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Original Research

Scaling of an evidence-based intervention program in older people with diabetes and frailty in Latin America. Diabfrail-Latam clinical trial protocol

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ABSTRACT

Objectives: Diabfrail-Latam is a project funded by the Horizon 2020 program of the European Commission (EC) and the Global Alliance for Chronic Diseases (GACD). The main objective of this protocol is to describe the clinical validation of a multimodal intervention aimed at older people with type 2 diabetes mellitus (T2DM) and frailty in Latin America, involving multicomponent physical exercise (based on VIVIFRAIL), nutritional education, and adjustment of therapeutic targets to be scaled up to other countries in Latin American region.
Methods: The Diabfrail-Latam CE is international, multicenter, single-blind and with two parallel groups with 1:1 randomization (multimodal intervention or usual clinical practice). More than 700 people over 65 years of age, frail or pre-frail, with T2DM, are expected to be recruited in four countries (Colombia, Peru, Mexico and Chile). The primary objective of this clinical validation is to evaluate the effectiveness of the multimodal intervention in improving functionality (measured by the Short Physical Performance Battery, SPPB) after one year of follow-up. Secondary objectives include changes in frailty status, adherence, feasibility, economic impact, biomarkers and caregiver burden. The intervention is expected to significantly improve functionality, reduce frailty progression, and demonstrate feasibility for large-scale implementation in Latin American health systems.
Conclusion: Diabfrail-Latam will allow to validate and adapt interventions that have demonstrated efficacy in previous studies in European population, providing solid evidence for scaling and replication in the Latin American region and its context.

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1. Introduction

Chronic diseases have become a major threat to the well-being of older people, both in Europe and in all regions of the world [1]. It is known to be highly prevalent among older adults, affecting approximately 30% of people aged 65 and older [2]. In 2024, the estimated number of people with diabetes mellitus (DM) aged 65–99 years was 158.3 million (23.7%), 80% of them in low and middle income countries-LMIC [3]. In this population, DM not only increases cardiovascular mortality, but also accelerates the onset of frailty, defined as a clinical syndrome characterized by the presence of three or more of the following criteria: unintentional weight loss, fatigue, muscle weakness, slow walking speed, and low physical activity [4,5]. DM has serious personal and social consequences, associated with an increased risk of disability affecting mobility and instrumental/non-instrumental activities of daily living [6]. DM is the third leading cause of disability-adjusted life-years in adults between 50 and 75 years of age, and the second in those over 75 worldwide, being the leading cause of disability in the older population in Latin American countries [7]. Likewise, these limitations impair the functional capacity of older people and their well-being, fundamental concepts for healthy aging proposed by the World Health Organization (WHO) [8]. Type 2 diabetes mellitus (T2DM) is the most frequent in the elderly and is associated with a significant public health burden in terms of increased healthcare costs [9,10]. Therefore, the management of T2DM in older adults requires an individualized strategic approach based on a comprehensive prior assessment of the patient [11].

In this scenario, multimodal nonpharmacological interventions have demonstrated benefits over the last five decades, particularly in improving functional capacity and reducing complications. However, there is little evidence on their large-scale implementation in Latin American health systems, which justifies the need for this study. A multimodal intervention consisting of 16 weeks of individualized resistance exercise, a 7-session educational program, and adjustment of therapeutic goals (blood pressure and HbA1c) was superior to usual clinical practice in improving physical function as measured by a functional capacity test, the Short Physical Performance Battery test (SPPB). In addition to these benefits, cost savings were achieved, mainly due to lower hospitalization expenses. The above has been largely demonstrated by the European MIDFRAIL clinical trial, conducted from December 2014 to February 2017, with more than 900 participants over the age of 70 who were frail or pre-frail and diagnosed with T2DM [4,10,12–16].

Diabfrail-Latam (GA 825,546) arises as the adaptation and validation of this European experience in Latin American countries, with specific innovations such as the use of the VIVIFRAIL exercise program, the inclusion of people from 65 years of age and the implementation in diverse health systems (public and private). Diabfrail-Latam is funded by the European Commission in the Horizon 2020 program in collaboration with the Global Alliance for Chronic Diseases (GACD). The main objective of Diabfrail-Latam project is to scale up the multimodal intervention already used in MIDFRAIL, introducing some modifications due to the characteristics of the population in countries in the Latin American and Caribbean region. Based on how people age in Latin America, some of the modifications include the use of the VIVIFRAIL physical exercise program [17–19], which promotes physical activity in the participant's home, and a change in the age criteria for inclusion from 70 to 65 years. In order to scale this intervention, the first step was to validate it and determine its effectiveness and practicability in the target population through a randomized clinical trial in four Latin American countries (Colombia, Peru, Mexico and Chile). This article presents the protocol of the validation clinical trial developed in the four countries mentioned above.

Feasibility will be determined by adherence to intervention and economic analysis.

In addition to its main objective, the Diabfrail-Latam clinical trial has the following secondary aims to analyze:

- Changes in frailty status (pathways of frailty: frail to pre-frail, pre-frail; frail to robust; pre-frail to robust; and vice versa).
- Incidence rate of symptomatic hypoglycemia (e.g., proven blood glucose less than 4 mmol/L. Symptoms or signs attributed to hypoglycemia that respond to specific treatment) and hypoglycemic coma.
- Incidence rate of hospital admissions (any admission involving at least one overnight stay in hospital).
- Episodes of permanent institutionalization (permanent transfer to any location other than the patient's own home, where staff are available to provide care if needed at any time of the day or night).
- Caregiver burden (provided there is a caregiver).
- Laboratory biomarkers with prognostic value of response to intervention.

This article presents the protocol of the validation clinical trial developed in the four countries mentioned above. Initially, the validation clinical trial was scheduled for the first quarter of 2020. However, due to the COVID-19 pandemic, the implementation of the protocol was significantly postponed. Finally, the clinical trial was launched in January 2022, after a two-year delay.

2. Methods and design

The present clinical trial is part of the Diabfrail-Latam project funded by the Horizon 2020 program of the European Commission and the Global Alliance for Chronic Diseases (GACD). Eleven institutions from eight countries (Spain, Italy, UK, USA, Colombia, Peru, Mexico and Chile) make up the Diabfrail-Latam consortium (Table 1).

Table 2 shows the nine work packages into which the Diabfrail-Latam project is divided.

2.1. Study design

This is a randomized, pragmatic, multicenter, international and open-label clinical trial conducted by investigators in four Latin American countries (Chile, Colombia, Mexico and Peru). It features a 1:1 random assignment to two groups: Usual Clinical Practice Group (UCG) and Intervention Group (IG). This protocol was written and based on the international standard of recommendations for clinical studies SPIRIT [20].

Recruitment began on January 1st, 2022 in a staggered manner depending on the evolution of the COVID-19 pandemic in each of the countries. Colombia was the first to start, followed by Peru, Chile, and Mexico, respectively. Recruitment was closed in all involved sites on April 21, 2023. All participants signed received verbal and written explanation and signed the inform consent form before any procedure of

Table 1
Diabfrail-Latam consortium.

Number of participants	Institution	Country
1 (Coordinator)	Consorcio Centro de Investigación Biomédica en Red MP (CIBER)	Spain
2	Panamerican Health Organization (PAHO)	USA
3	Università Cattolica del Sacro Cuore (UCSC)	Italy
4	Diabetes Frail Limited (DIFRAIL)	UK
5	Universidad de Castilla-La Mancha (UCLM)	Spain
6	Confederación Española de Organizaciones de Mayores (CEOMA)	Spain
7	Pontificia Universidad Javeriana (PUJ)	Colombia
8	Pontificia Universidad Católica de Chile (PUC)	Chile
9	Instituto Nacional de Geriatría, Mexico (INGer)	Mexico
10	Universidad de San Martín de Porres (USMP)	Peru
11	Universidad de Santiago de Chile (USACH)	Chile

Table 2
List of work packages.

Number of WP	Name of the work package	Work package leader
WP1	Coordination	CIBER
WP2	Guarantee of quality	UCSC
WP3	Clinical trial design and training	DIFRAIL
WP4	Clinical trial implementation and monitoring	INGER
WP5	Feasibility	PUC
WP6	Data collection and statistical analysis	CIBER
WP7	Dissemination, communication and exploitation	PAHO
WP8	Scaling	PAHO
WP9	Ethics	CIBER

the study.

A total of 5 centers involved more than 700 participants. In Colombia, Hospital San Ignacio and Javesalud. In Peru, Universidad San Martin de Porres. In Chile, Municipalidad de Requínoa, and in Mexico, Hospital de los Ángeles in Tijuana. Fig. 1 describes the overall design of the Diabfrail-Latam validation study.

Each center was monitored to ensure full adherence to the procedures described in the protocol and the comprehensiveness of the data collected. To this purpose, a monitoring strategy was designed that included remote review by a Contract Research Organization (CRO) under the supervision of the coordinating team (CIBER-Fundación de Investigación del Hospital de Getafe) and the leader of the guarantee of quality work package (Universidad Católica del Sacro Cuore).

All the ethics committees of each center involved in the study gave their approval. It was conducted in accordance with Good Clinical Practice (GCP), the legislation of each country and the Declaration of Helsinki [21]. It has been registered in ClinicalTrials.gov (NCT04504968) on August 7th 2020.

2.2. Participating subjects

Participants were included according to the following criteria:

- Individuals ≥65 years old, with a diagnosis of T2DM of at least 2 years.
- Frail or pre-frail according to the Fried Phenotype [5].
- Signed informed consent.
- Acceptance of the informal caregiver (in case of having one), to assess burden.
- Participants were excluded according to the following criteria:
- Unable or unwilling to provide informed consent or agree to study procedures.
- Plans to move out of the study area during the year of follow-up or plans to be out of the study area for more than 6 consecutive weeks in the year following the signing of informed consent.
- Montreal Cognitive Assessment (MoCA) test score less than 21/30 [22].
- Cancer treated within the past 3 years, except for skin cancers other than melanoma or those with excellent prognosis (e.g., early-stage prostate or breast cancer).
- Barthel Index Score less than 60 points [23].
- Inability to perform SPPB (total score = 0) [24].
- Amputation of upper and/or lower limbs that prevents physical activity.
- Current participation in a structured physical activity, physical therapy or cardiopulmonary rehabilitation program.
- Current participation in another clinical trial with lifestyle intervention, nutrition or pharmacological treatment.

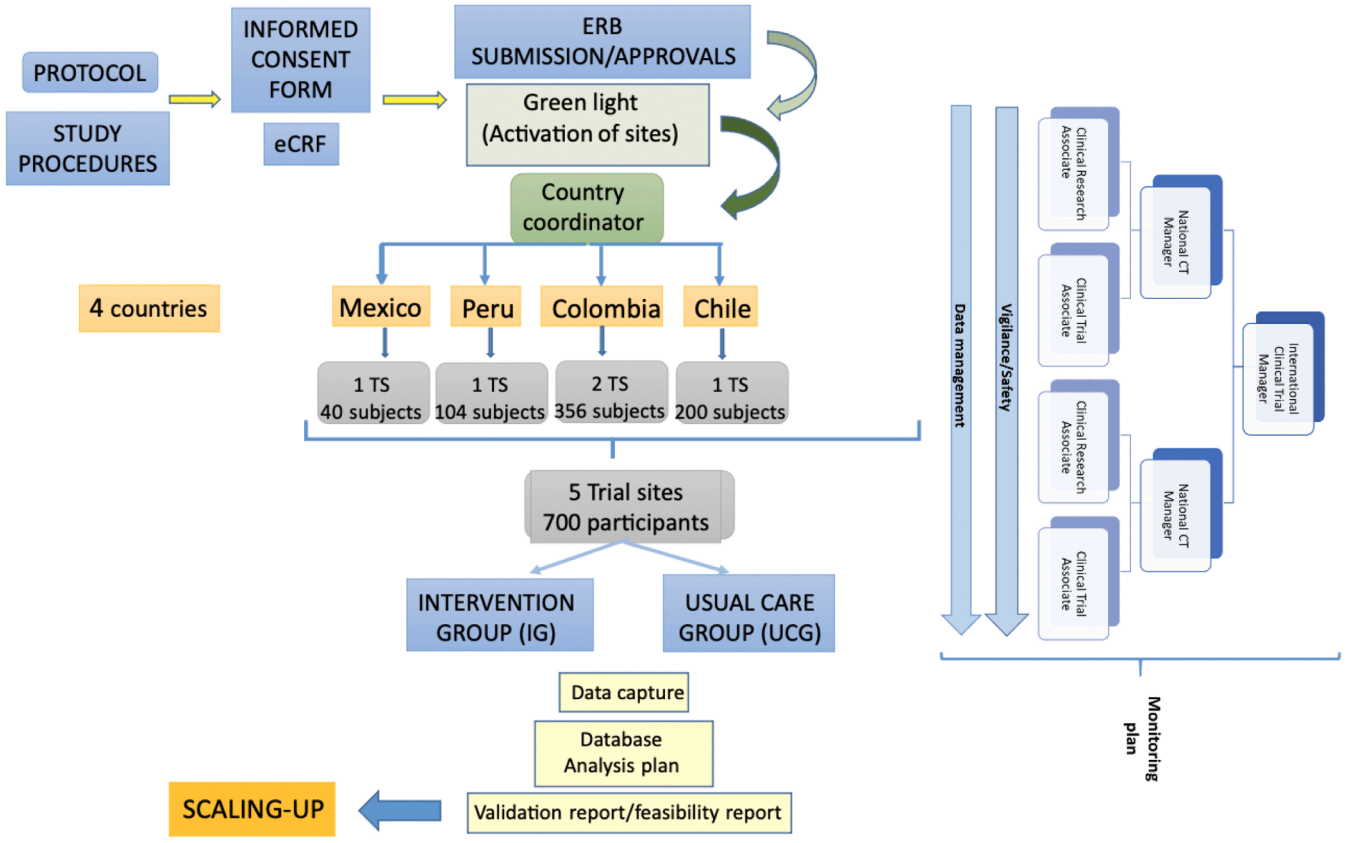


Fig. 1. Overall study design.

- Other conditions that, in the researcher's opinion, may interfere with participation in the study.
- Life expectancy of less than 12 months.
- Any other condition that is an absolute contraindication for the exercise program in the investigator's opinion.

2.3. Randomization

Randomization was 1:1 and was performed upon confirmation that the subject met all inclusion criteria and none of the exclusion ones. In the electronic data collection notebook (eCRF) designed within the REDCAP platform, a list of numbers with a random distribution to intervention group (IG) or usual clinical practice (UCG) was implemented for each participating country. Once the subject completed the screening visit and the inclusion/exclusion criteria page was filled out, the eCRF assigned the randomization group according to this list.

2.4. Usual clinical practice group (UCG)

Participants assigned to the usual clinical practice group received standard care as defined in each national health system, including regular medical follow-up, pharmacological treatment according to national guidelines, and general lifestyle counseling.

2.5. Intervention group (IG)

The multimodal intervention program consisted of 3 fundamental parts:

1. Optimization of glycemic and blood pressure control:

Given the increased vulnerability of frail older adults to treatment-related adverse events, glycemic and blood pressure targets were individualized according to recommendations for older people with diabetes. An HbA1c target of 7.6–8.5% and a blood pressure target of <150/90 mmHg were selected based on EDWPOP and EuGMS–EDWPOP recommendations for older adults with frailty and functional impairment [25,26]. This approach is consistent with the ADA recommendation to use less strict and individualized treatment targets in older adults with frailty, functional limitations, and increased risk of treatment-related adverse events [2].

How to achieve these targets was not predefined. Existing treatment protocols at each center were used to ensure that the target values were accomplished within the first six months from the baseline visit.

2. Exercise program:

The exercise program used was the VIVIFRAIL program, developed in Europe (EU Erasmus + program). The VIVIFRAIL multicomponent exercise intervention program consists of resistance, gait, balance and flexibility training.

The training program lasted 16 weeks. The researchers explained the program at the study center during the first three weeks, to match the educational program sessions. Afterwards, the program was carried out at home. Once the 16 weeks of training were over, the subjects continued with follow-up visits for the study until completing 52 weeks (1 year).

3. Nutritional and educational programs:

The design of the intervention focuses on increasing knowledge about diabetes, developing practical self-management skills for this condition, and increasing the likelihood of safely improving glycemic control. Minimizing the risk of hypoglycemia, ensuring optimal nutritional condition, and helping to maintain functional status are among the main objectives of the intervention.

The nutritional and educational program consisted of seven 45-min sessions twice a week over a period of 3–4 weeks. It had to be scheduled on the same day as the physical activity program. The pandemic forced us to choose an educational program designed to be carried out virtually.

2.6. Evaluation variables

Different variables were grouped into primary and secondary, measured and analyzed according to their relevance. The primary variable was the difference in function after 12 months of follow-up between the intervention and usual clinical practice groups according to changes in the SPPB scale. Table 3 describes the endpoints of the Diabfrail-Latam study.

Questionnaires were completed by participants, caregivers, and treating physicians during follow-up visits. The purpose was to evaluate the feasibility of the intervention program, define the pros and cons of its implementation, and assess its economic viability and adherence. The economic analysis was carried out using information collected in questionnaires designed for the study. Adherence was assessed in two ways: by means of self-reported diaries, and by means of watch-type devices worn for one week at different times during the follow-up by all participants randomized to the intervention group and a randomly selected cohort of participants in the UCG group.

2.7. Safety

At the baseline visit, all concomitant diseases were recorded in the

Table 3
Diabfrail-Latam clinical trial evaluation variables.

Evaluation variables	Definition
Primary	Difference in function after 12 months of follow-up between the intervention and usual clinical practice groups according to changes in the SPPB scale.
Secondaries	Quality of life measured by the Euro-QoL EQ 5D-3 L index [27] and the ADDQoL and ADDQoL Senior [28]. Trajectories in frailty status measured by changes in Frailty phenotype, Frail Trait Scale (FTS) [29] and FRAIL [30]. Worsening in Basic Activities of Daily Living according to changes of at least 10 points in the Barthel ADL index [23]. Impairment in instrumental activities of daily living according to worsening by at least 1 point on the Lawton IADL scale [31]. Episodes of symptomatic hypoglycemia (i.e., a recorded blood sugar level of less than 4 mmol/l (70 mg/dl), or clinical symptoms or signs attributed to low blood sugar and responsive to appropriate treatment). Episodes of hospital admission (i.e., any admission involving an overnight stay) assessed at each visit. Episodes of permanent institutionalization (i.e., a permanent transfer to any care setting other than the patient's own home, where contracted staff are available to provide care if needed at any time during the day or night) are assessed at each visit. Caregiver burden, as assessed by the Zarit scale [32]. Laboratory biomarkers with prognostic value. We will determine a set of classical biomarkers (blood count, glucose, glycosylated hemoglobin, HbA1c, creatinine and cholesterol) plus additional innovative biomarkers of lipid and metabolomics peroxidation. Feasibility of the intervention: it was analyzed by means of questionnaires to participants, caregivers/family members and treating physicians. Adherence to the intervention program using a questionnaire and the watch-like device “Kronowise 3.0″ for ambulatory monitoring (Kronohealth SL, Spain). Evaluation of economic and health care costs due to diabetes and its impact on disability and quality of life, using an economic model that encompasses direct health-related costs (internal, external, pharmaceutical), formal care costs (home care, day care centers) and informal care costs (caregiver).

eCRF, as well as the prescribed treatment. This treatment was maintained according to standard clinical practice. During follow-up, at each visit we asked about the appearance of new pathologies, changes in treatment or new medication. Any new disease or any complication of previous pathologies was recorded as an adverse event. If the adverse event was considered serious, it was recorded on a specific eCRF form and the medical monitor, the promoter and the center's reference committee were notified. An annual safety report was submitted to all RECs of the centers involved.

2.8. Follow-up visits

After the baseline visit, a total of 9 face-to-face visits will be performed during the 52 weeks of follow-up (1 year). The scheme of the follow-up visits for the validation study is shown in Fig. 2.

The outline of the different procedures to be performed during the visits is shown in Table 4.

2.9. Sample size calculation

The results obtained in the MIDFRAIL study were considered to calculate the sample size. 35% of the participants in the UCG group and 53% of those assigned to IG had an improvement of at least one point in the SPPB. This represents an absolute difference of 18%, in addition to a dropout rate of 21%. A sample size calculation was performed, assuming a conservative position: effect size of 14% and losses of 25%, with a result of 950 subjects. Several centers declined to participate due to the COVID 19 pandemic which led to a delay of approximately 2 years for the start of the clinical trial. The sample size was recalculated with the first 100 subjects recruited who completed the study. It was observed that the effect size was equal to that obtained in MIDFRAIL (18%), while the dropout rate was lower (12%). Taking this data into account, 695 subjects would provide sufficient statistical power to account for the main variable.

2.10. Statistical analysis

The main analysis will consist of comparing the change in function and quality of life of the intervention group versus the control group after one year of follow-up. Adjustments will be made for baseline functional status, using a hierarchical linear regression model (patients grouped by center or country) under an analysis of covariance (ANCOVA) approach. An intention-to-treat analysis will be performed adjusting for age and sex. In addition, a secondary analysis will be adjusted for number of comorbidities, frailty status (pre-frail/frail) and baseline PBPS. Differences between groups will be presented by regression coefficients, effect sizes, 95% confidence intervals and p values.

In addition, the variables improvement in function and improvement in quality of life will be created if sufficient statistical power is available. These two variables will be analyzed using hierarchical logistic regression models, and the results will be presented using odds ratios and relative risks.

After assessing adherence (defined as attending 5 of the 7 nutritional and educational sessions and performing more than 70% of the physical exercise program according to the questionnaires and the data obtained from Kronowise 3.0), an analysis of the previously described variables will also be performed, by means of a per-protocol analysis.

The analyses will be carried out using the R statistical package for Windows, version 3.6.1. In all cases, a p value < 0.05 will be considered statistically significant.

3. Expected results

The multimodal intervention is expected to improve functionality (SPPB), outperform usual care in frailty trajectories, reduce hospitalization and institutionalization, and generate economic benefits derived from lower utilization of health services. Likewise, it is expected to document a high feasibility of implementation and an adherence $\geq 80\%$, supporting the possibility of scaling the intervention to different contexts in Latin America.

4. Discussion

Low- and middle-income countries (LMICs) are in a rapid process of population aging, and face an epidemic of noncommunicable diseases that mostly affect the elderly, especially those in vulnerable conditions, such as frail older persons [33]. This reality has been highlighted on several occasions by institutions that are part of the Global Alliance for Chronic Diseases (GACD). Diabetes mellitus stands out among chronic diseases, not only accelerating the aging process, but also increasing the risk of frailty, complications and functional deterioration. These conditions highlight the need for comprehensive and personalized management for this vulnerable population.

Along with the increase in the prevalence of chronic noncommunicable diseases, the lack of physical activity has experienced an alarming upsurge globally, with all the negative implications associated with this condition [34]. In this context, the development and implementation of multicomponent programs that encourage regular practice of physical exercise, promote an increment of daily physical

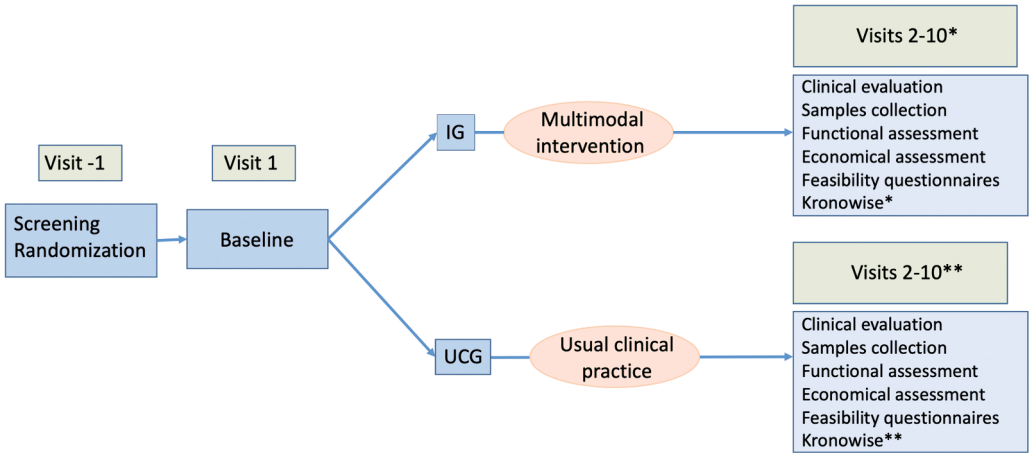


Fig. 2. Outline of follow-up visits. * IG: At visits V3 (week 9), V6 (week 26), and V9 (week 51), the Kronowise device is delivered to the participant. **UCG: At visits V3 (week 9) and V6 (week 26), the Kronowise device is delivered to participants randomized to the control group with Kronowise.

Table 4
Procedures to be accomplished at each visit.

Visit	Selection W1	Basa line (V1) W1	V2 W5 (± 3 days)	V3 W9 (±1W)	V4 W10 (± 1W)	V5 W17 (± 2W)	V6 W26 (± 2W)	V7 W 27 (± 2W)	V8 W 40 (± 2W)	V9 W51 (± 4W)	V10 W52 (± 4W)
Informed consent (patient)	X										
Informed consent (caregiver)	X										
Eligibility criteria	X										
Medical records	X	X	X		X	X		X	X		X
Concomitant medication	X	X	X		X	X		X	X		X
Demographic data	X										
Physical examination/MNA-SF		X	X		X	X		X	X		X
HR and BP		X	X		X	X		X	X		X
Complete BC, biochemistry, biomarkers		X**				X**		X	X		X**
Adverse events	X	X	X		X	X		X	X		X
Deliver Kronowise 3.0	X			X			X			X	
Capture Kronowise 3.0 data		X			X			X			X
Assessments											
SPPB	X	X	X		X	X		X	X		X
MoCA	X										
IADL (Lawton)	X		X		X	X		X	X		X
(BADL) Barthel Index	X		X		X	X		X	X		X
L. Fried Criteria	X	X	X		X	X		X	X		X
Frail		X	X		X	X		X	X		X
FTS 5		X	X		X	X		X	X		X
Economic questionnaire for subjects		X						X			X
Episodes of hypoglycemia		X	X		X	X		X	X		X
Permanent institutionalization		X	X		X	X		X	X		X
Hospitalization episodes		X	X		X	X		X	X		X
EQ 5D-3L		X				X		X	X		X
ADDQoL and ADDQoL Senior		X				X		X	X		X
Feasibility questionnaire		X	X		X	X		X	X		X
Adherence questionnaire		X	X		X	X		X	X		X
Reassess exercise passport			X		X						
Randomization	X										
Zarit Scale		X						X			X
Economic questionnaire for caregivers		X						X			X

** Blood test INCLIVA-UV (Spain).

activity and the adoption of healthy lifestyles are considered fundamental. These strategies are not only effective in preventing and treating metabolic diseases such as type 2 diabetes, but also in mitigating their consequences, including frailty [35]

The Diabfrail-Latam project aims to validate and scale a multimodal intervention to improve functionality and prevent frailty in older people with type 2 diabetes in Latin America. This protocol is based on the results of previously conducted European projects, mainly MIDFRAIL [12] and VIVIFRAIL [17–19], and represents an innovative adaptation in Latin American vulnerable populations. The MIDFRAIL study demonstrated that frail and pre-frail European individuals over 70 years of age with type 2 diabetes improved their physical performance as measured *By sppb* [12], and their frailty status [16]. These gains were achieved through a multicomponent program consisting of 16-week endurance physical exercise sessions, an educational and nutritional program, and adjustments of therapeutic targets (mainly HbA1c and BP). On the other hand, it saved costs mainly derived from hospitalization [10]. This improvement was maintained in the long term up to 18–24 months of follow-up [14,16].

Diabfrail-Latam, based on these findings, intends to validate and adapt these interventions to the specific realities of Latin America, not only in the four countries participating in the study (3 LMIC and 1 HIC), but throughout the region. This includes cultural, economic and social adjustments to ensure that the strategies are feasible and effective for this population. The methodology used shows the importance of sharing good practices to favor replication and adaptation, which can lead to better results and the optimization of time and resources.

Considering adherence to the program as well as its feasibility, the results should reach 35–49% in the improvement in patient control in the general population.

Collaboration with local institutions and the active participation of organizations such as the Pan American Health Organization (PAHO) make it possible for the program to be replicated and scaled up in other countries in the region.

5. Conclusion

The Diabfrail-Latam Project represents a strategic step towards the validation and scale-up of cost-effective multimodal interventions targeting older people with T2DM and frailty in Latin America. The previous evidence from MIDFRAIL and VIVIFRAIL, on which this protocol is based, describes a culturally adapted, feasible and potentially sustainable intervention in health systems in the region. Its results will provide robust evidence to guide the design of public policies and comprehensive care programs for the elderly, thereby favoring healthier and more functional aging.

Declaration of the use of generative AI and AI-assisted technologies in scientific writing and in figures, images and artwork

During the preparation of this work the author(s) did not use generative AI or AI-assisted technologies.

Data statement

No datasets were generated or analyzed for this manuscript, which reports the study protocol. Data generated during the study will be securely stored by the study sponsor and will be made available, where appropriate, in accordance with the sponsor's data-sharing policy and applicable regulations.

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CRediT authorship contribution statement

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.tjfa.2026.100211.

References

[1] GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the global burden of disease study 2019. Lancet L Engl 2020;396(10258):1204–22.
[2] American Diabetes Association Professional Practice Committee for Diabetes. 13. Older adults: standards of care in diabetes—2026. Diabetes Care 1 January 2026; 49(Supplement_1):S277–96.
[3] Genitsaridi I, Salpea P, Salim A, et al. 11th edition of the IDF diabetes atlas: global, regional, and national diabetes prevalence estimates for 2024 and projections for 2050. Lancet Diabetes Endocrinol 2026;14:149–56.
[4] Rodríguez-Mañas L, Bayer AJ, Kelly M, Zeyfang A, Izquierdo M, Laosa O, et al. An evaluation of the effectiveness of a multi-modal intervention in frail and pre-frail older people with type 2 diabetes–the MID-Frail study: study protocol for a randomised controlled trial. Trials 2014;15:34.
[5] Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol Biol Sci Med Sci 2001;56(3): M146–57.
[6] Volpato S, Maraldi C, Fellin R. Type 2 diabetes and risk for functional decline and disability in older persons. Curr Diabetes Rev 2010;6(3):134–43.
[7] Martinez R, Morsch P, Soliz P, Hommes C, Ordunez P, Vega E. Life expectancy, healthy life expectancy, and burden of disease in older people in the Americas, 1990-2019: a population-based study. Rev Panam Salud Publica Pan Am J Public Health 2021;45:e114.
[8] Informe Mundial sobre el envejecimiento y la salud 2015 [Internet]. [cited 2025 Apr 16]. Available from: https://www.who.int/es/publications/i/item/9789241565042.
[9] Oliva J, Lobo F, Molina B, Monereo S. Direct health care costs of diabetic patients in Spain. Diabetes Care 2004;27(11):2616–21.
[10] Peña-Longobardo LM, Oliva-Moreno J, Zozaya N, Aranda-Reneo I, Trapero-Bertran M, Laosa O, et al. Economic evaluation of a multimodal intervention in pre-frail and frail older people with diabetes mellitus: the MID-FRAIL project. Expert Rev Pharmacoecon Outcomes Res 2021;21(1):111–8.
[11] Castro-Rodríguez M, Carnicero JA, Garcia-Garcia FJ, Walter S, Morley JE, Rodríguez-Artalejo F, et al. Frailty as a major factor in the increased risk of death and disability in older people with diabetes. J Am Med Dir Assoc 2016;17(10): 949–55.
[12] Rodriguez-Mañas L, Laosa O, Vellas B, Paolisso G, Topinkova E, Oliva-Moreno J, et al. Effectiveness of a multimodal intervention in functionally impaired older people with type 2 diabetes mellitus. J Cachexia Sarcopenia Muscle 2019;10(4): 721–33.
[13] Izquierdo M, Laosa O, Cadore EL, Abizanda P, Garcia-Garcia FJ, Hornillos M, et al. Two-year follow-up of a multimodal intervention on functional capacity and muscle power in frail patients with type 2 diabetes. J Am Med Dir Assoc 2021;22 (9):1906–11.
[14] Álvarez-Bustos A, Laosa O, Marzetti E, Carnicero JA, Castro-Rodriguez M, Landi F, et al. Response rates and associated factors after a multicomponent intervention in frail older adults with diabetes. Age Ageing 2024;53(1):afad253.
[15] Sinclair AJ, Laosa O, Antonio Carnicero J, Rodriguez-Mañas L, Álvarez-Bustos A. Disability and quality of life measures in older frail and prefrail people with type 2 diabetes. The MIDFRAIL-study. Diabetes Res Clin Pr 2024;214:111797. https://doi.org/10.1016/j.diabres.2024.111797 [cited 2024 Oct 8];214. Available from:.
[16] Laosa O, Topinkova E, Bourdel-Marchasson I, Vellas B, Izquierdo M, Paolisso G, et al. Long-term frailty and physical performance transitions in older people with type-2 diabetes. The MIDFRAIL randomized clinical study. J Nutr Health Aging 2025;29(4):100512.
[17] Izquierdo M. [Multicomponent physical exercise program: vivifrail]. Nutr Hosp 2019;36(Spec No2):50–6.
[18] Izquierdo M, Casas-Herrero A, Martínez-Velilla N, Alonso-Bouzón C, Rodríguez-Mañas L. [An example of cooperation for implementing programs associated with the promotion of exercise in the frail elderly. European Erasmus + «Vivifrail» program]. Rev Esp Geriatr Gerontol 2017;52(2):110–1.
[19] Casas-Herrero A, Anton-Rodrigo I, Zambom-Ferraresi F, Sáez de Asteasu ML, Martinez-Velilla N, Elexpuru-Estomba J, et al. Effect of a multicomponent exercise programme (VIVIFRAIL) on functional capacity in frail community elders with cognitive decline: study protocol for a randomized multicentre control trial. Trials 2019;20(1):362.
[20] Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med 2013;158(3):200–7.
[21] World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310 (20):2191.
[22] Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005;53(4):695–9.
[23] Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. Md State Med J 1965;14:61–5.

[24] Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49(2):M85–94.
[25] Sinclair AJ, Paolisso G, Castro M, Bourdel-Marchasson I, Gadsby R, Rodriguez Mañas L. European diabetes working party for older people 2011 clinical guidelines for type 2 diabetes mellitus. executive summary. Diabetes Metab 2011; 37(Supplement 3):S27–38.
[26] Bourdel-Marchasson I, Maggi S, Abdelhafiz A, Bellary S, Demurtas J, Forbes A, et al. Essential steps in primary care management of older people with type 2 diabetes: an executive summary on behalf of the European geriatric medicine society (EuGMS) and the European diabetes working party for older people (EDWPOP) collaboration. Aging Clin Exp Res 2023;35(11):2279–91.
[27] EuroQol Group. EuroQol–a new facility for the measurement of health-related quality of life. Health Policy 1990;16(3):199–208.
[28] Speight J, Sinclair AJ, Browne JL, Woodcock A, Bradley C. Assessing the impact of diabetes on the quality of life of older adults living in a care home: validation of the ADDQoL Senior. Diabet Med 2013;30(1):74–80.
[29] García-García FJ, Carcaillon L, Fernandez-Tresguerres J, Alfaro A, Larrion JL, Castillo C, Rodriguez-Mañas L. A new operational definition of frailty: the frailty trait scale. J Am Med Dir Assoc 2014;15(5):371.e7–371.e13.
[30] Valdatta L, Perletti G, Maggiulli F, Tamborini F, Pellegatta I, Cherubino M. FRAIL scale as a predictor of complications and mortality in older patients undergoing reconstructive surgery for non-melanoma skin cancer. Oncol Lett 2019;17(1): 263–9.
[31] Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9(3):179–86. Autumn.
[32] Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. Gerontologist 1980;20(6):649–55.
[33] Davidson SL, Lee J, Emmence L, Bickerstaff E, Rayers G, Davidson E, et al. Systematic review and meta-analysis of the prevalence of frailty and pre-frailty amongst older hospital inpatients in low- and middle-income countries. Age Ageing 2025;54(1):afae279.
[34] Strain T, Flaxman S, Guthold R, Semenova E, Cowan M, Riley LM, et al. National, regional, and global trends in insufficient physical activity among adults from 2000 to 2022: a pooled analysis of 507 population-based surveys with 5.7 million participants. Lancet Glob Health 2024;12(8):e1232–43.
[35] Izquierdo M, Merchant RA, Morley JE, Anker SD, Aprahamian I, Arai H, et al. International exercise recommendations in older adults (ICFSR): expert consensus guidelines. J Nutr Health Aging 2021;25(7):824–53.