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OPEN-ENDED PRELIMINARY QUESTIONNAIRE

GENERAL QUESTIONS

1) What is the background of the definition of frailty?

-Physiological changes accompanying ageing process

-Additive impairments/disabilities

-A final outcome coming mainly from biological inputs, as education or social ones

-Other (please specify)

2) What is your clinical definition for frailty useful in the different settings where clinical approaches are carried out?

-At the office. Proposed definition

-General or geriatric ward. Proposed definition.

-Emergency Department. Proposed definition.

-Rehabilitation setting. Proposed definition.

-The same definition is useful in all the clinical settings. Proposed definition.

3) This same definition is useful for investigation purposes or is it needed another definition for research studies?

4) What do you think generally about the value of biomarkers for aging and frailty?

SPECIFIC QUESTIONS

Geriatric Focus Group and Non-Geriatric Physicians Focus Group:

-What specific parameters do you think are directly relevant to our definition of frailty?

- Which of these parameters should be included in an operative definition of frailty?

Health workers Focus Group and social and non-governmental focus group

-What specific criteria do you think are directly relevant to our definition of frailty?

-Which of these identified specific criteria should be included in our operative definition of frailty?

Basic scientist Focus Group

-What specific biomarkers do you think are directly relevant to our definition of frailty?

-Which of these identified specific biomarkers should be included in our definition of frailty?

PLEASE INDICATE YOUR AGREEMENT OR DISAGREEMENT WITH EACH STATEMENT BY CHECKING THE APPROPRIATE BOX, FROM 1 (STRONGLY DISAGREE) TO 10 (STRONGLY AGREE)

FRAMEWORK/DEFINITION:

1. Frailty is a definite entity

   1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

2. Frailty is a biological phenomenon

   1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

3. Frailty could be primary or secondary

   1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

4. Frailty is a clinical syndrome

   1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

5. Frailty is a physiological state

   1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

6. Frailty is characterized by decreased reserve and diminished resistance to stressors

   1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

7. The same definition of frailty should be valid across different clinical settings

   1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

8. The same definition of frailty should be valid across different clinical and non-clinical settings (e.g. community)

   1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

9. The definition must show reproducibility across time

   1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

10. Definitions of frailty differ according to the adverse health outcome being studied

    1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

11. The various components of frailty may differ in importance according to the adverse health outcome being studied

    1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

12. The concept of frailty and its operational definition can help in identifying and stratifying older persons at high risk of disability and/or other adverse outcomes

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

13. Frailty is multidimensional and may involve psychological, social, emotional and spiritual aspects in addition to physical components

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

14. Frailty is the outcome of the interaction between age-associated physiological changes and disease

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

15. Frailty could be both the cause of disease and/or the consequence of it

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

16. Frailty is the result of genetic, environmental and medical factors

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

17. Frailty can be the outcome of genetic and environmental factors without concomitant disease

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

18. Frailty is a natural physiologic change of aging

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

19. Frailty is related to aging but it is not exclusive to older people

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

20. Frailty is the outcome of age-associated physiological changes, disease and social issues

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

21. Frailty is a condition of older people with increased vulnerability in which minimal stress may cause functional impairment

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

22. Frailty might be reversible or attenuated by interventions

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

23. Frailty is a condition where prevention may still be possible and it is mandatory for clinicians and health workers to detect it as early as possible

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

24. Frailty is a dynamic, non-linear process

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

25. Frailty is different from vulnerability

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

26. Frailty is different from disability

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

27. Frailty increases vulnerability to impairments and the ensuing consequences

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

28. Frailty involves alterations in multiple, not individual, body systems

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

29. Frailty involves alteration in several domains of function

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

30. Frailty may be due to a number of different causes, but once activated it is sustained by physiological and psychological changes and social dynamics that may act independently of the triggering cause

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

31. Frailty should be defined in terms of molecular mechanisms and functional outcomes

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

32. Frailty cannot be defined in terms of a single molecular mechanism

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

33. Frailty should be defined in terms of mobility or loco motor activity

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

34. Establishing different levels of frailty severity would be useful for clinical purposes when allocating patients to different levels of care (acute geriatric unit, rehabilitation unit, day hospital, home care, social care, etc)

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

35. Frailty should be assessed in all old people > 75 years

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

36. Frailty should be assessed in all old people > 70 years

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

37. Frailty should be assessed in all old people > 80 years

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

38. Frailty diagnosis is useful at the population level

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

39. Frailty is a dynamic process, non-linear, different from vulnerability and disability

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

40. Frailty typically involves alteration in multiple, not individual, body systems

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

41. A diagnosis of Frailty is a several step process from suspicion to confirmation and involves a graduate scale of severity

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

42. Grading frailty severity would be useful in determining welfare (Health and social care) response

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

43. Definitions must be tested in clinical and non-clinical settings

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

44. The purpose of a diagnosis of frailty is to identify the non-robust, non-disabled older patient, that is at risk of developing disability in the near future

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

45. The purpose of a diagnosis of frailty is to identify the non-robust, non-disabled older patient, that is at risk of adverse health outcomes in the near future

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

46. A Frailty diagnosis is useful in primary care and community care

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

47. A Frailty diagnosis is useful in managing older people with chronic diseases

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

48. A Frailty diagnosis is only necessary in specialized settings in geriatric medicine

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

49. As Frailty is a dynamic process, its diagnosis must be based on repeated domain measurements over time

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

50. The evolution from frailty to disability is modulated by any type of stress and is not limited to disease, its treatment, and other environmental and social factors

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

51. The frailty process is modulated by disease, function and socio-economic forces

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

52. Repeated measurements are not needed for diagnosis, but are necessary to clinically manage the frailty process

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

BIOMARKERS

The term Biomarker refers to "a biological parameter intended as a quantitative measure of the rate of aging more accurate than chronologic age" (Ingram DK et al. Strategy for identifying biomarkers of aging in long-lived species. Exp Gerontol 2001; 36: 1025-1034)

53. Biomarkers are useful only in the second step of screening after an initial diagnosis is established

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

54. Biomarkers may be useful at any step of screening depending on their sensitivity and specificity

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

55. Biomarkers need to correlate with clinical endpoints/measures of frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

56. Additional clinically measurable parameters (e.g. number of medications, cardiovascular parameters, etc) should be part of the definition of frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

57. Biomarkers must be easily and broadly available

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

58. The positive predictive value of these markers should be estimated by the ability to predict vulnerability to stress in independent individuals

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

59. It is important to know the predictive value of biomarkers

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

60. There is no single biomarker that is adequate to predict or diagnose frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

61. Biomarkers are useful when they are used as a 'set of biomarkers'

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

62. Single frailty biomarkers may be as important as clusters of biomarkers

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

63. Inflammatory markers are not useful for assessing frailty in patients with chronic disease

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

64. Mental health assessments and cognitive status evaluation are highly recommended as part of the assessment of frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

65. Physical activity is important for the recovery of Frailty and should be done with all patients as appropriate to their condition

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

66. Frailty is related to life style, and increases with a sedentary life style

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

67. It is desirable to utilize a general stress test to distinguish between advancing age and frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

68. It is desirable to utilize a general stress test to diagnose frailty at each age

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

69. It is desirable to utilize a general stress test for the diagnosis of frailty and its prognosis

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

70. Different biomarkers have different prognostic value in different settings

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

71. Age could be an important contributor to frailty at the end of life

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

72. We should differentiate between frailty and a self-perceived state of frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

73. Within a Syndrome of Frailty different indicators of frailty carry a greater or less weighting

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

74. reduced model of frailty (mobility+nutrition+mood/cognition) may be of clinical utility

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

75. A reduced model of frailty (cognition+gait speed+weight loss) may be of clinical utility

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

76. Gait velocity is a valid marker of frailty. Thus, we could diagnose frailty based on gait velocity

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

77. Handgrip strength is a valid marker of frailty. Thus, we could diagnose frailty based on handgrip strength

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

78. The Classical Comprehensive Geriatric Assessment is very useful to detect disabilities, but is of limited utility to identify frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

79. Tasks (what the patient is able to do) are important clinical biomarkers of frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

80. Adverse health outcomes should not be limited to disability, institutionalization, hospitalization and death

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

81. Quality of life should be measured when measuring frailty outcomes

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

82. To identify and validate novel biomarkers of frailty , their response to challenges/stresses should be assessed

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

83. Gait velocity is useful to measure mobility

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

84. Handgrip strength is useful to measure muscle weakness/sarcopenia

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

85. Poor exercise tolerance is useful to measure frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

86. Weight loss is useful to measure malnutrition

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

87. Balance must be tested in people with a suspected diagnosis of frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

88. Assessing Self-efficacy is useful to measure coping

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

89. Socio-demographic characteristics (age, education, living arrangement, income, welfare systems, political background, social cohesion, economic development) should be measured in every frail patient for diagnoses

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

90. Socio-demographic characteristics (age, education, living arrangement, income, welfare systems, political background, social cohesion, economic development) should be measured in every frail patient for prognosis

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

91. Biomarkers should be predictive of the onset of frailty, disability and dependency

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

92. Standard clinical tests, e.g. rate of decrease in hand grip strength, may serve as valuable 'functional biomarkers'

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

93. The factors related to frailty are: mobility, nutrition, physical function, cognition, mood, strength

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

94. The domains related to frailty are: mobility, nutrition, physical function, cognition, mood, strength, social isolation, small social network

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

95. Poor social networks are an indication of social isolation

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

FRAILTY VS DISABILITY

96. Frailty is not disability

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

97. Frailty and disability may coexist but they do not require each other to be present

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

98. Disability is usually the main outcome of Frailty, so it cannot be included in the definition of Frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

99. Frailty is a risk factor for disability, although disability can exist without previous frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

100. Frailty has different predictive values for different health outcomes (including disability, falls, hospitalization, permanent institutionalization and death)

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

101. The predictive value of frailty depends on its severity

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

102. The frailty process is modulated by disease, functional loss and socio-economic forces

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

FRAILTY VS COMORBIDITY

103. Frailty is not co morbidity. Thus , co morbidity should not be included in the definition or characterization of frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

104. Frailty modifies the negative effects of co morbidities leading to adverse outcomes

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

105. Co morbidity is a modulator of the progression of frailty to disability

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

106. Co morbidity is one of the important contributing factors to frailty

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

ANIMAL MODELS

107. 'Animal models' – motor coordination, grip strength, VO2, learning ability reflect important aspects of frailty in rodent models

1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ 10☐

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SECOND ROUND QUESTIONNAIRE

1. Frailty is a biological phenomenon.
   Median: 7 Percentage of agreement to accept the statement: 43.2%
2. Frailty may be a clinical syndrome.
   Median: 8 Percentage of agreement to accept the statement 51.4%
3. The predictive value of Frailty depends of its severity.
   Median: 8 Percentage of agreement to accept the statement: 70.9%
4. Frailty may be due to aging.
   Median: 5 Percentage of agreement to refuse the statement: 37.3%
5. The same definition of frailty should be valid across different clinical settings.
   Median: 9 Percentage of agreement to accept the statement: 70.6%
6. The definition must show reproducibility across time.
   Median: 9 Percentage of agreement to accept the statement: 77.5%
7. Frailty is a condition of older people with increased vulnerability in which minimal stress may cause functional impairment.
   Median: 9 Percentage of agreement to accept the statement: 75.5%
8. Frailty might be reversible or attenuated by interventions.
   Median: 8 Percentage of agreement to accept the statement: 73%
9. Frailty is a condition where prevention may still be possible and it is mandatory for clinicians and health workers to detect it as early as possible.
   Median: 9 Percentage of agreement to accept the statement: 78.4%
10. Frailty is different from disability.
    Median: 9 Percentage of agreement to accept the statement: 76.4%
11. Frailty is a dynamic process, non-linear, different from vulnerability and disability.
    Median: 9 Percentage of agreement to accept the statement: 72.3%
12. Frailty typically involves alteration in multiple systems.
    Median: 9 Percentage of agreement to accept the statement: 77.6%
13. The purpose of diagnosing frailty is to identify the non-robust, non-disabled older patient, which is at risk of adverse health outcomes in the near future.
    Median: 8.5 Percentage of agreement to accept the statement: 78.7%
14. Frailty diagnosis is useful in primary care and community care.
    Median: 9 Percentage of agreement to accept the statement: 74.8%
15. A diagnosis of frailty is only necessary in settings specialized in geriatric medicine.
    Median: 2 Percentage of agreement to refuse the statement: 72.9%
16. A Frailty diagnosis is useful in managing older people with chronic diseases.
    Median: 9 Percentage of agreement to accept the statement: 72.7%
17. Mental health assessment and cognitive status evaluation are highly recommended as part of the assessment of frailty.
    Median: 9 Percentage of agreement to accept the statement: 76.9%
18. Additional clinically measurable parameters (e.g. number of medications, cardiovascular parameters, etc) should be part of the definition of frailty.
    Median: 7 Percentage of agreement to accept the statement: 41.4%
19. Frailty can be the outcome of genetic plus environmental factors.
    Median: 7 Percentage of agreement to accept the statement: 48.6%
20. Frailty could be both the cause of disease and/or the consequence of it.
    Median: 8 Percentage of agreement to accept the statement: 70.3%

21. The frailty process is modulated by disease.
    Median: 8 Percentage of agreement to accept the statement: 70.9%

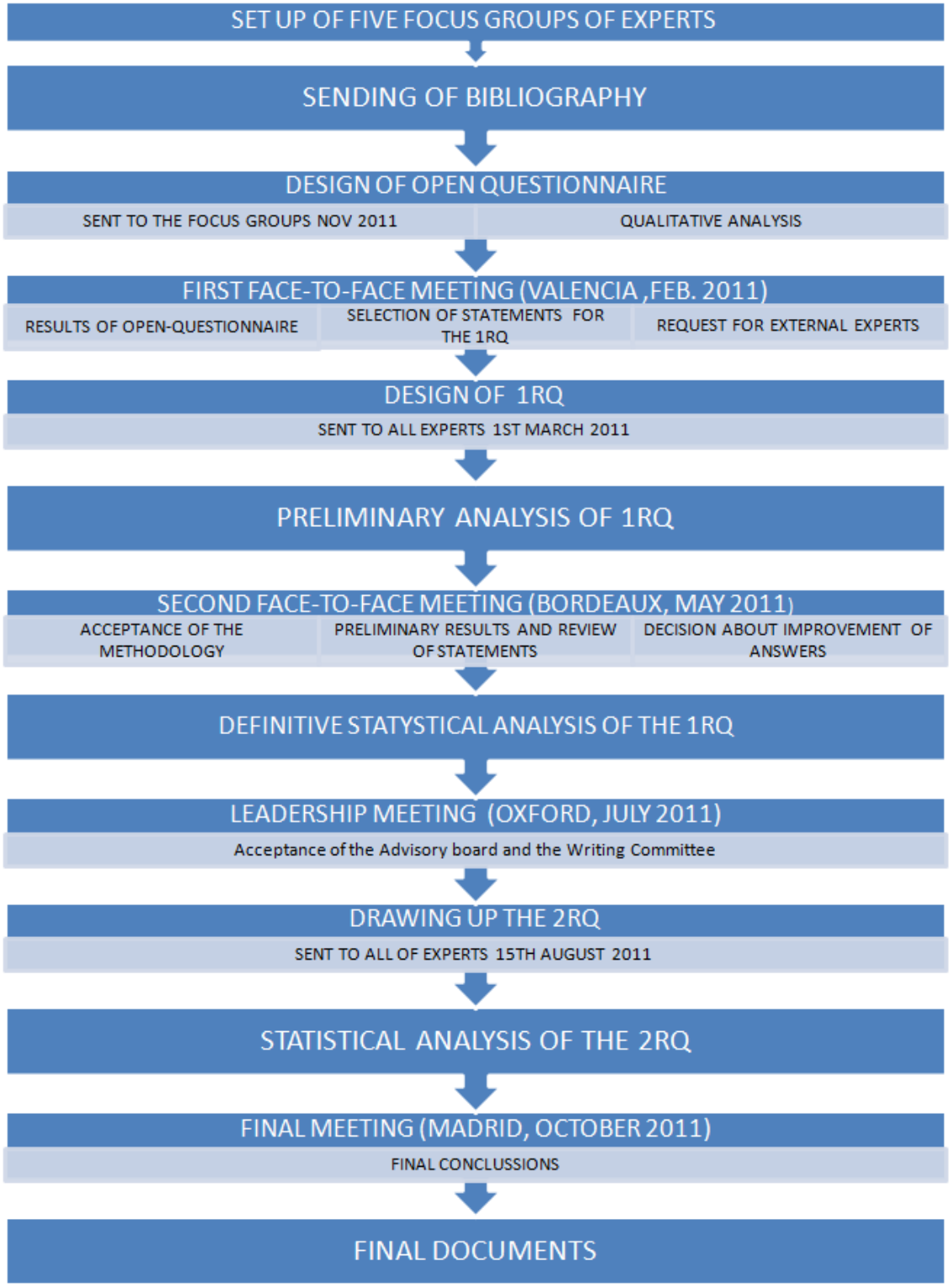
22. Frailty should be defined in terms of mobility or loco motor activity.
    Median: 5 Percentage of agreement to refuse the statement: 35.8%
23. The frailty process is modulated by functional status.
    Median: 8 Percentage of agreement to accept the statement: 70.9%
24. The frailty process is modulated by socio-economic forces.
    Median: 8 Percentage of agreement to accept the statement 70.9%
25. Frailty modifies the negative effects of co morbidities leading to adverse outcomes.
    Median: 8 Percentage of agreement to accept the statement: 73.8%
26. Inflammatory markers are not useful for assessing frailty in patients with chronic disease.
    Median: 5 Percentage of agreement to refuse the statement: 27.6%
27. Co morbidity is a modulator of the progression of frailty to disability.
    Median: 8 Percentage of agreement to accept the statement: 67.9%
28. Frailty should be a cluster of symptoms which could differ in different clinical settings. New
29. The components of frailty may vary from individual to individual. New
30. No single model can adequately reflect the complex nature of frailty. New
31. There is no single approach to the assessment of frailty. New
32. The assessment of frailty may vary from person to person. New
33. Physical activity should be considered an intervention for the management of frailty. New
34. Healthy life styles are important for the prevention and recovery of frailty. New
35. Determining nutritional status can be important in the diagnosis of frailty. New
36. Determining cognitive status can be important in the diagnosis of frailty. New
37. Determining psychological health can be important in the diagnosis of frailty. New
38. Examining sensory function can be important in the diagnosis of frailty. New
39. Determining social support can be important in the diagnosis of frailty. New
40. Examining economic forces can be important in the diagnosis of frailty. New
41. Physical performance tests can be important in the diagnosis of frailty. New
42. Assessing grip strength can be important in the diagnosis of frailty. New
43. Assessing gait speed can be important in the diagnosis of frailty. New
44. Mobility assessment can be important in the diagnosis of frailty. New
45. Frailty should be assessed in all old people older than 75 years old. New
46. Clinical biomarkers (grip strength, gait speed…) can be useful only after an initial diagnosis of Frailty. New
47. Laboratory biomarkers (CPR, IL1…) can be useful only after an initial diagnosis of Frailty. New
48. Clinical biomarkers (grip strength, gait speed…) can be useful at any step of the diagnostic process of frailty. New
49. Laboratory biomarkers (CPR, IL1…) can be useful at any step of the diagnostic process of frailty. New
50. Clinical biomarkers must be easily and broadly available. New
51. Handgrip strength is useful to measure muscle weakness. New
52. Handgrip strength is useful to measure sarcopenia. New

SECOND ROUND QUESTIONNAIRE

1. Frailty is a biological phenomenon.
   Median: 7 Percentage of agreement to accept the statement: 43.2%
2. Frailty may be a clinical syndrome.
   Median: 8 Percentage of agreement to accept the statement 51.4%
3. The predictive value of Frailty depends of its severity.
   Median: 8 Percentage of agreement to accept the statement: 70.9%
4. Frailty may be due to aging.
   Median: 5 Percentage of agreement to refuse the statement: 37.3%
5. The same definition of frailty should be valid across different clinical settings.
   Median: 9 Percentage of agreement to accept the statement: 70.6%
6. The definition must show reproducibility across time.
   Median: 9 Percentage of agreement to accept the statement: 77.5%
7. Frailty is a condition of older people with increased vulnerability in which minimal stress may cause functional impairment.
   Median: 9 Percentage of agreement to accept the statement: 75.5%
8. Frailty might be reversible or attenuated by interventions.
   Median: 8 Percentage of agreement to accept the statement: 73%
9. Frailty is a condition where prevention may still be possible and it is mandatory for clinicians and health workers to detect it as early as possible.
   Median: 9 Percentage of agreement to accept the statement: 78.4%
10. Frailty is different from disability.
    Median: 9 Percentage of agreement to accept the statement: 76.4%
11. Frailty is a dynamic process, non-linear, different from vulnerability and disability.
    Median: 9 Percentage of agreement to accept the statement: 72.3%
12. Frailty typically involves alteration in multiple systems.
    Median: 9 Percentage of agreement to accept the statement: 77.6%
13. The purpose of diagnosing frailty is to identify the non-robust, non-disabled older patient, which is at risk of adverse health outcomes in the near future.
    Median: 8.5 Percentage of agreement to accept the statement: 78.7%
14. Frailty diagnosis is useful in primary care and community care.
    Median: 9 Percentage of agreement to accept the statement: 74.8%
15. A diagnosis of frailty is only necessary in settings specialized in geriatric medicine.
    Median: 2 Percentage of agreement to refuse the statement: 72.9%
16. A Frailty diagnosis is useful in managing older people with chronic diseases.
    Median: 9 Percentage of agreement to accept the statement: 72.7%
17. Mental health assessment and cognitive status evaluation are highly recommended as part of the assessment of frailty.
    Median: 9 Percentage of agreement to accept the statement: 76.9%
18. Additional clinically measurable parameters (e.g. number of medications, cardiovascular parameters, etc) should be part of the definition of frailty.
    Median: 7 Percentage of agreement to accept the statement: 41.4%
19. Frailty can be the outcome of genetic plus environmental factors.
    Median: 7 Percentage of agreement to accept the statement: 48.6%
20. Frailty could be both the cause of disease and/or the consequence of it.
    Median: 8 Percentage of agreement to accept the statement: 70.3%

21. The frailty process is modulated by disease.
    Median: 8 Percentage of agreement to accept the statement: 70.9%

22. Frailty should be defined in terms of mobility or loco motor activity.
    Median: 5 Percentage of agreement to refuse the statement: 35.8%
23. The frailty process is modulated by functional status.
    Median: 8 Percentage of agreement to accept the statement: 70.9%
24. The frailty process is modulated by socio-economic forces.
    Median: 8 Percentage of agreement to accept the statement 70.9%
25. Frailty modifies the negative effects of co morbidities leading to adverse outcomes.
    Median: 8 Percentage of agreement to accept the statement: 73.8%
26. Inflammatory markers are not useful for assessing frailty in patients with chronic disease.
    Median: 5 Percentage of agreement to refuse the statement: 27.6%
27. Co morbidity is a modulator of the progression of frailty to disability.
    Median: 8 Percentage of agreement to accept the statement: 67.9%
28. Frailty should be a cluster of symptoms which could differ in different clinical settings. New
29. The components of frailty may vary from individual to individual. New
30. No single model can adequately reflect the complex nature of frailty. New
31. There is no single approach to the assessment of frailty. New
32. The assessment of frailty may vary from person to person. New
33. Physical activity should be considered an intervention for the management of frailty. New
34. Healthy life styles are important for the prevention and recovery of frailty. New
35. Determining nutritional status can be important in the diagnosis of frailty. New
36. Determining cognitive status can be important in the diagnosis of frailty. New
37. Determining psychological health can be important in the diagnosis of frailty. New
38. Examining sensory function can be important in the diagnosis of frailty. New
39. Determining social support can be important in the diagnosis of frailty. New
40. Examining economic forces can be important in the diagnosis of frailty. New
41. Physical performance tests can be important in the diagnosis of frailty. New
42. Assessing grip strength can be important in the diagnosis of frailty. New
43. Assessing gait speed can be important in the diagnosis of frailty. New
44. Mobility assessment can be important in the diagnosis of frailty. New
45. Frailty should be assessed in all old people older than 75 years old. New
46. Clinical biomarkers (grip strength, gait speed…) can be useful only after an initial diagnosis of Frailty. New
47. Laboratory biomarkers (CPR, IL1…) can be useful only after an initial diagnosis of Frailty. New
48. Clinical biomarkers (grip strength, gait speed…) can be useful at any step of the diagnostic process of frailty. New
49. Laboratory biomarkers (CPR, IL1…) can be useful at any step of the diagnostic process of frailty. New
50. Clinical biomarkers must be easily and broadly available. New
51. Handgrip strength is useful to measure muscle weakness. New
52. Handgrip strength is useful to measure sarcopenia. New



Box 1: Flow Chart of the Delphi Process

Table 1: **Rate of Statements Accepted, Excluded, Reviewed or Passed to the 2nd Round Questionnaire according to Each Block of Questions, Results from the First Round Questionnaire**

	Total	Accepted		Excluded		2nd Round		Reviewed	
		n	%	n	%	n	%	n	%
Framework	52	9	17.3	17	32.7	13	25.0	13	25.0
Biomarkers	43	2	4.7	28	65.1	1	2.3	12	27.9
Frailty vs disability	7	4	57.1	0	0.0	2	28.6	1	14.3
Frailty vs comorbidity	4	0	0.0	1	25.0	1	25.0	2	50.0
Animal models	1	0	0.0	1	100.0	0	0.0	0	0.0
Total	107	15	14.0	47	43.9	17	15.9	28	26.2

Table 2: List of Accepted Statements (in Light Blue, Statements Accepted after the 1st Round; in Dark Blue, Statements Accepted after the 2nd Round)

Statements	Missing value		Q≤3		Q≥8		Mean	50th	25th	75th	IQR	Classification 1	Classification 2
	n	%	n	%	n	%							
4. Frailty may be a clinical syndrome.	1	1.2	7	8.4	69	83.1	8.3	9	8	10	2	Framework	Concept
6. Frailty is characterized by decreased reserve and diminished resistance to stressors			2	1.8	95	85.6	8.7	9	8	10	2	Framework	Concept
7. The same definition of frailty should be valid across different clinical settings.	1	1.2	2	2.4	70	84.3	8.6	9	8	10	2	Framework	Concept
9. The definition must show reproducibility across time.	3	3.6	2	2.4	72	86.8	8.9	9	8	10	2	Framework	Concept
12. The concept of frailty and its operational definition can help in identifying and stratifying older persons at high risk of disability and/or other adverse outcomes			2	1.8	98	88.3	8.9	9	8	10	2	Framework	Prognosis
13. Frailty is multidimensional and may involve psychological, social, emotional and spiritual aspects in addition to physical components	1	0.9	4	3.6	90	81.8	8.7	10	8	10	2	Framework	Diagnostic
21. Frailty is a condition of older people with increased vulnerability in which minimal stress may cause functional impairment.	3	3.6	1	1.2	73	88.0	8.8	9	8	10	2	Framework	Prevention/ Treatment
22. Frailty might be reversible or attenuated by interventions.	1	1.2	2	2.4	71	85.5	8.7	9	8	10	2	Framework	Prevention/ Treatment
23. Frailty is a condition where prevention may still be possible and it is mandatory for clinicians and health workers to detect it as early as possible.	1	1.2	2	2.4	72	86.8	8.9	9	9	10	1	Framework	Concept
24. Frailty is a dynamic, non-linear process			3	2.7	93	83.8	8.7	9	8	10	2	Framework	Concept
26.Frailty is a dynamic process, non-linear, different from vulnerability and disability	1	1.2	2	2.4	79	95.2	9.1	9	9	10	1	Framework	Concept

Table 2. Continued

27. Frailty increases vulnerability to impairments and the ensuing consequences	2	1.8	1	0.9	97	89.0	8.7	9	8	10	2	Framework	Prognosis
28. Frailty involves alterations in multiple, not individual, body systems	2	1.8	6	5.5	89	81.7	8.4	9	8	10	2	Framework	Concept
29. Frailty involves alteration in several domains of function	1	0.9	3	2.7	88	80.0	8.3	9	8	10	2	Framework	Concept
32. Frailty cannot be defined in terms of a single molecular mechanism	3	2.7	5	4.6	96	88.9	9.0	10	9	10	1	Framework	Concept
39. Frailty is different from disability.	3	3.6	4	4.8	74	89.2	8.9	9	9	10	1	Framework	Concept
40. Frailty typically involves alteration in multiple systems.	2	2.4	3	3.6	75	90.4	9.0	9	9	10	1	Framework	Diagnostic
43. Definitions must be tested in clinical and non-clinical settings	1	0.9	8	7.3	92	83.6	8.4	9	8	10	2	Framework	Concept
45. The purpose of diagnosing frailty is to identify the non-robust, non-disabled older patient, which is at risk of adverse health outcomes in the near future.	2	2.4	4	4.8	73	88.0	8.7	9	8	10	2	Framework	Diagnostic
46. Frailty diagnosis is useful in primary care and community care.	2	2.4	0	0.0	74	89.2	9.1	9	9	10	1	Framework	Diagnostic
47. A Frailty diagnosis is useful in managing older people with chronic diseases.	2	2.4	3	3.6	67	80.7	8.6	9	8	10	2	Biomarkers	Diagnostic
48. A diagnosis of frailty is only necessary in settings specialized in geriatric medicine. *	4	4.8	67	80.7	6	7.2	2.3	1	1	3	2	Framework	Diagnostic
59. It is important to know the predictive value of biomarkers	2	1.8	1	0.9	91	83.5	9.5	9	8	10	2	Biomarkers	Diagnostic
60. There is no single biomarker that is adequate to predict or diagnose frailty	3	2.7	3	2.8	95	88.0	8.7	9	8	10	2	Biomarkers	Diagnostic
64. Mental health assessment and cognitive status evaluation are highly recommended as part of the assessment of frailty.	2	2.4	4	4.8	70	84.3	8.7	9	8	10	2	Frailty vs Disability	Diagnosis
96. Frailty is not disability			2	1.8	94	84.7	8.8	9	8	10	2	Frailty vs Disability	Concept
97. Frailty and disability may coexist but they do not require each other to be present	1	0.9	4	3.6	94	85.5	8.8	9	8	10	2	Frailty vs Disability	Concept

Table 2. Continued

99. Frailty is a risk factor for disability, although disability can exist without previous frailty			2	1.8	102	91.9	9.0	9	9	10	1	Frailty vs Disability	Concept
100. Frailty has different predictive values for different health outcomes (including disability, falls, hospitalization, permanent institutionalization and death)	3	2.7	3	2.8	88	81.5	8.4	9	8	10	2	Frailty vs Disability	Prognosis
101.The predictive value of Frailty depends of its severity.			5	6.0	69	83.1	8.3	9	8	9	1	Framework	Concept
102.The frailty process is modulated by disease	3	3.6	3	3.6	72	86.8	8.5	9	8	9	1	Frailty vs Disability	Prognosis
104. Frailty modifies the negative effects of co morbidities leading to adverse outcomes.	3	3.6	1	1.2	71	85.5	8.6	9	8	9	1	Frailty vs Comorbidity	Prognosis
N6.Physical activity should be considered an intervention for the management of frailty	1	1.2	3	3.6	72	86.8	8.4	8	8	10	2	Biomarkers	Prevention/ Treatment
N7.Healthy life styles are important for the prevention and recovery of frailty	1	1.2	3	3.6	73	88.0	8.5	9	8	9	1	Biomarkers	Prevention/ Treatment
N8.Determining nutritional status can be important in the diagnosis of frailty	1	1.2	2	2.4	68	81.9	8.4	8	8	10	2	Biomarkers	Diagnostic
N9.Determining cognitive status can be important in the diagnosis of frailty	2	2.4	2	2.4	71	85.5	8.5	9	8	10	2	Biomarkers	Diagnostic
N14.Physical performance tests can be important in the diagnosis of frailty.	1	1.2	1	1.2	78	94.0	8.8	9	8	10	2	Biomarkers	Diagnostic
N16.Assessing gait speed can be important in the diagnosis of frailty.	3	3.6	3	3.6	69	83.1	8.5	9	8	10	2	Biomarkers	Diagnostic
N17.Mobility assessment can be important in the diagnosis of frailty	2	2.4	2	2.4	72	86.8	8.6	9	8	10	2	Biomarkers	Diagnostic

*All agreements are for acceptance of the statements except for this statement which is rejected

Table 3: Rate of Accepted and Excluded Statements According to Each Block of Questions, Results from the Second Round Questionnaire

	Total			Accepted				Excluded			
	n	***Initial***	***New***	**Total**	**%**	***Initial***	***New***	**Total**	**%**	***Initial***	***New***
Framework	22	18	4	13	59.1	*13*	*0*	9	40.9	*5*	*4*
Biomarkers	24	3	21	8	33.3	*1*	*7*	16	66.7	*2*	*14*
Frailty vs disability	2(+2)	2(+2)	0	2	40.0	*2*	*0*	(+2)	60.0	*(+2)*	*0*
Frailty vs comorbidity	2	2	0	1	100.0	*1*	*0*	1	0.0	*1*	*0*
Total	52	25(+2)	25	24	46.2	*17*	*7*	28	53.8	*8+2*	*18*

"Initial" refers to statement previously present in the first round questionnaire; "New" refers to new statements added specially to the 2nd round questionnaire; (+2) refers to the question from the 1rst round questionnaire that have been divided into 3 different sentences for the 2nd round

Table 4: Rate of Accepted and Excluded Statements According to Each Block of Questions, Final Analysis

	Total			Accepted				Excluded			
	n	***Initial***	***New***	**Total**	**%**	***Initial***	***New***	**Total**	**%**	***Initial***	***New***
Framework	57	52	4	22	38.6	22	0	35	61.4	31	4
Biomarkers	63	43	21	10	15.9	3	7	53	84.1	39	14
Frailty vs disability	7(+2)	7(+2)	0	6	66.6	6	0	1(+2)	33.3	1(+2)	0
Frailty vs comorbidity	4	4	0	1	25.0	1	0	3	75.0	3	0
Animal models	1	1	0	0	0.0	0	0	1	100.0	1	0
Total	132(+2)	107(+2)	25	39	29.1	32	7	93(+2)	70.9	75(+2)	18

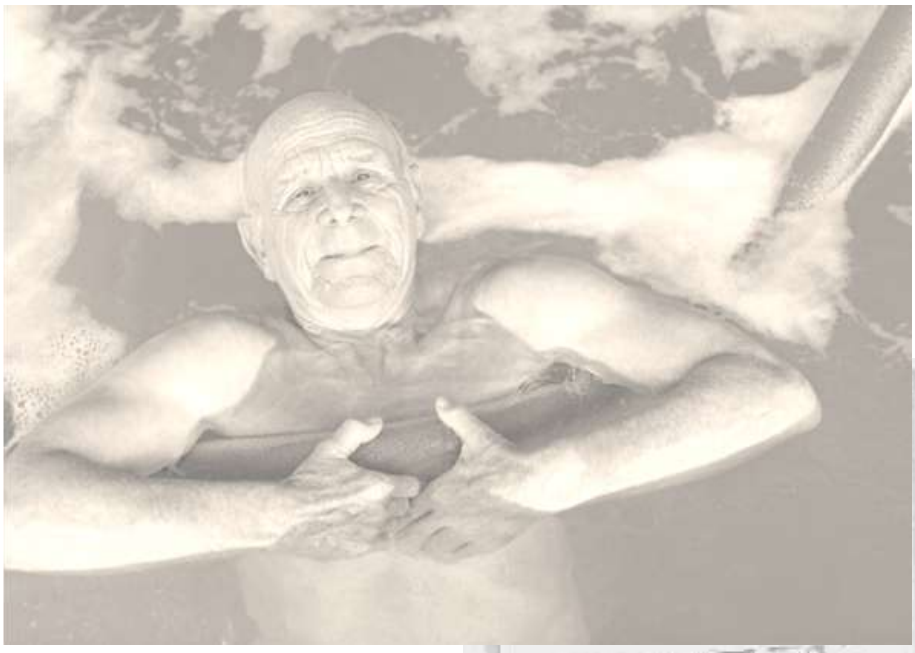
"Initial" refers to statement previously present in the first round questionnaire; "New" refers to new statements added specially to the 2nd round questionnaire; (+2) refers to the question from the 1rst round questionnaire that have been divided into 3 different sentences for the 2nd round

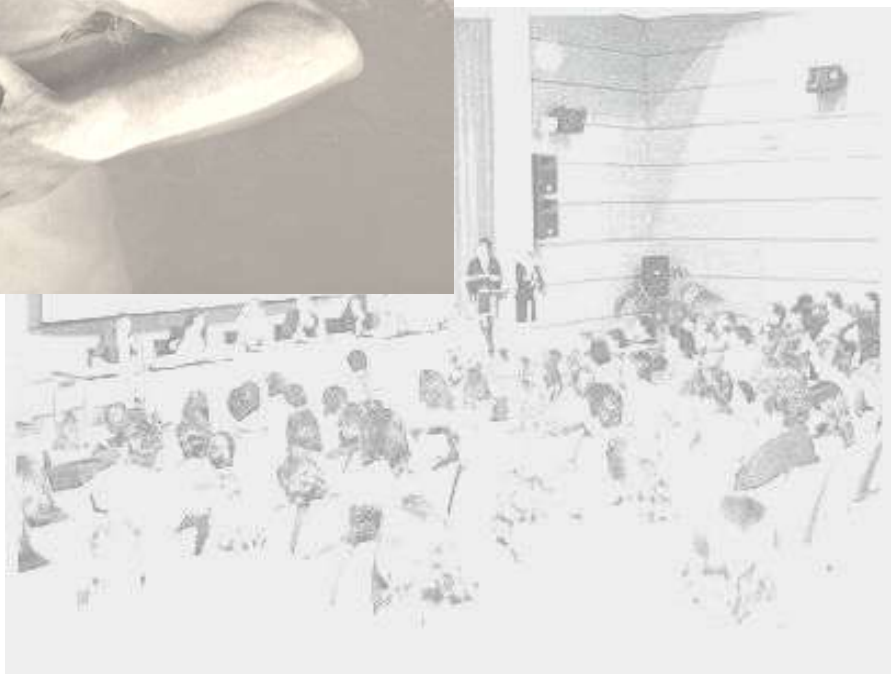
Table 5: Rate of Accepted and Excluded Statements According to the Alternative Classification, Final Analysis

	Total			Accepted				Excluded			
	n	***Initial***	***New***	**Total**	**%**	***Initial***	***New***	**Total**	**%**	***Initial***	***New***
Concept	36	33	3	16	44.4	16	0	20	55.5	17	3
Prognosis	15	15	0	5	33.3	5	0	10	66.7	10	0
Diagnosis	76(+2)	58	20	14	17.9	9	5	62(+2)	82.3	49	15
Prevention/Treatment	5	3	2	4	80.0	2	2	1	20.0	1	0
Total	132(+2)	107(+2)	25	39	29.1	32	7	93(+2)	70.9	75(+2)	18

"Initial" refers to statement previously present in the first round questionnaire; "New" refers to new statements added specially to the 2nd round questionnaire; (+2) refers to the questions from the 1rst round questionnaire that have been divided into 3 different sentences for the 2nd round


28.10.2011





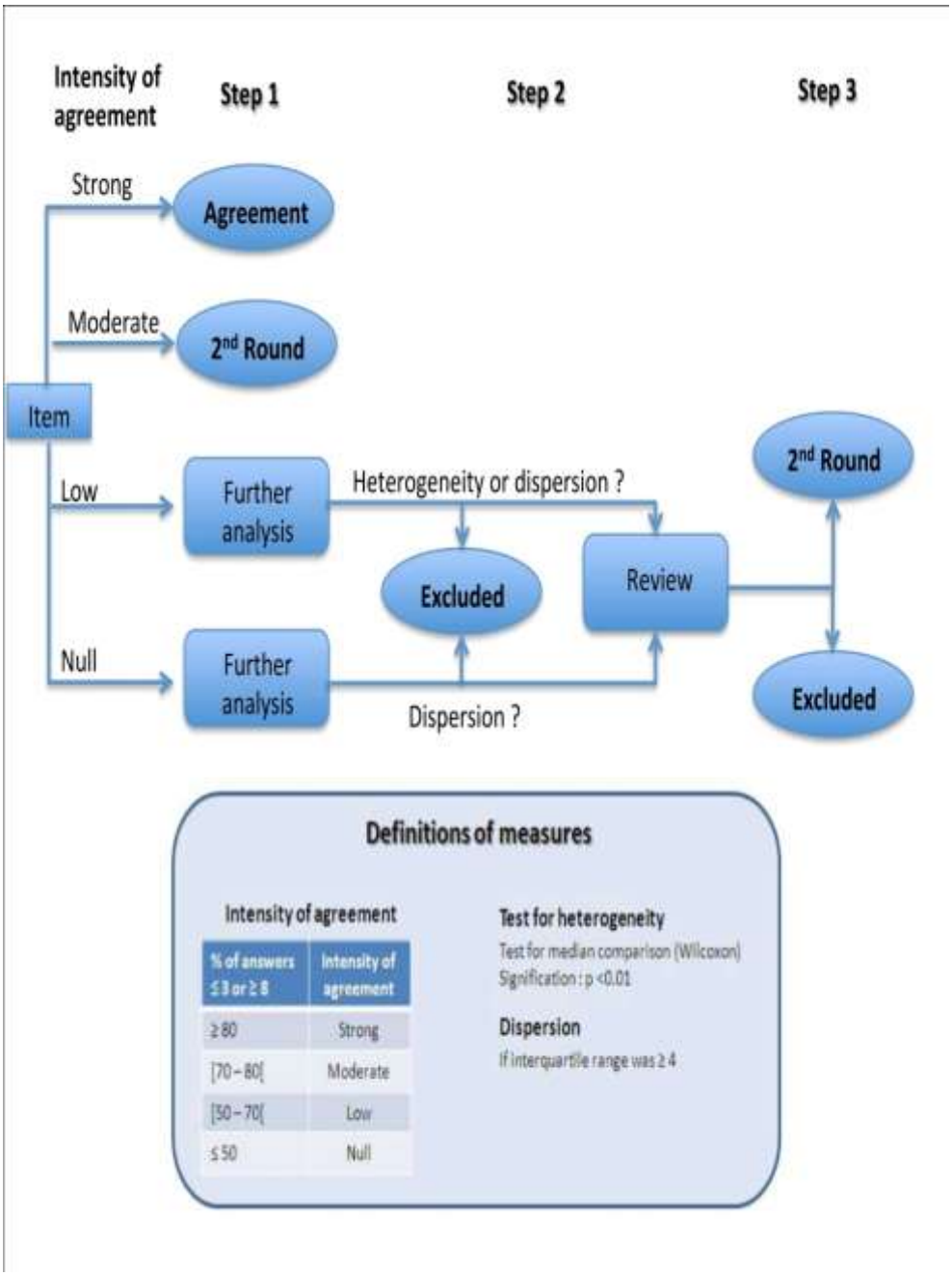


Figure 1. Flow chart of Statistical Method

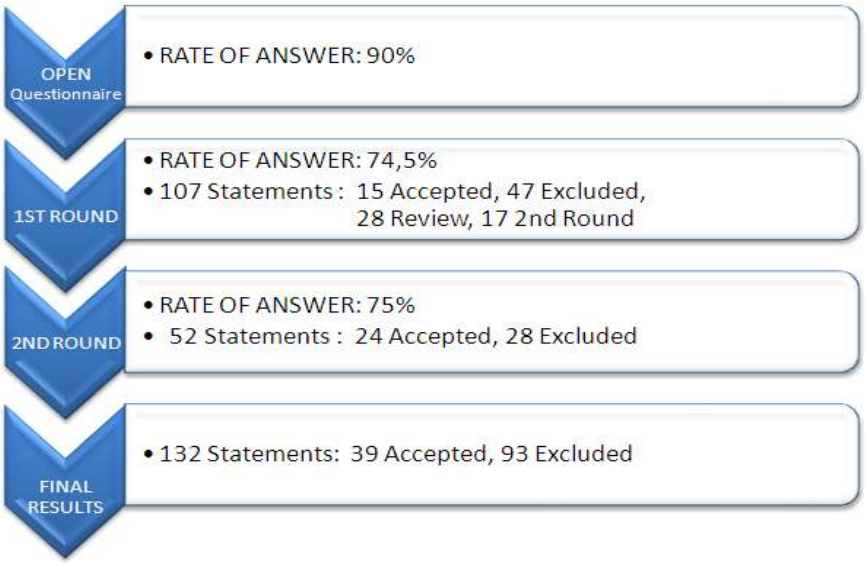


Figure 2: Flow Chart for the Results of the Delphi Process