Bridging the translational gap: improving the selection of interventions for early-phase clinical trials to prevent, delay, or treat sarcopenia

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Background

Sarcopenia, the age-related loss of muscle strength and mass, affects 10% to 27% of individuals aged 60 and older. It increases the risk of falls, hospital admissions, and early mortality, costing the UK about £2.5 billion annually in healthcare. Resistance exercise is the only effective intervention; however, patients struggle to maintain the intensity of exercise required. There is an unmet need for novel treatments for sarcopenia. A systematic approach is needed to identify promising interventions for testing and enhance translational medicine in this area.

Methods

A multidisciplinary team with expertise in sarcopenia, early-phase clinical trials, and geriatric medicine conducted a literature review to identify target product profiles and intervention selection tools for neuromuscular conditions. None were identified specifically for sarcopenia.

The group developed a target product profile for sarcopenia. Based on this profile, an intervention selection algorithm was created for early-phase trials, employing a combination of "stop/go" criteria and a traffic light system. This approach aimed to facilitate balanced decision-making in the selection of interventions for further testing.

The tool was tested by evaluating outputs from a recent horizon scan and was adapted iteratively based on the findings.

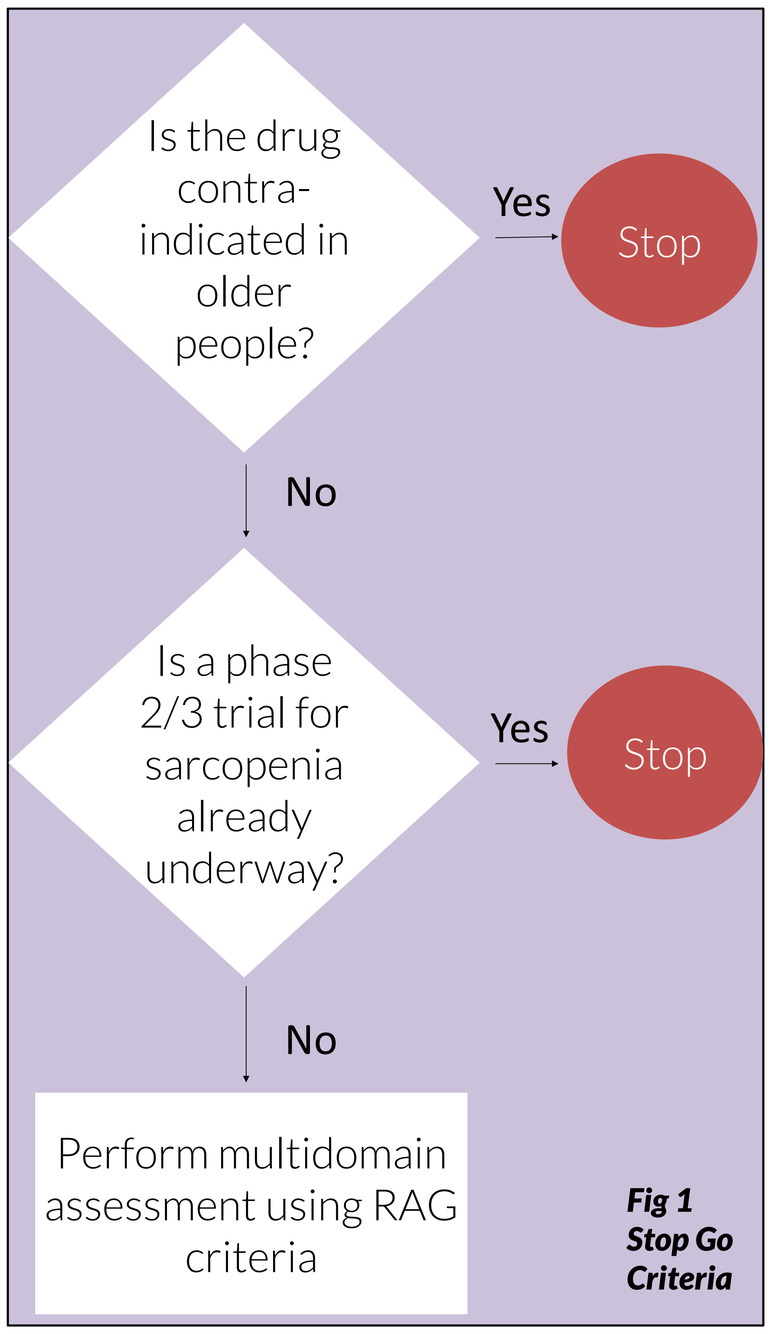

Fig 1 Stop Go Criteria

Results

The key domains identified for consideration include:

- The scope and depth of prior clinical testing
- The safety profile and tolerability of the treatment, particularly in older adults
- The presence or absence of a well-defined and plausible mechanism of action supported by reliable preclinical data demonstrating biological activity
- Pragmatic considerations, such as the agent's stability, the method of administration (e.g., oral, intravenous), and the frequency of administration.

Question	Red	Amber	Green
Can the drug be used long term?	It has been clearly stated that the drug cannot be used long term.	The drug can be used long term but there are side effects when it is used like this. To avoid or minimise the effect of this, preventative measures can be advised to the patient.	There is no problem with using the drug long term.
Is there a credible mechanism?	No credible mechanism has been established.	There is some evidence of a potential mechanism but it is incompletely understood and/or not shown in humans.	A credible mechanism has been demonstrated within humans.
What are the participants like?	No human studies	-Healthy individuals (old and young) -Individuals are only of one biological sex	The drug has been tested in a clinically relevant population (e/g ≥ 65, sarcopenia).

Fig 1 Example of RAG rating

Conclusions

A predefined target product profile, combined with an intervention selection tool, aids in systematically evaluating promising interventions for sarcopenia to undergo testing in clinical trials. Further evaluation and refinement of these tools by other key contributors is essential.

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