## List of supplementary materials

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## **Supplemental Appendix A: Search strategies**

## Central search

| Steps   | Search details   |
|---|--|
| #1:   | MeSH descriptor: [Knee Joint] explode all trees OR (knee):ti,ab,kw OR (knee*):ti,ab,kw   |
| #2:   | MeSH descriptor: [Osteoarthritis, Knee] explode all trees OR (arthr*):ti,ab,kw OR (osteoarthr*):ti,ab,kw OR (degenerative joint disease):ti,ab,kw  |
| #3:   | ("musculoskeletal manipulation") OR (MH "Manipulation, Orthopedic") OR (TI manual therapy OR AB Manual therapy) OR (TI manipulat* OR AB manipulat*) OR (TI mobili* OR AB mobili*)  |
| #4:   | (MeSH descriptor: [Randomized Controlled Trial] explode<br>all trees) OR ((randomized control* trial*):ti,ab,kw) OR<br>((randomized trial*):ti,ab,kw) OR (clinical):ti,ab,kw) OR<br>((random*):ti,ab,kw) OR ((random* control*):ti,ab,kw)) AND<br>((trial):ti,ab,kw) |
| #5:   | (MH "Adult+") OR (MH "Young Adult")  |
| #6: #1 AND #2<br>AND #3 AND #4<br>AND #5  |  |
| #7: #6 with the<br>following filters<br>(English and<br>publication date up<br>to April 2023) |  |

#### **CINAHL** search

| Steps | Search details  |
|-------|---|
| #1:   | (MH "Knee Joint+") OR (TI knee OR AB knee) OR (TI knee* OR AB knee*)  |
| #2:   | (MH "Osteoarthritis, Knee") OR (TI arthr* OR AB arthr*) OR (TI osteoarthr* OR AB osteoarthr*) OR (TI degenerative joint disease OR AB degenerative joint disease)                 |
| #3:   | ("musculoskeletal manipulation") OR (MH "Manipulation, Orthopedic") OR (TI manual therapy OR AB Manual therapy) OR (TI manipulat* OR AB manipulat*) OR (TI mobili* OR AB mobili*) |

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| #4:   | (MH "Randomized Controlled Trials+") OR (TI randomized control* trial* OR AB randomized control* trial*) OR (TI randomized trial* OR AB randomized trial*) OR (((TI clinical OR AB clinical) OR (TI random* OR AB random*) OR (TI random* control* OR AB random* control*)) AND (TI trial OR AB trial)) |
|---|---|
| #5:   | (MH "Adult+") OR (MH "Young Adult")   |
| #6: #1 AND #2<br>AND #3 AND #4<br>AND #5  |   |
| #7: #6 with the following filters (English and publication date up to April 2023) |   |

#### **Embase search**

| Steps  | Search details  |
|--|---|
| #1:  | 'knee'/exp OR knee:ab,ti OR knee*:ab,ti   |
| #2:  | 'knee osteoarthritis'/exp OR arthr*:ab,ti OR osteoarthr*:ab,ti OR 'osteoarthritis'/exp OR "degenerative AND joint AND disease":ab,ti  |
| #3:  | 'musculoskeletal manipulation'/exp OR 'orthopedic manipulation'/exp OR 'manual AND therapy':ab,ti OR manipulat*:ab/ti OR mobili*:ab,ti  |
| #4:  | ('randomized AND control* AND trial*':ab,ti OR 'randomized AND trial*':ab,ti OR 'randomized controlled trial'/exp OR (('clinical"ab,ti OR 'random*':ab,ti OR ('random* AND 'control*':ab,ti)) AND 'trial*':ab,ti) |
| #5:  | "adult'/exp OR 'young adult'/exp  |
| #6: #1 AND #2<br>AND #3 AND #4<br>AND #5                                     |   |
| #7: #6 with the following filters (English and publication years <1966-2023) |   |

## PubMed search

| Steps  | Search details   |  |  |  |
|--|--|--|--|--|
| #1:  | ((knee*[Title/Abstract]) OR (knee[Title/Abstract])) OR<br>("Knee Joint"[Mesh])   |  |  |  |
| #2:  | (((((degenerative joint disease[Title/Abstract]) OR ("Osteoarthritis"[Mesh])) OR (osteoarthr*[Title/Abstract])) OR (arthr*[Title/Abstract])) OR ("Osteoarthritis, Knee"[Mesh])       |  |  |  |
| #3:  | ((((mobili*[Title/Abstract]) OR (manipulat*[Title/Abstract])) OR (manual therapy[Title/Abstract])) OR ("Manipulation, Orthopedic"[Mesh])) OR ("Musculoskeletal Manipulations"[Mesh]) |  |  |  |
| #4:  | ((((((((((((((((((((((((((((((((((((((   |  |  |  |
| #5:  | ("Young Adult"[Mesh]) OR ("Adult"[Mesh])   |  |  |  |
| #6: #1 AND #2<br>AND #3 AND #4<br>AND #5   |  |  |  |  |
| #7: #6 with<br>the following<br>filters (English and<br>publication date up<br>to 3/31/2023) |  |  |  |  |

## Supplemental appendix B: Inclusion and exclusion criteria

|                              | Inclusion Criteria   | Exclusion Criteria  |
|------------------------------|--|---|
| Participants /<br>Population | Adults aged 18+     receiving treatments     for knee OA   | <ul> <li>Studies that include conditions other than knee joint complex osteoarthritis, unless those individuals also have knee joint complex osteoarthritis</li> <li>Animal studies</li> <li>Studies that include subjects that have had any knee surgery in the past 6 months, or have undergone a total or partial knee arthroplasty in the involved knee at any time</li> </ul>  |
| Interventions                | Includes knee joint mobilization or manipulation performed by a clinician, potentially alongside other interventions as long as the effect of the manual therapy intervention was being assessed | <ul> <li>Other forms of manual therapy treatment (e.g., massage, soft tissue mobilization, lymphatic massage/drainage, cupping, dry needling, acupuncture, acupressure) in the absence of joint mobilization or manipulation</li> <li>Manual therapy as part of a group of interventions where the effect of manual therapy was not assessed (e.g., a trial where everyone received manual therapy as part of standard care, and the purpose of the trial was to assess the effect of other interventions, such as exercise, education, medications, etc.)</li> <li>Stretching</li> </ul> |
| Study Design                 | <ul> <li>Randomized clinical trials</li> </ul>   | <ul> <li>All non-primary literature, including reviews,<br/>dissertations, theses, editorials, study protocols,<br/>abstracts, and clinical practice guidelines</li> </ul>  |
| Language                     | <ul> <li>English</li> </ul>  |   |

Abbreviations: OA, osteoarthritis.

#### Supplemental appendix C: Information about excluded trials

| Primary author and year of publication | Study title  | Exclusion reason         |  |
|--|--|--------------------------|--|
| Horng (2013)                           | The effects of collateral meridian therapy for knee osteoarthritis pain management: a pilot study  | Wrong intervention       |  |
| Iversen (2012)                         | Rehabilitation interventions for pain and disability in osteoarthritis: a review of interventions including exercise, manual techniques, and assistive devices   | Wrong study design       |  |
| Kitay (2009)                           | Efficacy of combined local mechanical vibrations, continuous passive motion and thermotherapy in the management of osteoarthritis of the knee  | Wrong intervention       |  |
| Gurudut (2020)                         | Comparative effect of graded motor imagery and progressive muscle relaxation on mobility and function in patients with knee osteoarthritis: a pilot study  | Wrong intervention       |  |
| Dunning (2018)                         | Periosteal electrical dry needling as an adjunct to exercise and manual therapy for knee osteoarthritis  | Wrong intervention       |  |
| Cuesta-Barriuso (2021)                 | The effectiveness of manual therapy in addition to passive stretching exercises in the treatment of patients with haemophilic knee arthropathy: A randomized, single-blind clinical trial                    | Wrong patient population |  |
| Abou-Raya (2013)                       | Effect of low dose oral prednisolone on symptoms and systemic inflammation in older adults with moderate to severe knee osteoarthritis: a randomized placebocontrolled trial                                 | Wrong intervention       |  |
| Abbott (2013)                          | Manual therapy, exercise therapy, or both, in addition to usual care, for osteoarthritis of the hip or knee: a randomized controlled trial. 1: clinical effectiveness  | Duplicate                |  |
| Bennell (2005)                         | Efficacy of physiotherapy management of knee joint osteoarthritis: a randomised, double blind, placebo-controlled trial  | Wrong intervention       |  |
| Romanowski (2020)                      | Manual therapy (postisometric relaxation and joint mobilization) in knee pain and function experienced by patients with rheumatoid arthritis: a randomized clinical pilot study                              | Wrong indication         |  |
| Cheawthamai (2014)                     | A comparison of home-based exercise programs with and without self-manual therapy in individuals with knee osteoarthritis in community   | Wrong intervention       |  |
| Khademi-Kalantari (2014)               | Effects of non-surgical joint distraction in the treatment of severe knee osteoarthritis   | Wrong intervention       |  |
| Schencking (2013)                      | A comparison of Kneipp hydrotherapy with conventional physiotherapy in the treatment of osteoarthritis: a pilot trial  | Wrong indication         |  |
| Espí-López (2017)                      | Effectiveness of inclusion of dry needling in a multimodal therapy program for patellofemoral pain: a randomized parallel-group trial  | Wrong intervention       |  |
| Safran-Norton (2019)                   | A consensus-based process identifying physical therapy and exercise treatments for patients with degenerative meniscal tears and knee OA: the TeMPO physical therapy interventions and home exercise program | Wrong study design       |  |

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| Rafiq (2021)         | The effect of rehabilitation protocol using mobile health in overweight and obese patients with knee osteoarthritis: a clinical trial   | Wrong intervention       |  |
|----------------------|---|--------------------------|--|
| Weleslassie (2021)   | Effectiveness of mobilization with movement on the management of knee osteoarthritis: a systematic review of randomized controlled trials   | Wrong study design       |  |
| Safran-Norton (2019) | A consensus-based process identifying physical therapy and exercise treatments for patients with degenerative meniscal tears and knee OA: the TeMPO physical therapy interventions and home exercise program                                | Wrong study design       |  |
| Grindstaff (2014)    | Manual therapy directed at the knee or lumbopelvic region does not influence quadriceps spinal reflex excitability  | Wrong indication         |  |
| Stanton (2018)       | Illusory resizing of the painful knee is analgesic in symptomatic knee osteoarthritis   | Wrong intervention       |  |
| Hart (2000)          | Combination of manual physical therapy and exercises for osteoarthritis of the knee   | Wrong study design       |  |
| Deyle (2012)         | Knee OA: which patients are unlikely to benefit from manual PT and exercise?  | Wrong study design       |  |
| Gomiero (2018)       | Sensory-motor training versus resistance training among patients with knee osteoarthritis: randomized single-blind controlled trial   | Wrong intervention       |  |
| Jardine (2012)       | The effect of osteopathic manual therapy on the vascular supply to the lower extremity in individuals with knee osteoarthritis: A randomized trial  | Wrong intervention       |  |
| Abbott (2019)        | Incremental clinical effectiveness and cost effectiveness of providing supervised physiotherapy in addition to usual medical care in patients with osteoarthritis of the hip or knee: 2-year results of the MOA randomised controlled trial | Wrong patient population |  |
| Robbins (2021)       | Low-level laser therapy and static stretching exercises for patients with knee osteoarthritis: a randomised controlled trial  | Wrong intervention       |  |
| Pereira Garbi (2021) | Aquatic physiotherapy in the functional capacity of elderly with knee osteoarthritis Wrong intervention   |                          |  |
| Schilke (1996)       | Effects of muscle-strength training on the functional status of patients with osteoarthritis of the knee joint  | Wrong intervention       |  |
| Altmis (2018)        | Mobilization with movement and kinesio taping in knee arthritis—evaluation and outcomes  Wrong intervent  |                          |  |
| Goslinska (2020)     | Wireless motion sensors-useful in assessing the effectiveness of physiotherapeutic methods used in patients with knee osteoarthritis-preliminary report   | Wrong intervention       |  |
| Pinto (2013)         | Manual therapy, exercise therapy, or both, in addition to usual care, for osteoarthritis of the hip or knee. 2: economic evaluation alongside a randomized controlled trial   | Wrong intervention       |  |
| Sayers (2012)        | Effect of high-speed power training on muscle performance, function, and pain in older adults with knee osteoarthritis: a pilot investigation  Wrong intervention   |                          |  |
| Bennell (2005)       | Efficacy of physiotherapy management of knee joint osteoarthritis: a randomised, double blind, placebo-controlled trial   | Duplicate                |  |

#### Supplemental appendix D: Study characteristics

| Primary author and year of publication | Stage of<br>knee OA     | Primary outcome(s)  | Treatment groups and participant characteristics*   |
|--|-------------------------|---|---|
| Abbott (2015) <sup>32</sup>            | All Stages              | Pain;<br>Stiffness; Physical<br>Function  | Exercise therapy without booster sessions (n=19 [8m/11f], 64 yr, BMI=29.2) Exercise therapy with booster sessions (n=19 [8m/11f], 65 yr, BMI=30.2) Exercise therapy plus manual therapy with no booster sessions (n=18 [6m/12f], 61 yr, BMI=27.6) Exercise therapy plus manual therapy with booster sessions (n=19 [7m/12f], 64 yr, BMI=29.8) |
| Ali (2016) <sup>33</sup>               | All Stages              | Pain;<br>Stiffness; Physical<br>Function  | Knee mobilization plus exercise (n=25 [numbers specific to gender not provided], participant age data not provided, BMI not provided) Electrophysical agents plus exercise (n=25 [numbers specific to gender not provided], participant age data not provided, BMI not provided)  |
| Alkhawajah (2019) <sup>34</sup>        | Chronic                 | Pain;<br>Stiffness; Physical<br>Function  | Mobilization with movement (n=20 [13m/7f], 56.5 yr, BMI=32.6) Sham mobilization (n=20 [12m/8f], 56.6 yr, BMI=33.3)  |
| Altinbilek (2018) <sup>35</sup>        | Chronic                 | Pain;<br>Stiffness; Physical<br>Function  | Knee mobilization plus exercise (n=44 [5m/39f], 53.9 yr, BMI=32.3)<br>Sham (n=15 [5m/10f], 56.9 yr, BMI=30.9)   |
| Bhagat (2020) <sup>36</sup>            | Chronic                 | Pain;<br>Physical Function  | Mobilization with movement (n=15 [5m/10f], 53.7 yr, BMI=?) Pragmatic Lumbar Spine Treatment (n=43 [27m/16f], 48.1 yr, BMI=?)  |
| Bove (2018) <sup>37</sup>              | Bove                    | Pain;<br>Stiffness; Physical<br>Function  | Exercise (n=75 [23m/52f], 58.3 yr, BMI=30.1) Exercise plus booster (n=76 [25m/51f], 58.4 yr, BMI=31.4) Exercise plus manual therapy (n=75 [26m/49f], 58.0 yr, BMI=31.1) Exercise plus manual therapy plus booster (n=74 [27m/47f], 58.5 yr, BMI=31.7)   |
| Courtney (2016) <sup>38</sup>          | Chronic                 | Pain  | Knee mobilization (n=29 [13m/16f], 59.4 yr, BMI=36.9)<br>Hands-on cutaneous input (Sham) (n=29 [13m/16f], 59.4 yr, BMI=36.9)  |
| Crossley (2015) <sup>39</sup>          | Subacute and<br>Chronic | Rate of Change of Pain<br>Severity;<br>Pain; Pain;<br>Stiffness; Physical<br>Function | Knee mobilization (n=44 [20m/24f], 56 yr, BMI=27.2)<br>Education (Control) (n=48 [19m/29f], 53 yr, BMI=27.9)  |
| Cruz-Montecinos (2016) <sup>40</sup>   | Not Provided            | Muscle Activation;<br>Pain;<br>Physical Function;<br>Stiffness                        | Knee mobilization (n=8 [numbers specific to gender not provided], 64.4 yr, BMI not provided) Control (n=8 [numbers specific to gender not provided], 61 yr, BMI not provided)   |

| Deyle (2005) <sup>14</sup>      | Not Provided | Pain;<br>Stiffness; Physical<br>Function   | Knee mobilization with exercise (n=60 [23m/37f], 64 yr, BMI=25.3) Home exercise program (n=60 [16m/44f], 62.2 yr, BMI=28.0) Knee mobilization with exercise group non-completers (n=6 [3m/3f], 62.2 yr, BMI=28.0) Home exercise program group non-completers (n=8 [4m/4f], 63.8 yr, BMI=28.0) |
|---------------------------------|--------------|--|---|
| Deyle (2000) <sup>13</sup>      | Not Provided | Pain;<br>Stiffness; Physical<br>Function   | Knee mobilization and exercise (n=42 [15m/27f], 60 yr, BMI=31.1) Subtherapeutic ultrasound and exercise (placebo) (n=41 [19m/22f], 62 yr, BMI=30.4)   |
| Dwyer (2015) <sup>41</sup>      | Chronic      | Pain;<br>Stiffness; Physical<br>Function;<br>ROM;<br>Patient Perceived<br>Satisfaction | Knee mobilization (n=26 [7m/19f], 63.5 yr, BMI=28.6) Exercise (n=26 [11m/15f], 60.9 yr, BMI=30.8) Knee mobilization and exercise (n=26 [11m/15f], 62.2 yr, BMI=30.6)  |
| Fitzgerald (2016) <sup>42</sup> | All Stages   | Pain;<br>Stiffness; Physical<br>Function   | Knee manual therapy and exercise and booster (n=74 [27m/47f], 58.5 yr, BMI=31.7) Knee manual therapy and booster (n=75 [26m/49f], 58.0 yr, BMI=31.1) Exercise and booster (n=75 [25m/51f], 58.4 yr, BMI=31.4) Exercise (n=75 [23m/52f], 58.3 yr, BMI=30.1)                                    |
| Forestier (2014) <sup>43</sup>  | Chronic      | Stiffness; Physical<br>Function;<br>Quality of Life                                    | Knee mobilization (n=113 [47m/66f], 64.1 yr, BMI=31.1)<br>Control (n=101 [42m/59f], 64.8 yr, BMI=28.9)  |
| Jeyakumar (2017) <sup>44</sup>  | Subacute     | Pain;<br>ROM   | Knee mobilization (Mulligan) (n=20 [12m/8f], 51 yr, BMI not provided) Knee mobilization (Maitland) (n=20 [11m/9f], 50 yr, BMI not provided) Conventional physiotherapy (n=20 [8m/12f], 52 yr, BMI not provided)   |
| Jin (2017) <sup>45</sup>        | Not Provided | Pain;<br>Stiffness; Physical<br>Function;  | Knee manual therapy (n=40 [9m/31f], 59.3 yr, BMI=24.97)<br>NSAIDs (n=40 [8m/32f], 61.9 yr, BMI=26.07)   |
| Kaya Mutlu (2018) <sup>46</sup> | Not Provided | Pain;<br>Stiffness; Physical<br>Function;  | Knee mobilization (MWM) (n=21 [10m/21f], 54.19 yr, BMI=30.82)<br>Knee mobilization (Accessory mobs) (n=21 [5m/16f], 56.29 yr, BMI=30.74)<br>Electrotherapy (n=22 [3m/19f], 57.77 yr, BMI=32.59)   |
| Kornkamon (2019) <sup>47</sup>  | Not Provided | Pain;<br>ROM;<br>Function  | PT generated manual therapy (n=8 [2m/6f], 74.0 yr, BMI not provided) Self-manual therapy (n=8 [2m/6f], 72.25 yr, BMI not provided) Control group (n=8 [0m/8f], 73.25 yr, BMI not provided)  |
| Lalit (2012) <sup>48</sup>      | Not Provided | Proprioception;<br>Pain;<br>Stiffness;<br>Physical Function                            | Knee mobilization (Maitland) (n=30 [numbers specific to gender not provided], 54.67 yr, BMI not provided) Knee mobilization (Mulligan) (n=30 [numbers specific to gender not provided], 51.67 yr, BMI not provided)   |
| Lizis (2019) <sup>49</sup>      | Chronic      | Pain   | Knee mobilization (n=64 [33m/37f], 62.3 yr, BMI=24.15)<br>Exercise (n=64 [30m/40f], 62.0 yr, BMI=23.57)   |

| Mahmooda (2020) <sup>50</sup>     | Subacute     | Pain;<br>ROM;<br>Stiffness;<br>Physical Function                            | Knee mobilization (Mulligan) (n=15 [0m/15f], participant age data not provided, BMI not provided) Myofascial release (n=15 [0m/15f], participant age data not provided, BMI not provided)  |
|-----------------------------------|--------------|---|--|
| Moss (2007) <sup>51</sup>         | Not Provided | Pain;<br>Stiffness;<br>Physical Function;<br>PPT                            | Knee mobilization (n=38 [numbers specific to gender not provided], participant age data not provided, BMI not provided) Manual contact (No mobilization) (n=38 [numbers specific to gender not provided], participant age data not provided, BMI not provided) Control (n=38 [numbers specific to gender not provided], participant age data not provided, BMI not provided) |
| Narang (2014) <sup>52</sup>       | All Stages   | Pain;<br>Stiffness;<br>Physical Function                                    | Knee mobilization (n=15 [numbers specific to gender not provided], participant age data not provided, BMI not provided) Routine physiotherapy (n=15 [numbers specific to gender not provided], participant age data not provided, BMI not provided)  |
| Nigam (2021) <sup>53</sup>        | Not Provided | Pain;<br>Stiffness;<br>Physical Function                                    | Knee mobilization (MWM) plus exercise and moist heat (n=20 [8m/12f], 58.5 yr, BMI=26.2) Exercise and moist heat (n=20 [7m/13f], 59.4 yr, BMI=25.6)   |
| Pollard (2008) <sup>54</sup>      | Chronic      | Pain  | Knee mobilization (n=26 [18m/8f], 56.5 yr, BMI not provided) Control (n=17 [11m/6f], 54.6 yr, BMI not provided)  |
| Pozsgai (2022) <sup>55</sup>      | Not Provided | Pain Pressure<br>Threshold;<br>Pain;<br>Physical Function;<br>Strength      | Knee mobilization (n=20 [0m/20f], 70.4 yr, BMI=19.07)<br>Sham (n=20 [0m/20f], 66.9 yr, BMI=30.95)  |
| Pryymachenko (2021) <sup>56</sup> | Not Provided | Incremental Cost-<br>Effectiveness;<br>Incremental Net<br>Monetary Benefits | Manual therapy and exercise and booster (n=19 [7m/12f], 64 yr, BMI=29.8)  Manual therapy and exercise (n=18 [6m/12f], 61.2 yr, BMI=27.6)  Exercise and booster (n=19 [7m/12f], 65.3 yr, BMI=30.0)  Exercise (n=19 [8m/11f], 63.9 yr, BMI=29.2)   |
| Rao (2018) <sup>57</sup>          | Not Provided | Pain;<br>Physical Function;<br>Stiffness                                    | Knee mobilization (Maitland) (n=32 [numbers specific to gender not provided], participant age data not provided, BMI not provided)  Knee mobilization (Mulligan) (n=31 [numbers specific to gender not provided], participant age data not provided, BMI not provided)   |
| Razek (2014) <sup>58</sup>        | Chronic      | Pain;<br>Stiffness;<br>Physical Function;<br>ROM                            | Knee mobilization with traditional physiotherapy (n=15 [5m/10f], 44.47 yr, BMI=29.09) Traditional physiotherapy (n=15 [4m/11f], 50.13 yr, BMI=28.45)   |

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| Reza (2021) <sup>59</sup>   | Not Provided     | Pain;              | Manual therapy and exercise (n=16 [9m/7f], 54.19 yr, BMI not provided)             |
|-----------------------------|------------------|--------------------|--|
|                             |                  | Stiffness;         | Exercise (n=16 [10m/6f], 53.25 yr, BMI not provided)                               |
|                             |                  | Physical Function  |  |
| Sharma (2013) <sup>60</sup> | Less Than 1 Year | Pain;              | Manual therapy and exercise (n=20 [numbers specific to gender not provided],       |
|                             |                  | Stiffness;         | participant age data not provided, BMI not provided)                               |
|                             |                  | Physical Function; | Exercise (n=20 [numbers specific to gender not provided], participant age data not |
|                             |                  | ROM                | provided, BMI not provided)  |
| Sit (2018) <sup>61</sup>    | Subacute and     | Pain;              | Patellar mobilization therapy (n=104 [19m/85f], 59.4 yr, BMI not provided)         |
|                             | Chronic          | Stiffness;         | Control (n=104 [22m/82f], 60.9 yr, BMI not provided)                               |
|                             |                  | Physical Function  |  |
| Syed (2014) <sup>62</sup>   | Not Provided     | Pain               | Myofascial mobilization and exercise (n=20 [3m/17f], 53.25 yr, BMI not provided)   |
|                             |                  |                    | Maitland mobilization and exercise (n=20 [7m/13f], 52.15 yr, BMI not provided)     |
| Taj (2023) <sup>63</sup>    | All Stages       | ROM;               | Knee mobilization (n=24 [4m/20f], 45.3 yr, BMI not provided)                       |
|                             |                  | Pain;              | Pain release group (n=24 [9m/15f], 45.4 yr, BMI not provided                       |
|                             |                  | Physical Function  |  |
| Tucker (2003) <sup>64</sup> | Not Provided     | Pain;              | Manual therapy (n=30 [12m/18f], 61.2 yr, BMI not provided)                         |
|                             |                  | Physical Function; | Sham (n=30 [11m/19f], 57.4 yr, BMI not provided)                                   |
|                             |                  | ROM                |  |
| Witwit (2022) <sup>65</sup> | Chronic          | Pain;              | Mobilization (n=21 [7m/14f], 54.8 yr, BMI=31.29)                                   |
|                             |                  | ROM                | Muscle energy technique (n=21 [9m/12f], 52.0 yr, BMI=31.56)                        |

Abbreviations: f, females; m, males; n, number of subjects; PPT, pain pressure threshold; ROM, range of motion; yr, age in years \*Group participant characteristics expressed as (number of subjects [males/females], mean age, mean Body Mass Index (BMI)

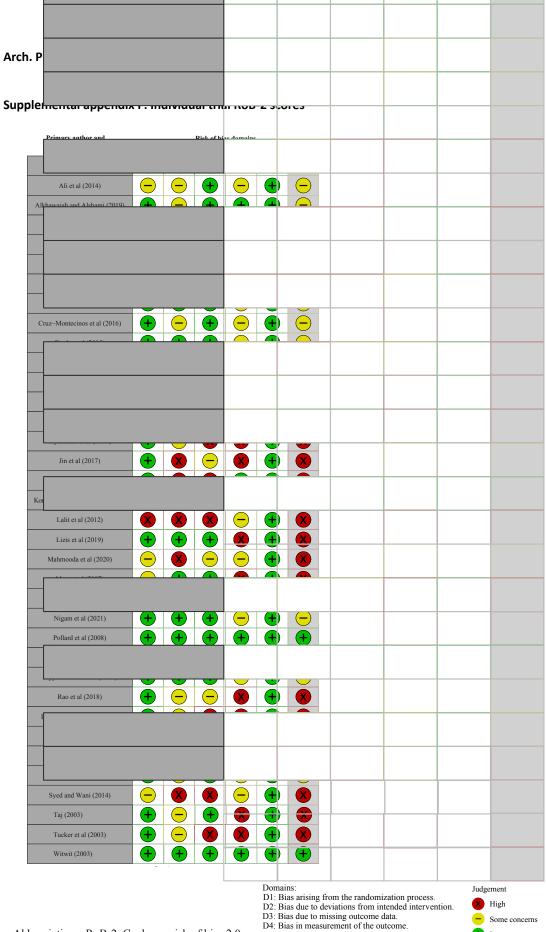
#### Supplemental appendix E: Manual therapy interventions

| Primary author and year of publication | Total # of participants | Length of follow-up | Manual therapy interventions  |
|--|-------------------------|---------------------|---|
| Abbott (2015) <sup>32</sup>            | N=75                    | 1 year              | Non-thrust joint mobilization directed at tibiofemoral and patellofemoral joints, with the option to perform techniques on hip, ankle, tibiofibular joints, and lumbopelvic spine, on an as needed basis. Twelve 30–45-minute treatment sessions. |
| Ali (2016) <sup>33</sup>               | N=50                    | 4 weeks             | Maitland mobilization with distraction directed at tibiofemoral and patellofemoral joints. Twelve 30-minute treatment sessions.   |
| Alkhawajah (2019) <sup>34</sup>        | N=40                    | 2 days              | Mulligan mobilization with movement (MWM) directed at tibiofemoral joint (2 sets of 10 repetitions). One treatment session. No information provided regarding duration of each manual therapy session.  |
| Altinbilek (2018) <sup>35</sup>        | N=59                    | 4 weeks             | Osteopathic manipulative treatment directed at tibiofemoral and patellofemoral joints. Each technique was performed in one-minute intervals. One treatment session with three minutes of mobilization and three minutes of joint compression.     |
| Bhagat (2020) <sup>36</sup>            | N=58                    | Immediate           | Mulligan MWM directed at tibiofemoral joint (3 sets of 10 repetitions). One treatment. No information provided regarding duration of each manual therapy session.   |
| Bove (2018) <sup>37</sup>              | N=300                   | 2 years             | Non-thrust joint mobilization directed at tibiofemoral joint, with the option to perform techniques on hip, ankle, and foot, on an as needed basis. Twelve treatment sessions, with manual therapy component lasting 15-20 minutes per session.   |
| Courtney (2016) <sup>38</sup>          | N=58                    | 2 weeks             | Oscillatory joint mobilization directed at the tibiofemoral joint (3 minutes x 2 repetitions). One treatment session. No information provided regarding duration of each manual therapy session.  |
| Crossley (2015) <sup>39</sup>          | N=92                    | 9 months            | Joint mobilization directed at tibiofemoral and patellofemoral joints, plus soft tissue mobilization. Eight treatment sessions. No information provided regarding   |

|                                      |       |            | duration of each manual therapy session.  |
|--------------------------------------|-------|------------|---|
| Cruz-Montecinos (2016) <sup>40</sup> | N=16  | 1 week     | Grade II Maitland joint mobilization directed at tibiofemoral and patellofemoral joints, plus soft tissue mobilization. One treatment session with manual therapy lasting about 40 minutes per patients.  |
| Deyle (2005) <sup>14</sup>           | N=134 | 1 year     | Joint mobilization, directed at tibiofemoral and patellofemoral joints, as well as hip, ankle, tibiofibular joints, and lumbopelvic spine, on an as needed basis, plus soft tissue mobilization and stretching. Eight 30-minute treatment sessions. |
| Deyle (2000) <sup>13</sup>           | N=83  | 1 year     | Joint mobilization, directed at tibiofemoral and patellofemoral joints, as well as hip, ankle, tibiofibular joints, and lumbopelvic spine, on an as needed basis, plus soft tissue mobilization and stretching. Eight 30-minute treatment sessions. |
| Dwyer (2015) <sup>41</sup>           | N=52  | 5 weeks    | Thrust and non-thrust joint mobilization directed at tibiofemoral and patellofemoral joints, as well as the hip, foot, and spine. Six 20-minute treatment sessions.   |
| Fitzgerald (2016) <sup>42</sup>      | N=300 | 1 year     | Non-Thrust joint mobilization directed at tibiofemoral joint, with the option to perform techniques on hip, ankle, and foot, on an as needed basis. Twelve treatment sessions, with manual therapy component lasting 15-20 minutes per session.     |
| Forestier (2014) <sup>43</sup>       | N=214 | 3 weeks    | Joint mobilization directed at the knees, hips, ankles, spine, shoulders, and wrists, plus soft tissue mobilization. Three 25-minute treatment sessions.  |
| Jeyakumar (2017) <sup>44</sup>       | N=60  | 3 weeks    | Mulligan MWM directed at the tibiofemoral joint or Maitland's MWM directed at the tibiofemoral joint. Both groups received 3 weeks of daily sessions including 3 bouts of the respective treatment for 30-seconds each.                             |
| Jin (2017) <sup>45</sup>             | N=80  | 6 weeks    | Joint mobilization and stretching directed at the tibiofemoral joint, plus soft tissue mobilization. Twelve 20-minute treatment sessions.   |
| Kaya Mutlu (2018) <sup>46</sup>      | N=64  | 1 year     | Mulligan MWM directed at the tibiofemoral joint, or passive joint mobilization (grade I-IV) directed at the tibiofemoral and patellofemoral joints. Twelve 50-minute treatment sessions.  |
| Kornkamon (2019) <sup>47</sup>       | N=24  | Not stated | Joint mobilization directed at tibiofemoral and patellofemoral joints, plus soft tissue mobilization. No information provided regarding number of treatment   |

|                                   |        |            | sessions or duration of each manual therapy session.   |
|-----------------------------------|--------|------------|--|
| Lalit (2012) <sup>48</sup>        | N=60   | 5 days     | Mulligan MWM directed at the tibiofemoral joint (3 sets of 3 repetitions), or Maitland's grade II-III joint mobilization (no dosage provided) directed at the tibiofemoral and patellofemoral joints. Three treatment sessions. No information provided regarding duration of each manual therapy session. |
| Lizis (2019) <sup>49</sup>        | N=128  | 5 weeks    | Joint mobilization (grade III) directed at the tibiofemoral and patellofemoral joints. Each mobilization was performed for 30 repetitions. Ten 30-45-minute treatment sessions.  |
| Mahmooda (2020) <sup>50</sup>     | N=30   | 2 weeks    | Mulligan MWM directed at tibiofemoral joint (no dosage provided). Ten treatment sessions. No information provided regarding duration of each manual therapy session.   |
| Moss (2007) <sup>51</sup>         | N= 114 | Not stated | Joint mobilization directed at the tibiofemoral joint (single 9-minute repetition of non-noxious mobilization). One 9-minute treatment session.  |
| Narang (2014) <sup>52</sup>       | N=30   | 15 days    | Kaltenbohn mobilization directed at tibiofemoral and patellofemoral joints (no dosage provided). No information provided regarding number of treatment sessions or duration of each manual therapy session.  |
| Nigam (2021) <sup>53</sup>        | N=40   | 6 months   | Mulligan MWM directed at the tibiofemoral joint (3 sets of 6-10 repetitions). Six treatment sessions. No information provided regarding the duration of each manual therapy session.   |
| Pollard (2008) <sup>54</sup>      | N=43   | 4 weeks    | Joint mobilization directed at the patellofemoral joint, including myofascial manipulation (no dosage provided). Three treatment sessions. No information provided regarding the duration of each manual therapy session.  |
| Pozsgai (2022) <sup>55</sup>      | N=40   | 2 weeks    | Maitland joint mobilization (grade III-IV) directed at tibiofemoral joint (30 seconds x 2 repetitions). One treatment session.   |
| Pryymachenko (2021) <sup>56</sup> | N=56   | 2 years    | Joint mobilization directed at the knee joint, plus soft tissue mobilization (no dosage provided). Twelve treatment sessions. No information provided regarding the duration of each manual therapy session.   |
| Rao (2018) <sup>57</sup>          | N=63   | Immediate  | Maitland joint mobilization (grade I-IV) (3 seconds – 5 minutes duration) and Mulligan MWM (no dosage provided) directed at the tibiofemoral joint. Two  |

|                             |       |          | treatment sessions. No information provided regarding the duration of each manual therapy session.  |
|-----------------------------|-------|----------|---|
| Razek (2014) <sup>58</sup>  | N=30  | 4 weeks  | Mulligan MWM (No dosage provided). Twelve treatment sessions. No information provided regarding the duration of each manual therapy session.  |
| Reza (2021) <sup>59</sup>   | N=32  | 4 weeks  | Joint thrust (no dosage provided) joint mobilizations were directed at the tibiofemoral joint, and non-thrust (10 repetitions) joint mobilizations directed at the patellofemoral joint. Six treatment sessions. No information provided regarding the duration of each manual therapy session.                                   |
| Sharma (2013) <sup>60</sup> | N=40  | 4 weeks  | Maitland joint mobilization (grade III-IV) directed at the tibiofemoral and patellofemoral joints (30 seconds x 2-6 repetitions), plus muscle stretching. No information provided regarding number of treatment sessions or duration of each manual therapy session.  |
| Sit (2018) <sup>61</sup>    | N=208 | 24 weeks | Joint mobilization directed at the patellofemoral joint (5 minutes). Three treatment sessions.  |
| Syed (2014) <sup>62</sup>   | N=40  | 2 weeks  | Maitland joint mobilization directed at tibiofemoral joint (gr II x 5 repetitions). Treatments provided on alternating days for 2 weeks. No information provided regarding the duration of each manual therapy session.   |
| Taj (2023) <sup>63</sup>    | N=48  | 6 weeks  | Maitland joint mobilization directed at the tibiofemoral and patellofemoral joints (3 repetitions, grade and duration not specified), plus muscle stretches for hamstrings, gastrocnemius, soleus, and rectus femoris. No information provided regarding number of treatment sessions or duration of each manual therapy session. |
| Tucker (2003) <sup>64</sup> | N=60  | 3 weeks  | Thrust joint mobilization directed at the tibiofemoral and patellofemoral joints (no dosage provided). Eight treatment sessions. No information provided regarding the duration of each manual therapy session.   |
| Witwit (2022) <sup>65</sup> | N=42  | 4 weeks  | Non-thrust joint mobilization (grade II-III) directed at the tibiofemoral joint (1 minute x 3 repetitions). Twelve treatment sessions.  |



Abbreviations: RoB-2, Cochrane risk of bias 2.0

D5: Bias in selection of the reported result.

+ Low