

1 ABSTRACT

2 Manual therapy has proven benefit in the management of knee osteoarthritis (OA), but the effects of the method of Mulligan's mobilization with
3 movement (MWM) have yet to be explored in knee OA. As a first step, this case series investigated MWM's immediate and short-term benefits
4 over three occasions of treatment in 19 patients with knee OA. Patients (71.1 \pm SD 13.9 years, 14 females and 5 males) received individually
5 prescribed MWM and performed self-MWM. Outcome measures included: 1) pain intensity (visual analogue scales) during walking, ascending
6 and descending stairs and sit-to-stand; 2) passive flexion and extension range of motion (ROM); 3) Activities of Daily Living Scale of the Knee
7 Outcome Survey (KOS-ADLS). Pain and ROM were assessed at baseline, after the initial treatment, before the second treatment and at exit at the
8 fourth consultation. The KOS-ADLS was assessed at baseline and at exit. Significant improvements from baseline were detected in flexion ROM
9 and pain scores in all tasks following the initial treatment ($P < 0.05/3$). The KOS-ADLS score improved significantly from baseline (67.1% SD
10 16.6%) to exit (86.3% SD 12.6%) ($P < 0.001$). MWM was associated with immediate pain-relief and improved knee function, suggesting its
11 potential as a component of early management of knee OA.

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13 **Key Words:** knee, musculoskeletal manipulations, osteoarthritis, pain

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1 INTRODUCTION

2 Knee osteoarthritis (OA) is a frequent cause of knee pain (Felson, Naimark and Anderson, 1987) which can be successfully managed by
3 physiotherapy (Page, Hinman and Bennell, 2011). Furthermore, two recent systematic reviews demonstrated the usefulness of manual therapy and
4 exercise for the management of knee OA (Jansen, 2011; French, Brennan, White and Cusack, 2011), while Deyle et al (2011) reported predictor
5 variables for patients unlikely to respond to these interventions. In addition, joint mobilization has been shown to be a useful modality to reduce
6 knee pain (Moss, Sluka and Wright, 2007). Mulligan's concept of mobilization with movement (MWM) is a contemporary form of joint
7 mobilization (Konstantinou, Foster, Rushton and Baxter, 2002), consisting of a therapist applied pain-free accessory gliding force combined with
8 active movement (Mulligan, 2004). There are reports of immediate pain-relief and improved function in response to these techniques in several
9 musculoskeletal disorders (Abbott, Patla and Jensen, 2001; Vicenzino, Paungmali, Buratowski and Wright, 2001; Paungmali, O'Leary, Souvlis
10 and Vicenzino, 2003; Collins, Teys and Vicenzino, 2004; Teys, Bisset and Vicenzino, 2008). The mechanisms by which MWM achieves
11 pain-relief are not well understood; however, biomechanical and neurophysiological mechanisms are probably involved (Vicenzino, Hall, Hing
12 and Rivett, 2011).

13 To our knowledge, there have been no reports to date of the effects of MWM on knee pain and disability associated with knee OA.
14 Although a prospective randomized controlled trial (RCT) is the appropriate methodology to investigate treatment effects of MWM on knee OA,
15 it is advantageous to have preliminary evidence of the immediate and short-term positive effects of MWM on knee OA patients both to justify the
16 cost of conducting a formal RCT and to assist the development of a well-designed trial. Thus as this first step, we conducted a prospective case
17 series in which the immediate and short-term effects of MWM on OA knee pain and associated disability were evaluated prior to the introduction

1 of a multimodal program inclusive of exercise at the fourth consultation.

2 METHODS

3 Patients

4 This case series reports on 19 patients with knee OA who attended an outpatient clinic at the Shinoro Orthopedic Hospital in Japan over a
5 2 month period from December 2010 to January 2011. Inclusion criteria for knee OA was grade 2 or 3 knee OA according to the Kellgren &
6 Lawrence classification (Kellgren and Lawrence, 1957). The diagnosis was made by an experienced orthopedic surgeon based on x-ray and MRI
7 findings using a standard classification of knee OA (Altman et al., 1986). The patients agreed to participate in this study before commencing
8 pharmacological pain management and other modalities of management for knee OA. The most painful side was treated with MWM in patients
9 with bilateral knee OA. Ethical principles were followed according to the Declaration of Helsinki and all participants provided written informed
10 consent following an explanation about the study.

11 Outcome Measures

12 Outcome measures included pain severity during performance of four functional tasks using a visual analogue scale (VAS), passive knee
13 joint range of motion (ROM), and level of disability determined by the KOS-ADLS Japanese version (Yoshida, Kubo, Irrgang and
14 Snyder-Mackler, 2010). Pain severity and ROM were assessed by an independent assessor who remained blinded to the previous scores on the
15 outcome measures. The measures were performed at baseline prior to the intervention on day 1, immediately after treatment on day 1, before the
16 second treatment session and at final follow-up before other modalities were added at the fourth consultation. This allowed us to examine
17 immediate and carry over effect of the initial treatment as well as the effects of MWM in the short-term after three treatments. As the KOS-ADLS

1 asks participants to rate knee symptoms and function over the previous few days, it was not appropriate to administer this questionnaire at the
2 second consultation. Thus, the KOS-ADLS was completed at baseline and at the final follow-up only.

3 **VAS pain score**

4 A 100-mm VAS (0mm = no pain, 100mm = worst pain ever) is considered a valid and reliable measure for pain intensity (Williamson
5 and Hoggart, 2005; Hawker, Mian, Kendzerska and French, 2011; Sindhu, Shechtman and Tuckey, 2011) and its test-retest reliability in
6 individuals with knee and hip OA is generally acceptable (intra-class correlation coefficients [ICC] = 0.55-0.89) (Wessel, 1995; Grafton, Foster
7 and Wright, 2005). Previous studies of knee OA have assessed pain (VAS) during functional tasks, including walking, ascending and descending
8 stairs, and sitting-to standing (Moss, Sluka and Wright, 2007; Ađlamiř, Toraman and Yaman, 2008; Azlin and Lyn, 2011; Huang et al., 2011) and
9 this measure was adopted in this case series. Hence, patients were asked to rate their knee pain using a VAS, during four tasks undertaken at their
10 usual pace; Task 1: a 20m walk test; Task 2: ascending and Task 3: descending seven stairs without using a handrail and with alternating steps;
11 Task 4: Five repetitions of sit to stand from a standard height chair with arms folded across their chest.

12 **ROM**

13 Passive ROM for knee flexion and extension was measured in supine lying using a standard goniometer. A systematic review
14 demonstrated generally acceptable inter-rater reliability (ICC = 0.59-0.90) for this goniometric measurement (van Trijffel, van de Pol, Oostendorp
15 and Lucas, 2010). In this study, three repetitions were performed in each direction and the average value recorded for analysis.

16 **KOS-ADLS**

1 The KOS-ADLS is a valid and reliable (test-retest reliability; ICC = 0.97) self-rating questionnaire used for various painful knee
2 conditions to evaluate symptoms and functional limitations over the previous few days (Irrgang et al., 1998). The symptom section has six
3 questions regarding pain, stiffness, joint swelling, giving way, weakness and limping. In this section, patients rate their disability level on a
4 6-point Likert scale (0 = complete loss of function due to the symptoms, 5 = no symptoms). The functional limitation section has eight questions
5 regarding walking, ascending and descending stairs, standing, kneeling, squatting, sitting, and rising from a chair and patients rate their disability
6 level on a 6-point Likert scale (0 = inability to perform it, 5 = no limitation). The total score (KOS-ADLS^{total}) is presented in percentiles (0% = the
7 highest disability, 100% = no disability). The KOS-ADLS^{total} also reflects psychological reactions such as fear of movement and anxiety (Scopaz,
8 Piva, Wisniewski and Fitzgerald, 2009). The KOS-ADLS^{total} was used as a measure of total disability level in this study and scores of the
9 symptom (KOS-ADLS^{symptom}) and functional limitation sub-sections (KOA-ADLS^{function}) were used to inform on the levels of symptom and
10 functional limitation, respectively, as secondary measures.

11 Intervention

12 Patients completed a course of therapist and self-applied MWM only for the first three clinic visits. There was a 2-3 day interval between
13 each consultation, and the total duration of the intervention period in this study ranged from 13 to 16 days. At the fourth clinic visit, participants
14 commenced a multimodal program inclusive of therapeutic exercise.

15 **Identification of the Glide Direction for the MWM Treatment Technique**

16 A physiotherapist, with two years experience in using MWM, applied all treatments for each patient. MWM consisted of a sustained
17 manual glide of the tibia (either medial, lateral, anterior, posterior or rotation) during active knee flexion and extension. These techniques are

1 described in detail in a textbook of MWM (Mulligan, 2004). Each patient was tested with sustained manual glides in each of the possible
2 directions during active knee flexion and extension in supine lying. Frontal plane glides were tested first and then sagittal plane glides followed
3 by rotation. The glide direction that reduced pain to the minimum level and improved range of knee motion most was chosen as the glide for the
4 MWM treatment technique. Overpressure was included at end range if ROM was pain-free. If pain was not present in supine lying, then the glide
5 direction for the MWM treatment technique was assessed in a weight bearing position in a similar manner. If in supine lying more than one glide
6 direction had similar beneficial effects, then these assessments were repeated in weight bearing to identify the most effective glide direction for
7 the treatment technique.

8 **Procedures for the Intervention**

9 At the first consultation, a therapist-applied MWM was performed (two sets of 10 repetitions) during active knee flexion and extension.
10 The therapist initially applied the pain-free manual glide force on the tibia with the knee resting in a mid range position. The glide force was
11 sustained while the patient performed 10 repetitions of self-paced active full range knee flexion and extension. Either of two protocols was used
12 depending on the assessment of the patient's pain during active knee flexion and extension in lying. (i) For patients with pain during active knee
13 flexion and extension in lying, the technique was performed initially in lying. The technique was progressed to weight bearing positions when the
14 movement in lying became pain free. The patient was taught a self-applied MWM in weight bearing position. (ii) For patients without pain during
15 active knee flexion and extension in lying, a therapist-applied MWM (two sets of 10 repetitions) was performed in the weight bearing position.
16 Patients were similarly instructed in the self-applied MWM in the weight bearing position (Figure 1).

17 The self-management regime involved at least 20 movement repetitions, performed every three hours (or at least 4-5 times per day).

1 Patients could perform the MWM exercise more frequently if they experienced any increase in pain with daily activities. Patients were also
2 advised to stop the self-applied MWM if this exercise caused pain, or their knee showed signs of increasing inflammation such as swelling, heat,
3 and/or redness greater than pre-treatment levels.

4 On the subsequent two consultations, the therapist-applied MWM intervention was repeated. Patients were treated in lying if they
5 continued to have pain during movement in the non weight bearing position. Otherwise, the therapist-applied MWM was performed in the weight
6 bearing position. The glide direction was again checked prior to application of the intervention. Patients' self-applied MWM were checked for
7 their correctness at each visit.

8 Statistical Analysis

9 Outcomes were analyzed using an intention to treat analysis. Preliminary analysis (Shapiro-Wilk test) revealed that data were not
10 normally distributed. Therefore, comparisons of the pain and ROM outcome measures across the assessment points were analyzed using
11 Friedman tests. As therapeutic effects of MWM were expected *a priori*, one-tailed analyses were used for comparison. The one-tailed Wilcoxon
12 signed rank test with Bonferroni adjustments was used to examine improvements in pain and ROM between the baseline and each assessment
13 point (three time points). The one-tailed Wilcoxon signed rank test was also used to analyze KOS-ADLS data. All statistical analyses were
14 performed with SPSS version 19.0 (IBM Corporation, New York, USA). Significance level was set at < 0.05 .

15 OUTCOMES

16 Eleven patients began treatment in lying at the initial consultation. After one set of 10 repetitions of the therapist-applied MWM, the
17 technique was progressed to weight bearing positions in these patients as the movement in lying became pain free. The other eight patients were

1 treated with a therapist-applied MWM in weight bearing position from the outset. Following the therapist-applied MWM, all patients were
2 instructed a self-applied MWM at the end of the initial consultation.

3 At each of the following consultations, no patient reported either exacerbation of pain or inflammation following the therapist and
4 self-applied MWM. The 11 patients, who had pain during active knee flexion and extension in lying and therefore began treatment in lying at the
5 initial consultation, had no pain during active knee flexion and extension in lying at the second visit. Hence, all patients were treated in the weight
6 bearing position. Examination confirmed that the direction of glide applied in the MWM at the initial consultation was appropriate.

7 Patients' characteristics and the direction of glide applied in the MWM are summarized in Table 1. There were no complications arising
8 from the MWM intervention. All patients completed each treatment session (no drop-outs). All patients verbally reported that they had undertaken
9 the prescribed self-applied MWM home exercise program.

10 VAS Pain Score during Functional Tasks

11 Table 2 presents the mean (SD) values of the pain VAS scores in the four tasks over the four assessment points. Significant time effects
12 ($P < 0.001$) were detected. The pain VAS scores were significantly lower than baseline over all assessment points in each task (all $P < 0.001$). The
13 greatest change occurred immediately after the first treatment and pain was minimal at the final assessment.

14 Passive Knee ROM

15 Table 3 presents the mean (SD) values for knee flexion and extension range. Significant time effects ($P = 0.007$) were detected in knee
16 flexion ROM. The one-tailed Wilcoxon signed rank tests demonstrated that there was significant improvement from baseline in knee flexion
17 ROM immediately after the initial treatment ($P = 0.012 < 0.05/3$) and at the final assessment point ($P = 0.013 < 0.05/3$). However, significant

1 time effects were not detected in knee extension ROM ($P = 0.059$).

2 KOS-ADLS

3 Table 4 presents the mean (SD) values for the KOS-ADLS^{total}, KOS-ADLS^{symptom} and KOA-ADLS^{function}. Analysis revealed that the
4 KOS-ADLS^{total} and its components, KOS-ADLS^{symptom} and KOA-ADLS^{function} improved significantly from baseline ($P < 0.001$).

5 DISCUSSION

6 This short-term prospective case series revealed that MWM was associated with an immediate reduction in pain during performance of
7 functional tasks. Such positive effects are similar to those reported for MWM administered for other extremity joint problems (Vicenzino and
8 Wright, 1995; O'Brien and Vicenzino, 1998; Backstrom, 2002; Paungmali, Vicenzino and Smith, 2003). Pain intensity scores in the functional
9 tasks were minimal on presentation for the fourth consultation, representing changes from baseline ranging from 30-48mm on the VAS, which are
10 clinically relevant improvements (Grafton, Foster and Wright, 2005).

11 Interestingly, the greatest reduction in pain occurred after the initial treatment application. The reduction was maintained until the second
12 consultation. Pain continued to decline after treatments 2 and 3 and most subjects had minimal or no pain on their final assessment. However, the
13 changes in pain between these subsequent assessment points were minimal. The reduction in pain intensity and its maintenance probably reflects
14 a combination of the effect of the therapist and patient applied MWM, but we are unable to separate the effects in this instance. Nevertheless, the
15 pain relieving effect of MWM for knee OA achieved predominantly at the initial application, suggests that MWM could be applied at the first
16 treatment session to reduce pain and that exercise programs may be able to be commenced at the second consultation. The pain relief afforded by
17 MWM might limit its de-motivating effects (Fraenkel and Fried, 2008) to start exercise and would position the patient well to undertake exercise

1 programs, which are recommended for the management of knee OA (Altman, Hochberg, Moskowitz and Schnitzer, 2000; Roddy et al., 2005). It
2 would be interesting to compare recovery time and compliance with exercise programs between a management plan where MWM is performed at
3 the initial consultation and exercise programs start at the second assessment and a management plan where exercise programs start at the initial
4 consultation.

5 The treatment with MWM resulted in significant improvement in KOS-ADLS scores. The KOS-ADLS scores at baseline are consistent
6 with other reports of disability in knee OA patients (Piva et al., 2004; Courtney et al., 2009; Zeni Jr, Axe and Snyder-Mackler, 2010; Zeni Jr and
7 Snyder-Mackler, 2010). Scores following the three treatments were representative of normal or nearly normal functional levels (Irrgang et al.,
8 1998) and were comparable with those documented following surgery for knee OA (Mizner et al., 2005; Briem et al., 2007) or knee hyaluronic
9 acid injections (Briem, Axe and Snyder-Mackler, 2009). Changes of the mean KOS-ADLS^{total} values were 19.2 in this study. Irrgang et al (1998)
10 showed that patients who achieved great improvements and somewhat improvements on a 5-point global perceived change after 4-week
11 physiotherapy had mean changes of approximately 25 and 11, respectively. Thus the treatment with MWM resulted in clinically relevant
12 improvement in disability due to knee pain and malfunction.

13 The mechanisms by which MWM achieves pain-relief are not well understood, however biomechanical and neurophysiological
14 mechanisms may be involved (Vicenzino, Hall, Hing and Rivett, 2011). Biomechanically it was initially proposed that MWM may address joint
15 partner bone alignment (ie, position fault) (Mulligan, 2004) and some observations of positional faults have been made (Hsieh et al., 2002;
16 Hubbard, Hertel and Sherbondy, 2006; Hubbard and Hertel, 2008). However, there is currently insufficient evidence to support correction of a
17 positional fault as the mechanism of action for pain relief following MWM (Vicenzino, Paungmali and Teys, 2007). Potential neurophysiological

1 mechanisms include changes in descending pain inhibitory systems (Paungmali, Vicenzino and Smith, 2003; Skyba et al., 2003; Paungmali,
2 O'Leary, Souvlis and Vicenzino, 2004), and changes in central pain-processing mechanisms (Paungmali, O'Leary, Souvlis and Vicenzino, 2004;
3 Hall, Hardt, Schafer and Wallin, 2006; Sterling et al., 2010). In addition, the large range movement used in the application of MWM with our
4 patients might alter concentrations of inflammatory mediators (Schmidt, 1996) and result in deactivation of silent/sleeping nociceptors activated
5 by such inflammatory mediators (Sambajon, Cillo Jr, Gassner and Buckley, 2003).

6 While the pain relief afforded by MWM would be associated with improvements of disability level (Schein et al., 2008), other factors
7 may also contribute to the immediate improvements in disability level following MWM. The MWM was largely conducted in a weight bearing
8 position and patients received simultaneous feedback of painless joint movements. This feedback might modulate psychological features such as
9 fear of movements (Vicenzino, Hall, Hing and Rivett, 2011), resulting in an increased activity level. In addition, MWM in a weight bearing
10 position requires muscle activity, which might have resulted in improved motor performance, which would position the patient well to gain long
11 term benefits from a formal exercise program. Further research into the possible psychological and motor benefits of MWM is required.

12 Knee flexion ROM improved from baseline at post initial treatment and the final assessment point but there was no statistically
13 significant change in knee extension ROM across the four assessment points. Generally, knee ROM appeared to improve less than improvements
14 in pain and disability. This may reflect the small number of patients who presented with limited passive knee ROM in our group (8/19 and 6/19
15 were regarded clinically as having limited knee flexion and extension, respectively). Knee ROM was assessed in supine lying rather than in a
16 weight bearing position. Perhaps, if assessment had been undertaken in a functional weight bearing position, greater limitation and changes of
17 movement might have been detected. Such measures might be more useful than our measure of passive ROM in future studies of treatment

1 effects.

2 In our cases, there were no patients who responded to an anterior or posterior glide. This finding corresponds with the clinical experience
3 of Mulligan, who mentioned that the typical direction of beneficial glide for hinge joints was usually medial or lateral (Mulligan, 2004). However,
4 the explanation why anterior or posterior glides are not beneficial for patients with knee OA remains unclear.

5 Case series represent one of the lowest levels of evidence. One limitation is the potential for bias within the sample population who were
6 not randomly selected and the lack of a control group. Our patients may not represent the entire population of people with knee OA and effects
7 may have reflected for example, patients' positive responses arising from their decision to consult an orthopedic surgeon for their knee pain. Such
8 factors underpin the need for a formal RCT. Nevertheless, this case series has demonstrated the potential benefit of MWM for knee OA sufficient
9 we believe to justify a future RCT. In addition, outcomes also point to the need for future research into the mechanisms of action of MWM.

10 A multimodal treatment approach incorporating manual therapy, muscle strengthening, stretching, range of motion and home exercise
11 has been shown to be beneficial for the long-term recovery of knee function and reduction of pain (Deyle et al., 2000; Deyle et al., 2005; Ko, Lee
12 and Lee, 2009; Jansen et al., 2011; Deyle et al., 2012). Given the effective pain relief associated with MWM in our cases, further studies could not
13 only explore the most optimal application of joint mobilization for relief of knee OA pain but also investigate the inclusion of MWM into
14 standardized joint mobilization techniques. .

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1 REFERENCES

- 2 Abbott JH, Patla CE, Jensen RH 2001 The initial effects of an elbow mobilization with movement technique on grip strength in subjects with
3 lateral epicondylalgia. *Manual Therapy* 6: 163-169.
- 4 Ağlamiş B, Toraman NF, Yaman H 2008 The effect of a 12-week supervised multicomponent exercise program on knee OA in Turkish women.
5 *Journal of Back and Musculoskeletal Rehabilitation* 21: 121-128.
- 6 Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, Christy W, Cooke TD, Greenwald R, Hochberg M, Howell D, Kaplan D, Koopman
7 W, Longley S, Mankin H, McShane D, Medsger Jr T, Meenan R, Minnellsen W, Moskowitz R, Murphy W, Rothschild B, Segal M,
8 Sokoloff L, Wolfe F 1986 Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of
9 the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis and Rheumatism* 29:
10 1039-1049.
- 11 Altman RD, Hochberg MC, Moskowitz RW, Schnitzer TJ 2000 Recommendations for the medical management of osteoarthritis of the hip and
12 knee: 2000 update. *Arthritis and Rheumatism* 43: 1905-1915.
- 13 Azlin NMN, Lyn KS 2011 Effects of Passive Joint Mobilization on Patients with Knee Osteoarthritis. *Sains Malaysiana* 40: 1461-1465.
- 14 Backstrom KM 2002 Mobilization with movement as an adjunct intervention in a patient with complicated de Quervain's tenosynovitis: a case
15 report. *Journal of Orthopaedic and Sports Physical Therapy* 32: 86-94.
- 16 Briem K, Axe MJ, Snyder-Mackler L 2009 Medial knee joint loading increases in those who respond to hyaluronan injection for medial knee
17 osteoarthritis. *Journal of Orthopaedic Research* 27: 1420-1425.

- 1 Briem K, Ramsey DK, Newcomb W, Rudolph KS, Snyder-Mackler L 2007 Effects of the amount of valgus correction for medial compartment
2 knee osteoarthritis on clinical outcome, knee kinetics and muscle co-contraction after opening wedge high tibial osteotomy. *Journal of*
3 *Orthopaedic Research* 25: 311-318.
- 4 Collins N, Teys P, Vicenzino B 2004 The initial effects of a Mulligan's mobilization with movement technique on dorsiflexion and pain in
5 subacute ankle sprains. *Manual Therapy* 9: 77-82.
- 6 Courtney CA, Lewek MD, Witte PO, Chmell SJ, Hornby TG 2009 Heightened Flexor Withdrawal Responses in Subjects With Knee
7 Osteoarthritis. *The Journal of Pain* 10: 1242-1249.
- 8 Deyle GD, Allison SC, Matekel RL, Ryder MG, Stang JM, Gohdes DD, Hutton JP, Henderson NE, Garber MB 2005 Physical therapy treatment
9 effectiveness for osteoarthritis of the knee: a randomized comparison of supervised clinical exercise and manual therapy procedures versus
10 a home exercise program. *Physical Therapy* 85: 1301-1317.
- 11 Deyle GD, Gill NW, Allison SC, Hando BR, Rochino DA 2012 Knee OA: Which patients are unlikely to benefit from manual PT and exercise?
12 *Journal of Family Practice* 61: E1-8.
- 13 Deyle GD, Henderson NE, Matekel RL, Ryder MG, Garber MB, Allison SC 2000 Effectiveness of manual physical therapy and exercise in
14 osteoarthritis of the knee. A randomized, controlled trial. *Annals of Internal Medicine* 132: 173-181.
- 15 Felson DT, Naimark A, Anderson J 1987 The prevalence of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. *Arthritis and*
16 *Rheumatism* 30: 914-918.
- 17 Fraenkel L, Fried T 2008 If You Want Patients with Knee Osteoarthritis (OA) to Exercise: Tell them about NSAIDS. *Patient* 1: 21-26.

- 1 French HP, Brennan A, White B, Cusack T 2011 Manual therapy for osteoarthritis of the hip or knee – A systematic review. *Manual Therapy* 16:
2 109-117.
- 3 Grafton KV, Foster NE, Wright CC 2005 Test-retest reliability of the Short-Form McGill Pain Questionnaire: assessment of intraclass correlation
4 coefficients and limits of agreement in patients with osteoarthritis. *Clinical Journal of Pain* 21: 73-82.
- 5 Hall T, Hardt S, Schafer A, Wallin L 2006 Mulligan bent leg raise technique--a preliminary randomized trial of immediate effects after a single
6 intervention. *Manual Therapy* 11: 130-135.
- 7 Hawker GA, Mian S, Kendzerska T, French M 2011 Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for
8 Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale
9 (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis
10 Care and Research* 63: S240-S252.
- 11 Hsieh CY, Vicenzino B, Yang CH, Hu MH, Yang C 2002 Mulligan's mobilization with movement for the thumb: a single case report using
12 magnetic resonance imaging to evaluate the positional fault hypothesis. *Manual Therapy* 7: 44-49.
- 13 Huang TL, Chang CC, Lee CH, Chen SC, Lai CH, Tsai CL 2011 Intra-articular injections of sodium hyaluronate (Hyalgan®) in osteoarthritis of
14 the knee. a randomized, controlled, double-blind, multicenter trial in the asian population. *BMC Musculoskeletal Disorders* 12:
- 15 Hubbard TJ, Hertel J 2008 Anterior positional fault of the fibula after sub-acute lateral ankle sprains. *Manual Therapy* 13: 63-67.
- 16 Hubbard TJ, Hertel J, Sherbondy P 2006 Fibular position in individuals with self-reported chronic ankle instability. *Journal of Orthopaedic and
17 Sports Physical Therapy* 36: 3-9.

- 1 Irrgang JJ, Snyder-Mackler L, Wainner RS, Fu FH, Harner CD 1998 Development of a patient-reported measure of function of the knee. Journal
2 of Bone and Joint Surgery. American Volume 80: 1132-1145.
- 3 Jansen MJ, Viechtbauer W, Lenssen AF, Hendriks EJM, de Bie RA 2011 Strength training alone, exercise therapy alone, and exercise therapy with
4 passive manual mobilisation each reduce pain and disability in people with knee osteoarthritis: a systematic review. Journal of
5 Physiotherapy 57: 11-20.
- 6 Kellgren JH, Lawrence JS 1957 Radiological assessment of osteo-arthrosis. Annals of the Rheumatic Diseases 16: 494-502.
- 7 Ko T, Lee S, Lee D 2009 Manual Therapy and Exercise for OA Knee: Effects on Muscle Strength, Proprioception, and Functional Performance.
8 Journal of Physical Therapy Science 21: 293-299.
- 9 Konstantinou K, Foster N, Rushton A, Baxter D 2002 The use and reported effects of mobilization with movement techniques in low back pain
10 management; a cross-sectional descriptive survey of physiotherapists in Britain. Manual Therapy 7: 206-214.
- 11 Mizner RL, Petterson SC, Stevens JE, Axe MJ, Snyder-Mackler L 2005 Preoperative quadriceps strength predicts functional ability one year after
12 total knee arthroplasty. Journal of Rheumatology 32: 1533-1539.
- 13 Moss P, Sluka K, Wright A 2007 The initial effects of knee joint mobilization on osteoarthritic hyperalgesia. Manual Therapy 12: 109-118.
- 14 Mulligan BR 2004 Manual Therapy NAGS SNAGS MWMS etc. Wellington, New Zealand, Plane View Services.
- 15 O'Brien TO, Vicenzino B 1998 A study of the effects of Mulligan's mobilization with movement treatment of lateral ankle pain using a case study
16 design. Manual Therapy 3: 78-84.
- 17 Page CJ, Hinman RS, Bennell KL 2011 Physiotherapy management of knee osteoarthritis. Int J Rheum Dis 14: 145-151.

- 1 Paungmali A, O'Leary S, Souvlis T, Vicenzino B 2003 Hypoalgesic and sympathoexcitatory effects of mobilization with movement for lateral
2 epicondylalgia. *Physical Therapy* 83: 374-383.
- 3 Paungmali A, O'Leary S, Souvlis T, Vicenzino B 2004 Naloxone fails to antagonize initial hypoalgesic effect of a manual therapy treatment for
4 lateral epicondylalgia. *Journal of Manipulative and Physiological Therapeutics* 27: 180-185.
- 5 Paungmali A, Vicenzino B, Smith M 2003 Hypoalgesia induced by elbow manipulation in lateral epicondylalgia does not exhibit tolerance.
6 *Journal of Pain* 4: 448-454.
- 7 Piva SR, Fitzgerald GK, Irrgang JJ, Bouzubar F, Starz TW 2004 Get Up and Go Test in Patients with Knee Osteoarthritis. *Archives of Physical*
8 *Medicine and Rehabilitation* 85: 284-289.
- 9 Roddy E, Zhang W, Doherty M, Arden NK, Barlow J, Birrell F, Carr A, Chakravarty K, Dickson J, Hay E, Hosie G, Hurley M, Jordan KM,
10 McCarthy C, McMurdo M, Mockett S, O'Reilly S, Peat G, Pendleton A, Richards S 2005 Evidence-based recommendations for the role of
11 exercise in the management of osteoarthritis of the hip or knee--the MOVE consensus. *Rheumatology* 44: 67-73.
- 12 Sambajon VV, Cillo Jr JE, Gassner RJ, Buckley MJ 2003 The effects of mechanical strain on synovial fibroblasts. *Journal of Oral and*
13 *Maxillofacial Surgery* 61: 707-712.
- 14 Schein JR, Kosinski MR, Janagap-Benson C, Gajria K, Lin P, Freedman JD 2008 Functionality and health-status benefits associated with
15 reduction of osteoarthritis pain. *Current Medical Research and Opinion* 24: 1255-1265.
- 16 Schmidt RF 1996 The articular polymodal nociceptor in health and disease. *Progress in Brain Research* 113: 53-81.
- 17 Scopaz KA, Piva SR, Wisniewski S, Fitzgerald GK 2009 Relationships of Fear, Anxiety, and Depression With Physical Function in Patients With

- 1 Knee Osteoarthritis. Archives of Physical Medicine and Rehabilitation 90: 1866-1873.
- 2 Sindhu BS, Shechtman O, Tuckey L 2011 Validity, Reliability, and Responsiveness of a Digital Version of the Visual Analog Scale. Journal of
3 Hand Therapy 24: 356-364.
- 4 Skyba DA, Radhakrishnan R, Rohlwing JJ, Wright A, Sluka KA 2003 Joint manipulation reduces hyperalgesia by activation of monoamine
5 receptors but not opioid or GABA receptors in the spinal cord. Pain 106: 159-168.
- 6 Sterling M, Pedler A, Chan C, Puglisi M, Vuvan V, Vicenzino B 2010 Cervical lateral glide increases nociceptive flexion reflex threshold but not
7 pressure or thermal pain thresholds in chronic whiplash associated disorders: A pilot randomised controlled trial. Manual Therapy 15:
8 149-153.
- 9 Teys P, Bisset L, Vicenzino B 2008 The initial effects of a Mulligan's mobilization with movement technique on range of movement and pressure
10 pain threshold in pain-limited shoulders. Manual Therapy 13: 37-42.
- 11 van Trijffel E, van de Pol RJ, Oostendorp RAB, Lucas C 2010 Inter-rater reliability for measurement of passive physiological movements in
12 lower extremity joints is generally low: a systematic review. Journal of Physiotherapy 56: 223-235.
- 13 Vicenzino B, Hall T, Hing W, Rivett D 2011 A new proposed model of the mechanisms of action of Mobilisation with Movement. In: Vicenzino B,
14 Hall T, Hing W, Rivett D editors (eds) Mobilisation with Movement: The Art and the Science, p 75-85. London, Churchill Livingstone.
- 15 Vicenzino B, Paungmali A, Buratowski S, Wright A 2001 Specific manipulative therapy treatment for chronic lateral epicondylalgia produces
16 uniquely characteristic hypoalgesia. Manual Therapy 6: 205-212.
- 17 Vicenzino B, Paungmali A, Teys P 2007 Mulligan's mobilization-with-movement, positional faults and pain relief: Current concepts from a

- 1 critical review of literature. *Manual Therapy* 12: 98-108.
- 2 Vicenzino B, Wright A 1995 Effects of a novel manipulative physiotherapy technique on tennis elbow: a single case study. *Manual Therapy* 1:
3 30-35.
- 4 Wessel J 1995 The reliability and validity of pain threshold measurements in osteoarthritis of the knee. *Scandinavian Journal of Rheumatology*
5 24: 238-242.
- 6 Williamson A, Hoggart B 2005 Pain: a review of three commonly used pain rating scales. *Journal of Clinical Nursing* 14: 798-804.
- 7 Yoshida Y, Kubo M, Irrgang JJ, Snyder-Mackler L 2010 A Report: Translation into Japanese of the Knee Outcome Survey (KOS-ADLS).
8 *Rigakuryoho Kagaku* 25: 811-819.
- 9 Zeni Jr JA, Axe MJ, Snyder-Mackler L 2010 Clinical predictors of elective total joint replacement in persons with end-stage knee osteoarthritis.
10 *BMC Musculoskeletal Disorders* 11: 86.
- 11 Zeni Jr JA, Snyder-Mackler L 2010 Clinical Outcomes After Simultaneous Bilateral Total Knee Arthroplasty: Comparison to Unilateral Total
12 Knee Arthroplasty and Healthy Controls. *The Journal of Arthroplasty* 25: 541-546.

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1 TABLE 2. 100mm-VAS during four tasks over the four assessment points and statistical outcomes.

Measures	Assessment 1	Assessment 2	Assessment 3	Assessment 4	P-value*	P-value [†] [Z-score]
	Baseline	Immediately after treatment 1	Prior to treatment 2	Exit at fourth consultation		
Walking	31.3 (23.6)	3.9 (4.6)	2.9 (5.4)	1.3 (2.8)	<0.001	Assessment 1 vs Assessment 2; <0.001 [3.5]
						Assessment 1 vs Assessment 3; <0.001 [3.5]
						Assessment 1 vs Assessment 4; <0.001 [3.5]
Ascending stairs	45.0 (21.5)	8.9 (11.6)	5.5 (8.3)	1.1 (2.7)	<0.001	Assessment 1 vs Assessment 2; <0.001 [3.6]
						Assessment 1 vs Assessment 3; <0.001 [3.7]
						Assessment 1 vs Assessment 4; <0.001 [3.7]
Descending stairs	50.5 (19.5)	10.3 (17.5)	8.9 (18.6)	2.6 (5.6)	<0.001	Assessment 1 vs Assessment 2; <0.001 [3.8]
						Assessment 1 vs Assessment 3; <0.001 [3.8]
						Assessment 1 vs Assessment 4; <0.001 [3.8]
Sit-to-stand	32.6 (21.6)	4.5 (7.8)	6.1 (13.5)	0.3 (1.1)	<0.001	Assessment 1 vs Assessment 2; <0.001 [3.4]
						Assessment 1 vs Assessment 3; <0.001 [3.2]
						Assessment 1 vs Assessment 4; <0.001 [3.4]

1 Mean (SD) values in millimeter are presented.

2 * Freidman test.

3 † One-tailed Wilcoxon signed rank test with Bonferroni adjustments (significant level $< 0.05/3=0.017$).

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1 TABLE 3. Knee ROM over the four assessment points and statistical outcomes.

Measures	Assessment 1	Assessment 2	Assessment 3	Assessment 4	P-value*	P-value [†] [Z-score]
	Baseline	Immediately after treatment 1	Prior to treatment 2	Exit at fourth consultation		
Flexion	123.2 (10.6)	126.3 (7.6)	125.8 (8.0)	127.1 (7.1)	0.007	Assessment 1 vs Assessment 2; 0.012 [2.3] Assessment 1 vs Assessment 3; 0.042 [1.7] Assessment 1 vs Assessment 4; 0.013 [2.2]
Extension	4.2 (7.1)	1.8 (4.2)	3.4 (7.5)	2.9 (7.3)	0.059	-

2 Mean (SD) values in degree are presented.

3 * Freidman test.

4 [†] One-tailed Wilcoxon signed rank test with Bonferroni adjustments (significant level < 0.05/3=0.017).

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1 TABLE 4. KOS-ADLS at baseline and the exit and statistical outcomes.

Measures	Assessment 1	Assessment 4	P-value*
	Baseline	Exit at fourth consultation	[Z-score]
KOS-ADLS ^{total}	67.1 (16.6)	86.3 (12.6)	<0.001 [3.8]
KOS-ADLS ^{symptom}	79.9 (13.7)	96.0 (5.2)	<0.001 [3.8]
KOA-ADLS ^{function}	57.5 (22.4)	79.3 (18.6)	<0.001 [3.6]

2 Mean (SD) values in percentile are presented.

3 * One-tailed Wilcoxon signed rank test (significant level < 0.05/3=0.017).

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