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Current Perspectives on the Biomechanical Modelling of the Human Lower Limb: A Systematic Review

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Abstract

The purpose of this systematic review is to report the characteristics and methods utilized in human lower limb or knee joint only biomechanical models to provide state-of-the-art knowledge on the topic. This review was conducted according to the preferred reporting items for systematic reviews and meta-analyses guidelines. PubMed, Scopus and Web of Science were searched up to 24th April 2018 to look for musculoskeletal models of the human lower limb or knee joint only without any associated pathology. A 15-item checklist was used to assess the methodological quality of the included studies. Twenty-one studies were included, with seventeen of them modelling the lower limb and four only the knee joint. The methodological quality of the studies varied considerably, with the reporting of model characteristics showing very low quality. Among studies including experimental setup, subjects were instructed to perform vertical jumping, running at different speeds, drop landing and isokinetic knee extension (5%), static conditions (9%), knee's flexion/extension (14%) and walking at constant (29%) and different (33%) speeds. A great variety of modelling strategies was found for the reproduction of the human musculoskeletal system in terms of number of segments, muscles and muscle models. The reviewed musculoskeletal models were able to reproduce human movement dynamics similar to results present in literature and to experimentally measured records. However, standardized methods for reporting the characteristics and methods of these models are missing and should be addressed in future studies.

1 Introduction

The human body comprises an internal framework named skeleton, composed by a series of bones. The part of the skeletal system that involves the lower limb is formed by the pelvic girdle, the bones of the thigh (femur and patella), lower leg (tibia and fibula) and foot (tarsus, metatarsus and phalanges) (Fig. 1a) [1]. The skeletal system is interconnected by the articular system, which for the lower limb includes the hip, knee and ankle joints (Fig. 1b).

The human neuromusculoskeletal system entails many intricate elements that interact with each other to enable a coordinated movement. In order to understand how this is achieved, an extensive range of studies were performed to obtain data characterizing muscle mechanics, geometric relationships between muscles and bones, and motions of joints [2]. Using this knowledge, computational models of the human body are being developed to study and analyze the biomechanics of healthy and pathological human movement. The combination of computational models with experimental information of human motion provides estimates of biomechanical parameters, such as musculotendon or joint forces, that are not easily measured in experimental human designs [2, 3]. The general structure of a biomechanical model of the human lower limb is presented in Fig. 1c and involves the segments and joints presented in Fig. 1a and b.

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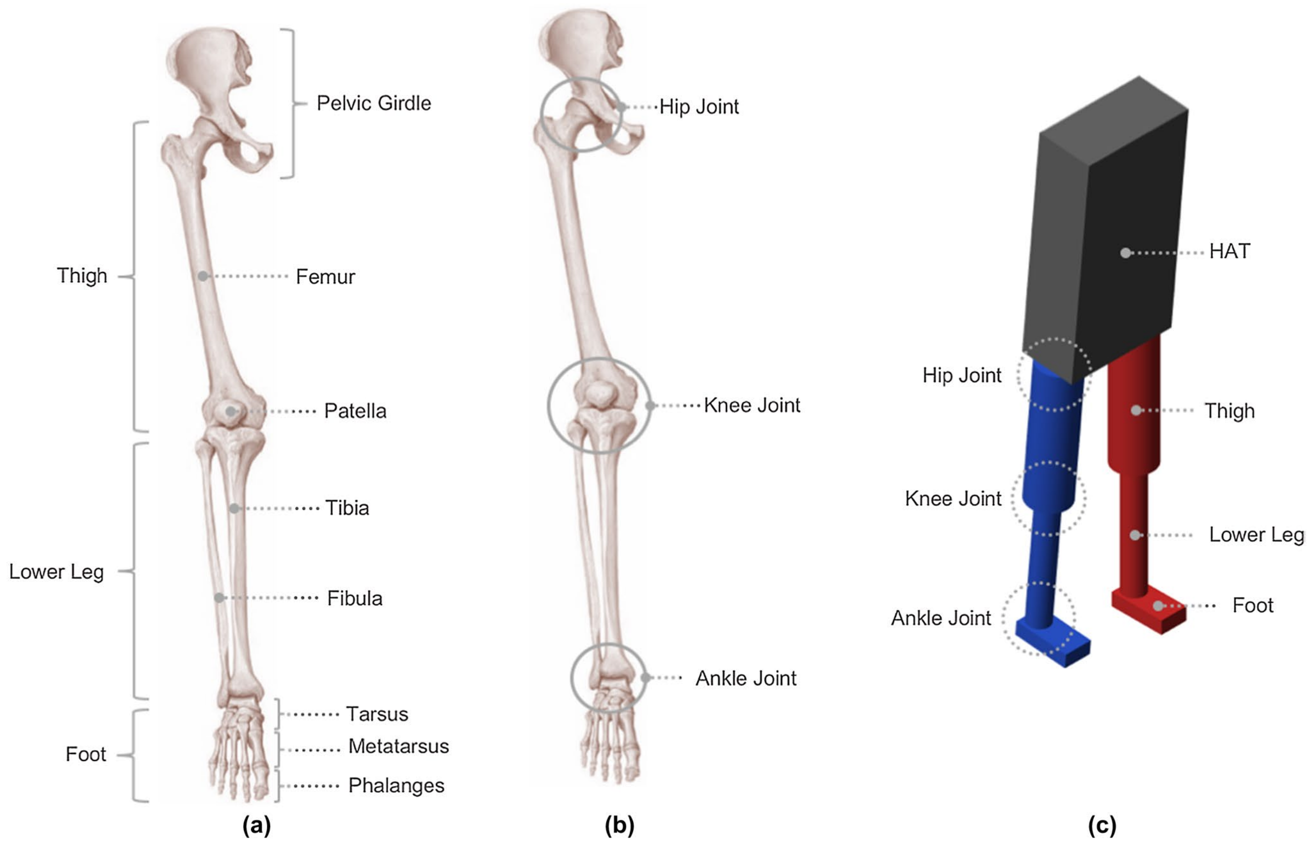

Fig. 1 Human lower limb **a** skeletal and **b** articular systems. Adapted from [1]. **c** General structure of a lower limb biomechanical model with the identification of its constituting segments and joints. Usually, the upper extremity is represented by a Head, Arms and Trunk (HAT) segment. (Color figure online)

The determination of muscle and joint forces, and many other biomechanical parameters that act in a determined human movement, is essential to enable the iterative development of cost-effective mobility assistive and rehabilitation devices tailored to the patients' specifications. Computer musculoskeletal simulation uses algorithms and equations to allow the experimentation of a diversity of scenarios on a valid digital representation of the human musculoskeletal system. By using simulation tools to predict the forces that those devices are required to provide or endure during the assistance procedure, which involves the use of the device in patients, the production process becomes less time and cost consuming than experiments performed with real prototypes. This is feasible since computer simulation provides valuable solutions by giving clear insights into what needs to be altered when the product is still under development.

Despite the extensive research on this topic, there is still lack of information on the description of the differences between existing biomechanical models, including the minimum number of muscles and segments, the formulation of the muscle model, the implementation of the joints and the number of degrees of freedom necessary for an accurate representation of the human musculoskeletal system, just to name a few. A systematization of the features comprised on the currently available biomechanical models representing the human lower limb is warranted and would enable the definition of guidelines for future developments of these models. This systematic review of the literature was performed with the purpose to identify and summarize the characteristics and methods reported in the development of biomechanical models representing the human lower limb or knee joint.

2 Methods

The present systematic review of literature was conducted according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [4].

2.1 Search Strategy

A comprehensive electronic database search was carried out on MEDLINE/PubMed, Scopus and Web of Science.

The searches were performed until April 24, 2018, and no publication year limit was applied. Articles that included the development and/or use of a musculoskeletal model of the human body and reported lower limb or knee joint kinetic, kinematic and/or muscular results were identified. The search strategy was determined using the AND/OR/NOT Boolean operators and combining the following key-words: human knee, knee, knee joint, biomechanical, biomechanical model, knee biomechanical, biomechanical analysis, musculoskeletal, musculoskeletal model, muscle force, mechanical force, muscle reaction, prosthesis, prostheses, pathology, injury, replacement, arthroplasty, loss, deficit, reduction, pain, disorder, rehabilitation, unhealthy, reconstruction, graft, disease. An example of the search is depicted in "Appendix 1".

2.2 Study Selection

All records were extracted to an Excel file (Microsoft® Office) and duplicates were removed by software filter and verified manually. The reference list of relevant articles resulting from database search were analyzed to identify other studies that could potentially be included in this systematic review. All titles, abstracts and keywords of the articles obtained were screened and identified relevant studies were retrieved and the respective full text analyzed for eligibility. Musculoskeletal computational biomechanical models of the human lower limb or knee joint were considered for inclusion. Studies were excluded if did not (1) focus on a generic musculoskeletal model, (2) alter some feature or further analyzed the musculoskeletal model, (3) focus only on healthy articulation, (4) refer to a study performed with normal movements, (5) refer to a study performed in humans, (6) include validation, (7) include three-dimensional (3D) models, (8) include or analyze the knee joint. Conference proceedings and studies that were not written in the English language were also excluded. To be considered as healthy, the joints must not present any injury or prothesis.

2.3 Data Collection and Extraction

A customized data extraction table was developed to extract key details from each included study considering: (1) aim, population demographics (i.e. age) and experimental setup (i.e. equipment used); (2) musculoskeletal model characteristics (i.e. number of muscles and muscle model); (3) alterations applied to the biomechanical model; (4) validation dataset used to assess model accuracy; (5) conditions used to model the biomechanical model and (6) study's main outcomes, limitations and general remarks. These characteristics were chosen to provide an overview of the methods each study used in the analyzes performed and of the results and conclusions obtained. When only partial information was described in the original article, references and authors' previous works were analyzed to provide comparable data across the selected studies.

2.4 Methodological Quality

To assess the methodological quality of the studies included in this systematic review, a checklist was developed on the basis of a previous review in the field of biomechanics [3]. Each question from the checklist was scored as zero (no information), one (limited details) or two (satisfying description). The 15-item quality checklist used in this review was: Q1: Are the research objectives clearly stated?, Q2: Is the scientific context clearly explained?, Q3: Is the musculoskeletal model adequately described?, Q4: If any, were the model alterations clearly described?, Q5: Were participant characteristics adequately described?, Q6: Were movement tasks, equipment design, and set up clearly defined?, Q7: Was the evaluation strategy appropriately justified?, Q8: Were the analytical methods clearly described?, Q9: Were the statistical methods justified and appropriately described (other than descriptive statistics)?, Q10: Was the validation procedure clearly described?, Q11: Were the direct results easily interpretable?, Q12: Were the main outcomes clearly stated and supported by the results?, Q13: Were the limitations of the study clearly described?, Q14: Were key findings supported by other literature?, Q15: Were conclusions drawn from the study clearly stated? The overall score (%) of each of article was calculated based on the work of Moissenet F, Modenese L, Dumas R [3] in which the score of each article is the "sum of the rated questions divided by the sum of applicable questions".

3 Results

3.1 Search Strategy

The database and hand searches provided a total of 414 citations. After duplicate citations were removed, 330 articles were screened, and 184 full texts were retrieved to be examined in detail. A total of 21 articles met the eligibility criteria and were included in this systematic review (Fig. 2).

3.2 Methodological Quality Assessment

The studies' scores ranged from 53.3 to 93.3%, with a mean of 74.1% ("Appendix 2"). The quality of the reviewed studies regarding Q1, Q2 and Q12 was very high, comprising each an average score of 2 ("Appendix 2"). Aside from these, most of the articles presented high quality regarding Q14, Q7, Q8, Q10 and Q11. Each item was scored with 1.6, 1.6, 1.7, 1.8 and 1.8, respectively. Q6, Q5 and Q13

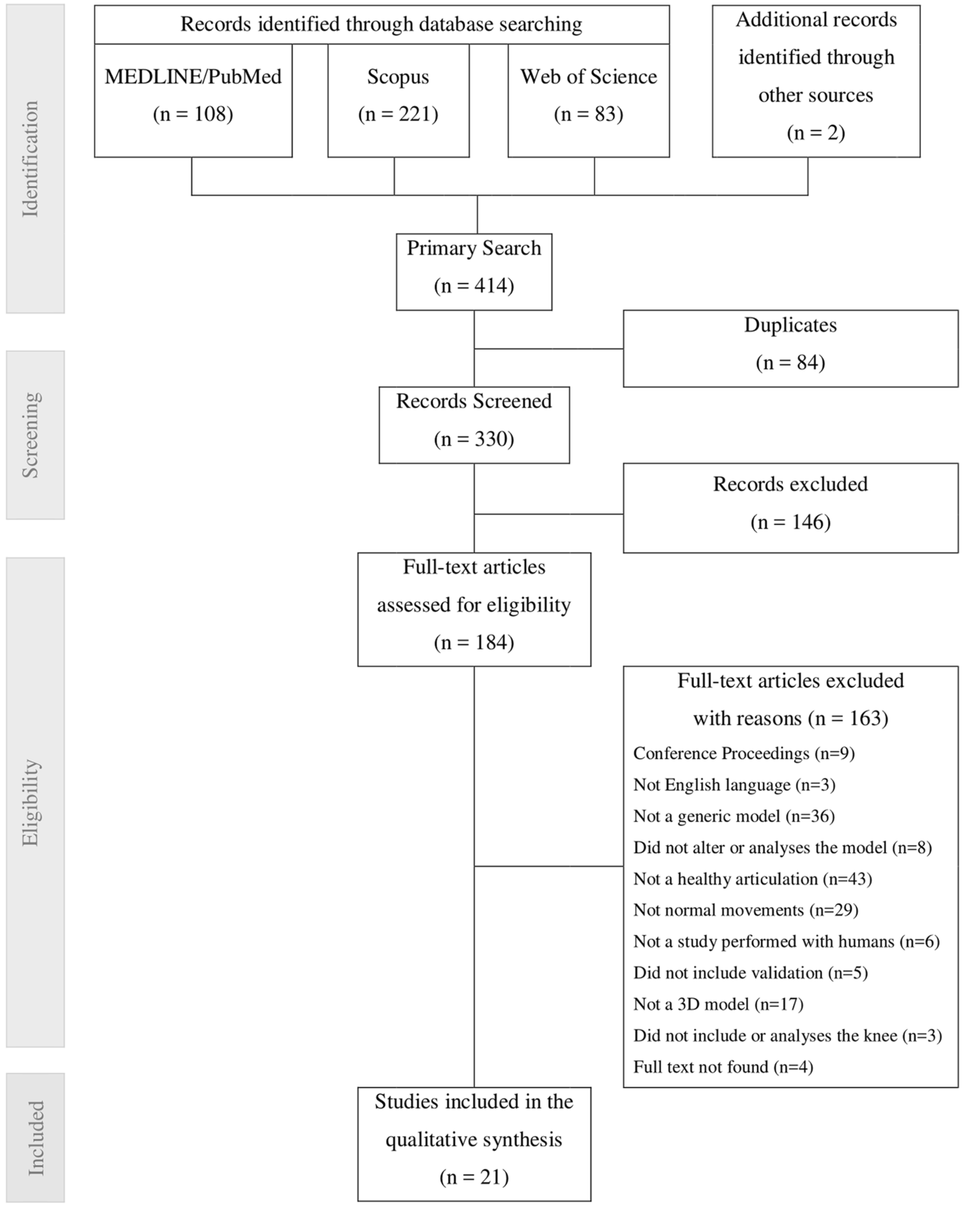

Fig. 2 Flowchart of the search strategy conducted in this review

were mediumly scored with an average of 1.3, 1.2 and 1.3, respectively. Six of the studies did not report any limitations (scored 0), while three presented a limited description of the limitations (scored 1). Most of the studies did not clearly present their conclusions (Q15) and, therefore, this item is averagely scored with 1.2. Since almost all studies did not adequately describe the musculoskeletal model utilized (Q3), the overall quality regarding this item is not high, being averagely scored with 1.1. To the studies including only a brief description of the model utilized (as it was more detailly explained in a previous work), a score of 1 was attributed. Many analyzed articles presented limited description of the alterations implemented to the model (Q4), as well as of the statistical analysis (Q9), being scored with 1 and 1.2 on average, respectively. Regarding to the alterations performed to the model, nine studies were attributed with a score of 0, since no alterations were performed, and four and eight studies presented medium and high quality (scored 1 and 2, respectively).

3.3 Population Demographics and Experimental Setup

The demographic characteristics of the 113 participants (25 females, 71 males and 17 unknowns) are presented in Table 1. Three studies [5–7] did not mention the subjects' gender. Four studies [8–11] did not perform experimental procedures. Of all studies including experimental procedures, two studies [6, 12] did not present information regarding the age, five studies [12–16] did not report the body

Table 1 Overview of the data extraction criteria for each study included in the present systematic review

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Arnold (2013) [5]	Aim: to evaluate the influence of force–length and force–velocity properties on lower limb muscle force generation (i.e. the force generated per unit activation) at different walking and running speeds Population: n = 6; Age: 29.2 ± 6.3; BM:72.4 ± 5.7; BH:180 ± 3 Performed movement: walking at speeds of 1.0–1.75 m/s and running at speeds of 2.0–5.0 m/s Measured variables: surface EMG in 11 muscles, positions of 30 lower limb markers and ground reaction forces Equipment used: eight camera motion capture system, force plate instrumented treadmill	Segments: pelvis, femur, patella, tibia, fibula, talus, calcaneus, metatarsals and phalanges Joints: hip, knee and ankle Software: SIMM [27] and OpenSim 2.4 Original Model: [26] Degrees of Freedom: 11 Number of muscles/ligaments: 35/0 Muscle Model: Hill-type Muscle Paths: line segments, wrapping surfaces or via points Simulation: Forward Dynamics Optimization Strategy: Inverse Kinematics Algorithm Optimization Parameters: Generalized Coordinates Objective Function: function that best tracked the subject's measured marker data	The model had its knee range of motion altered from 0 –100 deg to 0 –130 deg All muscles were strengthened to reflect young athletic subjects The maximum shortening velocity was increased The Achilles' tendon compliance was increased in accordance to ultrasound studies	Gastrocnemius medius tendon strain compared with [28–32] The hypothesis that the walk-to-run transition in human gait is influenced by the force generation ability of the plantarflexors correlated with studies of [33, 34] Simulated tendon stretch of the plantarflexors was compared with [34] Results with tendon compliance of 10% were compared to [35] The estimates of where lower limb muscles operate on the force–length curve were compared to [36–38]	Fibers were assumed to be connected serially within the fascicle ($l_{fibre} \approx l_{fascicle}$) Maximum fiber contraction velocity was set to 15 optimal fiber lengths/s F_{max} was increased by a factor of 2 for all muscles included in the model	Estimated Parameter(s): lower limb muscle fiber lengths, velocities and forces Limitations: lower highest walking speed than other studies; the plantarflexors had longer fibers and more complaint tendons than other studies; the theory that the relative activation of all 3 plantarflexors was the same was not considered; the model does not account for variable gearing in pennate muscles, sarcomere and fiber heterogeneity, changes to the force–velocity residual force enhancement, or the effects of short time history; small population size General Remarks: The force generation ability of 8 muscles was affected by speed of walking or running. Walking faster, increases knee extension and ankle plantarflexion moments. As humans run faster, hip FE moments increase.
Chen (2017) [21]	Aim: to propose a novel musculoskeletal biomechanical model of the lower limb, in order to estimate knee torque and muscle forces using sEMG Population: n = 8 (8 M/0 F); Age: 27 ± 4.7; BW: 65.2 ± 6.8; BH:169.8 ± 3.9 Performed movement: walking on level ground with speeds of 0.8, 1.0, 1.2 m/s and transition speed from 0.8 to 1.2 m/s separately Measured variables: kinematic data of 20 motion capture markers placed on the lower limbs, plantar forces and sEMG signals from 10 main muscles related to the knee joint movements of the right leg Equipment used: optical motion capture system, force plate and a wireless sEMG collection device	Segments: Pelvis, Thigh, Shank and Foot Joints: hip, knee and ankle Software: MATLAB ® 2013a Original Model: – Degrees of Freedom: no information Number of muscles/ligaments: 10/0 Muscle Model: muscle bio-electrical activation, muscle contraction mechanical and muscular function models Muscle Paths: no information Simulation: Forward Dynamics Optimization Strategy: Genetic Optimization Algorithm Optimization Parameters: σ, F_{amax}, l_{opti}, k_m and γ_m Objective Function: non-linear least squares algorithm to minimize difference between knee joint torque calculated from the model and from Newton–Euler method: $\min \sum_{i=1}^{ns} \left[T(i) - T_{iv}(i)\right]^2$	No alterations were performed since the authors developed a novel musculoskeletal model of the knee joint	RF activation curves for one subject were compared with the work from [39] All muscles activation curves for one subject were compared with the work from [40] The derived muscle parameters of one subject, including σ, F_{amax} and l_{opti}, were compared with the work from [26]. Statistical estimation results were compared with the work of [41] and [42]	The coordinates of the knee and ankle centers are the central position of lateral and external markers The hip joint center is defined using a method proposed by another author Muscle contraction force: $\pm 50\%$ of the maximum value from literature Other muscle parameters: $\pm 20\%$ of the maximum value from literature Eletromechanical delay set to 50 ms	Estimated Parameter(s): FE knee joint torque, maximum absolute error, mean residual error, root mean square error and cross-correlation coefficient Limitations: the geometric parameters for different subjects were altered by a scaling factor (ratio of body heights), which may affect the precision of the model General Remarks: a more reasonable approach is needed to scale the model, such as by X-ray inspection; the results indicate that the musculoskeletal model can accurately estimate the knee joint dynamic torque in walking; the model provides a novel platform for investigating the internal forces of individual muscles and their interaction

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Ciszkiewicz (2016) [8]	Aim: to develop a model of the patellofemoral joint by considering the linear displacement along the axis of the cylindrical joint and to use the model to analyze the femoral spatial displacements caused by the quadriceps muscle force No human experimental procedures were developed	Segments: patella, femur and tibia Joints: Knee (patellofemoral cylindrical joint) Software: no information Original Model: [43] Degrees of Freedom: 1 Number of muscles/ligaments: 1/3 Muscle Model: no information Muscle Paths: no information Simulation: no information Optimization Strategy: Nedler-Mead method Optimization Parameters: linear displacement along the axis of cylindrical joint of the patellofemoral joint Objective Function: minimization of the difference between the modelled and measured spatial displacements of the femur with respect to the tibia over the full range of the knee flexion	The authors used a cylindrical model of the patellofemoral joint developed by [43]. However, a linear displacement along the cylindrical joint axis was included and coupled with angular displacement	Simulation results regarding to the linear displacement are compared to [44] The results of the relation between the flexion angle of the knee joint and the arm of the quadriceps force moment are compared to results from [45] The maximum difference between the p_z^p obtained from the model is compared to results obtained from [43] The results obtained for the moment arm of the quadriceps muscle were compared to the ones obtained by [45]	The patellofemoral joint is assumed as an active leg added to the 5-5 parallel platform mechanism of the femur-tibia joint presented in [46] The segments are considered rigid bodies and the ligaments' lengths are constant The model has 2 nonsymmetrical platforms (femur and tibia), linked with two-point contact pairs and four legs	Estimated Parameter(s): instantaneous screw displacements of the femur with regard to the tibia, corresponding muscle forces and the angle between the muscle force and the instantaneous screw axis Limitations: no information General Remarks: The simulation results for the model developed show significant improvement of the modelled linear coordinates of the femur reference system with respect to tibia reference system. The model of the patella-femur joint where the linear displacement along axis of the cylindrical joint is considered can reproduce the actual patella displacements more accurately. The model can be used to study some medical conditions such as patellofemoral dislocation.

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Cleather (2011) [17]	Aim: to demonstrate the feasibility of using existing technology to solve the equations of motion during vertical jumping using optimization techniques and to explore the sensitivity of the solution to the choice of cost function Population: n = 12 (12 M/0 F); Age: 27.1 ± 4.3; BM: 83.7 ± 9.9 Performed movement: vertical jumps Measured variables: position of reflective markers placed on key anatomical landmarks and the ground reaction forces Equipment used: motion capture system synchronized with a force plate	Segments: pelvis, thigh, calf and foot (four-linked rigid segments of the right lower limb) Joints: right hip, knee and ankle Software: MATLAB® 2007 Original Model: [47–49] Degrees of Freedom: no information Number of muscles/ligaments: 163/14 Muscle Model: [50] Muscle Paths: via points Simulation: Inverse dynamics Optimization Strategy: optimization toolbox of MATLAB® (version 7.5; The Mathworks, Inc, 2007) Optimization Parameters: 186 unknown parameters Objective Function: 5 cases: minimize (1) muscle, ligament and joint loading (ALL), (2) only muscle (MO), (3) only ligament (LO), (4) muscle and ligaments (ML) and (5) joint reaction force (JO). The optimization procedure calculates ligament and joint contact forces	Five different objective cost functions were used in the optimization problem in order to calculate and compare the muscle, ligament and joint reaction forces	The forces and moments obtained in the study were compared to those presented by [47, 48] Inter-segmental moments were compared against results from [51–53] Magnitude of tibiofemoral joint (TFJ) loading was compared with [54–60] Ligament loadings were compared against the studies from [61–65] The alteration in length of the collateral ligaments were compared to results from [66]	The model is specified by the translations and rotations that describe the position and orientation of each segment The patella position and orientation are defined to be a function of knee flexion angle Upper bound of ligaments	Estimated Parameter(s): lower limb muscle and joint contact forces and ligament moments Limitations: the ligaments are modelled as active force actuators which are able to produce any force up to their failure limit, and without reference to their strain. The lack of dynamic muscle modelling, that is, the force generating capacity of the muscles is assumed to be constant and independent of the known force–length and force–velocity relations General Remarks: ligaments have an important role in stabilizing the ankle and knee during vertical jumping. Muscle, ligament and joint contact forces are very sensitive to the choice of cost function. The main conclusion drawn from this study is that this technique can produce viable solutions to a variety of different cost functions

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Geyer (2010) [9]	Aim: to develop a neuromuscular model of the human being with a motor control based on muscle reflexes, which are designed to include principles of legged mechanics, such as the reliance on compliant leg behavior No human experimental procedures were developed The simulation of the model starts with its left leg in stance and its right leg in swing at a normal walking speed of 1.3 m/s In other simulation, approaching from steady-state walking at the same initial walking speed of 1.3 m/s, the model encounters a sequence of stairs of 4 cm in height each. The simulation involves the model going up and down those stairs	Segments: HAT, 2 thighs, 2 shanks and 2 feet Joints: 2 hips, 2 knees and 2 ankles Software: MATLAB SimMechanics (v2.7) Original Model: – Degrees of Freedom: 12 Number of muscles/ligaments: 7 (each leg)/0 Muscle Model: Hill-type muscle model (parallel elastic, contractile, buffer elasticity and series elastic elements) Muscle Paths: no information Simulation: Forward Dynamics No optimization was performed. The model's parameters were derived from previous knowledge from other authors [36, 67–73], or by making plausible estimates	No alterations were performed since the authors developed a novel human musculoskeletal model	The model's steady-state patterns of muscle activations and joint torques and angles show qualitative agreement with human walking data from [74]	Muscle stimulations are limited in range from 0.01 to 1. Joint's range of operation are: $70° < \theta_H < 130°$ $\theta_K < 175°$ $\theta_A < 230°$ The ground contact model is a nonlinear spring-damper If $F_{stiction} \geq \mu_{stiction} F_y$, the horizontal ground model changes to sliding and if $\lvert \dot{x}_{CP} \rvert < 1$ cm/s the horizontal ground model changes to stiction	Estimated Parameter(s): GRF, lower limb muscle activations, joint torques and angles Limitations: No limitations were specifically reported by the authors; however, this can be considered: swing leg behavior is very sensitive to external disturbances and to internal reflex adjustments General Remarks: in walking, the human model generates strong agreement for all joints in stance and for the hip and knee in swing. In this latter phase, the ankle kinematics shows less agreement. The ankle torque is very similar to literature, while hip and knee torques show less agreement throughout gait. The activations of some individual muscles are predicted by the model. Besides walking gait, the model also tolerates sudden and self-adapts to changes of the ground level (slopes and stairs up and down). The ground reaction forces show the characteristic M-shape for walking

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
De Groote (2010) [13]	Aim: to investigate which MT parameters of the knee joint flexors and extensor muscles affect the calculated MT-force produced during gait and whether it is feasible to make subject-specific estimates of these parameters based on dynamometer experiments Population: n = 3 (2 M/1 F); Age: 26.5 ± 1.5 Performed movement: gait analysis and knee FE Measured variables: knee FE torques during maximal voluntary contraction at various knee angles and over the full ROM of the knee at different velocities Equipment used: 3D motion capture system, a synchronized force plate and a Biodex Dynamometer	Segments: HAT, pelvis, 2 thighs, 2 lower legs and 2 feet Joints: spherical joints connect the HAT to the pelvis and the latter to the thigh. The knee is modelled as a sliding joint and the ankle as a hinge joint Software: OpenSim Original Model: [75] Degrees of Freedom: 19 Number of muscles/ligaments: 43 (each leg)/0 Muscle Model: activation dynamics is a first-order model [76] and contraction dynamics is the Hill model [77, 78] Muscle Paths: no information Simulation: inverse kinematics (joint kinematics), inverse dynamics (joint torques), forward dynamics using the Hill muscle model (MT forces) Optimization Strategy: CIA and PIA Optimization Parameters: MT forces and activations Objective Function: minimizing the sum of: squared activations of all muscles (CIA); squared activations of all muscles over all time instants (PIA)	The generic musculoskeletal model was scaled according to each musculotendon specific parameters, namely, tendon slack length, optimal muscle fiber length, maximal isometric muscle force, optimal pennation angle and maximal muscle fiber velocity	The relationship between sensitivities for tendon slack length/optimal muscle fiber length and optimal muscle fiber length/maximal isometric muscle force were compared with results from [79, 80]	Bounds to classify sensitivities $\mathrm{MS}_{\mathrm{jk}}$ (Nm) from (1) dynamometer experiments: low ($MS_{jk} < 50$), medium ($50 \le MS_{jk} < 100$) and high ($100 \le MS_{jk}$); (2) gait: low ($MS_{jk} < 5$), medium ($5 \le MS_{jk} < 10$) and high ($10 \le MS_{jk}$);	Estimated Parameter(s): individual lower limb muscle contributions to the knee torque (musculotendon torques) and sensitivity of the optimal muscle fiber length, maximal isometric force and tendon slack length calculated using CIA, PIA and the Hill model forward simulation Limitations: no information General Remarks: the muscle contributions to the knee torque during gait and dynamometer experiments had a high sensitivity to only a limited number of MT parameters of the 13 knee flexors and extensors analyzed, suggesting that not all parameters need to be estimated. The authors also conclude that the angle–torque relation measured by dynamometer experiments contains information about musculotendon parameters necessary to reliably analyze gait

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Hoy (1990) [10]	Aim: to develop a musculoskeletal model of the human lower extremity in order to use it in computer simulations studies to develop better knowledge on the contributions of individual muscles to isometric moments about joints in the sagittal plane in a variety of lower extremity positions. With the development of this model, the authors aim at complementing experimental studies in order to obtain better comprehension of muscle and tendon functions during lower extremity motor tasks No human experimental procedures were developed	Segments: trunk, thigh, shank and foot Joints: hip, knee and ankle Software: no information Original Model: – Degrees of Freedom: no information Number of muscles/ligaments: 18/0 Muscle Model: the authors developed their own musculotendon actuator model, which incorporates a CE, to represent the static properties of active muscle, in series with a linear elastic element (tendon) Muscle Paths: straight line from origin to insertion Simulation: no information No optimization strategy was implemented; however, two criteria were used in order to determine l_s^T for each actuator: (1) l_s^T was selected so that actuators were near l_0^M at joint angles corresponding to the in vivo passive moment, and (2) l_s^T of individual actuators was adjusted so that the summed moment about each joint peaked at a joint angle corresponding to the in vivo measurements [81]	No alterations were performed since the authors developed a novel human musculoskeletal model	The relative contributions of hamstrings, adductor magnus, gluteus maximus and gracilis to summed hip extensor moment were compared to results obtained from [82, 83] The relative contributions of gastrocnemius and soleus to the summed ankle moment were compared to results from [84] The peak moment, the joint angle at which it occurred, and the change in moment with change in adjacent joint angle were compared to results from: hip [85, 86], knee [87, 88] and ankle [84, 89] Hip joint axis for hip joint moments were compared to [83, 86] The peak magnitude of the summed moment and the joint angle where the peak moment occurs correspond to in vivo data. The simulated moments varied with changes in joint angle as the experimental moments do	All muscle fibers are parallel and insert at the same pennation angle on tendon, and muscle volume and CSA are constant The authors reduced the number of muscles by neglecting some muscles and lumping others Muscles are fully activated The ratio of muscle PCSA to tendon PCSA is constant	Estimated Parameter(s): tendon slack length, l_s^T, musculotendon force and joint moment Limitations: no information General Remarks: the joint angle where an actuator develops peak force depends on moment arm, l_0^M and l_s^T. The range of joint angles where an actuator can develop active force depends both on moment arm and l_0^M. The contribution of each actuator to the summed moment about a joint depends on joint angle. The joint angle where force peaks agrees with the joint angle where moment arm peaks for some actuators. The joint angle where moment peaks differs among the actuators crossing a joint. The isometric function of an actuator depends on both the moment arm and on the musculotendon specific parameters

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Kaufman (1991) [25]	Aim: to successfully apply a physiological model of the knee joint capable of accounting for nonequilibrium dynamic loading and predicting individual knee muscle forces Population: n = 5 (5 M/0 F); Age: 27 ± 2; BW: 81 ± 13; BH:178 ± 4 Performed movement: flexion and extension of the knee joint (isokinetic movement) at two constant angular velocities: 60°/s and 180°/s Measured variables: angular displacement of the knee joint and myoelectric activity of seven muscles surrounding the knee joint Equipment used: isokinetic dynamometer, triaxial electrogoniometer, intramuscular wire electrodes	Segments: shank, tibia, fibula and patella Joints: knee Software: no information Original Model: – Degrees of Freedom: 1 (knee flexion/extension) Number of muscles/ligaments: 8/0 Muscle Model: the mathematical model of [90] was used to model the muscle active length-tension relation. The muscle force–velocity relation of [91] was used to account for eccentric and concentric contractions Muscle Paths: the muscles included were represented by force vectors directed tangentially to their origin and insertion Simulation: Inverse Dynamics Optimization Strategy: Linear and nonlinear optimization Optimization Parameters: muscle forces Objective Function: linear criteria: minimize (1) the sum of muscle forces and (2) muscle activation. Nonlinear criterion: the sum of muscle stresses (muscle forces divided by physiological cross-sectional area) cubed	No alterations were performed since the authors developed a novel knee model	Myoelectric activity from each muscle was acquired simultaneously with the motion and force data and was used for comparison with the forces calculated by the biomechanical model. The muscle force prediction of each muscle was statistically correlated with the corresponding myoelectric activity of that muscle The antagonistic activity during extension of the hamstrings and the quadriceps were compared with the results from [92] The antagonistic activity of linear programming technique was compared to those of [93] Co-activation of the flexor muscles was justified by the results of [94, 95]	The knee joint was assumed to have 1 DOF The patellar tendon line of action and the moment arm vary with knee flexion Muscle force constraints were utilized for all three optimization criteria	Estimated Parameter(s): knee joint individual muscle force Limitations: nonlinear criteria presented fluctuations on muscle force predictions, which are not physiologically justifiable General Remarks: the study demonstrated that the objective function of minimizing muscle activation was the best of the other linear and nonlinear objective functions, and that its results showed an improved muscle force prediction. In general, the results showed good agreement between the force prediction and the myoelectric activity

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Lemieux (2017) [6]	Aim: the aim of this study is to use a musculoskeletal model of the entire body equipped with a special knee kinematic in order to simultaneously estimate the paths, magnitudes and orientations of the medial and lateral femorotibial contact forces for the stance phase of gait using bone geometry constraints. Besides this aim, the authors propose a new method of estimation of the path of the contact force in the lateral and medial knee compartment The characteristics of the population and the experimental setup was used from previous data [96] Population: n = 1, BW = 75.4, BH = 174 Performed movement: walking Measured variables: ground reaction forces and gait kinematics Equipment used: ViconNexus® Motion Capturing System, four Kistler force plates and eight MX cameras	Segments: 31 Joints: spherical hip joint, a hinge patellofemoral joint, hinge knee joint, a hinge ankle joint, hinge subtalar joint, sacrum-pelvis joint, spherical glenohumeral joint, a hinge elbow joint, a hinge radio-ulnar joint and a universal wrist joint Software: AnyBody Modelling System (AnyBody A/S, Aalborg University, Denmark) Original Model: GaitUniMiami (AMMR v1.5) Degrees of Freedom: 38 in general and 7 per leg Number of muscles/ligaments: 55/0 Muscle Model: Hill-type Muscle Paths: no information Simulation: Inverse Dynamics Optimization Strategy: min/max muscle recruitment criterion provided by the AnyBody Modelling System Optimization Parameters: contact and muscle forces and moments Objective Function: minimize the overall fatigue of the muscular system by maximizing load sharing among the available muscles, constrained by: (1) the unknown internal forces and moments have to fully equilibrate the external forces and moments provided as inputs, and (2) each muscle (i) amongst all muscles (n) must apply a pulling force lower or equal to its strength. Objective function: $minimize G\left(f^{(M)}\right)$ $subject\ to C * f = d$ $0 \leq f_i^{(M)} \leq N_i, i \in \left\{1,\ldots,n^M\right\}$	The knee joint was equipped with the extension mechanism developed by [75], providing an additional translational DOF	The locations of the CF obtained by the CZ method were compared with [97] The contact patterns of the CP (contact point) and CZ methods were compared to the results of [97] The range of peak medial, lateral and total CF obtained by both methods was compared with [98–107] The results obtained by limiting the amount of CF were compared to those from [108] The patterns of vastii and gastrocnemius forces were compared to [100, 101, 109–111] Biceps femoris force throughout the stance phase of gait was compared to results from [100, 101, 109–112] The contribution of the biceps femoris in this study was justified regarding results from [112] The frontal moment created by the medial contact force estimated in this study was compared to the external knee adduction moment of [113]	The knee extensor mechanism simulates a "node sliding on an ellipse" constraint". This node could move in the anteroposterior direction, but its position is correlated to the flexion angle CP method: in the sagittal plane, the contact force orientations were perpendicular to the ellipse and to the long axis of the tibia. In the frontal plane, these forces were aligned with the sagittal plane of the femur CZ method: the orientation of each contact force was set to be perpendicular to their corresponding medial/lateral femoral ellipsoid. Both: The CF strength was 6 times BW	Estimated Parameter(s): magnitude, path and orientation of medial and lateral femorotibial CF. Muscle forces and moments from muscles crossing the knee Limitations: the use of the CP method limited the estimation of the shear components. The model does not account for the influence of the ACL and thus the findings were not fully representative of an intact knee internal load distribution. The use of the min/max criterion may be questionable since it exploits muscles with very poor working conditions. Since inverse dynamics simulation was used, there are no muscle activity inputs like in forward dynamics and EMG-drive methods, and hence muscle activations can deviate from their normal pattern. A generic model was used, which involved muscle–tendon parameters, bone geometries and gait data from different sources, making the model not sufficiently realistic to be used as a predictive tool. The simulated knee extensor mechanism used for both CP and CZ models is a simplification of the complex knee kinematics that occurs during walking, and hence the model's predictions may have been influenced by this simplification. The medial and lateral contact zones were estimated using a proximity map between the femur and tibia bone geometries without considering the cartilage geometries, which would lead to different estimations of CF. The CF should be estimated allowing shear translations and simulating soft tissues. General Remarks: The CZ method allows the path, magnitude and orientation of the femorotibial CF to be sensitive to knee bone geometries and to the allowable CF. This method could associate CF with pathology

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Lerner (2014) [22]	Aim: to use a musculoskeletal model to analyze the loading environment of the knee joint (magnitude, mediolateral distribution, and rate of tibiofemoral loading) relative with the walking speed. To examine the relationship between knee extension NMMs and compressive tibiofemoral forces Population: n = 10 (7 M/3 F); Age: 23.6 ± 2.5; BM: 67.2 ± 12; BH: 178 ± 9; Performed movement: walking on a treadmill at speeds and grades ranging from 0.5 to 1.75 m/s and − 3° to 9°, respectively Measured variables: kinetic, kinematic and electromyographic data Equipment used: dual-belt, inclinable, force-measuring treadmill with force plates embedded underneath, seven-camera, three-dimensional motion capture system, bipolar surface electrodes	Segments: 12 (femur, patella, tibia/fibula, talus, foot and toes) combined with an upper body segment Joints: hip, tibiofemoral, ankle, subtalar, and metatarsophalangeal joints Software: OpenSim Original Model: [75] Degrees of Freedom: 19 Number of muscles/ligaments: 92/0 Muscle Model: no information Muscle Paths: wrapping points Simulation: Inverse Kinematics to determine the joint angles across each gait cycle and Inverse Dynamics to calculate the model's generalized forces that reproduced the measured kinematics, given the ground reaction forces at 0.75, 1.25 and 1.50 m/s Optimization Strategy: (1) Optimization for the inverse kinematics analysis, (2) Weighted Static Optimization Optimization Parameters: (1) experimental and virtual marker trajectories, (2) muscle forces Objective Function: (1) minimize the errors between the experimental and the virtual marker trajectories and the markers defined on each scaled model, (2) minimize the sum of squared muscle activations while reproducing the required NMMs at all joint in the model	The knee joint was altered to include an optimal abduction and adduction DOF. Three force actuators and three torque actuators were applied to the pelvis to account for dynamic irregularities	Electromyographic data was collected during the experiments and used for qualitative comparison with the estimated muscle forces. The results of pattern and magnitude of compressive tibiofemoral loading during stance were compared with results from [20, 56, 107, 114–116] The effects of speed on sagittal plane net muscle moment were compared to results from [117, 118] Increases in compressive tibiofemoral forces due to intersegmental forces were compared to results from [119] The gastrocnemius force production was compared to the acquired EMG data and with results from [33]	The tibiofemoral joint was modelled as a single degree of freedom planar joint with the function of knee flexion/extension The patellofemoral joint was based on a study from [75, 120] Since the model does not include ligaments, to control this DOF, it was locked during model kinematics calculation	Estimated Parameter(s): knee net muscle moments and forces, tibiofemoral joint forces (magnitude, mediolateral distribution and rate of tibiofemoral loading) and the relationship between net muscle moments and tibiofemoral forces across different walking speeds Limitations: the authors used a generic model, containing several simplifications, scaled to the anthropometries of each subject. The individual muscle forces predicted by the model were not validated, since the authors reported there is no direct way to do that. The model and methodologies used were chosen based on minimizing the differences between model estimates of loading and in vivo data from a subject with an instrumented knee replacement. General Remarks: muscles spanning the knee joint are the primary contributors to the compressive tibiofemoral force and increase their relative contributions with increased walking speeds

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Lim (2017) [7]	Aim: to quantify the effects of step length and step frequency on lower-limb muscle function during walking Population: n = 10; Age: 24.2 ± 2.7; BM: 67.7 ± 10.5; BH: 169.7 ± 9.3; Performed movement: walking at six different speeds ranging from slow to fast, using a prescribed combination of step length and step frequency at each speed Measured variables: kinematic data (markers positions), GRF and EMG of 6 muscles Equipment used: 3D motion capture system, two strain gauged force place and surface electrodes	Segments: 10 (pelvis, HAT, 2 thighs, 2 shanks, 2 hindfoot and left and right toes) Joints: third lumbar vertebra, hip, knee and ankle Software: no information Original Model: [121] Degrees of Freedom: 21 Number of muscles/ligaments: 54 muscle–tendon units/0 Muscle Model: Hill type with series elastic tendon Muscle Paths: straight lines and space curves Simulation: Inverse Dynamics Optimization Strategy: Static Optimization Optimization Parameters: (1) joint angles and (2) individual muscle forces Objective Function: minimizing the sum of the squares of (1) the differences between the positions of virtual markers defined in the musculoskeletal model and reflective markers mounted on the participant; (2) muscle activations subject to the physiological bounds imposed by each muscle's force–length-velocity properties	Subject-specific musculoskeletal models were created by scaling segment lengths, inertial properties and muscle attachment sites 5 foot ground interaction points were defined on the foot segment of the model to simulate the force applied to the foot during ground contact	The results on the effects of changes in step length and frequency on joint motion are in accordance with results reported by [122–127] The contributions of vastic muscle (VAS) and gluteus maximum (GMAX) to vertical support were compared to [124, 127] The relation between limb posture, vertical support and walking speed was compared to results from [124, 126] The values of step length and frequency together with hip, knee and ankle joint angles were compared to results from [122, 123, 128, 129]	Each of the 5 foot ground interaction points could be fully constrained, partially constrained or unconstrained in space depending on the phase of foot ground contact	Estimated Parameter(s): lower limb peak joint angles, peak joint moments, peak muscle forces, normalized muscle-fiber lengths, and peak muscle contributions to vertical support and forward progression Limitations: each participant used a prescribed step length and step frequency at each walking speed; the use of cost function (2) General Remarks: although increases in both step length and frequency required larger contributions from the forces developed by GMAX, GMED, VAS, GAS and SOL to both vertical support and forward progression, an increase in step length resulted in greater differences in the contributions of VAS, GMAX and limb posture to vertical support

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Lloyd (1996) [14]	Aim: to determine the load sharing between muscles and other soft tissues of the knee for normal subjects voluntarily generating FE and varus or valgus isometric moments Population: n = 7 (7 M/0 F); Age: 29.6 ± 5.3; BH: 180 ± 8; Performed movement: subjects were instructed to produce moments at the hip and the knee which result in FE and varus-valgus moments at the knee and no FE or internal–external rotation at the hip Measured variables: external loads just above the ankle, joint angles of the hip, knee, and ankle and the averaged NTE Equipment used: load device, load cell, intramuscular and surface electrodes	Segments: femur, tibia and fibula Joints: knee Software: SIMM™ Musculographics Inc. Original Model: – Degrees of Freedom: no information Number of muscles/ligaments: 13/0 Muscle Model: Hill-based model and a non-linear tendon function proposed by [10, 77] Muscle Paths: the muscles were represented as lines in series, wrapping around bones when necessary Simulation: no information Optimization Strategy: quasi-Newton non-linear minimization method Optimization Parameters: optimal fiber length, tendon slack length, subject's global gain factor Objective Function, U: $minU = \sum_{\substack{joint\\angle}} \sum_{\substack{force\\direction}} E_{act}^2 + \sum_{\substack{joint\\angle}} E_{rest}^2$ error term E_{act} and E_{rest} (the subscripts rest and act represent the states when the subject is at-rest and generating active moments, respectively)	No alterations were performed since the authors developed a novel knee biomechanical model	The FE moment arms from the anatomical model were compared to those found in [75] The knee angles in the present study are in the range that showed no EMG joint angle dependency in accordance with [130] The author's results showed that the neuromuscular control system relies upon soft tissues to support a large portion of isometric varus or valgus loads and thus stabilize the joint. This was compared to results from [106, 131]	25 additional points of passive moment taken from literature were used as inputs to the model to ensure more realistic properties Each muscle's activation was assumed to be equal to the average of the NTE of 4 trials Linear relation between EMG and isometric muscle force Moment balance between the external and internal moments	Estimated Parameter(s): knee joint FE moments, soft tissue ratio and coefficient of variation Limitations: the fact that FE moment arms probably change from individual to individual has not been assessed. Variation of joint contact position in the sagittal plane was not considered and probably it would affect the FE moment arms. In the model, it was assumed that each muscle had the same uniform length tension relationship, and this may not reflect the reality. Measuring EMG maximums at different joint angles was not possible since this would have lengthened the duration of the experiment and that would increase the potential for fatigue to affect the results. General Remarks: Muscles were mainly used to support FE loads at the knee, but in so doing, they were also able to support some part of the varus or valgus loads. Since they couldn't support all the load, the soft tissues were required

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Lopes (2016) [15]	Aim: to develop a general-purpose superellipsoid-plane contact model in order to determine the 3D foot–ground contact forces during human movement. Simulation results and execution times were compared with a point-like viscoelastic contact model using a common forward simulation of walking Population: n = 10 (7 M/3 F); Age: 33 ± 12; Performed movement: walking at four randomly speeds: 0.6, 0.9, 1.2, 1.5 m/s Measured variables: positions and orientations of the body segments and ground reaction forces Equipment used: eight-camera motion capture system, reflective markers and force plates	Segments: trunk (a single body representing the pelvis, torso, head and arms) and two legs (each composed by thigh, shank, patella, calcaneus, mid-foot and toes) Joints: hip, knee, ankle, mid-foot and toes Software: SIMM/Dynamics Pipeline (MusculoGraphics Inc., Santa Rosa, CA) Original Model: [132–134] Degrees of Freedom: 13 Number of muscles/ligaments: 25 Hill-type musculo- -tendon actuators per leg/ligaments were modelled as passive torques acting on each joint Muscle Model: Hill-type Muscle Paths: no information Simulation: Forward Dynamics Optimization Strategy: Dynamic Optimization Optimization Parameters: muscle excitations parameters and initial generalized velocities Objective Function: minimize the squared differences in joint kinematics and ground reaction forces as: $minJ = \sum_{i} \sum_{m=1}^{17} W_{i,m} \frac{\left(Y_{i,m} - \hat{Y}_{i,m}\right)^2}{SD_{i,m}^2}$ m – variable m: m = 1,…,17	Two ways of computing contact: the ellipsoid–plane contact model (1) and the point-like foot–ground contact model (2)	The results produced by the two contact models implemented (the ellipsoid–plane contact model and the point-like foot–ground contact model) were compared between each other and compared with the average obtained by the experimental results	The (1) was represented by a set of 6 independent ellipsoid–plane surface pairs, rigidly attached to each foot segment and placed within the shoe's boundary The (2) was represented using 31 independent viscoelastic elements with Coulomb friction and they were attached beneath each foot	Estimated Parameter(s): GRF, lower limb joints kinematics, average execution time and average stiffness measure Limitations: 2D simulation. Additional movements should be simulated. Further optimization to improve tracking results. The analytical deduction of the closest points is only applicable to smooth convex surfaces that present an explicit relationship between surface points and surface normals. Limited comparison between contact element layouts General Remarks: Both models produced realistic GRF and kinematics with similar computational efficiency. However, the superellipsoid–plane model (1) was more computationally efficient that the point-like model (2). The (1) elements are more versatile than (2) elements. (1) is geometrically accurate and easily integrated within multibody simulation

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Martelli (2015) [19]	Aim: to investigate the repertoire of muscle synergies during walking Population: n = 1 (0 M/1 F); Age: 81; BH: 167; BW: 63 Performed movement: walking Measured variables: EMG of 15 lower limb muscles, skin-mounted marker trajectories and ground reaction forces. Equipment used: TelEMG system, Vicon Motion Capture and Kistler Instrument AG	Segments: 13 Joints: no information Software: MATLAB (The MathWorks, Natick, MA) and OpenSim [2] Original Model: [75, 135–137] Degrees of Freedom: 15 Number of muscles/ligaments: 84/0 Muscle Model: Hill-type muscle–tendon unit Muscle Paths: no information Simulation: Inverse Kinematics and Inverse Dynamics Optimization Strategy: SO Optimization Parameters: muscle stresses Objective Function: minimizing the squared sum of muscle stresses	Musculoskeletal anatomy was adjusted to match computed-tomography images and a dissection of an 81-year-old female donor	Muscle's lever arm and joint torques were compared to [138–142] The muscle lever arms were compared to [139–145] The joint torque pattern was compared to results from [146] Kinematics, kinetics, hip contact forces and muscle patterns compared to [135, 136, 147] The variability of physiological possible and plausible muscle forces were compared to [147, 148]	Muscle and joint forces were calculated by constraining muscle forces between zero and the peak muscle force. Plausible muscle forces were constrained within six selected EMG boundaries	Estimated Parameter(s): lower limb joint forces, torques and muscle activations, possible/plausible muscle forces Limitations: some muscle forces that were not constrained between EMG-driven muscle force boundaries showed higher variability. The EMG signal was normalized using the peak muscle activation calculated by SO. The results cannot be generalized. Joint torque was set to the values from inverse dynamics. The peak isometric muscle stress was the upper boundary of published values General Remarks: the model yielded joint torques within published values, hip contact forces in agreement with in vivo measurements and muscle force patterns in good qualitative agreement with corresponding the EMG recordings. The results provide a viable numerical approach for studying physiological and pathophysiological conditions

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Mikosz (1988) [12]	Aim: to develop a 3D stochastic mathematical muscle model of the knee joint to study the influence of both mechanical and physiological factors on the prediction of muscular forces about the joint Population: n = 4 (4 M/0 F) Performed movement: one experiment was conducted under static conditions at knee flexion angles of 10°, 20° and 40°. Subjects were tested while lying supine on a specially designed load table. Other movement: level walking Measured variables: in vivo EMG Equipment used: fine-wire monopolar electrodes, multi-component force plate, optoelectronic digitizer, a 10-meter walkway and a minicomputer	Segments: proximal portion of the tibia, distal portion of the femur and patella Joints: Knee Software: no information Original Model: – Degrees of Freedom: no information Number of muscles/ligaments: 13/1 Muscle Model: no information Muscle Paths: straight-line Simulation: no information Computational Technique: the authors do not consider the use of a cost function. They consider a computational technique that involves equilibrating the $\bar{M}_{\text{ext}}$ generated by foot-floor contact, gravitational and inertial forces at the knee joint to an $\bar{M}_{\text{int}}$ generated by muscular forces and soft tissue: $\mathcal{F} = \left(\bar{M}_{ext} - \bar{M}_{int}\right)^2$ Due to the non-linear nature of this equation, a quasi-Newton algorithm was used to find the minimum	No alterations were performed since the authors developed a novel knee model	Muscle force predicted by the model was compared to the recorded myoelectric activity	Muscle angle does not change with knee flexion Muscles act primarily to maintain the dynamic moment equilibrium at the knee and resist external moments Muscle force was constrained to physiological maximum force Contact region was constrained to tibial plateau Muscles produce tension force	Estimated Parameter(s): knee joint individual muscle forces, joint contact force, location of the resultant force on the surface of the tibia Limitations: the angle of the muscles does not change with knee flexion, which may limit the application of the model. Muscle length remains constant. Velocity of contraction does not affect muscle tension. General Remarks: the model was able to simulate the moving contact point between the tibia and femur, since it increased the mechanical advantage of the quadriceps muscles by 50%, which correlated to in vivo EMG measurements. Muscle force predictions during normal gait show the capability of the model to determine the presence of synergistic and antagonistic muscle action.

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Neptune (2011) [16]	Aim: to generate a muscle-actuated forward dynamics simulation of normal walking to determine how individual muscles and gravity contribute to whole-body angular momentum in the sagittal plane Population: n = 10 (5 M/5 F); Age: 27.7; Performed movement: walking for 30 s at 1.3 m/s Measured variables: kinematic, ground reaction force and muscle EMG data Equipment used: split-belt instrumented treadmill, bipolar surface electrodes	Segments: HAT and two legs (thigh, shank, patella, rear-foot, mid-foot and toes) Joints: hip, knee, ankle, mid-foot, and toe Software: SIMM (Musculo-Graphics, Inc.) Original Model: [149] Degrees of Freedom: 13 Number of muscles/ligaments: 25/0 Muscle Model: Hill-type Muscle Paths: no information Simulation: Forward Dynamics Optimization Strategy: Dynamic Optimization Optimization Parameters: EMG-based excitation patterns Objective Function: minimizing the difference between simulated and experimentally measured walking data	To identify how individual muscles and gravity contribute to whole-body angular momentum in the sagittal plane, the authors quantified their contributions to the time rate of change of whole-body angular momentum over the gait cycle using: $\dot{H} = \bar{r} \times \bar{F}_{GRF}$	Whole-body angular momentum trajectory was compared to [150] The forward/backward moment generated by SOL/GAS, respectively, is coherent with [151] The actions of SOL and GAS regarding gravity's angular momentum generated by gravity were compared to [152, 153] The capacity of the ankle dorsiflexors to make backward angular momentum was compared [154–156] Tibialis anterior (TA) and GAS' response to regulate whole-body angular momentum was related to [157, 158] HAM and gluteal muscles activity control the trunk to create a hip extensor moment [159–161] GAS, HAM and GMAX are the primary muscle groups to generate backward momentum [162]	Foot–ground contact was modelled using 30 visco-elastic elements with Coulomb friction distributed over foot segments The excitation magnitudes were allowed to vary between 0 and 1 Timing parameters from EMG data were used to restrict the excitation timing to guarantee muscles were generating force at the correct time in the gait cycle	Estimated Parameter(s): GRF, lower limb kinetics (internal and external), kinematics and muscle excitations Limitations: the authors did not include swinging arms in the musculoskeletal model. Another limitation is that the individual muscle contributions to the time rate of change of angular momentum are dependent on the simulated center-of-mass and center-of-pressure positions and each muscle's contribution to the ground reaction forces, which cannot be experimentally validated. The simulation used group average kinematic/kinetic data rather than subject-specific walking mechanics. General Remarks: The walking simulation correlated well with the group-averaged kinematic, GRF and EMG data. Simulation analysis showed that in early stance active muscles and gravity generate backward angular momentum, except the ankle plantar flexors

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Roelker (2017) [23]	Aim: to determine the effects of four OpenSim models, namely Caruthers, Gait2392, Arnold and Hamner, (with different parameters, including coordinate systems, number of segments, and muscles properties) on gait mechanics (kinematics and kinetics) and estimates of muscle forces and activations Population: n = 6 (2 M/4 F); Age: 21 ± 2.3; BW: 69.1 ± 8.3; BH: 170 ± 5; Performed movement: walking at a self-selected speed of 1.30 ± 0.14 m/s Measured variables: kinematic, kinetic EMG and GRF data Equipment used: eight-camera motion system to capture the motion of reflective markers placed on each subject, six embedded force plates to measure GRF and a 16-channel surface EMG system (Ag/AgCl dual-electrodes)	Segments: 22 (Caruthers), 10 (Gait2392), 12 (Arnold) and 12 (Hamner) Joints: no information Software: OpenSim 3.1 Original Model: Caruthers [24, 115, 163], Gait2392 [164–166], Arnold [166, 167] and Hamner [108] Degrees of Freedom: 46 (Caruthers), 23 (Gait2392), 23 (Arnold) and 29 (Hamner) Number of muscles/ligaments: 94 (Caruthers), 92 (Gait2392), 96 (Arnold) and 92 (Hamner). Muscle Model: no information Muscle Paths: no information Simulation: Forward Dynamics Optimization Strategy: Weighted Least Squares (Inverse Kinematics) (1) and Static Optimization (2) Optimization Parameters: marker and model distances (1) and muscle activations (2) Objective Function: minimize weighted least squares problem between marker and model distances (1) and minimize the sum of squared muscle activations (2)	Scaling was performed to match each model to the anatomy of the population used in the study	The principal cause of variation in kinematics was attributed to discrepancies in pelvis neutral position and knee joint model between model groups. This conclusion is supported by other literature [168] The simulated muscle activations were compared to results from EMG Joint moments predicted by simulated muscle forces were compared to results from inverse dynamics and experimental moments	Scaling: $e_v - e_e < 2.5$ cm. Max bony landmark marker error was 4 cm. Mass properties of each segment were scaled so that total model's mass was equal to the subject's mass. IK: max marker error less than 4 cm. $\mathrm{RMS} < 2$ cm. RRA/SO: Max residual forces, moments (RRA, SO) and reserves (SO): less than 25 N, 75 Nm and 50 Nm. Max translational and rotational errors: less than 5 cm and 5 $^\circ$ (RRA)	Estimated Parameter(s): peak lower extremity sagittal plane joint angles were determined for hip extension, hip flexion, knee flexion during early and late stance, knee flexion during late stance and ankle dorsiflexion and plantarflexion. Peak hip extension moment, hip flexion moment, knee flexion moment during late and early stance, knee extension moment, ankle dorsiflexion and plantarflexion moment. Muscle activations and forces Limitations: joint centers were not included in the marker sets and were not used in scaling General Remarks: several model parameters could affect simulated estimates of gait mechanics and muscle function between the models. The parameters that have a higher impact on simulation results are the pelvis and knee coordinate system definition and muscle parameters. Gait2932 is a sufficient model to study walking in healthy adults

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Sasaki (2010) [20]	Aim: to use a muscle-driven forward dynamics simulation of normal walking to identify how individual muscles contribute to the axial tibio-femoral joint force (force component parallel to the longitudinal axis of the tibia) Population: n = 10 (5 M/5 F); Age: 29.6 ± 6.1; BM: 65.6 ± 10.7; BH: 169.7 ± 10.9; Performed movement: walking on a split-belt instrumented treadmill at 1.2 m/s Measured variables: kinematics, GRF and EMG data Equipment used: split-belt instrumented treadmill, modified Helen Hays marker set to acquire kinematic data and equipment for EMG and GRF acquisition	Segments: trunk segment (head, torso and arms) and two legs (femur, tibia, patella, calcaneus, mid-foot and toes) Joints: hip, knee, ankle, mid-foot and toe Software: SIMM (MusculoGraphics Inc., Santa Rosa, CA) Original Model: – Degrees of Freedom: 13 DOFs in the sagittal-plane Number of muscles/ligaments: 25 per leg/0 (passive torques applied to represent the forces of ligaments) Muscle Model: Hill-type muscle actuators Muscle Paths: no information Simulation: Forward Dynamics Optimization Strategy: Dynamic Optimization Optimization Parameters: muscle excitation patterns Objective Function: kinematics and GRF between experimental and simulation data were minimized: $J = \sum_{i} \sum_{m} W_{i,m} \frac{(Y_{i,m} - \hat{Y}_{i,m})^2}{SD^2_{i,m}}$ where $w_{i,m}$, is the weighting factor for variable m, $Y_{i,m}$, is the experimental measure of variable m, $\hat{Y}_{i,m}$, is the simulation data corresponding to $Y_{i,m}$, and $SD_{i,m}$, is the standard deviation of variable m at time step i.	No alterations were performed since the authors developed a novel model	The knee joint loading pattern during stance was compared to results from [56, 57, 102, 106, 114, 121, 169–173] The contribution of vastii and gastrocnemius muscles to the knee joint loading pattern during stance was compared to results from [102, 103, 106, 107] The peak axial force that occurs in early stance was compared to results from [55, 57, 114, 173, 174]	The motion of the patella/tibia relative to the femur were functions of knee flexion angle The excitation timing for each muscle was constrained to EMG data Displacement of the tibia relative to the femur is a function of knee flexion angle Re-optimization mimicked quadriceps avoidance gait pattern	Estimated Parameter(s): GRF, lower limb joint angles, muscle excitation patterns, axial knee joint contact force Limitations: simulations restricted to the sagittal plane. The AP displacement of the tibia relative to the femur may influence the magnitude of knee joint forces. The analysis is based upon a generic model. The analysis does not attempt to distribute the tibio-femoral joint forces between medial/lateral compartments of the tibia. Some muscles and connective tissues crossing the knee joint were not included in the model, which may contribute to the knee joint force. General Remarks: the vastii and gastrocnemius muscles are the main contributors to knee joint force in stance. Muscles that do not cross the knee can influence the joint force. Small changes in kinematics can have a significant effect on the magnitude of the knee joint forces

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Shelburne (2004) [11]	Aim: to calculate and explain the pattern of ACL loading during normal level walking No human experimental procedures were developed	Segments:10(1),5(thigh, shank, patella, hindfoot toes) (2) Joints: pelvis, third lumbar vertebra, hip, knee, ankle and hindfoot/toes joint (1); hip, tibiofemoral, patellofemoral, hindfoot and toes (2) Software: no information Original Model: [175, 176] (1)/- (2) Degrees of Freedom: 23 (1)/no information (2) Number of muscles/ligaments: 54/0 (1), 13/5 (2) Muscle Model: [77, 177] (1)/ forces estimated based on the CSA of each muscle (2) Muscle Paths: straight lines, via points and via cylinders Simulation: no information Optimization Strategy: Dynamic Optimization (1) and Static Equilibrium Problem (2) Optimization Parameters: muscle excitation histories, muscle forces and body segmental motions (1); knee-ligament forces (2) Objective Function: minimum metabolic energy spent per unit distance moved (1); given the muscle forces, GRF, FE and internal/external (IE) rotation knee angles, and the other joint angles, find the positions of the shank and patella relative to the thigh, and the joint torques (2)	No alterations were performed to model (1) Model (2) was developed by the authors	The pattern of muscle forces predicted by the dynamic optimization solution were consistent with EMG activity. GRF and joint angles obtained from walking simulation were also similar to the same measures obtained from subjects. These results were compared to results from the walking simulation of [121] While the pattern of ACL loading during gait cycle is similar to results from [169, 170, 178, 179], the value of peak ACL force presented significant differences, when comparing to the same authors Peak ACL force for normal level walking was also compared to results from [169, 170, 178–184]	Bilateral symmetry (1). (2): The contacting surfaces of the tibia and the femur were defined as deformable. The patellar tendon was assumed to be inextensible Each ligament bundle was assumed to be elastic. Lower limb was assumed in static equilibrium	Estimated Parameter(s): body segmental motions, GRF and leg muscle forces (1), and pattern of knee muscle forces, knee joint angle, GRF, forces transmitted to the knee ligaments, anterior shear force acting on the leg Limitations: the assumption of static equilibrium in the calculation of knee-ligament loading, neglecting the effects of centrifugal and inertial forces. The predictions of knee-ligament loading were compromised by the fact that the dynamic optimization solution for walking was not fully converged General Remarks: the simulation predicted that the ACL bears load throughout stance and that its peak force occurred at the beginning of single-leg stance (contralateral toe off). The pattern of ACL force was explained by the shear forces acting at the knee.

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Tsai (2012) [18]	Aim: to investigate how incorporating direct measurements of muscle anatomic parameters using magnetic resonance imaging (1) influences knee moment predictions when compared with generic (2) and scaled (3) models Population: n = 7 (4 M/3 F); M/F Age: 25.7 ± 3.8/29.7 ± 5.5; M/F BW: 73.2 ± 6.8/54.3 ± 2.5; M/F BH: 175 ± 4/164 ± 2; Performed movement: MRI (1): static partial weight bearing by having subjects pushing against a load of 111 N at 0°, 15°, 30°, 45° and 60° knee flexion; Biomechanical testing (2 and 3): drop landing and isokinetic knee extension Measured variables: muscle volumes and moment arms (1), muscle activation levels, kinematic data and GRF (2 and 3) Equipment used: 3.0-T MRI system, isokinetic dynamometer, bipolar surface electrodes, 8-camera motion analysis system, force plates	Segments: pelvis, femur, tibia, patella and foot Joints: hip, knee and ankle Software: SIMM Software (MusculoGraphics, Inc. Chicago, IL) Original Model: – Degrees of Freedom: no information Number of muscles/ligaments: 10/0 Muscle Model: Hill-type muscle model Muscle Paths: no information Simulation: Forward Dynamics No optimization procedures were adopted	No alterations were performed, since the model was developed by the authors	Net knee joint moment calculated by the EMG driven model (MRI model) exhibited better agreement and a smaller error when compared with the standard knee joint moment measurements than the generic and scaled models Knee joint moments errors were compared to results from [41] MRI-measured muscle volumes were compared to results from [185–187] The magnitudes and patterns of the polynomial curve relationships between moment arms and joint angles for the muscle included in the model were compared with results from [188, 189]	Muscle activation of vastus intermedius muscle was estimated as the average of the vastus medialis and vastus lateralis normalized EMG amplitudes during each task Semimembra-nosus and biceps femoris short head muscles were assumed to have the same activation of semitendinosus biceps femoris long head A 40-ms eletromechanical delay was used	Estimated Parameter(s): net knee sagittal plane moments, moment arms Limitations: the errors in each of the 3 models may be attributed to the estimation of muscle activation directly from normalized EMG and the use of generic muscle parameters. The errors during isokinetic exercise may be due to the constant velocity at which the isokinetic task was performed. The use of fiber lengths and pennation angles from other literature may have limited the calculation of subject-specific PCSA for each muscle. The moment arm and the knee joint center estimation methods influenced the prediction of moments. Moment arms were estimated from a limited number of knee positions. The 111 N load does not result in muscle forces comparable to those experienced in the performed movements General Remarks: models that include direct measurements of muscle anatomic parameters may provide more accurate results of kinetics than generic and scaled

Table 1 (continued)

First author, year	Aim, population demographics and experimental setup	Musculoskeletal model characteristics	Model alterations	Validation dataset	Modelling Conditions	Outcomes, Limitations and General Remarks
Xiao (2010) [24]	Aim: to evaluate: how estimated muscle forces change due to the number of muscles included; the sensitivity of individual muscles forces to perturbation in muscle parameters; how other muscles respond to perturbation of one muscle Population: n = 3 (3 M/0 F); Age: 20.7 ± 0.7; BW: 76.6 ± 11.7; BH: 178.1 ± 7.2; Performed movement: walking on a split-belt, motorized treadmill at self-selected speeds (1.296 ± 0.051 m/s) Measured variables: 3D locations of markers and GRF Equipment used: 6-camera motion analysis system and treadmill	Segments: 13 Joints: 12 Software: OpenSim Original Model: [2, 163] Degrees of Freedom: 23 Number of muscles/ligaments: 34 muscle–tendon units/0 Muscle Model: Hill-type Muscle Paths: no information Simulation: Forward Dynamics Optimization Strategy: Computed Muscle Control Optimization Parameters: muscle excitation patterns Objective Function: minimization of the weighted squared sum of muscle forces	The generic model was scaled to subject-specific geometry and mass based on marker positions obtained during a static position trial	The OpenSim simulations of the all models (the generic model used was perturbed in terms of number of muscles, which increased from 34 to 64, and in other simulation in terms of a subset of model parameters for leg muscles, for instance, maximum isometric force) were compared to the experimental walking data	The authors fixed the perturbation size (+10% and -10%) for the three muscle parameters tested (optimum fiber and tendon slack lengths and maximum isometric force)	Estimated Parameter(s): lower limb kinematics, muscle forces Limitations: no limitations were reported General Remarks: the change of one muscle force was compensated by muscles in the same functional group and/or antagonistic muscle group. Only magnitude of the estimated muscle forces is affected by the change in the number of muscles included in the model. This indicates that it is not always necessary to use as many muscles in the model as possible. Also, accurate attention must be considered in using values of tendon slack length and optimal fiber length for ankle plantarflexors and knee extensors.

n, number of participants; BM, body mass (kg); BW, body weight (kg); BH, body height; M, male participant; F, female participant; EMG, electromyography; deg, degree; SIMM, Software for Interactive Musculoskeletal Modeling; $l_{fascicle}$, fascicle length; l_{fibre}, fiber length; F_{max}, maximum contraction force; FE, flexion/extension; sEMG, surface electromyography; σ, standard deviation; F_{amax}, maximum muscle contraction force;l_{opti}, optimal muscle length; k_m, rigidity; γ_m, damping; $T(i)$, model knee torques; $T_{iv}(i)$, Newton–Euler method knee torques; ns, samples; RF, rectus femoris muscle; p_z^p, component of the translational displacements of the patella reference frame origin with regard to the femur reference frame origin; TFJ, Tibiofemoral joint; HAT, head, arms and trunk; θ_A, ankle joint angle; θ_H, hip joint angle; θ_K, knee joint angle; GRF, ground reaction force; $F_{stiction}$, stiction horizontal GRF; $\mu_{stiction}$, stiction coefficient; F_y, vertical ground reaction force; $\dot{x}_{CP}$, contact point position from which stiction engages; MT, musculotendon; ROM, range of motion; 3D, three dimensional; PIA, physiological inverse approach; CIA, 'classical' inverse approach; MS_{jk}, muscle sensitivities; CE, contractile element; l_0^M, optimal muscle fiber length; l_s^T, tendon slack length; CSA, cross-sectional area; PCSA, physiological cross-sectional area; DOF, degree of freedom; G, objective function; $f^{(M)}$, muscle force; f, unknown internal forces and moments; d, external forces and moments; C, matrix containing other inputs such as coefficients and constants for the unknown forces and moments (e.g. moment arms) found at each step; N_i, muscle strength; CF, contact force; CZ, contact zone; CP, contact point; ACL, anterior cruciate ligament; NMMS, net muscle moments; VAS, vasti muscle; GMAX, gluteus maximum; GMED, gluteus medius; GAS, gastrocnemius; SOL, soleus; NTE, normalized trial EMG; $\mathrm{E}^2_{\mathrm{act}}$, error term for subjects generating active moments; $\mathrm{E}^2_{\mathrm{rest}}$, error term for subject at rest; U, J, objective function; $W_{i,m}$, weighting factor for variable m at step time i; $Y_{i,m}$, experimental measurement of variables m at step time i; $\hat{Y}_{i,m}$, simulation data related to $\mathrm{Y}_{\mathrm{i,m}}$ at step time i; $\mathrm{SD}^2_{\mathrm{i,m}}$, standard deviation of experimental variable m at step time i; 2D, two dimensional; SO, static optimization; $\mathcal{F}$, square difference between internal and external moments; $\bar{M}_{ext}$, external reaction moment; $\bar{M}_{int}$, internal moment vector; $\dot{H}$, time rate of change of sagittal plane whole-body angular momentum; $\bar{r}$, moment arm vector form each foot's center-of-pressure to the body's center-of-mass; $\bar{\mathrm{F}}_{\mathrm{GRF}}$, vector of each muscle's and gravity's contribution to GRF; TA, tibialis anterior muscle; HAM – hamstrings muscle; $\mathrm{e_v} - \mathrm{e_e}$, error between virtual and experimental marker location; IK, inverse kinematics; RMS, root mean square; RRA, residual reduction algorithm; AP, anterior/posterior; IE, internal/external; MRI, magnetic resonance imaging

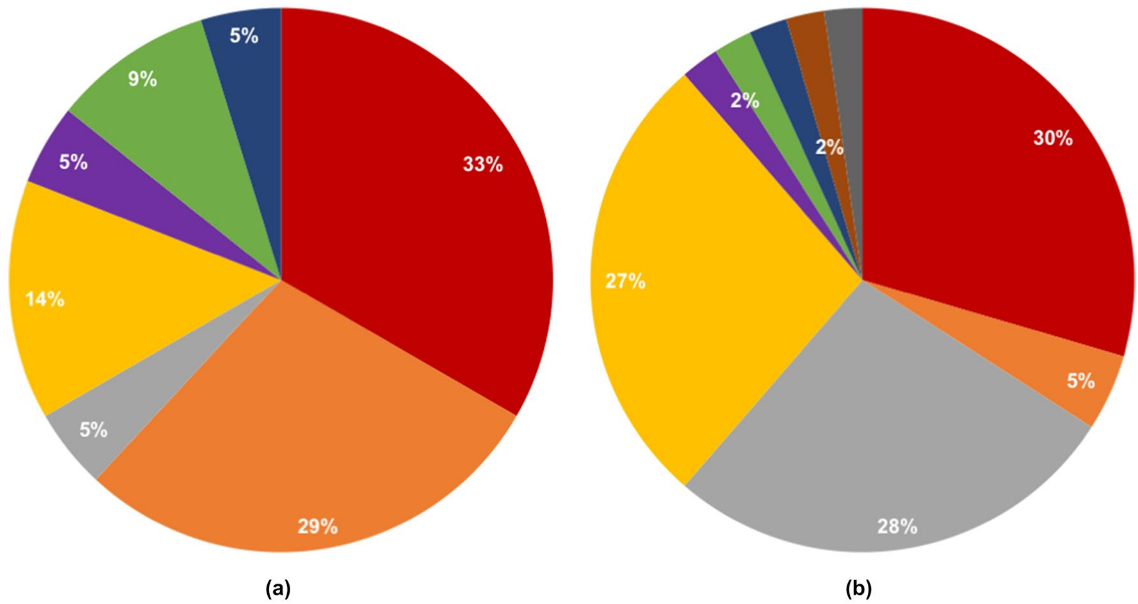

Fig. 3 **a** Distribution of the movement performed by the subjects of the reviewed articles. Flexion and extension of the knee joint. Vertical jumping. Walking at constant speed. Walking at different speeds. Running at different speeds. Static conditions. Drop landing and isokinetic knee extension. **b** Distribution of the measured variables of the reviewed articles. Electromyographic signals. Ground reaction forces. Kinetic data. Kinematic data of markers placed on key anatomical landmarks. Knee flexion and extension torques. Angular displacement of the knee joint. External loads above the ankle. Joint angles of hip, knee and ankle. Muscle volumes and moment arms. (Color figure online)

mass/weight and five studies [12, 13, 15–17] did not mention the body height of the subjects. Note that some studies presented the mass of the subjects as body mass or as body weight (both expressed in kg).

Four studies [5, 12, 13, 18] analyzed more than one movement (Fig. 3a). Thirteen studies considered the subjects' walking gait, with six being performed at constant speed [6, 12, 13, 16, 19, 20] and seven at different speeds [5, 7, 15, 21–24]. One study analyzed vertical jumps [17] and another study analyzed a drop landing task and isokinetic knee extension [18]. Three studies analyzed the knee's flexion and extension [13, 14, 25] and two acquired data in static conditions [12, 18]. One study analyzed running at different speeds [5].

Studies reported different measured variables during the experimental procedure, with fifteen [5–7, 14–25] measuring more than one variable (Fig. 3b). The kinematic data of markers placed on key anatomical landmarks was measured by thirteen studies [5–7, 15–24], and the electromyography (EMG) activity of lower limb muscles was measured in twelve studies [5, 7, 12, 14, 16, 18–23, 25]. Twelve studies [5–7, 15–21, 23, 24] measured ground reaction forces (GRF) and two [22, 23] kinetic data. Knee flexion and extension torques [13], angular displacement of the knee joint [25], external loads applied above the ankle joint and hip, knee and ankle joint angles [14], and muscle volumes and moments arms [18] were the variables of interest of four different studies.

An array of different of equipment was used to perform experimental movement analysis (Table 1). Motion capture systems were used in thirteen studies [5–7, 13, 15, 17–24], force plates were used in also thirteen studies [5–7, 12, 13, 15, 17–23] and eleven studies [7, 12, 14, 16, 18–23, 25] used EMG collection devices. Five studies [5, 16, 20, 22, 24] used treadmills and only one [18] used a magnetic resonance imaging (MRI) system. Three studies [13, 18, 25] used dynamometers and other equipment, such as load device and load cell [14], triaxial electrogoniometer [25], and a optoelectronic digitizer, a 10-m walkway and a minicomputer [12].

3.4 Musculoskeletal Model Characteristics

Four studies [8, 12, 14, 25] used a musculoskeletal model of the knee joint, whilst the remaining utilized models of the lower limb. The characteristics of the musculoskeletal models are presented in Table 1. Fourteen studies [5, 8–10, 12–18, 20, 21, 25] detailly described the composition of their models in terms of segments and joints, whilst the other seven studies [6, 7, 11, 19, 22–24] only referred to either one or neither of them (segments or joints) or their number. Most of the studies reported the software used for the construction of the biomechanical model and its simulation, including the

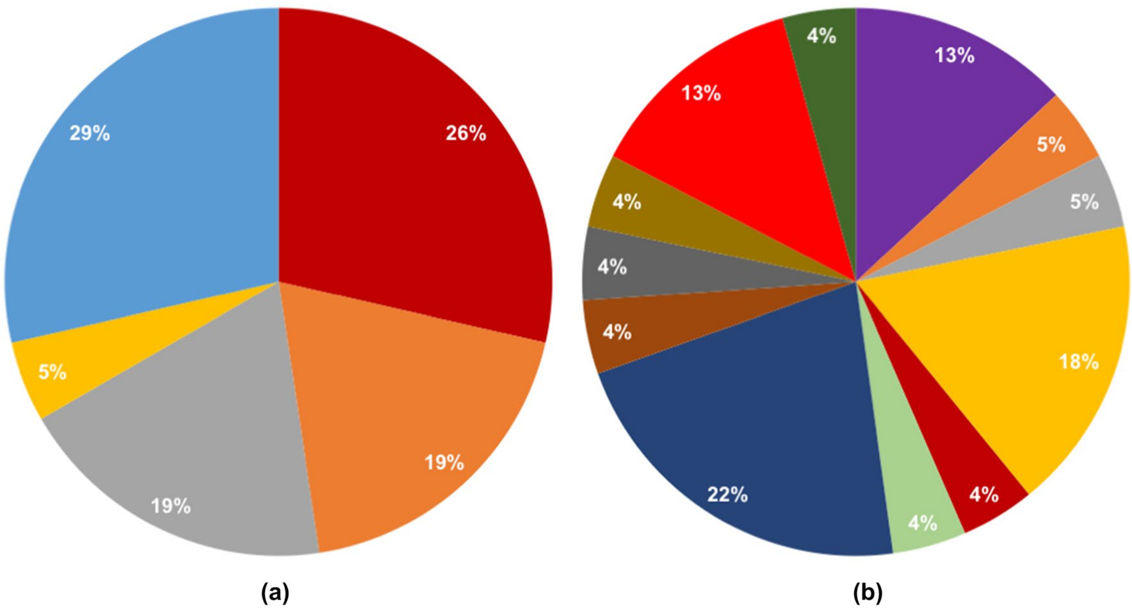

Fig. 4 **a** Distribution of the software used to construct and to simulate the biomechanical models of the studies. Anybody Modelling System. OpenSim. Matlab. SIMM. No information. **b** Distribution of the optimization strategy used. Quasi-Newton non-linear minimization method. Static optimization. Linear/non-linear optimization. Optimization toolbox of Matlab. Dynamic optimization. Computed Muscle Control. Genetic Algorithm. Inverse Kinematics. Nedler-Mead method. No information. CIA and PIA. Min/max recruitment criterion. (Color figure online)

SIMM, Matlab, OpenSim and AnyBody Modelling Systems (Fig. 4a). Six studies [7, 8, 10–12, 25] did not provide information on the software used.

Eight studies [9, 10, 12, 14, 18, 20, 21, 25] did not use a previously developed biomechanical model, creating their own instead. In turn, thirteen studies [5–8, 11, 13, 15–17, 19, 22–24] used models previously reported in the literature. The number of degrees of freedom varied from 1 to 46, with six studies [10, 12, 14, 17, 18, 21] not referring this parameter. All studies included muscles (hill-type muscle model, models developed by other authors or by the study authors themselves) and five studies [8, 11, 12, 15, 17] also included ligaments to more accurately mimic the musculoskeletal system. Twelve studies did not refer the muscle path [6, 8, 9, 13, 15, 16, 18–21, 23, 24]. When reported, the muscle paths were considered as wrapping surfaces or points, line segments, space curves and via cylinders or points.

As simulation strategy, ten studies [5, 9, 13, 15, 16, 18, 20, 21, 23, 24] used forward dynamics, seven studies [6, 7, 13, 17, 19, 22, 25] used inverse dynamics and three studies [13, 19, 22] used inverse kinematics. Three studies [13, 19, 22] used more than one simulation strategy, and five studies [8, 10–12, 14] did not mention it. Overall, the studies used an optimization strategy to look for parameters that, once input into the biomechanical model, made it pertain a gait as desired regarding the aim of the study. The optimization strategies utilized can be seen in Fig. 4b.

3.5 Alterations Performed to the Musculoskeletal Model

In all reviewed studies using a previously developed biomechanical model, it was analyzed the alterations performed to the original model in order to adapt it to the authors' needs. For instance, Arnold et al. [5] used a model developed by Arnold et al. [26] and increased the knee range of motion (ROM), strengthened the muscles to reflect young athletic subjects, increased the maximum shortening velocity and increased the Achilles tendon compliance in accordance to ultrasound studies. Other alterations found in the reviewed studies consisted in utilizing different cost or objective functions to optimize the biomechanical model, to perform the scaling of the model so it could mimic different subjects with different anthropometric characteristics, to alter the ground contact model, amongst the others presented in Table 1.

3.6 Validation Datasets

The validation process mostly consisted in comparing the study's results with the ones existing in the literature. Besides this strategy, four studies [12, 22, 23, 25] compared the obtained simulated muscle activation patterns with the experimentally measured EMG activity. One study [15] compared the results of the contact models implemented between each other, as well as with the obtained experimental results. In addition to comparing their results to other authors, Roelker et al. [23] also compared joint moments predicted by simulated muscle forces to results from inverse dynamics analysis and experimental moments. Tsai et al. [18] compared the net knee joint moment calculated by the MRI, the generic and scaled models between each other. Xiao and Higginson [24] compared the OpenSim simulations of all models to experimental walking data.

3.7 Modelling Conditions

Different modelling conditions were utilized to limit the results' search space and to obtain results within normal physiological conditions (Table 1). Modelling conditions comprised data associated with muscle, tendon and ligament characterization [5, 8–14, 16–21, 24, 25], models' geometric considerations and properties [6, 8, 11, 12, 15, 17, 20, 21], ground contact model [7, 9, 16], degrees of freedom [22, 25], joints modelling [8, 9, 22], moments [14], and scaling and marker errors [23].

3.8 Estimated Parameters

The most common estimated parameters included muscle and joint forces and moments, muscle activation patterns, joint angles and muscle fibers velocities. Other examples can be found in Table 1. Ten studies only analyzed these parameters in relation to the knee joint [6, 8, 11–14, 18, 21, 22, 25], whilst the remaining studied the entire lower limb.

4 Discussion

The present systematic review gathered and analyzed the characteristics and methods employed in the development of human lower limb and knee joint musculoskeletal models available in the scientific literature. This information can be used by model developers and users to compare, adapt and fine-tune their musculoskeletal models according to their specific needs.

Studies used different number of body segments to construct their musculoskeletal model, with some studies using more segments than others. However, depending on the purpose for which it is to be used, more or less complexity may be added to the model. For instance, if a single joint is being studied, it should be prioritized a more detailed and complex biomechanical modelling of that specific joint (e.g. knee joint), rather than using a model representing the entire lower limb or including the torso and upper limbs. Generally, studies that included only the knee joint [8, 12, 25] incorporated the patella, except for Lloyd and Buchanan [14]. This segment may be removed if a less computational burden is desired and if it is beyond the study's aim, that is, if the movement of the patella does not significantly affect the parameter(s) under analysis. Lloyd and Buchanan [14] aimed to determine the load sharing between muscles and other soft tissues comprised around the knee joint, and modelling the patella was not necessary for this purpose as it did not influence the evaluation of those parameters. Besides the patella, to model the knee joint, lower limb models mostly incorporated the femur and the tibia bone segments and excluded the fibula, thus, diminishing model's modelling complexity. Only two knee studies [14, 25] have included the fibula on the representation of the leg.

The number and type of segments included in the models representing the entire lower limb varied substantially, comprising at least four segments. The simplest models [9, 10, 17, 21] contain a unique segment representing the entire upper extremity (pelvis, HAT or trunk), and three segments characterizing each lower limb (thigh, leg and foot). The use of at least these four segments is therefore suggested to be used in lower limb musculoskeletal models to analyze the dynamics of human movement. Incorporating a more detailed modelling of the human anatomy—for instance including the fibula, patella and bones of the foot—increases the computational burden, decreasing simulation's efficiency and may not be essential for obtaining the study's results. Also, modelling the human torso and upper limbs should be considered when their influence on the physiological task being tested is relevant, otherwise can be omitted or represented by a HAT/trunk/pelvis segment. The choice of the musculoskeletal model complexity should be tailored to the purpose of the study, as well as to how much detail the model should comprise to obtain the study's parameters and outcomes according to the human physiological dynamics desired. This should be considered during the model development to avoid non-essential components that can result in additional computational burden.

The analyzed models involving the entire human lower limb included at least the three major articulations of this anatomical structure, namely hip, knee and ankle joints [5, 9, 10, 17, 18, 21]. Besides utilizing these three joints, De Groote et al. [13] also included a spherical joint connecting the HAT to the pelvis and Lemieux et al. [6] used a musculoskeletal model of the entire body, including joints of the upper limb (shoulder, elbow, radio-ulnar and wrist joints). Lerner et al. [22] contains a more detailed representation of the foot, including the subtalar and metatarsophalangeal joints, while Lim et al. [7] also comprises the third lumbar vertebra. Other models have included the mid-foot and toes [15, 16, 20], whilst Xiao and Higginson [24] only referred that twelve joints were used and did not describe them. Shelburne et al. [11] used two models in their study. A three-dimensional model of the body was utilized to calculate muscle forces of the leg and was composed by joints at the pelvis, third lumbar vertebra, hip, knee, ankle and hindfoot/toes. The other model was used to calculate knee-ligament forces and was composed by the hip, tibiofemoral, patellofemoral, hindfoot and toes joints. Considering this analysis, it is recommended that at least the hip, knee and ankle joints are included in the musculoskeletal model to properly model the human lower limb. Also, based on the analyzed literature, a segment modelling the upper extremity is required and, therefore, joints connecting it to the lower limbs are important—for instance, Geyer and Herr [9] used the hip joint to connect the HAT to both lower limbs. More specific joints, such as the patellofemoral joint, should be utilized if a more detailed study is intended to be carried out and/or if their inclusion influence the study's results.

The modelling of the muscles has an important role to simulate their action during physiological tasks. The Hill-type muscle model was the most commonly utilized [5–7, 9, 13–16, 18–20, 24], but a few studies opted to develop their own muscle model. Chen et al. [21] incorporated 10 muscles and created a muscle model including muscle bioelectrical activation, muscle contraction mechanical and muscular function models. Similarly, Hoy et al. [10] developed a musculotendon actuator model, including a contractile element in series with a linear elastic tendon. Cleather and Bull [17], Kaufman et al. [25] and Shelburne et al. [11] used muscle models developed by other authors. Since the majority of the studies used the Hill-type muscle model, it may be adequate for simulations of human movement. However, this model describes the force–velocity relation only for concentric muscular contractions and it is only related to maximally activated muscles, not being applicable to muscle actions performed during most daily activities [190]. Therefore, to test more specific situations or situations that are not predicted by this muscle model, for instance, if eccentric muscular contractions are intended to be studied, this model is not adequate and another one should be utilized. Even though these limitations exist, authors continue to use the Hill-type muscle model and their results are adequate and within physiological conditions. The choice of the muscle model to incorporate in the musculoskeletal model should rely on the purpose of the study. Independently of the number of segments, joints, muscles and muscle model utilized, the studies presented good agreement with the physiological dynamics of human movement reported in literature or in experimentally measured data. This is a crucial step before implementing the model in experimental settings.

The methodological quality of the analyzed studies should also be addressed. The major concern identified was the poor description of model parameters (only two studies achieved high quality) which is crucial to compare results and drawing out conclusions among models. There was no standardization of the description of the biomechanical models which precluded direct comparison between all studies in all variables. It is recommended the use of the parameters displayed in the summary table developed in the presented systematic review as a strategy to implement in future studies, avoiding inconsistent reporting and harmonizing biomechanical modelling of the lower limb and knee joint. The strategy should be applied to reporting of participant characteristics and definition of movement tasks, equipment design and experimental set up. The reporting of alterations performed to the model, statistical methods, study limitations and conclusions must also be clearly and systematically described in future studies.

Some limitations of this systematic review are important to be mentioned. This review only included studies related to musculoskeletal models of the lower limb or knee joint only that studied normal physiological human movement, such as walking, jumping or running. Therefore, models including exclusively the hip and ankle joints were not included. Conference proceedings, articles that were not written in English and studies that did not focus only on healthy articulations or studied pathological conditions were not considered. In addition, studies including subject specific and/or two-dimensional musculoskeletal models were also not considered. This led to the exclusion of several studies that, although reported important aspects, did not fulfil the eligibility criteria.

5 Conclusion

Musculoskeletal models of the human lower limb and knee joint only were analyzed and the characteristics and methods utilized in their development were systematically reported. Even though the twenty-one reviewed studies were able to reproduce the dynamics of physiological tasks similar to results reported in literature and to experimentally measured records, there is a high reporting heterogenicity between the models analyzed and a lack of precise standardization methods reported (such as the data collection and extraction table presented in this review), which hinder more definitive conclusions. The characteristics reported in this review can be used by model developers and researchers to build or fine-tune their models. Future studies should aim to clearly and systematically report the model parameters discussed in this review to harmonize the biomechanical modelling of the lower limb and knee joint.

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Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest.

Appendix 1

See Table 2.

Table 2 Example of search strategy for the PubMed database

Search	Search terms	Results
1	Human knee	128,399
2	Knee	150,217
3	Knee joint	87,080
4	1 OR 2 OR 3	150,217
5	Biomechanical	126,978
6	Biomechanical model	27,185
7	Knee biomechanical	17,075
8	Biomechanical analysis	42,501
9	Musculoskeletal	72,992
10	Musculoskeletal model	6607
11	5 OR 6 OR 7 OR 8 OR 9 OR 10	194,850
12	Muscle force	43,700
13	Mechanical force	38,554
14	Muscle reaction	51,148
15	12 OR 13 OR 14	121,664
16	Prosthesis	526,750
17	Prostheses	488,550
18	Pathology	3,223,371
19	Injury	1,285,113
20	Replacement	282,517
21	Arthroplasty	78,248
22	Loss	849,172
23	Deficit	111,768
24	Reduction	1,064,506
25	Pain	737,223
26	Disorder	4,540,414
27	Rehabilitation	556,766
28	Unhealthy	10,538
29	Reconstruction	333,707
30	Graft	301,612
31	Disease	4,112,261
32	16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31	10,171,703
33	4 AND 11 AND 15 NOT 32	108

Appendix 2

See Table 3.

Table 3 Methodological quality assessment results obtained from the selected studies. Q1: Are the research objectives clearly stated?, Q2: Is the scientific context clearly explained?, Q3: Is the musculoskeletal model adequately described?, Q4: If any, were the model alterations clearly described?, Q5: Were participant characteristics adequately described?, Q6: Were movement tasks, equipment design, and set up clearly defined?, Q7: Was the evaluation strategy appropriately justified?, Q8: Were the analytical methods clearly described?, Q9: Were the statistical methods justified and appropriately described (other than descriptive statistics)?, Q10: Was the validation procedure clearly described?, Q11: Were the direct results easily interpretable?, Q12: Were the main outcomes clearly stated and supported by the results?, Q13: Were the limitations of the study clearly described?, Q14: Were key findings supported by other literature?, Q15: Were conclusions drawn from the study clearly stated?

First author, year	Questions															Score (%)
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	
Arnold (2013) [5]	2	2	2	2	1	2	2	2	2	2	2	2	2	2	1	93.3
Chen (2017) [21]	2	2	1	0	2	2	2	2	2	2	2	2	1	2	2	86.7
Ciszkiewicz (2016) [8]	2	2	1	2	0	0	2	2	0	2	2	2	0	2	2	70.0
Cleather (2011) [17]	2	2	1	2	1	2	2	2	1	2	2	2	2	2	1	86.7
Geyer (2010) [9]	2	2	1	0	0	0	2	1	1	2	2	2	0	2	1	60.0
De Groote (2010) [13]	2	2	1	2	1	2	2	1	0	2	1	2	0	1	1	66.7
Hoy (1990) [10]	2	2	1	0	0	0	2	2	0	2	2	2	0	2	1	53.3
Kaufman (1991) [25]	2	2	1	0	2	2	2	2	2	2	2	2	0	1	2	80.0
Lemieux (2017) [6]	2	2	1	2	1	1	2	1	0	2	1	2	2	2	1	73.3
Lerner (2014) [22]	2	2	1	1	2	2	2	2	2	2	2	2	2	2	1	90.0
Lim (2017) [7]	2	2	1	2	2	2	1	2	1	2	1	2	2	2	1	83.3
Lloyd (1996) [14]	2	2	1	0	2	1	1	2	1	2	1	2	1	2	1	70.0
Lopes (2016) [15]	2	2	1	2	1	1	2	2	0	1	2	2	2	0	1	70.0
Martelli (2015) [19]	2	2	1	1	1	1	1	1	1	2	2	2	2	2	1	73.3
Mikosz (1988) [12]	2	2	1	0	1	1	2	1	0	1	1	2	2	0	1	56.7
Neptune (2011) [16]	2	2	2	1	1	1	1	2	0	2	2	2	2	2	1	76.7
Roelker (2017) [23]	2	2	1	1	2	2	1	2	2	1	2	2	1	1	2	80.0
Sasaki (2010) [20]	2	2	1	0	2	1	1	2	0	2	2	2	2	2	1	73.3
Shelburne (2004) [11]	2	2	1	0	0	0	1	1	0	2	2	2	2	2	1	60.0
Tsai (2012) [18]	2	2	1	0	2	2	2	1	2	2	2	2	2	1	1	80.0
Xiao (2010) [24]	2	2	1	2	2	2	1	2	0	1	2	2	0	1	2	73.3
Average	2.0	2.0	1.1	1.0	1.2	1.3	1.6	1.7	1.2	1.8	1.8	2.0	1.3	1.6	1.2	74.1

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