Supplementary Material

Pre-meeting survey questions were sent to the five identified experts. Table 1 shows the questions included.

Table 1: Pre-meeting survey

Pre-meeting survey questions
What are the early signs/symptoms of age-associated cellular decline/change?
How could early age-associated cellular decline be differentiated from other conditions with similar symptoms?
What are the risk factors for age-associated cellular decline?
Describe the profile of individuals at high risk of age-associated cellular decline/change
Describe the profile of someone at moderate risk of age-associated cellular decline/change
Which of the features of age-associated cellular decline are clinically relevant and important triggers for intervention?

Please note the following are a sample of the responses that were received ahead of the meeting workshop. Key words and themes were highlighted. Responses went on to become the multiple-choice answers for the workshop.

Table 2: Sample responses from pre-meeting survey

	Q1. What are the early signs/symptoms of age-associated cellular decline/change
Respondent	**Response**
1	Fatigue is an important candidate symptom for early assessment of age-associated cellular decline. The advantage is that there are already published studies that evaluated fatigue and also several measures have been evaluated, although no gold standard exists. Exhaustion can also be considered a useful symptom, particularly when related to activities that previously did not cause it. Lack of energy might also be a symptom of age-associated cellular decline. This symptom, as well as the other symptoms, could be evaluated by considering not only the current feeling of the individual, but also their desire/aspiration or perception compared to subjects of the same age. At the same time, the absence of a feeling of being full of energy might be an important symptom, particularly in adults. Concerning signs: the presence of even minimally impaired mobility could be an important measure of age-associated cellular decline. Slow walking might be an early sign, particularly in comparison with subjects of the same age. Having some difficulties walking for 400 meters, or difficulty in climbing some, e.g. four flights of stairs without resting, could be important signs.
2	• Decreased autophagia and mythophagia • Decreased biogenesis/mitogenesis, cellular senescence • increased proinflammatory markers • Insulin resistance, with low function of the insulin signaling route impairing mTOR-dependent phenomena oxidative stress with a major involvement of the Nrf2 pathway • Defective signaling
3	• Physical, muscular exhaustion / fatigue • Reduced appetite • Low-quality of sleep • Psychological • Low mood (e.g., depressive symptoms) • Subjective memory complaints
4	There are no highly specific signs or symptoms of early age-associated cellular decline. There are nonspecific symptoms such as fatigue, poor exercise tolerance, poor resilience in dealing with acute illnesses or injuries. Even less specific are factors such as depression, lack of motivation to be physically or socially active, poor appetite. Nonspecific signs would include low gait speed, poor grip strength, slow time to do five chair rises, low distance covered in a ‘6-minute walk’. As in the approach to frailty, it might be possible to combine several nonspecific symptoms and signs to increase the probability that the individual has early cellular decline before moving on to lab tests that may add to the specificity.
5	• Insulin resistance • Obesity • Inflammation • Cognitive decline • Endothelial vascular dysfunction

mTOR, mechanistic target of rapamycin; Nrf2, nuclear factor erythroid 2–related factor 2

Workshop survey questions and prioritization scores

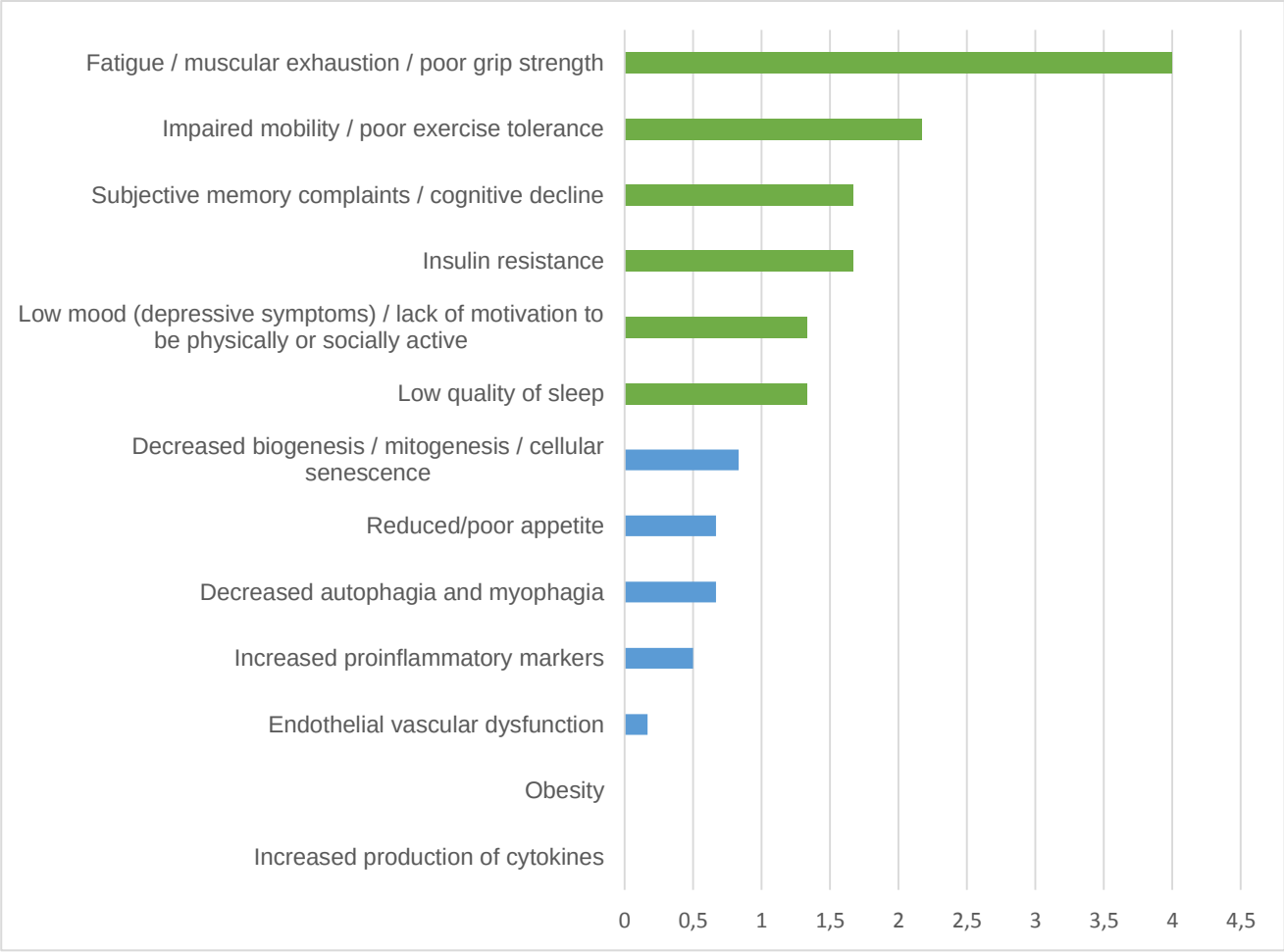
The modified nominal group technique (NGT) was used to establish consensus among the interdisciplinary expert panel.

During the virtual workshop, advisors were asked to prioritize their responses anonymously using electronic polling software. The top five responses (where a score of 5 was the highest) were analyzed to identify the highest ranked answers following the close of the meeting.

1. **What are the early signs/symptoms of age-associated cellular decline? Please rank the following statements in order of importance (ensuring that the top 5 are the most important).**

Prioritization scores:

Figure 1: Average of top five ranking items[a]

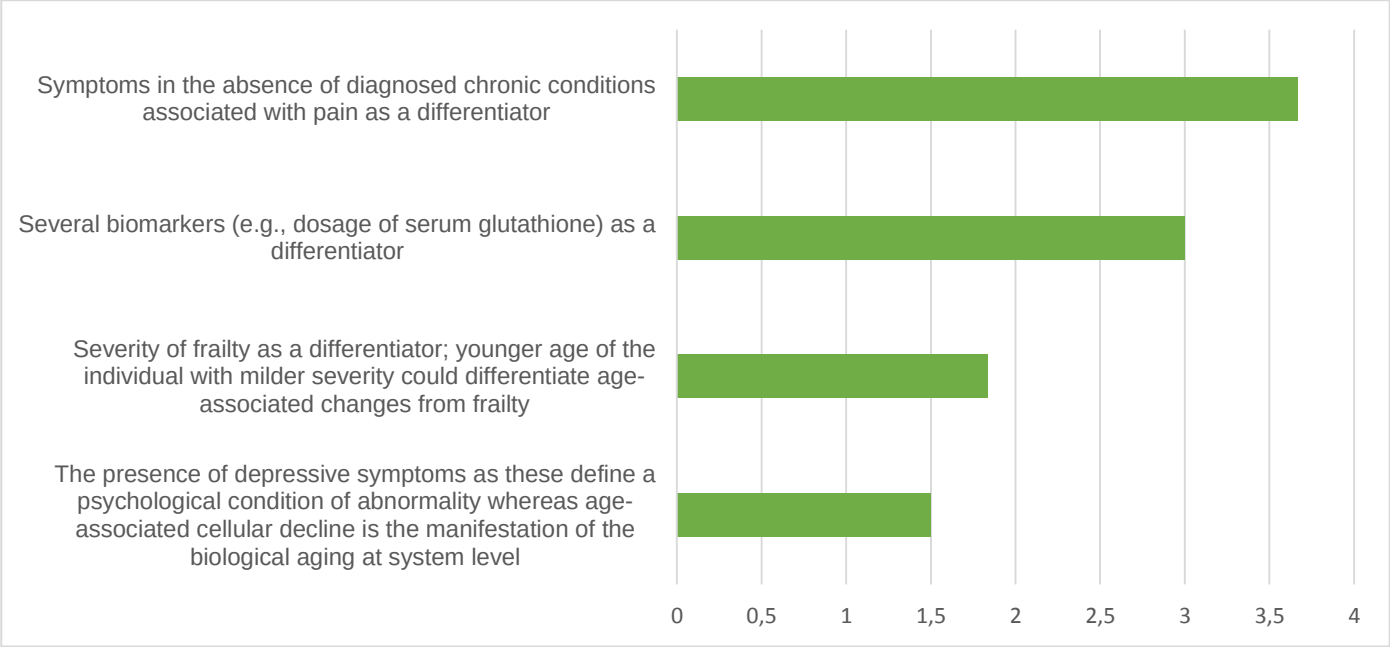


[a]There are six responses owing to the Chair voting twice.

2. How could early age-associated decline be differentiated from other conditions with similar symptoms? Please rank the following statements in order of importance.

Prioritization scores:

Figure 2: Average of top five ranking items[a]

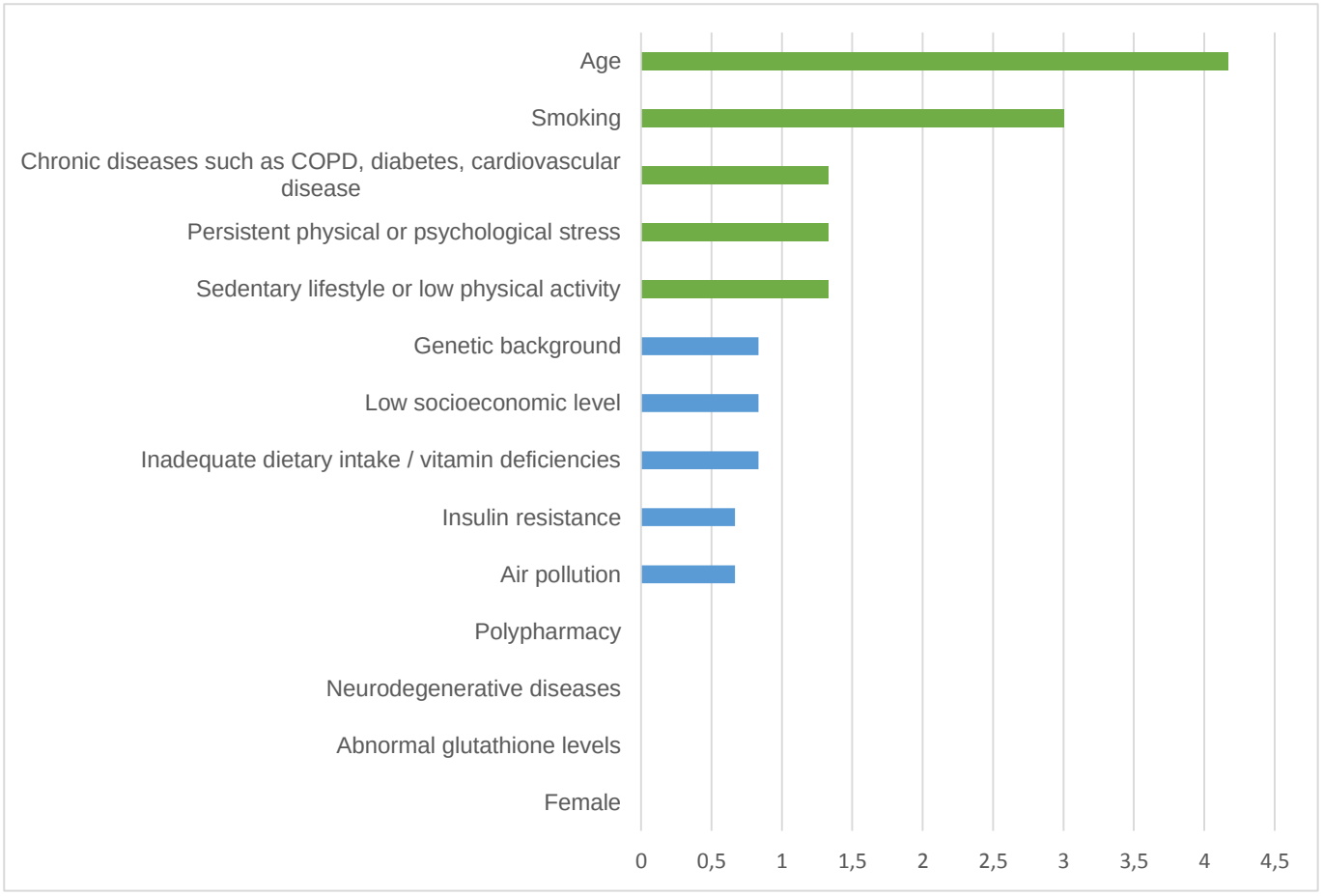


[a]There are six responses owing to the Chair voting twice.

3. What are the risk factors for age-associated cellular decline? Please rank the following statements in order of importance.

Prioritization scores:

Figure 3: Average of top five ranking items[a]



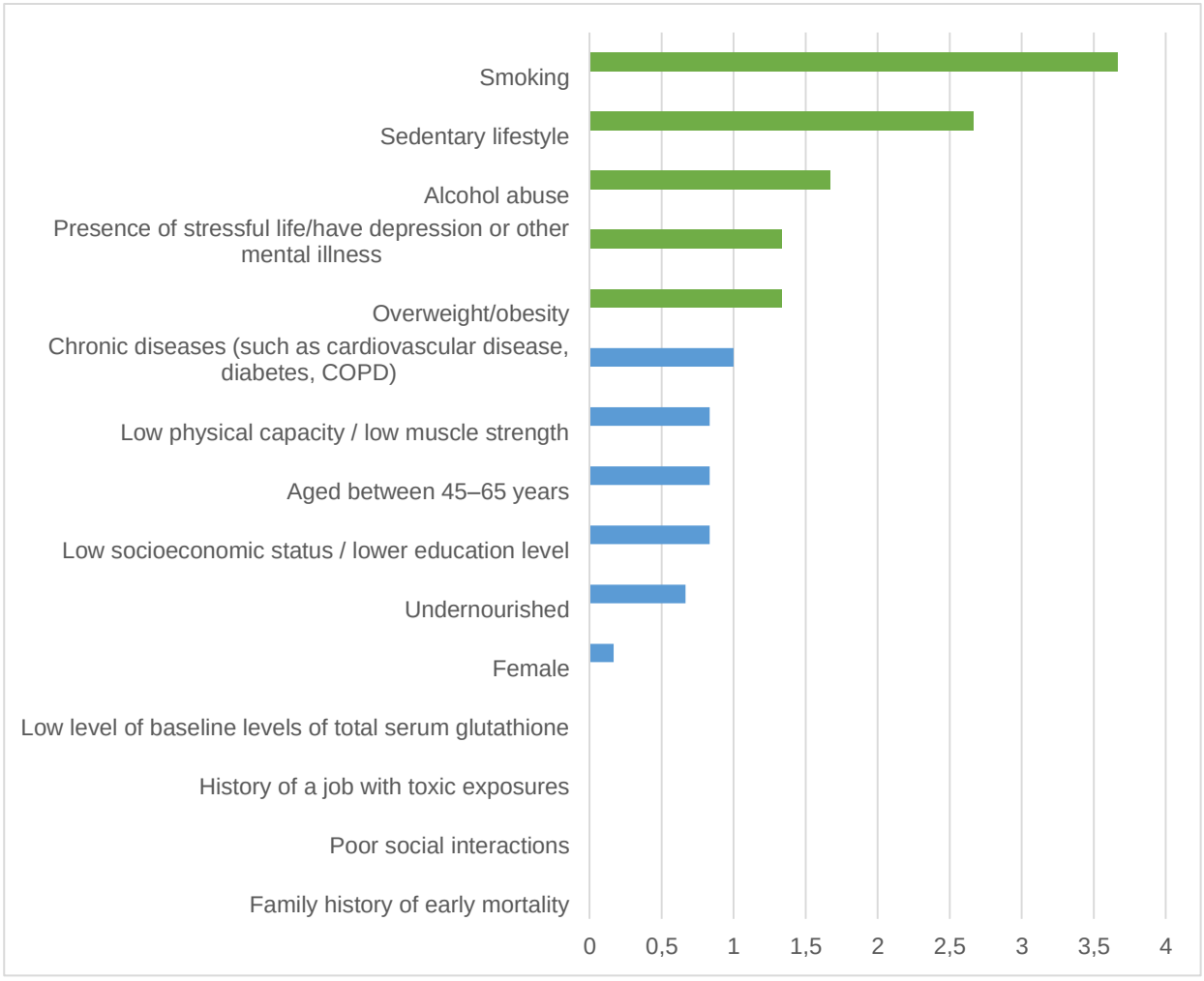
[a]There are six responses owing to the Chair voting twice.

COPD, chronic obstructive lung disease.

4. Describe the profile of individuals at high risk of age-associated cellular decline/change. Please rank the following statements in order of importance (ensuring that the top 5 are the most important).

Prioritization scores:

Figure 4: Average of top five ranking items[a]



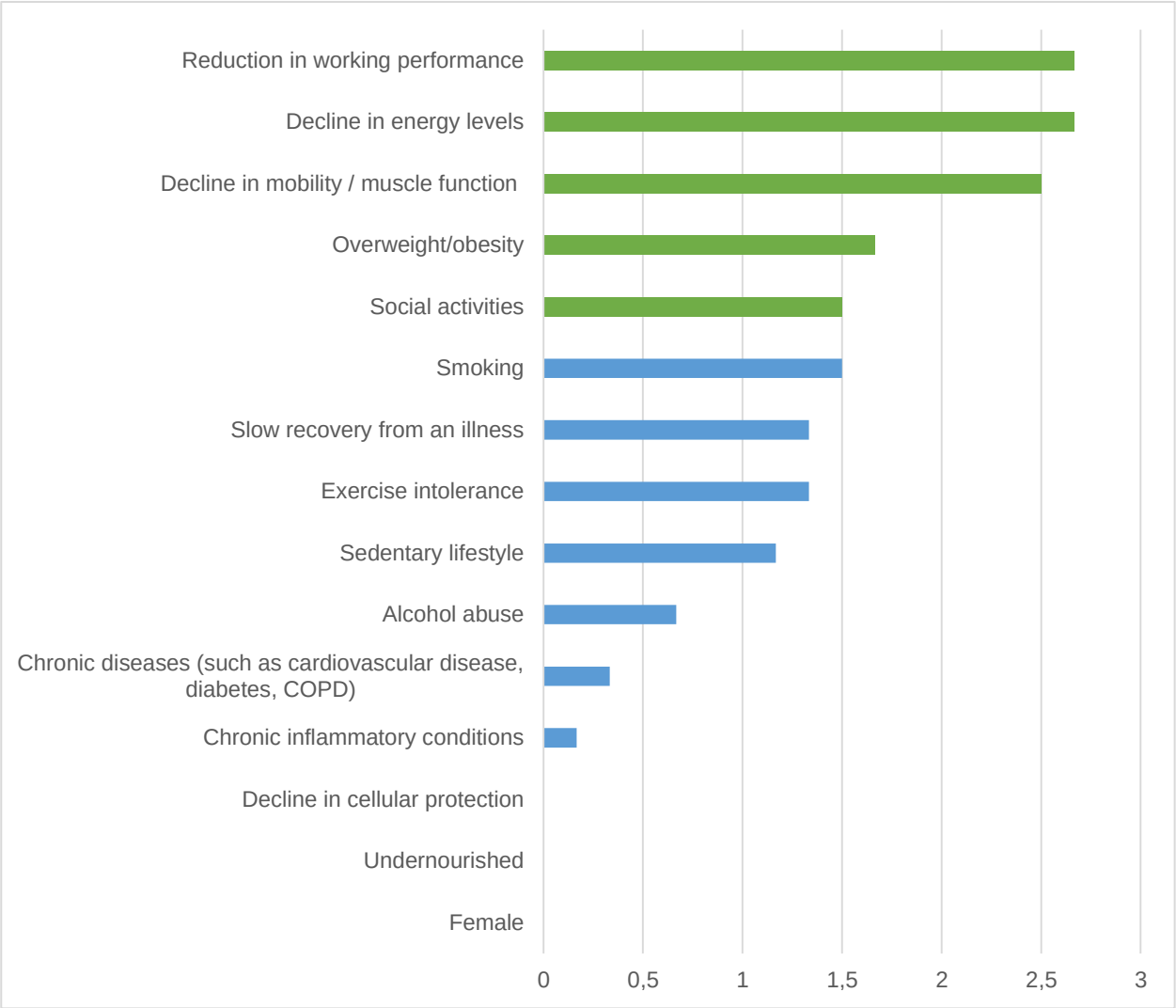
[a]There are six responses owing to the Chair voting twice.

COPD, chronic obstructive lung disease.

5. Which of the features of age-associated cellular decline are clinically relevant and important triggers for intervention? Please rank the following statement in order of importance (ensuring that the top 5 are the most important).

Prioritization scores:

Figure 5: Average of top five ranking items[a]



[a]There are six responses owing to the Chair voting twice.

COPD, chronic obstructive lung disease.