity) (2,3).

Co-existing diseases: Two or more diseases in the same individual with no clear statement of an index or primary disease. The multiple conditions may or may not have a relation with one another (4).

Co-occurring diseases: Concomitant diseases implying a relation with one another. The nature of the causal relationship requires a formal causal analysis (4).

Multimorbidity: The complex interactions of several co-existing or concurrent diseases. No index condition is identified (3–5).

Resource-oriented intervention: low-cost interventions that focus on the existing individual resources or inner potentials of the patient, as well as on available resources within the community or social structures, to improve and maintain personal health and promote well-being (6,7).

Patient-centred approach: a model of care in which an individual's specific health needs and desired outcomes guide clinical decisions and quality measures. Patients are viewed as active partners alongside their families and health care providers, who not only address medical concerns but also consider emotional, mental, spiritual, social, and financial factors. This approach emphasises shared decision-making, respect for patient and family values, and the creation of coordinated, accessible, and compassionate care that promotes safety, effectiveness, and overall well-being (8).

Technology-assisted intervention: an intervention that involves an electronic or digital device, application, or software used for delivering the intervention (9).

Implementation Research: the systematic study of processes, activities, and strategies that support the successful integration of evidence-based health interventions and treatments into routine practice across specific settings. Implementation research comprises three types of outcomes: client outcomes, service outcomes, and implementation outcomes (10,11).

Service Outcomes: standard of care outcomes, including efficiency, safety, effectiveness, equity, patient-centeredness, and timeliness (10).

Client Outcomes: tangible impacts of interventions on the target population. This includes satisfaction, function and symptomatology (10).

Implementation Outcomes: effects of processes to implement new interventions, programs or services. These outcomes serve as indicators of the implementation continuum, as well as intermediate outcomes in relation to service or clinical outcomes. Implementation outcomes serve as necessary preconditions for attaining subsequent desired changes in clinical or service outcomes. Eight implementation outcomes are considered according to Proctor's proposed model: acceptability, adoption, appropriateness, costs, feasibility, fidelity, penetration and sustainability (11).

Acceptability: is the perception among implementation stakeholders that an intervention, service, practice, or innovation is satisfactory within a particular setting. It is usually assessed at the individual provider or client level (e.g. patient). It can serve as an early indicator of adoption. Acceptability can be evaluated using a survey, qualitative interviews, or administrative data. This construct is considered to be subject to change across the implementation continuum (11).

Adoption: the intention or action to employ an intervention, service, practice, or innovation. It can be assessed from the perspective of the individual provider or the organisation. It can serve as an early to mid-indicator in the implementation continuum. Adoption may be evaluated using administrative records, structured observations, surveys, or qualitative interviews (11).

Appropriateness: the perceived suitability, relevance, or compatibility of an intervention, service, practice, or innovation for a specific setting, provider, or consumer, or its fit to address a problem. It may overlap with acceptability, but there is a conceptual distinction (e.g., being relevant in a given context does not necessarily make the intervention acceptable to a patient or provider). Appropriateness can be assessed at the level of the individual provider, the consumer, or the organisation. Data are usually collected through surveys or qualitative interviews (11).

Costs: the implementation cost refers to the expenses incurred during the implementation process, which depend on the specific intervention, the chosen implementation strategy, and the prevailing setting conditions (11).

Feasibility: the extent to which an intervention, service, practice, or innovation can be successfully used or carried out within a given setting. It may overlap with appropriateness, but a conceptual distinction is relevant (e.g., an intervention may be appropriate for a setting but unfeasible due to external causes such as costs). Feasibility is considered an early indicator for implementation. It can be assessed at the level of individual providers and organisations. Measurement tools include surveys and administrative data (11).

Fidelity: the extent to which an intervention, service, practice, or innovation is implemented as intended by the original protocol or program developers. Fidelity is usually defined in terms of adherence, the

amount (e.g., dose) delivered, and the quality of delivery. It is considered an early to mid-implementation outcome. Fidelity is usually assessed at the individual provider level through direct observation, checklists, or self-report (11).

Penetration: the integration of an evidence-based intervention, service, practice, or innovation within a service setting. It is considered a mid-to-late implementation outcome. Penetration is usually assessed at the organisational level using case audits or checklists (11).

Sustainability: the degree to which a newly implemented service, practice, or intervention is maintained within a specific setting. It is considered a late implementation outcome, as it requires an intervention to already be in place. Sustainability is usually assessed at the organisational level using case audits, checklists, questionnaires, or semi-structured interviews (11).

Hybrid Trials: Clinical trials that assess both the effectiveness and implementation of a given intervention in the same trial (12).

Hybrid Type 1 Trial: A Hybrid trial that has a primary objective of assessing the effectiveness of an intervention with a secondary aim of assessing the context for implementation. This hybrid trial does not evaluate a formal implementation strategy (12) .

Hybrid Type 2 Trial: A hybrid trial with two coprimary objectives, one for effectiveness and the other for implementation. For the implementation primary objective, this type of hybrid trial seeks to assess the feasibility or impact of a formal implementation strategy for a given intervention (12).

Hybrid Type 3 Trial: A hybrid trial with a primary objective of evaluating the impact of an implementation strategy, with a secondary aim of exploring clinical outcomes associated with implementation (12).

Objective Social Outcomes Index (SIX): a score that summarises various indicators of social outcomes, specifically employment, living situation, and social contacts, which has been extensively utilised in mental health research and can be employed as a routine care measure. The resulting score ranges from 0 to 6 (13).

Client Service Receipt Inventory (CSRI): a structured tool used to collect information on clinical services as well as clinical and community resources for patients. Multiple adaptations have been constructed for specific health conditions and can also be adapted for particular contexts. In this trial, it will be used as an instrument for collecting information on health resource use (14).

Manchester Short Assessment of Quality of Life (MANSA): is a brief instrument for assessing quality of life, focusing on satisfaction with life as a whole, employment, financial status, friendships, leisure activities, accommodation, personal safety, the people with whom the individual lives, family, and health. The questionnaire includes 16 items: 4 evaluate objective quality of life, and 12 measure satisfaction with various life domains. Satisfaction is rated on a 7-point scale, where 1 signifies “could not be worse” and 7 signifies “could not be better”. The objective items use a dichotomous scale, with responses limited to “yes” or “no”. The mean score is calculated by summing the satisfaction scores (15).

5-Level EQ-5D version (EQ-5D-5L): an instrument part of the EQ-5D family of instruments to describe and value Health Related Quality of Life in adults. It is a cognitively undemanding instrument, therefore requiring only a few minutes to complete. It consists of two parts, a short descriptive system questionnaire and a visual analogue scale. The descriptive system measures mobility, self-care, usual activities, pain/discomfort and anxiety/depression, with five response levels each. The visual analogue scale assesses the overall current health on a vertical visual analogue scale. The five dimensions can be represented as a 5-digit code that reflects a respondent's health profile (eg. 21111). These codes are categorical and do not carry arithmetic meaning. To derive summary scores for EQ-5D-5L health states, an appropriate value set must be applied (16).

World Health Organisation Quality of Life Questionnaire Brief Version (WHOQOL-BREF): Is an instrument valid for the assessment of well-being. It consists of 26 items assessing four domains of QoL: physical, psychological, social and environmental. The instrument has a current validated version in Spanish for Colombia. Each item scored on a 5-point Likert scale (1 = very poor/very dissatisfied, 5 = very good/very satisfied); domain scores are calculated according to WHO guidelines and transformed to a 0–100 scale, with higher scores indicating better quality of life (17).

5. BACKGROUND

Chronic non-communicable diseases (NCDs), such as cardiovascular conditions, diabetes, and respiratory illnesses, represent a growing public health challenge in low- and middle-income countries (LMICs), where they account for over 80% of global NCD-related deaths (18,19). Parallel to this, mental health conditions, particularly depression, anxiety, and psychotic disorders, contribute significantly to the global burden of disease, with comorbidity between physical and mental disorders further amplifying morbidity and mortality risks (20–22). Low socioeconomic status, social inequities, and under-resourced health systems are critical drivers of these intersecting epidemics in LMICs (23).

In Latin America, the lifetime prevalence of anxiety disorders ranges from 13% to 20%, and for major depressive disorder from 7% to 12%, depending on the country and study population(24). In Colombia, 2022 administrative data reported prevalence rates ranging from 1.8 to 8.1 per 1,000 people for depression, depending on the region, with a national prevalence of 5.1 per 1,000. Anxiety prevalence ranged from 3.4 to 16.4 per 1,000, with a national prevalence of 12.2 per 1,000 (25). Despite this high burden, even under the high chance of underdiagnosis of the reported data, treatment gaps remain vast—up to 75% of people with mental health conditions in Latin America receive no formal care (24). Structural barriers, stigma, and limited access to trained providers contribute to this treatment gap. The World Health Organisation has emphasised the need for scalable, evidence-based interventions to address mental health in LMICs, particularly in regions like Latin America, where resource constraints and high unmet need intersect (26).

In Colombia in 2022, the prevalence of diabetes was 26.6 per 1,000 people, varying from 11.3 to 31.4 per 1,000 across regions. Hypertension prevalence was higher, at 90 per 1,000 nationally, with regional variation from 30.3 to 96.6 per 1,000. For overweight and obesity, a significant underreport was suspected,

with national prevalence at 15.2 per 1,000 people and regional variation between 6.8 and 24.0 per 1,000 (25).

There is a well-documented bidirectional relationship between chronic physical illnesses and mental health conditions. Individuals with co-existing disorders face increased disability, reduced quality of life, greater healthcare utilisation, and elevated mortality rates (27–29). Despite this, integrated approaches to addressing mental and physical health are rare in LMICs. As a result, health systems often fail to detect and treat mental health problems among patients with NCDs, contributing to poor health outcomes and increased systemic costs (30,31). Also, The World Health Organisation has emphasised the need for scalable, evidence-based interventions to address mental health in LMICs, particularly in regions like Latin America, where resource constraints and high unmet need intersect (26).

Digital health technologies have emerged as promising, scalable tools to bridge the treatment gap for mental health care. These technologies are low-cost, can be delivered by non-specialist providers, and offer flexible, user-centred approaches tailored to resource-constrained settings (31,32). One such intervention is DIALOG+, a digital, app-based therapeutic tool developed by the Unit for Social and Community Psychiatry at Queen Mary University of London. DIALOG+ facilitates structured conversations between health professionals and patients, covering 11 life domains and using elements of solution-focused and cognitive-behavioural therapy to guide brief, person-centred interventions (32–34)

Evidence from high-income countries (HICs), including randomised controlled trials in the UK and implementation studies in Europe, shows that DIALOG+ is effective in improving quality of life, reducing psychiatric symptoms, and enhancing communication between patients and providers (7,35).

6. RESEARCH PROBLEM AND RATIONALE

Despite the proven effectiveness of DIALOG+, mainly for patients with mental NCD in Colombia, implementation strategies are lacking. Evidence is primarily oriented towards effectiveness in mental health conditions in particular contexts, such as school settings, victims of armed conflict or adolescents (36,37).

Although exploratory data suggest the utility, feasibility, and effectiveness of DIALOG+ for patients with physical NCD (33), and the impact of such conditions on mental health and QoL is well recognised, no controlled trial has yet provided effectiveness data for DIALOG+ in patients with co-existing physical and mental health conditions.

Previous data from a recent pilot study conducted in Colombia by the NIHR LatAm Centre identified key system-level barriers to implementation. These include the additional consultation time required to deliver the intervention, which may increase costs due to clinician time and reduce capacity to meet primary care demand (38). Another barrier is the high turnover of health professionals, particularly in remote regions, which disrupts the continuity of DIALOG+ delivery and affects the therapeutic alliance between patient and provider (39).

To address these challenges while acknowledging the known limitations of the original intervention in the Colombian context, the NIHR LatAm Centre has proposed an adaptation of the original DIALOG+ intervention based on previous pilot studies. Modifications include adjustments to the app's structure and language, as well as the way the intervention is delivered, with contracted professionals/staff providing the intervention in appointments exclusively assigned for this purpose. Given these modifications, the adapted intervention will be referred to as Dynamic DIALOG+(DD+). Therefore, given the absence of an implementation strategy for DD+, a Hybrid I effectiveness-implementation trial will be conducted. This design will allow simultaneous testing of both effectiveness and implementation outcomes of the modified intervention in patients with co-existing physical and mental NCDs in Colombia.

The study will generate essential evidence to guide the future implementation and scale-up of digital health interventions aimed at improving health-related QoL in Colombia. The combined effectiveness and implementation data from the modified intervention will provide the basis for designing a country-specific implementation strategy and sufficient evidence to determine scale-up and long-term sustainability within the national health system. To achieve this, the Hybrid I model enables the parallel assessment of effectiveness and implementation, reducing the operational and cost burden of research and accelerating the integration of an effective intervention into routine care.

The structure of the trial that will be presented includes the screening of potential participants for probable underdiagnosed medical conditions such as diabetes, HBP, obesity, anxiety, depression and hazardous alcohol consumption. Therefore, implementing screening trial procedures through standard and validated methods will support efforts to identify underdiagnosed patients. For diabetes screening, a capillary or, eventually, a venous blood sample is necessary to adequately assess the diagnosis, with the benefits of an accurate diagnosis outweighing the puncture risk. Also, as stated later, no samples will be kept or used for other purposes.

7. RESEARCH QUESTIONS

- In adults living in Colombia with co-existing physical and mental non-communicable diseases, does the DD+ intervention, compared to usual care, lead to quality of life improvement?
- Is the DD+ intervention implementable in the local Colombian context for patients with co-existing physical and mental NCDs, considering identified barriers and facilitators, and in terms of its feasibility, appropriateness, acceptability, adoption, and fidelity?
- In adults living in Colombia with co-existing physical and mental non-communicable diseases, does the DD+ intervention, compared to usual care, lead to enhancing social functioning and service utilisation, and in reducing depressive and anxiety symptoms?
- In adults living in Colombia with co-existing physical and mental non-communicable diseases, does the DD+ intervention, compared to usual care, lead to an improvement of clinical outcomes for diabetes, obesity or HBP?

- Does the effect of DD+ intervention in patients with co-occurring physical and mental non-communicable diseases at 6 months remain stable when the intervention frequency is reduced to every two months for the subsequent 6 months?
- What is the additional cost and cost-effectiveness of implementing and delivering the patient-centred, solution-focused intervention DD+ as part of usual care for adults with co-existing physical and mental non-communicable diseases in Colombia?

8. OBJECTIVES AND OUTCOME MEASURES

Table 1. Objectives and outcome measures

Objectives	**Outcome Measures**	**Timepoints of evaluation**
Primary Objective Evaluate the effectiveness of DD+ intervention for improving QoL of patients with co-existing physical and mental NCDs in Colombia.	Change in QoL at 6 months measured by MANSA.	- Baseline Assessment -6-month follow-up-
Secondary Objective **(Implementation)** Analyse the implementation context for DD + intervention for patients with co-existing physical and mental NCD to improve their QoL in local Colombian contexts. Through the following specific objectives: - Identify barriers and facilitators for implementation of DD + intervention for patients with physical and mental NCD to improve their QoL in local Colombian contexts. - Assess the feasibility of DD+ intervention for	- Barriers and facilitators for implementation through qualitative interviews. - Feasibility measured through qualitative interviews. - Feasibility of Intervention Measure (FIM) - Feasibility measured as completion proportion (participants who agreed to participate, consented to do so, and were allocated to active treatment and completed the intervention as planned in relation to all those who agreed to participate and consented to do so) - Appropriateness measured through qualitative interviews. - Intervention Appropriateness Measure (IAM)	- Baseline Assessment -6-month follow-up-

patients with physical and mental NCD to improve their QoL in local Colombian contexts. - Assess the Appropriateness of DD + intervention for patients with physical and mental NCD to improve their QoL in local Colombian contexts. - Assess the acceptability of DD + intervention for patients with physical and mental NCD to improve their QoL in local Colombian contexts. - Assess the adoption of DD + intervention for patients with physical and mental NCD to improve their QoL in local Colombian contexts. - Assess the fidelity of DD + intervention for patients with physical and mental NCD to improve their QoL in local Colombian contexts.	- Acceptability measured through qualitative interviews. - Acceptability of Intervention Measure (AIM)	
Secondary Objective (Effectiveness) Evaluate the effectiveness of the DD+ intervention in enhancing social functioning and in reducing depressive symptoms and anxiety among individuals with co-existing physical and mental NCDs in Colombia.	- Change in Social Functioning measured with Objective Social Outcomes Index (SIX) - Change in depressive symptoms, measured with Patient Health Questionnaire-8 (PHQ-8) - Change in anxiety symptoms, measured with Generalised Anxiety Disorder- 7(GAD-7)	- Baseline Assessment -6-month follow-up- - 12-month follow-up
Secondary Objective (Effectiveness)	- Change in HbA1c measured through a capillary sample.	- Baseline Assessment

Evaluate the effectiveness of DD+ intervention in the reduction of HbA1c, systolic mmHg, diastolic mmHg, abdominal circumference and BMI	- Change in systolic/diastolic mmHg measured through an automatic blood pressure cuff - Change in abdominal circumference measured with standard measuring tape	-6-month follow-up- - 12-month follow-up
Secondary Objective (Effectiveness) Evaluate the stability of treatment when reducing the frequency of DD+ visits (bimonthly visits in the 6 to 12-month period)	- Change in QoL measured by MANSA.	-12-month follow-up
Secondary Objective (Cost effectiveness) Assess the additional cost and cost-effectiveness for implementation and delivery of patient-centred solution-focused intervention with DD+ into usual care for adults with co-existing physical and mental NCDs in Colombia.	- Cost in USD - Cost per Quality Adjusted Life Year (QALYs) gained - Changes in clinical variables (blood pressure, glycosylated haemoglobin, body weight and waist circumference.	-6-month follow-up- - 12-month follow-up

9. RESEARCH HYPOTHESIS

Hypothesis 1- <u>Effectiveness</u>: DD+ is effective for improving QoL in patients with co-existing physical (Diabetes or HBP) and mental (depression, anxiety or alcohol misuse) NCD.

Hypothesis 2- <u>Implementation</u>: DD+ is potentially implementable in the Colombian health care system in the context of Amazonas, Guaviare, Cauca and Bogotá D.C for improving QoL in patients with co-occurring physical (Diabetes or HBP) and mental (depression, anxiety or alcohol misuse) NCD.

10. STUDY DESIGN

10.1. General Design

To assess the effectiveness and implementation context of DD+, we will conduct a Hybrid I Randomised Controlled Trial (RCT) using a mixed-methods approach (11,12,40). A health economic analysis will also be included to evaluate the cost of delivering the intervention in the local setting. Effectiveness will be assessed through an RCT, implementation will be evaluated through a descriptive mixed-methods implementation study, and cost-effectiveness will be assessed through an embedded health economic analysis.

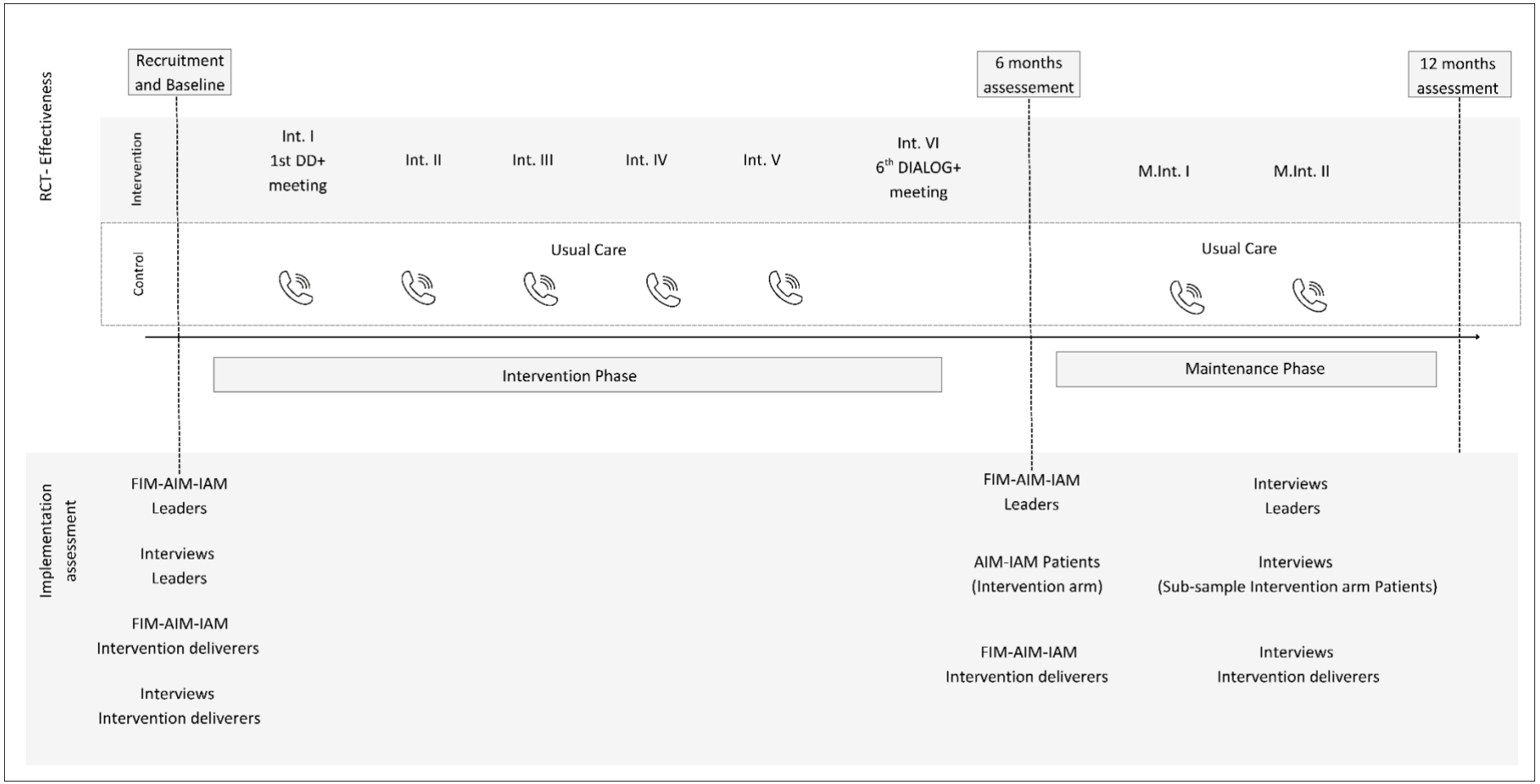
Patients in selected HC (Health Centres) will be pre-screened for chronic physical and mental health conditions. Those who meet the initial criteria will be recruited. After accepting to participate and signing informed consent, they will undergo full screening for physical and mental health conditions and QoL. Patients with co-existing physical and mental NCD will be randomised to the active intervention or the control group. Healthcare practitioners (contracted research study professional/staff) trained in DD+ will deliver the assigned intervention to each active intervention participant once per month for six months. Participants allocated to the control group will continue their usual or routine care as established by the HC professionals and procedures. Participants in the control group will be contacted periodically by phone (**Figure 1).**

Participants in both study arms will be assessed for outcome measures at baseline, 6, and 12 months. **Table 2** displays the timing and content of study procedures, including interventions, assessments, and interviews across all study visits.

To assess the **implementation context**, a mixed-methods approach will be used, with the following steps: a) At the 6-month assessment, all patients in the intervention arm will complete the AIM and IAM scales. b) At the 6-month assessment, a subsample of the intervention group participants will be invited to individual interviews to enhance explanatory power and to assess additional implementation criteria, including fidelity, adoption, and feasibility. c) During the trial recruitment period, FIM, IAM, and AIM scales will be administered to clinical and managerial leaders from each health centre and to the staff responsible for delivering the intervention. These data will be complemented with semi-structured interviews to enhance explanatory power and to assess additional implementation criteria, including fidelity and adoption. d) After the 6-month assessment, clinical and managerial leaders, as well as the staff responsible for delivering the intervention, will again complete the FIM, IAM, and AIM scales, together with a complementary semi-structured interview.

Methods and procedures for the effectiveness assessment are presented in the following sections. Details on the implementation context assessment are provided later in Section 13. IMPLEMENTATION CONTEXT ASSESSMENT. The full set of procedures for patients is described in the effectiveness section as an integral guide to study activities, in order to avoid mistakes or confusion during data collection.

Figure 1. Study Phases Overview



Abbreviations: AIM= Acceptability of Intervention Measure; IAM= Intervention Appropriateness Measure; FIM= Feasibility Intervention Measure, Int= Intervention Dynamic DIALOG+(DD+).

Table 2. Summary of study visits procedures for patients

Month				**M1**	**M2**	**M3**	**M4**	**M5**	**M6**	**M6**	**M9**	**M12**	**M12**
Reference date for window calculation			Screening	Baseline	Int. I +30D	Int. II +30D	Int. III +30D	Int. IV +30D	Int. V +30D	Int. VI	6-MA + 90D	M.Int I +90D	M.Int II
Window (days)			+10	±10	±10	±10	±10	±10	±10	±15	±10	±10	±10
Study visit name		Screening*	Baseline*	Int. I	Int. II	Int. III	Int. IV	Int. V	Int VI	6-MA	M.Int I	M.Int II	12-MA
Study visit number	0	1	2	3	4	5	6	7	8	9	10	11	12
Invitation	X												
Informed consent		X											
MANSA QoL		X								X			X
WHOQOLBREF			X							X			X
EQ5D			X							X			X
Socio-demographics			X										
PHQ-8		X								X			X
GAD-7		X								X			X
AUDIT-C		X								X			X
HbA1 measurement		X								X			X
HBP measurement		X								X			X
Obesity assessment		X								X			X
Eligibility checklist		X											
SIX			X							X			X
CSRI				X						X			X
AIM										X			
IAM										X			
Dialog+**				X	X	X	X	X	X		X	X	
Telephone follow-up¥				X	X	X	X	X	X		X	X	
Qualitative Interview¶										X			

Abbreviations: M=Month; D=Day; Int= Intervention DIALOG+; M.Int = Maintenance Intervention DIALOG+; PHQ-8=Patient Health Questionnaire-9; GAD-7=Generalized Anxiety Disorder-7; HBP= High Blood Pressure; SIX=Objective Social Outcomes Index; CSRI= Client Service Receipt Inventory; AIM= Acceptability of Intervention Measure; IAM= Intervention Appropriateness Measure; FIM= Feasibility Intervention Measure; 6-MA: six months assessment.

*The screening visit and baseline visit may be performed on the same day or on a different day.

**Intervention arm only

¥Control arm only

¶A sample of 24 patients allocated to the intervention group will be interviewed. The window for qualitative interviews can be extended by 15 additional days beyond the indicated timeframe.

10.2. Setting

The study will be conducted and participants recruited in primary health care centres, outpatient psychiatric facilities or outpatient services from hospitals in Bogotá, San José del Guaviare (Guaviare), Boquerón (Guaviare), Leticia (Amazonas), Cali (Valle del Cauca), Toribio-Tacueyó (Norte del Cauca) and Santander de Quilichao (Norte del Cauca) in Colombia. The HCs to be included may be either a rural or urban HC. As part of previous work, the NIHR Latam research centre has been working with the community, building trust and collaborating on research.

Recruiting, screening, intervention provision and continuing care will happen at each site.

11. PARTICIPANTS

11.1. Reference Population

Reference population: patients receiving outpatient care for chronic NCDs and mental health conditions in Colombia.

11.2. Study Population

Study population: patients receiving outpatient care at primary care centres or mental health care outpatient facilities with a diagnosis of diabetes, HBP or obesity and at least one mental health condition, such as anxiety, depression or hazardous alcohol consumption in selected health centres in Bogotá, Guaviare, Cauca, and Norte del Cauca.

11.3. Eligibility criteria

Patients with a clinical diagnosis of at least one long-term chronic NCD of interest (diabetes, high blood pressure, or obesity) and at least one mental health condition of interest (anxiety, depression or alcohol misuse) will be eligible to participate.

11.3.1. Inclusion criteria

- Male or female, aged between 18 and 65 at the time of the screening visit;
- Meet either of the following condition combinations:
    a. Diagnosis of at least one long-term physical chronic non-communicable disease of interest (diabetes, high blood pressure, or obesity) **and** positive screening of at

least one mental health condition of interest (anxiety, depression or hazardous alcohol consumption). **Table 3** displays the positive screening criteria.

b. Diagnosis of at least one mental health condition of interest (anxiety, depression or hazardous alcohol consumption) **and** a positive screening of at least one long-term chronic NCD of interest (diabetes, high blood pressure, or obesity). **Table 3** displays the positive screening criteria.

c. Diagnosis of at least one mental health condition of interest (anxiety, depression or hazardous alcohol consumption) **and** one long-term physical chronic non-communicable disease of interest (diabetes, high blood pressure, or obesity).

- currently receiving outpatient care for physical or mental NCD at one of the study sites;
- have a low quality of life score as measured by MANSA of ≤5
- speak and understand Spanish;
- have legal residency status in Colombia.

11.3.2. Exclusion criteria

- Diagnosis of dementia, or
- clinical diagnosis of schizophrenia or other psychotic disorders, or
- an inpatient at the time of recruitment, irrespective of the cause, or
- absence of health insurance, or
- inactive health insurance at the moment of recruitment

Table 3 .Positive Screening Criteria

Condition	Screening Tool / Measure	Positive Screening Definition
Depression	PHQ-8	Score ≥ 10 (41)
Anxiety	GAD-7	Score ≥ 10 (41)
Alcohol Use (Hazardous alcohol consumption)	AUDIT-C	Score ≥ 4 in men OR ≥ 3 in women (42)
Prediabetes/Diabetes	Glycated haemoglobin (HbA1c)	≥ 5.7% (prediabetes level or above) (43)
Obesity	BMI / Abdominal circumference	BMI ≥ 30 OR ≥ 91 cm in men OR > 89 cm in women (44)
Hypertension	Blood pressure (average of 3 readings, ≥5 min apart)	Systolic ≥ 130 mmHg and/or Diastolic ≥ 80 mmHg (45)

12. PROTOCOL PROCEDURES

Itemised list of procedures for DIALOG+/DD+ RCT patient participants

- Identify sites where RCT will take place
- Identify and invite to participate in a roll-in basis patients across all sites
- Potentially eligible patients sign the consent form
- Potentially eligible participants complete MANSA with the researcher. Those scoring less or equal to 5 go on to complete the full baseline assessment.

- Potentially eligible participants complete physical and mental NCDs screening.
- Researcher confirms the inclusion criteria
- Researcher completes the baseline assessment with participants
- Randomise participants to either the intervention group or the control group (standard care)
- Patients continue to receive treatment as usual. Those in the intervention arm will complete DIALOG+/DD+ once a month for 6 months.
- Researchers complete a 6-month follow-up assessment with patients
- A purposive sample of 24 intervention patients will be contacted for an individual semi-structured interview
- Conduct face-to-face individual interviews with 24 participants.
- Researchers complete a 12-month follow-up assessment

12.3. Recruitment

Recruitment centres will correspond to each study site (health centres). Participants will be recruited through one of the following mechanisms:

- Waiting room invitation: Local research staff will approach eligible patients in the waiting area, provide the study information sheet, and offer a screening visit. This visit can be scheduled for the following day or performed that same day, depending on the capacity of the HC and the local research team.
- Practitioner referral: HC practitioners will be briefed on the study and may invite eligible patients during routine consultations. Interested patients may authorise the research team to contact them to provide further details and schedule a screening visit.
- Study advertisements: Visual materials will be displayed in health centres with contact details for interested patients. Patients may contact the research team to join the study.

Upon acceptance, potential participants will meet individually with a researcher to sign the consent form and complete the eligibility screening.

12.4. Informed Consent

Individuals who respond to the study information with interest will be contacted and invited by phone or letter to attend a face-to-face meeting with a researcher. Researchers will review information sheets with interested individuals and take the time to address any questions or concerns that are raised. At this stage, contact details will be confirmed and availability ascertained for attendance at intervention sessions, interviews, or appointments.

All participants will be asked to provide informed consent at the enrolment visit by signing and dating an informed consent form prior to any data collection commencing. The form will contain the exact nature of the study, what it will involve for the participant, the implications and constraints of the protocol, the

known side effects and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, without affecting their legal rights, and with no obligation to give the reason for withdrawal.

If signed on paper, the participant will retain one copy of the informed consent form, and the research team will keep the other, storing it in a locked filing cabinet and uploading a copy to the participant's records in the REDCap secure system (Research Electronic Data Capture). If electronically signed, the participant should receive a copy of the signed consent form on their phone or by email. If there is no available electronic source to deliver the copy, the researcher responsible for obtaining informed consent must provide a physical copy of the signed form to the participant.

All local researchers authorised to obtain informed consent will receive training based on Good Clinical Practice. Researchers must be suitably qualified with proven knowledge of current local and international clinical research regulations.

The researchers will assess each patient's level of understanding during the recruitment and consent process, alongside discussion with patients' clinicians where necessary. If there are any doubts regarding the patient's capacity to consent to take part in research, this will need to be resolved before proceeding with study participation. If any doubts about their capacity emerge during the recruitment process, or capacity to consent appears to change during their participation in the study, their capacity to consent will be re-evaluated before continuing with study participation.

12.5. Screening and Eligibility Assessment

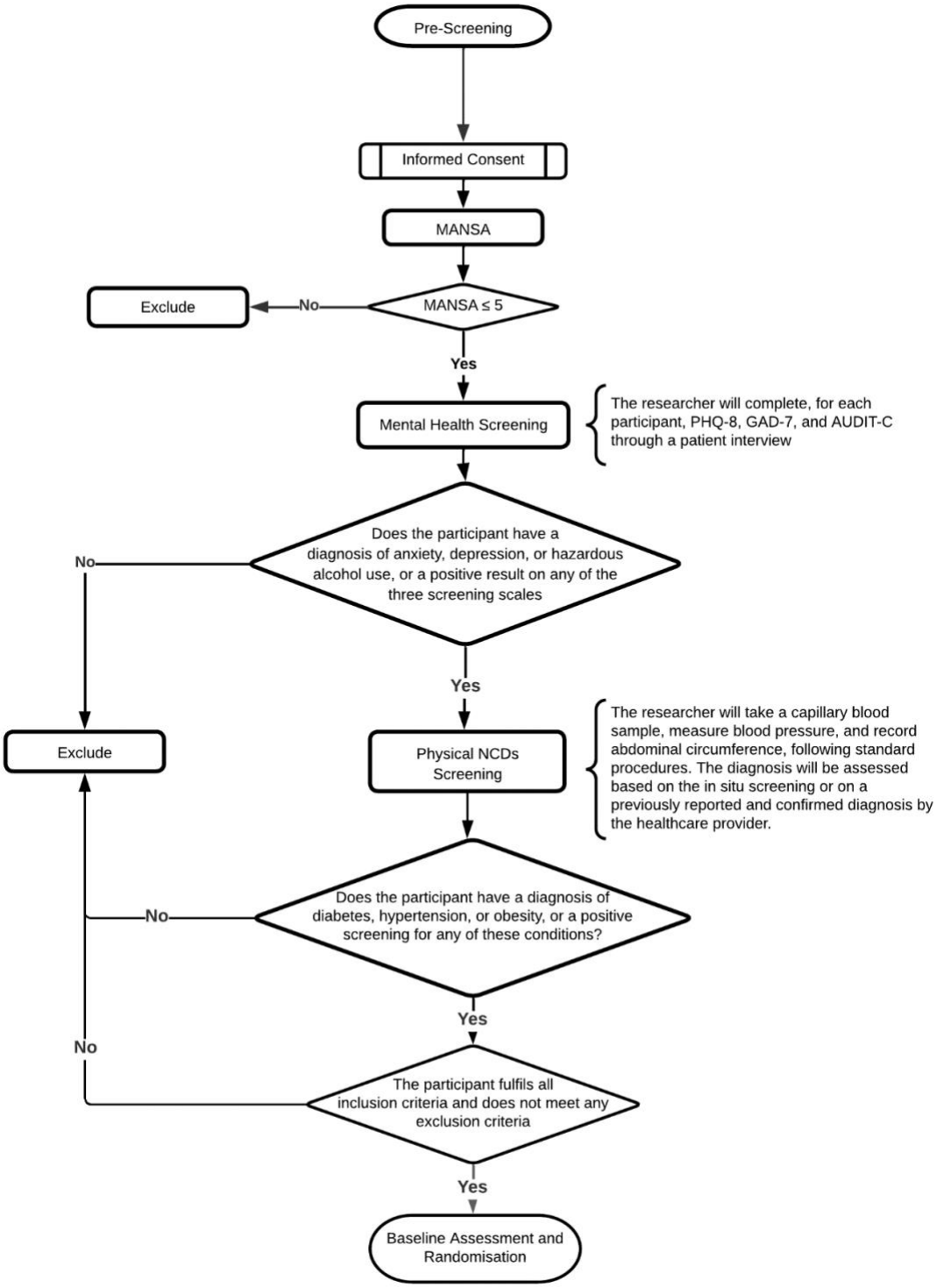
Participants must have at least one long-term chronic non-communicable disease (NCD) of interest, such as diabetes, high blood pressure or obesity, and at least one mental health condition, including anxiety, depression, or hazardous alcohol consumption. Consequently, a screening phase is necessary to thoroughly assess the inclusion criteria. Participants can be recruited from specialised mental health centres or primary health centres focused on physical non-communicable diseases.

To complete the eligibility assessment, patients will complete the MANSA, where only individuals with a MANSA score of ≤ 5 points will be eligible to continue with the study.

After QoL assessment, all participants under the MANSA threshold will be screened for mental health conditions with PHQ-8, GAD-7 and AUDIT-C scores irrespective of a previous mental health diagnosis. Afterwards, all participants will be screened for diabetes, HBP, and obesity. Diabetes screening will be based on HbA1 measurement or a previous confirmed diagnosis when the patient is under treatment. HBP will be based on double standard measurement at the screening visit or a previous confirmed diagnosis by the healthcare provider. Obesity will be evaluated using the abdominal circumference measurement at the screening visit.

Error! Reference source not found. presents a flow diagram that summarises the process from recruitment up to randomisation for each participant.

Figure 2. Participant selection and enrolment flow diagram



12.6. Baseline Assessment

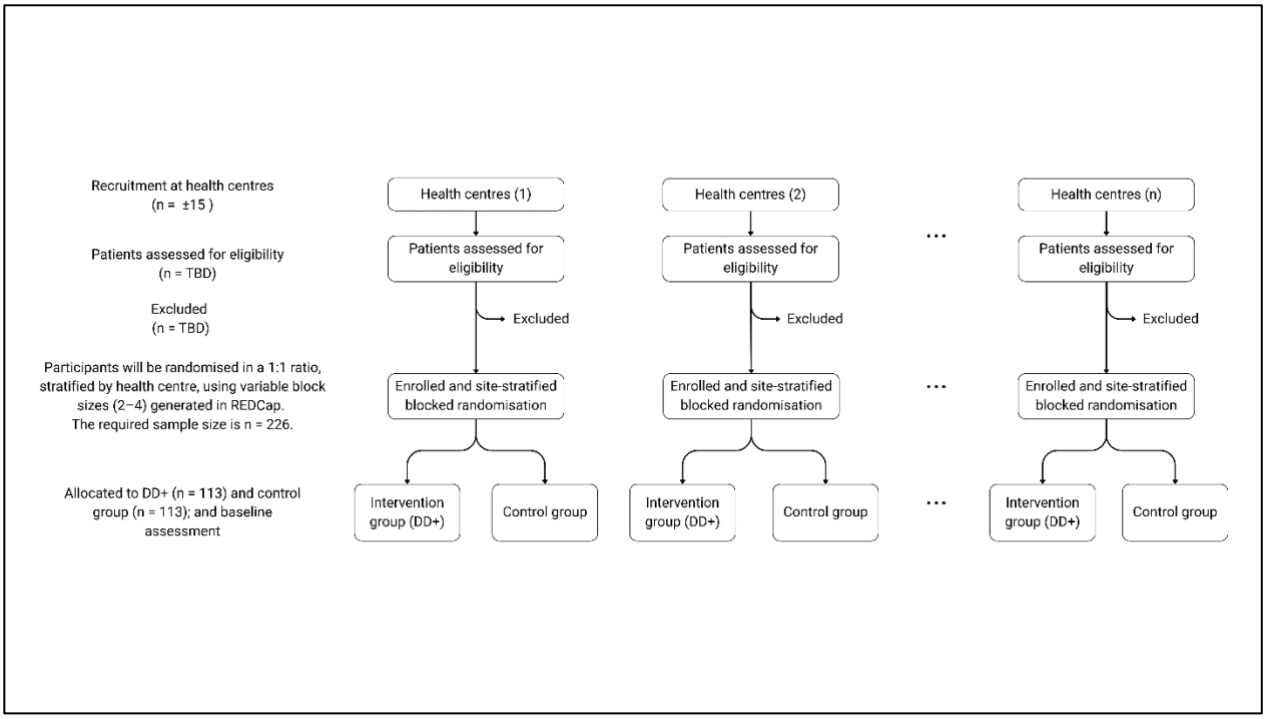
Measurements performed for screening and eligibility assessment will be part of the Baseline Assessment. Additionally, participants will complete a socio-demographic questionnaire with the help of a researcher. The researcher will administer the following scales to patients (See **Table 2**):

- Objective Social Outcomes Index (SIX)
- Socio-demographic questionnaire
- EQ5D
- WHOQOL-BREF
- CSRI

12.7. Randomisation

The unit of randomisation will be the individual participant. Site-stratified blocked randomisation, with a variable block size ranging from two to four, will be performed on a rolling basis during the recruitment period. A randomisation schedule will be defined for each health centre (study site). Within each stratum, participants will be randomised in a 1:1 ratio to either DD+ or the control group. Randomisation will be performed using REDCap or via a phone call, following the corresponding randomisation schedule.

Figure 3. Study Randomisation Summary



TBD= To Be Determined; DD+= Dynamic DIALOG+

12.8. Blinding and code-breaking

Due to the nature of the DD+ intervention and the usual care control group, patients cannot be blinded to the intervention. Researchers responsible for recruitment, screening, baseline assessment, and scheduling intervention appointments will be unblinded. Researchers conducting outcome evaluations will be blinded to participant allocation, and participants will be instructed not to disclose details of their allocation to the research team at any time during the study.

Blinded statisticians will perform statistical analysis. Qualitative interviews and analysis will be conducted by unblinded researchers.

12.9. Description of study intervention

DD+ consists of a patient-centred assessment whereby the clinician invites the patient to rate their satisfaction with different life domains and treatment aspects. This is followed by a four-step solution-focused approach to identify the patient's resources and develop solutions to deal with the patient's concerns. The intervention is available as an app and makes use of a tablet computer (e.g. ipad or android device) within routine clinical meetings.

Each session begins with the patient using the tablet to rate their satisfaction with eight life domains (mental health, physical health, job situation, accommodation, leisure activities, friendships, relationship with family/partner, personal safety) and three treatment aspects (medication, practical help, meetings with professionals). The tablet allows patients to be more actively involved in the meeting, with the tablet easily passed between the clinician and patient. Each satisfaction item is rated on a scale from 1 ("totally dissatisfied") to 7 ("totally satisfied"), and followed by a question on whether the patient wants additional help with that domain. The ratings are summarised on screen, allowing for comparisons with ratings from previous meetings. Clinicians are instructed to offer positive feedback on any improving or high-scoring domains.

The ratings are followed by a four-step solution-focused approach to identify the patient's existing resources that can be used to address the concerns raised. The four steps are: Understanding (Why is the patient dissatisfied? What went nevertheless well?); Looking Forward (What is the best-case scenario? What is the smallest step forward?); Exploring Options (What can the patient, the clinician or others do?); and finally Agreeing on Actions (e.g. homework and referrals).

DD+ will be delivered by a blinded trial member once a month for six months in a specific appointment for this purpose.

The control group will continue their routine care in the health centre as indicated by the HC clinical team.

12.10. Subsequent Visits

Participants will be followed up at predefined time points as outlined in **Table *2***. Each visit will be identified by name and visit number and associated with the specific time window, when applicable. Details of each visit, including type, timing, and procedures, are described below.

Unless stated otherwise, all scales or instruments should be completed directly in REDCap. In the event of unforeseen circumstances, a paper-based CRF can be used. When using paper forms, the researcher in charge of data collection must enter or upload the completed scale or instrument into REDCap as soon as possible, and no later than two working days after collection.

Visit 0- Invitation and pre-screening

As mentioned in Section 12.1 (Recruitment), potential participants may be invited through waiting room invitation, practitioner referral, or study advertisements. Upon acceptance, potential participants will meet individually with a researcher to sign the consent form and complete the eligibility screening. The procedures described from visit 1 onwards apply to all participants, irrespective of any previous known diagnosis.

Visit 1 – Screening Visit

The screening visit is the initial assessment of the participant by the research team, excluding any previous communications intended to invite the potential participant or arrange the time for visit 1. The place of the visit will correspond to each of the participating HCs. The first activity in the screening visit will be the delivery of the information about the trial as a formal invitation for the participant. If interested, the researcher will proceed with the informed consent procedure, broadening the information about study aims and procedures. Upon acceptance and signing of the informed consent, the following procedures will take place or all participants irrespective of previous diagnosis status:

- The MANSA scale will be completed by the participant with the researchers' aid. A MANSA score of five or less points is a prerequisite for continuing in the trial, as stated in the inclusion criteria.
- The researcher will complete mental health screening scales through patient interview (PHQ-8, GAD-7, AUDIT-C).
- The researcher will screen participants for diabetes, obesity and HBP following standard procedures. The diagnosis will be assessed based on the in-situ screening or a previously reported and confirmed diagnosis by the healthcare provider. Screening criteria are presented in **Table 3**.
    a. The researcher will take a capillary blood sample for assessing HbA1c levels (Afinion™ HbA1c Abbott),
    b. Measure blood pressure with standard electronic equipment. During the visit, the assessment will be done at three moments, with at least five minutes between measurements. HBP measurement will follow the checklist and recommendations from the 2025 AHA Guideline for the Prevention, Detection, Evaluation, and Management of HBP, as well as the established study standard procedures (46).

c. Record abdominal circumference measuring at the midway between the bottom of the ribs and the top of the hips, while the participant breathes out naturally, before taking the measurement (47).
d. Record height and weight using validated instruments and as stated in the standard procedures.

The screening visit is finalised with the determination of the participant's eligibility. The assessment will be made by the researcher after filling out the selection criteria checklist.

Visit 2- Baseline Assessment Visit

Depending on logistical issues and the availability of the research team and participants, the screening visit and baseline assessment may be performed on the same day or a different day, considering a window of no more than ten calendar days. The baseline consists of the completion of a sociodemographic questionnaire and the remaining instruments for this visit (EQ5D, WHOQOLBREF, SIX, CSRI). The researcher will complete the baseline assessment through a patient interview. This process will take approximately 60 minutes. Visit 2 finalise with participant randomisation.

Visits 3 to 8 – Intervention visits

After randomisation, visits 3 to 8 will take place once a month (average month duration of 30 calendar days), with a 10-day window.

- Patients will be assigned to a routine clinical visit with a trial clinician. The local trial research coordinator will facilitate the appointment assignment.
- A member of the research team will accompany the patient and clinician to support them in any technical or logistical issues.
- Patient and clinician will privately go through the intervention meeting: DD+ with the solution-focused approach.

At visit 6, a researcher will update the CSRI with participants, either at the health centre during the DD+ intervention visit or by phone within five days after the visit.

Visits 3 to 8 – Control group follow-up

Participants allocated to the control group will be followed up on monthly by phone call to assess any health events, and to remind the 6-month follow-up visit.

Visit 9- Main and secondary 6-month outcome assessment.

Within 30 days after Visit 8, a researcher will schedule Visit 9 with participants. The researcher will complete the clinical scales described in Table 1 through patient interviews. Also, HbA1c, HBP and abdominal circumference will be reassessed. For the qualitative implementation assessment, twenty-four patients will be sampled and interviewed as defined in Section 13. Semi-structured interviews will be audio-recorded and are expected to last between 30 and 60 minutes.

Visit 10 and 11- Maintenance period intervention visits

At 90 (±10) days from visit 9 (visit 10) and 90 (±10) days from visit 10 (visit 11), participants in the intervention arm will go through the DD+ intervention.

Visits 10 and 11 – Control group follow-up

At 90 (±10) days from visit 9(visit 10) and 90 (±10) days from visit 10 (visit 11), participants in the control arm will receive a follow-up phone call.

Visit 12- Main and secondary 12-month outcome assessment

At ±10 days after visit 11, a researcher will schedule visit 12 with participants. The researcher will complete clinical scales and CSRI through patient interviews. Visit 12 will be the last study visit.

12.11. Sample Handling

Capillary blood samples will be taken from participants at the baseline visit, 6-month, and 12-month assessments. Samples will be processed immediately by a research team member at the HC and used exclusively for HbA1c estimation. Due to the collection method and the small amount of blood extracted, transport or storage of biological samples is neither possible nor expected. Biological residues will be disposed of according to each HC's procedures. If no such procedure exists, disposal will follow local regulations and will be specified in the SOP documents.

12.12. Early Discontinuation/Withdrawal of Participants

During the course of the study, a participant may choose to withdraw early from the study treatment at any time. This may happen for several reasons, including but not limited to:

- The occurrence of what the participant perceives as an intolerable Adverse Events (AE).
- Inability to comply with study procedures
- Participant decision

Any participant will be given three options when withdrawing from the study:

1. Withdrawal from active follow-up/ treatment and further communication, but allow the study team to continue to access their medical records and any relevant clinical data that is recorded as part of routine standard of care.
2. Withdrawal from active follow-up/ treatment and further communication, keeping the consent to use data already collected up to the time of withdrawal.
3. Complete withdrawal from the study, including data and samples collected up until the point of withdrawal. The data and samples already collected would not be used in the final study analysis. However, if the analysis of their data or samples has already been integrated into interim or final analysis, it should be explained to the participant.

In addition, the Investigator may discontinue a participant from the study treatment at any time if the Investigator considers it necessary for any reason, including, but not limited to:

- Ineligibility (either arising during the study or retrospectively having been overlooked at screening)
- Significant protocol deviation
- Significant non-compliance with treatment regimen or study requirements
- Clinical decision

For any of the aforementioned situations, the type of withdrawal and reason for withdrawal will be recorded in each participant's CRF.

If the participant withdraws due to an adverse event, the researcher will arrange fortnightly telephone calls until the adverse event has been resolved or the end-of-study definition is reached. Clinical management of the participant will be the responsibility of the health system the participant is affiliated with. As stated elsewhere, the security record of the intervention does not foresee AE related to the intervention or serious adverse event (SAE).

If a REC/IRB determines that it is in the best interests of the participants to terminate the study, written notification will be provided to the country's PI and CI. This may be due to, but not limited to: serious safety concerns, success or failure of the primary outcome, serious breaches, acts of fraud, critical findings or persistent non-compliance that negatively affects patient safety or data integrity. If the study is terminated, participants will be returned to their normal follow-up and routine care within the health system of each country. Other REC/IRB will be informed of the decision to determine study status in sites under their jurisdiction. PIs may pause study procedures until a final decision is taken.

12.13. Definition of End of Study

The end of the study is defined as the date when the last patient completes Visit 10. All IRBs/RECs that have approved the study will be informed of the end of the study, site closure, and archiving procedures initiated.

13. IMPLEMENTATION CONTEXT ASSESSMENT

13.1. Participants

For the implementation assessment, clinical and managerial leaders from each health centre, intervention deliverers, and trial participants will be included.

13.2. Eligibility Criteria

For patients, the eligibility criteria are the same as those described in Section 11.3. For managerial and clinical leaders, as well as DD+ deliverers, the requirements are detailed in Table 4. It should be noted that the DD+ deliverers will be employed as part of the trial personnel; however, their insights into how the intervention is delivered are considered highly valuable for thoroughly assessing the implementation context.

Table 4. Eligibility criteria implementation assessment

Participant	Inclusion Criteria	Exclusion Criteria
Managerial or clinical leaders	-Clinical or administrative manager of a HC included as a study centre - ≥ 18 years	
DD+ providers	-DD+ facilitators employed and trained for the trial -18 to 65 years -Technical or professional healthcare worker (e.g. physician, nurse, nurse assistant, physical therapist, respiratory therapist, social worker)	

13.3. Sample and sampling

13.3.1. Patients

The AIM and IAM instruments will be administered to all participants in the intervention arm. For the qualitative interviews aimed at assessing feasibility and providing additional explanatory depth for implementation outcomes, a purposive sampling strategy based on a maximum variation matrix will be used. This strategy will consider participants' adherence to intervention visits, age, and sex. Participants attending at least 3 out of 6 intervention visits will be classified as having high adherence, while those attending 2 or fewer visits will be classified as having low adherence.

Table 5 displays the maximum variation matrix for sampling patients for qualitative semi structured interviews. The number in each cell indicates the number of participants with those characteristics to be sampled.

Table 5. Maximum Variation Matrix

	Male 18-24	**Female 18-24**	**Male 25-44**	**Female 25-44**	**Male 45-65**	**Female 45-65**
High adherence participants	2	2	2	2	2	2
Low adherence participants	2	2	2	2	2	2

* The upper limit of each age interval includes participants up to that age plus 364 days.

13.3.2. Managerial or clinical leaders

All managerial/clinical leaders from the HC will be invited to participate. Up to one leader per centre will be invited.

13.3.3. Dynamic DIALOG+ providers

Up to two DD+ previously trained providers per region (Bogotá, Cauca, Guaviare, Amazonas) will be invited to participate.

13.3. Informed Consent

For patients, the informed consent process, as stated in, will include information about the possibility of being invited to participate in qualitative interviews. Clinical and managerial leaders invited to participate will undergo an informed consent process. DD+ providers will sign a specific informed consent form related to their participation in this part of the study. Despite their contractual relationship with the trial, their participation will remain voluntary.

13.4. Implementation context assessment procedures

Procedures for patients are also described in Table 1, as an integral guide to study procedures, to avoid mistakes or confusion during data collection. The assessments relevant to the implementation context for all participants are presented in Table 6.

Table 6. Study procedures for Implementation Context Assessment

	Sociodemographic Questionnaire	Baseline QI	6-MA QI	FIM Baseline	AIM Baseline	IAM Baseline	FIM 6-MA	AIM 6-MA	IAM 6-MA
Patients	X		X					X	X
Leaders	X	X	X	X	X	X	X	X	X
DD+ Providers	X	X	X	X	X	X	X	X	X

At the 6-month assessment, all patients in the intervention arm will complete the acceptability and appropriateness scales as part of the outcome assessment visit. In addition, 24 patients selected through purposive sampling will participate in individual in-depth interviews to assess further implementation criteria, including fidelity, adoption, and feasibility. These interviews will also provide explanatory depth to the quantitative findings from the scales, ensuring relevant information is gathered to inform future implementation.

During the trial recruitment period, feasibility, acceptability, and appropriateness scales as well as a brief sociodemographic questionnaire will be administered to clinical and managerial leaders from each health centre, as well as to staff responsible for delivering the intervention. Instruments will be completed directly in REDCap or, if necessary, using paper-based CRFs, under the supervision of local research team members. The estimated completion time for the three scales is approximately 15 minutes. Complementary in-depth interviews will also be conducted, audio-recorded, and analysed to enhance explanatory power and explore additional implementation criteria, such as fidelity and adoption.

After the 6-month assessment, clinical and managerial leaders will again complete the feasibility, acceptability, and appropriateness scales, followed by a new round of qualitative semi-structured interviews.

Each interview is expected to last between 30 and 60 minutes.

14. SAFETY REPORTING

The study will take place within the context of the primary care and mental health care systems in Colombia, where a resource-oriented intervention will be evaluated for its effectiveness. The interventions and research assessments will take place in addition to routine health treatment. Adverse Events, immediate hazards or the need for Urgent Safety Measures are not anticipated.

14.1. Serious Adverse Events

14.1.1. Definition of Serious Adverse Events

A serious adverse event is any untoward medical occurrence that:

- results in death
- is life-threatening
- requires inpatient hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- consists of a congenital anomaly or birth defect.

Other 'important medical events' may also be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.

14.1.2. Reporting Procedures for Serious Adverse Events

A SAE occurring to a participant should be reported to the REC/IRB that gave a favourable opinion of the study. Reports of related and unexpected SAEs should be submitted within seven working days of the PI becoming aware of the event. Local investigators should inform the PI immediately after becoming aware of the event and within the first 24 hours of identifying the SAE.

Based on previous safety reports and research experience with DD+, a low likelihood of a 'related' event is expected.

14.1.3. Follow-up of Serious Adverse Events.

After the initial SAE report, investigators will proactively follow up with each participant by fortnightly phone calls until the issue is resolved. The local research team will ensure participants receive appropriate medical treatment and follow-up as required, according to each participant's medical insurance, until resolution.

14.2. Adverse Events

14.2.1. Adverse Event Definition

In the context of a psychosocial intervention such as DD+, an AE will be defined as an untoward event, unfavourable change, unwanted medical occurrence, or unintended sign or symptom having been absent at baseline, or, if present at baseline, appears to worsen and is temporally associated with the intervention (48). The adverse event does not necessarily have a causal relationship with the intervention.

14.2.2. Reporting Procedures for Adverse Events

AEs occurring to a participant will be recorded in the main research file (REDCap) and the participant's clinical records, if appropriate. Reports of AE should be submitted as soon as possible to the local PI and CIs after being identified by a researcher and within the next seven working days.

Based on previous safety reports and research experience with DD+, a low likelihood of a 'related' event is expected. Due to the nature of the intervention and the low risk of AE, causality assessment will be jointly conducted by the local PI and CI within the next 30 working days after the report.

14.3. Urgent Safety Measures

In the case of urgent safety measures being required, the local PI will inform the CIs and the REC/IRB of the event as per REC/IRB and other relevant requirements and guidelines.

14.4. Annual Safety Reporting

The local PI will send over annual reports as required by the REC/IRB using their existing templates and guidelines.

14.5. Overview of the Safety Reporting Responsibilities

The PI (Adriana Buitrago-López) will ensure that safety monitoring and reporting are conducted in accordance with the requirements of the REC and any other relevant organisations/institutions that are involved in overseeing and monitoring research activities.

15. STATISTICS AND ANALYSIS

An independent statistician, blinded to participant allocation status, will conduct all analyses. Blinding will be maintained throughout data cleaning and statistical procedures to minimise bias.

15.1. Study Variables

Table 7 presents the study variables, their measurement scales, operationalisation, and the time points at which each variable will be collected.

Table 7. Study Variables

Variable	Measurement Scale	Operationalisation	Follow-up
Date of assessment	Date	Date on which the assessment is conducted, recorded in the format DD/MM/YYYY	Baseline, 6 months, 12 months
Health centre ID	Nominal	Unique three-digit code identifying the health centre	Baseline, 6 months, 12 months
Participant ID	Nominal	Unique three-digit code assigned to the participant	Baseline, 6 months, 12 months
Interviewer ID	Nominal	Unique three-digit code assigned to the interviewer	Baseline, 6 months, 12 months
Clinician ID	Nominal	Unique three-digit code assigned to the clinician	Baseline, 6 months, 12 months
Date of birth	Date	DD/MM/YYYY	Baseline
Sex	Nominal	1. Male 2. Female 3. Prefer not to say	Baseline
Spanish literacy	Ordinal	1. Can read and write 2. Can read but not write 3. Cannot read or write	Baseline
Marital status	Nominal	1. Single 2. Cohabiting 3. Divorced or separated 4. Married 5. Widowed	Baseline
Place of residence	Nominal	1. Hamlet/Rural district (*corregimiento)* *2*. Rural village (*Vereda)* *3*. Municipal centre (*Cabecera municipal)* *4*. Indigenous reserve (*Resguardo indígena*) 5. Other (specify)	Baseline
Ethnic Self-Identification	Nominal	1. Indigenous (*Indígena*) 2. Black, Afro-Colombian, Raizal or Palenquero (*Población Negra, Afrocolombiana, Raizal y Palenquera*) 3. Gitano (*Gitano(a) o Rrom*) 4. No ethnic group (*Ningún grupo étnico*)	Baseline
Indigenous group	Text	If the participant identifies as Indigenous, they must provide the name and a description of the Indigenous group or community to which they belong (open-ended response)	Baseline
Social status or situation	Nominal (multiple selection)	1. Farmer 2. Victim of armed conflict 3. Displaced due to violence 4. Community leader 5. None 6. Other (specify)	Baseline
Household composition	Nominal (multiple selection)	1. Lives alone 2. Parents 3. Children 4. Other relatives 5. Friends 6. Partner 7. Others (specify)	Baseline
Current health conditions	Nominal (multiple selection)	1. None 2. Diabetes 3. Obesity or overweight 4. Hypertension 5. Dyslipidaemia 6. Asthma 7. COPD 8. Tuberculosis 9. Hepatitis 10. Cancer 11. Poor dental health 12. Alcohol consumption 13. Anxiety 14. Depression 15. Bipolar disorder 16. Other (specify)	Baseline
Health insurance scheme	Nominal	1. Uninsured 2. Subsidised scheme 3. Contributory scheme 4. Special scheme 5. Complementary plan or private insurance 6. Don't know	Baseline
Education degree	Ordinal	1. No formal education 2. Incomplete primary 3. Complete primary 4. Incomplete secondary 5. Complete secondary 6. Technical or vocational qualification 7. University degree 8. Other (specify)	Baseline

Main occupation	Nominal	1. Employed 2. Studying 3. Housework 4. None 5. Other (specify)	Baseline
Type of work	Nominal	1. Full-time 2. Part-time 3. Unpaid work (domestic, caregiving, volunteer) 4. Not applicable	Baseline
HbA1c (Glycated hemoglobin)	Ratio	Blood test measuring % of glycated hemoglobin	Baseline, 6 months, 12 months
Systolic Blood Pressure (SBP)	Ratio	Measured in mmHg	Baseline, 6 months, 12 months
Diastolic Blood Pressure (DBP)	Ratio	Measured in mmHg	Baseline, 6 months, 12 months
Blood Pressure Control	Dichotomous	Achieving <130/80 mmHg	Baseline, 6 months, 12 months
Height	Ratio	Measured in meters or centimeters	Baseline, 6 months, 12 months
Weight	Ratio	Measured in kilograms	Baseline, 6 months, 12 months
BMI	Ratio	Calculated as weight (kg) / height² (m²)	Baseline, 6 months, 12 months
Waist Circumference	Ratio	Measured in centimeters (cm)	Baseline, 6 months, 12 months
AUDIT-C (Alcohol Use Disorders Identification Test) Score	Interval	A brief 3-item screening tool assessing alcohol use: drinking frequency, typical quantity, and frequency of heavy drinking (six or more drinks per occasion). Each item is scored 0–4; scores are summed to give a total of 0–12. Higher scores indicate greater alcohol consumption and increased risk of alcohol-related problems	Baseline, 6 months, 12 months
Manchester Short Assessment of Quality of Life (MANSA)	Interval	Measure of subjective quality of life across multiple life domains. It comprises 16 items, including 12 subjective ratings of satisfaction across core life domains, each scored on a 7-point Likert scale (1 = extremely negative, 7 = extremely positive), and four objective yes/no items on social contact, victimisation, and legal issues. The overall score is the mean of the 12 satisfaction ratings, with higher values indicating better perceived quality of life.	Baseline, 6 months, 12 months
Objective Social Outcomes Index (SIX)	Ordinal	The index covers four domains: employment (0–2), accommodation (0–2), living arrangements (0–1), and friendship/social contact (0–1). The total score is obtained by summing the domain scores, yielding a range from 0 to 6, with higher values indicating better objective social outcomes.	Baseline, 6 months, 12 months
Patient Health Questionnaire-8 (PHQ-8)	Interval	An 8-item validated self-report screening measure of depressive symptoms over the past two weeks. Each item is scored on a 4-point scale (0 = not at all, 3 = nearly every day), resulting in a total score ranging from 0 to 24, with higher values indicating greater depressive symptom severity.	Baseline, 6 months, 12 months
Generalised Anxiety Disorder-7 (GAD-7)	Interval	A 7-item validated self-report screening measure of anxiety symptoms over the past two weeks. Each item is scored on a 4-point scale (0 = not at all, 3 = nearly every day), resulting in a total score ranging from 0 to 21, with higher values indicating greater anxiety symptom severity.	Baseline, 6 months, 12 months
WHOQOL-BREF	Interval	26-item validated tool assessing quality of life across four domains (Physical health, Psychological health, Social relationships, Environment) and two overall items on general QoL and health satisfaction. Each item scored on a 5-point Likert scale (1 = very poor/very dissatisfied, 5 = very good/very satisfied); domain scores	Baseline, 6 months, 12 months

		are calculated according to WHO guidelines and transformed to a 0–100 scale, with higher scores indicating better quality of life.	
Acceptability of Intervention Measure (AIM) - Score	Interval	Comprises 4 items assessing the acceptability of an intervention: approval, appeal, liking, and welcoming of the intervention. Each item is rated on a 5-point Likert scale: 1 (Completely disagree) to 5 (Completely agree). Total score is calculated by averaging the item scores.	Baseline, 6 months
Intervention Appropriateness Measure (IAM) - Score	Interval	Comprises 4 items assessing the perceived appropriateness of the intervention: whether it seems fitting, suitable, applicable, and a good match. Rated on a 5-point Likert scale: 1 (Completely disagree) to 5 (Completely agree). Total score is calculated by averaging item scores.	Baseline, 6 months
Feasibility of Intervention Measure (FIM) - Score	Interval	Comprises 4 items assessing the feasibility of the intervention: whether it seems implementable, possible, doable, and easy to use. Items are rated on a 5-point Likert scale: 1 (Completely disagree) to 5 (Completely agree). Scores are averaged across items to obtain a total score.	Baseline, 6 months
Feasibility of Intervention Completion	Ratio	Feasibility was measured as the proportion of participants who agreed to participate, provided informed consent, were allocated to the active treatment, and completed the intervention as planned, relative to all those who initially agreed to participate and consented.	6 months
Death status	Nominal	Has the individual passed away by the end of the follow-up period? (Yes/No). This is essential for determining the QALY value, as it implies a quality-of-life value of 0 for that individual.	12 months
Costs of health service use, medication and productivity lost. Out-of-pocket expenses.	Ratio	In the CSRI instrument, we collect participants' use of inpatient hospital service, use of health care services, current medication, family support, out-of-pocket expenses and employment.	Baseline, 6 months, 12 months
Costs of DIALOG+, and costs of supervision and training to health professional	Ratio	The Health Economics Inventory forms	Training phase, implementation and monthly in the intervention arm. The research team will calculate costs.

15.2. Sample Size Determination

The sample size calculation for this study will be based on parameters derived from previous DIALOG+ trials (35). A standard deviation of 0.9 for the MANSA and a correlation of 0.4 between baseline and follow-up measurements will be assumed, while an effect size of 0.4 points on the MANSA will be considered the minimal clinically important difference (MCID) for quality of life in this patient population. Based on these parameters, a total of 90 participants per group will be required to achieve 90% power at the 5% two-sided significance level. To account for an anticipated 20% attrition rate, the final sample size will be set at 226 participants (113 per group).

15.3. Analysis populations

The primary and Secondary (Effectiveness) analysis will follow the intention-to-treat (ITT) principle, including all randomised participants in the groups to which they were originally allocated, regardless of treatment received, adherence, or withdrawal. Participants who discontinue or deviate from the intervention will remain in their assigned group for analysis (49). Missing data will be imputed as specified in the following subsection.

15.4. Procedure for Accounting for Missing, Unused, and Spurious Data.

For the primary and secondary analysis of the outcome and in line with the intention-to-treat (ITT) principle, missing data will be addressed using multiple imputation by chained equations (MICE) (50). The imputation model will incorporate treatment group and relevant baseline covariates including study clinician age, sex, clinician, and baseline MANSA score or other measures that are relevant according to the objective of the analysis. The imputation will be conducted under the assumption that data are missing at random (MAR). Rubin's rules (51) will be applied to pool the estimates across multiple imputed datasets, thereby reflecting the uncertainty associated with the imputation process. This approach aims to preserve the structure of the data and reduce bias due to missingness.

A sensitivity analysis will be conducted to assess the impact of missing data assumptions, comparing multiple imputation estimates with those from a complete-case analysis.

15.5. Interim analyses

Data will be processed and analysed upon completion of the 6- and 12-month follow-up periods, respectively. However, no formal interim analyses are planned to support decisions regarding modification

or early termination of the trial in accordance with the proposed study timeline. The trial management team will periodically monitor recruitment progress, data quality, and participant safety. Any serious adverse events will be reported in accordance with applicable ethical and regulatory requirements, as outlined in the study protocol.

15.6. Descriptive Analyses

Descriptive statistics will be employed to summarise baseline sociodemographic characteristics, clinician-related variables, and psychometric measures across both intervention and control groups. Categorical variables will be presented as absolute frequencies and corresponding percentages. For continuous variables, means and standard deviations (SD) will be reported when distributions are symmetrical; otherwise, medians and interquartile ranges (IQR) will be used. Discrete numerical variables will also be summarised using medians and IQRs.

Missing data will be documented in detail. The number and proportion of missing values for each variable will be reported by study arm.

15.7. Primary Objective

The primary outcome data (MANSA scores) will be summarised at baseline and 6 months. At each time point, the number of observations, means, and standard deviations will be reported separately for the intervention and control groups to support interpretation of changes over time.

A mixed-effects linear regression model will be used to evaluate the effect of the intervention on MANSA scores at 6 months. Fixed effects will include treatment group (intervention vs control) and the baseline MANSA score to adjust for initial differences. Clinician or healthcare practitioners clusters will be modelled as a random effect to account for intra-cluster correlation.

The model will estimate the adjusted mean difference in MANSA scores between the two groups, with corresponding 95% confidence intervals (CIs) and p-values.

Formally, the model can be expressed as:

$$y = X\beta + Z\gamma + \varepsilon$$

y is the vector of observed MANSA scores, X i the design matrix for fixed effects, β i the vector of fixed-effect parameters (including the treatment group and baseline MANSA), $Z\gamma$ represents the random effects, with Z being the design matrix for random effects and γ the corresponding random-effect parameters (clinician clusters) and ε is the vector of residual errors.

In lay terms:

Mixed-effects model = Fixed effects (treatment arm + covariates) + Random effects (clinician clusters). The mixed-effects model accounts for both fixed effects—such as treatment group and relevant covariates—and random effects arising from the clustering of participants within clinicians.

15.8. Secondary Objective (Feasibility)

For the participants, the AIM and IAM will be administered at 6 months. Descriptive statistics will be presented for each instrument means and standard deviations (SD) will be reported for approximately symmetric distributions, and medians and interquartile ranges (IQR) for skewed distributions. No formal statistical hypothesis testing is planned.

For healthcare practitioners and leaders, the AIM, IAM, and FIM will be administered at baseline and at 6 months. Each measure will be summarised using means and SD when the distribution is approximately symmetric; otherwise, medians and IQR will be reported. Change scores between the baseline and 6-month assessments will be calculated and reported descriptively.

Feasibility of Intervention Completion will be calculated as the number of participants who agreed to participate, provided informed consent, were allocated to the active treatment, and completed the intervention as planned, divided by the total number of participants who provided informed consent.

No formal statistical hypothesis testing will be conducted.

15.9. Secondary Objective (Effectiveness)

Mixed-effects models will be used to evaluate the effect of the intervention on the secondary outcomes (see **Table *1***) at 6- and 12-month follow-up assessments. Analyses will be conducted under the intention-to-treat principle. Each model will include fixed effects for treatment group (intervention vs control), time, the baseline score of the corresponding outcome, and other relevant baseline covariates. A random effect for clinical professional group (cluster) will be included to account for intragroup correlation. The models will report adjusted mean differences between groups, with corresponding 95% confidence intervals (CIs) and p-values.

15.10. Software

All primary and secondary analyses will be performed using R statistical software (R Foundation for Statistical Computing) (52), via the RStudio interface (53).

15.11. Health Economics Analysis

15.11.1. **Measurement of health economic data**

Resource use specific to DD+ will capture both start-up (training, initial supervision, and device setup) and steady-state delivery (clinician time per DD+ session and documentation, routine/top-up supervision, app/support). These data will be obtained from site time sheets/logs and finance records in a health economics inventory form.

All other healthcare and patient-level resource use (whether under DD+ or usual care) will be collected at baseline, 6 months, and 12 months using a custom, interview-based health-economics inventory (CSRI-style) tailored to primary care for patients with co-occurring physical and mental NCDs in Colombia. Total cost per participant will be computed for 0–6 and 0–12 months from the health-system perspective.

15.11.2. Value of resource utilization

The amount of resource usage for each cost element will be combined with the relevant unit costs. Hourly trainer clinician wage rate will be used as the unit cost to calculate costs to training sessions and supervision, transportation expenses will be included in the implementation phase. On the other hand, hourly Health professional wage rates will be used to calculate the cost of their training, documentation and deliver DIALOG+. Unit costs for other health care services such as visits to a general practitioner, nurse, nutritionist, phycologist, social worker, psychiatrist, internal medicine or other subspecialist, and hospitalizations will be obtained from the tariff manual ISS 2001 + 30% and hospital bills (for sensibility analysis). The unit cost of the current medication prescribed to patients will be sourced from the Colombian drug price information system (SISMED in Spanish) based on the weighted price of each medication for the year. Costs will be reported in U.S. dollars (USD), using the average representative market exchange rate published by the Central Bank of Colombia (*Banco de la República)* for the study year. Sensitivity analyses will explore the impact of applying the minimum and maximum values of this exchange rate within the same year.

15.11.3. Discounting

No discount rate will be applied because the time horizon is 12 months.

15.11.4. Geographical Jurisdictions

The study will be carried out separately in 15 centers of Colombia.

15.11.5. Measurement of effectiveness outcomes for health economic evaluation

For the economic evaluation EQ-5D-5L will be the primary outcome. The EQ-5D-5L describes health on 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), each with 5 levels, yielding 3,125 possible health states denoted by a five-digit code (e.g., 11223). These health-state profiles are converted to utility weights using a Latin American value set; utilities are anchored at 1 = full health and 0 = dead, with negative values allowed for “worse-than-dead” states. This enables QALY estimation. EQ-5D-5L will be collected at baseline, 6-months and 12-months after randomisation.

There is no published Colombia-specific EQ-5D-5L value set. Therefore, in this trial we will use a Latin American value-set strategy: the Peru EQ-5D-5L value set for the base case, with Uruguay EQ-5D-5L and England EQ-5D-5L in sensitivity analyses to test robustness to the choice of tariffs.

Utilities will be assigned to each participant's EQ-5D-5L state at baseline, 6 months, and 12 months, and QALYs over 12 months will be computed using the area-under-the-curve (trapezoidal) method with linear interpolation between time points. Guidance on analysis and reporting follows (54).

15.11.6. Analysis of population and missing data

The economic analysis set will include all randomised participants, in line with the intention-to-treat (ITT) principle. Missing data on costs and other outcome variables in the health economic analysis will be examined. Mean imputation and multiple imputation methods will be applied to address missing data.

15.11.7. Analysis of cost-effectiveness

We will compute the ICER as the additional cost per additional QALY gained ($\Delta C/\Delta E$). Interpretation will use Colombia-relevant willingness-to-pay (WTP) benchmarks. Specifically, we will present cost-effectiveness acceptability curves (CEACs) across a WTP range and highlight the empirically estimated Colombia threshold of about US$5,181 per QALY (≈ COP 17 million in 2019 prices) from Espinosa et al. (55) (IETS) updated to the study price year (2025) using DANE CPI. DIALOG+ will be described as cost-effective when the ICER lies below a WTP value deemed acceptable in Colombia, and we will report the probability of cost-effectiveness at the updated reference threshold and other policy-relevant WTP points.

Differences between trial arms in costs and outcomes will be estimated on an intention-to-treat basis, initially unadjusted and subsequently adjusted for pre-specified baseline covariates. If participant characteristics differ systematically between arms, adjusted models will include age, sex, NCD condition group (hypertension/obesity/T2DM), mental health condition group (anxiety, depression or alcohol misuse), baseline utility (EQ-5D-5L), baseline MANSA and WHOQOL-BREF, baseline total cost, and site (fixed effects).

Incremental costs will be estimated using mixed-effects generalized linear models appropriate for skewed data (primary: Gamma family with log link, or log-normal), including by random effect in the model for healthcare practitioners who delivered DIALOG+ considering clusters. Incremental cost-effectiveness will be estimated with linear mixed models including the same covariates.

Based on the results for quality of life, blood pressure control, glycated hemoglobin, and within-trial cost-effectiveness, we plan to conduct a modeled cost-effectiveness extension study over a 5-year time horizon from the healthcare perspective. In addition, a budget impact analysis with the same horizon will be carried out to support acceptability among decision-makers in the country.

15.11.8. Sampling uncertainty

Sampling uncertainty around the ICER will be quantified using cost-effectiveness planes and cost-effectiveness acceptability curves (CEACs). CEACs will report the probability that DIALOG+ is cost-effective across a range of willingness-to-pay (WTP) values per QALY relevant to Colombia. We will highlight

Colombian specific WTP benchmarks (e.g., values referenced by IETS and recent empirical estimates) and present results at the study price year.

15.11.9. Sensitivity analyses

We will conduct a prespecified set of deterministic and scenario analyses to assess robustness. The base case uses QALYs (EQ-5D-5L); therefore, we will report the incremental cost for each 0.1-point increase in MANSA and for each 5-point increase in WHOQOL-BREF. The base case uses a Latin American value set (Uruguay/Peru); sensitivity analyses will include alternative value sets (e.g., England). Some cost sources come from the ISS 2001 tariff manual plus 30%, but considering outdated tariffs, we will consider hospital bills for sensitivity analysis. And finally, we will include the steady state (baseline) vs. full rollout (training/supervision/annualized leave configuration). Over the time horizon: 12-month base case with an additional 6-month analysis to assess short-term cost-effectiveness.

15.11.10. Software

Economic data analysis will be performed using R statistical software (R Foundation for Statistical Computing) (52), via the RStudio interface (53).

15.12. Qualitative Data Analysis for feasibility of the DD+ intervention

For the analysis of semi-structured interviews, a thematic analysis approach will be used, adapted from the guidelines presented by Miles & Huberman (1994) and Gale et al. (2013), to evaluate the feasibility of the intervention. The analysis will follow these steps:

i) **Transcription**. Interviews will be transcribed verbatim. Identifiers such as names will not be included in the transcription; however, the type of participant (e.g. clinician, patient) will be indicated.

ii) **Immersion**. Researchers responsible for the analysis will review the transcripts in depth, taking notes on initial impressions. If necessary, immersion will be supported by listening to the original audio recordings.

iii) **Development of the analytical framework**. Researchers will apply both deductive coding (based on pre-defined feasibility criteria) and inductive coding to generate new codes. Specifically, at least two members of the research team will familiarise themselves with the transcripts and then conveniently select one or two interviews or focus groups to test the deductively constructed coding framework. Emerging coding will be applied throughout the process to enrich the analysis. New codes will be discussed iteratively by the research team and adopted if they align with the study objectives.

iv) **Data synthesis in an analytical matrix**. Key findings will be summarised in a structured matrix.

v) **Data analysis**. The final interpretation will be based on the completed data matrix as well as the researchers' reflections and insights.

16. STUDY LIMITATIONS AND BIAS CONTROL

Due to the diversity of settings in terms of geographic location and sociodemographic characteristics, the risk of bias due to lack of representativeness of the Colombian population will be low. The randomisation procedure is also expected to generate balanced groups, reducing the risk of differential selection bias and minimising the chances of differential losses. However, since participants in the control group will have less contact with the study team and will be aware of their allocation due to unblinding, there is a risk of higher losses in this group. To mitigate this, routine phone calls will be made to control participants as reminders for the 6- and 12-month follow-up assessments.

A risk of contamination bias exists due to the public availability of the DIALOG+ application in the Play Store. However, for the active group, the intervention will be delivered by a trial clinician in the intervention appointments. In contrast, the follow-up visits for the control group will be through brief phone calls. Neither the trial clinician nor the researcher in charge of the follow-up call will be part of the patient care team. Furthermore, the fact that the application is publicly available will not be explicitly disclosed to participants to minimise the risk of bias.

The lack of blinding may also introduce bias through QoL outcome overestimation. However, outcome assessors and statisticians will remain blinded to allocation to reduce the risk of overestimating the effect or its magnitude. The risk of allocation concealment failure exists, but it is limited because the allocation will be automatically provided by the REDCap platform and only disclosed at the end of the baseline assessment visit.

A risk of outcome misclassification also exists. Although the diagnostic scales and tests used are validated and widely applied, the absence of measurement errors cannot be guaranteed. However, any misclassification is not expected to be differential. Finally, the risk of confounding is low due to randomisation, but not negligible. Therefore, statistical analyses for primary and secondary outcomes will adjust for relevant covariates, and the interpretation of results will consider the distribution of known variables among intervention and control groups.

17. DATA MANAGEMENT

17.1. Source Data

Source data are all original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial that are necessary for the reconstruction and evaluation of the trial. Source documents are the original documents, data, and records from which trial data are obtained.

In this study, source documents will include:

- Signed informed consent form. The specific source document may be a paper-based or an electronically signed consent form.
- Sociodemographic questionnaire. The source document will be the eCRF (Redcap) when applicable or the paper-based questionnaire.
- Eligibility assessment tools and the complete baseline assessment instrument set. The source document will be the eCRF when applicable or the paper-based instruments.
- HBP, diabetes, obesity, depression, anxiety or alcohol misuse report provided by clinicians or HCs. The source document will be the eCRF when applicable or the paper-based data collection form.
- Follow-up assessment scales or instruments. The source document will be the eCRF when applicable or the paper-based instruments.

All source documents will be stored securely under conditions that preserve confidentiality and data integrity. The local PI will be responsible for overseeing and ensuring the secure storage of all research documents. REDCap is a secure system designed for research purposes. Physical documents must be stored in locked, secure cabinets. Participants will be identified in all study-specific documents, except for the signed informed consent forms, only by their unique study participant number/code. Personal identifiers, such as names or other directly identifying information, will not be used in any study data.

17.2. Access to Data

Direct access will be granted to authorised representatives from the IRB/REC and host institutions for monitoring and/or audit of the study to ensure compliance with local and international regulations.

17.3. Data Recording and Record Keeping

All trial data will be entered into REDCap, either directly or after collection on paper. Participants will be identified in the database using a unique, trial-specific code. Names or other identifying details will not be included in any trial data file, except for the consent form.

Records must be stored securely to prevent unauthorised access, loss, or damage, and must be readily available for inspection by ethics committees or other pertinent authorities upon reasonable request. Each academic institution must retain all essential documents for a minimum of 3 years after the end of the trial, or as per applicable regulatory or institutional requirements, whichever is longer. Appropriate for both electronic and physical paper-based documents. The local PI will be the formal custodian of these documents.

All REDCap data will also be transferred to [PUJ/QMUL] as coded, de-identified data for analysis. Retention time for transferred data will be up to 10 years after the end of the trial.

18. QUALITY ASSURANCE PROCEDURES

The study may be monitored, or audited in accordance with the current approved protocol, GCP, relevant regulations and standard operating procedures.

18.1. Risk assessment

We do not foresee any significant ethical, legal or management issues arising from this study. To minimise any risks or adverse effects of taking part in the research, the following measures will be taken:

- The purpose of the study will be clearly explained to participants, and it will be stressed that participants do not have to share any information they are uncomfortable with.
- The topic guides for the interviews will be piloted, and questions will be worded more generally rather than focusing on the individual (i.e. instead of how did it make you feel, how might this make a person feel).
- Participants will be reminded about their right to withdraw (without giving a reason) at any point in the study.
- Participants will be informed that the research team are able to contact their clinicians if they would like further support.
- In the unlikely event that any patient becomes highly distressed during the interviews, data collection will be terminated immediately and, where appropriate, their clinician contacted.
- For patients without a previous diagnosis of anxiety, depression or hazardous alcohol consumption, each local research team will establish a plan prior to commencing the recruitment to ensure that these patients can access formal diagnosis and treatment within the local health system.

In case any adverse event or unforeseeable risk occurs during the trial, the local teams will develop and implement a plan to prevent similar events in the future.

18.2. Study monitoring

Regular monitoring will be carried out according to the procedures established by each approving IRB/REC. In addition, central monitoring will be coordinated by the NIHR LatAm Research Centre, with monitoring visits scheduled every three months, unless earlier visits are required based on previous monitoring findings.

Following written standard operating procedures, the monitors will verify that the clinical study is conducted and data are generated, documented and reported in compliance with the protocol, GCP and the applicable regulatory requirements.

18.3. Study Committees

No oversight committees will be assembled for this trial. Based on the safety record of DD+ the probability of safety issues is low and will be managed as stated in the safety reporting section (32,33,36,56). A data monitoring committee is not deemed necessary, as no early study termination is expected either for safety reasons or for early proof of effectiveness, given the relatively low expected effect size and the importance of the implementation objective within the hybrid trial framework.

The management of the trial will be held by the chief investigator, primary investigator and central research coordinator.

19. PROTOCOL DEVIATIONS

A study-related deviation is any departure from the ethically approved study protocol, study documents (e.g. consent process or administration of the intervention), Good Clinical Practice (GCP), or applicable regulatory requirements.

A protocol deviation may be identified by a researcher during scheduled or unscheduled monitoring visits. In all cases, the local research team should review the deviation. The investigator must explain the reason and take appropriate measures to prevent it from happening again, where applicable.

The local PI may notify the IRB/REC, as required by local regulations or IRB/REC procedures.

All protocol deviations must be documented in the protocol deviation form and filed in the study master file, either physically or electronically.

A standard operating procedure will be described for identifying non-compliances and assessing whether a non-compliance /deviation may be a potential Serious Breach.

20. SERIOUS BREACHES

A “serious breach” is a breach of the protocol or of the conditions or principles of Good Clinical Practice which is likely to affect to a significant degree:

(a) the safety or physical or mental integrity of the trial subjects; or

(b) the scientific value of the research.

If a serious breach is suspected, the CI must be contacted within one working day. The CI, local PI, and relevant research team members will review the breach and notify the IRB/REC, as required by local regulations or IRB/REC procedures.

21. ETHICAL AND REGULATORY CONSIDERATIONS

21.1. Declaration of Helsinki

CIs, local PIs, researchers and associated personnel will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

21.2. Guidelines for Good Clinical Practice

The Investigator will ensure that this study is conducted in accordance with relevant local regulations and with Good Clinical Practice guidelines.

21.3. Colombian Regulations and risk stratification

According to Resolution 8430 from 1993, this study is considered a higher-than-minimum risk research (Investigación con riesgo mayor al mínimo), given that it will employ a random procedure to assign the treatment.

21.4. Approvals

The protocol, informed consent form, participant information sheet, and any proposed advertising materials will be submitted for REC/IRB approval. When required, these documents will also be submitted to the host institutions for approval.

The Investigator will submit all substantial amendments to the originally approved documents and, where necessary, obtain approval from the relevant parties before implementation.

21.5. Other Ethical Considerations

The intervention and related trial procedures pose a low risk of physical or mental harm to participants. However, the DD+ questions, the solution-focused therapy, the assessment instruments, and the qualitative interviews may cause distress to some participants. Preventive measures for this eventuality have been described.

Additionally, the screening process using the GAD-7 and PHQ-8 may identify new cases of depression or anxiety. In such cases, it is essential to have a clear referral plan in place to ensure that these participants receive an accurate diagnosis and appropriate treatment within the local healthcare system.

Implementing screening trial procedures through standard and validated methods will support efforts to identify patients who are underdiagnosed. For diabetes screening, a capillary or, eventually, a venous blood sample is necessary to adequately assess the diagnosis, with the benefits of an accurate diagnosis outweighing the puncture risk.

Capillary blood samples will be taken from participants at the baseline visit, 6-month, and 12-month assessments. Samples will be processed immediately by a research team member at the HC and used exclusively for HbA1c estimation. Due to the collection method and the small amount of blood extracted, transport or storage of biological samples is neither possible nor expected. Biological residues will be disposed of according to each HC's procedures. If no such procedure exists, disposal will follow local regulations and will be specified in the SOP documents. Therefore, no sample will be stored or used for purposes other than determining HbA1c level.

When involving potential participants from Indigenous or other ethnic communities, particular attention will be paid to ensuring that the informed consent process and all study activities are conducted in a culturally appropriate and respectful manner. Prior to initiating recruitment, the research team will request the relevant permissions in accordance with each community's requirements, engage in dialogue with community leaders when necessary, and seek their approval. An additional consent form will be in place in case indigenous or communitary authorities are required to sign the document on behalf of the community. Whichever the procedure, each participant will be addressed individually to obtain informed consent or verbal assent. The study will respect traditional community decision-making processes and local leadership structures, seeking community engagement prior to recruitment, in accordance with national ethical guidelines and international best practices for research with Indigenous and ethnic populations

21.6. Reporting

The CI shall submit once a year throughout the study, or on request, an Annual Progress report to the IRB/REC. Additionally, Reports will also be submitted to host institutions or other relevant entities, as appropriate, to comply with local regulations. In addition, an End of Study notification and final report will be submitted to the same parties.

21.7. Transparency in Research

Prior to the recruitment of the first participant, the trial will have been registered on the International Clinical Trials Registry Platform (ISRCTN), a primary clinical study publicly accessible registry recognised by the World Health Organisation (WHO) and the International Committee of Medical Journal Editors (ICMJE) publicly accessible database. The platform was chosen to comply with the Funder and partner institutions' requirements.

The trial information will be kept up to date during the trial, and the CI or their delegate will upload results to all those public registries within 12 months of the end of the trial declaration.

21.8. Data protection and patient confidentiality

All investigators and study staff will comply with the requirements of the Law 1581 (2012) and Decree 1377 (2013) and any other associated legislation of Colombia regarding the collection, storage, processing and disclosure of personal information and will uphold the law's core principles throughout the study.

21.8.1. Personal Information

All data will be pseudonymised to maintain patient confidentiality. All participants will be assigned a participant ID number used for all data processing purposes. Patient identifiable data (participants' names, contact details, socio-demographic data) and the list linking these data with the participant ID number will be stored on computers using a secure drive, within password-protected folders, which will only be accessible to the research team. All hard copies of data, including socio-demographic forms, consent forms, and patient receipts, will be kept in lockable filing cabinets within the premises of Pontificia Universidad Javeriana at the department of clinical epidemiology and biostatistics and only accessible by the research team. Temporal custody of documents may be held by local research coordinators at the study sites. Details of post-trial record keeping are provided in Section 17.3.

21.8.2. Audio recordings

The individual interviews will be audio-recorded using an encrypted device with explicit permission (as indicated on the consent form) from participants. Audio recordings will be stored in password-protected folders on computers using a secure drive, which will only be accessible to the research team. The audio recordings will be destroyed immediately after transcription. All transcriptions will be completed by a professional transcription service or by the research team with the aid of secure, password-protected and encrypted AI services. Prior to transcription, all identifiable information will be removed and/ or replaced with pseudonymised labels, and audio recordings will be transferred to the transcription service in a secure way.

21.9. Expenses and Benefits

Reasonable travel expenses for any visits additional to usual care will be reimbursed on production of receipts, or a mileage allowance provided as appropriate. Additionally, each patient participant will receive an incentive in the form of a prepaid bonus, depending on the available commercial facilities in each region, which will be offered to each participant. The value of the bonus will be $50,000 COP. In addition, the 24 participants in the qualitative interviews will receive an additional pre-paid bonus of the same value. Considering the 12-month follow-up period and the time commitment required from participants, the incentive is considered proportional and not coercive. All participants (patients) will receive the same incentive, and a record of delivery will be signed by both the participant and the researcher.

Clinical/managerial leaders and intervention deliverers will be offered snacks and transportation, if needed, for each interview they participate in. Table 8 summarises reimbursement for each type of participant.

Table 8. Reimbursements

Type of participant	Visit/timepoint	Description
Patient	Baseline assessment	Snack and transportation
Patient	Baseline assessment	$50.000 COP prepaid bonus
Patient	DD+ visits (each)	Snack and transportation
Patient	6-months assessment	Snack and transportation
Patient	6-months assessment	$50.000 COP prepaid bonus
Patient	12-monts assessment	Snack and transportation
Patient	12-month assessment	$50.000 COP prepaid bonus
Patient	Qualitative interviews	$50.000 COP prepaid bonus
Clinical/managerial leaders	Qualitative interviews	Snack and transportation
Intervention deliverers	Qualitative interviews	Snack and transportation

22. FINANCE AND INSURANCE

22.1. Funding

This research is funded by the National Institute for Health Research (NIHR) through its Global Health Research Centre programme (Grant number NIHR203266), using UK aid from the UK Government to support global health research.

22.2. Budget

Available as a supplementary material

22.3. Insurance

DD + intervention is a low-risk intervention, as previous studies using the DIALOG+ and DD+ intervention have not reported serious adverse events or complications attributable to the intervention. Therefore, the intervention does not exceed the level of risk associated with other routine clinical activities. Also, the assessment scales used are validated scales that may be used as part of standard care and do not represent an additional trial-related risk to participants.

Given this evidence and the minimal-risk nature of the procedures, additional insurance coverage for the trial is not deemed necessary.

22.4. Contractual arrangements

Appropriate contractual arrangements will be put in place with all study sites (Health Centres), including data transfer agreements for trial data.

23. DISSEMINATION

This section describes the expected results and products and outlines the strategy for dissemination. This will target different stakeholders, including health service commissioners and policymakers, clinicians, patients, carers, academics and the general public. The dissemination activities will aim to communicate findings to inform research, policy and practice. Dissemination activities will take via the following means and products:

- Website: a Group specific website has been launched. This will include updates, findings, profiles of Group members, links to participating institutions, manuals for all developed interventions, relevant literature. All the information will be available in English and Spanish.
- Social media through NIHR LatAm research centre accounts (X, Linkedln, Instagram)
- Publications: in peer-reviewed journals (open access), wide distribution newspapers and journals; and presentations at national and international scientific events and professional events, with lead authorship from researchers from partner centres
- Presentations at national and international conferences.
- Interventions: freely available DIALOG+ App including modifications suggested by trial results.
- Regional dissemination event in each partner country: involving researchers, clinicians, patients and their families, who participated in the research activities, and relevant stakeholders from the wider regional networks.

It is anticipated that data will need to be made publicly available by the time the main findings are known. Data sharing with external interests will be considered only after publication of the findings that reflect the given data. Pontificia Universidad Javeriana- Department of Clinical Epidemiology and Bioestatistics will manage the sets of data generated as a result of the research activities described in this protocol. The data management procedures (including storage) will be in line with Data Protection legislation and Information Governance requirements. All rights to the data arising from the study will be owned by the CIs.

Regarding research capacity strengthening, throughout the trial, training for research assistants with different levels of expertise will take place. Senior researchers will tutor early-career researchers during the development of the trial to gain abilities related to trial conduction and data analysis. Also, master's and doctoral students will be involved in the trial as research assistants as part of their academic training.

23.1. Authorship eligibility guidelines

Authorship will be determined by contribution to the study design, data collection, data analysis and writing up of the study following the ICMJE recommendations to base the authorship on the following criteria:

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or reviewing it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement 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.

24. RECORD, RETENTION AND ARCHIVING

Documents will be stored at the main study site in Colombia, at Pontificia Universidad Javeriana, and Dr Carlos Gómez will be the custodian of the data. This will be done according to the regulation for data storage and protection at Pontificia Universidad Javeriana, Bogotá.

25. ENVIRONMENTAL IMPACT

Foreseen environmental impacts are related to the use of paper-based materials, energy consumption due to electronic devices used during the trial, and the use of transportation means for mobilising participants and research team members. The potential benefits of implementing DIALOG+ and DD+ for the community's health and well-being overcome the potential environmental impact of conducting the trial.

To minimise the environmental impact, the research team will take the following actions:

- Avoiding the use of paper-based material whenever possible by using electronic data capturing systems. In cases where paper-based material is necessary due to technical or compliance issues, recycled paper will be used.
- Monthly review of the conditions of electronic tablets, cell phones and computers to ensure an optimum energy usage.
- Thoroughly justify the need for study site visits and any other activity requiring motorised transportation.

26. RESEARCH GROUP BACKGROUND

Researcher	Relevant Qualifications	Trial responsibilities
Victoria Jane Bird	- Psychologist - PhD in Psychiatry - Professor of Mental Health Care (Unit for Social and Community Psychiatry)	Chief Investigator
Carlos Gómez-Restrepo	- Medical Doctor - Psychiatrist - Psychoanalyst - Magister in Clinical Epidemiology - PhD in Public Health - Dean. Faculty of Medicine. Pontificia Universidad Javeriana	Chief Investigator
Adriana Buitrago López	- Registered Nurse - Magister in Clinical Epidemiology - Doctor in Science in Clinical Epidemiology - PhD in Health Sciences - Assistant professor- Department of Clinical Epidemiology and Biostatistics	Country Principal Investigator
Sana Sajun	- Magister in Public Health	Trial Manager and researcher
Miguel Uribe Restrepo	- Medical Doctor - Psychiatrist - Magister in Public Health	Clinical advisor and researcher
Magda Cepeda-Gil	- Medical Doctor - Magister in Epidemiology -	
Yazmin Cadena Camargo	- Medical Doctor - Magister in Public Health - PhD Pregnancy among adolescents in an internal displaced population in Bogota (CAPHRI).	Qualitative methods advisor and researcher

	- Director. Department of preventive and social medicine. Faculty of Medicine. Pontificia Universidad Javeriana	
Esperanza Peña Torres	- Registered Nurse - Magister in Health Administration - Magister in Clinical Epidemiology - Dean. Faculty of Nursing. Pontificia Universidad Javeriana	Health economics advisor and researcher
Camilo Alberto Gonzalez	- Medical Doctor - Internal medicine and nephrologist - Magister in epidemiology - Magister in Health Economics	Health economics advisor and researcher
Juan Camilo Marín	- Medical Doctor - Magister in Clinical Epidemiology - Research Coordinator. Department of Clinical Epidemiology and Biostatistics- NINR Global Health Research Centre	Clinical trial coordinator
David Niño Torres	- Statistician - Biostatistics Master Student - Statistician Department of Clinical Epidemiology and Biostatistics- NINR Global Health Research Centre	Statistician
Andrea López Gonzalez	- Medical Doctor - Clinical Epidemiology Master Student - Research Assistant Department of Clinical Epidemiology and Biostatistics- NIHR Global Health Research Centre	Associate Researcher

27. ANNEXES

Table 9. Annexes

	Category	Document Name	Description
Annex A	CRF	A_T1_CO_CRF_AplicadoresYLideres_20250930_v2.0_ES	CRF for leaders and DD+ deliverers.
Annex B	CRF	B_T1_CO_CRF_Pacientes_20250930_v2.0_ES	CRF for patients
Annex C	Interview Guide	C_T1_CO_GUIDE_Aplicadores_20250930_v2.0_ES	Qualitative Interview Guide for deliverers
Annex D	Interview Guide	D_T1_CO_GUIDE_Lideres_20250930_v2.0_ES	Qualitative Interview Guide for Leaders
Annex E	Interview Guide	E_T1_CO_GUIDE_Pacientes_20250930_v2.0_ES	Qualitative Interview Guide for Patients
Annex F	Timeline	F_T1_CO_MASTERSHEET_Cronograma_20250930_v1.0_EN	Trial timeline
Annex G	Budget	G_CO_BUDGET_BOND_20250605_v1.0_ESP	Trial Budget

28. REFERENCES

1. Noncommunicable Diseases (NCDs) overview | NCD Alliance [Internet]. [cited 2025 Aug 12]. Available from: https://ncdalliance.org/explore-ncds/ncds

2. Comorbidity - MeSH - NCBI [Internet]. [cited 2025 Aug 12]. Available from: https://www.ncbi.nlm.nih.gov/mesh/?term=comorbidity

3. Harrison C, Fortin M, Akker M van den, Mair F, Calderon-Larranaga A, Boland F, et al. Comorbidity versus multimorbidity: Why it matters. J Comorb [Internet]. 2021 Jan 1 [cited 2025 Aug 12];11:2633556521993993. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7930649/

4. Meghani SH, Buck HG, Dickson VV, Hammer MJ, Rabelo-Silva ER, Clark R, et al. The conceptualization and measurement of comorbidity: a review of the interprofessional discourse. Nurs Res Pract [Internet]. 2013 [cited 2025 Aug 13];2013:1–10. Available from: https://pubmed.ncbi.nlm.nih.gov/24187618/

5. Multimorbidity - MeSH - NCBI [Internet]. [cited 2025 Aug 12]. Available from: https://www.ncbi.nlm.nih.gov/mesh/?term=multimorbidity

6. Prüfer F, Joos S, Miksch A. What Do Resource-Oriented Approaches Mean to General Practitioners and How Can They Be Facilitated in Primary Care? A Qualitative Study. Evid Based Complement

Alternat Med [Internet]. 2013 [cited 2025 Sep 14];2013:187641. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3748733/

7. Priebe S, Fung C, Sajun SZ, Alinaitwe R, Giacco D, Gómez-Restrepo C, et al. Resource-oriented interventions for patients with severe mental illnesses in low-and middle-income countries: trials in Bosnia-Herzegovina, Colombia and Uganda. BMC Psychiatry [Internet]. 2019 Jun 14 [cited 2024 Aug 21];19(1). Available from: https://bmcpsychiatry.biomedcentral.com/articles/10.1186/s12888-019-2148-x

8. What Is Patient-Centered Care? | NEJM Catalyst [Internet]. [cited 2025 Sep 14]. Available from: https://catalyst.nejm.org/doi/full/10.1056/CAT.17.0559

9. Syriopoulou-Delli CK, Gkiolnta E. Review of assistive technology in the training of children with autism spectrum disorders. Int J Dev Disabil [Internet]. 2022 [cited 2025 Sep 14];68(2):73–85. Available from: https://scholar.google.com/scholar_url?url=https://www.tandfonline.com/doi/pdf/10.1080/20473869.2019.1706333&hl=en&sa=T&oi=ucasa&ct=usl&ei=Xn_IaLdJ-tSJ6g_liKHICg&scisig=AAZF9b-2NEsjYwpCfrDUd9M8YrG8

10. Proctor EK, Landsverk J, Aarons G, Chambers D, Glisson C, Mittman B. Implementation Research in Mental Health Services: an Emerging Science with Conceptual, Methodological, and Training challenges. Adm Policy Ment Health [Internet]. 2008 Jan [cited 2025 Sep 1];36(1):10.1007/s10488-008-0197–4. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3808121/

11. Proctor E, Silmere H, Raghavan R, Hovmand P, Aarons G, Bunger A, et al. Outcomes for Implementation Research: Conceptual Distinctions, Measurement Challenges, and Research Agenda. Adm Policy Ment Health [Internet]. 2010 Mar [cited 2025 Sep 1];38(2):65. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3068522/

12. Ullman AJ, Beidas RS, Bonafide CP. Methodological progress note: Hybrid effectiveness-implementation clinical trials. J Hosp Med [Internet]. 2022 Nov 1 [cited 2025 Aug 13];17(11):912. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC9804495/

13. Priebe S, Watzke S, Hansson L, Burns T. Objective social outcomes index (SIX): A method to summarise objective indicators of social outcomes in mental health care. Acta Psychiatr Scand [Internet]. 2008 Jul 1 [cited 2025 Aug 10];118(1):57–63. Available from: /doi/pdf/10.1111/j.1600-0447.2008.01217.x

14. Client Service Receipt Inventory (CSRI) | Client Service Receipt Inventory [Internet]. [cited 2025 Sep 21]. Available from: https://www.pssru.ac.uk/csri/client-service-receipt-inventory/

15. Björkman T, Svensson B. Quality of life in people with severe mental illness. Reliability and validity of the Manchester Short Assessment of Quality of Life (MANSA). Nord J Psychiatry [Internet]. 2005 [cited 2025 Sep 21];59(4):302–6. Available from: https://www.tandfonline.com/doi/pdf/10.1080/08039480500213733

16. EuroQol Research Foundation. EQ-5D-5L User Guide [Internet]. 2025 [cited 2025 Sep 21]. Available from: https://euroqol.org/information-and-support/documentation/user-guides.

17. Skevington SM, Lotfy M, O'Connell KA. The World Health Organization's WHOQOL-BREF quality of life assessment: Psychometric properties and results of the international field trial a Report from the WHOQOL Group. Quality of Life Research [Internet]. 2004 Mar [cited 2025 Sep 21];13(2):299–310. Available from: https://link.springer.com/article/10.1023/B:QURE.0000018486.91360.00

18. Patel V, Saxena S, Lund C, Thornicroft G, Baingana F, Bolton P, et al. The Lancet Commission on global mental health and sustainable development. Lancet. 2018 Oct 27;392(10157):1553–98.

19. World Health Organization. Noncommunicable diseases progress monitor 2022 [Internet]. 2022 [cited 2023 Mar 28]. Available from: https://www.who.int/publications/i/item/9789240047761

20. Vigo D, Thornicroft G, Atun R. Estimating the true global burden of mental illness. Lancet Psychiatry [Internet]. 2016 Feb 1 [cited 2025 Sep 10];3(2):171–8. Available from: https://pubmed.ncbi.nlm.nih.gov/26851330/

21. Lund C, De Silva M, Plagerson S, Cooper S, Chisholm D, Das J, et al. Poverty and mental disorders: breaking the cycle in low-income and middle-income countries. Lancet [Internet]. 2011 [cited 2025 Sep 10];378(9801):1502–14. Available from: https://pubmed.ncbi.nlm.nih.gov/22008425/

22. Prince M, Patel V, Saxena S, Maj M, Maselko J, Phillips MR, et al. No health without mental health. The Lancet [Internet]. 2007 Sep 8 [cited 2025 Sep 10];370(9590):859–77. Available from: https://www.thelancet.com/action/showFullText?pii=S0140673607612380

23. Saxena S, Thornicroft G, Knapp M, Whiteford H. Resources for mental health: scarcity, inequity, and inefficiency. Lancet [Internet]. 2007 Sep 8 [cited 2025 Sep 10];370(9590):878–89. Available from: https://pubmed.ncbi.nlm.nih.gov/17804062/

24. Pan American Health Organization. The Burden of Mental Disorders in the Region of the Americas, 2018 [Internet]. PAHO; 2018 [cited 2025 Sep 11]. Available from: https://iris.paho.org/handle/10665.2/49578

25. Marin-Urrego J, Buitrago-López A, Gómez-Restrepo C, Lopez-Alvarez E, Tapia-Pijuan R, Alvarado-Arnez L, et al. Understanding the community management of long-term physical and mental health conditions in Bolivia, Colombia, and Guatemala: a situational analysis. Manuscript Submited-Pending . 2025;

26. World Health Organization. Guidance on community mental health services: promoting person-centred and rights-based approaches [Internet]. World Health Organization; 2021 [cited 2025 Sep 11]. Available from: https://iris.who.int/handle/10665/341648

27. Thornicroft G, Chatterji S, Evans-Lacko S, Gruber M, Sampson N, Aguilar-Gaxiola S, et al. Undertreatment of people with major depressive disorder in 21 countries. Br J Psychiatry

[Internet]. 2017 Feb 1 [cited 2025 Sep 10];210(2):119–24. Available from: https://pubmed.ncbi.nlm.nih.gov/27908899/

28. Kakuma R, Minas H, Van Ginneken N, Dal Poz MR, Desiraju K, Morris JE, et al. Human resources for mental health care: Current situation and strategies for action. The Lancet [Internet]. 2011 [cited 2025 Sep 10];378(9803):1654–63. Available from: https://pubmed.ncbi.nlm.nih.gov/22008420/

29. Collins PY, Patel V, Joestl SS, March D, Insel TR, Daar AS, et al. Grand challenges in global mental health. Nature [Internet]. 2011 Jul 7 [cited 2025 Sep 10];475(7354):27–30. Available from: https://www.nature.com/articles/475027a

30. Priebe S, Kelley L, Omer S, Golden E, Walsh S, Khanom H, et al. The effectiveness of a patient-centred assessment with a solution-focused approach (DIALOG+) for patients with psychosis: a pragmatic cluster-randomised controlled trial in community care. Psychother Psychosom. 2015 Aug 23;84(5):304–13.

31. Naslund JA, Aschbrenner KA, Araya R, Marsch LA, Unützer J, Patel V, et al. Digital technology for treating and preventing mental disorders in low-income and middle-income countries: a narrative review of the literature. Lancet Psychiatry [Internet]. 2017 Jun 1 [cited 2025 Sep 10];4(6):486–500. Available from: https://pubmed.ncbi.nlm.nih.gov/28433615/

32. Ramírez SM, Cabarique C, Ortiz N, Uribe-Restrepo JM, Bird V, Priebe S, et al. Experience with the use of the DIALOG+ intervention in patients with severe mental illness in outpatient services in Colombia. Rev colomb psiquiat. 2022;

33. van Loggerenberg F, McGrath M, Akena D, Birabwa-Oketcho H, Méndez CAC, Gómez-Restrepo C, et al. Feasibility, experiences and outcomes of using DIALOG+ in primary care to improve quality of life and mental distress of patients with chronic conditions: an exploratory non-controlled trial in Bosnia and Herzegovina, Colombia and Uganda. Pilot Feasibility Stud [Internet]. 2021 Dec 1 [cited 2025 Aug 12];7(1):180. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8481761/

34. Omer S, Golden E, Priebe S. Exploring the mechanisms of a patient-centred assessment with a solution focused approach (DIALOG+) in the community treatment of patients with psychosis: a process evaluation within a cluster-randomised controlled trial. PLoS One. 2016 Feb 9;11(2):e0148415.

35. McNamee P, Matanov A, Jerome L, Kerry S, Walker N, Feng Y, et al. Clinical- and cost-effectiveness of a technology-supported and solution-focused intervention (DIALOG+) in treatment of patients with chronic depression—study protocol for a multi-site, cluster randomised controlled trial [TACK]. Trials [Internet]. 2022 Dec 1 [cited 2025 Aug 3];23(1):1–13. Available from: https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-022-06181-4

36. Gómez-Restrepo C, Sarmiento-Suárez MJ, Alba-Saavedra M, Calvo-Valderrama MG, Rincón-Rodríguez CJ, Bird VJ, et al. Development and Implementation of DIALOG+S in the School Setting

as a Tool for Promoting Adolescent Mental Well-Being and Resilience in a Post-Armed Conflict Area in Colombia: Exploratory Cluster Randomized Controlled Trial. JMIR Form Res [Internet]. 2023 Oct 4 [cited 2025 Aug 12];7:e46757. Available from: https://pubmed.ncbi.nlm.nih.gov/37792465/

37. Birabwa-Oketcho H, Nakasujja N, Alinaitwe R, Bird V, Priebe S, Sewankambo N. The effectiveness of a solution-focused approach (DIALOG+) for patients with severe mental illness and epilepsy in Uganda: a randomised controlled trial. Psychiatry Res Commun. 2023 Mar;3(1):100097.

38. Adam T, Amorim DG, Edwards SJ, Amaral J, Evans DB. Capacity constraints to the adoption of new interventions: Consultation time and the Integrated Management of Childhood Illness in Brazil. Health Policy Plan [Internet]. 2005 Dec [cited 2025 Aug 12];20(SUPPL. 1). Available from: https://pubmed.ncbi.nlm.nih.gov/16306069/

39. Mullan L, Armstrong K, Job J. Barriers and enablers to structured care delivery in Australian rural primary care. Australian Journal of Rural Health [Internet]. 2023 Jun 1 [cited 2025 Aug 12];31(3):361–84. Available from: /doi/pdf/10.1111/ajr.12963

40. Weiner BJ, Lewis CC, Stanick C, Powell BJ, Dorsey CN, Clary AS, et al. Psychometric assessment of three newly developed implementation outcome measures. Implementation Science [Internet]. 2017 Aug 29 [cited 2025 Aug 10];12(1):1–12. Available from: https://implementationscience.biomedcentral.com/articles/10.1186/s13012-017-0635-3

41. Vilela-Estrada AL, Villarreal-Zegarra D, Toyama M, Carbonel A, Fung C, Carbonetti FL, et al. Psychometric properties of the patient health questionnaire-8 and general anxiety disorder-7 in adolescents and young adults from three Latin American cities: Internal structure, invariance, internal consistency and divergent validity. J Affect Disord [Internet]. 2025 Jun 1 [cited 2025 Sep 21];378:138–46. Available from: https://perfilesycapacidades.javeriana.edu.co/es/publications/psychometric-properties-of-the-patient-health-questionnaire-8-and

42. Johnson JA, Lee A, Vinson D, Seale JP. Use of AUDIT-Based Measures to Identify Unhealthy Alcohol Use and Alcohol Dependence in Primary Care: A Validation Study. Alcohol Clin Exp Res [Internet]. 2013 Jan [cited 2025 Sep 21];37(SUPPL.1):E253–9. Available from: /doi/pdf/10.1111/j.1530-0277.2012.01898.x

43. Committee ADAPP, ElSayed NA, McCoy RG, Aleppo G, Balapattabi K, Beverly EA, et al. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2025. Diabetes Care [Internet]. 2025 Jan 1 [cited 2025 Sep 21];48(Supplement_1):S27–49. Available from: https://dx.doi.org/10.2337/dc25-S002

44. Buendía R, Zambrano M, Díaz Á, Reino A, Ramírez J, Espinosa E. Puntos de corte de perímetro de cintura para el diagnóstico de obesidad abdominal en población colombiana usando bioimpedanciometría como estándar de referencia. Revista Colombiana de Cardiología [Internet]. 2016 Oct 15 [cited 2025 Sep 21];23(1):19–25. Available from:

http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0120-56332016000100005&lng=en&nrm=iso&tlng=es

45. Members* WC, Jones DW, Ferdinand KC, Taler SJ, Johnson HM, Shimbo D, et al. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Hypertension [Internet]. 2025 Oct [cited 2025 Sep 21];82(10). Available from: /doi/pdf/10.1161/HYP.0000000000000249?download=true

46. Jones DW, Ferdinand KC, Taler SJ, Johnson HM, Shimbo D, Abdalla M, et al. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation [Internet]. 2025 Aug 14 [cited 2025 Sep 8]; Available from: /doi/pdf/10.1161/CIR.0000000000001356?download=true

47. NICE. Identifying and assessing overweight, obesity and central adiposity | Overweight and obesity management | Guidance | NICE. Overweight and obesity management. NICE guideline. 2025.

48. Klein JP, Rozental A, Sürig S, Moritz S. Adverse Events of Psychological Interventions: Definitions, Assessment, Current State of the Research and Implications for Research and Clinical Practice. Psychother Psychosom [Internet]. 2024 Oct 11 [cited 2025 Aug 12];93(5):308–15. Available from: https://dx.doi.org/10.1159/000540212

49. Jakobsen JC, Gluud C, Wetterslev J, Winkel P. When and how should multiple imputation be used for handling missing data in randomised clinical trials - A practical guide with flowcharts. BMC Med Res Methodol [Internet]. 2017 Dec 6 [cited 2025 Aug 3];17(1):1–10. Available from: https://bmcmedresmethodol.biomedcentral.com/articles/10.1186/s12874-017-0442-1

50. van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. J Stat Softw [Internet]. 2011 Dec 12 [cited 2025 Aug 3];45(3):1–67. Available from: https://www.jstatsoft.org/index.php/jss/article/view/v045i03

51. Rubin DB. Multiple Imputation for Nonresponse in Surveys. 1987 Jun 9 [cited 2025 Aug 3]; Available from: https://onlinelibrary.wiley.com/doi/book/10.1002/9780470316696

52. Team RC. R Core Team 2023 R: A language and environment for statistical computing. R foundation for statistical computing. https://www.R-project.org/. R Foundation for Statistical Computing. 2023;

53. Posit team. RStudio: Integrated Development for R. RStudio, Inc., Boston, MA. 2023.

54. Devlin N, Parkin D, Janssen B. Methods for Analysing and Reporting EQ-5D Data. Methods for Analysing and Reporting EQ-5D Data. 2020;

55. Espinosa O, Rodríguez-Lesmes P, Orozco L, Ávila Di, Enríquez H, Romano G, et al. Estimating cost-effectiveness thresholds under a managed healthcare system: experiences from Colombia. Health Policy Plan [Internet]. 2022 Mar 4 [cited 2025 Sep 10];37(3):359–68. Available from: https://dx.doi.org/10.1093/heapol/czab146

56. van Loggerenberg F, McGrath M, Akena D, Birabwa-Oketcho H, Méndez CAC, Gómez-Restrepo C, et al. Feasibility, experiences and outcomes of using DIALOG+ in primary care to improve quality of life and mental distress of patients with chronic conditions: an exploratory non-controlled trial in Bosnia and Herzegovina, Colombia and Uganda. Pilot Feasibility Stud. 2021 Dec 1;7(1).

29. AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made
0	1	30.09.2025	-	-
1	2	13.11.2025	David Niño, Andrea López, Juan Camilo Marín	Ethics Committee requirements.

List details of all protocol amendments here whenever a new version of the protocol is produced.