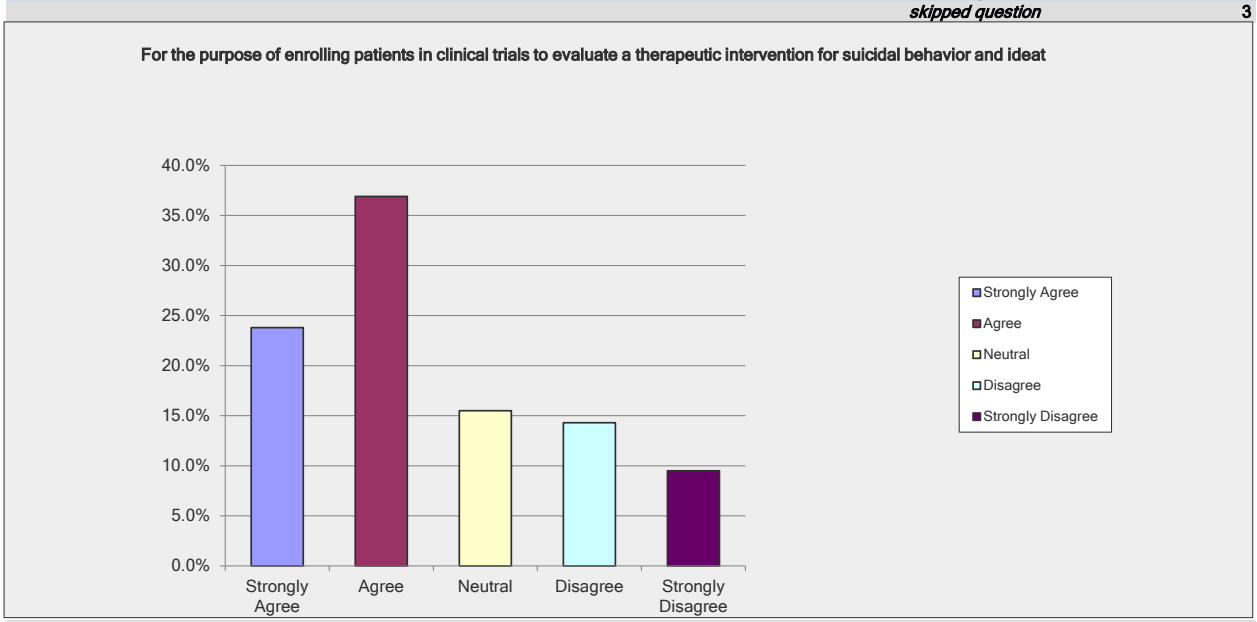
## SIB Consensus Pre-meeting Survey: Clinical Trial Design & Methodology

| | |
|---|---|
| Recipients | 128 |
| Responded | 87 |
| Unresponded | 41 |
| % Responded | 68% |

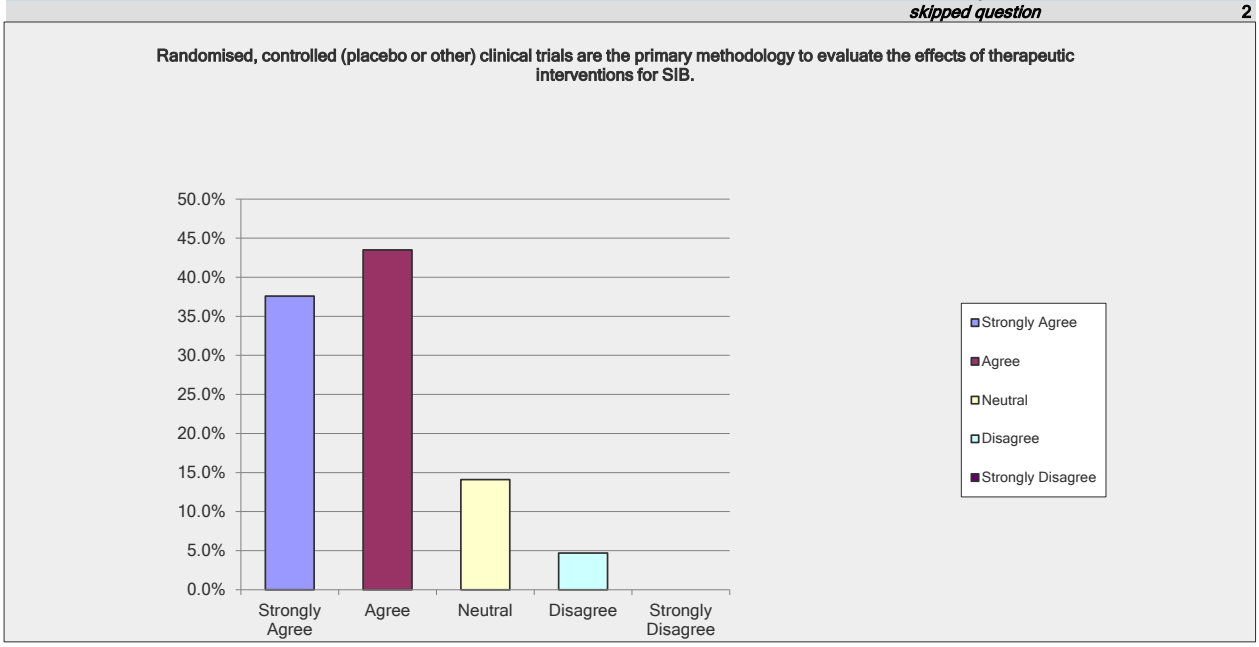
### Q1.For the purpose of enrolling patients in clinical trials to evaluate a therapeutic intervention for suicidal behavior and ideation (SIB), SIB should be studied as a trans-nosological condition or syndrome, i.e., patients with SIB should be enrolled without regard to whether SIB occurs within the course of another disorder such as Major Depression or Post-Traumatic Stress Disorder.

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 23.8% | 20 |
| Agree | 36.9% | 31 |
| Neutral | 15.5% | 13 |
| Disagree | 14.3% | 12 |
| Strongly Disagree | 9.5% | 8 |
| | *answered question* | 84 |
| | *skipped question* | 3 |



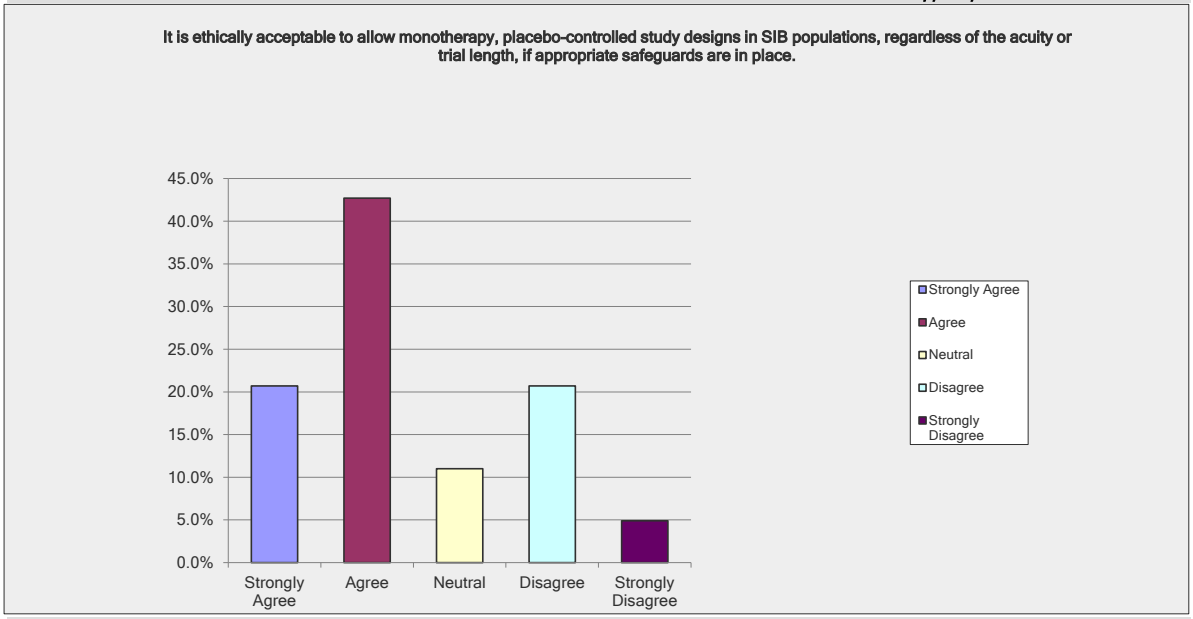

### Q2.Randomised, controlled (placebo or other) clinical trials are the primary methodology to evaluate the effects of therapeutic interventions for SIB.

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 37.6% | 32 |
| Agree | 43.5% | 37 |
| Neutral | 14.1% | 12 |
| Disagree | 4.7% | 4 |
| Strongly Disagree | 0.0% | 0 |
| | *answered question* | 85 |
| | *skipped question* | 2 |



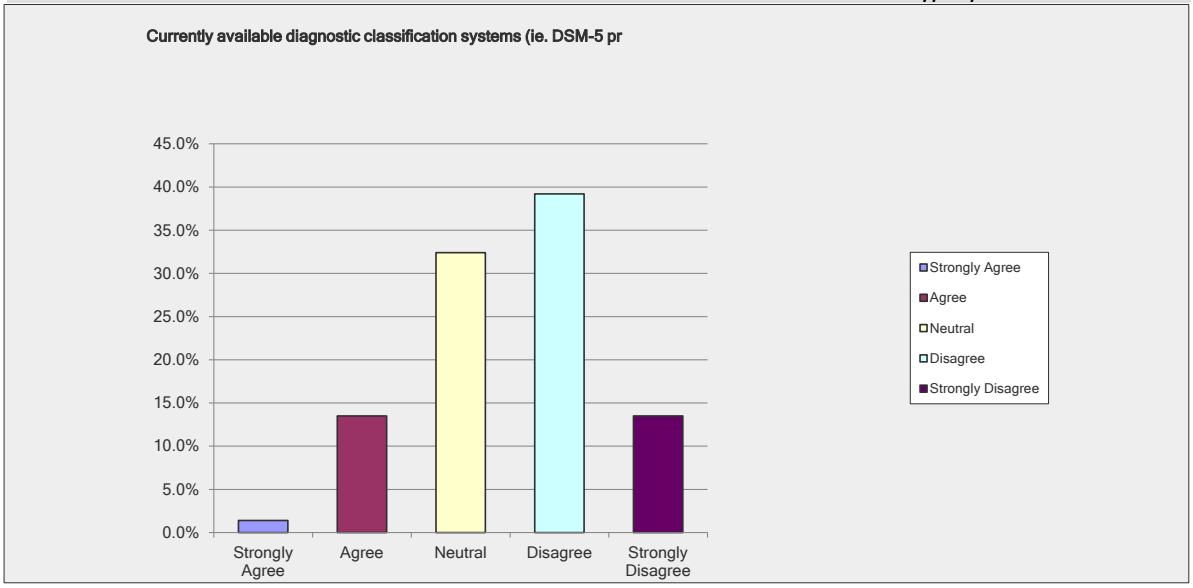
**Q3.It is ethically acceptable to allow monotherapy, placebo-controlled study designs in SIB populations, regardless of the acuity or trial length, if appropriate safeguards are in place.**

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 20.7% | 17 |
| Agree | 42.7% | 35 |
| Neutral | 11.0% | 9 |
| Disagree | 20.7% | 17 |
| Strongly Disagree | 4.9% | 4 |
| | *answered question* | 82 |
| | *skipped question* | 5 |



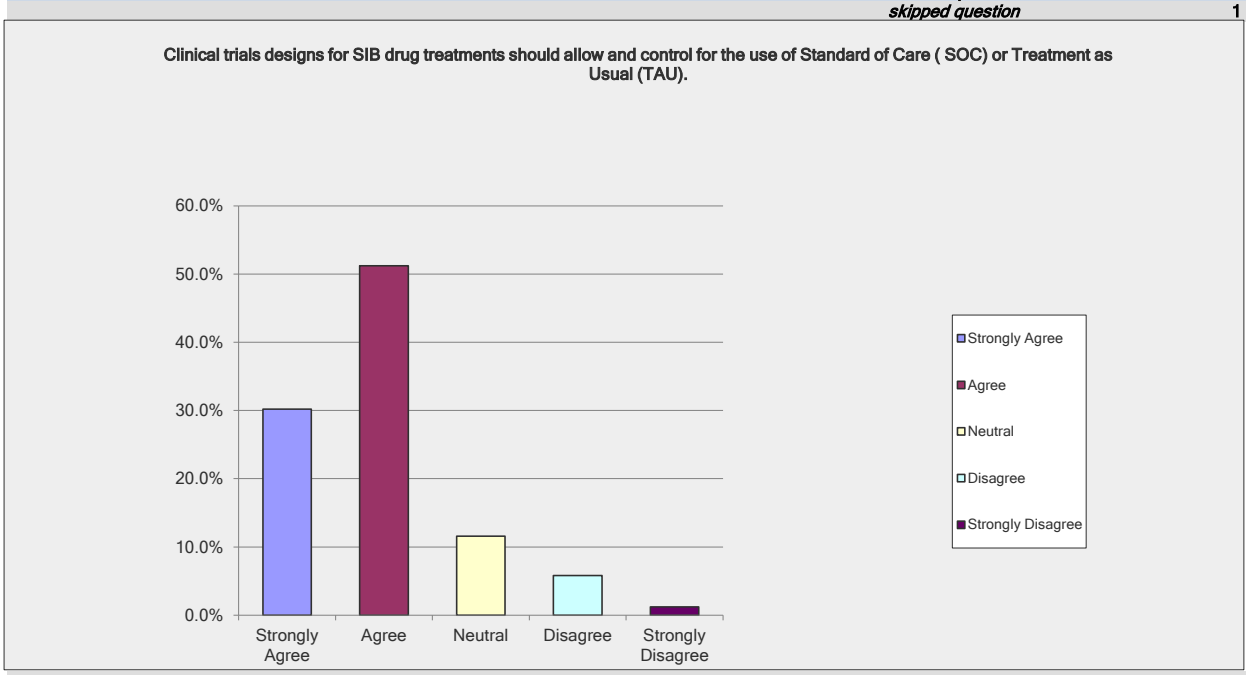

**Q4.Currently available diagnostic classification systems (ie. DSM-5 provisional criteria) provide sufficient guidance and operational criteria to classify patients along the suicidality spectrum (e.g., acuity) to ensure that the appropriate patient populations are enrolled in SIB trials to evaluate therapeutic interventions.**

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 1.4% | 1 |
| Agree | 13.5% | 10 |
| Neutral | 32.4% | 24 |
| Disagree | 39.2% | 29 |
| Strongly Disagree | 13.5% | 10 |
| | *answered question* | 74 |
| | *skipped question* | 13 |



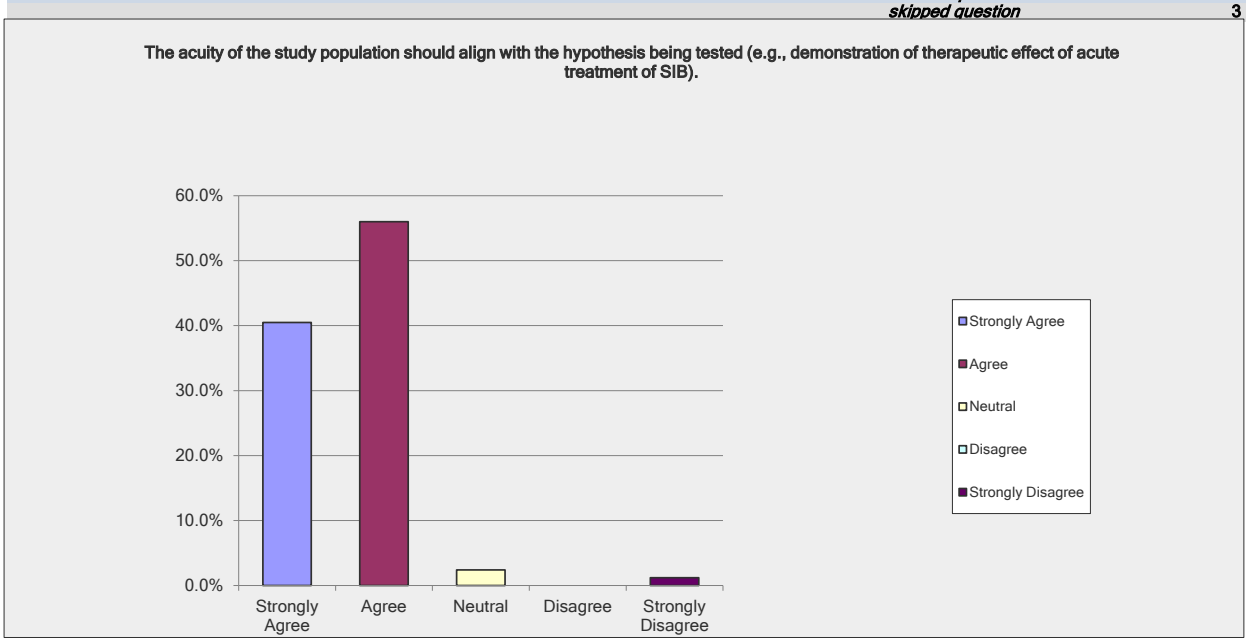
## Q5.Clinical trials designs for SIB drug treatments should allow and control for the use of Standard of Care ( SOC) or Treatment as Usual (TAU).

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 30.2% | 26 |
| Agree | 51.2% | 44 |
| Neutral | 11.6% | 10 |
| Disagree | 5.8% | 5 |
| Strongly Disagree | 1.2% | 1 |
| *answered question* | | 86 |
| *skipped question* | | 1 |



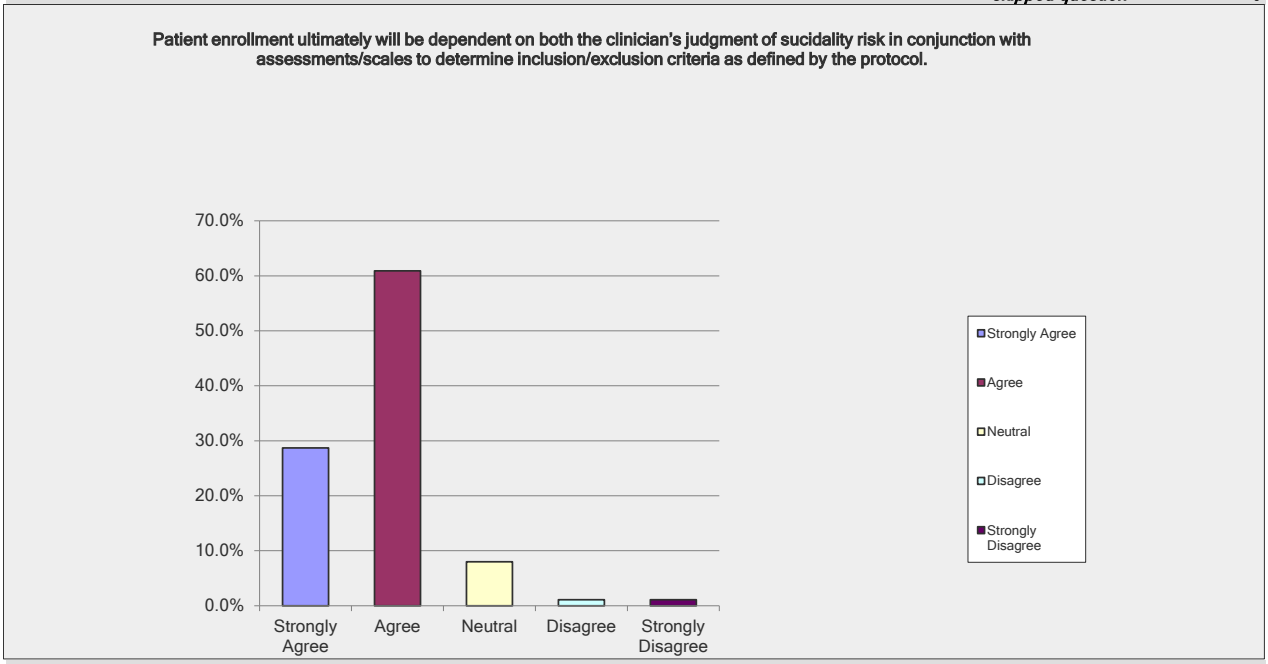

## Q6.The acuity of the study population should align with the hypothesis being tested (e.g., demonstration of therapeutic effect of acute treatment of SIB).

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 40.5% | 34 |
| Agree | 56.0% | 47 |
| Neutral | 2.4% | 2 |
| Disagree | 0.0% | 0 |
| Strongly Disagree | 1.2% | 1 |
| *answered question* | | 84 |
| *skipped question* | | 3 |



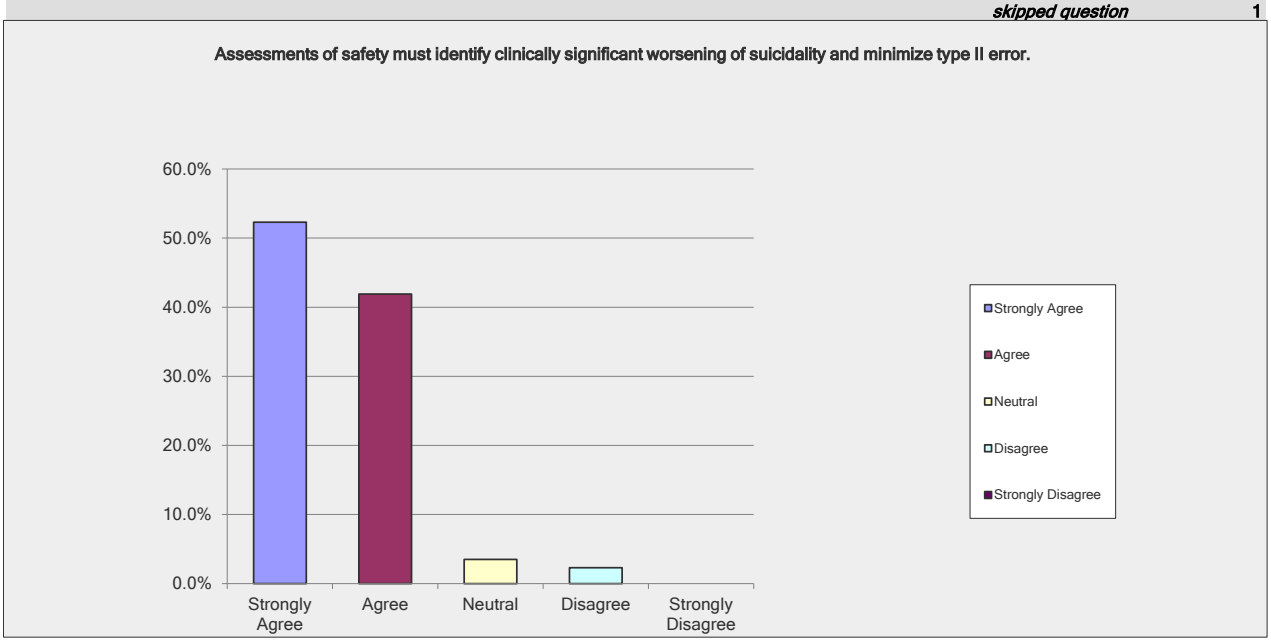
## Q7.Patient enrollment ultimately will be dependent on both the clinician's judgment of sucidality risk in conjunction with assessments/scales to determine inclusion/exclusion criteria as defined by the protocol.

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 28.7% | 25 |
| Agree | 60.9% | 53 |
| Neutral | 8.0% | 7 |
| Disagree | 1.1% | 1 |
| Strongly Disagree | 1.1% | 1 |
| *answered question* | | 87 |
| *skipped question* | | 0 |



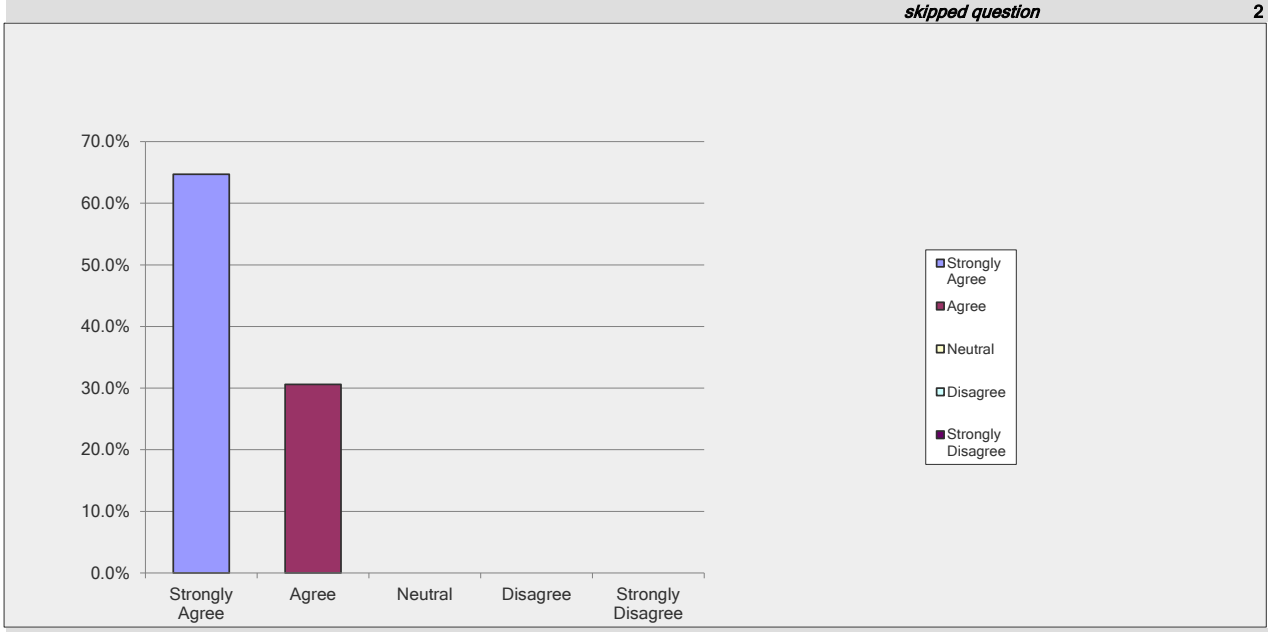

## Q8.Assessments of safety must identify clinically significant worsening of suicidality and minimize type II error.

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 52.3% | 45 |
| Agree | 41.9% | 36 |
| Neutral | 3.5% | 3 |
| Disagree | 2.3% | 2 |
| Strongly Disagree | 0.0% | 0 |
| *answered question* | | 86 |
| *skipped question* | | 1 |



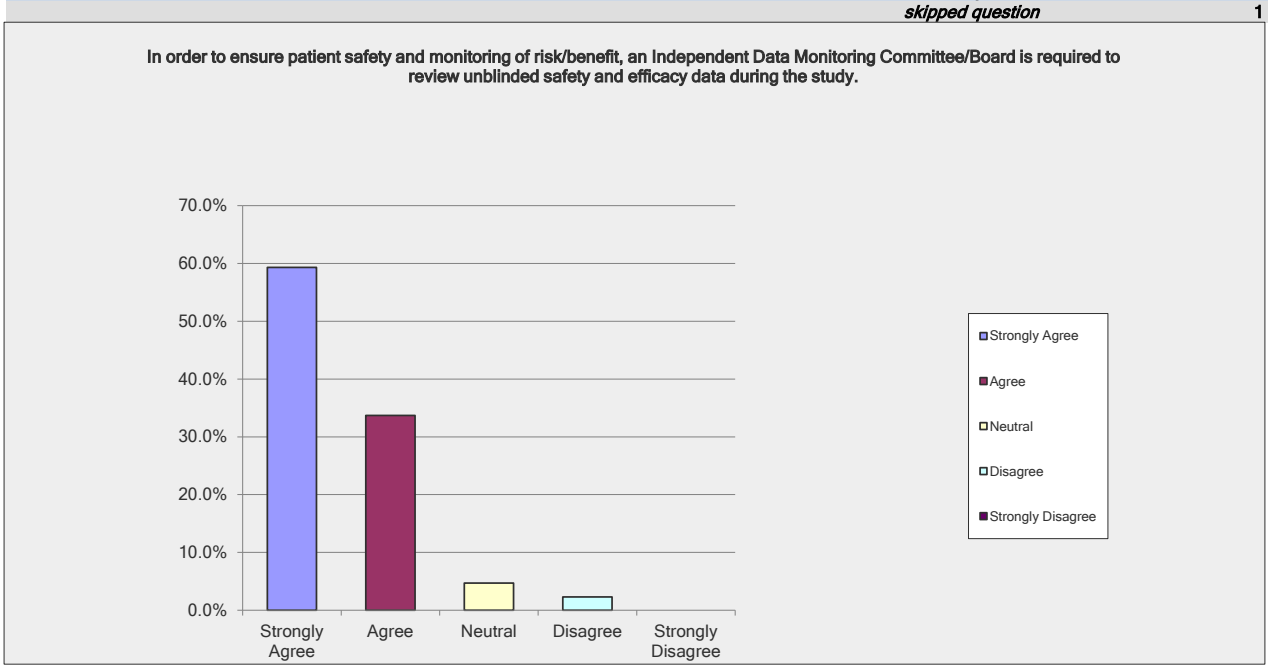
**Q9.The protocol should specify actions to be taken in case of worsening of symptoms or worsening of comorbid conditions (e.g., schizophrenia, depression, bipolar, etc.), including criteria for early withdrawal of treatment and outpatient studies should consider criteria for hospitalization.**

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 64.7% | 55 |
| Agree | 30.6% | 26 |
| Neutral | 0.0% | 0 |
| Disagree | 0.0% | 0 |
| Strongly Disagree | 0.0% | 0 |
| *answered question* | | 85 |
| *skipped question* | | 2 |



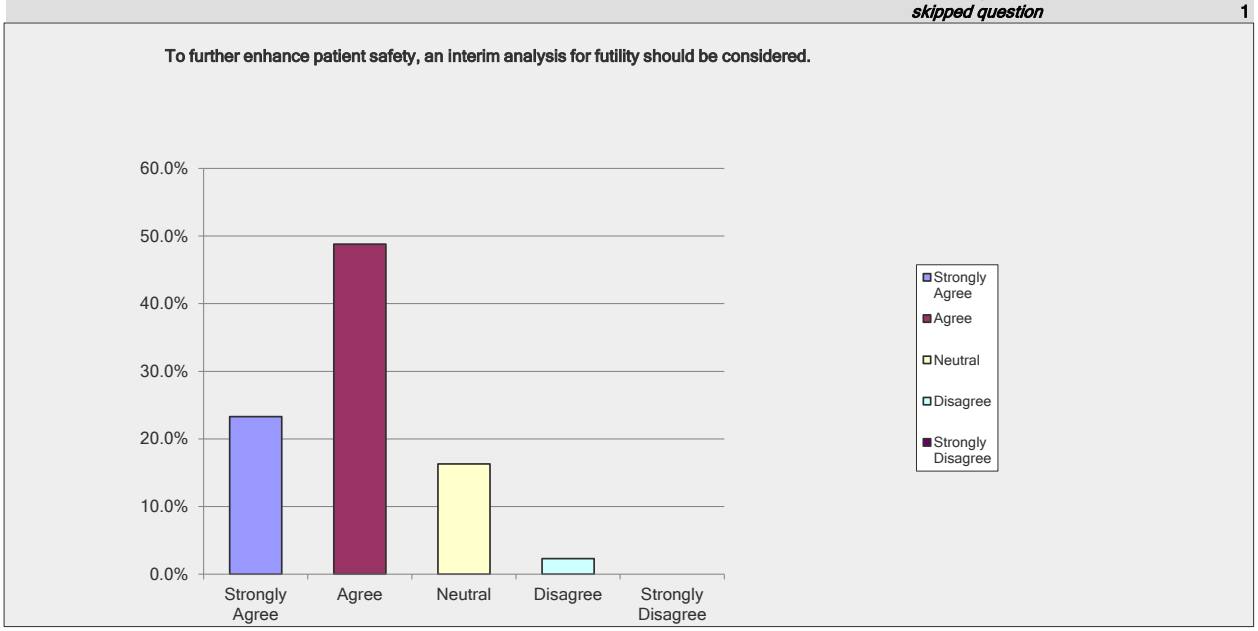

**Q10.In order to ensure patient safety and monitoring of risk/benefit, an Independent Data Monitoring Committee/Board is required to review unblinded safety and efficacy data during the study.**

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 59.3% | 51 |
| Agree | 33.7% | 29 |
| Neutral | 4.7% | 4 |
| Disagree | 2.3% | 2 |
| Strongly Disagree | 0.0% | 0 |
| *answered question* | | 86 |
| *skipped question* | | 1 |



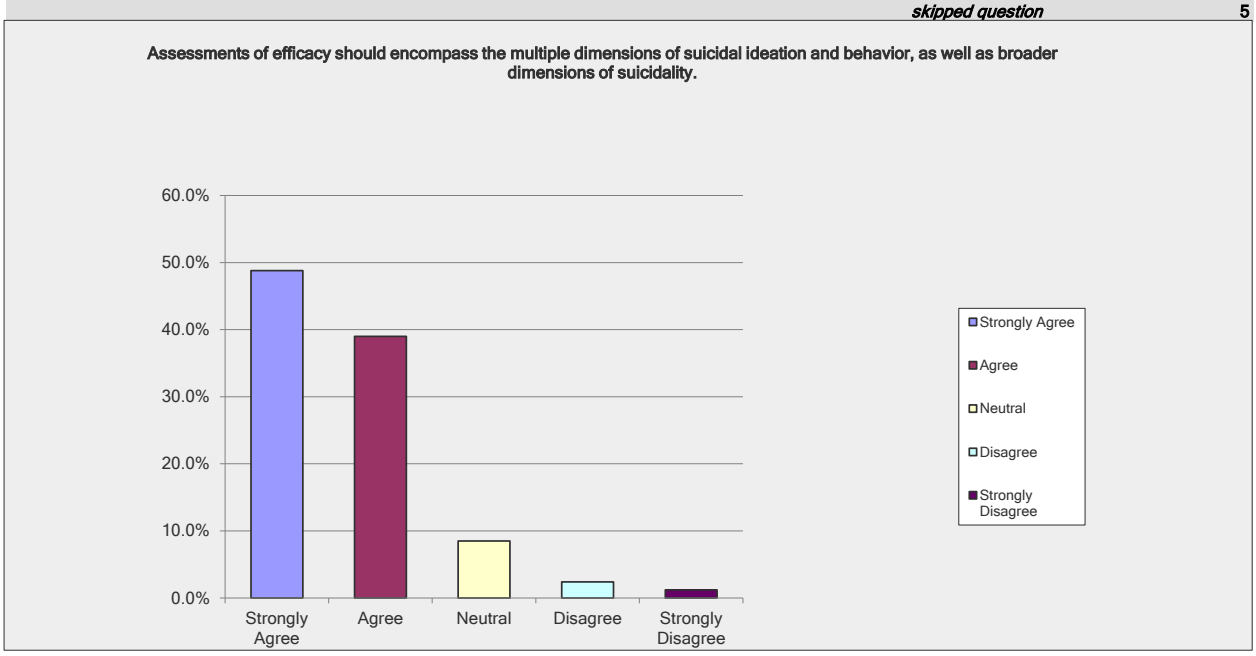
## Q11.To further enhance patient safety, an interim analysis for futility should be considered.

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 23.3% | 20 |
| Agree | 48.8% | 42 |
| Neutral | 16.3% | 14 |
| Disagree | 2.3% | 2 |
| Strongly Disagree | 0.0% | 0 |
| *answered question* | | 86 |
| *skipped question* | | 1 |



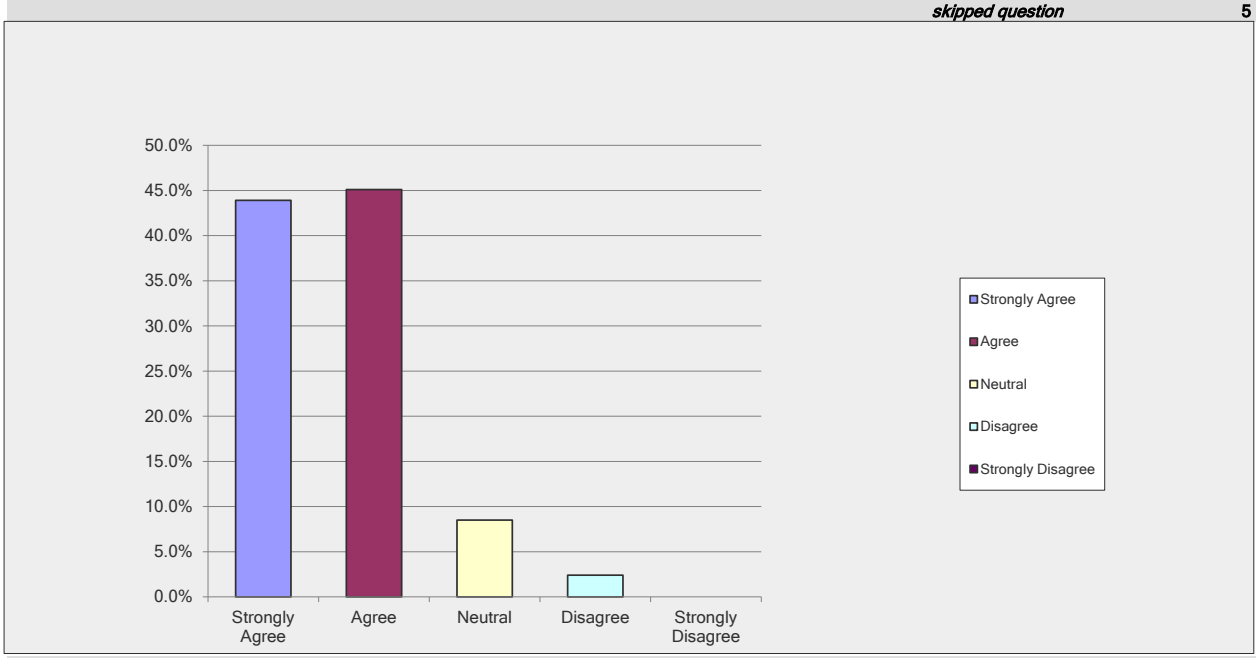

## Q12.Assessments of efficacy should encompass the multiple dimensions of suicidal ideation and behavior, as well as broader dimensions of suicidality.

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 48.8% | 40 |
| Agree | 39.0% | 32 |
| Neutral | 8.5% | 7 |
| Disagree | 2.4% | 2 |
| Strongly Disagree | 1.2% | 1 |
| *answered question* | | 82 |
| *skipped question* | | 5 |



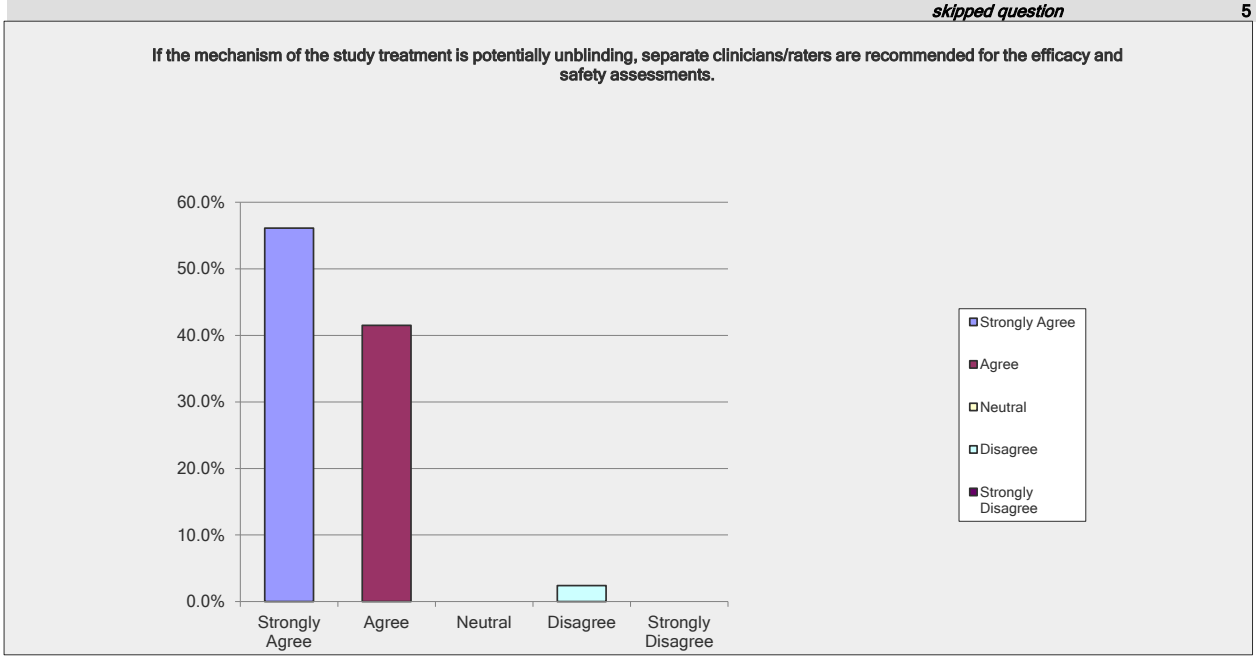
**Q13.The length of the acute treatment period should be the minimum necessary to answer the study hypothesis and the length of an open-label extension or post-treatment follow-up period should be sufficient to ensure safety and adequately address secondary outcomes.**

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 43.9% | 36 |
| Agree | 45.1% | 37 |
| Neutral | 8.5% | 7 |
| Disagree | 2.4% | 2 |
| Strongly Disagree | 0.0% | 0 |
| *answered question* | | 82 |
| *skipped question* | | 5 |



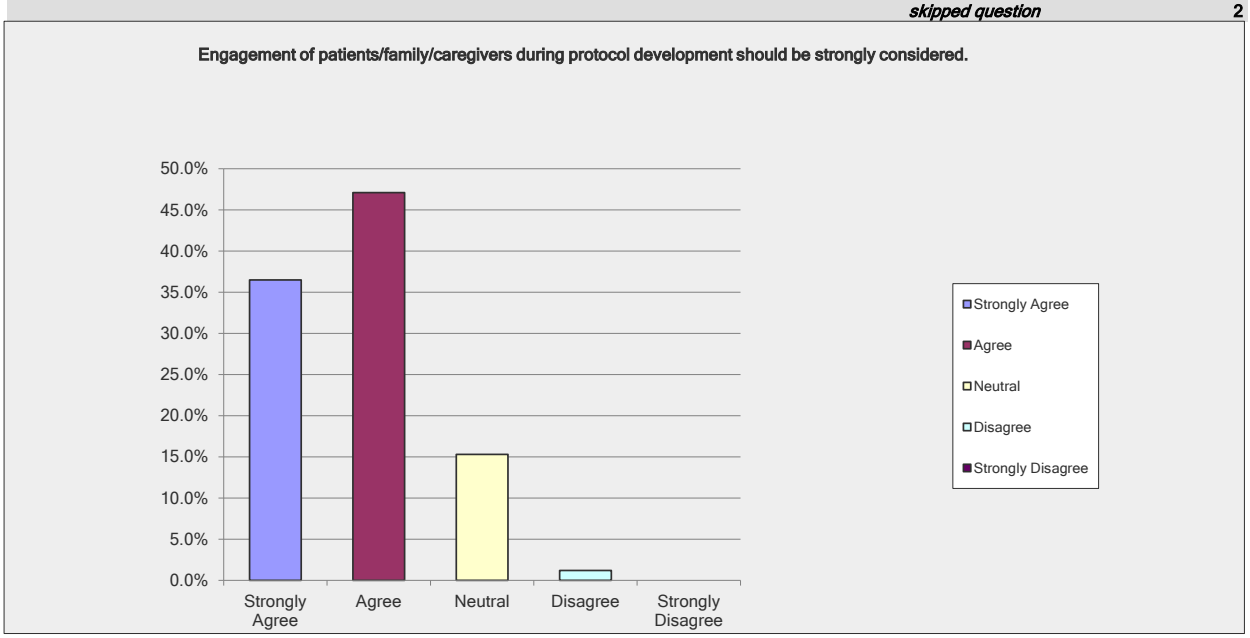

**Q14.If the mechanism of the study treatment is potentially unblinding, separate clinicians/raters are recommended for the efficacy and safety assessments.**

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 56.1% | 46 |
| Agree | 41.5% | 34 |
| Neutral | 0.0% | 0 |
| Disagree | 2.4% | 2 |
| Strongly Disagree | 0.0% | 0 |
| *answered question* | | 82 |
| *skipped question* | | 5 |



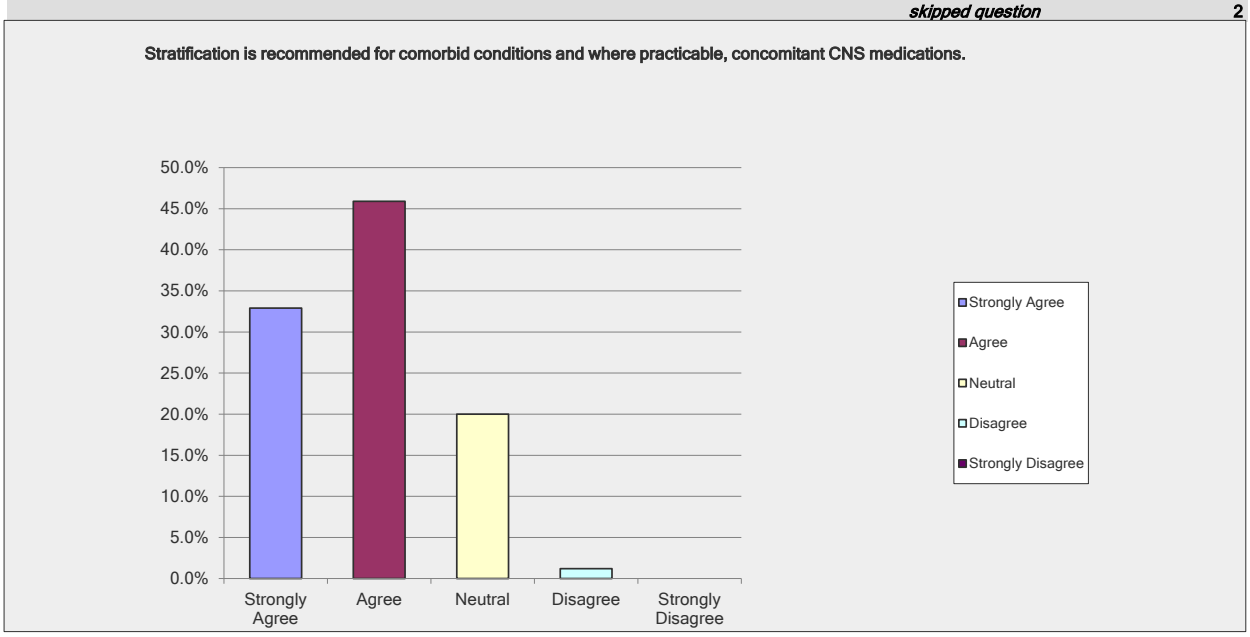
## Q15.Engagement of patients/family/caregivers during protocol development should be strongly considered.

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 36.5% | 31 |
| Agree | 47.1% | 40 |
| Neutral | 15.3% | 13 |
| Disagree | 1.2% | 1 |
| Strongly Disagree | 0.0% | 0 |
| *answered question* | | 85 |
| *skipped question* | | 2 |



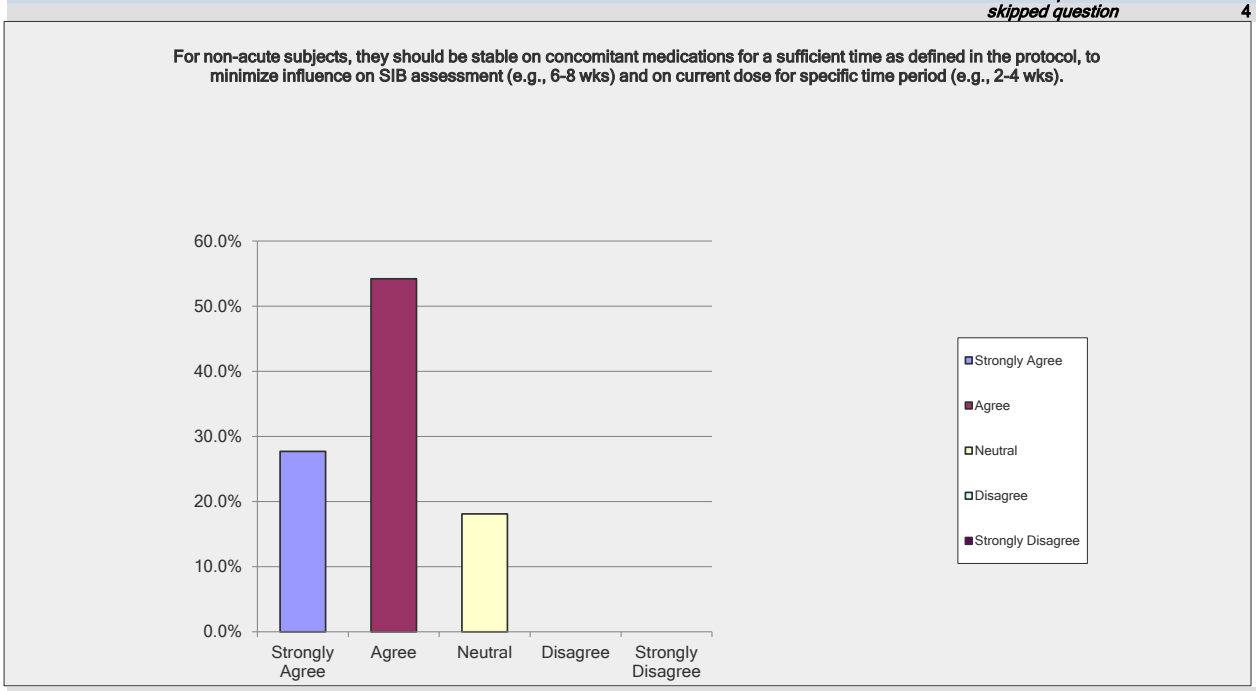

## Q16.Stratification is recommended for comorbid conditions and where practicable, concomitant CNS medications.

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 32.9% | 28 |
| Agree | 45.9% | 39 |
| Neutral | 20.0% | 17 |
| Disagree | 1.2% | 1 |
| Strongly Disagree | 0.0% | 0 |
| *answered question* | | 85 |
| *skipped question* | | 2 |



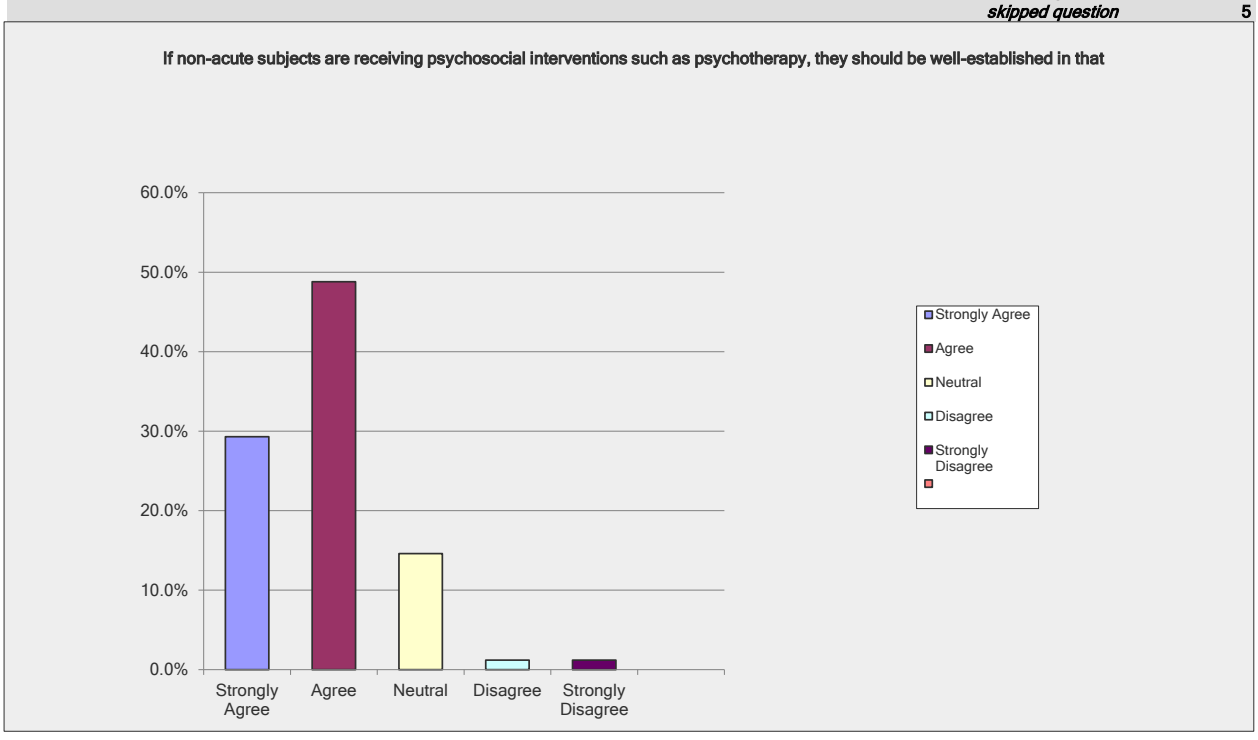
**Q17.For non-acute subjects, they should be stable on concomitant medications for a sufficient time as defined in the protocol, to minimize influence on SIB assessment (e.g., 6-8 wks) and on current dose for specific time period (e.g., 2-4 wks).**

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 27.7% | 23 |
| Agree | 54.2% | 45 |
| Neutral | 18.1% | 15 |
| Disagree | 0.0% | 0 |
| Strongly Disagree | 0.0% | 0 |
| *answered question* | | 83 |
| *skipped question* | | 4 |



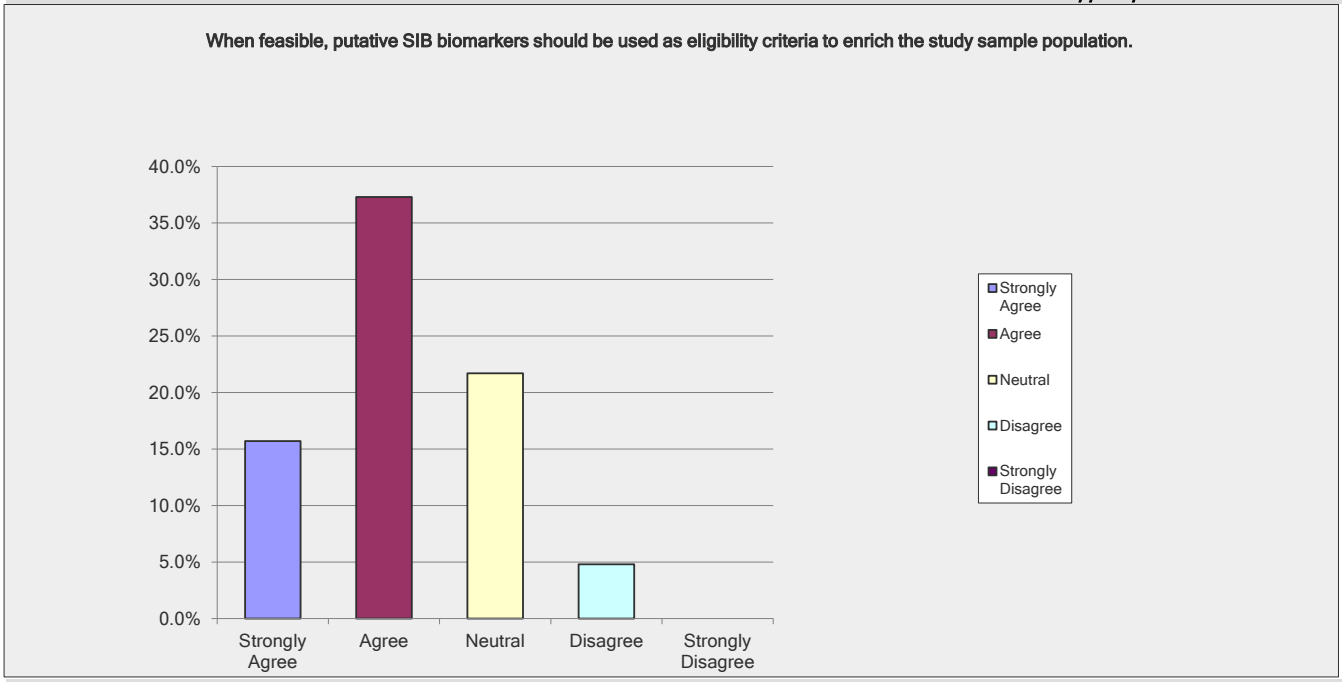

**Q18.If non-acute subjects are receiving psychosocial interventions such as psychotherapy, they should be well-established in that therapy as defined in the protocol (e.g., have been receiving care for 3-6 mos or shorter duration for brief crisis interventions, as appropriate) with no anticipated changes (in frequency, modality, or therapeutic approach) for the duration of the trial.**

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 29.3% | 24 |
| Agree | 48.8% | 40 |
| Neutral | 14.6% | 12 |
| Disagree | 1.2% | 1 |
| Strongly Disagree | 1.2% | 1 |
| *answered question* | | 82 |
| *skipped question* | | 5 |



## Q19.When feasible, putative SIB biomarkers should be used as eligibility criteria to enrich the study sample population.

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 15.7% | 13 |
| Agree | 37.3% | 31 |
| Neutral | 21.7% | 18 |
| Disagree | 4.8% | 4 |
| Strongly Disagree | 0.0% | 0 |
| *answered question* | | 83 |
| *skipped question* | | 4 |




## Q20.In addition to meeting core requirements for clinical validation and qualification of use in regulatory clinical trials (i.e., diagnostic accuracy), SIB biomarkers should also demonstrate clinical utility.

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 29.6% | 24 |
| Agree | 42.0% | 34 |
| Neutral | 22.2% | 18 |
| Disagree | 6.2% | 5 |
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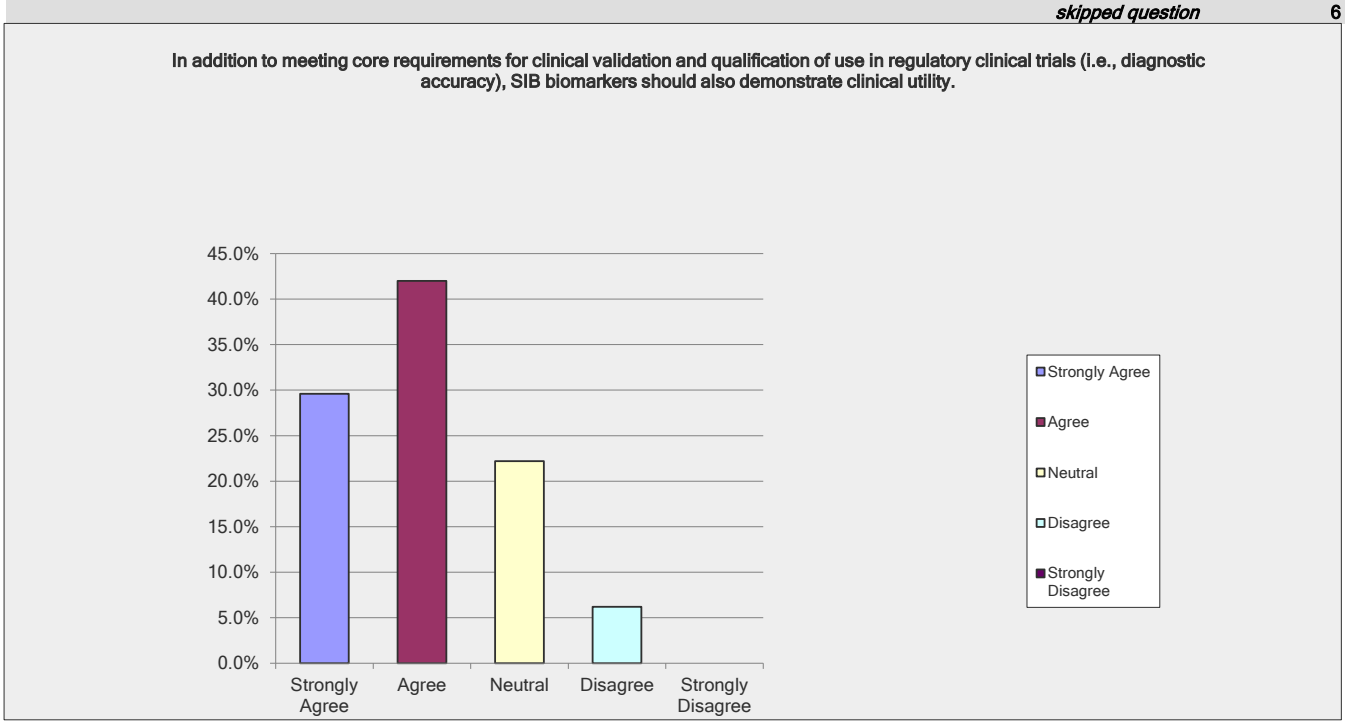
| *skipped question* | | 6 |



## Q21.Policies should be developed to encourage biobanking as well as to ensure a broader access to biobank specimens.

| Answer Options | Response Percent | Response Count |
|---|---|---|
| Strongly Agree | 45.6% | 36 |
| Agree | 40.5% | 32 |
| Neutral | 13.9% | 11 |
| Disagree | 0.0% | 0 |
| Strongly Disagree | 0.0% | 0 |
| *answered question* | | 79 |
| *skipped question* | | 8 |