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Short communication

The effectiveness of pulmonary rehabilitation for Post-COVID symptoms: A rapid review of the literature

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ABSTRACT

Background: Multi-disciplinary rehabilitation is recommended for individuals with post-acute sequelae of COVID-19 infection (i.e., symptoms 3–4 weeks after acute infection). There are emerging reports of use of pulmonary rehabilitation (PR) in the post-acute stages of COVID-19, however the appropriateness of PR for managing post-COVID symptoms remains unclear. To offer practical guidance with regards to post-COVID PR, a greater understanding of the clinical effectiveness literature is required.

Methods: A rapid review of the published literature was completed. An electronic database search of the literature published between July 1, 2020 and June 1, 2021 was performed in MEDLINE, Pubmed, and EMBASE. Primary studies evaluating the clinical effectiveness of PR for individuals with post-COVID symptoms were included.

Results: Nine studies evaluating the effectiveness of PR were identified; most were small, experimental or quasi-experimental studies, including 1 RCT, and were primarily of low quality. After attending PR, all studies reported improvements in exercise capacity, pulmonary function, and/or quality of life for individuals with post-COVID symptoms who had been hospitalized for their acute COVID-19 infection. Few studies evaluated changes in post-COVID symptom severity or frequency and, of these, improvements in dyspnea, fatigue, anxiety and depression were observed following PR. Further, no studies evaluated non-hospitalized patients or long-term outcomes beyond 3 months after initiating PR.

Conclusions: With limited high-quality evidence, any recommendations or practical guidance for PR programmes for those with post-COVID symptoms should consider factors such as feasibility, current PR capacity, and resource constraints.

1. Introduction

The SARS-CoV-2 coronavirus (COVID-19) has resulted in unparalleled morbidity, mortality [1], and there is evolving evidence that a notable proportion of COVID-19 survivors experience residual and long-term effects [2]. Data published to-date indicate that symptoms appearing 3–4 weeks after acute COVID-19 infection can include dyspnea, fatigue, exercise intolerance, and worsened health-related quality of life (HRQL) [2–4].

To manage these post-acute sequelae of SARS-CoV-2 [5], herein referred to as post-COVID symptoms, groups such as the World Health Organization recommend multi-disciplinary rehabilitation. Given that acute COVID-19 frequently includes respiratory complications, and the prevalence of post-COVID respiratory symptoms [3,4], many suggest that participation in a pulmonary rehabilitation (PR) programme may be appropriate for COVID-19 survivors [5]. To support the development of practical guidance for post-COVID PR, a rapid literature review was completed to determine the clinical effectiveness of PR for individuals with post-COVID symptoms.

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Table 1
Characteristics of included studies.

Author (Year) Country	Study Design	Participants, N	Participant Characteristics			Acute COVID-19 History			Post-COVID conditions, n (%)
			Age, mean years (SD)	Female, n (%)	Pre-existing comorbidities, n (%)	Hospitalized, n (%)	ICU, n (%)	Complications, n (%)	
Bertacchini (2021)Italy	Case series	8	67.5 (10.7)	4 (50)	0	8 (100)	*Mechanical ventilation* n = 8 (100)	Pulmonary embolism n = 2 (25)	NR
Betschart (2021) Switzerland	Feasibility pilot study	12	Median: 61 (range: 26–84)	4 (33)	Cardiovascular disease: n = 6 (50); Arterial hypertonia: n = 3 (25); Chronic renal disease: n = 5 (42); Chronic pulmonary disease: n = 3 (25); Diabetes mellitus: n = 1 [8] Adipositas (BMI ≥25): n = 1 Other internal disease: n = 2 [16] Polyneuro-pathia: n = 1 [8]	12 (100)	NR	NR	Dyspnea n = 11 (92)
Bickton (2021) Malawi	Case report	1	46	0	0	1 (100)	NR	Severe acute infection	Dyspnea, Fatigue
Daynes (2021) United Kingdom	Before and after	*Intervention:* n = 30 *Control:* historical, same as Intervention group	58 [16]	14 (48)	Asthma: n = 3 [10]; COPD: n = 1 [3]	30 (100)	5 [14]	NR	Reduced exercise capacity, fatigue, respiratory symptoms[a]
Liu (2020) China	Random-ized Controlled Trial	*Intervention:* n = 36 *Control (no PR):* n = 36	*Intervention:* 69.4 [8]. *Control:* 68.9 (7.6). *Only post-COVID patients aged 65 years or older were enrolled*	*Intervention:* n = 12 (33). *Control:* n = 11 (31)	*Intervention:* Hypertension: n = 10 (28); Diabetes type 2: n = 9 (25) Osteoporosis: n = 8 (22) *Control:* Hypertension: n = 8 (22); Diabetes type 2: n = 9 (25) Osteoporosis: n = 6 [17]	72 (100)	NR	NR	*Intervention:* Multilobular lesion: n = 25 (69); Unilobular lesion: n = 11 (31); Pleural effusion: n = 4 [11] *Control:* Multilobular lesion: n = 23 (64); Unilobular lesion: n = 13 (36); Pleural effusion: n = 3 [8]
Maniscalco (2021) Italy	Before and after	*Intervention:* n = 95	Without comorbidities: 61.5 (1.6). With comorbidities: 65.3 (1.2)	Without comorbidities: 8 [16]. With comorbidities: 7 [15]	Hypertension: n = 27; Valvular heart disease: n = 7;	95 (100)	NR	All recovering from acute COVID-19 pneumonia	Dyspnea, muscle fatigue, reduced exercise capacity[a]

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Table 1 (*continued*)

Author (Year) Country	Study Design	Participants, N	Participant Characteristics			Acute COVID-19 History			Post-COVID conditions, n (%)
			Age, mean years (SD)	Female, n (%)	Pre-existing comorbidities, n (%)	Hospitalized, n (%)	ICU, n (%)	Complications, n (%)	
		*divided into 2 subgroups: 1. Without comorbidities n = 49 2. With comorbidities n = 46 *Control:* historical, same as Intervention group (n = 95)			Cardiac arrhythmia: n = 9; Heart failure n = 2; Ischemic heart disease: n = 11; Hypertrophic cardio-myopathy n = 9; COPD: n = 9; Asthma: n = 3; Pulmonary fibrosis: n = 2				
Paneroni (2021) Italy	Pilot study	*Intervention:* n = 24. *Control:* historical, same as intervention group (n = 24)	66.0 ± 8.7	13 (54)	NR	24 (100)	**Invasive mechanical ventilation:* 12 (29.2); **CPAP:* 17 (70.8); **Tracheo-stomy:* 7 (29.2); **Oxygen therapy:* n = 24 (100)	All survivors of COVID-19 pneumonia	Fatigue: n = 17 (70.8); Muscle pain: n = 12 (50); Exercise-induced dyspnea: n = 12(50); Sleep disorders: n = 10 (41.7)
Spielmanns (2021) Switzerland	Controlled before and after	*Intervention:* post-COVID-19 patients n = 99. *Comparator:* retrospective lung disease patients in 2019 (non-COVID) n = 419	*Intervention:* 67.7 ± 10.2. *Comparator:* 69.3 ± 11.3	*Intervention:* 42 (42). *Comparator:* 213 (51)	Hypertension: n = 54 (54); Smokers or Ex-Smokers: n = 27 (27); Adiposities: n = 25 (25); Musculoskele-tal disease: n = 25 (25); Dyslipidemia: n = 20 (20.2); Neurological disease: n = 20 (20); Chronic renal failure: n = 19 (19); Coronary artery disease: n = 18 (18.2); Malignancy: n = 15 [15]; COPD: n = 11 [11]	*Intervention:* 99 (100). *Comparator:* NR	*Intervention:* 65 (66)	Sepsis: n = 37 (37); Delirium: n = 36 (35); ARDS severe: n = 27 (27); ICU acquired weakness: n = 24 (24); Anemia: n = 24 (24); Electrolyte disturbance: n = 18 [18]; Acute renal failure: n = 14 [14]; Atrial Fibrillation: n = 13 [13] Myocarditis 12 [12]	NR
Tozato (2021) Brazil	Case series	4	Range: 43-72	2 (50)	Hypertension: n = 3 (75); Previous smoker: n = 1 (25);	4 (100)	2 (50)	Kidney injury: n = 1 (25)	Dyspnea: n = 3 (75); Fatigue: n = 1 (35);

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Table 1 (*continued*)

Author (Year) Country	Study Design	Participants, N	Participant Characteristics			Acute COVID-19 History			Post-COVID conditions, n (%)
			Age, mean years (SD)	Female, n (%)	Pre-existing comorbidities, n (%)	Hospitalized, n (%)	ICU, n (%)	Complications, n (%)	
					HIV: n = 1 Prostate cancer: n = 1 (25)				Tetraparesis: n = 1 (25); Cardio-respiratory deficits: n = 1 (25)

[a] Numbers or proportions not reported; COPD: chronic obstructive pulmonary disease; COVID-10: Coronavirus Disease 2019; CPAP: continuous positive airway pressure; NR: not reported; PR: pulmonary rehabilitation; SD: standard deviation.

2. Methods

A rapid review of the published literature was completed in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [6], where applicable. An electronic database search of the literature published between July 1, 2020 and June 1, 2021 was completed in MEDLINE, Pubmed, and EMBASE. For the search strategy, medical subject headings (MeSH terms) for respiratory symptoms and conditions (e.g., dyspnea, cough, respiratory failure, airway disease) were combined with key word terms for "post-COVID" and the concept of "pulmonary rehabilitation". The search was limited to English language. Abstracts and full-texts were screened in duplicate. Articles were included if: they were primary studies designed as a randomized controlled trial (RCT), quasi-experimental study, observational cohort study, or implementation experience; secondary data from evidence syntheses; and focused on PR for patients with post-COVID symptoms. A program was considered as PR if it contained, at minimum, exercise and education/counselling [7].

3. Results

Nine studies were included (Supplementary Figure 1) [8–16] and study characteristics are summarized in Table 1. Most studies were case reports or pilot (n = 5) or controlled before and after (n = 3); only 1 randomized controlled trial (RCT) was included. Sample sizes were small to moderate (<100 participants) and included primarily older participants (~60 years old or older). All study participants were hospitalized due to acute COVID-19 infection and, in 5 studies [8,11,14–16] participants were admitted to the intensive care unit (ICU) and/or required mechanical ventilation.

Details of PR programs and study findings are presented in Table 2. Most PR were multi-disciplinary, tailored to the participants' conditions or rehabilitation goals, and frequently consisted of exercise training, education, and/or counselling. All participants were admitted to PR after hospitalization due to acute COVID-19; only 4 studies reported the timing of admission [8,9,11,15] which ranged from 10 to 125 days following onset of acute symptoms or COVID-19 diagnosis. The length of follow-up varied across studies, from 3 weeks to 3-months from the start of the PR.

Broadly, all studies reported improvements in post-COVID patient outcomes following PR (Table 2). The experimental and the controlled before and after studies commonly reported statistically significant improvements in exercise tolerance (e.g., 6-min walk test distance [6MWD]), HRQL, and pulmonary function (e.g., forced vital capacity, forced vital capacity in 1 s, FEV1/FVC, and diffusion capacity for carbon monoxide). Select studies also reported improvements in dyspnea or other respiratory symptoms, fatigue, and anxiety and depression. No worsening of outcome measures, nor adverse events were reported (n = 309 participants across included studies).

In the one RCT, 36 participants were randomized to the intervention (two 10-min PR sessions/week for 6 weeks) and demonstrated at 6-weeks post-PR significant improvements in 6MWD, HRQL, pulmonary function, and self-rated anxiety compared to their baseline values and to control participants (n = 36; no rehabilitation intervention) [12]. No statistically significant differences in functional independence measures or self-rating depression scores within (i.e., pre-post) and between groups were observed. Limitations of this RCT include a small sample size, inclusion of only older adults (i.e., age 65 years or older), and unclear blinding of assessors and participants to the group allocation [12].

4. Discussion

We identified 9 primary studies that suggest that PR may lead to improvements in exercise capacity, HRQL, and/or pulmonary function among patients with post-COVID symptoms who had been hospitalized.

Table 2
Summary of findings from primary studies evaluating PR programmes.

Author (Year)	Characteristics of Pulmonary Rehabilitation (PR) Programme				Length of Follow-up	Outcome Measures	Summary of Findings
	Setting	Components	Frequency & Duration	Timing of Initiation			
Bertacchini (2021)	In-hospital unit, followed by post-discharge tele-rehabilitation	Callisthenic, strengthening, balance exercise, paced walking, chest physiotherapy (bronchial hygiene techniques), lung expansion procedures, nutritional, psychological assessment	A minimum of one, 20-min daily session up to two-three, 30-min daily sessions, 1 month duration	43–88 days post-COVID diagnosis	94–174 days post-COVID diagnosis	Oxygenation (SpO2/FiO2); physical function [Short Physical Performance Battery test (SPPB)] and disability (Barthel index)	Following the in-patient PR and tele-rehabilitation: - Only one patient still had a significant oxygenation deficit (−26.7% compared to baseline) - Three patients had no deficit, with an average value of SPPB (SPPB score: 10.0 ± 2.1) that remained at 88.5% of the pre-illness value; SPPB tests improved more were those relating to balance and walking speed - One patient had a significant disability (−35% compared to the pre-COVID-19 phase); sub-items of Barthel Index referring of washing, toilet use and transfers improved more than others
Betschart (2021)	Outpatient	Training consisted of twice weekly, interval-based aerobic cycle endurance (ACE) training, followed by resistance training (RT); education and physical activity coaching were also provided.	Twice a week, the minimum number of sessions expected for completion was 16. Training consisted of a combination of 30 min of aerobic cycle endurance (ACE) training followed by 30–40 min of resistance training (RT) at intensities of 50% peak work rate.	41.5 (21–73) post-COVID diagnosis	NR	6-min walk test (6MWT), Euroqol 5-level EQ-5D (EQ-5D-5L) Visual Analogue Scale, Post-COVID-19 Functional Status scale (PCFS)	Nine out of 12 patients demonstrated a clinically significant improvement in 6MWD (>30 m), ranging from 80 m to 170 m from initial to post-training assessment. The distance covered during the 6MWT increased with a group mean of 88 m (95% CI, 52 m–125 m). Patients' values also increased in relation to age- and gender-specific norm values. The group difference to the lower limit of normal (LLN) increased with 97 m (95% CIs, 59 m–134 m). Median percentage norm of 6MWD changed from 80% (range 50–103%) to 107% (range 57–125%). There was a statistically significant improvement in HRQoL from a mean of 65%–81% (95% CI, 4–25%) on the VAS (0–100%) Six out of 10 patients with initially perceived restrictions due to the COVID-19 (PCFS) presented no more restrictions at post-training (PCFS: 0). Four patients remained with PCFS scores of 2 and 1.
Bickton (2021)	Virtual and tele-rehabilitation (WhatsApp text messaging,	Education and patient-tailored progressive exercise sessions (i.e.,	At least 2 sessions per day, 3 days per week, over 3 weeks	NR; patient in early convalescence after discharge	3 weeks after start of PR	mMRC, Chronic obstructive pulmonary disease assessment test	All respiratory severity scores had fallen by more than their

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Table 2 (*continued*)

Author (Year)	Characteristics of Pulmonary Rehabilitation (PR) Programme				Length of Follow-up	Outcome Measures	Summary of Findings
	Setting	Components	Frequency & Duration	Timing of Initiation			
	video, and audio calls)	breathing, aerobic, strength training)				(CAT), Checklist of individual strength fatigue subscale (CIS-Fatigue)	thresholds for clinical significance: - mMRC: before = 3; after = 1 - CAT: before = 8; after = 2 - CIS-Fatigue: before = 43; after = 11
Daynes (2021)	NR	Strength training of upper and lower limbs and educational discussions with handouts, education sessions (breathlessness, cough, fatigue, fear and anxiety, memory and concentration, taste and smell, eating well, getting moving again, sleeping well, managing daily activities and, returning to work)	6 weeks in duration, with two supervised sessions per week	Mean 125 days post-COVID infection	6 weeks after start of PR	The incremental and endurance shuttle walking test (ISWT/ESWT), CAT, Functional Assessment of Chronic. Illness Therapy Fatigue Scale (FACIT), Hospital Anxiety and Depression Scale (HADS), EQ5D, and the Montreal Cognitive Assessment (MoCA)	Individuals that completed rehabilitation demonstrated statistically significant improvements in exercise capacity, respiratory symptoms, fatigue and cognition. Post-PR, there was a mean [SD] within group improvement in the ISWT of 112 m [105] ($p < 0.01$), and 544 s [377] ($p < 0.01$). The FACIT improved by 5 points [7] ($p < 0.01$), the EQ5D thermometer improved by 8 [19] ($p = 0.05$) and MoCA by 2 points [2] ($p < 0.01$). The CAT score improved by a score of 3[6] ($p < 0.05$). The HADS anxiety and depression scores improved by 0[4] and 1 [4] respectively which was not statistically significant, however the baseline scores were low.
Liu (2020)	NR, patients were reported from acute care facilities designated for COVID-19 patients	Respiratory muscle training [2]; cough exercise [3]; diaphragmatic training [4]; stretching exercise; and [5] home exercise	Once a day for 10 min, 2 sessions per week for 6 weeks	NR; patients described as post-acute and 6 or more months after the onset of other acute diseases without COPD or other respiratory conditions	6 weeks after start of PR	Primary Outcome Measures: Respiratory function (FEV1; FVC; DLCO [%]); Secondary Outcome Measures: Exercise endurance (6-min walk distance), Activities of Daily Living (ADL; Functional Independence Measure) and Quality of Life (QoL; Short Form [SF]-36), psychological status assessment (anxiety, depression scores).	Compared to the control group, the intervention group demonstrated significant improvements in pulmonary function (FEV1[L], FVC[L], FEV1/FVC%, DLCO%). QoL, based on SF-36 scores in 8 dimensions, significantly increased post-intervention for those in the intervention group and between the intervention and control groups, suggesting an improvement in QoL. Anxiety and depression scores decreased post-intervention in the intervention group, but only anxiety was significantly decreased within and between intervention and control groups. There was no statistically significant difference in ADL in the intervention group before or after the PR, nor compared with the control group.
Maniscalco (2021)	PR ward	Physical exercise training, dietary	5-week pulmonary rehabilitation program			Pulmonary function (FVC, FEV1, FVC/	Regardless of having pre-existing

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Table 2 (*continued*)

Author (Year)	Characteristics of Pulmonary Rehabilitation (PR) Programme				Length of Follow-up	Outcome Measures	Summary of Findings
	Setting	Components	Frequency & Duration	Timing of Initiation			
		counselling, and psychosocial counselling	with daily sessions (6 sessions/week; total of 30 sessions)	NR; patients described as post-COVID-19	5 weeks after start of PR	FEV1, DLCO), 6MWD, 6MWT, arterial blood gas levels (PaO2 and PaCO2)	comorbidities, participants experienced statistically significant improvements in pulmonary function (FVC, FEV1, DLCO%), blood gases, and the ability to exercise after PR. PR also resulted in reduced dyspnea and muscle fatigue in both subgroups.
						Dyspnea scores, Muscle fatigue scores	Compared to patients with underlying cardiorespiratory comorbidity, the DLco %-predicted was the only parameter that showed a statistically significant improvement for patients without comorbidities after PR.
Paneroni (2021)	Tele-rehabilitation	Aerobic reconditioning and muscle strengthening and healthy lifestyle education.	1-month program of 1-h daily sessions at home and video call with physiotherapist twice a week to monitor progress.	NR	1-month after start of PR	6MWT, 1 min Sit-to-Stand (1MSTS), Barthel Dyspnoea Index	At the end of the program, exercise capacity and dyspnea significantly improved: - Distance walked in 6MWT increased in 75.0% of patients and 70.8% improved 6MWT above the minimal clinically important difference (30 m). - Number of sit-to-stands increased in 62.5% and 50% improved 1MSTS above the minimal clinically important difference (3 rises) - Barthel dyspnea improved in 83.3%; in 50% of patients the dyspnea decrease was 6.5 points above the minimal clinically important difference
Spielmanns (2021)	Inpatient	Individualized endurance exercise, strength training, respiratory physiotherapy, educational sessions, including self-management, coping skills, self-medication, management of infections and exacerbations, dyspnea, use of oxygen, and nutrition interventions, and smoking cessation, if needed.	A total of 25–30 therapy sessions, 5–6 days a week, for 3-weeks	10 days after onset of infection and asymptomatic for 2 days	3-weeks after start of PR (at discharge)	FIM, Cumulative Illness Rating Scale (CIRS), 6MWT, duration of PR, and Feeling Thermometer (FT)	Prior to PR, there were no significant differences in the baseline FT and FIM parameters between groups; however, the 6MWT distance was significantly smaller for the post-COVID-19 group relative to the lung disease group. After the PR program, there were significant improvements the FIM, 6MWT, and FT parameters in both the post-COVID-19 group and historical lung disease group. Improvements in FT, FIM and 6MWT distance following PR were significantly higher for the post-COVID-19 compared to the improvements observed in the lung disease group.

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Table 2 (*continued*)

Author (Year)	Characteristics of Pulmonary Rehabilitation (PR) Programme				Length of Follow-up	Outcome Measures	Summary of Findings
	Setting	Components	Frequency & Duration	Timing of Initiation			
Tozato (2021)	NR	Protocol based on cardio-pulmonary rehabilitation (CPR) principles, including aerobic and resistance training	3-months (frequency NR)	NR	3-months after start of PR	6MWT distance; Borg scale dyspnea; Double product (heart rate and systolic blood pressure); Maximal repetitions of knee extensions, should abduction, elbow flexion; Handgrip	After CPR, there was cardiovascular recovery as assessed by the double product, reduced exertion dyspnea, increased peripheral muscle strength, and functional independence as reported and observed throughout the rehabilitation.

The few studies that evaluated changes in post-COVID symptom severity or frequency reported improvements in dyspnea, fatigue, anxiety and depression. No studies evaluated non-hospitalized patients, healthcare resource utilization, nor longer-term outcomes beyond 3 months following PR. The included study populations were variable in terms of time post-acute COVID-19 infection. Although we did not perform a risk of bias or quality assessment, most studies were likely low quality due to smaller sample sizes, short follow-up, and/or non-randomized study designs. The reported findings should, therefore, be interpreted with caution.

Potential practical limitations to implementing post-COVID PR were also not addressed in the literature. In many jurisdictions, PR was halted due to the COVID-19 pandemic and/or delivered at reduced capacity due to the need to deliver PR virtually, leaving considerable waitlists for non-COVID respiratory patients to attend PR. Referring post-COVID patients to PR will likely place large demands on existing programs, increase waitlists or require substantial resources for expansion, and potentially deny individuals with respiratory conditions access to a well-established therapy [17]. Further, patients with post-COVID symptoms may have different rehabilitation needs compared to the usual patients participating in PR. For instance, some COVID-19 survivors experience persistent dyspnea and diminished exercise capacity, despite no substantial impairment in pulmonary function [18]. While the need for post-COVID rehabilitation is recognized, PR may not be the solution and differences in presentation between post-COVID and chronic respiratory patients suggest value in a more specific “post-COVID rehabilitation”.

5. Conclusions

Evidence evaluating PR for patients with post-COVID symptoms is emerging, yet limited and of uncertain quality. A challenge to understanding the potential benefit of post-COVID PR is the current limited knowledge of the long-term trajectory of post-COVID symptoms. It is unclear whether natural recovery occurs over time and, if so, at what rate and to what extent. Further, the appropriateness and effectiveness of PR versus other forms of rehabilitation for post-COVID conditions is unknown. Such comparative studies are needed to better elucidate the ideal form of rehabilitation for this growing patient population.

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Author contributions

Design of the study (LJJS, RWD, GYL, MPS, JW, JB, PH, MKS) acquisition and management of data (LJJS,MKS), analysis and interpretation of data (LJJS, MKS); preparation of manuscript (LJJS, MKS); review of manuscript (LJJS, RWD, GYL, MPS, JW, JB, PH, MKS); approval of manuscript (LJJS, RWD, GYL, MPS, JW, JB, PH, MKS).

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Appendix A. Supplementary data

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