The Effect of Menstrual Cycle Phase-based Rehabilitation for Females Following Anterior Cruciate Ligament Reconstruction: A Randomised Controlled Trial

Emma O'Loughlin *PhD, BSc (Hons) Physiotherapy*
Sports Performance Research Institute New Zealand (SPRINZ), Auckland University of Technology, Auckland, New Zealand; Department of Surgery and Anaesthesia, University of Otago, Wellington, New Zealand

Duncan Reid *DHSc, MHSc (Hons) PGDipHSc (Manipulative Physiotherapy)*
Sports Performance Research Institute New Zealand (SPRINZ), Auckland University of Technology, Auckland, New Zealand

Stacy Sims *PhD, MSc, BA*
Sports Performance Research Institute New Zealand (SPRINZ), Auckland University of Technology, Auckland, New Zealand; Stanford Lifestyle Medicine, Stanford University, Palo Alto, California, USA

Peter Larsen *PhD, BSc (Hons)*
Department of Surgery and Anaesthesia, University of Otago, Wellington, New Zealand

ABSTRACT

Recent research reports that follicular phase-based resistance training, where females predominantly perform resistance training in the first half of their menstrual cycle (MC), appears to result in better responses than regular training. The objective of this study was to compare the effects of MC phase-based rehabilitation (MCPBR) versus usual care (UC), following anterior cruciate ligament reconstruction (ACLR). Forty-three females participated in a 12-week intervention commencing six weeks post-ACLR. The primary outcome was knee extension strength limb symmetry index (LSI), and the secondary outcome was self-reported function (measured using the Knee Injury and Osteoarthritis Outcome Score, International Knee Documentation Committee Questionnaire, and Knee Self Efficacy Scale), measured at baseline and endpoint. Participants were randomly assigned to MCPBR (n = 21) or UC (n = 22). Participants' MCs were monitored using calendar tracking, basal body temperature tracking, and urinary ovulation testing. Thirty-six females provided data for the final analysis. The *M (SD)* knee extension LSI for participants following MCPBR was 81.2% (13.2%), compared to 73.5% (21.8%) for those following UC (p = 0.17). The *M (SD)* one repetition maximum knee extension of the injured leg was 38.8 kg (14.1 kg) following MCPBR and 30.4 kg (11.7 kg) following UC (p = 0.06). Self-reported function was similar between groups. The findings of this study show that MCPBR and UC result in similar knee extension LSI and function and therefore do not support the recommendation of MCPBR for ACL rehabilitation in a New Zealand context. Future research should investigate females' experience of MCPBR following ACLR.

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Key Words: Anterior Cruciate Ligament, Female Athlete, Menstrual Cycle, Rehabilitation, Resistance Training

INTRODUCTION

Rates of female anterior cruciate ligament (ACL) injuries have increased in recent years, with the likelihood of sustaining an ACL injury three to six times greater for females than for males (Herzog et al., 2018; Sutherland et al., 2019; Zbrojkiewicz et al., 2018). This may be due to a combination of anatomical, biomechanical, physiological, and gender-related environmental factors (Hewett et al., 2006; Parsons et al., 2021). Post-ACL reconstruction (ACLR) females have reduced quadriceps strength recovery, worse self-reported knee-related function, and are less likely to return to sport compared to males (Devana et al., 2022; Kuenze et al., 2019). Reduced quadriceps strength may put athletes with ACLR at a higher risk of further subsequent ACL injuries (Grindem et al., 2016) and early onset post-traumatic osteoarthritis (Tourville et al., 2014). Females are under-represented in ACLR research and, subsequently, there are no female-specific guidelines to specifically approach their rehabilitation (Culvenor et al., 2022; Filbay & Grindem, 2019; Mok et al., 2022; Van Melick et al., 2016).

Restoring lower limb strength is a key focus of rehabilitation following ACLR, with particular emphasis on the quadriceps (Kuenze et al., 2014). Subsequently, research recommends resistance training as part of post-ACLR rehabilitation (Culvenor et al., 2022). The response to resistance training depends on nutrition, sleep, and hormonal responses (Douglas et al., 2016; Hawley et al., 2011). Specifically for females, the hormone oestrogen is known to have an anabolic effect on skeletal muscle (Lowe et al., 2010). In contrast, progesterone has anti-oestrogenic effects and is considered catabolic (Kriengsinyos et al., 2004). Recent reviews have recommended that non-injured, naturally cycling females, where possible, concentrate their resistance training in the follicular phase of their menstrual cycle (MC) to benefit from rising levels of oestrogen and low levels of progesterone (Oosthuyse & Bosch, 2010; Thompson et al., 2020).

MC phase-based resistance training has not been investigated in females post-ACLR. Therefore, the primary objective of this study was to investigate if menstrual cycle phase-based rehabilitation (MCPBR), where females post-ACLR periodise resistance training to the follicular phase of the menstrual cycle (MC), results in improved quadriceps strength symmetry following ACLR, compared to usual physiotherapy rehabilitation. The secondary objective was to investigate if MCPBR resulted in improved self-reported functional outcomes and self-efficacy in females following ACLR compared to usual physiotherapy care (UC).

METHODS

Study design

This randomised, single-blind, two-arm study was registered with the Australian and New Zealand Clinical Trials Registry (Trial registration number: ACTRN12621000517875). The study is reported in line with the Checklist for Statistical Assessment of Medical Papers statement (Mansournia et al., 2021).

Participants

Females residing in New Zealand, aged 16 years or older, post-ACLR with a regular MC were eligible for the trial. Females using a copper or progestin-only intrauterine device were eligible for inclusion (Ortiz & Croxatto, 2007). For the first year after insertion, the progestin-only intrauterine device causes anovulatory cycles, with ovulatory cycles resuming thereafter (Apter et al., 2014). Exclusion criteria included using the oral contraceptive pill, those who were under 16 years old, more than six weeks post-operation, had an allograft surgery, or revision surgery (Janse de Jonge et al., 2019). Surgeons and physiotherapists identified potential participants in their clinics between August 2021 and November 2022 and gave them a study advert. The research team advertised the study in the media and online. All interested participants contacted the primary researcher (EOL). All participants completed screening questions via an online Google Forms questionnaire, received trial information, and provided written consent pre-operatively.

Randomisation and blinding

The primary researcher (EOL) generated a randomisation list online (www.random.org) and randomly allocated participants to one of two groups. The study used block randomisation to obtain equal groups of 10 control and intervention participants throughout the study. After randomisation, the primary researcher informed the physiotherapist of the participant's group assignment. Participants were informed about the nature of the study, including that the study investigated the effects of certain exercises at certain parts of the menstrual cycle, but were not told whether they were in the control or intervention group. The participants were blind to their group assignment.

Changes to trial protocol

The trial protocol originally excluded females with meniscal repairs and greater than grade two cartilage damage. However, in focus groups conducted prior to trial commencement, physiotherapists identified that these patients would be able to engage in rehabilitation without limitation (O'Loughlin et al., 2023). Therefore, these participants were included in the trial. Secondly, physiotherapists were to measure participants' one repetition maximum (1RM) leg extension strength of both lower limbs at the start and end of the trial. However, physiotherapists noted that post-operative pain on the injured side would limit the initial test. Therefore, only non-injured limb strength was measured at the start of the trial (Figure 1, Table 1).

Location

Twenty-eight private physiotherapy clinics across New Zealand participated in the trial. All physiotherapists had experience treating ACL injuries. All clinics had access to either a leg extension machine or handheld dynamometer to measure leg strength. The research team educated physiotherapists regarding the study protocols and the MC, provided a written instruction booklet (Appendix A), and created an online resource to ensure methods were standardised across clinics and physiotherapists. Physiotherapists only treated control or intervention participants, not both.

Outcomes

The primary and secondary outcomes are outlined in Table 1.

Interventions

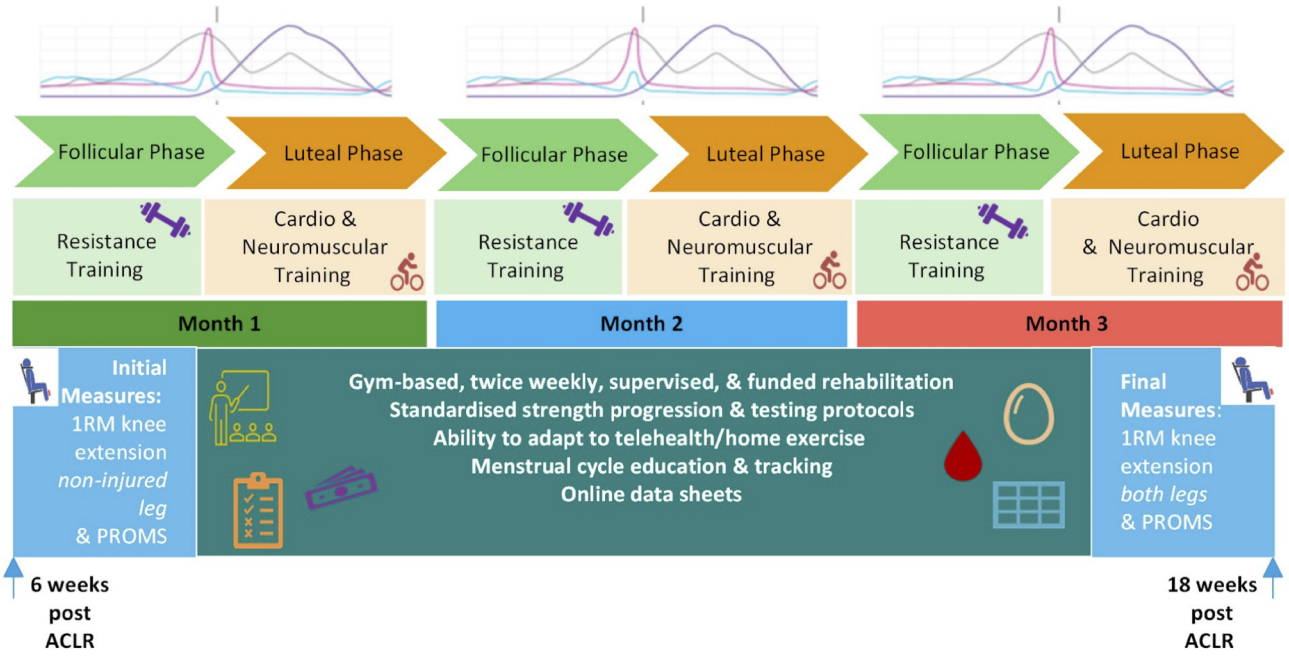
The research team sent all participants an education pack, which included education and testing kits to verify their MCs (Appendix B). These testing kits included a basal body thermometer, a urinary cup, and 20 ovulation strip tests. Each participant had an individual online datasheet where they entered this MC information, which the primary researcher and physiotherapist could also access. The primary researcher assisted with queries regarding MC tracking.

All participants attended twice-weekly, supervised, fully funded, individual 30 min gym-based physiotherapy appointments for 12 weeks, commencing at 6 weeks post-ACLR. Non-injured lower limb knee extension strength was measured at the start of the trial, and knee extension of both lower limbs was measured at the end of the trial, at 18 weeks postoperatively (Figure 1, Table 1). Several patient reported outcomes were measured at the start and end of the trial (Figure 1, Table 1). The American College of Sports Medicine guidelines recommend that people undertake resistance training 2–3 times per week. (Ratamess et al., 2009). While there is no established optimal amount of strength training post-ACLR (Nichols et al., 2021), for the general population, evidence shows greater gains from additional training frequency (Grgic et al., 2018). However, these additional gains can be negated if the overall training volume per week is the same (Grgic et al., 2018). Focus group participants recommended scheduling twice-weekly sessions to complete all their exercises during supervised physiotherapy sessions (O'Loughlin et al., 2023). Twice weekly frequency was chosen to focus on quality sessions with substantial exercise volume to elicit muscle strength gains while balancing study constraints. The study commenced at 6 weeks post-operatively as focus group physiotherapists recommended this timeframe as being when post-operative swelling and pain decreases to a point where a loading programme can be commenced without restriction (O'Loughlin et al., 2023).

Physiotherapists offered participants telehealth and home exercise sessions if they were unable to attend the in-person sessions during the programme. Participants could not perform lower limb resistance training outside their rehabilitation sessions. However, participants could complete cardiovascular,

Figure 1

Menstrual Cycle Phase-based Rehabilitation Programme



Note. Visual representation of the menstrual cycle (MC) phase-based quadriceps resistance training programme. Training commenced at six weeks post-surgery and continued until 18 weeks post-surgery. Participants attended twice weekly to a gym-based setting for supervised rehabilitation. These sessions were adapted if needed, i.e., telehealth. The researcher, physiotherapist, and participants entered all data into an online datasheet. Females received MC education and inputted information into their datasheet to establish their MC phase. Participants engaged in resistance training in the follicular phase sessions and cardiovascular and neuromuscular exercises in the luteal phase sessions. Physiotherapists used standardised strength testing to measure outcomes and standardised progression protocols to prescribe strength exercises. Funding was available for females to attend sessions. Image used with permission (O'Loughlin et al., 2023). PROMS = patient reported outcome measures.

neuromuscular, trunk exercises and upper limb resistance training outside their rehabilitation sessions. Participants recorded the frequency, content, and duration of exercise outside physiotherapy in their online datasheet. Physiotherapists also recorded each participant's rehabilitation attendance and session content in their online datasheet.

Tailoring to the menstrual cycle

Participants were randomised into two groups – either MCPBR or UC. The details of their twice-weekly supervised, fully funded, gym-based physiotherapy sessions depended on the group assignment.

MCPBR

Participants completed resistance training during the follicular phase of their MC. Participants were considered in their follicular phase from day one of menses, as noted on their individual datasheet. Squat, leg press, and knee extension exercises were compulsory in each follicular phase rehabilitation session (Figure 1). The luteal phase-based training commenced once a positive urinary ovulation test and/or a consistent rise in basal body temperature was recorded on their datasheet. Physiotherapists prescribed neuromuscular and cardiovascular exercises for the luteal phase at low to moderate intensity, as measured by the Borg Rate of Perceived Exertion scale (Figure 1). The research protocol did not define these exercises; however, the research team provided a guide (Appendix A).

UC

Participants completed their twice-weekly supervised, fully funded, gym-based physiotherapy rehabilitation as guided by their physiotherapist, most often in keeping with referring surgeons' post-operative protocols. The research team provided a general guide for ACL rehabilitation based on recent consensus statements (Appendix A) (Van Melick et al., 2016).

MC verification and synchronisation

Participants used a three-step method, which included calendar tracking, basal body temperature checking, and urinary ovulation testing, to confirm their MC phases. Participants commenced tracking their MC from study enrolment, usually at their ACLR surgery date, to provide 6 weeks of initial MC data before the programme commenced. This enabled the research team and physiotherapist to understand each participant's individual usual MC timeframe and ovulation dates. Participants were excluded from post hoc analysis if there was more than one month where their temperature and urinalysis did not verify ovulation. In addition, participants were excluded if their cycles differed by greater than seven days outside their norm for more than two cycles.

Sample size estimation

Based on previous studies, the research team estimated that with an alpha level of 0.05 and 90% power, a sample size of 27 in each group would enable an 80% probability of detecting

Table 1

Trial Outcome Measurement and Interpretation

Construct and measure	Assessment method and interpretation
LSI (%) of 1RM, injured versus non-injured leg	Physiotherapists experienced with collecting strength measurements post-ACL injury carried out a 1RM knee extension strength test, using a knee extension machine or handheld dynamometer (see Appendix A): Percentage difference between limbs = 1RM strength of the affected limb divided by the 1RM unaffected limb, multiplied by 100. Recent research defines 90% LSI as the standard target for max quadriceps strength of the injured versus non-injured leg following ACLR (Urhausen et al., 2022). Recent research recommends 1RM testing on a knee extension machine following ACL due to sufficient construct and criterion validity (Urhausen et al., 2022). Future trials are needed to establish the reliability of 1RM strength testing on knee extension machines following ACLR (Roos et al., 1998). In contrast, isometric extensor strength tests using handheld dynamometry offer sufficient intra-rater reliability (Urhausen et al., 2022).
Self-reported knee function: KOOS (Roos et al., 1998)	Addresses participants' pain, symptoms, activities of daily living, sport and recreation function, and knee-related quality of life (Roos et al., 1998). The score is a percentage score from 0–100, with 0 representing extreme problems and 100 representing no problems. The KOOS is valid and reliable for patients undergoing ACLR (Roos et al., 1998).
Self-reported knee function: IKDC (Collins et al., 2011)	The IKDC includes seven questions on knee symptoms – pain, swelling, locking, and giving way, as well as questions on knee function and activity (Collins et al., 2011). Scores range from 0 points (indicating the lowest level of function or the highest level of symptoms) to 100 points (indicating the highest level of function and the lowest level of symptoms). The IKDC is considered valid and reliable for use in a broad patient population, including following ACLR (Higgins et al., 2007).
Self-efficacy regarding knee injury: K-SES (Ezzat et al., 2020)	The K-SES consists of 22 items subdivided into four categories: daily activities, sports and leisure activities, physical activities, and future knee function (Ezzat et al., 2020). Participants respond to each item on an 11-point Likert scale from 0–10, where 0 indicates poor self-efficacy and 10 indicates strong self-efficacy. The English K-SES is considered a valid and reliable measure for knee-specific self-efficacy in individuals following a sport-related intra-articular knee injury in the previous 5 years (Ezzat et al., 2020).

Note. All measurements were obtained at 6 and 18 weeks post-ACLR, with the exception of 1RM knee extension strength of the leg, which was assessed at 18 weeks post-ACLR only. ACL = anterior cruciate ligament; ACLR = anterior cruciate ligament reconstruction; LSI = limb symmetry index; 1RM = one repetition maximum; KOOS = the Knee Injury and Osteoarthritis Outcome Score; IKDC = the International Knee Documentation Committee Questionnaire; K-SES = Knee Self-Efficacy Scale.

a 20% knee extension strength limb symmetry difference between the two groups (Harput et al., 2019; Reis et al., 1995). As this study used handheld dynamometers and knee extension machines to measure strength, which may be less reliable than isokinetic dynamometry as used in previous studies, numbers were boosted by 10% to 30 per group (Urhausen et al., 2022).

Statistical analysis

The distribution of continuous variables was assessed using the Spiro-Wilk test. Variables that were normally distributed are expressed as *M* (*SD*). Variables that were not normally distributed were expressed as *Mdn* (interquartile range). Categorical variables were expressed as count (%). Categorical variables were compared between groups using the Chi-squared test, and continuous variables using either unpaired t-test (normally distributed) or Mann-Whitney U test (not normally distributed). The primary endpoint, limb symmetry index (LSI) and 1RM injured were compared between groups using the Mann-Whitney U test. The secondary endpoints of 1RM non-injured, Knee Injury and Osteoarthritis Outcome Score (KOOS), International Knee Documentation Committee (IKDC), and Knee Self Efficacy Scale (K-SES) scores, as outlined in Table 1, were examined over time and between groups using repeated measures ANOVA. In all cases, $p < 0.05$ indicated statistical significance.

Ethics, diversity, and inclusion statement

The researchers discussed the project with the Mātauranga Māori Committee at the Auckland University of Technology. The research team sought advice from Māori regarding the wording of the trial forms and translated the trial name and the participant information sheet into te reo Māori. The study provided fully funded physiotherapy sessions to ensure participants of different socioeconomic statuses could participate. Furthermore, the research team was gender balanced and included junior and senior researchers.

RESULTS

Participants

The trial included 43 females from 75 potential participants recruited between July 2021 and November 2022 (Figure 2). The trial was stopped due to constraints in the availability of key personnel. Participant characteristics are reported in Table 2. Participants' surgical graft type and concomitant injuries were noted from their surgical notes. There were no significant differences in baseline outcomes between groups (Appendix C, Table C1). Participants in the MCPBR group attended a *M* (*SD*) of 19.9 (3.6) appointments, while participants in the UC group attended 17.9 (5.4) appointments over the course of the trial ($p = 0.18$, Appendix C, Table C2).

Primary outcome

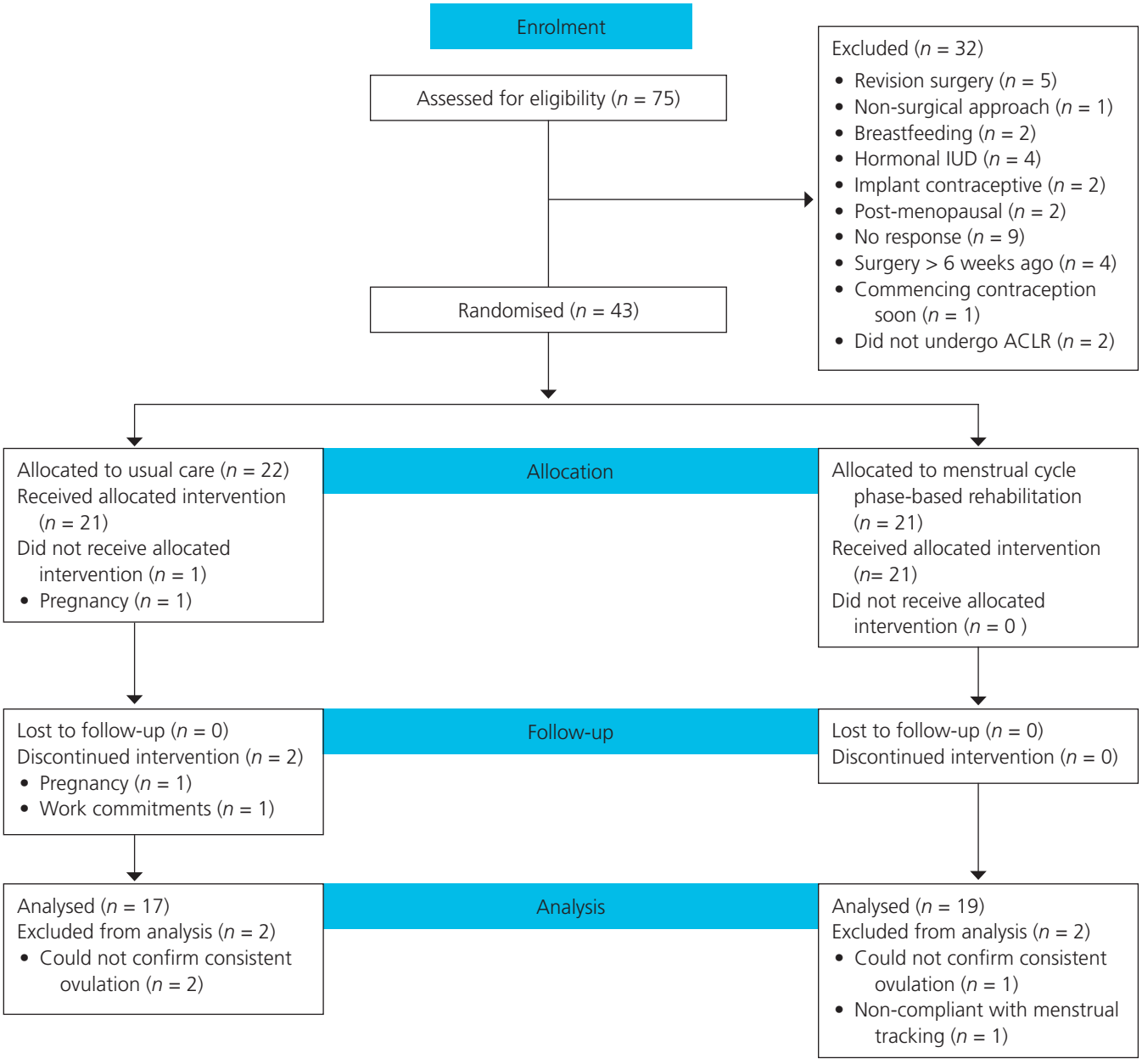
All outcomes are presented as *M* (*SD*). There were no statistically significant between-group differences in knee extension LSI at 18 weeks post-ACLR ($p = 0.17$, Table 3, Figure 3). The mean LSI was 81.2% (13.2%) following MCPBR compared to 73.5% (21.8%) following UC (Table 3, Figure 3). The mean knee extension 1RM for the injured leg was 38.8 kg (13.4 kg) following MCPBR and 30.4 kg (11.7 kg) following UC, resulting in a mean difference of 8.4 kg (95% CI [–0.3, 17.1], $p = 0.06$), as detailed in Table 3 and Figure 3. The mean knee extension 1RM for the non-injured leg increased from 41.0 kg (10.8 kg) to 47.3 kg (12.4 kg) following MCPBR, and from 38.1 kg (7.9 kg) to 40.7 kg (9.5 kg) following UC, demonstrating a significant time effect ($p = 0.01$). However, there was no significant treatment effect, with a mean difference of 5.7 kg (95% CI [–1.8, 13.2], $p = 0.18$), as detailed in Table 3 and Figure 3.

Secondary outcomes

Total and sub-scale KOOS and IKDC scores improved significantly for both groups throughout the trial from baseline to endpoint (Table 3, Figure 3). There was no between group treatment effect (Table 3). Similarly, total K-SES scores improved significantly for both groups, but there were no between-group effects (Table 3).

Figure 2

Flow of Participants Through the Study



Note. ACLR = anterior cruciate ligament repair; IUD = intrauterine device.

Table 2

Participant Characteristics

Characteristic	Usual care group (*n* = 22)		MCPBR group (*n* = 21)		*p*
	n [a]	% [a]	*n* [a]	% [a]	
Age, *M* (*SD*)	30.4 (7.6)		32.8 (8.4)		0.33
Ethnicity					
New Zealand European	11	50	13	62	0.65
Māori	4	18	2	9	
Samoan	1	5	1	5	
Chinese	2	10	1	5	
Indian	0	0	2	9	
Other European	3	14	1	5	
Other Asian	1	5	1	5	
Menstrual cycle status					
Natural	17	77	20	95	0.22
Copper IUD	1	5	0	0	
Hormonal IUD	4	18	1	5	
Contralateral injury					
No	18	82	19	90	0.96
Yes	3	14	3	10	
Resistance training status					
Untrained	9	41	9	43	0.25
Moderate	8	36	3	14	
Well trained	5	23	7	33	
Graft type					
Hamstring	15	68	17	81	0.34
Bone-patella-bone	7	32	4	19	
Cartilage damage					
None	15	68	17	81	0.62
Grade 1	2	10	2	9.5	
Grade 2	4	18	2	9.5	
Grade > 2	1	5	0		
Meniscal treatment					
No	14	64	10	47	0.56
Meniscectomy	4	18	5	24	
Meniscal repair	4	18	6	29	
Associated ligamentous injury					
None	18	82	18	86	0.53
MCL	2	10	3	14	
LCL	1	5	0	0	
Multiple (LCL and MCL)	1	5	0	0	
Delay to surgery (days), *Mdn* (IQR)	178	(97–299)	128	(78–392)	0.98

Note. IUD = intrauterine device; IQR = interquartile range; LCL = lateral collateral ligament; MCL = medial collateral ligament; MCPBR = menstrual cycle phase-based rehabilitation.

[a] Except where indicated.

DISCUSSION

Primary outcome

The main finding of this study was that the MCPBR and UC groups had similar knee extension LSI at the end of the study. Females had a *M* (*SD*) LSI of 81.2% (13.2%) following MCPBR and 73.5% (21.8%) following UC. While these were not statistically different, even small differences in LSI can be clinically important for females after ACLR, as there is a 3% reduction in re-injury rate for every 1% point increase in strength symmetry post-ACLR (Grindem et al., 2016). Recent studies recommend 90% LSI as the standard target for 1RM extension strength symmetry following ACLR (Lynch et al., 2015). Thirty-three percent of females in the MCPBR group and 25% in the UC group met the 90% LSI goal. These LSI cut-offs are pertinent as criterion-based rehabilitation has surpassed

Table 3

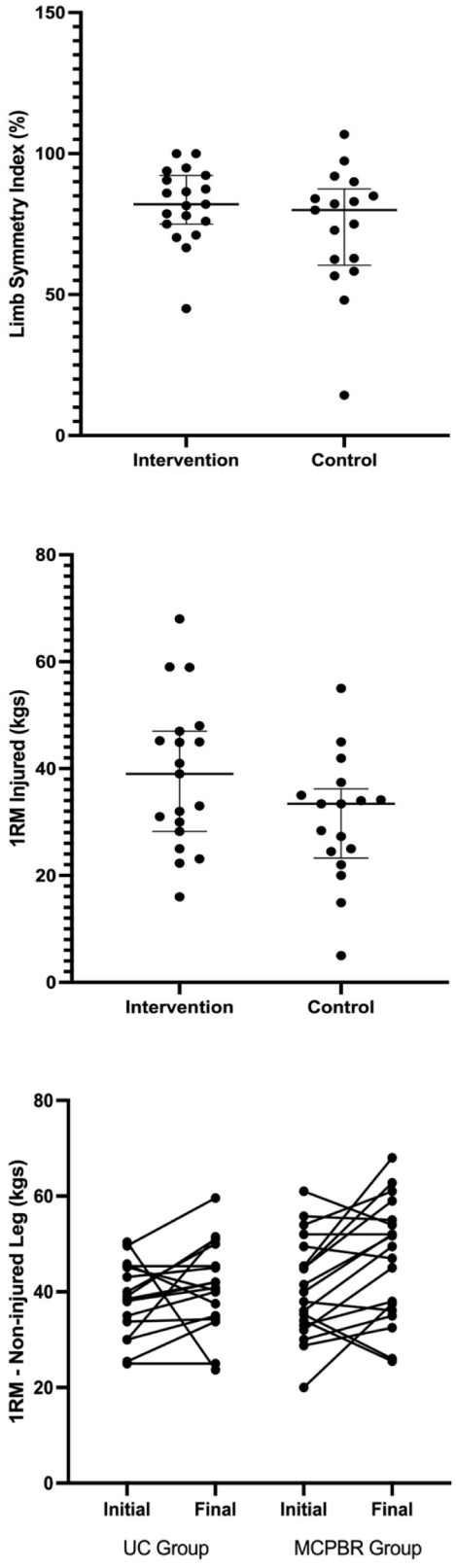
Summary of Participant Primary and Secondary Outcomes

Outcome	Usual care group (*n* = 17)				MCPBR (*n* = 19)				Difference between groups				*p*	
	Baseline		Final		Baseline		Final		Baseline		Final			
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M* difference	95% CI	*M* difference	95% CI		
Quadriceps strength LSI (%)	–		73.5	21.8	–		81.8	13.2	–		8.3	[–3.7–20.4]	0.17	
1RM injured (kg)	–		30.4	11.7	–		38.8	14.1	–		8.4	[–0.3–17.1]	0.06	
													Time effect	Rx effect
1RM non-injured (kg)	38.1	7.9	40.7	9.5	41.0	10.8	47.3	12.4	4.3	[1.0–7.6]	5.7	[–1.8–13.2]	0.01	0.18
KOOS (%)														
Total	59.8	15.1	73.2	14.9	65.0	13.0	73.2	11.9	10.6	[5.8–15.4]	-0.02	[–9.1–9.1]	< 0.001	0.28
Pain	56.4	18.8	81.0	11.1	53.3	13.4	82.3	9.8	26.8	[22.3-31.4]	1.3	[–5.8–8.3]	< 0.001	0.81
Symptoms	50.1	13.4	75.4	20.2	48.2	13.9	74.3	18.5	25.7	[19.9–31.5]	–1.1	[–14.2–11.9]	< 0.001	0.76
ADL	70.9	18.7	89.1	12.2	71.4	17.2	93.4	6.7	20.2	[14.9–25.3]	4.3	[–2.2–10.8]	< 0.001	0.56
Sports	25.6	19.4	63.8	19.0	31.3	27.8	64.5	18.8	35.5	[29.1–41.9]	0.7	[–12.1–13.5]	< 0.001	0.63
QoL	31.0	16.4	56.6	20.6	22.4	15.6	52.5	14.8	27.7	[21.0–34.5]	–4.1	[–16.2–7.9]	< 0.001	0.23
IKDC (%)	39.6	11.6	68.6	13.3	37.4	13.7	64.1	11.9	27.7	[23.5–31.9]	–4.6	[–13.1–3.9]	< 0.001	0.36
K-SES														
Total (max 180)	61.1	33.3	127.4	31.7	50.6	35.1	129.1	39.7	72.7	[60.9–84.5]	1.7	[–22.7–26.2]	< 0.001	0.67
Movement (max 80)	19.6	14.2	56.0	18.1	17.9	17.4	59.6	21.5	39.2	[33.2–45.2]	3.6	[–9.9–17.2]	< 0.001	0.85
Leisure (max 80)	29.1	18.2	57.1	15.3	21.8	16.5	57.6	14.0	32.1	[26.4–37.7]	0.5	[–9.4–10.4]	< 0.001	0.47
Future (max 20)	12.5	6.0	14.2	3.6	10.8	5.1	12.8	5.5	1.9	[0.05–3.8]	–1.5	[–4.6–1.7]	0.001	0.28

Note. Quadriceps limb symmetry index (LSI) and one repetition maximum (1RM) injured were compared between groups using the Mann-Whitney U test. The secondary endpoints of 1RM non-injured, KOOS, IKDC, and K-SES scores were examined over time and between groups using repeated measures ANOVA. ADL = activities of daily living; CI = confidence interval; KOOS = the Knee Injury and Osteoarthritis Outcome Score; IKDC = the International Knee Documentation Committee Questionnaire; K-SES = Knee Self-Efficacy Scale; MCPBR = menstrual cycle phase-based rehabilitation; QoL = quality of life; Rx = treatment.

Figure 3

Strength Outcomes Following MCPBR and Usual Care



Note. UC = usual care; MCPBR = menstrual cycle phase-based rehabilitation; 1RM = one repetition maximum.

time-based rehabilitation (Culvenor et al., 2022). Only 32.5% of ACLR patients achieve an average 90% LSI 1RM knee extension at six months post-ACLR (Cristiani et al., 2019). Therefore, both study groups in this trial had comparatively high levels of LSI at this early time point compared to these previously reported figures. The relatively high mean LSI following UC, in addition to the relatively high pre-determined estimated mean difference (20% difference between groups) in the sample size calculation, may also have affected the ability of MCPBR to demonstrate a substantive improvement over the UC group. The effect size in this study was smaller than initially estimated (approximately 10%). Future studies, using a primary outcome of limb symmetry index, would require a sample size of 200 participants to demonstrate a 10% difference between groups (90% power and $\alpha = 0.05$).

There was no significant difference in the maximum strength of the injured leg between the MCPBR and the UC group. Although no baseline measures were available, the estimated strength differences at the final measurement suggest that the MCBPR group may have been stronger than the UC group. However, the small sample size limits the ability to draw firm conclusions. Similarly, while there was a significant change in the strength of participants' non-injured leg over the course of the trial, there was no significant difference between the MCPBR and UC groups. However, the estimated strength gain differences suggest greater improvement in the MCPBR group. If the MCPBR group participants' non-injured leg became stronger alongside their injured leg, this could have affected the final limb symmetry index score, making it less reflective of the strength changes over the course of the trial.

Previous research describes superior strength gains following MC phase-based resistance training in non-injured populations (Sung et al., 2014; Wikström-Frisén et al., 2017). In these two studies, participants engaged in a higher volume of resistance training (five sessions per week) during the follicular phase. In contrast, in the current study, MCPBR participants attended biweekly rehabilitation across all MC phases, but resistance training was restricted to the follicular phase only. No training limitations were placed on the UC group, and physiotherapists prescribed quadriceps exercises more frequently to the UC group than to the MCPBR group. Consequently, the MCPBR group engaged in less quadriceps loading as compared to UC, which may have negatively affected responses. Future studies should ensure a similar level of resistance training between groups.

Secondary outcomes

All KOOS subscales improved throughout the study for both MCPBR and UC groups. There was no significant difference between groups for KOOS change or absolute values at the start or finish. Previous literature has identified a patient acceptable symptom score (PASS score) for KOOS (Muller et al., 2016). In this study, 61% of participants in both MCPBR and UC groups met the six-month KOOS ADL subscale PASS criteria at only 18 weeks post-ACLR. This compares favourably to previous research, where 55% of patients from the Norwegian Knee Registry considered their symptoms acceptable at their six-month follow-up (Ingelsrud et al., 2015). Similarly, IKDC scores and present knee self-efficacy improved for all participants, and there were no between-group differences.

Clinical implications

Based on the results of this study, MCPBR is not currently recommended in a New Zealand context for ACL rehabilitation. However, patients and physiotherapists may consider undertaking such rehabilitation if that is their preference, as there is no evidence yet that such a programme may lead to poorer outcomes than usual care.

Strengths

This study was a novel design explicitly aimed at improving outcomes for females by benefitting from female hormone fluctuations and female-specific preferences for ACLR rehabilitation. This study was the first to adapt previous MC phase-based training designs and apply them to a rehabilitation context. Second, this study was designed utilising recommendations given by females. Because the programme was tailored to meet the preferences of females, this could explain why the attrition rate was lower than anticipated based on the sample size estimation. Similarly, adherence to MCPBR was positive, with participants attending most scheduled appointments, and only one participant was excluded due to non-compliance with MC verification methods. Finally, the research team excluded a further three females post priori due to being unable to verify regular ovulation, which ensures that the results reflect the truth in the population studied rather than methodological error and ensures a high level of internal validity (Patino & Ferreira, 2018).

Limitations

This study did not meet the numbers required for statistical power, limiting its ability to detect a true effect if it existed. Therefore, this study may not have identified real differences between MCPBR and UC when there may have been some. Difficulty recruiting the targeted sample size may reflect the timing of the trial during ongoing COVID-19 lockdowns in New Zealand, and the small proportion of eligible ACL injuries: females with a eumenorrheic MC. This small sample size may also have meant there was a risk of sampling bias and an increased variability of outcomes, both of which may increase the chance of Type I and Type II errors. Additionally, subgroup analyses were unable to be conducted due to the small sample size, which may have provided extra insight into how results may have varied across different subpopulations, such as those who carried out more or less quadriceps strengthening.

Participants carried out twice weekly strengthening in their physiotherapy sessions; however, they were not allowed extra resistance training outside of this prescribed training environment. This may have limited some participants – particularly trained individuals – from reaching their maximum ability of strength gain over the 12-week period. Furthermore, participants did not have an initial strength test of their injured leg, which could have meant baseline differences were erroneously interpreted as treatment effects or, concurrently, Type II errors may have occurred if true baseline differences were not accounted for and masked**.** Although physiotherapists were provided with protocols and training to standardise measurements, the number of different physiotherapists may have led to variability in the strength measurements. Similarly, both knee extension machines and handheld dynamometry were used to collect strength measures, depending on what was available in the treating physiotherapy clinic, which also may have led to variability in the strength measurements. No long-term data were collected, including return to function or re-injury rates. Finally, this study did not discuss females' experiences of engaging with MCPBR.

CONCLUSION

Results from this study demonstrate that participating in MCPBR and UC resulted in similar LSI and self-reported function for females at 18 weeks post-ACLR. However, the study was underpowered to detect a difference in the primary outcome, which limits the ability to draw definitive conclusions. This study does not support the premise that MCPBR needs to be recommended for ACL rehabilitation in a New Zealand context. Conversely, patients and physiotherapists may consider undertaking this rehabilitation if this is a patient's preference, as there is no evidence yet that such a programme may lead to poorer outcomes than usual care. Future research should investigate a larger cohort of females, including strength measures of both legs over a longer period. Similarly, it would be pertinent to understand females' acceptability of engaging with MCPBR.

KEY POINTS

1. This rehabilitation programme synchronised ACLR rehabilitation to females' MCs.
2. Participants had similar limb symmetry following MCPBR versus UC. Therefore, this study does not support that MCPBR needs to be recommended for ACL rehabilitation in a New Zealand context.
3. Patients and physiotherapists may consider undertaking such rehabilitation if that may be their preference, as there is no evidence yet that such a programme may lead to poorer outcomes than usual care.

DISCLOSURES

The primary author (EOL) received a scholarship from the New Zealand Manipulative Physiotherapists Association (NZMPA) in 2020 and at the time of the study was an employee of the Accident Compensation Corporation (ACC). ACC provided funding for her PhD fees as part of her continuing professional development allowance. In addition, DR had a research fund that provided funding for the trial. No conflicts of interest exist that may be perceived to interfere with or bias this study.

PERMISSIONS

This study was approved by the New Zealand Health and Disability Ethics Committee 21/CEN/92 and the Auckland University of Technology Ethics Committee application 20/224. Permission has been granted by the *New Zealand Journal of Sports Medicine* to republish Figure 1 in the *New Zealand Journal of Physiotherapy*.

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CONTRIBUTIONS OF AUTHORS

EOL, DR, and SS designed the study and created the study protocol; PL conducted statistical analysis; all authors contributed to writing and editing the manuscript.

ADDRESS FOR CORRESPONDENCE

Emma O'Loughlin, Department of Surgery and Anaesthesia, University of Otago, Wellington, New Zealand.

Email: emma.oloughlin@otago.ac.nz

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APPENDIX A

MENSTRUAL CYCLE PHASE BASED ACLR REHABILITATION GUIDE FOR PHYSIOTHERAPISTS

Part A: Guide for Intervention Group

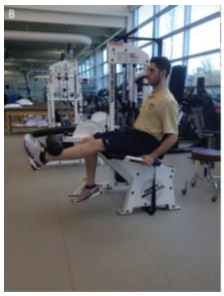
This includes:

- Instructions for first and last appointments.
- Instructions on how to measure quadriceps strength.
- Instructions for verifying menstrual cycle phase with participant.
- Instructions for periodisation of rehabilitation.
- Instructions regarding which strengthening exercises to complete with participant, and a guideline for the progression of these.
- Examples of exercises appropriate for the luteal phase rehabilitation sessions.

Initial appointment – 6 weeks post-operation

1. Screen operation notes and notify researcher if client does not meet inclusion criteria.
2. Check Google Sheets to ensure calendar tracking, basal body temperature and ovulation prediction results have been entered by participant.
3. Establish participant's menstrual cycle (MC) phase and enter result into Google Sheet.
4. Client to complete KOOS 12 form and enter result into Google Sheet.
5. Client to complete IKDC subjective knee evaluation form and enter result into Google Sheet.
6. Client to complete K-SES form and enter result into Google Sheet.
7. Ensure appointments booked x 2/week for 12 weeks and enter dates into Google Sheet.
8. Obtain 1RM knee extension strength of the uninjured leg and enter into Google Sheet.

How to assess 1RM (Sinacore et al., 2017)



- Requires a knee extension machine.
- All 1RM testing should begin with the uninvolved limb and alternated between limbs.
- The tester will instruct the patient to extend the knee against the resistance of the machine in a slow and controlled fashion.
- Trials are deemed successful when the patient has achieved the targeted angle of knee extension and maintained it for 2 s.
- Resistance is increased after a successful trial on each limb by 2 to 14 kg, at the tester's discretion, depending on the difficulty of the previous repetition.
- Failure is defined as three unsuccessful attempts to lift the weight to the targeted angle, with a rest interval of up to 60 s given between attempts.
- The final 1RM values for the involved and uninvolved legs are to be recorded.
- Testing can be done at 90–0° knee extension or 90–45° knee extension. As time progresses, clearly the resistance of the test needs to increase.

Periodisation of rehabilitation programme

How to establish if the participant is in follicular phase:

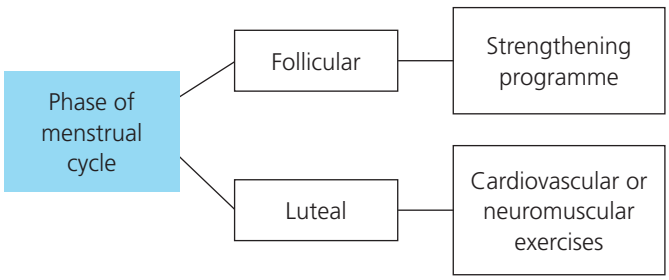
1. They have logged their recent menses into their calendar.
2. They have not yet logged a positive urinary ovulation predictor kit result.

How to establish if the participant is in luteal phase:

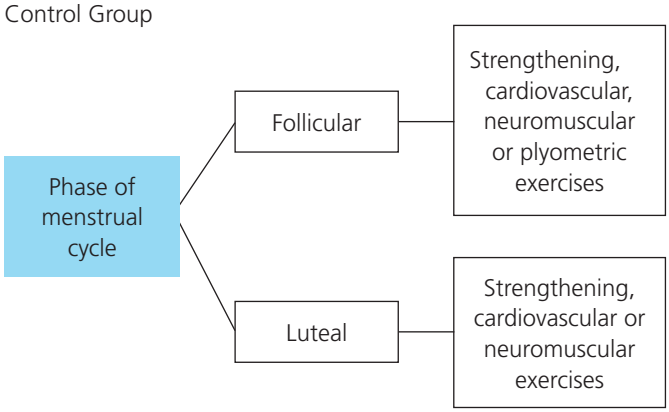
1. Their calendar indicates that ovulation should have occurred.
2. They have entered several raised basal body thermometer reading.
3. They have entered in a positive urinary kit result.

Periodisation

Intervention Group



Control Group



Follicular phase guide

Please complete these three exercises per session in the follicular phase.

Olympic leg press – Closed kinetic chain

Squat – Closed kinetic chain

Seated knee extension – Open kinetic chain

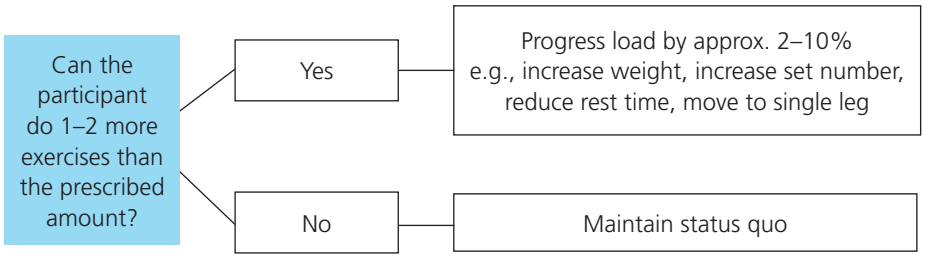
*Open chain exercises should be incorporated as per surgeons' instructions. Open chain should start at 90-45°, then full arc 90-0° but without resistance. Strong isometric quadriceps holds are to be encouraged at the end of the full arc.

*From 8–12 weeks (week 4 of research study) onwards you can introduce resistance and graduate this over the next 4–6 weeks.

Progression Guide

Week 6–10	Week 11–14	Week 15–18
Double leg leg press and double leg squat 60% of 1RM 8–12reps 2–3 sets	Double leg press and double leg squat 70–80% of 1RM 6–8 reps 2–3 reps Progress to single leg	Single leg press and single leg squat 70–80% of 1RM 4–6 reps 2–3 sets
Leg extension 90-45°, then 90-0° Strong isometric holds Start to add resistance approx. week 8	Double leg knee extension 60% of 1RM 8–12 reps 2–3 sets	Single leg knee extension 70–80% of 1RM 6–8 reps 2–3 sets

Do I progress the client?



Remember! Any increase in pain and swelling following exercise sessions indicates the exercises were too hard – drop back to previous week until the knee settles.

*Strength exercises should be done at the start of each session (before neuromuscular control or mobility exercises).

*Multi-joint exercises (leg press and squat) should be done before single joint (leg extension) exercises.

Luteal phase guide

All exercises stated below are examples of exercises that are suitable (depending on the participant's ability) to complete within the luteal phase sessions.

Cardiovascular exercises
Walking
Ergo machine
Rowing
Cycling

Neuromuscular exercises
Toe stand Toe/heel walk
Bosu/wobble board stand/single leg stand/mini squat/step ups
Step up/downs
Lateral step up/downs
Single leg stand/balance – Star exercise, balance and reach
Grapevine
Medicine ball core exercise
Graduated agility exercises with good movement form
Consider controlled vertical hopping (on the spot) when movement patterns are appropriate

Final appointment – 18 weeks post–operation

1. Check Google Sheets to ensure calendar tracking, basal body temperature, ovulation prediction, outcome measures and exercise records are entered.
2. Client to complete KOOS 12 form and enter result into Google Sheet.
3. Client to complete IKDC subjective knee evaluation form and enter result into Google Sheet.
4. Client to complete K-SES form, enter result into Google Sheet.
5. Obtain isometric quadriceps strength measures with handheld dynamometer on bilateral lower limbs and enter result into Google Sheet.
6. Obtain 1RM knee extension strength of bilateral lower limbs and enter result into Google Sheet.
7. Email researcher to acknowledge end of protocol with patient.

Part B: Guide for Control Group

- It is expected the control group will also receive an evidence based, phased, and criterion based progressive ACLR rehabilitation programme.
- Below is an adapted postoperative rehabilitation guide from Van Melick et al. (2016) and Adams et al. (2012) which can be used as a guide for best practice post op ACLR rehabilitation for the control group.

Phase 2. Range of motion/strength/muscle reactivation/ balance (2–12 weeks)

Goals

- Build knee strength
- Restore normal range of motion
- Restore balance and walking confidence

Intermediate postoperative phase (weeks 3–5) milestones

- Knee flexion ROM to within 10° of uninvolved side
- Quadriceps strength greater than 60% of uninvolved side

Treatment

- Tibiofemoral mobilisations with rotation for ROM if joint mobility is limited
- Progress bike duration (10 min minimum)
- Begin graduated balance and proprioceptive activities

Late post-operative phase (Weeks 6–8) milestones

- Quadriceps strength greater than 80% of uninvolved side
- Normal gait pattern
- Full knee ROM (compared to uninvolved side)
- Knee effusion of trace or less

Treatment

- Progress exercises in intensity and duration
- Continue exercise programme at fitness facility (if all milestones are met)
- Maintain or gain quadriceps strength (greater than 80% of uninvolved side)
- Sports-specific activities – graduate from easy to more challenging over time

Phase 3. Function: In a controlled environment and with good movement patterns – running, jumping, hopping, landing (3–6 months)

Goals

- Restore strength to 80% of uninvolved limb
- Restore functional movements – running, jumping, landing, hopping, landing

Follow-up functional testing (4 months, 5 months, 6 months, 1 year post-operative)

- Milestones functional phase (3–6 months)
- Maintain gains in strength (greater than or equal to 90% to 100%)
- Consider controlled vertical hopping (on the spot) when movement patterns are appropriate
- Return-to-sport criteria (see below)
- Recommend changes in rehabilitation as needed. Progression may emphasise single-leg activities in gym, explosive types of activities (cutting, jumping, plyometrics, landing training)

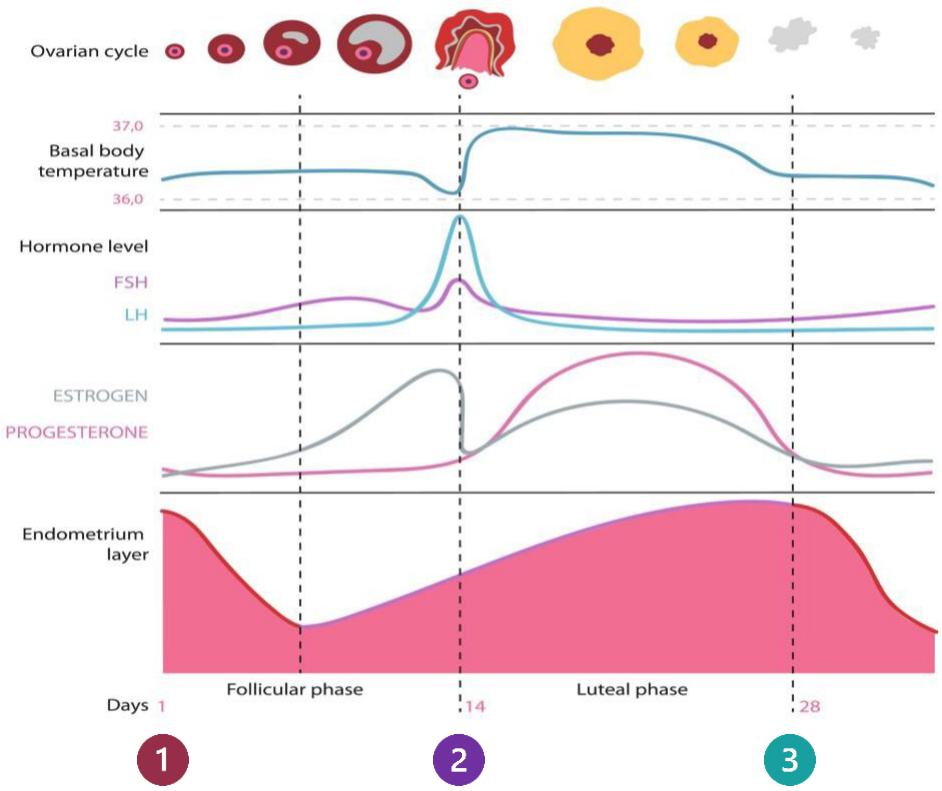
APPENDIX B

PARTICIPANT EDUCATION PACK

Thank you for your interest in taking part in 'A Female Specific Menstrual Cycle Phased Anterior Cruciate Ligament Rehab Programme'.

The research team will track your menstrual cycle as part of the programme. This education pack aims to educate you about your menstrual cycle, and the processes involved to track your menstrual cycle.

The Menstrual Cycle



1. When you get your period, this is the first day of the follicular phase.
   Ovulation occurs on approximately day 14. This is when your ovary releases an egg.
2. Once ovulation occurs, you are in the luteal phase.
   Your basal body temperature and luteinising hormone (LH) levels rise around ovulation.
   The luteal phase lasts about two weeks.
3. When you get your period again, you have finished the luteal phase.
   You will now start a new menstrual cycle.

Tracking Your Menstrual Cycle

The research team will send you a link to your own online logbook (a Google Sheet), and will post you a basal body thermometer and an ovulation predictor kit to help track your menstrual cycle.

Tracking your menstrual cycle is a **3 step process**.

1 Record your period in your online logbook. When? Daily when you have your period.

- The length of the menstrual cycle is the duration from your first menstrual bleeding day to the day before the next bleeding begins.

2 Measure your basal body temperature.

When? Daily.

- The process for basal body temperature tracking is simple, but it does require a small commitment.
- Every morning before getting out of bed, take your temperature and note it in your logbook.
- The thermometer needs to be placed under the tongue and left there until it beeps.
- Take your temperature as close to the same time every day as you can.
- You should have a minimum of five hours of sleep before measuring.

3 Use an ovulation prediction kit

When? Daily, starting 10 days from the start of your period, until a positive result is recorded.

- If you have a short cycle, you should start using an ovulation test kit 4 day prior to your cycle's midpoint. *(The research team can help you with this)*.
- Your ovulation kit instructions can be found here: https://www.pregmate.com/pages/ovulation-test-strips-instructions-for-use
- In short:
  1. Dip the strip into the urine for 3-5 seconds.
  2. Lay the strip flat.
  3. Read results in 5 minutes.

  Positive: If two colour lines are visible and the test line is equal to or darker than the control line.

  Negative: Only one line appears in the control area or the test line is lighter than the control line.
- Record the results in your logbook.
- **How long should I continue to perform the test?** At least 5 days or until the LH surge has been detected.

Any questions? Contact the research team at ccq8275@autuni.co.nz or 0221723949

The research team is here to help you understand this information and is available via email or phone at any time, to answer any questions you may have.

APPENDIX C

Table C1

Initial Outcome Scores

Outcome	Usual care group (n = 17)		MCPBR group (n = 19)		p
	M	*SD*	*M*	*SD*	
1RM non-injured (kg)	38.4	7.7	40.8	10.5	0.37
KOOS					
Total (%)	59.8	15.1	65.0	13.0	0.14
Pain (%)	56.4	18.8	53.3	13.4	0.28
Symptoms (%)	50.1	13.4	48.2	13.9	0.68
ADL (%)	70.9	18.7	71.4	17.2	0.94
Sports and recreation (%)	25.6	19.4	31.3	27.8	0.48
Quality of life (%)	31.0	16.4	22.4	15.6	0.21
IKDC (%)	39.6	11.6	37.4	13.7	0.61
K-SES					
Total	61.1	33.3	50.6	35.1	0.21
Self-efficacy movements	19.6	14.2	17.9	17.4	0.76
Self-efficacy leisure	29.1	18.2	21.8	16.5	0.22
Future self-efficacy	12.5	6.0	10.8	5.1	0.51

Note. ADL = activities of daily living; KOOS = Knee Osteoarthritis Outcome Score; IKDC = the International Knee Documentation Committee Questionnaire; K-SES = Knee Self-Efficacy Scale; MCPBR = menstrual cycle phase-based rehabilitation; 1RM = one repetition maximum.

Table C2

Programme Engagement and Adherence

Variable	Usual care group (n = 16)		MCPBR group (n = 18)		p
	M [a]	*SD* [a]	*M* [a]	*SD* [a]	
Total physiotherapy sessions attended	18.0	5.5	19.7	3.7	0.27
Total physiotherapy sessions attended in follicular phase	8.5	3.5	9.3	1.9	0.35
Total physiotherapy sessions attended in luteal phase, *Mdn* (IQR)	11 [6–12]		11 [7–12]		0.44
Total home exercise physiotherapy sessions completed, *Mdn* (IQR)	0 [0–4]		0 [0–2]		0.70
Total telehealth physiotherapy sessions completed, *Mdn* (IQR)	0 [0–0]		0 [0–0]		0.28
Total physiotherapy sessions which included quadriceps strengthening exercises	17.4	6.1	9.6	2.2	< 0.0001
Total physiotherapy sessions which included knee extension exercises	9.3	7.3	8.9	3.2	0.85
Total days active outside physiotherapy	45.3	18.5	40.2	23.2	0.45
Total days no exercise outside physiotherapy	22.0	13.9	21.3	18.2	0.89
Measurement equipment used for strength tests, *n* (%)					
Knee extension machine	10	(63)	14	(78)	0.33
Handheld dynamometer	6	(37)	4	(22)	

Note. IQR = interquartile range; MCPBR = menstrual cycle phase-based rehabilitation.

[a] Except where indicated.