Supplementary files

Supplementary file 1. The preliminary list of recommendations for reporting delirium biomarker studies provided to meeting attendees*

Item number	Item	Consensus achieved in prior Delphi surveys*
1	**The study objective should include the following:**	
1(a)	The biomarker under study (including source)	87.5%
1(b)	The time of collection in relation to delirium onset	87.6%
1(c)	The clinical endpoint(s) including their definition	81.3%
1(d)	The clinical covariates	85%
1(e)	The methods of biomarker collection	75%
1(f)	A description of which delirium pathophysiological theory the study will address	80%
2	**In defining the population:**	
2(a)	Delirium cases should be diagnosed by a trained assessor or specialist doctor	93.8%
2(b)	Delirium should be assessed using a validated delirium diagnosis tool	81.3%
2(c)	Delirium should be prospectively evaluated	87.5%
2(d)	Adult and paediatric populations should be considered separately	81.3%
3	**Delirium biomarker studies should support the person with delirium and their proxy decision maker by:**	
3(a)	Providing a clear participant information that explains the study to the person with delirium and/or their proxy decision maker	93.8%
3(b)	Providing clear procedures to assist staff in interacting and supporting the patient during biomarker collection and other data collection	75%
3(c)	Explaining the value of the research in lay terms and how it can contribute to the understanding of delirium	75%
3(d)	Clear processes for informed consent	75%
4	**When selecting control(s) group:**	
	As delirium is a complex clinical condition with many influencing clinical variables several control groups will strengthen the ability to interpret the findings	70%
4(a)	**The following control groups would be appropriate to consider:**	
	Participants without delirium	93.8%
	Participants with the same illness severity, with and without delirium	85%
	Participants with delirium superimposed onto dementia	70%
4(b)	**In studies which follow participants longitudinally, the following are appropriate additional comparator groups:**	

	Participants with delirium of a shorter duration	75%
	Participants who do not develop delirium	87.5%
5	**The biomarker in a delirium study should be:**	
5(a)	Chosen *a priori*	100%
5(b)	Supported by a biologically plausible rationale	75%
5(c)	Supported by a clear hypothesis	81.3%
6	**The type of biological specimen chosen should:**	
6(a)	Be based on the capacity to measure the proposed biological process being evaluated	100%
6(b)	Have high specificity and sensitivity	83.8%
7	**Description of the assay procedure should include the following as a minimum:**	
7(a)	A detailed assay protocol that includes the reagents/kits used	81.3%
7(b)	An assay validation for assay repeatability and robustness	75%
7(c)	The inter- and intra- assay coefficients of variation	75.6%
7(d)	Methods of preservation, storage and processing of the biological sample	87.6%
7(e)	The assay validity	93.8%
7(f)	The sensitivity limits of the assay	93.8%
7(g)	A scoring and reporting protocol	87.5%
7(h)	Method of blinding should be explicit	81.3%
8	**In biomarker studies, confounding variables need to:**	
8(a)	Be decided *a priori*	81.3%
8(b)	Take into account the population being studied/the clinical condition	75%
8(c)	Be clearly defined and justified	81.3%
8(d)	Be accounted for in the analysis	93.8%
9	**The minimum clinical covariates that should be taken into account are:**	
	Age, gender, concurrent medication, comorbidities, prior cognitive impairment, illness severity, sepsis, prior neurological conditions, frailty, inflammation, delirium risk and delirium precipitants	75%
10	**Timing of collection**	
10(a)	Timing of the sample collection should be determined based on the clinical scenario and/or the hypothesis being tested	87.5%
10(b)	In longitudinal sampling of populations AT RISK OF DELIRIUM, it is recommended that samples are collected prior to delirium onset, during delirium episode, and after delirium resolution	100%
10(c)	In longitudinal sampling of populations WITH DELIRIUM, it is recommended that samples are collected at delirium onset and again after delirium resolution	87.5%
11	**Sample size**	

11(a)	Sample size should be decided *a priori* based on previous studies/pilot data	81.3%
11(b)	Sample size should be determined based on the estimated effect size of the biomarker in predicting the outcome	87.5%
12	**The analysis plan should plan for clinical and biomarker missing data due to:**	
12(a)	Clinical issues such as overall deterioration, worsening cognition, and death	100%
12(b)	Practical challenges of biomarker collection in people with delirium	75%
13	**Univariate analyses of biomarker and clinical endpoints of interest should report the following:**	
13(a)	Estimated effect size	81.3%
13(b)	Whether biomarker result was dichotomised using a cut-point and/or threshold	87.6%
13(c)	How missing data were handled	75%
13(d)	Number of included participants	87.5%
14	**Multivariate analyses of biomarker and clinical endpoints of interest should report the following:**	
14(a)	Estimated effect size	100%
14(b)	Whether biomarker result was dichotomised using a cut-point and/or threshold	100%
14(c)	How model assumptions were verified	93.8%
14(d)	How missing data were handled	75%
14(e)	Number of included participants	93.8%
14(f)	Covariates	87.5%

**Items highlighted in red achieved a 70-80% consensus and were the key items for discussion in the consensus meeting*

Supplementary file 2. Participant wording suggestions in open-text form

Item number	Checklist item	Wording suggestions	Updated wording for the REDEEMS
1(e)	The study objective should include: the method of biomarker collection	1. "Describe the collection of biological sample, time, storage and method of measurement of all analytes" 2. "Include time of collection in relationship to the study timeline and include biomarker specimen processing method" 3. Remove 'study objective'	The study should include: a description of the method of biomarker collection
1(f)	The study objective should include: A description of which delirium pathophysiological theory the study will address	1. Remove 'study objective' 2. Write 'biological hypothesis' instead of 'pathophysiological theory' 3. Add a plural term on theory 4. "The study needs to contextualize the experiment in a biologically plausible way" 5. "Hypothesis" 6. "Should refer to the hypothesis that it addresses but should not insist on limiting to a specific pathophysiological theory. If not testing a specific hypothesis you should state unbiased or exploratory"	The study should include: A description of the biological hypotheses(/is) it is addressing. If the study is not testing a specific hypothesis, it should state that it is undertaking an un-biased or exploratory approach
3(a)	Delirium biomarker studies should support the person with delirium and their proxy decision maker by: Providing clear procedures to assist staff in interacting and	N/A	Exclude

	supporting the patient during biomarker collection and other data collection		
3(b)	Delirium biomarker studies should support the person with delirium and their proxy decision maker by: Explaining the value of the research in lay terms and how it can contribute to the understanding of delirium	N/A	Exclude
3(c)	Delirium biomarker studies should support the person with delirium and their proxy decision maker by: Clear processes for informed consent	N/A	Exclude
4(a)	When selecting control(s) group: As delirium is a complex clinical condition with many influencing clinical variables, several control groups will strengthen the ability to interpret the findings	1. "Consider more than one control group" 2. Remove the word 'groups' and just have the word 'controls' 3. "Consider more than one control to support your study aim"	Exclude
4(b)	The following control groups would be important to consider: Participants with delirium superimposed onto dementia	N/A	Exclude
4(c)	In studies which follow participants longitudinally, the following are appropriate additional comparator groups: Participants with delirium of a shorter duration	N/A	Exclude
5(b)	The biomarker in a delirium study should be: Supported by a biologically plausible rationale	N/A	Merge with item 1
7(b)	Description of the assay procedure should include the following as a minimum: An assay validation for assay repeatability and robustness	1. "An assay validation for repeatability and robustness"	Description of the assay procedure should include the following as a minimum: An assay validation for repeatability and robustness
7(c)	Description of the assay procedure should include the following as a minimum: The	N/A	Remain the same

	inter- and intra- assay coefficients of variation		
8(b)	In biomarker studies, confounding variables need to take into account the population being studied/the clinical condition	None	Remain the same
9	The minimum clinical covariates that should be taken into account are: Age, gender, concurrent medication, comorbidities, prior cognitive impairment, illness severity, sepsis, prior neurological conditions, frailty, inflammation, delirium risk and delirium precipitants	N/A	Exclude
12(b)	The analysis plan should plan for clinical and biomarker missing data due to: Practical challenges of biomarker collection in people with delirium	1. “Remove the word ‘practical’” 2. “The analysis plan should plan for clinical and biomarker missing data”	The analysis plan should account for clinical and biomarker missing data
13(c)	Univariate analyses of biomarker and clinical endpoints of interest should report the following: How missing data were handled	N/A	Merge with item 12
14(d)	Multivariate analyses of biomarker and clinical endpoints of interest should report the following: How missing data were handled	N/A	Merge with item 12