Virtual Rehabilitation in Long-COVID: A Randomized Controlled Trial

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Background & Objectives

- Following a COVID-19 infection, numerous patients have reported over 200 persistent and disabling symptoms such as mobility issues, fatigue, brain fog, etc.
- There is a paucity of randomized controlled trials (RCT) focusing on rehabilitation for individuals with long COVID.
- Given the diverse range of symptoms in these individuals, questions persist regarding whether **symptom-based exercise** could improve functional mobility among other health outcomes. Moreover, the adverse events (AE) occurring with the intervention with fluctuating symptoms over time have yet to be investigated.

Objective: To investigate whether an 8-week virtual rehabilitation program improves functional mobility and symptoms compared to usual care in individuals with long COVID.

Methods

- Prospective, multicentered, assessor-blind RCT.
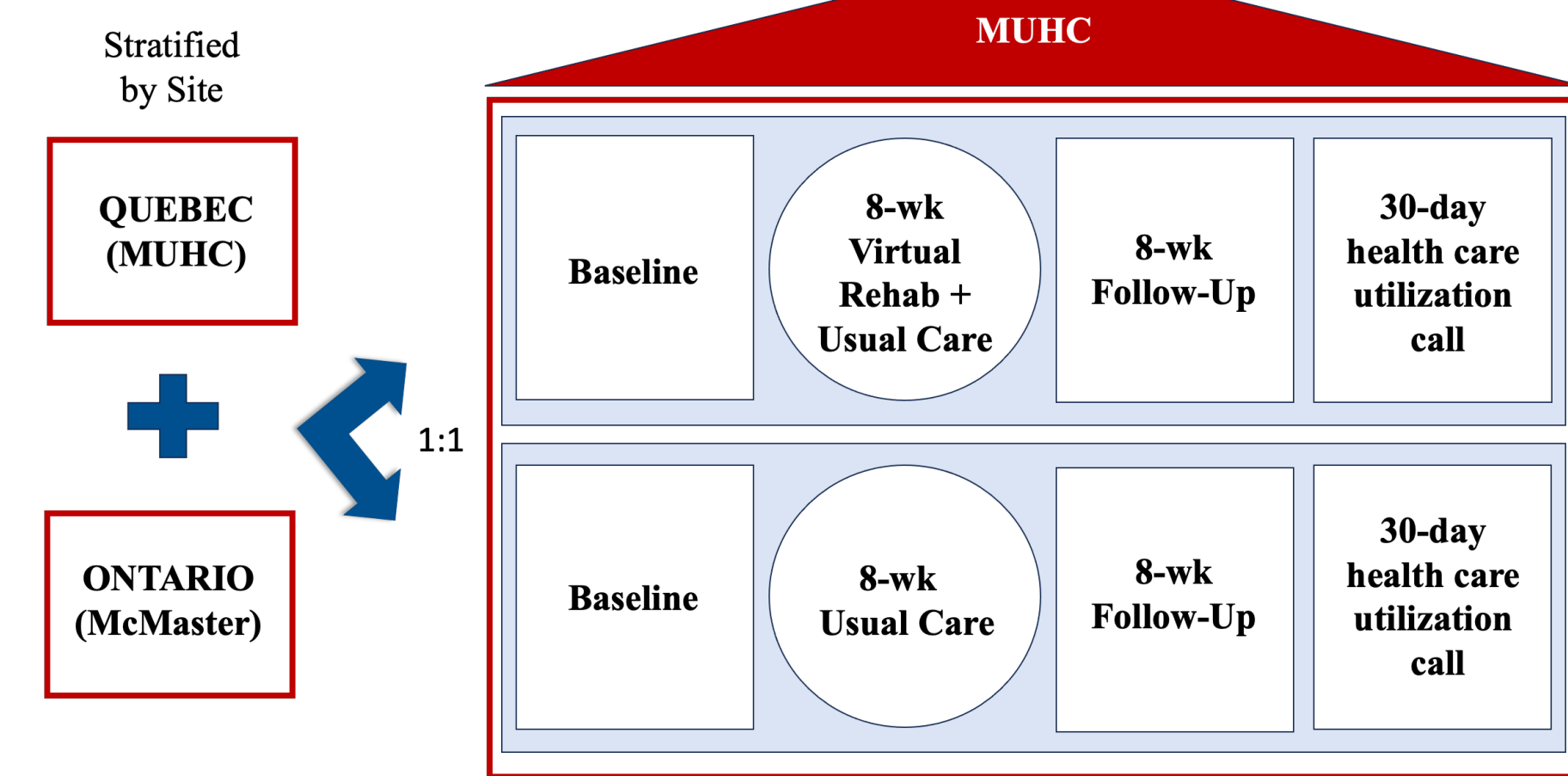
- **Usual Care:** a set of written generic instructions guiding them on how to manage their symptoms and safely engage in physical activity.

Intervention: aerobic, upper and lower limb strengthening, flexibility

| Week	Supervised sessions (40 min)	Independent sessions	
1-2	3 sessions/wk	0 sessions/wk	Educational sessions (10 min/session)
3-4	2 sessions/wk	1 session/wk	
5-8	1 session/wk	2 sessions/wk	

	Educational Topics
Week 1	Goal setting and breathing management during exercise and ADLs
Week 2	Dealing with physical fatigue, post-exertional malaise, energy conservation techniques
Week 3	Posture training and injury prevention
Week 4	Dealing with cough (coughing techniques)
Week 5	Sleep hygiene, dealing with brain fog, mental fatigue
Week 6	Nutrition
Week 7	Dealing with stress and anxiety. Impact of LC into work/social life, include information on PTSD
Week 8	Review of goal setting and improving social outlook (return to work, social isolation and loneliness)

Primary outcome: AM-PAC mobility scale.

Secondary outcomes: One minute sit-to-stand (1MSTS), Timed-up and go (TUG), Transition dyspnea index (TDI), Fatigue Visual Analog Scale, Quality of life questionnaire (SF-12), Hospital anxiety and depression scale (HADS), Health Status (EQ-5D-5L), De-Paul Symptom Questionnaire, Impact of Event Scale – Revised (IES-R), and adverse events (AEs).

Results
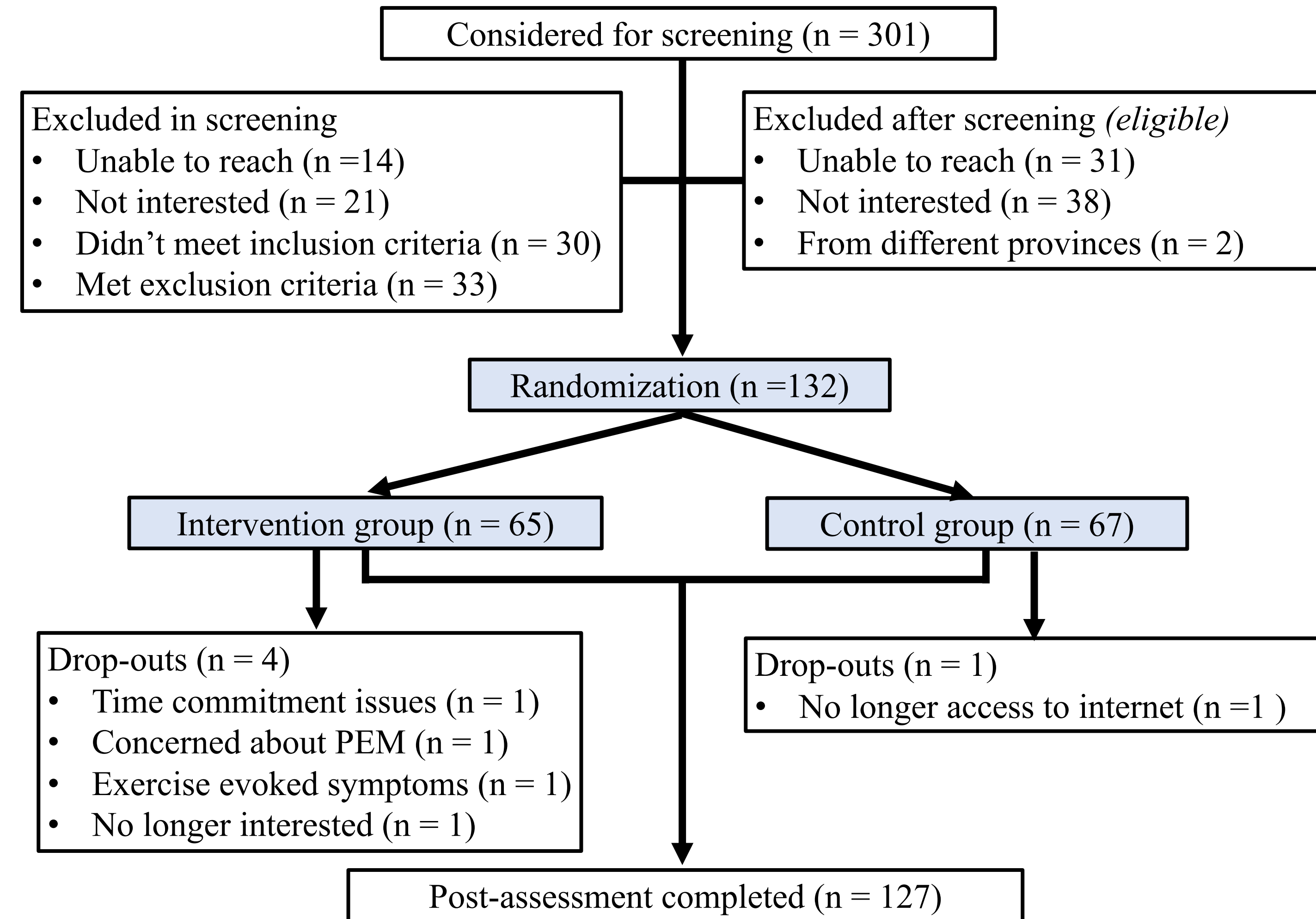
Demographics	All	Control	Intervention	P-value
Age (years)	48.0 ± 11.8	48.0 ± 11.7	57 ± 87.7	0.988
Sex, n(%)	99 (75.0)	53 (71.9)	46 (70.8)	0.269
BMI kg/m^2	31.3 ± 17.0	33.4 ± 22.2	29.2 ± 9.2	0.776
Covid frequency once, n(%)	85 (69.1)	43 (69.4)	42 (68.9)	1.000
Not hospitalized due to COVID, n(%)	103 (78.0)	52 (77.6)	51 (78.5)	0.906
Supplemental O2, n(%)	6 (4.5)	6 (9.0)	0 (0)	0.028*
Current Level of Activity, seldom active, n(%)	103 (78.0)	53 (79.1)	50 (76.9)	0.762
PEM (sum all the score) (0-5)	3.7 ± 1.6	3.7 ± 1.6	3.5 ± 1.5	0.349

PEM = post-exertional malaise

- In the intervention group, a total of 87 adverse events were reported among 47 participants:

Causality related to intervention	System	Grade	Resolved/ Ongoing
Definitely related =26 (n = 17)	Musculoskeletal=18 (n = 12)	**Mild = 27 (n = 24)**	Resolved = 71
Probably or Possibly related = 22 (n = 20)	Respiratory = 15 (n = 12)	**Mod. = 58 (n=32)**	Ongoing = 15
Not related = 39 (n = 29)	Cardiovascular = 4 (n = 4)	Severe = (n = 2)	Withdrawal = 1
	Multisystem = 16 (n = 10)		
	Gastrointestinal = 3 (n = 3)		
	Involving PEM = 22 (n = 18)		
	Other = 9 (n = 8)		

Partners

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Outcomes	Control	Intervention	
	Change Pre- to Post-Intervention	Change Pre- to Post-Intervention	Comparing the Change P-value
AM-PAC mobility	1.5 (0.0, 2.9)	2.6 (0.8, 4.4)	0.323
1MSTS	2.4 (0.9, 4.0)	3.7 (2.3, 5.2)	0.232
TUG	-0.7 (-1.3,- 0.0)	-0.4 (-1.0, 0.1)	0.651
SF-12 Mental (0-100)	3.2 (0.7, 5.8)	6.4 (3.9, 8.9)	0.087
SF-12 Physical (0-100)	0.8 (-1.3, 2.9)	2.5 (0.2, 4.8)	0.283
EQ-5D-5L Mobility (0-5)	-0.1 (-0.3, 0.2)	-0.3 (-0.5, -0.1)	0.174
EQ-5D-5L Self-Care (0-5)	0.1 (-0.1, 0.2)	0.0 (-0.2, 0.2)	0.731
EQ-5D-5L Usual Activities (0-5)	-0.2 (-0.5, -0.0)	-0.2 (-0.5, 0.0)	0.945
EQ-5D-5L Pain/Discomfort (0-5)	-0.1 (-0.3, 0.1)	-0.3 (-0.6, -0.1)	0.152
EQ/5D/5L Anxiety/Depression (0-5)	-0.1 (-0.3, 0.2)	-0.3 (-0.5, -0.0)	0.195
EQ-5D-5L VAS (0-100)	3.5 (-0.9, 7.8)	10.3 (5.4, 15.1)	0.040*
VAS Fatigue (0-10)	-0.9 (-1.4, -0.4)	-1.7 (-2.4, -1.1)	0.054
HADS – Anxiety (0-21)	0.1 (-0.7, 0.9)	-1.2 (-2.0, -0.5)	0.015*
HADS – Depression (0-21)	-0.7 (-1.6, 0.2)	-1.7 (-2.7, -0.7)	0.136
PEM Sum of all scores (0-5)	-1.6 (-2.3, -0.9)	-1.8 (-2.5, -1.2)	0.618
TDI Functional Score	0.4 ± 0.8	0.8 ± 1.0	0.011*
TDI Magnitude Score	0.6 ± 1.3	0.8 ± 1.5	0.157
TDI Effort Score	0.5 ± 1.4	1.1 ± 1.5	0.006*
TDI Total Score	1.5 ± 3.0	2.7 ± 3.6	0.007*
Health Care Utilization – Doctor Visits, n(%)	30 (46.2)	34 (55.7)	0.292
Health Care Utilization – ER Visits, n(%)	3 (4.6)	1 (1.6)	0.620
Health Care Utilization – Hospitalization, n(%)	1 (1.5)	1 (1.6)	1.000

Per-Protocol Analysis
- A per-protocol analysis was conducted, **removing 25 participants** in the intervention group who did not progress the training (in terms of intensity, duration, time or type of exercise).
- No difference in baseline characteristics between controls and intervention group who progressed the training.
- Health Care Utilization: **higher number of doctor visits in the group who did not progress** (16 (44.4) vs. 19 (78.2), p = 0.033.
- Compared to controls, there was statistically significant improvement in **AM-PAC mobility, Dyspnea (TDI), 1MSTS, SF-12 Mental Score, EQ-5D-5L VAS, VAS Fatigue, HADS Anxiety and Depression, and PEM** in the group that was able to progress the training.

Conclusion

An 8-week virtual rehabilitation program improved dyspnea, quality of life and anxiety in individuals with long COVID. Among those who were able to advance the exercise program, improvements were also seen in mobility, dyspnea, perceived health, fatigue, anxiety, depression, and post-exertional malaise. AEs were common but mild or moderate.