Reframing sarcopenia as a disease of the ageing motor system

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Sarcopenia is a major driver of disability, frailty, and loss of independence in ageing populations. Current consensus definitions have shifted from low muscle mass to low muscle strength and impaired physical performance as the defining clinical features. The underlying disease model, however, has remained predominantly muscle-centric, a framing that has generated important advances in muscle biology but has also guided decades of muscle-focused research in which drugs that increase muscle mass have produced inconsistent functional benefits. Muscle mass and intrinsic muscle quality account for an important but incomplete proportion of age-related declines in strength and mobility. Ageing disrupts the entire motor system, from supraspinal centres, spinal circuitry, and peripheral nerves to neuromuscular junctions and muscle, reducing neural drive, coordination, and force generation. We propose reframing sarcopenia as a disease of the ageing motor system. Although existing strength-based and performance-based criteria capture the clinical syndrome, there is scope for improvement. The disease model and diagnostic framework should evolve to reflect the distributed biology of sarcopenia, guiding integrated assessment, mechanistic stratification, and therapies that target both neural and muscular mechanisms. Without this shift, meaningful therapeutic progress will remain challenging.

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Introduction

Sarcopenia was initially framed as the age-related loss of skeletal muscle mass, and early epidemiological studies linked declining lean mass with disability, falls, and mortality.[1] This poverty-of-flesh framing was reinforced by decades of research that implicitly equated greater muscle mass with better function.[1,2] Over the past decade, however, consensus definitions of sarcopenia have shifted away from framing muscle mass as the primary defining feature of sarcopenia.[1,2] Multiple international working groups now emphasise poor muscle strength and physical performance (eg, poor grip strength, gait speed, and chair stands) for diagnosis and staging,[3–6] with muscle mass as a supportive or confirmatory measure.[3–6] This shift reflects a robust empirical finding that strength and performance predict adverse outcomes more strongly and consistently than muscle mass in older adults.[1,2,7]

Despite this definitional evolution, in which low strength and poor performance are treated as the defining features and not as incidental findings, the underlying conceptual model of the disease has remained predominantly muscle-centric.[3–6,8] Mechanistically, weakness and slowness are still considered primarily as downstream consequences of muscle dysfunction, even though the diagnostic definitions of weakness and slowness have advanced.[3–6] The nervous system is sometimes acknowledged but rarely placed at the centre of the conceptual framework. According to reviews, figures, and trial designs, sarcopenia is a myopathic disorder, as though muscles act in isolation despite Sherrington's final common pathway principle, whereas the brain, spinal cord, and peripheral nerves required for coordinating and modulating muscle activation, trophic support, and maintenance are ignored or relegated to the margins.[3–6]

This conceptual lag has translational consequences beyond semantics. When sarcopenia is defined by deficits in voluntary strength and movement, then, by definition, sarcopenia is a disorder of the motor system. The term motor system indicates the entire central and peripheral apparatus that generates and controls movement—namely, the brain and supraspinal centres, spinal cord, peripheral nerves, neuromuscular junctions, and muscle fibres. Approaching sarcopenia as a muscle-only disorder risks continued misalignment between biological targets and the functional outcomes that define the condition. This misdirection, for example, perpetuates clinical trials and therapeutic strategies that increase muscle mass without meaningfully improving mobility and independence.[9] A condition defined by the inability to generate force and move effectively demands a conceptual model and framework that encompasses descending and sensorimotor circuits and contractile tissue.

In this Personal View, we distinguish between sarcopenia as a clinical syndrome, defined by weakness and impaired physical performance, and the disease model, which refers to the distributed biology of ageing across the motor system that produces this phenotype.

Muscle-focused models alone are not enough to predict motor output impairment

The most immediate challenge to a purely muscle-based view of sarcopenia is quantitative. Muscle loss explains only a modest or trivial proportion of strength decline in older adults.[7,10] Individuals with similar muscle mass can show markedly different strength and physical capabilities.[11] Conversely, pronounced weakness and mobility restriction can develop despite only slight reductions in lean tissue, whereas others undergo substantial muscle loss yet retain preserved function.[7,12] Furthermore, the model remains incomplete even when it is extended to include intrinsic muscle contractile function. When strength measures are replaced with mobility measures, such as walking speed, muscle measures become even weaker predictors than they originally were,[10] because gait speed is an integrated outcome influenced by balance, sensory function, pain, cardiorespiratory fitness, cognition, and

muscle function. Hence, gait speed alone does not identify which system is curtailing performance. Muscle power (ie, the product of force and velocity) illustrates this muscle function dissociation particularly clearly. Muscle power declines earlier and more steeply than either muscle mass or maximal strength, tracks functional decline and disability more closely, and depends not only on contractile properties but also on motor-unit recruitment, firing-rate modulation, and neural drive.[13–17] Muscle power, therefore, reflects the motor system nature of sarcopenia more directly than muscle mass or strength and corresponds to everyday tasks, such as rising from a chair, climbing stairs, recovering balance, and avoiding falls,[13–15] by which mobility is typically judged.

The field's experience with pharmacological and nutritional interventions is equally instructive. Substantial financial resources have been devoted to the development of muscle-targeted compounds.[2,9] However, several trials of anabolic agents or protein supplementation that increased lean mass and muscle mass in older adults produced only modest or variable gains in functional outcomes.[2,9] These results are frequently framed as inefficient translations of muscle gain into strength. Another equally plausible interpretation is that interventions have often targeted the wrong component of the system or only one of several necessary nodes. Conversely, exercise can improve strength, power, and physical performance in older adults even when muscle mass does not measurably increase, underscoring that functional gains might occur independent of changes in muscle mass.[18–20]

None of these observations imply that muscle tissue is unimportant. However, the insufficient explanatory power of muscle measures to predict declines in physical function and the disappointing functional returns of purely hypertrophic strategies suggest that the key drivers of age-related weakness and slowness have not been accounted for. Those drivers reside not only within the muscle but also throughout the motor system. Current frameworks do not account for how age-related changes in the nervous system fundamentally modulate muscle force generation.

Ageing alters the motor system from brain to muscle

Voluntary movement reflects coordinated activity across a distributed motor system. Supraspinal centres plan and modulate actions; sensory inputs are integrated to shape motor output; descending pathways convey commands; and spinal motoneurons amplify and translate neural drive into motor-unit discharge and force. At each of these levels, ageing introduces changes that can reduce the fidelity, timing, and magnitude of the outgoing neural drive to muscle[11,21] (figure 1). At the spinal level, motoneuron loss and motor-unit remodelling[22–24] help to prevent myofibre atrophy and preserve muscle mass but can impair fine motor control and reduce motor output.[11] Age-related changes in persistent inward currents and other intrinsic electrophysiological properties reduce neuromodulation of firing-rate acceleration, firing-rate amplification, and self-sustained firing, challenging rapid generation of high force.[25–30] Peripheral nerve demyelination, low conduction velocity, and impaired neuromuscular transmission can constrain motor-unit recruitment and flexible force scaling.[11,21] The sensory side of the motor system is affected in parallel. Age-related structural and functional decline of muscle spindles and their proprioceptive afferents (including spindle atrophy and partial loss of sensory innervation) impairs position sense and movement perception, contributing to slow and less accurate movement, poor balance, and weakness through reduced proprioceptive support of motor output.[31–36] Finally, movement is also reorganised. Older adults adopt more cautious movement strategies (eg, greater co-contraction[37] and greater reliance on visual feedback), which might not only improve stability but also impose energetic[38] and mechanical penalties that contribute to slower gait, impaired balance, and reduced adaptability to environmental demands. These adaptations are shaped not only by neuromuscular changes but also by cognitive and perceptual factors (eg, attention, executive function, fear of falling, and risk perception), which interact with motor decline to shape movement behaviour.[39,40] Gait slowness, commonly used to operationalise sarcopenia, is an integrated, low-specificity phenotype that possibly reflects age-related degradation of neural drive and sensorimotor control,[41] in addition to the changes in mechanical and histological properties of muscles. Precisely, because gait integrates multiple physiological systems, walking speed is highly predictive of adverse outcomes and is also a challenging therapeutic target for any therapy aiming at a single node of the system.[41] These neural impairments are not minor modifiers of muscle output; instead, they are of sufficient magnitude to explain a substantial proportion of the missing weakness and slowness that muscle-focused models leave unexplained. This pattern also illustrates a broader point: this framework does not replace a muscle-first model with a neuron-first model. Neural and muscular ageing are coupled and mutually reinforcing. Reduced neural drive might promote disuse and atrophy, whereas declining muscle quality, altered sensory feedback, and inflammation, in turn, might further impair motor control. Sarcopenic weakness is best understood as emerging from this coupled decline rather than from the failure of any single tissue.

Clinical phenotypes point to motor system involvement

The clinical presentation of sarcopenia often includes features suggestive of neural involvement: weak and slow force generation, increased force variability, altered coordination, reduced steadiness, impaired balance, and reduced adaptability to perturbations.[21,42–45] Boundaries with other age-related motor disorders (eg, mild neuropathies, parkinsonian syndromes, and cerebellar disease) can be

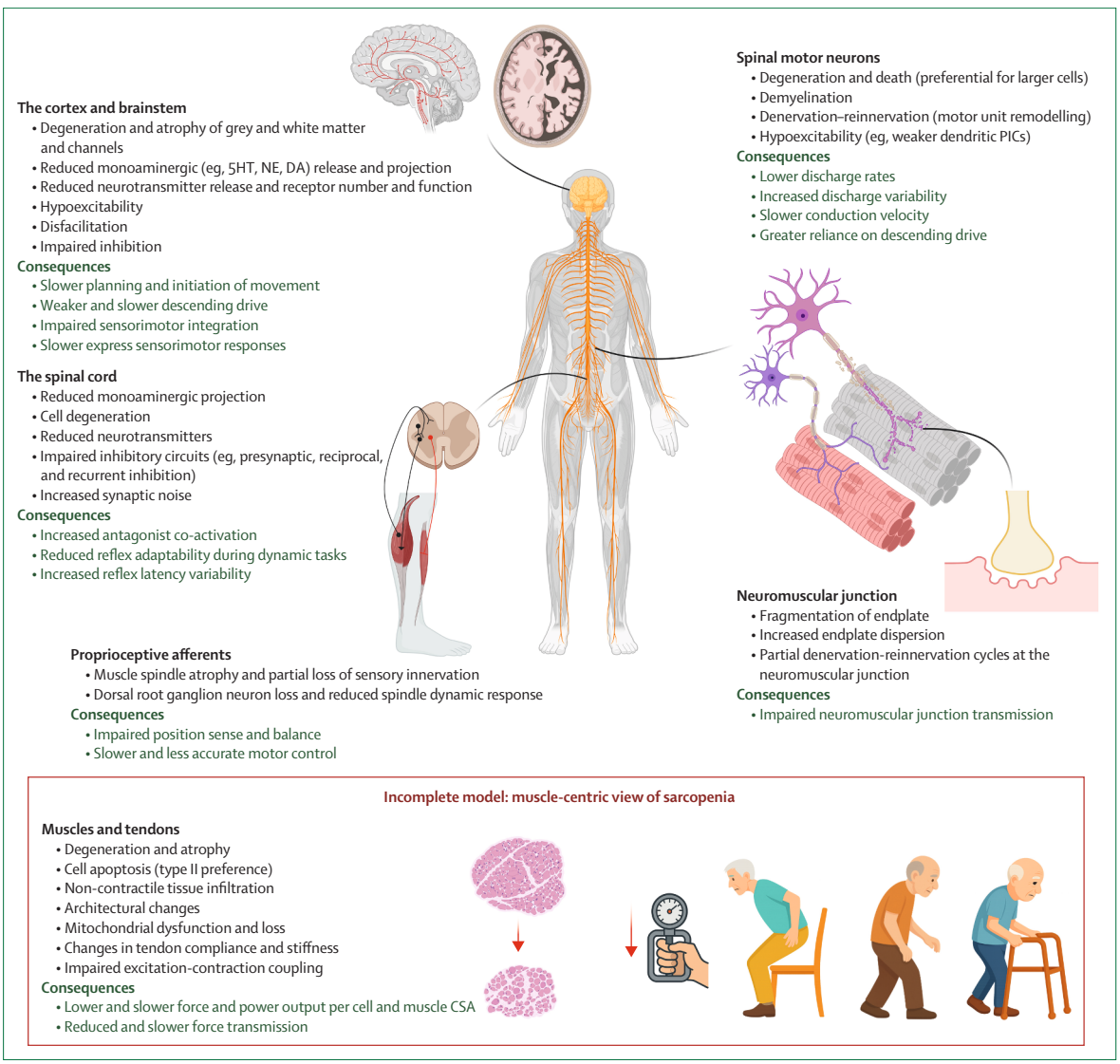

Figure 1: **Contrasting the current muscle-centric model of sarcopenia with a proposed motor system model**
The figure illustrates a comprehensive view of the motor system model of sarcopenia, in which age-related changes across the cortical and subcortical centres, the spinal cord, spinal motoneurons, and neuromuscular junctions interact with changes in the skeletal muscle to impair force generation and voluntary movement. The lower panel depicts the prevailing muscle-centric model, which emphasises muscle atrophy and muscle-related functional impairment, whereas the broader motor system remains largely uncharacterised. Note: The summarised mechanisms and circuits shown are examples of major age-related changes affecting the motor system and are not intended to be comprehensive. This figure was created using BioRender.com. CSA=cross-sectional area. DA=dopamine. 5HT=serotonin. NE=norepinephrine. PIC=persistent inward current.

blurred, and some older adults can have multiple subclinical lesions across the brain, spinal cord, peripheral nerves, neuromuscular junctions, and muscles that together hinder mobility. However, diagnostic frameworks for sarcopenia rarely incorporate systematic assessment of the broader motor system. Grip strength and gait speed capture the outcome of dysfunction but provide little insight into which components are impaired, and brief maximal tests might not reflect the repeated submaximal force demands of daily life. In this context, it is not surprising that trials recruiting participants solely on the basis of low muscle mass or weak grip, without central or peripheral motor profiling, have yielded heterogeneous or sometimes disappointing results.[9] This approach risks treating a multilevel motor system syndrome as a single, uniform myopathy.

Accordingly, caution is warranted when treating sarcopenia as a single-aetiology disease state, because even master athletes face age-related declines in muscle mass and function that reflect normal ageing.[44,46] However, genetic susceptibility and factors such as comorbid disease, medications, inactivity, surgery, and trauma can accelerate

this trajectory into pathophysiology. A major clinical challenge is detecting sarcopenia early, before motor impairment compromises mobility and independence.

Scope and boundaries of the motor system framework

Reframing sarcopenia as a disorder of the ageing motor system raises a legitimate question on its scope. The motor system is a broad construct, and many age-related conditions (eg, osteoarthritis, Parkinson's disease, stroke, peripheral neuropathy, and cerebellar or vestibular disorders) impair movement. The proposed framework is bound to provide a mechanistic account of the sarcopenic syndrome (reduced voluntary strength, low muscle power, and impaired physical performance) when these features arise from interacting, age-related changes distributed across muscles, the neuromuscular junction,[47] peripheral nerves, spinal motoneurons,[44,45] spinal circuitry, and supraspinal control.[48] The framework, which is not intended to reclassify every cause of impaired mobility as sarcopenia, extends, instead of replacing, existing mechanistic understanding of muscle movement. For example, the contributions of motoneuron loss or dysfunction and neuromuscular junction remodelling have long been acknowledged in sarcopenia research;[1,2,22–24] nevertheless, they have generally been viewed as modifiers operating around a fundamentally muscle-centric disease process. We argue that these neural changes are constitutive components of the syndrome rather than peripheral modifiers and should, therefore, be repositioned from the margins to the centre of mechanistic explanation and therapeutic targeting.

This framework places overt neurological, rheumatological, and orthopaedic diseases as differential diagnoses or comorbid contributors rather than as forms of primary sarcopenia. A condition in which a single dominant pathology accounts for an older adult's weakness or immobility defines a secondary cause of functional impairment and should be diagnosed and managed accordingly. Primary age-related sarcopenia, by contrast, is characterised by the distributed, multilevel, and frequent subclinical changes described above, in which no single overt lesion or pathology predominates but their cumulative effect on voluntary force generation and movement is clinically meaningful. The same logic applies to subclinical diseases because several age-related neural changes overlap with early or mild neuropathies;[21] a degree of diagnostic ambiguity is unavoidable. Resolving this ambiguity in individual patients is the purpose of the selective neuromuscular characterisation.

The framework also preserves a distinct and necessary role for the intrinsic biological ageing of skeletal muscle. Age-related changes in fibre size and type, excitation–contraction coupling, mitochondrial function, perfusion, extracellular matrix, and intramuscular fat infiltration reduce the capacity of a muscle to generate force,[2,7,12] and these changes remain essential subjects of mechanistic study. Whether these changes alone are sufficient to produce clinically meaningful functional impairment is an important conceptual question. We argue that isolated, severe intrinsic muscle disease can impair function but constitutes a myopathy, whereas, in typical age-related sarcopenia, muscular changes are neither isolated nor quantitatively sufficient to fully account for the observed deficits in strength and mobility.[7,10] The distinction is, therefore, not between muscle and the nervous system as competing sites but between isolated myopathic change and the coupled, multilevel decline that characterises the sarcopenic syndrome. Although muscle remains the indispensable effector of the motor system, we contest the assumption that it should remain the primary explanatory and therapeutic focus.

Finally, the framework distinguishes normal motor system ageing from disease. Decline across the motor system is universal to some degree: even master athletes show motor-unit remodelling and reductions in neural and muscular function with age.[46] Sarcopenia is not synonymous with this background trajectory. Rather, it denotes the point at which distributed motor system decline, accelerated by genetic susceptibility, comorbidity, sedative or anticholinergic medication burden, inactivity, surgery, or trauma, becomes sufficient to compromise mobility and independence. Framed this way, the model does not pathologise ageing itself; it characterises when and why age-related changes in the motor system become a clinically actionable disorder.

Shifting to a motor system model can address unresolved issues

The proposed reframing of sarcopenia has practical consequences at several levels.

First, this revised framework should reorient mechanistic research. Instead of focusing only on how muscle fibres atrophy, accumulate fat and non-contractile tissue, or lose contractile function, we should systematically map how age-related changes across the sensorimotor, neuromotor, and muscular systems (figure 1) interact over time. Longitudinal, multilevel studies that relate these measures to changes in strength, physical performance, and clinical outcomes are essential to resolve causal pathways.

Second, this framework has implications for biomarker development and patient stratification. Trial-ready measures of neural function could help to define distinct motor system phenotypes and identify the rate-limiting component(s) to target in individuals with weakness and mobility limitation. Some individuals might be primarily challenged by impaired central or spinal drive despite relatively preserved muscle mass, whereas others might show adequate neural drive but intrinsically weak muscles. These phenotypes are unlikely to respond similarly to the same intervention.

Third, a motor system model clarifies why the muscle-centric therapeutic strategies have produced

disappointing functional outcomes.[9] If weakness and mobility loss reflect distributed dysfunction across the motor system, interventions targeting muscle mass alone will often be insufficient unless paired with approaches that improve neural activation and functional translation. Resistance training is effective because it simultaneously loads muscle, challenges the neural circuitry that generates and coordinates force,[49,50] and enhances perfusion and mitochondrial function supporting muscle performance.[51] Moreover, exercises involving multiple sensory stimuli, postural challenges, continuous motor learning, and social stimulation, such as dancing, might engage motor system circuits more broadly.[52] This multisystem action possibly explains why exercise remains the most reliable intervention for improving sarcopenia outcomes[50] and also suggests that progress will depend on combination therapies that target multiple physiological systems rather than a single pathway.

Finally, the model should influence clinical practice. When an older adult presents with weakness and slow gait, evaluation should not stop at measuring strength and estimating muscle mass. Evaluation should also consider the neural contributions to motor output, as outlined in the next section. Aligning evaluation with the underlying biology could guide referral to neurology, physiatry, or other specialties when appropriate. Clinicians should also consider iatrogenic contributors, particularly sedative and anticholinergic burden, which can blunt motor drive and suppress functional capacity. Medication optimisation and deprescribing should thus be viewed as pragmatic adjuncts to rehabilitation when the clinical goal is improved mobility and independence.

A staged approach to implementation

A reasonable concern is that incorporating the motor system into the assessment of sarcopenia would impose impractical complexity to routine care. It need not. The framework is best implemented as a two-stage process that is motor system-aware from the first contact: clinical screening to identify the sarcopenic presentation while deliberately assessing signs of neural and muscular involvement, followed by mechanistic phenotyping where feasible and likely to change decisions. Consistent with the distinction between the syndrome and the underlying disease model, the clinical presentation (ie, weakness, mobility limitation, or low muscle strength and power) should be identified first. Motor system mechanisms can then be explored to characterise patient subtypes rather than to make initial diagnosis. The principle is to screen pragmatically with the whole motor system in view and to phenotype in detail only when additional information is clinically actionable.

The clinical motor system screening stage should remain feasible in primary care and geriatric practice but should not simply be equated with the measures in current use. Existing screening evaluates grip strength, gait speed, chair-rise time, and brief batteries such as the short physical performance battery,[3–6] supplemented with bedside assessment signs, such as tendon reflexes, sensation, coordination, rapid alternating movements, and qualitative gait (or emerging methods) for understanding neural involvement. These measures are valuable, and gait speed in particular is an important prognostic marker in geriatric medicine.[41] However, their limitations are well recognised; cut-points vary across working groups,[3–6,53] case-finding sensitivity is modest, brief maximal tests do not reflect the repeated submaximal force demands of daily life, and both performance measures and bedside examination signs are physiologically non-specific. The existing measures, thus, capture the outcome of motor system dysfunction while revealing little about the components that are impaired. A minimal universal core assessment can be applied to all older adults at this stage, with a brief, structured neuromuscular assessment reserved for those whose weakness is pronounced, rapidly progressive, or disproportionate to the apparent muscle loss, thereby supporting the time-constrained clinician to avoid unnecessary assessment in all individuals.

The greater opportunity is to improve the specificity of screening. The current bedside repertoire is of modest specificity. The appropriate response is not to discard but to develop it and validate practical motor system-relevant measures for point-of-care use. Promising near-term candidates include muscle power[13] and the rate of force development, which largely reflect neural drive and contractile speed rather than the maximal force;[54] measures of hand motor control (eg, the multifinger force deficit[43,55] and pegboard tests[56,57]); force steadiness or variability as accessible indexes of motor-unit control;[58–60] and dual-task gait[61] with reactive stepping or balance,[62] which is used to assess central and sensorimotor integration.[63,64] Low-cost instrumented or application-based implementations of these constructs could keep them feasible for routine clinical use instead of being confined to research laboratories. Establishing the reliability, cut-points, and discriminative and predictive validity of such measures is, in our view, among the most impactful near-term priorities for the field and offers the clearest route, realised in clinical care rather than only in research settings, to improve current screening techniques by ensuring practicality.

The mechanistic phenotyping stage is appropriate primarily in specialist clinics, research cohorts, and clinical trials, in which the process can identify mechanisms, stratify participants, and test target engagement. Relevant tools include surface and high-density electromyography with motor-unit analyses, motor-unit number estimation, nerve conduction studies, measures of neuromuscular transmission, transcranial magnetic stimulation-derived indexes of corticospinal excitability and inhibition, multimodal functional neuroimaging (eg, electroencephalography, magnetoencephalography, and MRI), and skeletal muscle imaging. Such measures can differentiate sarcopenic, non-sarcopenic, and athletic ageing

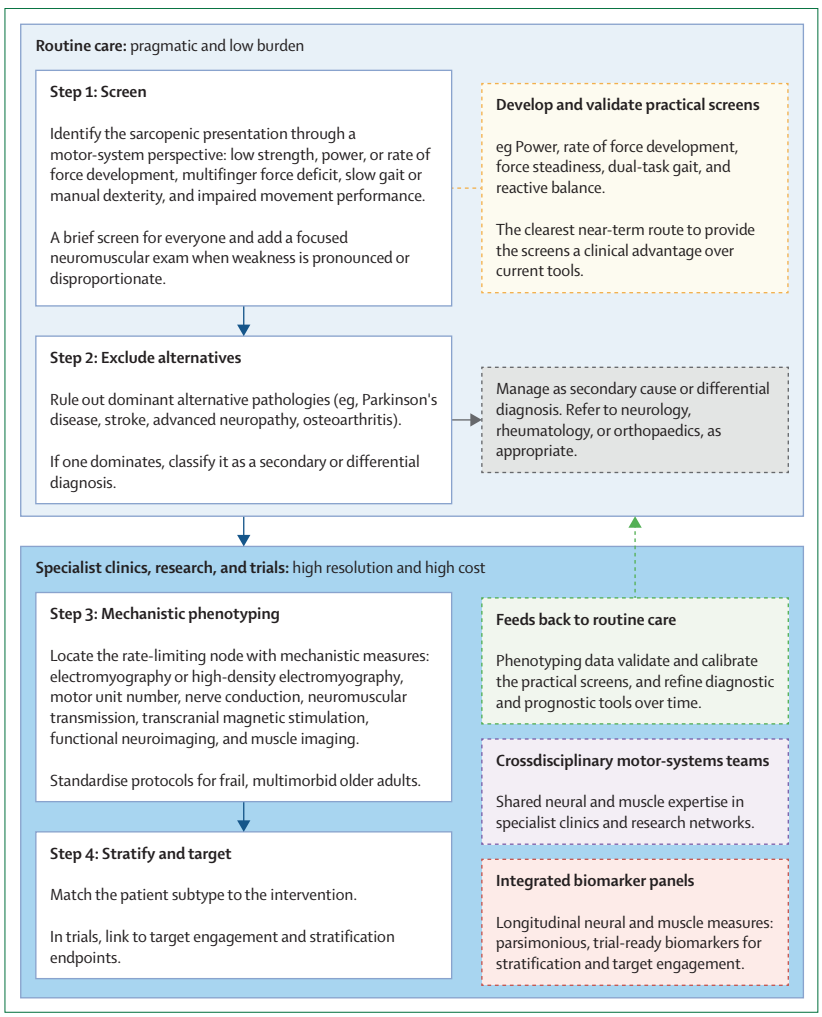

***Figure 2*: A staged, motor system-aware pathway for sarcopenia**
During routine assessment, older adults receive a brief motor system-informed screen of strength, power, gait, and physical performance, with selective neuromuscular examination when weakness is pronounced, rapidly progressive, or disproportionate to muscle loss. Dominant alternative pathologies (eg, Parkinson's disease, stroke, advanced neuropathy, or severe osteoarthritis) are excluded and managed as secondary or differential diagnoses. In specialist clinics, research cohorts, and trials, mechanistic phenotyping locates the rate-limiting component of the motor system to support participant stratification and target-engagement endpoints. A central near-term priority (highlighted boxes) is the development and validation of practical, motor system-relevant screens. The pathway is iterative, with data from mechanistic phenotyping feeding back to routine care (indicated using a green dashed loop), validating and calibrating the practical screens, and refining diagnostic categories and prognostic tools over time. Realising the pathway depends on crossdisciplinary motor system teams and on integrated biomarker panels. This figure was created using BioRender.com.

phenotypes[44] and identify the rate-limiting component of the motor system in an individual. This information cannot be obtained from screening measures, and this advantage is most relevant when the aim is to select or develop a targeted intervention. A precondition for translating this stage is the development and standardisation of protocols that are tolerable and reliable for older adults with frailty and multimorbidities, for whom many established electrophysiological tests are burdensome. This two-stage structure (figure 2) keeps routine screening low-burden and motor system-aware while reserving resource-intensive assessments for situations where these assessments are likely to change clinical decisions.

Practical challenges and limitations

Implementing the proposed framework for sarcopenia will require caution, and several limitations should be considered. Detailed mechanistic phenotyping is unlikely to be feasible or cost-effective as universal screening; time constraints, the restricted availability of neurological and neuromuscular expertise in primary care, and uneven access to electrophysiology and advanced imaging are real and substantial barriers. A further and more fundamental limitation is evidential. The measures on which current sarcopenia screening protocols depend are prognostically well validated (eg, gait speed[41]); however, they are mechanistically blind, and their performance as case-finding and diagnostic instruments is more modest than that implied by their prognostic standing. Conversely, the incremental value of the proposed motor system measures, whether refined screens or deep mechanistic phenotyping, is yet to be established, either for prediction over and above existing measures or for guiding treatment.

Two considerations temper the abovementioned concerns without resolving them. First, the two-stage approach outlined above is designed precisely to contain cost and complexity by concentrating resource-intensive assessment in the specialist and research settings. These settings facilitate decision making and keep routine screening feasible. Second, the value of a motor system approach is best judged not against prognosis alone but against two questions the current toolkit cannot answer: whether more specific yet practical screens that indicate which component of the motor system is failing can be developed and whether mechanistic phenotyping can match patients to interventions more effectively than performance-based assessment. Framed this way, the relevant tests are concrete: whether motor system measures improve screening specificity, patient stratification, treatment matching, and ultimately functional outcomes and cost-effectiveness beyond what current practice delivers.

These queries remain open empirical questions, and we present the framework as a mechanistic and therapeutic reorientation; the diagnostic and economic value of the proposed framework must, hence, be illustrated rather than assumed. The work needed to establish the framework's diagnostic and economic value is two-fold and already tractable. In the nearer term, such works must include developing and validating practical, motor system-relevant screening measures with defined cut-points and established discriminative performance, and in research and trial settings, such works must embed mechanistic phenotyping in longitudinal cohorts and trials as a stratification and target-engagement tool to test its incremental predictive and decision-analytical contribution. Both tasks are central priorities in the agenda outlined below.

A practical agenda for embracing sarcopenia as a motor system disease

Operationalising the reframing of sarcopenia requires coordinated efforts, for which we highlight five priorities (figure 3).

Identify mechanisms and biomarkers of motor system ageing

Research should move beyond isolated measures towards integrated, longitudinal characterisation of the motor system. Combining robust neural and muscle measures in well-phenotyped cohorts can reveal how changes at different levels coevolve and which combinations best predict subsequent functional decline. This information can then be used to derive parsimonious biomarkers of motor system health, understood here as physiological, electrophysiological, imaging, and performance-based measures, subsequently followed by two translational goals: practical point-of-care screens for the clinic (according to the near-term priority outlined earlier) and mechanistic measures suited for trial stratification and target engagement.

Build crossdisciplinary motor system teams

Sarcopenia research and care remain largely siloed, often anchored in geriatrics or endocrinology. To advance the motor system model, close collaboration with neurologists (eg, neuromuscular disease and movement disorder subspecialists), rehabilitation physicians and therapists, and basic and applied neuroscientists is essential. Multidisciplinary clinics and research networks focused on age-related mobility disorders should be structured to span brain, nerve, and muscle expertise, rather than treating them as separate domains.

Integrate motor system assessment into clinical pathways

Consensus statements and guidelines could explicitly endorse the staged, motor system-aware pathway as outlined earlier: a motor system-informed screen for older adults under assessment; a selective neuromuscular examination when weakness is pronounced, asymmetric, rapidly progressive, or disproportionate to muscle loss; and mechanistic phenotyping in specialist and research settings. Embedding this framework in guidelines and funding the validation of practical screen tools that it requires could inform refined diagnostic categories and prognostic tools over time.

Develop motor-targeted interventions

The therapeutic approaches for sarcopenia should build on muscle-focused and anabolic strategies by explicitly addressing how gains in muscle mass and quality translate into motor output. Potential avenues include compounds that modulate motoneuron excitability or neuromuscular transmission, which have shown promising preclinical results.[65,66] Alternative approaches could include non-invasive brain or spinal stimulation techniques, exercises (eg, resistance training, task-specific motor learning frameworks, balance training, and reactive stepping training), nutritional interventions (eg, serotonergic precursors), and technologies that provide enriched sensorimotor feedback. Trials should incorporate motor system biomarkers to test target engagement, identify responders, and link neural changes to gains in strength and performance. Broadly, because the motor system ages within the wider biology of the organism, geroscience-based strategies that target shared mechanisms of ageing might offer a complementary, system-level route to preserving motor function alongside interventions aimed at specific neural or muscular targets.

Define sarcopenia according to the proposed motor system-based framework

Formal definitions influence how clinicians think, how trials are designed, how public funding is allocated, and how payers reimburse care. We propose that future

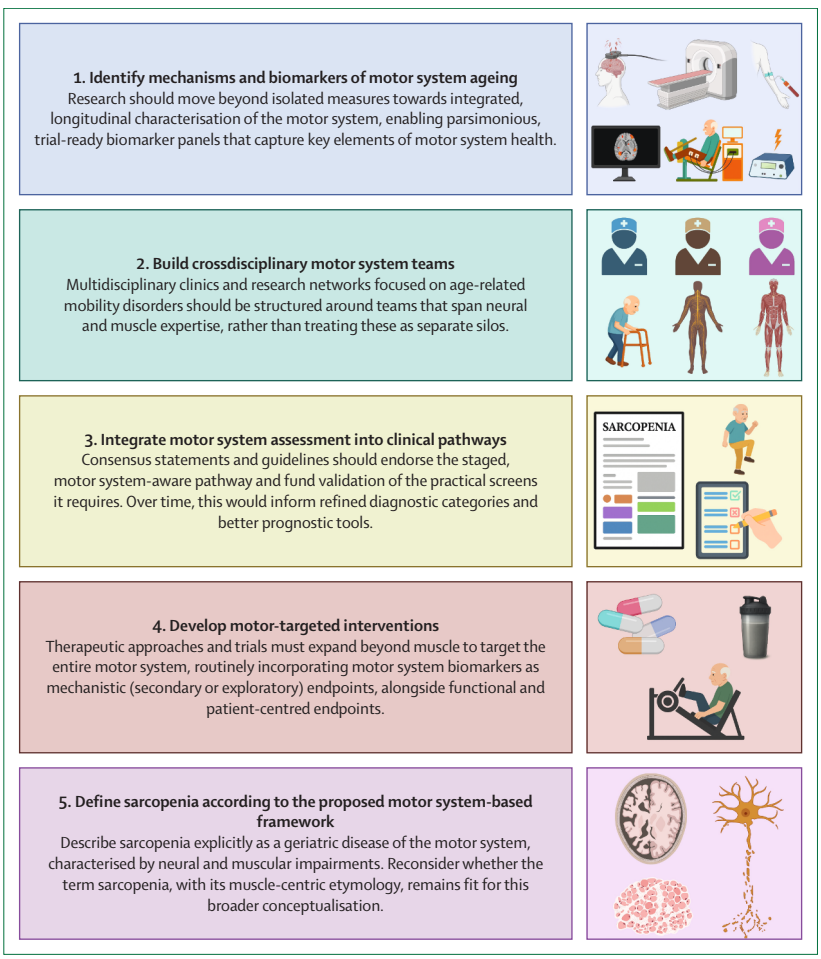

Figure 3: **A suggested practical agenda for embracing sarcopenia as a motor system disease**
The figure outlines five complementary directions for shifting sarcopenia research and care from a muscle-centric model to a motor system-based framework. This agenda is intended as a constructive guide for major sarcopenia working groups to support the integration of this model into future discussions, research priorities, and consensus updates. This figure was created using BioRender.com.

consensus explicitly describe sarcopenia as a geriatric disease of the motor system, characterised by reduced voluntary strength and impaired physical performance arising from interacting neural and musculoskeletal changes. Whether the term sarcopenia, with its muscle-centric etymology, remains appropriate for this broader model is an open question. Names of diseases of other specialities have been revisited[67] to better reflect pathophysiology and reduce conceptual bias, and a similar discussion might be warranted for sarcopenia as well. For now, clearly articulating the motor system framing would be a substantial step forward.

Conclusion

The field of sarcopenia research has made substantial advances in recognising that the condition is not simply about how much muscle an older adult has but what they can do. Yet, we have not fully recognised the corollary: what older adults can do depends on the entire motor system. Continuing to treat sarcopenia as a primary muscle disease while defining it by impairments in movement creates a fundamental inconsistency that constrains mechanistic insights and therapeutic progress.

Embracing a motor system model will not diminish the importance of muscles; rather, such an approach will place muscles within the distributed system that produces strength and movement. For researchers, following the proposed framework means designing studies and biomarkers that integrate mechanisms at neural and muscular levels. For clinicians, following the proposed framework means broadening assessment and management pathways to account for central and peripheral motor contributions. For the field of sarcopenia research as a whole, this framework means acknowledging that age-related weaknesses and mobility limitations are best understood, and ultimately managed, through an integrated motor system perspective. If sarcopenia is a signature characteristic of ageing, then its conceptual model should reflect the biology of human movement. Reframing sarcopenia as a motor system disease model is not merely semantic but necessary for aligning biology, clinical outcomes, and successful therapeutic strategies.

Contributors

LBRO and BCC conceived the study. All authors contributed to the development of ideas and critically reviewed and approved the final manuscript.

Declaration of interests

We declare no competing interests.

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