Trial Protocol

Early-warning Intervention for Heat and Cold in Older Hypertensive Patients: Impact on Blood Pressure and Electrocardiogram

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This protocol contains the following items:

1. Trial Protocol
2. Statistical Analysis Plan.

The trial protocol and statistical analysis plan have not changed throughout the trial.

Protocol Synopsis

Title	**Early-warning Intervention for Heat and Cold in Older Hypertensive Patients: Impact on Blood Pressure and Electrocardiogram**
Intervention	1. A digital heat health risk early warning tool intervention combined with self-monitoring 2. A digital cold health risk early warning tool intervention combined with self-monitoring
Study Objectives	1. To assess the intervention's effectiveness in reducing blood pressure and its underlying biological mechanisms. 2. To assess the intervention's effectiveness in reducing the risk of electrocardiogram abnormalities and its underlying biological mechanisms.
Study Design	The study is a cluster-randomized controlled trial of a digital heat health risk early warning tool intervention combined with self-monitoring.
Primary Endpoint(s)	**1. Change from Baseline in Blood Pressure Measurement** 1.1 Systolic Blood Pressure (SBP) 1.2 Diastolic Blood Pressure (DBP) **2. Change from Baseline in the Risk of Electrocardiogram (ECG) Measurement** 2.1 Overall Warning Level for Abnormal ECG.
Secondary Endpoint(s)	**1. Change from Baseline in Blood Pressure Measurement** 1.1 Proportion of Older Individuals Meeting the Standard for Blood Pressure Control (SBP/DBP <120/80 mm Hg) 1.2 Proportion of Older Individuals Meeting the Standard for Blood Pressure Control (SBP/DBP <140/90 mm Hg) **2. Change from Baseline in the Risk of Electrocardiogram (ECG) Measurement** 2.1 Left Ventricular Hypertrophy 2.2 Sinus Arrhythmia 2.3 Right Bundle Branch Block 2.4 Ventricular Premature Beats 2.5 Atrial Premature Beats 2.6 Q Waves 2.7 T-Wave Changes 2.8 ST Changes **3. Change from Baseline in Temperature Exposure Measurement** 3.1 Temperature 3.2 Humidity **4. Change from Baseline in Heatwave Perception Assessment**

	4.1 Heatwave Awareness and Concern **5. Change from Baseline in Cold Spell Perception Assessment** 5.1 Cold Spell Awareness and Concern **6. Change from Baseline in Cardiovascular and Cerebrovascular Symptoms Assessment** **7.Change from Baseline in Respiratory System Symptoms Assessment** **8. Change from Baseline in Sleeping Quality Assessment** 8.1 Pittsburgh Sleep Quality Index (PSQI) **9.Change from Baseline in Generalized Anxiety Disorder Assessment** 9.1 Generalized Anxiety Disorder Scale (GAD-7) Score. **10. Change from Baseline in Cognitive Function Assessment** 10.1 Mini-Mental State Examination (MMSE) Score. **11. Change from Baseline in Depression Assessment** 11.1 Patient Health Questionnaire-9 (PHQ-9) Score. **12.Change from Baseline in Social Support Perception Assessment** 12.1 Perceived Social Support Scale (PSSS) **13.Change from Baseline in Time-Activity Patterns Measurement** 13.1 Time-Activity Patterns **14.Change from Baseline in Medication Adherence Measurement** 14.1 Self-management Behavior 14.2 Medication Adherence **15. Changes in liver function biomarkers (e.g., albumin (ALB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), etc.) from baseline** **16. Changes in kidney function biomarkers (e.g., uric acid (UA), blood urea nitrogen (BUN), creatinine (CREA), etc.) from baseline** **17. Changes in cardiovascular biomarkers (e.g., creatine kinase-MB (CK-MB), creatine kinase (CK), etc.) from baseline** **18. Changes in inflammatory biomarkers (e.g., interleukin-6 (IL-6), interleukin-1β (IL-1β), etc.) from baseline** **19. Changes in metabolic biomarkers (e.g., lactate dehydrogenase (LDH), high-density lipoprotein (HDL), low-density lipoprotein cholesterol (LDL) , etc.) from baseline**
Accrual Objective	342
Study Duration	6 months total duration covering two distinct periods which focuses on heat wave and cold spell (From June 15th 2023 to August 31st

	2023, and December 1st 2023 to February 28th 2024).
Treatment Description	This cluster-randomized trial will be conducted in various districts across Tianjin, China. As part of the early warning interventions for heat and cold, three communities from each of the two selected districts will be randomly chosen and assigned to one of three groups: the combined intervention group, the self-monitoring group, or the control group. Participants in the combined intervention group will receive health risk warnings for heat and cold via digital tools, specifically through a WeChat mini-program, which provides real-time updates on early warnings and health advisories. Additionally, they will be instructed to perform daily self-monitoring of their blood pressure (BP) and electrocardiogram (ECG) using automated home devices. Participants in the self-monitoring alone group will engage in daily BP and ECG monitoring but not receive any health warnings. In contrast, the control group will monitor their BP and ECG only during baseline assessments and routine health check-ups (the day after the first heat wave in July and August 2023, as well as following the first cold spell in January and February 2024). All participants will be required to record their daily time-activity patterns. During the baseline and subsequent check-ups, data will be collected on participants' demographics, medical history, lifestyle factors (e.g., diet, smoking, physical activity), environmental exposures, mental health status (including stress levels, emotional stability, and psychological resilience), sleep quality, medication adherence, cardiovascular and cerebrovascular symptoms, respiratory system symptoms, and perceptions of heatwaves and cold spells. In addition, blood, urine, and stool samples will be gathered for further analysis.
Inclusion Criteria	(i) Individuals aged 60 to 65 years old; (ii) Individuals with a diagnosis of hypertension; (iii) Individuals with untreated blood pressure above 140/90 mmHg.
Exclusion Criteria	(i) having a history of coronary heart disease, heart failure, or stroke

Glossary of Abbreviations

BP	Blood Pressure
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
ECG	Electrocardiogram
MMSE	Mini-Mental State Examination
GAD-7	Generalized Anxiety Disorder-7
PSQI	Pittsburgh Sleep Quality Index
PHQ-9	Patient Health Questionnaire-9
PSSS	Perceived Social Support Scale
HPSMBRS	Hypertension Patient Self-Management Behavior Rating Scale
HPMARS	Hypertension Patient Medication Adherence Rating Scale
CVD	Cardiovascular disease
LVH	Left ventricular hypertrophy
BMI	Body Mass Index
CK-MB	Creatine Kinase-MB
CK	Creatine Kinase
LDH	Lactate Dehydrogenase
CREA	Creatinine
UA	Uric Acid
BUN	Urea Nitrogen
PRA	Plasma Renin Activity
ALD	Aldosterone
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ALB	Albumin
CRP	C-Reactive Protein
IL-6	Interleukin-6
PCT	Procalcitonin
LDH	Lactate Dehydrogenase
TRIGL	Triglycerides
HDL	High-Density Lipoprotein
LDL	Low-Density Lipoprotein Cholesterol
HCY	Homocysteine
RBBB	Right bundle branch block
VPBs	Ventricular premature beats
APBs	Atrial premature beats
MI	Myocardial infarction

1.Background and Rationale

Hypertension is a significant public health issue, predominantly affecting older adults, who are notably susceptible to the adverse effects of heat or cold exposure. Digital technologies effectively support lifestyle changes, promote medication adherence, and offer timely interventions to improve blood pressure management. However, they frequently fail to consider the critical environmental impact of heat or cold. This study develops a digital tool that delivers heat or cold health warnings, integrating it with traditional self-monitoring to provide a comprehensive approach to managing hypertension, especially in the context of global climate change.

2.Study Objectives

The primary objective of the study is to evaluate the effectiveness of the intervention in improving blood pressure control, reducing the risk of electrocardiogram abnormalities and abnormal mental health conditions, as well as understanding its underlying biological mechanisms. Additionally, the study aims to assess how the intervention impacts other health-related factors, including physical activity, environmental exposures, medication adherence, and participants' perceptions of heatwaves and cold spells. Finally, the intervention's effect on biological sample testing indicators will be analyzed to provide a comprehensive evaluation of its impact on participants' overall health.

3.Study Design

3.1 Description of Study Design

This cluster-randomized trial will be conducted in various districts across Tianjin, China. As part of the early warning interventions for heat and cold, three communities from each of the two selected districts will be randomly chosen and assigned to one of three groups: the combined intervention group, the self-monitoring group, or the control group. The study will be divided into pre-intervention and intervention phases. The pre-intervention period for the heat health early-warning information intervention spans from July 1st, 2023, to July 7th, 2023, followed by the intervention period from July 8th to September 9th, 2023. Similarly, during the cold spell health early-warning information intervention, the pre-intervention phase occurs from December 1st, 2023, to December 7th, 2023, and the intervention.

Participants in the combined intervention group will receive heat health risk warnings via digital tools, specifically a WeChat mini-program, providing real-time updates on early warnings and health advisories. Additionally, they will be instructed to perform daily self-monitoring of their blood pressure (BP) and electrocardiogram (ECG) using automated home devices. Participants in the self-monitoring alone group will engage in daily BP and ECG monitoring but not receive any health warnings. In contrast, the control group will monitor their BP and ECG only during baseline assessments and routine health check-ups (the day after the first heat wave in July and August 2023, as well as following the first cold spell in January and February 2024).

All participants will be required to record their daily time-activity patterns. During the baseline and subsequent check-ups, data will be collected on participants' demographics, medical history, lifestyle factors (e.g., diet, smoking, physical activity), environmental exposures, sleep quality, mental health status (including stress levels, emotional stability, and psychological resilience), medication adherence, cardiovascular and cerebrovascular symptoms, respiratory system symptoms, and perceptions of heatwaves and cold spells. In addition, blood, urine, and stool samples will be gathered for further analysis.

3.2 Primary and Secondary Outcomes

3.2.1 Primary Outcomes

3.2.1.1 Change from Baseline in Blood Pressure Measurement

a. Systolic Blood Pressure (SBP)

b. Diastolic Blood Pressure (DBP)

3.2.1.2 Change from Baseline in the Risk of Electrocardiogram (ECG) Measurement

Overall warning level for abnormal ECG

3.2.2 Secondary Outcomes

3.2.2.1 Change from Baseline inBlood Pressure Measurement

a. Proportion of older individuals meeting the standard for blood pressure control (SBP/DBP <120/80 mm Hg)

b. Proportion of older individuals meeting the standard for blood pressure control (SBP/DBP <140/90 mm Hg)

3.2.2.2 Change from Baseline in the Risk of Electrocardiogram (ECG) Measurement

a. Left ventricular hypertrophy

b. Sinus arrhythmia

c. Right bundle branch block

d. Ventricular premature beats

e. Atrial premature beats

f. Q waves

g. T-wave changes

h. ST changes

3.2.2.3 Change from Baseline in Temperature Exposure Measurement

a. Temperature

b. Humidity

3.2.2.4 Change from Baseline in Heatwave Perception Assessment

Heatwave Awareness and Concern

3.2.2.5 Change from Baseline in Cold Spell Perception Assessment

Cold Spell Awareness and Concern

3.2.2.6 Change from Baseline in Cardiovascular and Cerebrovascular Symptoms Assessment

3.2.2.7 Change from Baseline in Respiratory System Symptoms Assessment

3.2.2.8 Change from Baseline in Sleeping Quality Assessment

Pittsburgh Sleep Quality Index (PSQI)

3.2.2.9 Change from Baseline in Generalized Anxiety Disorder Assessment

Generalized Anxiety Disorder Scale (GAD-7) score

3.2.2.10 Change from Baseline in Cognitive Function Assessment

Mini-Mental State Examination (MMSE) score

3.2.2.11 Change from Baseline in Depression Assessment

Patient Health Questionnaire-9 (PHQ-9) score

3.2.2.12 Change from Baseline in Social Support Perception Assessment

Perceived Social Support Scale (PSSS)

3.2.2.13 Change from Baseline in Time-Activity Patterns Measurement

Time-Activity Patterns

3.2.2.14 Change from Baseline in Medication Adherence Measurement

a. Self-management Behavior

b. Medication Adherence

3.2.2.15 Changes in liver function biomarkers (e.g., albumin (ALB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), etc.) from baseline

3.2.2.16 Changes in kidney function biomarkers (e.g., uric acid (UA), blood urea nitrogen (BUN), creatinine (CREA), etc.) from baseline

3.2.2.17 Changes in cardiovascular biomarkers (e.g., creatine kinase-MB (CK-MB), creatine kinase (CK), etc.) from baseline

3.2.2.18 Changes in inflammatory biomarkers (e.g., interleukin-6 (IL-6), interleukin-1β (IL-1β), etc.) from baseline

3.2.2.19 Changes in metabolic biomarkers (e.g., lactate dehydrogenase (LDH), high-density lipoprotein (HDL), low-density lipoprotein cholesterol (LDL) , etc.) from baseline

3.3 Randomization

This cluster-randomized trial will be conducted in various districts across Tianjin, China. As part of the early warning interventions for heat and cold, three communities from each of the two selected districts will be randomly chosen and assigned to one of three groups: the combined intervention group, the self-monitoring group, or the control group. Due to the cluster design and intervention nature, the older individuals with hypertension, doctors in Community Health Planning Services, and research staff collecting outcome data will be aware of the group assignments.

4.Participants

4.1 Inclusion Criteria

Inclusion rules for the study participants were:

4.1.1 individuals aged 60 to 65 years old

4.1.2 individuals with a diagnosis of hypertension

4.1.3 individuals with untreated blood pressure above 140/90 mmHg

4.2 Exclusion Criteria

Exclusion criteria were as follows:

4.2.1 having a history of coronary heart disease, heart failure, or stroke

4.3 Sites

In the summer of 2022, a global warming trend led to record-breaking temperatures across all continents, the highest in over 100,000 years[1,3]. This summer, the Tianjin region has also experienced an unprecedented heatwave, with a total of 27 days of high temperatures. Among them, the temperature exceeded 40℃ for 4 days[4]. Meanwhile, the winter of 2022 saw a severe cold spell affecting the region, with temperatures plummeting to historic lows, reaching as low as -14°C[5]. These extreme conditions significantly heightened the health risks associated with cold weather, especially for vulnerable populations.

5.Known and Potential Risks and Benefits to Participants

The daily self-monitoring of BP and ECG will be trained by a professional, which will not cause health risks and discomfort. All information and samples, including blood, urine, and stool, tested about the subject will be kept strictly confidential and will only be used for this project. Participation in the survey is voluntary, and the rights of respondents who do not agree to participate in this survey, or withdraw at any time after the start of the survey, will not be affected in any way.

Respondents will receive a feedback report on the results of the self-monitoring of BP, exposure to temperature, time-activity patterns, and a small gift to thank to the respondents for participating.

6.Intervention

6.1 Combined Intervention

This study will utilize a digital heat or cold health risk early warning tool developed as a WeChat mini-program in the combined intervention group. The tool features capabilities for disseminating early heat or cold-health warning information.Throughout the intervention period, the heat or cold health risk early warning model, established by the National Institute of Environmental Health at the Chinese Center for Disease Control and Prevention, classified heat or cold-related health hazards into five levels: "no warning," "concern level," "warning level one," "warning level two," and "warning level three." Upon issuing a heat or cold health risk early warning, only the older individuals in the intervention group rwill receive these early warnings and health advice through the digital tool.

Additionally, participants in the combined intervention group will be instructed to self-measure their blood pressure (BP) three times each morning (from 6:00 a.m. to 8:00 a.m.) and evening (from 6:00 p.m. to 8:00 p.m.) at home, and to self-administer electrocardiogram (ECG) measurements twice during the same morning and evening timeframes.

6.2 Self-Monitoring Alone

Participants in the self-monitoring alone groups will be instructed to self-measure their blood pressure (BP) three times each morning (from 6:00 a.m. to 8:00 a.m.) and evening (from 6:00 p.m. to 8:00 p.m.) at home, and to self-administer electrocardiogram (ECG) measurements twice during the same morning and evening timeframes.

6.3 Criteria for Discontinuing or Modifying

The participation of subjects is voluntary and can be withdrawn at any time, and their rights will not be affected in any way.

6.4 Strategies for Adherence

During the investigation, all tests will be conducted by professionally trained medical personnel and will not cause any adverse effects. Participants will receive timely feedback on their blood pressure (BP) and electrocardiogram (ECG) results. This real-time monitoring will allow them to manage their health proactively, with immediate warnings and recommendations provided based on their health status and exposure to temperature variations. Additionally, participants will be given feedback on their questionnaire scores, including heat wave and cold spell perception scores, Pittsburgh Sleep Quality Index (PSQI) score, Mini-Mental State Examination (MMSE) score, Generalized Anxiety Disorder-7 (GAD-7) scores, Patient Health Questionnaire-9 (PHQ-9) score, and Perceived Social Support Scale (PSSS) score. These measures will provide insight into their psychological well-being and overall quality of life. Biomarkers identified from other omics and other targeted biomarkers of interest will bealso assessed. These biomarkers will provide detailed information on participants' physiological responses and health status.

6.5 Permitted or Prohibited Interventions

During the intervention study period, if the subject takes medication regularly, it can be carried out normally according to the doctor's instructions.

7. Study Procedures

7.1 Enrollment

The research subjects will be selected based on chronic disease management records, combined with the above inclusion and exclusion criteria, and the research subjects with good compliance and willing to complete the study according to the requirements of the project were selected.

7.2 Randomization

The process of conducting cluster randomization using a random number table starts with the random selection of districts. Each district is assigned a unique numerical identifier, and the random number table is then used to select the appropriate number of districts for inclusion in the study. After selecting the districts, the next step involves randomly choosing communities within these selected districts. Similar to the districts, each community is assigned a unique number, and the random number table is again used to carry out the community selection process.

Once the communities are chosen, they are randomly assigned to one of three intervention groups: the combined intervention group, the self-monitoring group, or the control group.

7.3 BP Measurement

All participants will self-monitor their BP once during the pre-intervention phase and daily throughout the intervention phase. Moreover, during the intervention period, participants in the intervention and monitoring groups will measure their BP themselves three times each morning (6:00 a.m. to 8:00 a.m.) and evening (6:00 p.m. to 8:00 p.m.) at home. BP measurements will be taken in a seated position after 5 minutes of quiet rest, using a self-monitored electronic sphygmomanometer (Model Maibobo, Shenzhen Yike Network Technology Co., Ltd., China), following a standard protocol. The Global System for Mobile Communication network can transmit these measurements to the digital health tool.

7.4 ECG Measurement

All participants will self-monitor their ECG once during the pre-intervention phase and daily throughout the intervention phase. The handheld electrocardiographic recorder, CarePatch (ECG-H01, Hangzhou Proton Technology Co., Ltd., China), will be used to monitor the electrocardiographic conditions of the study participants, providing outputs such as normal status, overall ECG warning level, Left ventricular hypertension, Sinus arrhythmia, Sinus tachycardia, Sinus bradycardia, Right bundle branch block, Ventricular premature beats, Atrial premature beats, Abnormal Q waves, T-wave changes and ST changes, which represent electrocardiographic abnormalities.

7.5 Exposure Temperature Measurement

Daily personal temperature exposure will be recorded using a portable temperature and humidity sensor (Renke, COS-04) during two intervention periods. When participants are outdoors, the temperature and humidity sensor will be worn on the upper chest and placed on the desk in the living room when indoors.

7.6 Heatwave Perception Questionnaire

The Heatwave Perception Questionnaire aims to assess individuals' awareness and concerns regarding heatwaves, particularly their potential health impacts on people with hypertension. Given the frequent occurrence of heatwaves in northern China during the summer, which poses significant health risks, this questionnaire captures participants' perceptions of heatwave-related health risks and their level of preparedness. Respondents rate their responses on a continuous scale from 0 to 100, with 0 representing "not at all" or "very low" and 100 representing "very much" or "very high," allowing them to express the degree of their perception and concern. The questions include: how much attention they pay to information about heatwaves and hypertension, how frequent they believe heatwaves occur in their area, how much they know about the risks heatwaves pose to individuals with hypertension, how concerned they are about these risks, how severe they believe the health impacts are, and how effective

they think protective measures like air conditioning can be in mitigating these impacts. This questionnaire provides valuable insights into heatwave awareness, risk perception.

7.7 Cold Spell Perception Questionnaire

The Cold Spell Perception Questionnaire is designed to assess individuals' awareness and concerns regarding cold spell events, particularly their potential health impacts on people with hypertension. Given the frequent occurrence of cold spells in northern China during winter, which pose significant health risks, this questionnaire captures participants' perceptions of cold spell-related health risks and their level of preparedness. Respondents rate their responses on a continuous scale from 0 to 100, with 0 representing "not at all" or "very low" and 100 representing "very much" or "very high," allowing them to express the degree of their perception and concern. The questions include: how much attention they pay to information about cold spells and hypertension, how frequent they believe cold spells occur in their area, how much they know about the risks cold spells pose to individuals with hypertension, how concerned they are about these risks, how severe they believe the health impacts are, and how effective they think protective measures (such as using heaters, dressing warmly, sealing windows, resting, avoiding outdoor activities, eating warm foods, exercising moderately, and staying informed of cold spell warnings) can be in mitigating these impacts. This questionnaire provides valuable insights into cold spell awareness, risk perception.

7.8 Cardiovascular and Cerebrovascular Symptoms Questionnaire

The Cardiovascular and Cerebrovascular Symptoms Questionnaire assesses symptoms over the past week. Participants are asked to indicate the frequency and characteristics of chest pain or discomfort, including whether it occurs during physical exertion and how long it takes to relieve. They are also asked about the duration of pain compared to usual, severe chest pain lasting more than 30 minutes, and any numbness, tingling, or loss of sensation on one side of the body lasting more than 5 minutes. Additionally, the questionnaire inquires about episodes of difficulty speaking or understanding others and whether the participant sought medical attention for these symptoms. If medical attention was sought, the main symptoms are identified. The medical history section includes questions on previous diagnoses of angina, myocardial infarction, and stroke, with space for the dates of first diagnoses.

7.9 The Respiratory System Symptoms Questionnaire

The Respiratory System Symptoms Questionnaire evaluates symptoms experienced over the past week. Participants are asked to indicate the frequency of various respiratory symptoms, including cough ($\geqslant$4 times daily), sputum production ($\geqslant$2 times daily, not just clearing the throat), cough with sputum, wheezing, shortness of breath, dyspnea, chest tightness, fever, chest pain, and difficulty in breathing not caused by medication. Additional symptoms assessed include wheezing sounds (e.g., "hehe"), nasal symptoms (such as sneezing, runny nose, or nasal congestion), hemoptysis or blood-streaked sputum, snoring, and daytime sleepiness. Each symptom is rated on a scale from 1 (all the time) to 5 (never).

7.10 Sleeping Assessment Questionnaire

The Pittsburgh Sleep Quality Index (PSQI) is a widely used self-report questionnaire designed to measure sleep quality and disturbances over a one-month period[6]. The PSQI consists of 19 individual items that assess seven key components of sleep: subjective sleep quality, sleep latency (the time it takes to fall asleep), sleep duration, habitual sleep efficiency (the ratio of total sleep time to time spent in bed), sleep disturbances, use of sleep medication, and daytime dysfunction.Each of the seven components is scored from 0 to 3, with the total PSQI score ranging from 0 to 21. A total score greater than 5 indicates poor sleep quality, while a lower score suggests good sleep quality. The PSQI has been

validated in various populations and is frequently used to assess sleep problems in both clinical and research settings.

7.11 Cognitive Assessment Scale

The Mini-Mental State Examination (MMSE) will be used to assess participants' cognitive function, particularly focusing on memory, attention, language, and executive function in older adults[7]. The MMSE evaluates five main areas: orientation (to time and place), memory (short-term and long-term), attention and calculation (concentration and basic arithmetic), language (fluency and comprehension), and executive function (complex task performance). Each area is scored on a scale from 0 to 5, with a total score ranging from 0 to 30. Typically, a score above 24 indicates normal cognitive function, while a score below 24 may suggest cognitive impairment.

7.12 Generalized Anxiety Disorder Scale

The Generalized Anxiety Disorder Scale (GAD-7) will be used to assess the severity of generalized anxiety disorder symptoms among participants[8]. The GAD-7 evaluates seven key symptoms of anxiety: feeling nervous, anxious, or on edge; not being able to stop or control worrying; worrying too much about different things; trouble relaxing; being so restless that it is hard to sit still; becoming easily annoyed or irritable; and feeling afraid as if something awful might happen. Each symptom is rated on a scale from 0 (not at all) to 3 (nearly every day), resulting in a total score ranging from 0 to 21. A score of 5 or above indicates the presence of generalized anxiety disorder symptoms, with higher scores reflecting greater symptom severity.

7.13 Depression Assessment Scale

The Patient Health Questionnaire-9 (PHQ-9) will be used to assess the severity of depressive symptoms among participants[9]. This self-report tool evaluates nine key symptoms of depression experienced over the past two weeks, including loss of interest or pleasure in activities, feeling down or hopeless, trouble sleeping, fatigue, poor appetite or overeating, feelings of worthlessness or failure, difficulty concentrating, physical agitation or slowing, and thoughts of self-harm or suicide. Each symptom is rated on a scale from 0 (not at all) to 3 (nearly every day), with total scores ranging from 0 to 27. Scores of 5, 10, 15, and 20 indicate mild, moderate, moderately severe, and severe depression, respectively.

7.14 Social Support Assessment Scale

The Perceived Social Support Scale (PSSS) will be utilized to assess participants' subjective perception of the social support they receive[10]. The PSSS evaluates three key sources of support: family, friends, and significant others. It consists of 12 items, with four items each related to family, friends, and significant others. Participants rate their agreement with each statement on a scale from 1 (very strongly disagree) to 7 (very strongly agree), resulting in a total score ranging from 12 to 84, where higher scores indicate higher perceived social support.

7.15 Time-activity Patterns Measurement

All participants will complete self-reported time-activity diaries via the digital heat health risk early warning tool during two intervention periods. The duration spent in various settings (such as outdoor environments, workplaces, transportation, home, and other indoor areas) and at different intensity levels of physical activity were recorded. Severe physical activities include shoveling, digging, plowing, running, carpentry, construction, and carrying. Moderate activities comprise housework, walking, yard work, light carpentry, and biking. Light activities are office work, driving, walking, and babysitting. Sedentary activities include eating, reading, writing, watching TV, listening to the radio, and using the computer.

7.16 Medication Adherence Indicators Measurement

The measurement of indicators of medication-taking behavior for hypertension is obtained through the Hypertension Patient Self-Management Behavior Rating Scale (HPSMBRS) and the Hypertension Patient Medication Adherence Rating Scale (HPMARS), yielding scores for self-management behavior and medication adherence, respectively.

7.17 Cardiovascular Health Biomarkers Measurement

Cardiovascular indicators are crucial for assessing heart health and detecting potential damage to heart muscle and other cardiovascular tissues. Creatine Kinase-MB (CK-MB) is an isoenzyme primarily found in the heart muscle, and elevated levels in the blood can signal myocardial infarction or heart damage. Creatine Kinase (CK) is an enzyme involved in energy production in muscles, and increased levels may indicate muscle stress or damage. Lactate Dehydrogenase (LDH) is an enzyme that plays a role in cellular energy production; elevated levels can suggest tissue damage, including from cardiovascular events. These indicators are typically measured through blood tests that assess the enzyme activity and concentration in the bloodstream.

7.18 Liver Function Health Biomarkers Measurement

Liver indicators help in evaluating liver function and detecting liver-related conditions. Alanine Aminotransferase (ALT) is an enzyme predominantly found in the liver, with elevated levels often indicating liver inflammation or damage. Aspartate Aminotransferase (AST) is another enzyme present in the liver, heart, and muscles, with high levels potentially suggesting liver injury or other organ damage. Albumin (ALB) is a protein synthesized by the liver, and its levels reflect liver function and nutritional status; low levels can signal liver disease or malnutrition. C-Reactive Protein (CRP) is produced by the liver in response to inflammation; increased CRP levels can indicate systemic inflammation or infection. These indicators are assessed through blood tests that measure enzyme activity, protein concentration, and inflammation markers.

7.19 Kidney Function Health Biomarkers Measurement

Kidney indicators are vital for monitoring kidney function and identifying potential renal issues. CREA (Creatinine) is a waste product from muscle metabolism, and elevated levels can indicate impaired kidney function. Uric Acid (UA) is produced from the breakdown of purines and high levels can be associated with gout or renal problems. Urea Nitrogen (BUN) is a byproduct of protein metabolism, and high levels can reflect kidney dysfunction. Plasma Renin Activity (PRA) is involved in regulating blood pressure and electrolyte balance; abnormal levels can suggest kidney disease or hypertension. Aldosterone (ALD) is a hormone that affects sodium and potassium levels and blood pressure; its measurement can help diagnose adrenal or renal disorders. These indicators are evaluated through blood tests that measure waste products, hormone levels, and other renal function markers.

7.20 Inflammatory Indicators Measurement

Inflammatory markers are essential for detecting and monitoring inflammatory conditions and infections. Interleukin-6 (IL-6) and Interleukin-1 β (IL-1 β) are cytokines that plays a role in immune response and inflammation; elevated levels can indicate various inflammatory diseases. Procalcitonin (PCT) is a protein that increases in response to bacterial infections and sepsis; high levels are used to diagnose severe infections. Measurement of these markers is done through blood tests that detect cytokine levels and protein concentrations, providing insights into the body's inflammatory and immune responses.

7.21 Metabolic Indicators Measurement

Metabolic indicators assess metabolic health and risk factors for chronic diseases. Lactate Dehydrogenase (LDH) also noted under cardiovascular indicators, is involved in energy metabolism and its levels can indicate metabolic disturbances. Triglycerides (TRIGL) are a type of fat in the blood, and elevated levels are linked to increased cardiovascular disease risk. High-Density Lipoprotein (HDL) is beneficial for heart health, with higher levels associated with a lower risk of heart disease. Low-Density Lipoprotein Cholesterol (LDL) can contribute to cardiovascular problems when elevated. Homocysteine (HCY) is an amino acid whose high levels are associated with a greater risk of cardiovascular disease. These indicators are typically measured through blood tests that analyze lipid profiles and metabolic markers.

8. Statistical Considerations and Analytical Plan

8.1 Sample Size Calculation

In this study, the sample size is calculated according to the formula $n=\frac{2\sigma^2(Z_\alpha+Z_\beta)^2}{d^2}$. σ is the assumed population standard deviation used for both of the three groups, $\sigma = 14$. μ_1 and μ_2 are the assumed population means, based on previously studied parameters of blood pressure (S B P) research, where $\mu_1=127$, $\mu_2=120$, d=7. Using the PASS15.0 software, where $\alpha=0.1$ and $\beta=0.2$[11]. The sample size calculated for this study is 153, taking into account a 10% loss to follow-up rate, the final sample size is determined to be 171. During two intervention periods, a total of 342 participants will be enrolled in the study.

8.2 Statistical Analysis

For continuous variables such as age and BMI, data that follow a normal distribution will be described using the mean and standard deviation (Mean $\pm$ SD). In cases where the data do not follow a normal distribution, the median and interquartile range (Median, IQR) will be used instead. For categorical variables, like gender and smoking status, percentages will be used to represent the distribution across the groups. Group differences will be analyzed using one-way ANOVA for normally distributed data and the Kruskal-Wallis test for non-normally distributed data.

The proportion of participants achieving a systolic blood pressure (SBP) below 140 mm Hg (or 120 mm Hg) and a diastolic blood pressure (DBP) below 90 mm Hg (or 80 mm Hg) each week or routine health check-up is calculated by $\text{Control rate}_i = \frac{\text{Control number}_i}{\text{Total number}_i}$, where Control rate_i denotes the proportion of participants who will achieve an SBP below 140 mm Hg (or 120 mm Hg) and a DBP below 90 mm Hg (or 80 mm Hg) at each week or routine health check-up. Control number_i refers to the count of participants who will meet the control criteria at the end of each week or routine health check-up. The Total number_i indicates the participant count at the end of each week or routine health check-up.

We will use a linear mixed-effects model to explore the effectiveness of combining this digital tool with traditional self-monitoring in elderly patients with hypertension, comparing its impact on blood pressure control to self-monitoring alone and the absence of any intervention.

Changes in BP, risks of ECG abnormalities, environmental exposures, mental health status (including stress levels, emotional stability, and psychological resilience), medication adherence, perceptions of heatwaves and cold spells, and indicators of biological sample testing compared with the pre-intervention period in each group will be analyzed using a linear mixed-effects model, as shown in Formula 1.

$$Y_i = \beta_{0i}\text{period} + \beta_{ni}X_{ni} + Z_i\Gamma_i + \varepsilon_i \quad (1)$$

where Y_i represents the outcomes measured in both the pre-intervention and intervention periods. The term period represents different intervention periods (pre-intervention and intervention period); X_{ni} represents matrixes of covariates (smoking and drinking status, and daily outdoor temperature). β_{ni} is the parameter vector of covariates, Γ_i is the individual random effect, Z_i is the parameter vector of the random effect, and ε_i is the residual.

The effect of the intervention will be assessed using a linear mixed-effects model, as indicated in Formula 2.

$$Y_i = \beta_{0i} group + \beta_{ni} X_{ni} + Z_i \Gamma_i + \varepsilon_i \quad (2)$$

The term group denotes various interventions (the combined intervention, self-monitoring alone and control groups); X_{ni} represents matrixes of covariates (age, sex, BMI, age, education, smoking and drinking status, baseline BP indicators, and daily outdoor temperature), Y_i is the change in outcomes for each group, compared to the baseline, and β_{ni}, Γ_i, Z_i, and ε_i have equivalent meanings to those in Formula 1.

8.3 Analytical Tools

All statistical analyses were carried out in R software version 4.1.1. Statistical tests were two-sided, and $p < 0.05$ was considered statistically significant.

9.Criteria for Participant and Study Completion and Premature Study Termination

9.1 Participant Completion

Study participants who meet the inclusion exclusion criteria and complete all interventions during the study.

9.2 Participant Stopping Rules and Withdrawal Criteria

Subjects may terminate the study early for the following reasons:

1. Study participants may voluntarily withdraw at any point in the course of the study.
2. Subject "lost to follow-up"
3. Participant died.
4. If any clinical adverse events, other medical conditions, or circumstances occur that make it not in the best interest of the subject to continue participating in the study, the study subject will discontinue further study intervention.

10.Protocol Deviations

The investigator will conduct the study in strict accordance with the protocol and will not allow deviations from the protocol. In the event of any changes, disagreements, or deviations during the course of the study, corrective actions will be developed by the site and implemented immediately.

11.Ethical Considerations

Participation in the trial is voluntary and the subject may withdraw from the study at any time for any reason. Subjects (or their legal representatives) participating in the trial will be issued and read an informed consent form, signed and dated informed consent form prior to any study procedures, and the informed consent materials will be presented in the participant's primary language.

12.Quality Control and Quality Assurance

Before the investigation, each technical person responsible for BP, ECG, exposure monitoring, questionnaire survey and computer testing should participate in technical training and pass the training assessment; Each technical person should be familiar with the division of labor and tasks and responsibilities. During the investigation, all technical personnel should carry out various tasks in strict

accordance with the investigation process and operating procedures; When you encounter a problem, you should report it to the relevant person in charge and ask for help as soon as possible. The replacement of research subjects and monitoring instruments should be recorded, and the monitoring data obtained should be handed in in a timely manner, and the data collector should check the quality of the monitoring data in a timely manner, and feedback to the investigator for correction if necessary.

13.References

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