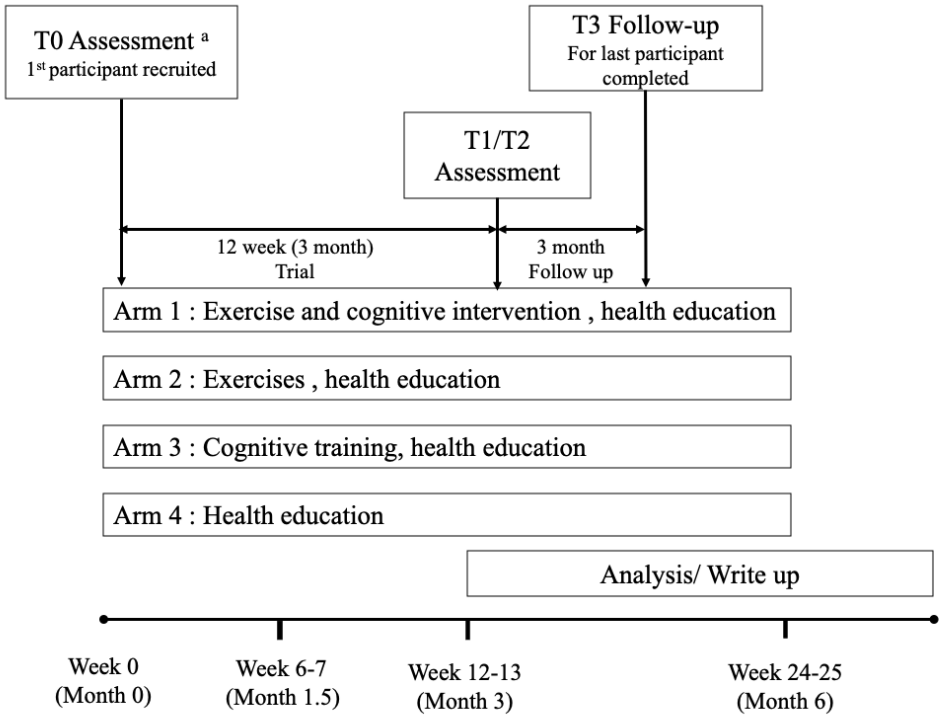
Supplemental Material

Hong C, *et al*. *BMJ Open* 2024; 14:e081122. doi: 10.1136/bmjopen-2023-081122

Appendix A: Timeline of the trial



(a) Baseline assessment (T0) will be completed within one-week of participants starting the specific intervention.

Appendix B: Informed Consent Form

知情同意书

我们将要开展一项《中国轻度认知障碍老年人远程监督居家运动-认知综合干预研究》，您符合该项研究的入组条件，因此，我们想邀请您参加该项研究。本知情同意书将向您介绍该研究的目的、步骤、获益、风险、不便或不适等，请仔细阅读后慎重做出是否参加研究的决定。当研究者向您说明和讨论知情同意书时，您可以随时提问并让他/她向您解释您不明白的地方。您可以与家人、朋友讨论之后再做决定。若您目前正参加其他临床研究，请务必告知您的研究人员。

项目负责人：罗雅楠，北京大学公共卫生学院

研究资助方：美国中华医学基金会

联系人：洪晨璐（13141224025）

1. 研究背景及研究目的

轻度认知障碍（Mild cognitive impairment，MCI）是介于认知功能正常衰老与痴呆症之间的过渡阶段，严重威胁了全球公众健康。每年有5%-20%的轻度认知障碍患者发展成为痴呆症，近三分之二的痴呆患者表现为MCI。2018年，全球约5000万老年人遭受不同程度的认知障碍，据预测，2030年规模将增加到8200万。在中国，有超过20%的老年人患有MCI，每年约有6%的MCI老年患者发展为痴呆。非药物干预是MCI的主要治疗方法，研究表明运动干预可降低MCI或痴呆患者负面健康结局风险并对其功能产生积极影响。认知训练对认知障碍患者的整体认知、记忆力、执行功能或注意力等方面有显著作用。运动-认知综合干预比单一干预益处更大。此外，研究显示，以家庭为基础的运动-认知综合干预是一种有前景的轻度认知障碍非药物治疗方法，其风险成本低、干预时间灵活且空间需求较小，“双管齐下”的治疗效果优于单一运动或认知干预，可以帮助医疗资源匮乏地区人群获得治疗机会。

目前，尚缺乏适用于我国MCI老年患者关于远程监督下以家庭为基础的运动-认知综合干预方案及高等级效果评价证据。关于远程监督居家运动-认知综合干预在老年MCI患者中的效果的研究较少、样本量小以及前期研究难以控制所有混杂因素、非随

机化，疗效不一。因此，本研究旨在设计一项满足中国MCI老年患者需求的远程监督居家运动-认知综合干预项目，通过开展随机对照试验以评价干预方案效果。

2. 哪些人将被邀请参加这项研究？

纳入标准（1）年龄在60-75岁之间；（2）轻度认知障碍；（3）无经常性的运动习惯；（4）独立行走5分钟以上的运动能力；（5）可完成简单智能手机操作；（6）受试者或授权委托人签订知情同意书，研究期间有时间参与并完成计划；（7）有家人或其他照护者支持；（8）家中有智能手机或平板电脑并有网络连接。

排除标准：（1）有其他精神障碍、其他神经功能障碍、有骨科合并症导致严重的关节疼痛、合并心血管疾病合并未有效控制的高血压、糖尿病、肾脏疾病；存在无法配合完成调查随访的其他疾病；（2）有劳力性胸部不适；无原因的呼吸困难；眩晕、晕厥、黑蒙；踝关节水肿；剧烈、快速或不规则的心跳产生的不适感；短距离行走时下肢灼烧感或“抽筋样”感觉等不适宜的运动症状；（3）有β-受体阻滞剂如美托洛尔、比索洛尔、普奈洛尔、卡维地洛等药物；抗精神病药物等用药史;（4）当前正参与另一项干预治疗。

3. 多少人将参与这项研究？

本研究计划招募总计 160 名轻度认知障碍老年患者。

4. 该研究是怎样进行的？

在本研究中，杭州市第七人民医院、大连市第七人民医院、宁夏回族自治区宁安医院、云南省精神病院负责轻度认知障碍老年人的管理以及远程监督居家运动-认知综合干预的业务管理和技术指导。北京大学负责设计远程监督居家运动-认知综合干预方案、评估和干预培训、数据分析及政策建议；轻度认知障碍老年人的招募、居家干预的实施由杭州市第七人民医院、大连市第七人民医院、宁夏回族自治区宁安医院、云南省精神病院负责。研究将招募 160 例（每个中心招募 40 例）60-75 岁无运动习惯的老年轻度认知障碍患者，进行随机对照试验，开展为期 3 个月的干预训练，从而评价干预方案效果并量化其成本效益。如果您同意参与该项目，您将被随机分配到下述四个组之一。四个组分别是：运动-认知综合干预及健康教育组、单一运动干预及健康教育组、单一认知干预及健康教育组、健康教育组。您将无法预测或者选择您会被随机分到哪一组。

5. 这项研究会持续多久？

本次研究开展为期3个月的干预训练，在第0周、第6-7周、第12-13周进行评估，并在第 6 个月时进行随访。

6. 参加本项研究的风险是什么？

调查过程中的某些问题可能会让您感到不舒服，您可以拒绝回答。干预过程中可能存在运动安全问题，如果您感到不舒服，出现了下列不宜继续进行研究的情况：（1）现患病情加重；（2）严重不良事件的发生，如在完成本研究运动干预方案的过程中发生的不良事件（如跌倒、骨折、肌肉拉伤、心血管疾病诱发等），您可以立即终止研究，并拟采取以下措施控制风险：（1）从安全性角度考虑，提高研究对象的遴选标准，通过运动评定与筛查以排除不能独立行走和存在运动禁忌症者，并在开展大样本试验研究前进行小样本安全性试验，以进一步明确该运动干预的可行性；（2）对参与运动干预的老年人进行相关运动安全教育（包括合适服装和运动鞋的选择等运动前的安全提示、需立即停止运动征兆和安全须知，不适宜进行运动的情况等安全知识）；（3）运动分为准备、运动和整理三个阶段，开始和结束时都要做柔韧性运动可减少心血管意外和意外伤害的风险；（4）尽量选择安静、地面干燥平整、环境温度适宜的场所进行运动；（5）建议在运动干预的现场摆置桌椅，以供自感劳累或者体力不支的老人休息；（6）建议运动干预现场由家庭护理人员或者家人全程陪同，以防发生意外时能够及时处理（尽管推荐的动作安全系数均较高且研究对象是严格筛选的），产生的相关费用由项目组承担，受试者不需要自行承担任何费用。

7. 参加本项研究的获益是什么？

我们不能保证您会从参与研究中获得任何直接利益。本研究旨在研究认知-运动综合干预是否是一种有用的干预措施，可改善认知障碍老年人的健康状况（情绪、睡眠、身体状况）、认知功能及其他内在能力，预防轻度认知障碍向痴呆症的发展。但如果干预研究有效的话，您的健康和生活质量可能有所改善。此外，您能够通过参与该项干预活动研究培养行为习惯。您的参与还有助于该研究科学设计一项满足中国 MCI 老年患者需求的远程监督居家运动-认知综合干预项目，评价远程干预方案效果并量化其成本效益。

8. 是否一定要参加并完成本项研究？

您是否参加这个研究完全是自愿的。如果您不愿意，可以拒绝参加，这对您目前或未来的医疗不会有任何负面影响。即使您同意参加以后，您也可以在任何时间改变主意，告诉研究者退出研究，您的退出不会影响您获得正常的医疗服务。在您退出之后，研究者将主动删除已经收集的个人信息，研究者将严密保存您的相关信息直至最终销毁，期间不会继续使用或透露这些信息。

9. 关于研究费用和补偿

本研究主要涉及的费用主要包括设备费用（臂带、康复手机软件）、材料费（指导手册、记录手册等）、交通费（调查人员等）、通讯费（电话联系受试者），各部分费用均来自项目组经费。您参加本项研究调查不会被收取任何费用。干预结束后，我们会为您准备一些小礼品。

10. 发生研究相关伤害的处理？

若发生为实现研究目的而执行研究方案造成的意外伤害，我们会提供必要的医疗措施，并依法给予赔偿或者补偿。

11. 我的信息会保密吗？

如果您决定参加本项研究，您参加研究及在研究中的个人资料均属保密。您的所有电子材料信息将以研究编码而非您的姓名加以标识。在未获得您的许可之前，任何可识别您身份的信息将不会透露给研究小组以外人员。所有研究成员和研究相关方都会按要求对您的身份保密。您的个人信息将妥善保存，仅供研究人员查阅。为确保研究按照规定进行，必要时，政府管理部门、学校当局或伦理委员会成员按规定可以在研究单位查阅您个人资料。这项研究结果发表时，将不会披露您个人的任何资料。

12. 如果我有问题或困难，该与谁联系？

如果您有与本研究相关的任何问题，请联系：洪晨璐（13141224025）。如果您有与受试者自身权益相关的问题，可与北京大学生物医学伦理委员会联系，联系电话：010-82805751，电子邮件：llwyh@bjmu.edu.cn。

您是否知情同意？ 1.是 2.否

研究者声明

“我已告知受试者《中国轻度认知障碍老年人远程监督居家运动-认知综合干预研究》的研究背景、目的、步骤、风险及获益情况。给予他/她足够的时间阅读知情同意书、与他人讨论，并解答了其有关研究的问题；我已告知该受试者当遇到与研究相关的问题时可随时与我们团队联系人联系，遇到与自身权利/权益相关问题时随时与北京大学生物医学伦理委员会联系，并提供了准确的联系方式；我已告知该受试者可以退出本研究；我已告知该受试者将得到这份知情同意书的副本，上面包含我和他/她的签名。”

研究者签名　　日期　　年　　月　　日

受试者声明

“我已被告知《中国轻度认知障碍老年人远程监督居家运动-认知综合干预研究》的研究背景、目的、步骤、风险及获益情况。我有足够的时间和机会进行提问。我对问题的回答很满意。我也被告知，当我有问题，想反映困难、顾虑，对研究有意见，或想进一步获得信息，或为研究提供帮助时，应当与谁联系。我已经阅读了这份知情同意书，并且同意参加本研究。我知道我可以在研究期间任何时候无需任何理由退出本研究。我被告知我将得到这份知情同意书的副本，上面包含我和研究者的签名。”

受试者签名　　日期　　年　　月　　日

Informed Consent Form

We are going to conduct a "home-based and remotely supervised combined exercise and cognitive intervention on older adults with mild cognitive impairment (COGITO)" in China. You meet the conditions for inclusion in the study, therefore, we would like to invite you to participate in our study. This informed consent form will introduce you to the purpose, procedures, benefits, risks, inconvenience or discomfort of the study. Please read it carefully before making a decision on whether to participate in the study. As the investigator explains and discusses the informed consent form, you are free to ask questions and have him/her explain what you do not understand. You can discuss it with family and friends before you make a decision. Be sure to inform your investigator if you are currently participating in other clinical studies.

Principal Investigator: Luo Yanan, School of Public Health, Peking University

Funding: China Medical Board

Contact person: Hong Chenlu (Phone number 13141224025)

1. Background and purpose

Mild cognitive impairment (MCI) is an intermediate phase between normal aging-associated cognitive deterioration and dementia. 5-20% of people with MCI develop dementia per year, and almost two-thirds of those who developed dementia had MCI before cognitive changes.

In 2018, approximately 50 million older adults worldwide experienced various degrees of cognitive impairment, a number projected to reach 82 million by 2030. In China, over 20% of older adults suffer from Mild Cognitive Impairment (MCI), with approximately 6% of them progressing to dementia each year. Non-pharmacological interventions are the primary approach to treating MCI, with research indicating that exercise interventions can mitigate the risk of adverse health outcomes in MCI or dementia patients and positively impact their functioning. Cognitive training has demonstrated significant effects on overall cognition, memory, executive function, and attention in individuals with cognitive impairment. Comprehensive motor-cognitive interventions yield greater benefits compared to singular interventions. In addition, home-based interventions have gained popularity as a cost-effective alternative due to their flexible scheduling, reduced space requirements, and lower cost, which also can help maintain the delivery of healthcare services to patients. Combined exercise and

cognitive training is superior to isolated exercise or cognitive intervention, and can provide treatment opportunities for individuals residing in regions with limited medical resources.

At present, there remains a lack of well-established intervention strategies in the field. There are few studies on the effect of home-based exercise-cognition comprehensive intervention under remote supervision in elderly patients with MCI, which is characterized by small sample size, difficulty in controlling all confounding factors, non-randomization in previous studies, and various efficacy. Therefore, this study aimed to develop a remote supervision home-based exercise-cognition comprehensive intervention program to meet the needs of elderly patients with MCI in China and validate its effectiveness so as to prevent dementia

2. Who will be invited to participate in this study?

Inclusion criteria: (1) Aged 60-75 years old; (2) Mild cognitive impairment; (3) No regular exercise habit; (4) Able to walk independently for at least 5 minutes; (5) With good visual, hearing, and language abilities to read Chinese; (6) able to provide written informed consent; (7) With family/caregiver support; (8) Has access to smartphone or internet at home

Exclusion criteria: (1) Has a medical history of psychiatric diseases, neurological, cardiovascular, disorders co-morbidities and other conditions interfering with completing cognitive assessments, cognitive intervention, and exercise intervention; (2) Has a medication history such as Beta-blockers and/or anti-psychotic such as metoprolol, bisoprolol, atenolol, propranolol, carvedilol, etc.; (3) Signs and symptoms that fail to meet the exercise preparticipation health screening recommendations; (4) Currently participating in any other intervention programme.

3. How many people will participate in this study?

A total of 160 older adults with MCI were planned to be enrolled in this study.

4. How will the study be conducted?

In this study, Kunming Psychiatric Hospital, Hangzhou Seventh People's Hospital, Dalian's Seventh People's Hospital and Ning An Hospital of Ningxia are responsible for managing older adults with mild cognitive impairment and providing management and technical guidance for home-based and remote monitoring interventions. Peking University is responsible for designing the intervention program, as well as for assessment and intervention training, data analysis, and policy recommendations. Recruitment of older adults with mild

cognitive impairment and implementation of home-based interventions are conducted by Kunming Psychiatric Hospital, Hangzhou Seventh People's Hospital, Dalian's Seventh People's Hospital and Ning An Hospital of Ningxia. The study aims to recruit 160 participants (40 from each centre) aged 60-75 years with no regular exercise habits and mild cognitive impairment, and conduct a randomized controlled trial. A three-month intervention will be carried out, with assessments at week 0, weeks 6-7, and weeks 12-13, followed by a follow-up at the 6th month. If you agree to participate in this project, you will be randomly assigned to one of the following four groups: combined exercise-cognition intervention and health education group, exercise intervention and health education group, cognitive intervention and health education group, or health education group. You will not be able to predict or choose which group you will be assigned to.

5. How long will this research last?

This study will conduct a 3-month intervention training period, with assessments at week 0, weeks 6-7, and weeks 12-13, followed by a follow-up at the 6th month.

6. Risks of participating in this study

During the course of the investigation, certain questions may cause discomfort, and you have the right to decline to answer them. There may be potential safety concerns during the intervention process, particularly related to physical activity. If you experience discomfort or encounter any of the following situations that warrant discontinuation of the study: (1) Exacerbation of existing health conditions; (2) Occurrence of severe adverse events, such as falls, fractures, muscle strains, or cardiovascular incidents during the implementation of the exercise intervention plan, you may choose to terminate your participation in the study. In such cases, the following measures will be implemented to mitigate risks: (1) Enhanced selection criteria for study participants to ensure safety, including pre-screening for independent mobility and exclusion of individuals with contraindications to exercise. Prior to conducting large-scale experimental trials, small-scale safety testing will be conducted to further evaluate the feasibility of the exercise intervention. (2) Provision of relevant safety education to elderly individuals participating in the exercise intervention, including guidance on appropriate attire and footwear selection, pre-exercise safety reminders, signs indicating the need to immediately stop exercising, and other safety considerations. (3) Implementation of a three-stage exercise regimen comprising warm-up, exercise, and cooldown phases to minimize the risk of cardiovascular accidents and accidental injuries. Flexibility exercises should be performed both

at the beginning and end of the session. (4) Selection of quiet, dry, level, and appropriately temperature-controlled environments for exercise sessions. (5) Recommendation to place tables and chairs at the exercise intervention site to allow elderly participants to rest if they feel fatigued or physically strained. (6) Suggestion to have family caregivers or relatives accompany participants throughout the exercise intervention session to promptly address any accidents that may occur, despite the high safety coefficient of recommended exercises and stringent participant selection criteria. Any related expenses incurred will be covered by the project team, and participants will not be responsible for any costs.

7. Benefit of participating in this study

We do not guarantee that you will have any direct benefit from participating in the study. The purpose of this study was to investigate whether combined exercise and cognitive intervention can effectively enhance the health (emotional, sleep, and physical conditions), cognitive function, and other intrinsic abilities of older individuals with cognitive impairment, thereby potentially preventing the progression of mild cognitive impairment to dementia. If the intervention proves effective, your health and quality of life may improve. Additionally, participation in this study may help you develop positive behavioural habits. Your involvement will also contribute to the scientific advancement of telemonitoring home-based combined exercise and cognitive intervention program tailored to the needs of older adults with Mild Cognitive Impairment (MCI) in China. Furthermore, it will facilitate the evaluation of telerehabilitation approach and the its cost-effectiveness.

8. Do I have to participate in and complete this study?

Your participation in this study is entirely voluntary. If you do not wish to participate, you are free to decline, and this will not have any negative impact on your current or future medical care. Even if you agree to participate initially, you have the right to change your mind at any time and inform the researcher of your decision to withdraw from the study. Your withdrawal will not affect your access to normal medical services. Upon your withdrawal, the researcher will promptly delete any collected personal information. Your relevant information will be securely retained until final destruction, and during this period, it will not be used or disclosed further.

9. Research costs and compensation

The expenses covered in this study primarily include equipment costs (such as arm bands and rehabilitation mobile phone software), material costs (including instruction manuals and

record manuals), transportation costs (for investigators, etc.), and communication costs (for contacting subjects by telephone). All expenses are funded by the project team, and you will not incur any fees for participating in this study. Upon completion of the intervention, small gifts will be provided to participants.

10. Treatment of study-related injuries

In the event of any accidental injury arising from participation in the study, necessary medical measures will be taken, and compensation or indemnification will be provided in accordance with applicable laws and regulations.

11. Will my information be kept confidential?

If you choose to participate in this study, your participation and personal data will be treated with utmost confidentiality. All data will be identified with a study code rather than your name. Any information that could identify you will not be disclosed outside the study group without your explicit consent. Your identity will be safeguarded by all study personnel and stakeholders as required. Your personal information will be securely stored and accessed only by authorized researchers. Personal information will not be disclosed in any publications resulting from this study.

12. Who should I contact if I have any questions?

If you have any questions regarding this study, please contact: Hong Chenlu (13141224025). If you have questions about the subject's rights, you can contact the the Institutional Review Board of Peking University at 010-82805751 (e-mail llwyh@bjmu.edu.cn).

Investigator Statement

"I have informed the participant about the research background, objectives, procedures, risks and benefits associated with the home-based and remotely supervised combined exercise and cognitive intervention on older adults with mild cognitive impairment (COGITO). Sufficient time has been provided for the participant to review the informed consent form, engage in discussions with others if desired, and seek clarification on any aspects of the study. I have ensured that the participant understands they can reach out to our team contact in case of study-related concerns, and the Peking University Bioethics Committee for any issues related to their rights or interests, providing accurate contact information for both. The participant has been made aware of their option to withdraw from the study at any time.

Furthermore, I have informed the participant that a copy of this informed consent form, bearing both their and my signature, will be provided to them for their records."

Signature of the investigator Date

Subject Statement

"I have been informed of the research background, objectives, procedures, risks, and benefits associated with the home-based and remotely supervised combined exercise and cognitive intervention on older adults with mild cognitive impairment (COGITO) in China. Ample time and opportunity have been provided for me to ask questions, and I am satisfied with the answers provided. I have been informed about whom to contact should I encounter difficulties, have concerns, wish to provide feedback on the study, or require further information or assistance. I have thoroughly reviewed this informed consent form and willingly consent to participate in the study. I understand that I have the right to withdraw from the study at any time, without needing to provide any justification. I have been assured that I will receive a copy of this informed consent form, containing both my and the investigator's signatures."

Subject Signature Date

Hong C, *et al*. *BMJ Open* 2024; 14:e081122. doi: 10.1136/bmjopen-2023-081122

Appendix C: Template for intervention description and replication checklist for the COGITO programme

Description	COGITO is designed to facilitate home-based and remotely supervised combined exercise and cognitive intervention on older adults with mild cognitive impairment, using digital health techniques.	
Why	There is strong evidence supporting the benefits of physical activity or cognitive training in the MCI population but limited access to such homed-based and remotely supervised intervention practice. Our intervention programme is designed based on behaviour change theories of HAPA-TPB theory, aimed at enhancing adherence through digital techniques, thereby enabling remote supervision.	
What	Materials provide to participants	Training materials include 'How to' guides and recorded videos demonstrating the operation of two intervention techniques (COGITO Mini-programme and RehabApp) and detailed exercise videos presenting to introduce the exercise training sessions. Additionally, participants receive an instruction manual and health education manual covering various topics related to cognitive health. They are provided access to virtual groups and blogs for peer support, personalized schedules for intervention activities and reminders, and personalized physical activity or cognitive training diaries to monitor progress against recommended weekly targets.
	Materials used to train intervention providers	Local intervention providers undergo two training sessions led by researchers before they commence participant training. They are provided with comprehensive training materials, including instructional manuals for supervision and assessment sessions introducing the purpose of the intervention, the overall instruction plan, and intervention precautions.

	Procedures, activities, and/or processes used in the intervention	Intervention providers conduct offline training sessions at the centre for groups of participants, integrating the first intervention with intervention training. During these sessions, intervention providers will ask older adults and their family members to watch demonstration videos of COGITO intervention instructions and precautions, as well as operational videos of the two intervention techniques. Hands-on demonstrations are also conducted for using Bluetooth heart rate armbands and elastic bands, and assistance is provided to install and activate the COGITO Mini-programme and RehabApp accounts.
Who (intervention provider)	The training, supervision or assessment sessions and needed materials on COGITO programme will be provided by experts in the field of physical activity and cognition from geriatrics hospital, psychiatric hospital or mental health centres and higher education institutes, including: • Geriatricians • Geriatric psychiatrists • Nurse • Physiotherapists • Researchers with expertise in the field of geriatric exercise rehabilitation and cognition	
How (mode of delivery)	The COGITO programme will be individually delivered at participants' homes and can be accessed through two intervention techniques: RehabApp and COGITO Mini-programme. RehabApp will provide a variety of exercise training options (including aerobic training, resistance training, and mind-body training) along with demonstration videos to guide each exercise session. Additionally, RehabApp, in conjunction with the arm-worn heart rate telemetry device, will record participants' exercise training time, heart rates, ratings of perceived exertion, adverse events, and other online	

	monitoring data. These functions collectively will enable supervisors to receive real-time feedback for improved training supervision and allow participants to monitor their progress. The COGITO Mini-programme will offer various cognitive training exercises, including memory, executive function, attention, and sensory training. Additionally, the COGITO Mini-programme will record cognitive training time, provide educational blogs, and send message notifications. Furthermore, supervisors will conduct weekly telephone calls with participants and make monthly home visits to encourage task completion and address any difficulties encountered during training. These interventions will be based on information from both RehabApp and the COGITO Mini-programme to enhance compliance.	
Where (location)	Participants will be able to use COGITO programme to conduct exercise or cognitive training at home with a variety of devices via their smartphone or tablet. The COGTIO programme training and assessment will be undertaken in five centres in China: Kunming Psychiatric Hospital, Hangzhou Seventh People's Hospital, Dalian's Seventh People's Hospital and Ning An Hospital of Ningxia. These are all local mental health centres, serving a socioeconomically and ethnically diverse population.	
When and how much	The frequency of delivery	Participants will be encouraged to attend a minimum of twice weekly intervention sessions.
	Target intensity	Participants will be coached on how to use Rating of Perceived Exertion (RPE) to rate the intensity of their intervention sessions as around 5-6 scores.
	Target duration	The duration of the exercise intervention will be 30 minutes and the cognitive training followed the target duration of 20 minutes. In the intervention group of combined exercise and cognitive training, will be 50 minutes (30 minutes duration of exercise intervention and 20 minutes duration of cognitive intervention)

	The total duration of delivery	The total duration of the home-based intervention will be 12 weeks. At the end of the 12-week programme, participants will be encouraged by phone and face-to-face assessment to maintain their engagement until 6 months.
Tailoring	Personalized maximum and recommended target heart rates in the exercise prescription will be set based according to baseline assessment and progressed using Borgs rating of perceived exertion. Moreover, participants gain access to personalized schedules for intervention activities and reminders, and personalized physical activity or cognitive training diaries to monitor progress against recommended weekly targets. Additional tailored support to use two COGITO intervention techniques will be provided to those who reported challenges with two techniques, including: • Telephone support • 'How to' guides and video demonstrations that can be shared via WeChat or email • Prompts and trouble-shooting with individuals if adherence is reduced	
How well	We will implement process evaluation to assess quality of intervention implementation. Data on adherence and fidelity will be collected from participants' training logs, online monitoring data, supervisory documents, adherence records, and satisfaction surveys conducted through qualitative interviews.	

Appendix D: Compliance enhancing and health behaviour changing techniques used in the 12-week combined exercise and cognitive intervention based on HAPA-TPB theory

Intervention phase	Intervention objectives	Preliminary plan
Preintenders (behavioural intention formation phase)	Enhance task self-efficacy	• Before the intervention (week 0), conduct a baseline assessment of physical function and set personalized maximum and recommended target heart rates in the exercise prescription. • During the intervention training session for participants, family members, or caregivers (week 0), provide clear and detailed explanations of the intervention prescription with instructional videos and prompts for aspects prone to errors, and emphasize gradual progression and real-time personalized heart rate reminders during training.
	Enhance expectations about outcomes	• During intervention training session, inform participants who improved their functionality post-intervention will be rewarded. • During home visit, participants based on Wechat Mini-programme ranking will receive rewards.
	Enhance subjective norms	During the intervention training session (week 0), families or caregivers are informed with intervention goals and asked to assist participants in achieving those goals. Full family participation in each intervention is suggested. Supervisors distribute intervention promotional materials to trigger a sense of obligation to participate in the training based on moral norms. Supervisors encourage participants to communicate with other participants; mini-programme ranking; provide exercise status of concurrent participants during supervision based on demonstrative norms. Providing Mini-programme's likes, family encouragement and approval for participants according to instructive norms.
	Enhance social support	• Participants and family members will join health communication community within the Wechat COGITO Mini-programme and design likes function on the COGITO Mini-programme . • Suggest family members or caregivers to accompany and provide encouragement during intervention training. • Supervisors will provide immediate assistance to resolve difficulties for participants.
	Enhance attitude	• Conduct health education and provide cognition health education manuals, lectures recommendation or promotional videos about the benefits of exercise and cognitive training within health blog. • Encourage discussion and comments in the health community within the COGITO Mini-programme.
Intenders (From preintenders to	Planning	Action planning: Supervisors will help participants to design exercise prescription based on the FITT-VP principle including: frequency, intensity, time, type, volume and progression and provide cognition prescription including frequency, types and time.

intenders)		Coping planning: Training participants and families or caregivers to introduce potential difficulties and coping plans; weekly telephone supervision and monthly home visit are required to help discuss coping issues.
	Improve maintenance self-efficacy	• Participants will receive a detailed digital prescription of exercise and cognition through the application, including instructional guidance, training frequency, intensity, duration, etc. • Participants are informed that supervisors will conduct weekly telephone and monthly home visit to solve training difficulties and they can contact supervisors anytime for help.
Action	Enhance recovery self-efficacy	• Each week, participants will receive reminders and points-based ranking from the application to help them to engage in their training and serve as a motivating reference. • The application tracks the training progress and records any adverse events that may occur. • Participants can monitor their training advancements in real-time, while supervisors utilize the application to monitor participants' physical well-being and their adherence to the training routine. • At the beginning of this intervention (week 1), supervisors offer health education to participants who encounter discomfort or stress due to the intervention, effectively alleviating their pressures. • At week1, 2, 3, 5, 6, 7, 9, 10, 11, supervisors offer telephone supervision and at week 4, 8, 12, supervisors provide monthly home visits to identify and address any challenges participants have encountered. • Additionally, participants can utilize the communication platform within the application to share their experiences, exchange insights, and mutually support one another. Moreover, this platform also serves as a channel for participants to receive encouragement from both their family members and supervisors.
	Reduce risk perception	Supervisors provide immediate solutions based on adverse event records from the application. At the end of week 1, summarize issues from first week's intervention (e.g., low enthusiasm for exercise/cognitive training, psychological discomfort or pain due to intervention, technical difficulties, misunderstanding of intervention programmes, unfavorable intervention environment, anxiety or stress unrelated to intervention) and offer specific coping solutions at week 2. From week 1 to week 12, conduct weekly telephone supervision and monthly home visits to identify and address difficulties.
	Enhance social support	Community support: Exchange and share in the Wechat Mini-programme. Family support: Encourage family members to accompany and provide encouragement. Peer interaction: Interaction and likes within the Wechat Mini-programme. Supervisor support: Provide weekly encouragement and problem solving.

Appendix E: Reporting checklist for protocol of a clinical trial based on the SPIRIT guidelines

Instructions to authors Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	appendix G
Protocol version	#3	Date and version identifier	5
Funding	#4	Sources and types of financial, material, and other support	14
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	14

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	14
Roles and responsibilities: sponsor and funder	#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	n/a
Roles and responsibilities: committees	#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	3
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	3
Objectives	#7	Specific objectives or hypotheses	4
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, non-inferiority, exploratory)	4-5
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	5
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)	5, Table 1
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
Interventions: modifications	#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)	10
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	10-11
Interventions: concomitant care	#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	6-8, Table 2
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts),	5,11, appendix A

		assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	
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	10
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	5
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	5-6
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	5-6
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	5-6
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	5-6

Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
Methods: Data collection, management, and analysis			
Data collection plan	#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	11
Data collection plan: retention	#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	7
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	11
Statistics: outcomes	#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	6-8
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12-13

Statistics: analysis population and missing data	#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)	12
Methods: Monitoring			
Data monitoring: formal committee	#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	8
Data monitoring: interim analysis	#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	12
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	7
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	13-14
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial	n/a

		participants, trial registries, journals, regulators)	
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	5
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
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	11
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	n/a
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	14
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	appendix B
Dissemination policy: trial results	#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	13-14
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	n/a

Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	13-14
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	8, appendix B
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	n/a

Appendix F: The Template for Intervention Description and Replication (TIDieR) Checklist

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	_3-4; appendix C_____	_____ __
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	_3-4; appendix C_____	_____ ____
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	_10_; appendix C____	_____ ____
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	_10-11_; appendix C____	_____ ____
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant),	___appendix C___	_____ ____

	describe their expertise, background and any specific training given.		
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	_8-9_; appendix C____	_____ ____
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	_5, 8,10_; appendix C_	_____ ____
	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	_8, Table 2_; appendix C_	_____ ____
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	_10_; appendix C____	_____ ____
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	_____	_____ ____
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	_7-8; appendix C___	_____ ____

12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	_____	_____ ____

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

‡ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).

Appendix G: All items from the World Health Organisation Trial dataset

Data category	Information
Primary registry and trial identifying number	ChiCTR2300073900
Date of registration in primary registry	25th July 2023
Secondary identifying numbers	n/a
Source of funding	China Medical Board
Primary sponsor	China Medical Board
Secondary sponsor(s)	n/a
Contact for public queries	hongchenlu@bjmu.edu.cn
Contact for scientific queries	hongchenlu@bjmu.edu.cn
Public title	COGITO
Scientific title	Home-based and remotely supervised combined exercise and cognitive intervention on older adults with mild cognitive impairment (COGITO)
Countries of recruitment	China
Health condition(s) or problem(s) studied	Mild cognitive impairment (MCI)
Intervention(s)	• Combined exercise and cognitive intervention, and health education • Exercise intervention and health education • Cognitive intervention and health education • Health education
Key inclusion and exclusion criteria	• Diagnosed with MCI • No regular exercise habits • Community-dwelling participants • With good visual, hearing, and language abilities to read Chinese (not illiterate) and able to perform simple smartphone operations • Able to walk independently for at least 5 minutes • Has access to smartphone or internet at home • With family/caregiver support • Able to complete the examinations, intervention and follow-up procedures to fulfil study requirements and participants or authorized representatives able to provide written informed consent • Exclude individuals with medical history and medications or signs and symptoms that may not benefit from the intervention or fail to meet the exercise preparticipation health screening recommendations
Study type	Randomised controlled trial
Date of first enrolment	April 2024
Target sample size	160 participants
Recruitment status	Ongoing recruitment
Primary outcome(s)	Global cognitive function (ADAS-COG, CSI-D)
Key secondary outcomes	• ADL • EQ-5D-5L • PSQI • Intrinsic capacity (MNA-SF, SPPB, PHQ-9) • Social support (LSNS) • Healthcare utilization and cost

List of abbreviations and definitions of terms

ABBREVIATIONS	
COGITO	Combined exercise and cognitive intervention in Chinese older adults with mild cognitive impairment
MCI	Mild cognitive impairment
HAPA-TPB	the Health Action Process Model and the Theory of Planned Behaviour
ADAS-Cog	Alzheimer's Disease Assessment Scale-Cognitive
CSI-D	Community Screening Instrument for Dementia
WHO	World Health Organization
BDNF	Brain-derived neurotrophic factor
CI	Cognitive intervention
EI	Exercise intervention
HE	Health education
TCSA	Thoven Cognitive Self-Assessment
COGSCORE	Cognitive score within the Community Screening Instrument for Dementia
RELSCORE	Informant score within the Community Screening Instrument for Dementia
DFSCORE	Discriminant function score within the Community Screening Instrument for Dementia
EQ-5D	Quality of life EuroQol-5D
ADL	Activity Daily of Life
PSQI	Pittsburgh Sleep Quality Index
MNA-SF	Mini Nutritional Assessment Short-Form
SPPB	Short Physical Performance Battery
PHQ-9	Patient Health Questionnaire
FP	Frailty Phenotype
IPAQ-SF	International Physical Activity Questionnaire-Short Form

LSNS	Lubben Social Network Scale
FITT-VP	Frequency, Intensity, Time, Type of exercise, Volume and Progression Exercise Prescription
HRR	Heart rate reserve
ES	Effect sizes
GCP	Good Clinical Practice
SOP	Standard operating procedures
ITT	Intention-to-treat
LOCF	Last Observation Carried Forward
ICER	Incremental Cost-Effectiveness Ratio
BCR	Benefit-Cost Ratio
CFIR	Consolidated Framework for Implementation Research