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Lifestyle Walking Intervention in Patients With Heart Failure With Reduced Ejection Fraction: The WATCHFUL Trial

MUDr. Michal Širanec

2nd Department of Medicine – Department of Cardiovascular Medicine
First Faculty of Medicine, Charles University in Prague and General University Hospital in Prague

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Circulation

Lifestyle Walking Intervention in Patients With Heart Failure With Reduced Ejection Fraction: The WATCHFUL Trial

Tomas Vetrovsky, Michal Siranec, Tereza Frybova, Iulian Gant, Iveta Svobodova, Ales Linhart, Jiri Parenica, Marie Miklikova, Lenka Sujakova, David Pospisil, Radek Pelouch, Daniela Odrazkova, Petr Parizek, Jan Precek, Martin Hutyra, Milos Taborsky, Jiri Vesely, Martin Griva, Miroslav Semerad, Vaclav Bunc, Karolina Hrabcova, Adela Vojkuvkova, Michal Svoboda and Jan Belohlavek

See fewer authors

and on behalf of the WATCHFUL Investigators

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Physical activity in heart failure

- Physical activity (PA) and exercise - for all HFrEF patients to improve exercise capacity, QoL, and reduce HF hospitalization
- Optimal strategy to increase PA remains elusive
- Traditional supervised, structured exercise-based cardiac RHB programs
  - availability and accessibility are limited; lower adherence rates
  - short-term impact
- Lifestyle PA interventions as an alternative approach

McDonagh TA, et al. Eur Heart J. 2021 Sep 21;42(36):3599-3726.; Piepoli MF. Et al. Eur J Heart Fail. 2015 Jun;17(6):631-8.; Bjarnason-Wehrens B. et al., Eur J Cardiovasc Prev Rehabil. 2010 Aug;17:410-8.

Objectives

- to determine if a 6-month lifestyle walking intervention combining self-monitoring and regular phone counseling improves functional capacity assessed by the six-minute walk test (6MWT) in stable patients with HFrEF compared to usual care

- **Primary outcome**
  - the difference in the distance walked during the 6MWT at 6 months

- **Secondary outcomes**
  - daily step count and minutes of moderate-to-vigorous physical activity
  - NT-proBNP and hsCRP biomarkers, left ventricular ejection fraction, anthropometric measures (BMI, waist and hip circumference), depression score, self-efficacy, quality of life, survival risk score

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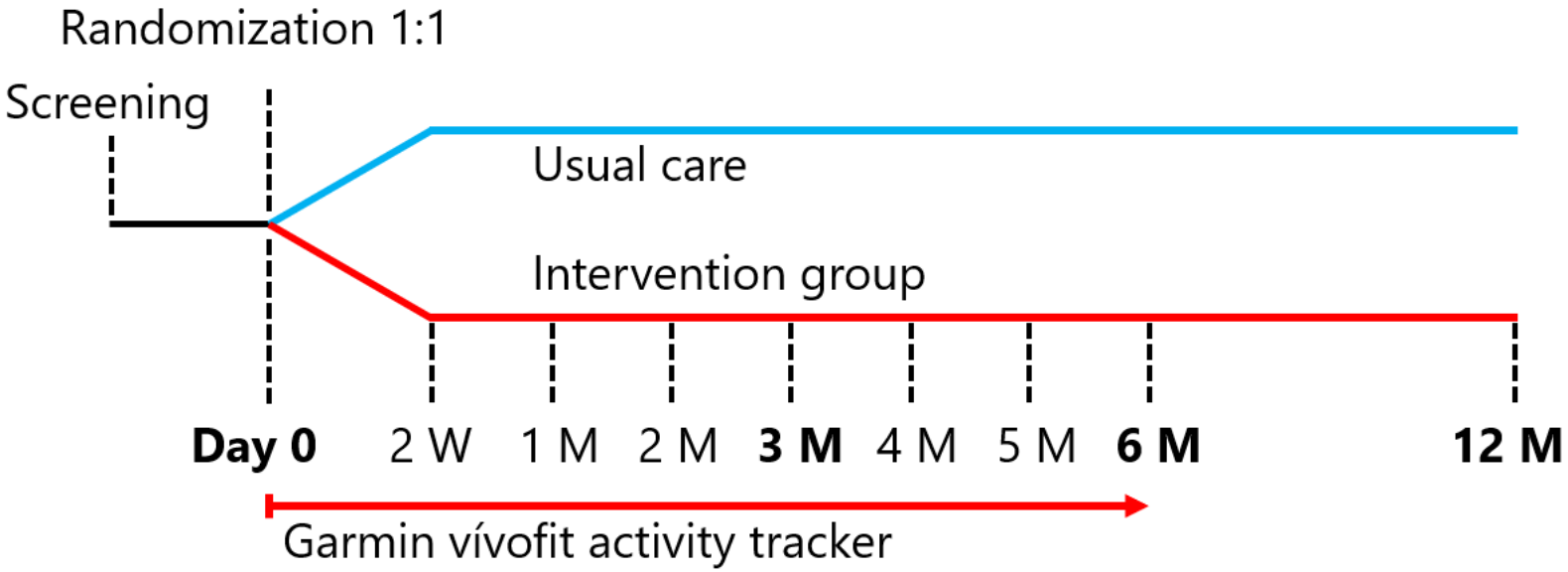
Study design

➢ 6-month, multicenter, parallel-group, randomized, controlled trial

Inclusion criteria
- Stable HFrEF
- LVEF < 40%
- NYHA class II or III
- Age ≥18 years

Exclusion criteria
- 6MWT distance > 450 m or unable to complete the test
- decompensated heart failure, uncontrolled arrhythmia, effort-induced angina, symptomatic aortic stenosis, persistent hypotension, recent events (<3 months) such as MI, PCI, ICD/CRT implantation, ICD shocks



Intention-to-treat principle

Phone counselling:
2 W, 1 M, 2 M, 4 M, 5 M
Clinical visits:
baseline, 3 M, 6 M, 12 M
MVPA by Actigraph wGT3X-BT:
baseline, 6 M, 12 M

Vetrovsky T, Siranec M, et al. Circulation. 2023 Nov 13. doi: 10.1161/CIRCULATIONAHA.123.067395.; MVPA, moderate-to-vigorous physical activity

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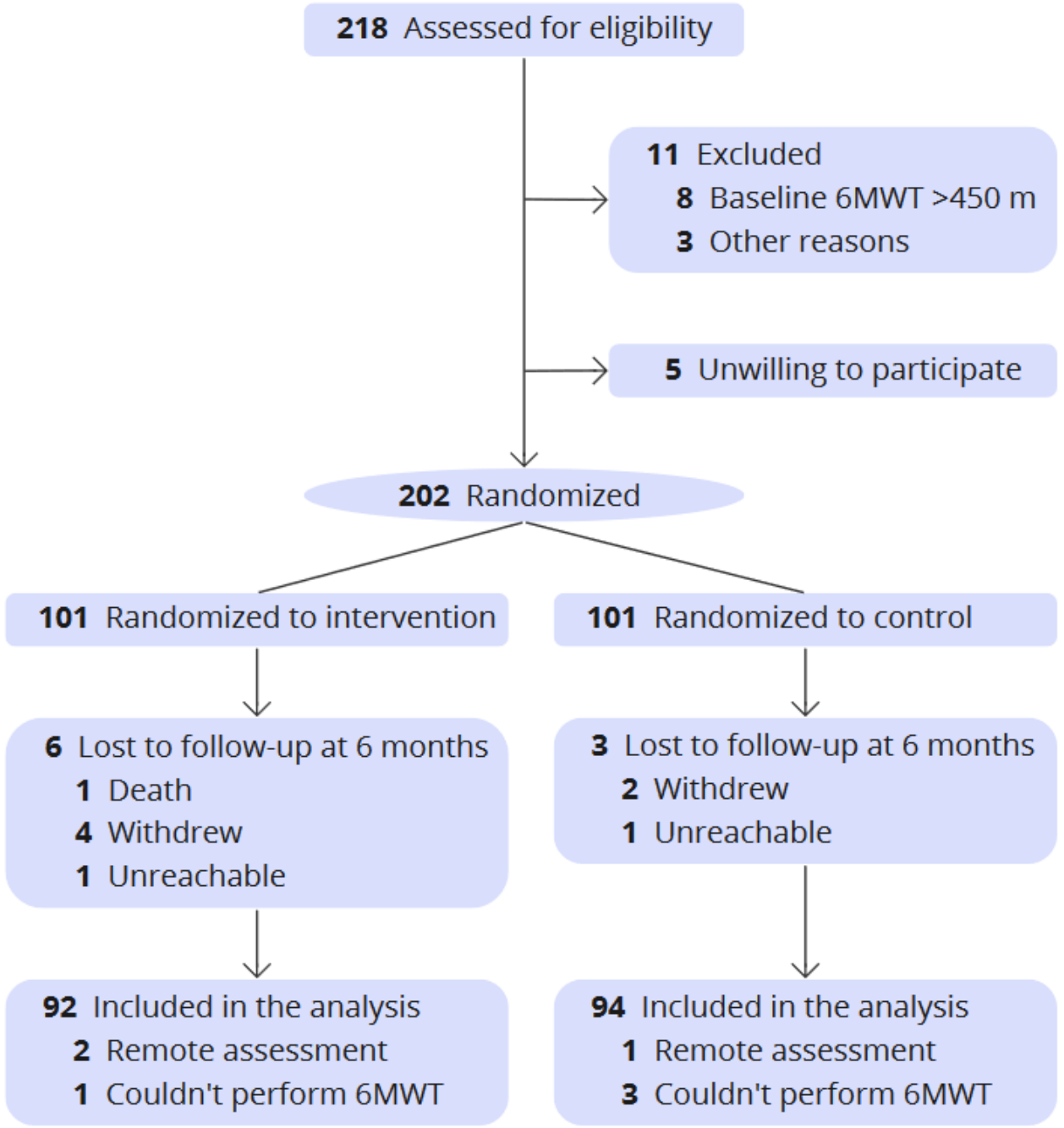
Study timeline & patient disposition

- August 2018: first patient enrolled
- June 2023: last patient 6M visit

- 202 randomized patients
- six clinical centers in the Czech Republic



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Intervention group

- 6-month behavioral lifestyle intervention aimed at integrating additional physical activity (walking) into daily routines
  - **behavior change techniques**
  - **self-monitoring** of daily step count by a wrist-worn Garmin vívofit activity tracker (from baseline to 6 months)
  - **recording** daily steps in a paper diary
  - **goalsetting** - incremental increase of at least 3,000 steps above baseline gradually over 6 weeks or a more achievable goal
  - **phone counseling sessions** - step goals, action plans, barriers, feedback on progress

GARMIN **vívo**fit
www.garmin.com

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Baseline characteristics

CHARACTERISTIC	ALL PATIENTS (N = 202)	INTERVENTION GROUP (N = 101)	CONTROL GROUP (N = 101)
Age at time of randomization, years, median (IQR)	65.0 (56.0–72.8)	65.0 (56.0–72.0)	65.0 (56.0–73.0)
Sex, n (%)			
Male	156 (77.2%)	78 (77.2%)	78 (77.2%)
Female	46 (22.8%)	23 (22.8%)	23 (22.8%)
Average daily step count, median (IQR)	5,071 (3,148–7,357)	4,851 (3,049–7,357)	5,343 (3,168–7,265)
Average daily minutes of MVPA, median (IQR)	10.9 (3.2–27.3)	11.1 (3.6–27.3)	10.2 (2.6–27.7)
Distance walked during the 6MWT, m, median (IQR)	385.0 (329.0–425.0)	390.0 (325.0–430.0)	371.0 (329.8–420.0)
Body mass index, kg/m^2, median (IQR)	29.0 (25.8–33.4)	29.7 (26.0–33.6)	28.5 (25.1–33.0)
Waist circumference, cm, median (IQR)	107.0 (97.0–118.0)	109.0 (99.0–118.0)	104.0 (96.8–117.2)
NYHA class, n (%)			
II	183 (90.6%)	92 (91.1%)	91 (90.1%)
III	19 (9.4%)	9 (8.9%)	10 (9.9%)
Left ventricular ejection fraction, %, median (IQR)	32.5 (25.0–36.8)	34.0 (26.0–37.0)	32.0 (25.0–36.0)
NT-proBNP, ng/L, median (IQR)	597.0 (287.0–1,483.0)	597.0 (276.0–1,483.0)	613.5 (293.5–1,480.0)

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Baseline characteristics

CHARACTERISTIC	ALL PATIENTS (N = 202)	INTERVENTION GROUP (N = 101)	CONTROL GROUP (N = 101)
Ischemic heart disease, n (%)			
Yes	121 (59.9%)	67 (66.3%)	54 (53.5%)
No	81 (40.1%)	34 (33.7%)	47 (46.5%)
Device therapy, n (%)			
ICD or CRT-D	114 (56.4%)	57 (56.4%)	57 (56.4%)
CRT-P or CRT-D	52 (25.7%)	31 (30.7%)	21 (20.8%)
Medication, n (%)			
ß blocker	195 (96.5%)	99 (98%)	96 (95%)
ARNI	114 (56.4%)	58 (57.4%)	56 (55.4%)
ACEi	63 (31.2%)	32 (31.7%)	31 (30.7%)
ARB	16 (7.9%)	8 (7.9%)	8 (7.9%)
MRA	159 (78.7%)	78 (77.2%)	81 (80.2%)
SGLT2i	37 (18.3%)	17 (16.8%)	20 (19.8%)
Loop diuretics	160 (79.2%)	77 (76.2%)	83 (82.2%)

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Primary outcome

- the difference in the distance walked during the 6MWT at 6 months

ANALYSIS (NUMBER OF PATIENTS INCLUDED IN THE ANALYSIS)	CHANGE IN INTERVENTION GROUP*, MEAN (95% CI)	CHANGE IN CONTROL GROUP*, MEAN (95% CI)	ADJUSTED BETWEEN-GROUP DIFFERENCE (95% CI)	P-VALUE
Intention-to-treat analysis of the complete cases (n = 186)	35.5 (22.7; 48.3)	28.8 (18.6; 39.0)	7.4 (-8.0; 22.7)	0.345
Intention-to-treat analysis following the imputation of missing cases (n = 202)	35.2 (23.5; 47.0)	26.9 (17.2; 36.5)	8.7 (-5.6; 22.9)	0.231
Per-protocol analysis (n = 137)	37.1 (21.3; 52.9)	30.1 (18.9; 41.2)	5.7 (-12.6; 24.0)	0.539

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Subgroup analyses of the primary outcome

		Adjusted difference between groups (95% CI)	P-value for interaction
COVID-19 pandemic	before the onset (n = 49)	19.1 (-9.1; 47.2)	0.270
	after the onset (n = 137)	2.7 (-15.3; 20.8)	
Baseline 6MWT	< median (n = 92)	-0.5 (-25.1; 24.0)	0.264
	≥ median (n = 94)	17.5 (-2.5; 37.4)	
Baseline daily step count	< median (n = 73)	0.8 (-28.4; 29.9)	0.343
	≥ median (n = 76)	21.1 (-2.3; 44.4)	
Age	< median (n = 92)	16.0 (-6.2; 38.2)	0.214
	≥ median (n = 94)	-3.4 (-24.8; 18.1)	
Sex	male (n = 143)	7.5 (-10.6; 25.5)	0.979
	female (n = 43)	6.0 (-25.2; 37.2)	
NYHA class	II (n = 169)	4.8 (-11.7; 21.4)	0.326
	III (n = 17)	23.9 (-22.2; 70.1)	
Body mass index	<30 kg/m² (n = 106)	13.2 (-6.0; 32.4)	0.536
	≥30 kg/m² (n = 80)	2.9 (-22.4; 28.1)	
Baseline NT-proBNP	< median (n = 90)	18.1 (-0.9; 37.2)	0.180
	≥ median (n = 96)	-3.1 (-26.9; 20.7)	
Baseline MAGGIC score	< median (n = 81)	12.9 (-14.3; 40.1)	0.434
	≥ median (n = 104)	1.5 (-18.0; 21.1)	

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Secondary outcomes

OUTCOME (NUMBER OF PATIENTS WITH COMPLETE DATA)	CHANGE IN INTERVENTION GROUP, MEAN (95% CI)	CHANGE IN CONTROL GROUP, MEAN (95% CI)	ADJUSTED BETWEEN-GROUP DIFFERENCE (95% CI)
Average daily step count (n = 131)	790 (332; 1,247)	-667 (-1,183; -152)	1420 (749; 2,091)
Average daily minutes of MVPA (n = 131)	4.9 (1.0; 8.7)	-3.1 (-6.8; 0.6)	8.2 (3.0; 13.3)
NT-proBNP, ng/L (n = 190)	114 (-370; 598)	-220 (-516; 75)	349 (-193; 892)
hsCRP, mg/L (n = 126)	1.7 (-0.9; 4.2)	-0.3 (-2.2; 1.7)	2.1 (-1.0; 5.1)
LVEF, % (n=189)	3.9 (2.5; 5.4)	3.7 (2.4; 5.0)	0.3 (-1.5; 2.2)
Weight, kg (n=193)	0.1 (-0.7; 1.0)	1.1 (0.3; 1.9)	-1.0 (-2.1; 0.1)
Waist circumference, cm (n=190)	-0.3 (-1.2; 0.5)	1.8 (-0.5; 4.2)	-1.5 (-3.7; 0.8)
Hip circumference, cm (n=190)	0.0 (-1.3; 1.2)	1.9 (-0.4; 4.1)	-0.9 (-3.1; 1.3)
MAGGIC risk score (n = 189)	-0.5 (-1.1; 0.0)	-1.1 (-1.7; -0.5)	0.4 (-0.4; 1.2)

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Secondary outcomes

OUTCOME (NUMBER OF PATIENTS WITH COMPLETE DATA)	CHANGE IN INTERVENTION GROUP, MEAN (95% CI)	CHANGE IN CONTROL GROUP, MEAN (95% CI)	ADJUSTED BETWEEN-GROUP DIFFERENCE (95% CI)
BDI-II (n=177)	-0.7 (-1.6; 0.1)	0.1 (-0.8; 1.0)	-0.8 (-1.9; 0.4)
SF-36: Physical functioning (n=177)	1.3 (-1.3; 4.0)	0.2 (-2.9; 3.3)	1.3 (-2.5; 5.2)
SF-36: Role-Physical (n=177)	3.5 (-4.0; 10.9)	-4.7 (-12.4; 3.0)	8.3 (-1.3; 17.8)
SF-36: Bodily pain (n=177)	-4.1 (-10.0; 1.8)	0.3 (-3.4; 4.0)	-4.9 (-11.0; 1.2)
SF-36: General health (n=177)	6.3 (3.2; 9.4)	1.3 (-2.0; 4.5)	4.5 (0.7; 8.4)
SF-36: Vitality (n=177)	2.6 (-0.2; 5.3)	-0.5 (-3.3; 2.2)	2.4 (-1.3; 6.0)
SF-36: Social functioning (n=177)	-1.2 (-5.6; 3.3)	-1.8 (-5.7; 2.1)	0.5 (-4.9; 5.9)
SF-36: Role-Emotional (n=177)	8.9 (0.7; 17.1)	0.7 (-7.3; 8.8)	4.3 (-5.0; 13.7)
SF-36: Mental health (n=177)	-1.2 (-4.2; 1.8)	-1.6 (-3.9; 0.6)	0.8 (-2.7; 4.3)
GSE (n=177)	0.2 (-1.0; 1.3)	-0.2 (-1.7; 1.3)	0.5 (-1.1; 2.1)

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Summary of results

- 218 screened patients, 202 randomized (65 years; 22.8% female; 90.6% NYHA II; left ventricular ejection fraction 32.5%; 6MWT 385m; 5071 steps/day; 10.9 minutes of MVPA per day)

- no between-group differences for the 6MWT at 6 months (7.4 m, 95% CI -8.0 to 22.7, p=0.345, N=186)
- increased average daily step count by 1420 (95% CI: 749; 2091) and daily minutes of MVPA by 8.2 (95% CI: 3.0; 13.3) in the intervention group
- no between-group differences for any other secondary outcomes

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Safety

ADVERSE EVENT CATEGORY	ALL PATIENTS (N = 202)	INTERVENTION GROUP (N = 101)	CONTROL GROUP (N = 101)
Hospitalization for heart failure	4	1	3
Visit to the emergency room for heart failure	1	0	1
Increase in diuretic dose	4	1	3
Other CV events including hospitalizations for CV reasons	13	5	8
Non-CV events including hospitalizations for non-CV reasons	9	8	1
ICD discharge	6	4	2
Fall, injury	2	0	2
Infection	9	5	4
Others	3	2	1
Death	1	1*	0
Total	52†	27	25

*The only death was for non-CV reason. †In total, 52 adverse events were recorded in 42 patients.

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Conclusions

- lifestyle walking intervention combining self-monitoring with an activity tracker and phone counseling in HFrEF patients increased daily step count by about 25%
- it failed to demonstrate a corresponding improvement in functional capacity
- further research is needed to understand the disconnect between increased physical activity and functional outcomes
- comprehensive approach is needed

  exercise-based rehabilitation with simple lifestyle PA interventions, utilizing tools (activity trackers, mobile apps) to support long-term behavioral change and enhance health outcomes for HFrEF patients

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The WATCHFUL study team

- *Investigators:* Tomáš Větrovský[1]; Michal Širanec[2]; Jan Bělohlávek[2]; Iveta Svobodová[2]; Aleš Linhart[2]; Jiří Parenica[3]; Marie Miklíková[3]; Lenka Šujaková[3]; David Pospíšil[3]; Radek Pelouch[4]; Daniela Odrážková[4]; Petr Pařízek[4]; Jan Přeček[5]; Martin Hutyra[5]; Miloš Táborský[5]; Jiří Veselý[6]; Martin Gřiva[7]; Jiří Šťastný[7]; Miroslav Semerád[1]; Václav Bunc[1]
- *Study nurses and coordinators:* Tereza Frýbová[2]; Iulian Gant[2]; Markéta Křečková[2]; Alena Bláhová[2]; Petra Zavadilová[2]; Dana Janíková; Monika Menšíková[4]; Ivana Sílová[6]
- *Statisticians:* Karolína Hrabcová[8]; Adéla Vojkůvková[8]; Michal Svoboda[8]

- [1] Faculty of Physical Education and Sport, Charles University, Prague
- [2] 2nd Department of Medicine – Department of Cardiovascular Medicine, First Faculty of Medicine, Charles University and General University Hospital in Prague
- [3]Department of Internal Medicine and Cardiology, University Hospital Brno and Faculty of Medicine of Masaryk University, Brno
- [4]1st Department of Internal Medicine – Cardioangiology, Faculty of Medicine in Hradec Kralove, Charles University in Prague and University Hospital Hradec Kralove
- [5] Department of Internal Medicine I - Cardiology, University Hospital Olomouc
- [6] Edumed s.r.o., Broumov and Faculty of Medicine in Hradec Kralove, Charles University, Prague
- [7] Department of Cardiology, Tomas Bata Regional Hospital, Zlin
- [8] Institute of Biostatistics and Analyses, Ltd., Brno