

Appendix C. Summary and risk of bias tables

| Yoo et al., 2009 | |
|-------------------------|--|
| Methods | Randomized, controlled trial |
| Participants | <p>The study location was a university hospital in (Korea University) and a community health centre (Guro-Gu Public Health Centre) in Korea. Fifty-seven (n=57) were from the general hospital and sixty-six (n=66) from the Public Health Centre.</p> <p>“62 participants were randomized to the intervention group and 61 participants were randomized to the control group.</p> <p>The inclusion criteria were (i) a diagnosis of both Type 2 diabetes and hypertension at least 1 year previously by a physician; (ii) HbA1C 6.5-10.0%; (iii) blood pressure >130/80 mmHg; and (iv) body mass index (BMI) \geq23.0 kg/m² (overweight according to Asia-Pacific criteria).</p> <p>The exclusion criteria were (i) severe diabetic complications (e.g. diabetic foot or severe diabetic retinopathy); (ii) liver dysfunction with aspartate aminotransferase or alanine aminotransferase >2.5 times the reference level, or renal dysfunction (serum creatinine > 132 μmol/l); (iii) medical history of congestive heart failure, angina pectoris, myocardial infarction, or stroke based on a physician’s diagnosis; (iv) pregnancy or lactation; or (v) other medical problems that could affect study results or trial participation.”</p> |
| Interventions | <p>INTERVENTION: A Ubiquitous Chronic Disease Care System using cellular phones and the internet</p> <p>“Patients in the intervention groups received a cellular phone (LG-SV280; LG Electronics, Seoul, Korea) with a modular blood glucose measuring device (Anycheck; Insung Information Co., Seoul, Korea), strips, and lancets. They also received an automatic blood pressure monitoring device (T5M; Omron, Kyoto, Japan), as well as body weight scales (HD308; Tanita, Tokyo, Japan). The UCDC system sent out an alarm on the cellular phone to remind the participant to measure their blood glucose, blood pressure twice a day (before breakfast and bedtime) and body weight once a day (before breakfast). The Anycheck device attached to their cellular phone conducted the glucose measurements and automatically sent the results to a central study database. As soon as participants transmitted their glucose measurement through their cellular phones, they immediately received messages of encouragement, reminders, and recommendations according to a pre-defined algorithm that was developed by endocrinologists, dieticians and nurses at Korea University based on the American Diabetes Association (ADA) Guidelines and the Korean Staged Diabetes Management Guidelines. Second, the UCDC system automatically recorded participant’s exercise time using the short message service (SMS), which was predefined according to each patient’s daily schedule. Participants received information via SMS three times a day regarding healthy diet and exercise methods, along with general information about diabetes, hypertension and obesity. Furthermore, using the internet website, physicians could follow participant’s trends in blood glucose levels, blood pressure and body weight changes, allowing them to send individualized recommendations to patients when needed (http://kumc.drub.co.kr).”</p> <p>CONTROL: Conventional Healthcare</p> <p>“Patients in the control group visited their clinic according to their routine schedule and received the usual out-patient treatment from their physicians during the study period.”</p> |
| Outcomes | Multiple metabolic parameters were assessed after 12 weeks: |

| | |
|--------------|--|
| | Body weight, BMI and waist circumference, systolic and diastolic office blood pressure, right/left baPWV, Hba1c, fasting glucose, Homeostasis model assessment insulin resistance, total cholesterol, HDL-cholesterol, LDL-Cholesterol, Triglyceride, levels of adiponectin, hsCRP, IL-6 |
| Notes | |

| Risk of Bias | | |
|--|---------------------------|---|
| Bias | Authors' Judgement | Support for Judgement |
| Random Sequence Generation (Selection Bias) | Unclear risk | Insufficient information about the sequence generation process to permit judgement of 'Low risk' or 'High risk' |
| Allocation concealment (selection bias) | Unclear risk | Insufficient information to permit judgement of 'Low risk' or 'High risk'. |
| Selective reporting (reporting bias) | High risk | Outcomes were only compared between control and intervention group for those with a statistically significant result. |
| Other bias | Unclear risk | Insufficient information |
| Blinding of outcome assessment (detection bias) Patient outcome | Unclear risk | Insufficient information to permit judgement of 'Low risk' or 'High risk'; |
| Blinding of participants (performance bias) Patient outcome | Unclear risk | Insufficient information to permit judgement of 'Low risk' or 'High risk'; |
| Blinding of personnel (performance bias) Patient outcome | Unclear risk | Insufficient information to permit judgement of 'Low risk' or 'High risk'; |
| Incomplete outcome data (attrition bias) Patient outcome | Low risk of bias | Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias). |

| Wakefield et al., 2011 (1) and 2012 (2) | |
|--|---|
| Methods | Single-Centre Randomized Controlled Clinical Trial |
| Participants | <p>The study was conducted at the Iowa City VA Medical Centre (ICVAMC) in the United States. The target population was comprised of patients with type 2 diabetes mellitus and hypertension treated by a veteran affairs (VA) primary care provider.</p> <p>107 participants were randomized to usual care, 93 participants were randomized to the high-intensity intervention and 102 were randomized to the low-intensity intervention.</p> <p>“The inclusion criteria were coexisting diabetes and hypertension, a landline telephone in the home, receipt of primary care from the VA in the previous 12 months, and anticipation of receiving primary care for the duration of study enrolment.</p> <p>Exclusion criteria were legal blindness, residency in a long-term care facility, and diagnoses indicating dementia or psychosis.”</p> |
| Interventions | “The intervention consisted of a nurse management component and close surveillance via home telehealth. Both Intervention groups received the home- |

| | |
|-----------------|---|
| | <p>telehealth device (Viterion-Bayer Panasonic) uses a standard telephone line to enable data transmission between the patient's home and the study centre. Using the device, intervention patients entered blood pressure and blood glucose measurements and responded to standardized questions based on their group assignment. Patients then received appropriate automated responses depending on how they answered the device prompt. Correct responses were reinforced, and incorrect responses were reviewed and explained. The device automatically downloads data each night, making the patient information available for the nurses to review the next day. The device also allows individualized messages to be transmitted to subjects. Trended data on BP, BG and responses to prompts were viewed via a secure Web site by the nurse. These data enabled the nurse to efficiently provide close surveillance in order to provide earlier intervention when clinical parameters were out of control or the subject indicated through his responses to the device prompts that additional health information or support was needed. Both intervention groups received care management from a study nurse. At enrolment, the subject's primary care physician was contacted for BP and BG parameters that should trigger a call to the physician for changes in the treatment plan. Each weekday, the study nurse reviewed responses from intervention group subjects and determined whether the subject needed follow-up, additional health information, increased monitoring, compliance strategies, problem resolution facilitation, or contact with the subject's physician. "</p> <p>INTERVENTION: High-Intensity Intervention "Subjects were instructed to measure blood pressure daily and blood glucose as directed by their physicians (no change in frequency of home blood pressure monitoring). A branching disease management algorithm was programmed into the device and focused on diet, exercise, smoking cessation, foot care, advice for sick days, medications, weight management, preventive care, behaviour modification and lifestyle adjustments. Subjects received standard prompts each day and a rotation of questions and education content."</p> <p>INTERVENTION: Low-intensity group "Subject were instructed to measure BP daily and BG as directed by their physician. Subjects in this group responded to a small subset of questions from the larger set of questions used with the high-intensity group. Every day subjects in this group were asked "Have you taken all your medication as prescribed?" In addition, subjects were prompted with one additional question each day focused on diet, exercise, foot care, or medication side effects. The questions did not use the branching algorithms used for the high-intensity group, rather they used yes/no or multiple responses."</p> <p>CONTROL: Usual care "Usual care subjects scheduled follow-up appointments with the primary care clinic in the usual manner. They had access to their nurse care manager employed by the medical centre. "</p> |
| Outcomes | <p>Outcomes were assessed at 6 months (end of the intervention) and 12 months (to determine the maintenance of outcomes following completion of the intervention). The primary outcomes were: HbA1c and SBP. Secondary outcomes were Depressive symptoms measured using the Geriatric Depression Scale (GDS) and patient adherence measured on the self-reported medication taking scale for hypertension and a validated regimen adherence scale for diabetes mellitus. Secondary outcomes (primary outcomes reported in Wakefield et al. 2016). Patient adherence measured on the self-reported medication taking scale for hypertension and a validated regimen adherence scale for diabetes mellitus. Self-efficacy was measured using the Self-Efficacy to Manage Disease in General scale. This scale contains 5 items that rate the patient's confidence in managing a chronic illness using Likert-type scale responses.</p> |

| Notes | | |
|--|--------------------|--|
| Risk of Bias | | |
| Bias | Authors' Judgement | Support for Judgement |
| Random Sequence Generation (Selection Bias) | Unclear risk | Insufficient information to permit judgement of 'Low risk' or 'High risk'; |
| Allocation concealment (selection bias) | Low risk | "Group assignments were made by the study nurses using sequentially numbered, sealed, opaque envelopes prepared in advance by the project director" (p.255) |
| Selective reporting (reporting bias) | Unclear | No protocol published before publication of results. In publication of results all outcomes reported. |
| Other bias | Unclear risk | Insufficient data |
| Blinding of outcome assessment (detection bias) Patient outcome | Unclear | Insufficient information to permit judgement of 'Low risk' or 'High risk'; |
| Blinding of participants (performance bias) Patient outcome | Unclear | Insufficient information to permit judgement of 'Low risk' or 'High risk'; |
| Blinding of personnel (performance bias) Patient outcome | Unclear | Insufficient information to permit judgement of 'Low risk' or 'High risk'; |
| Incomplete outcome data (attrition bias) Patient outcome | Low risk | Insufficient information to permit judgement of 'Low risk' or 'High risk'. To account for missing data, primary analyses were performed using a multiple-imputation approach |

| Rifkin et al., 2013 | |
|----------------------------|---|
| Methods | Single-centre Randomized controlled trial (feasibility) |
| Participants | <p>Patients attending the Chronic Kidney Disease (CKD)/Hypertension clinic at the Veteran Affairs San Diego, California</p> <p>30 participants were randomized to the intervention, 15 were randomized to the control arm.</p> <p>"Inclusion criteria were stage 3 CKD (estimated glomerular filtration rate of less than 60 ml/min/1.73m²); established hypertension [(systolic blood pressure (SBP) >140 or diastolic blood pressure (DBP) >90 in-clinic or on reported home readings]; and age more than 50 years. Patients had to be community-dwelling and currently self-managing their medications.</p> <p>Exclusion criteria were the presence of a clear secondary cause for HTN (e.g. aldosterone producing tumour), or estimation by clinic physicians that the individual was within 6 months of requiring dialysis or dying from other causes."</p> |
| Interventions | <p>INTERVENTION</p> <p>"The intervention consisted of two integrated subunits: the A&D Medical UA-767PBT fully automated oscillometric BP unit (A&D Medical, San Jose, California, USA) and the home health hub (HHH). The HHH receives BP and pulse data through Bluetooth from the BP unit, and relays the data through the internet to a secure</p> |

| | |
|-----------------|--|
| | <p>website. The website allowed for viewing of BP data sorted by participant. Patients were asked to measure and record their BP at home according to their physicians' instructions; no study specific instructions were given regarding the frequency of measurement. On a weekly basis the study physicians and pharmacist met to review BP logs of each participant. If a patient had consistently above-goal readings during the prior week, one of the study physicians or pharmacists called to discuss the readings, provide counselling, or adjust medications. Additional in-person follow-up was scheduled at the discretion of the study team. The number of BP readings transmitted by the system for each participant was totalled on a monthly basis, and monthly running averages were created for each participant."</p> <p>CONTROL</p> <p>"Patients were asked to measure and record their BP at home according to their physicians' instructions; no study specific instructions were given regarding the frequency of measurement. They were told that study personnel would be checking in with them at the end of 6 months for an end-of-study visit related to BP."</p> |
| Outcomes | Outcomes reported were systolic blood pressure (mmHg), diastolic blood pressure (mmHg), Mean arterial pressure (mmHg), creatinine (mg/dl), eGFR (ml/min/1.73m ²), total number of medications, number of blood pressure medications, Morisky Medication Adherence Scale. |
| Notes | |

| Risk of Bias | | |
|--|---------------------------|---|
| Bias | Authors' Judgement | Support for Judgement |
| Random Sequence Generation (Selection Bias) | Unclear risk | Insufficient information |
| Allocation concealment (selection bias) | Low risk | "Random assignment occurred after the consent and initial enrolment interview, using opaque envelopes containing odd (intervention) or even (control) study numbers." (p.3) |
| Selective reporting (reporting bias) | High risk | No prespecified outcome parameters; no pre-published protocol or pre-specified outcomes in methods section. |
| Other bias | High risk | "Limitations of the current study include the small sample size and short duration; we cannot predict whether the intervention would be robustly effective over longer periods of time. Given our small sample, our results do not reach statistical significance for BP between groups, although we believe the magnitude of the difference we found is clinically important." |
| Blinding of outcome assessment (detection bias) Adherence measure | High risk. | No blinding for outcome assessment. |
| Blinding of outcome assessment (detection bias) Patient outcome | High risk. | No blinding for outcome assessment. |
| Blinding of participants (performance bias) | High risk. | No blinding of participants |

| | | |
|--|------------|---|
| Adherence measure | | |
| Blinding of participants (performance bias) Patient outcome | High risk. | No blinding of participants |
| Blinding of personnel (performance bias) Adherence measure | High risk. | No blinding of personnel. |
| Blinding of personnel (performance bias) Patient outcome | High risk. | No blinding of personnel. |
| Incomplete outcome data (attrition bias) Adherence measure | Low risk. | Two participants per arm (11% control arm, and 5.5% intervention arm) lost to follow-up. Otherwise complete outcome data. |
| Incomplete outcome data (attrition bias) Patient outcome | Low risk. | Two participants per arm (11% control arm, and 5.5% intervention arm) lost to follow-up. Otherwise complete outcome data. |

| | |
|--------------------------|---|
| Mira et al., 2014 | |
| Methods | Single-blind randomized controlled trial |
| Participants | <p>Patients were recruited from health centres in the health districts of Alicante and Bilbao, Spain.</p> <p>102 patients were randomized, 51 in the control group and 51 in the experimental group.</p> <p>“Inclusion criteria were multimorbid patients taking multiple medications, older than 65 years, with a Bartel score of more than 60, living in their own home, and able to manage the administration of their medication at home.</p> <p>Exclusion criteria were refusing to participate in the study or more than 90 years old.”</p> |
| Interventions | <p>INTERVENTION</p> <p>“The intervention group was composed of people who used this tool for 3 months. A tablet-based medication self-management application (ALICE) was designed to help patients to remember to take all their medications at the correct doses, distinguish between drugs to avoid confusions, avoid known potential interactions and common errors in use of the medications, and know how to properly store the medications. The application was also designed to remember doctors’ recommendations for healthy habits, such as physical exercise and diet. The tablet used was a BQ Verne Plus 3G 7-inch with an easy-to-use touch screen with a tactile screen and an iPad 2 were used. The ALICE app was designed to work with</p> |

| | |
|-----------------|---|
| | <p>personalized prescriptions and recommendations given to patients. A second function established a customized system of alerts and reminders to remind patients when to take their medications and to put into practice healthy habits (e.g. intake with meals). A third function was to enable monitoring of the level of adherence to the prescriptions and medical advice, the tablet connecting via a wireless or 3 G network with the study monitoring system. When it's time to take a medication, an alarm sounds and the patient accesses the main menu of the application. The app reports the medications the patient must take in a day and reports medicines that the patient has forgotten to take that day.”</p> <p>CONTROL “The control group was composed of participants who did not use the application.”</p> |
| Outcomes | The primary outcomes was adherence to treatment measured by the 4-item Morisky Medication Adherence Scale (MMAS-4). Further outcomes were the number of missed doses and of medication errors, the self-perceived health status, the level of glycated haemoglobin (mmol/mol), the cholesterol level and blood pressure (Systolic and diastolic). |
| Notes | |

| Risk of Bias | | |
|--|---------------------------|--|
| Bias | Authors' Judgement | Support for Judgement |
| Random Sequence Generation (Selection Bias) | Unclear | Insufficient information to permit judgement of 'Low risk' or 'High risk': „Patients were randomly assigned to the control or experimental group“ |
| Allocation concealment (selection bias) | Unclear | Insufficient information to permit judgement of 'Low risk' or 'High risk'; |
| Selective reporting (reporting bias) | Low risk | In protocol primary outcome measure was adherence (MMAS-4) and the secondary outcome measure was “safety medication use”. In published results there are also self-perceived health status, glycated haemoglobin, cholesterol and blood pressure reported. |
| Other bias | High risk | “The small number of participants and the number of months using ALICE affected our ability to detect differences between the group using the ALICE application and the control group (e.g., in relation to biomarkers) as well as our ability to generalize the results.” There is some evidence that the MMAS-4 overestimates the adherence, yielding higher rates than those obtained from pill counts.” (p.11) |
| Blinding of outcome assessment (detection bias) Adherence measure | Low risk | “To maintain the blinding and be able to link the pre and post measurements, patients were assigned codes based on their date of birth and initials.” (p. 4) |
| Blinding of outcome assessment (detection bias) Patient outcome | Low risk | “To maintain the blinding and be able to link the pre and post measurements, patients were assigned codes based on their date of birth and initials.” (p. 4) |
| Blinding of participants (performance bias) | High risk | Not blinded |

| | | |
|--|-----------|--|
| Adherence measure | | |
| Blinding of participants (performance bias) | High risk | Not blinded |
| Blinding of personnel (performance bias) | Unclear | Insufficient information to permit judgement of 'Low risk' or 'High risk'. |
| Blinding of personnel (performance bias) | Unclear | Insufficient information to permit judgement of 'Low risk' or 'High risk'. |
| Incomplete outcome data (attrition bias) | Low risk. | No loss to follow-up, no exclusion from analysis. |
| Incomplete outcome data (attrition bias) | Low risk. | No loss to follow-up, no exclusion from analysis. |

| | |
|-----------------------------|--|
| Donesky et al., 2017 | |
| Methods | Controlled, nonrandomized trial |
| Participants | <p>Patients were recruited at pulmonary rehabilitation programs in the San Francisco Bay Area and from previous research studies of COPD and heart failure.</p> <p>Seven (n=7) patients were assigned to the tele-yoga intervention and 8 (n=8) to the control intervention.</p> <p>“Inclusion criteria were (i) provider diagnosed COPD, (ii) provider permission for participation, (iii) speak English, (iv) be older than the age of 40 years, (v) have NYHA class I-III systolic or diastolic heart failure, (vi) have access to television and a broadband internet connection, (vii) have space to practice yoga at their home and (viii) be willing to have a research assistant connect videoconferencing equipment to their home television.</p> <p>Exclusion criteria were (i) hospitalization within the three months before enrolment, (ii) cognitive impairment as determined by a score of <3 on the Mini-Cog or (iii) oxygen saturation <85% on 6 liters of nasal oxygen.”</p> |
| Interventions | <p>INTERVENTION</p> <p>“Those assigned to the TeleYoga group were provided a yoga mat, automatic blood pressure cuff, oximeter, and scale. Videoconferencing equipment was installed in the homes of the intervention group participants during the baseline home visit. They were taking their own blood pressure, weight, heart rate, and oxygen saturation levels before and after each class and reported them to the TeleYoga nurse.</p> |

| | |
|-----------------|---|
| | <p>Participants were visually monitored for safety during each session by the TeleYoga nurse via the multipoint videoconferencing system interface. The nurse called each participant on the telephone before and after each TeleYoga session to assess symptoms of HF and COPD. TeleYoga classes were offered twice weekly for 8 weeks to participants in their homes using videoconferencing. The yoga intervention was provided by the same certified yoga instructor/physical therapy assistant. The yoga protocol was based on the previously tested yoga programs for COPD and HF, originally developed by a certified Iyengar yoga instructor with experience working with individuals with chronic disease. Classes began with 10 minutes of relaxation followed by ca. 35 minutes of poses and concluded with 15 minutes of meditation and relaxation. All participants could see the yoga teacher (and vice versa) and received personalized instruction but could not see each other. If participants had questions they could talk with the teacher.”</p> <p>CONTROL “Participants assigned to the attention control group received educational materials in the mail once per week for 8 weeks. The intervention nurse called each week for 15-30 minutes to discuss the educational information so as to provide an equal number of phone or mail contacts as in the intervention group. The educational materials covered the following topics: evaluating health information, problems sleeping, elder abuse, flu vaccinations, accessing information about therapy, accessing information about medications online, depression and a low sodium diet.”</p> |
| Outcomes | <p>Outcomes measured were physical function, Quality of Life, and symptoms. Physical function was defined as muscle strength and endurance. Strength was tested via upper body (biceps) and lower body (quadriceps) testing using the total number of arm curls using two-pound hand weights and chair stands completed in 30 seconds. Endurance was measured with the home-adapted 6-min walk test that measured number of feet walked within 6 minutes. Validated QOL questionnaires included the St. George’s respiratory questionnaire that is used for patients with COPD and the Kansas City Cardiomyopathy Questionnaire (KCCQ) used for measurement in heart failure patients. Symptoms of depression, dyspnoea, and insomnia were evaluated at baseline and after study completion. Depression was evaluated using the validated Personal Health Questionnaire. Dyspnoea was measured using the Dyspnea-12 questionnaire and dyspnoea and distress related to dyspnoea were measured using the modified Borg scale at the end of the 6-min walk. Sleep was measured using the General Sleep Disturbance Scale.</p> |
| Notes | |

| Risk of Bias | | |
|--|---------------------------|--|
| Bias | Authors’ Judgement | Support for Judgement |
| Random Sequence Generation (Selection Bias) | High risk | “The first seven patients were enrolled in the intervention group and the following eight in the control group” (p. 2). |
| Allocation concealment (selection bias) | High risk | “The first seven patients were enrolled in the intervention group and the following eight in the control group” (p. 2) |
| Selective reporting (reporting bias) | Low risk | All outcomes from the methods section were also reported in the results section. |
| Other bias | High risk | “The characteristics of the four participants who declined enrolment in the study could not be compared with the study participants. Reports of vital signs before and after TeleYoga sessions were not observed, and there is a possibility that they were fabricated to please investigators, although this is thought |

| | | |
|--|--------------|---|
| | | highly unlikely. The time allotment (“dose”) of the intervention and control intervention was not equal.” |
| Blinding of outcome assessment (detection bias) Patient outcome | Unclear risk | Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’; |
| Blinding of participants (performance bias) Patient outcome | Unclear risk | Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’; |
| Blinding of personnel (performance bias) Patient outcome | Unclear risk | Insufficient information to permit judgement of ‘Low risk’ or ‘High risk’; |
| Incomplete outcome data (attrition bias) Patient outcome | Low risk. | One person lost to follow-up in intervention and in control arm. Otherwise no loss to follow-up. |

| Bernocchi et al., 2017 | |
|-------------------------------|--|
| Methods | Randomized open controlled multicentre trial |
| Participants | <p>Patients were recruited consecutively from the Cardiology and Pulmonary Departments of three rehabilitation hospitals in Italy (Salvatore Maugeri Foundation IRCCS Institutes of Lumezzane and Montescano; and San Raffaele Pisana IRCCS, Rome).</p> <p>Fifty-six participants were included in the intervention group and fifty-six participants were recruited in the control group.</p> <p>“Inclusion criteria were (i) Age over 18 years, (ii) Chronic obstructive pulmonary disease (COPD) GOLD classification (classes B, C, and D) (iii) Systolic and/or diastolic heart failure (HF) New York Heart Association (NYHA) classes II, II, and IV (iv) At least one hospitalization or visit due to HF or COPD exacerbation in the previous 12 months (v) Signed informed consent</p> <p>Exclusion criteria were (i) Physical activity limitations due to noncardiac and/or pulmonary conditions (ii) Limited life expectancy (iii) Severe cognitive impairments”</p> |
| Interventions | <p>INTERVENTION</p> <p>“Patients in the intervention group received an educational intervention from a nurse tutor (NT) and a physiotherapist tutor (PT) and were followed by both during the Telereab-HBP, which lasted 4 months. The NT made a weekly structured phone call to each participant collecting information about the disease status and symptoms, offering advice regarding diet, lifestyle and medications, previously defined with the cardiologist and pulmonologist supervising the programme. Patients were provided with a pulse oximeter (GIMA, Milan, Italy), and a portable one-lead electrocardiograph (Card Guard Scientific Survival Ltd., Rehovot, Israel) for real time monitoring of vital signs. The PT designed a personalized exercise programme for each patient who were provided with mini-ergometer, pedometer and diary. The</p> |

| | |
|-----------------|---|
| | <p>number/intensity of training sessions according to patients' progress were adjusted during 4 months or in the case of problems. The "basic level" of programme consisted of 15-25 min of exercise with mini-ergometer without load and 30 minutes of callisthenic exercises, performed three times/week and free walking twice a week. The "high level" consisted of 30-45 minutes of mini-ergometer with incremental load (from 0 to 60 W), 30-40 minutes of muscle reinforcement exercises using 0.5 kg weights and pedometer-based walking, performed from 3 to 7 days/week."</p> <p>CONTROL</p> <p>"On discharge from in-hospital rehabilitation, patients in the control group received the standard care program including medications and oxygen prescription, visits from the general practitioner, and in-hospital check-ups on demand. Patients were free to conduct physical activity without any monitoring or reinforcement provided by the hospital. At study enrolment, patients were instructed in an educational session about the desirability of maintaining a healthy lifestyle and were invited to practice daily physical activity as preferred."</p> |
| Outcomes | <p>The primary outcome was exercise tolerance improvement measured by difference in the meters walked in the 6MWT. The secondary outcomes were: (1) reduction of hospitalizations for cardiovascular and/or respiratory diseases, (2) reduction of hospitalizations for all causes, (3) improvement of QoL in the MLHFQ and the CAT, (4) reduction in impairment/disability evaluated by the Barthel Index, (5) reduction in dyspnoea evaluated by the MRC scale, (6) reduction in dyspnoea and fatigue at rest evaluated by the Borg scale, (7) improvement of physical activity profile evaluated by the PASE questionnaire and daily steps reported by patients, and (8) improvement of oxygenation (PaO₂/FiO₂). In the intervention group only, it was also evaluated: (1) adherence to at least 70 % of the prescribed rehabilitation sessions, (2) qualitative evaluation of patients' compliance to the rehabilitation program, (3) use of health services, calculated as total and per-person number of PT and NT scheduled and unscheduled calls, total and per-person number of PT home visits, total and per-person number of educational sessions, and total and per-person time spent by the PT and NT in the study.</p> |
| Notes | |

| Risk of Bias | | |
|--|---------------------------|---|
| Bias | Authors' Judgement | Support for Judgement |
| Random Sequence Generation (Selection Bias) | Low risk | A computer-generated table to allocate patients in fixed blocks of 4. |
| Allocation concealment (selection bias) | Low risk | In order to prevent selection bias, the allocation sequence was concealed from the investigators enrolling and assessing patients, in sequentially numbered, opaque, sealed envelopes. (Study Protocol, p. 2) |
| Selective reporting (reporting bias) | Low risk | All outcomes from the protocol were reported in the final article |
| Other bias | Low risk | - |
| Blinding of outcome assessment (detection bias) Adherence measure | Low risk | Due to the nature of the intervention, neither the patients nor the physicians were blinded to patients' group allocation; however, outcome assessors and data analysts will be blinded. (Study Protocol p.3) |
| Blinding of outcome assessment (detection bias) Patient outcome | Low risk | Due to the nature of the intervention, neither the patients nor the physicians were blinded to patients' group allocation; however, outcome assessors and data analysts will be blinded. (Study Protocol p.3) |

| | | |
|--|-----------|--|
| Blinding of participants (performance bias) Adherence measure | High risk | Due to the nature of the intervention, neither the patients nor the physicians were blinded to patients' group allocation; however, outcome assessors and data analysts will be blinded. (Study Protocol p.3) |
| Blinding of participants (performance bias) Patient outcome | High risk | Due to the nature of the intervention, neither the patients nor the physicians were blinded to patients' group allocation; however, outcome assessors and data analysts will be blinded. (Study Protocol p.3) |
| Blinding of personnel (performance bias) Adherence measure | High risk | Due to the nature of the intervention, neither the patients nor the physicians were blinded to patients' group allocation; however, outcome assessors and data analysts will be blinded. (Study Protocol p.3) |
| Blinding of personnel (performance bias) Patient outcome | High risk | Due to the nature of the intervention, neither the patients nor the physicians were blinded to patients' group allocation; however, outcome assessors and data analysts will be blinded. (Study Protocol p.3) |
| Incomplete outcome data (attrition bias) Adherence measure | High risk | "Overall, 11 (20%) patients in the intervention group were lost to follow-up, and 21 (37.5%) in the control group (p=0.0365)" (p. 3) |
| Incomplete outcome data (attrition bias) Patient outcome | High risk | "Overall, 11 (20%) patients in the intervention group were lost to follow-up, and 21 (37.5%) in the control group (p=0.0365)" (p. 3) |