Supplementary material

Table A1

Supplementary table A1. SPIRIT Cheklist of the flADex Trial.

SPIRIT-Outcomes (combination of the SPIRIT 2013 checklist and the 2022 extension) *

Section/item	Item_No	Description	Addressed headings; pags.
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Title page; 0
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Trial design and ethics; 7
	2b	All items from the World Health Organization Trial Registration Data Set	N/A
Protocol version	3	Date and version identifier	Trial design and ethics; 7
Funding	4	Sources and types of financial, material, and other support	Funding; 20, 21
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	0
	5b	Name and contact information for the trial sponsor	N/A
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Front pag;1

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Background; 4, 5
	6b	Explanation for choice of comparators	Overview of experimental condition; 9-11
Objectives	7	Specific objectives or hypotheses	Trial objectives; 5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Trial design and ethics; 6. Figure 1
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Trial design and ethics; 6, 7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Eligibility criteria, screening of participants and recruitment; 7, 8. Table 1
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Overview of experimental conditions; 9-11
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	Safety and adverse events; 15, 16
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	Resistance exercise condition; 10

	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Outcomes; 11-15. Tables 2, 3
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Eligibility criteria, screening of participants and recruitment; 7, 8 / Overview of experimental conditions; 9. Figures 2; 3
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Sample size; 16
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Eligibility criteria, screening of participants and recruitment; 7. Figure 2
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Randomization; 8, 9
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Randomization; 8, 9

Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Randomization; 8, 9
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Blinding; 9
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	Blinding; 9
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Outcomes; 11-15. Tables 2, 3
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Data management and sharing; 17, 18
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Data analysis plan; 16, 17
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Data analysis plan; 16, 17
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Data analysis plan; 16, 17
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Safety and adverse events; 15, 16
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Trial design and ethics; 6, 7
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Trial design and ethics; 6, 7
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Trial design and ethics; 6, 7
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	Trial design and ethics; 6, 7
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Data management and sharing; 17, 18
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Declarations of interest; 2
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Data management and sharing; 17, 18
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	Safety and adverse events; 15, 16
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	Data management and sharing; 17, 18

	31b	Authorship eligibility guidelines and any intended use of professional writers	Data management and sharing; 17, 18
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Data management and sharing; 17, 18
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	-
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	Secondary outcomes; 13

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.

Supplementary material A2. Exercise conditions

Below are descriptions of the exercises to be implemented in the flADex trial. All training conditions will be administered to participants in a randomized order.

A2.1. Resistance exercise condition

The resistance exercise condition will last 30 minutes and contains a combination of upper and lower body exercises using elastic bands and body weight exercise of the major muscle groups. The RPE target will be of 4-6 for a moderate intensity. The exercises will be divided into two levels and the level chosen will depend on the physical condition of the participants.

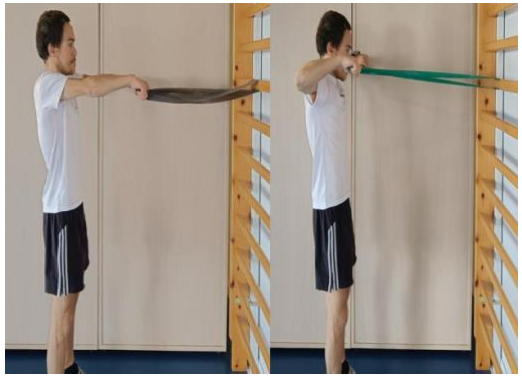
Warm up (4 minutes)			
Exercise	**Target muscle**	**Graphical presentation**	**Instruction**
Cat-camel	Lumbar, thoracic, and cervical muscles		**Starting position:** Begin standing with hands on the wall, forming a 90º angle, and make sure to stand straight. **Execution:** Move from a position of lumbar, thoracic, and cervical neutrality to maximum positions of flexion (kyphosis and retroversion), raising the spine. Continue with the extension (lordosis and anteversion), moving the spine downward.

Thoracic mobility	Extensor of the vertebral column	 	**Starting position:** Begin standing with one leg forward. Keep the arms extended, facing forward. One hand remains fixed (the same as the forward leg), while the other moves to the opposite side, opening the chest. **Execution:** Rotate the thorax as much as possible, keeping the body straight.
Hip and knee mobility	Hip flexors and extensors, dorsiflexors and plantarflexors		**Starting position:** Stand up. Hands are placed on the hips, and the foot you want to mobilize is positioned forward over the other, pointing towards the wall. **Execution:** Flex the knee and ankle as much as possible, trying to touch the wall with the knee. Move the forward foot backward to increase the difficulty.

Shouder and hip mobility	Shoulder, spinal and hip flexors and extensors	 	**Starting position:** Standing position. **Elastic band position:** The elastic band is stretched to the maximum without exerting tension with straight arms. **Execution:** Move the straight arms from the hips to above the head. Abducting the arms to generate tension in the elastic band. When the arms are above the head, perform a squat.

Exercise session (26 minutes)

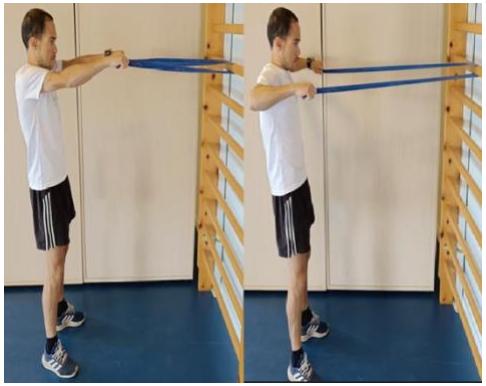
Training session			
Exercise	**Target muscle**	**Graphical presentation**	**Instruction**
Glute bridge for hamstring	Hamstring and gluteus		**Starting position**: Supine position with bent knees and feet at hip-width, heels on the mat and toes pointing at the ceiling. **Execution:** Move the hip towards the ceiling, keep the spine neutral and the scapulas flat against the floor. Lift the hips as high as possible. Then, lower the hip in a controlled manner to the starting position. **Key points:** Perform pelvic retroversion and squeeze the gluteus muscles when hip is high. Push the feet and hands against the floor.
Front plank	Lumbopelvic musculature		**Starting position:** Prone position with the forearms on the mat supporting the body and elbows at 90º. The knees and feet are at hip-width. **Execution:** Raise the hip and knees until the trunk is parallel to the mat. Hold the position for 10 seconds and return to the starting position. **Key points:** Contract the gluteus muscles and abdomen, keep the lumbopelvic neutrality and exhale during the concentric phase.

Standing face pull *	Trapezius		**Starting position:** Standing position with the feet at hip-width and grab the elastic band with straight arms in pronation with maximum elongation but without tension. **Elastic band position:** Nose height. **Execution:** Pull the elbows towards the face and bend the elbows to 90º. Keep the elbows on shoulder-height. **Key points:** Keep the elbows at shoulder-height, and the shoulders down.
Incline push up	Pectoral		**Starting position:** Standing position one meter in front of the object (e.g., a table). Place the hands on the edge of the table slightly wider than shoulder-width. Arms are straight. **Execution:** Bend the arms, so that the chest approaches the object as much as possible. Hold for a second, extend the arms and return to starting position. **Key points:** Maintain a plank position, push with the hands, and align the gluteus muscles and the trunk.

Squat	Quadriceps and gluteus		**Starting position:** Standing position with the legs hip-width. **Execution:** Lower into a squatting position and keep the lumbar in a neutral position. During this movement, the hip, knee and ankle are bent. After this, extend the legs and return to starting position. **Key points:** Push with the legs to get up and keep the knees aligned with the legs during the whole exercise.
Press pallof *	Lumbopelvic musculature		**Starting position:** Standing position with the elbows bent at 90º and the feet at hip-width. Grab the elastic band on the side at the maximum elongation without tension. **Elastic band position:** Chest level. **Execution:** Exhale, stretch the arms and hold for 3 seconds. Return to the starting position while inhaling. Focus on breathing when stretching the arms. Perform 20” continuously to each side. **Key points:** Control the breathing, move slowly, and controlled during the eccentric phase**.**

Lunge	Quadriceps and gluteus		**Starting position:** Standing position, with one leg in front of the other and with approximately 0.6m. Back leg stands on the toes and the hands are placed on the hips. **Execution:** Bend both knees to 90º. Stand back up and lift the back foot from the ground. Swing the back foot forward and step forward. **Key points:** Align the front knee and leg, push the foot against the floor, and push with the front leg.
Seated shoulder press *	Deltoid		**Starting position:** Sitting position and pass the elastic band under the seat of the chair. Grab the elastic band neutrally. **Elastic band position:** Underneath the seat of the chair. **Execution:** Push the arms above the head until the arms are straight. Align the wrists with the arm during the movement. **Key points:** Push from the feet to the shoulder.

Training session 2			
Exercise	**Target muscle**	**Graphical presentation**	**Instructions**
Glute bridge for hamstring	Hamstring and gluteus		**Starting position**: Supine position with bent knees and feet at hip-width, heels on the mat and toes pointing at the ceiling. **Execution:** Move the hip towards the ceiling, keep the spine neutral and the scapulas flat against the floor. Lift the hips as high as possible. Then, lower the hip in a controlled manner to the starting position. **Key points:** Perform pelvic retroversion and squeeze the gluteus muscles when hip is high. Push the feet and hands against the floor.
Kneeling plank	Lumbopelvic musculature		**Starting position:** Prone position with the forearms supported on the mat. The knees and feet are at hip-width on the mat. **Execution:** Raise the hip and keep the knees and feet on the mat. The trunk is parallel position with the mat and the elbows are bent at 90º. Hold the position for 10 seconds and return to the starting position. **Key points:** Strengthen the gluteus muscles and core and maintain the lumbopelvic in a neutral position. Exhale during the concentric phase.

Standing face pull *	Trapezious		**Starting position:** Standing position with the feet at hip-width and arms straight. Grab the elastic band in pronation with maximum elongation but without tension. **Elastic band position:** Nose height. **Execution:** Pull the elbows towards the face and bend the elbows at 90º. Keep the elbows on shoulder-height. **Key points:** Keep the elbows at shoulder-height and the shoulders down.
Wall push up	Pectoral		**Starting position:** Standing position one meter in front of the wall. The hands are placed at the wall on shoulder height and width. **Execution:** Bend the arms, so that the face approaches the wall as much as possible. **Key points:** Maintain the plank position, push with the hands, and align the gluteus muscles with the trunk.

Squat with crossed arms	Quadriceps and gluteus		**Starting position:** Standing position in front of the chair with the legs at hip-width and the hands crossed on the chest. **Execution:** Lower into a squatting position and lightly touch the chair, then get up from the chair. **Key points:** Push with the legs to get up from the chair, keep the knees aligned with the legs during the whole exercise.
Press pallof *	Lumbopelvic musculature		**Starting position:** Standing position with the elbows bent at 90º and the feet at hip-width. Grab the elastic band on the side at the maximum elongation without tension. **Elastic band position:** Chest level. **Execution:** Exhale, stretch the arms and hold for 3 seconds. Return to the starting position while inhaling. Focus on breathing when stretching the arms. Perform 20” continuously to each side. **Key points:** Control the breathing, move slowly, and controlled during the eccentric phase**.**

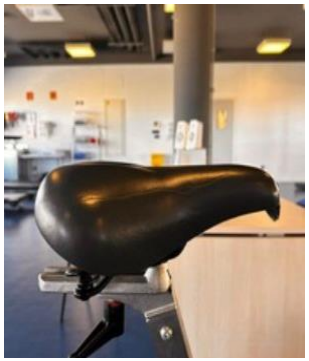
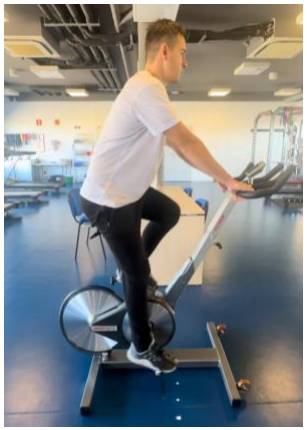
Lunge	Quadriceps and gluteus		**Starting position**: Standing position with one foot in front of the other with the distance of approximately 0.6 m. Place the hands on the hips. **Execution:** Bend both knees to approximately 90°. With this movement, the back knee is hovering just of the floor and the front knee and ankle are aligned. Return to the starting position by extending the knees. Perform 20" continuously with each leg. **Key points:** Align the front knee and the foot and push the feet against the floor.
Seated shoulder press *	Deltoid		**Starting position:** Sitting position with legs fully supported. Pass the elastic band under the seat of the chair and grab it neutrally. **Elastic band position:** Under the chair seat. **Execution:** Push the arms up until elbows are straight. Align the wrists with the arm during the exercise. **Key points:** Push from the feet to the shoulder.

A2.2. Moderate aerobic exercise condition

The aerobic exercise condition will last 30 minutes of continuous moderate intensity aerobic exercise on a bike. The intensity target will be at 60%-70% of their maximal heart rate (HRmax).

Warm-up (4 minutes)

Step	Graphical presentation	Instruction
1		Adjust the saddle height so that your extended leg has a slight bend at the knee while pedaling.

2		Ensure the saddle is horizontal to prevent discomfort; adjust the angle to make it parallel to the ground.
3		Adjust the handlebars to a height that allows you to maintain an upright and comfortable posture.

4		Check the distance between the saddle and the handlebars; it should allow you to reach them without overstretching or being too cramped.
5		Before starting, verify that all adjustments are secure and tight, avoiding any looseness or unexpected movements.

Exercise session (26 minutes)

Exercise	Target muscle	Graphical presentation	Instruction
Bike	Quadriceps, hamstrings, glutes, calf, hip muscles, abdominal muscles, and lower back muscles		A continuous aerobic exercise is performed on a stationary bike, which will be within the at 60%-70% of their maximal heart rate (HRmax)..