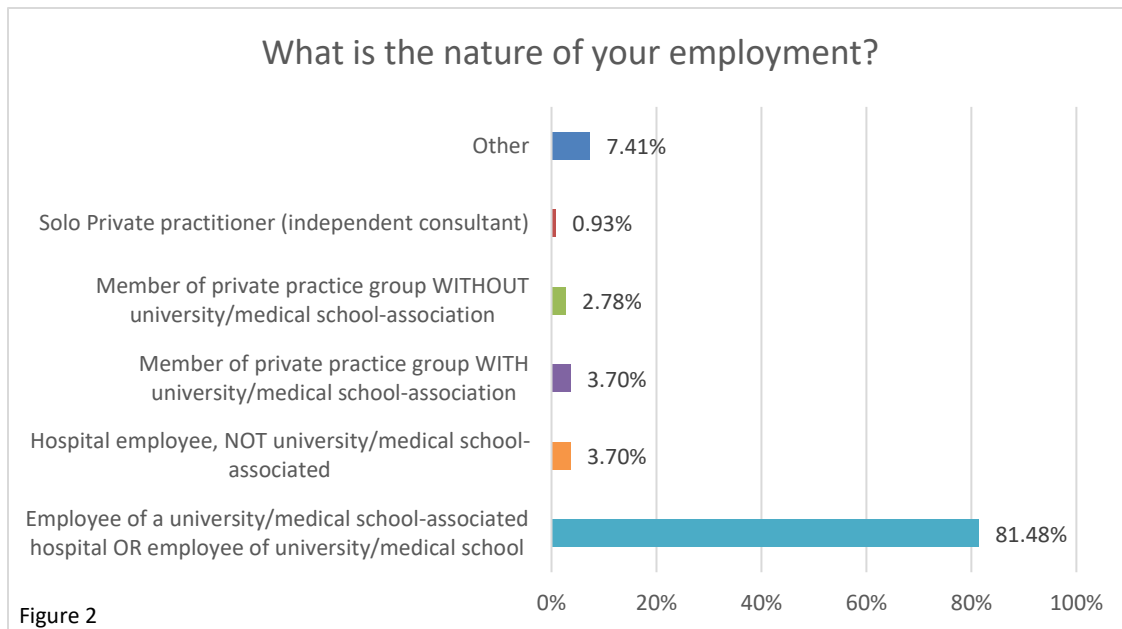
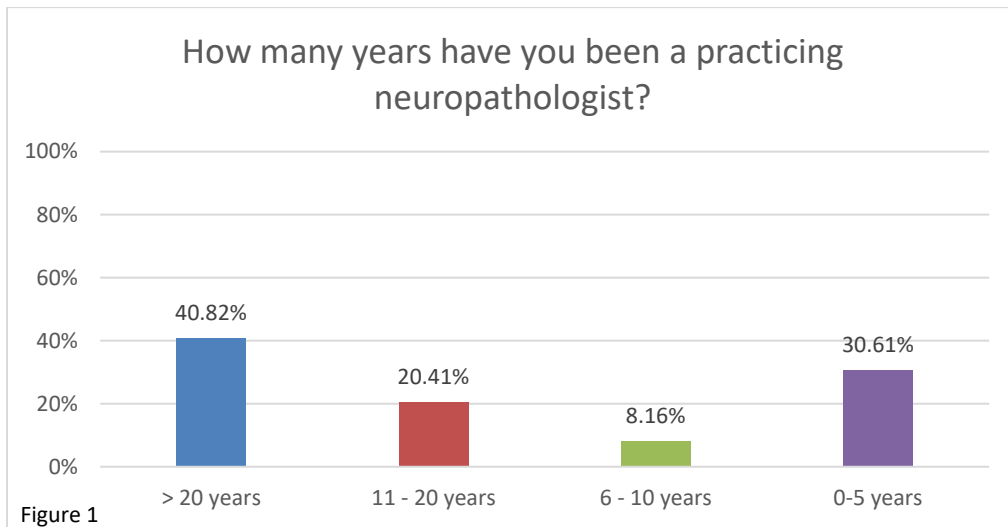


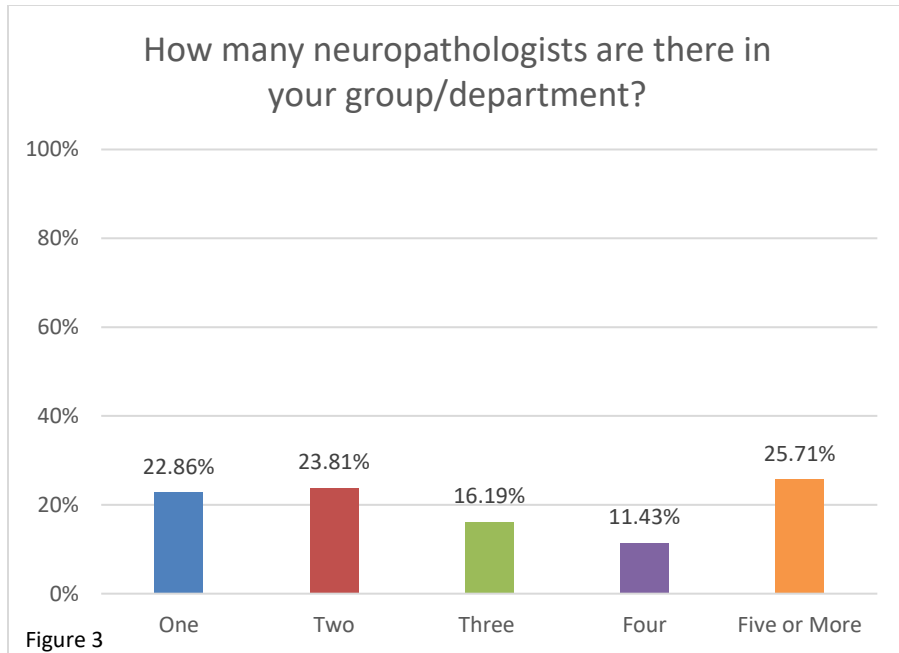
AOE Analysis of AANP’s Fall 2020 Membership Survey

A survey was sent to the membership base of the American Association of Neuropathologists (AANP) in the fall of 2020. This survey is used for planning of future annual meeting topics by providing a better understanding of current neuropathology practice characteristics. A total of 128 members provided responses to the 29 clinical assertion statement questions within the survey and the summary of these results are described below.

The survey asked individuals to provide responses to demographic questions, shown in figures 1-3, to help further contextualize the results.



Other includes: Retired (5), Medical Student (1), Volunteer (1), Animal/preclinical development in biopharma (1)



Clinical Assertion Statements

The survey asked members to rate 29 different clinical assertion questions using a 5-point Likert-type scale from 1=Disagree Completely to 5=Agree Completely, with a neutral option of 3=Neither Disagree nor Agree. These questions were developed to determine a member's level of knowledge regarding 10 separate topics in neuropathology. Data is presented as mean +/- standard deviation. Percentages indicate the number of responses in the incorrect/neutral position of total responses.

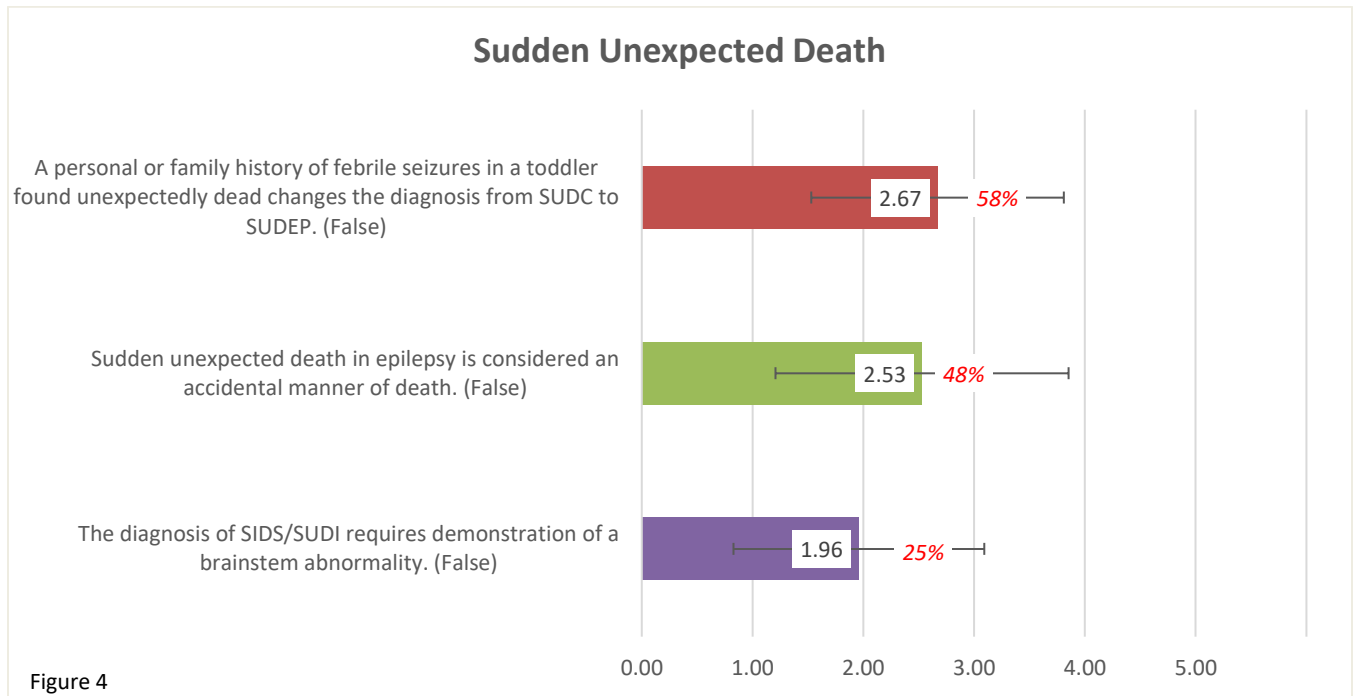


Figure 4 provides the results for the three questions evaluating knowledge in the area of **sudden unexpected death**. All three statements are false. All statements had mean scores in the desired direction. However, statement one had 58% of the respondents who answered at the neutral/incorrect position which may indicate where additional education is appropriate. In sum, areas of appropriate additional education include:

- A personal or family history of febrile seizures in a toddler found unexpectedly dead changes the diagnosis from SUDC to SUDEP. (False)

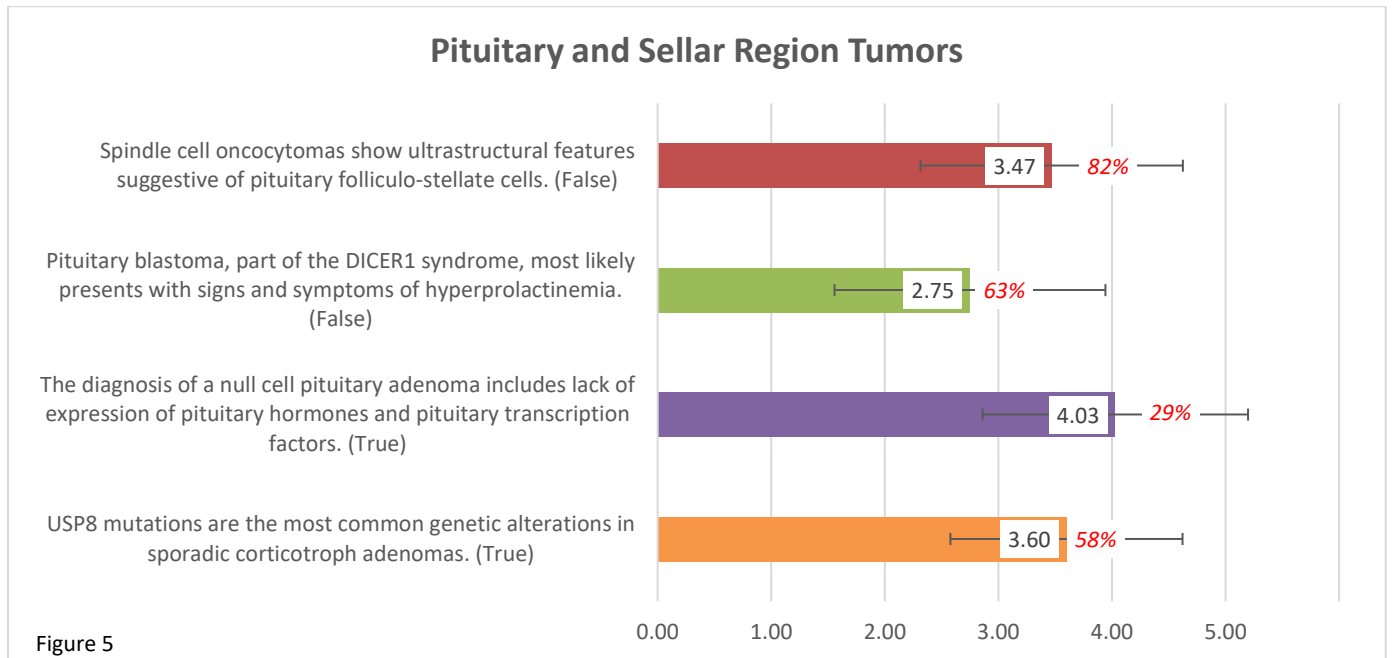


Figure 5 provides the results for the four questions evaluating knowledge in the area of **pituitary and sellar region tumors**. Statements one and two are false, while statements three and four are true. Statement one had a mean score on the incorrect side of the scale indicating that additional education is appropriate. Statements two and four had mean scores in the desired direction, however 63% and 58% of responses, respectively, were incorrect or neutral, indicating additional education is needed. Statement three had a mean score in the desired direction. In sum, areas of appropriate additional education include:

- Spindle cell oncocytomas show ultrastructural features suggestive of pituitary folliculo-stellate cells. (False)
- Pituitary blastoma, part of the DICER1 syndrome, most likely presents with signs and symptoms of hyperprolactinemia. (False)
- USP8 mutations are the most common genetic alterations in sporadic corticotroph adenomas. (True)

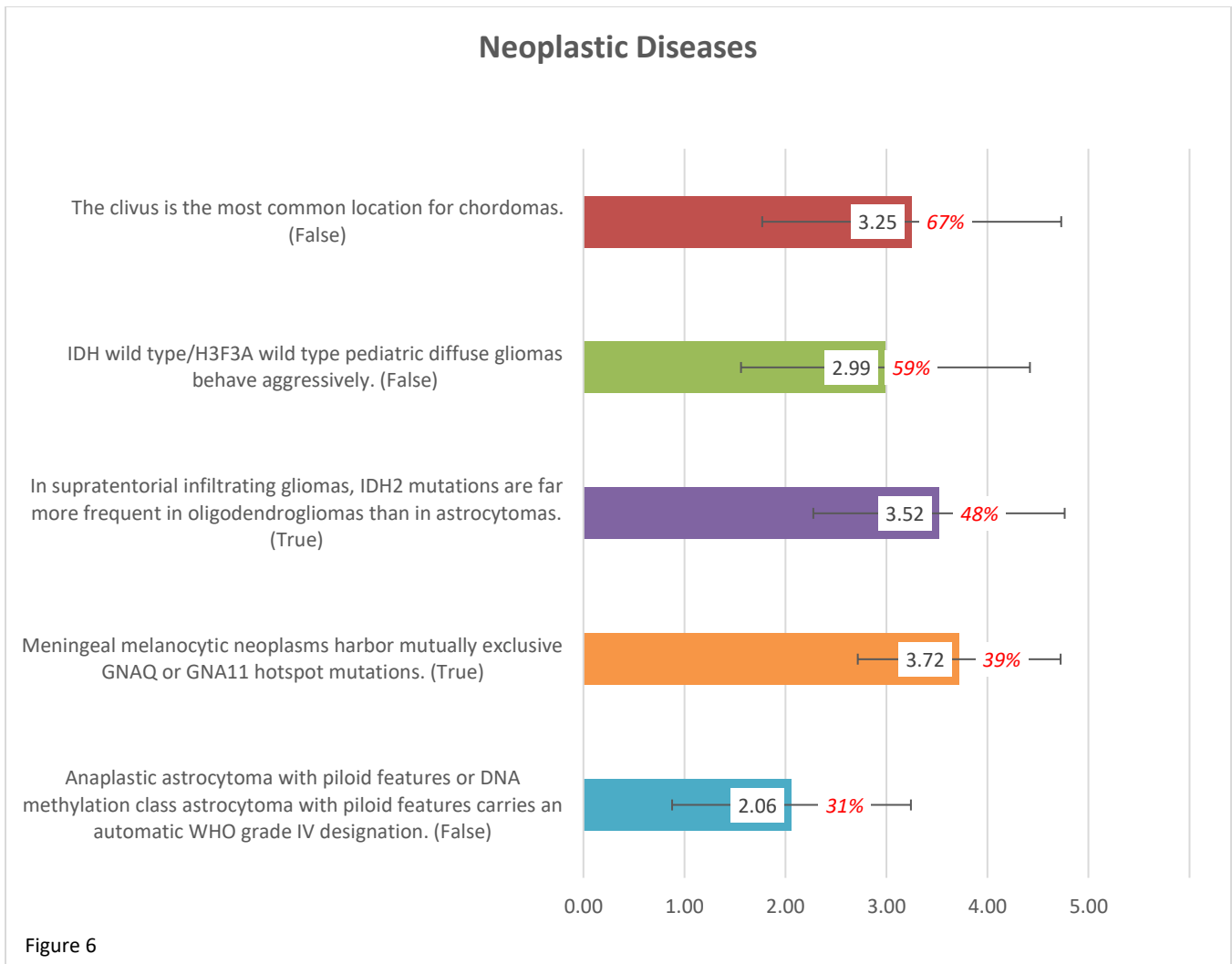


Figure 6 provides the results for the five questions evaluating knowledge in the area of **neoplastic diseases**. Statements one, two and five are false, while statements three and four are true. Statement one and two have a mean close to the neutral position, additionally, 67% and 59% of responses were incorrect or in the neutral position, respectively, indicating education is appropriate related to these statements. Statement three, four and five had a mean score in the desired direction. In sum, areas of appropriate additional education include:

- The clivus is the most common location for chordomas. (False)
- IDH wild type/H3F3A wild type pediatric diffuse gliomas behave aggressively. (False)

Neurodegenerative Disease and Age-Associated Brain Changes

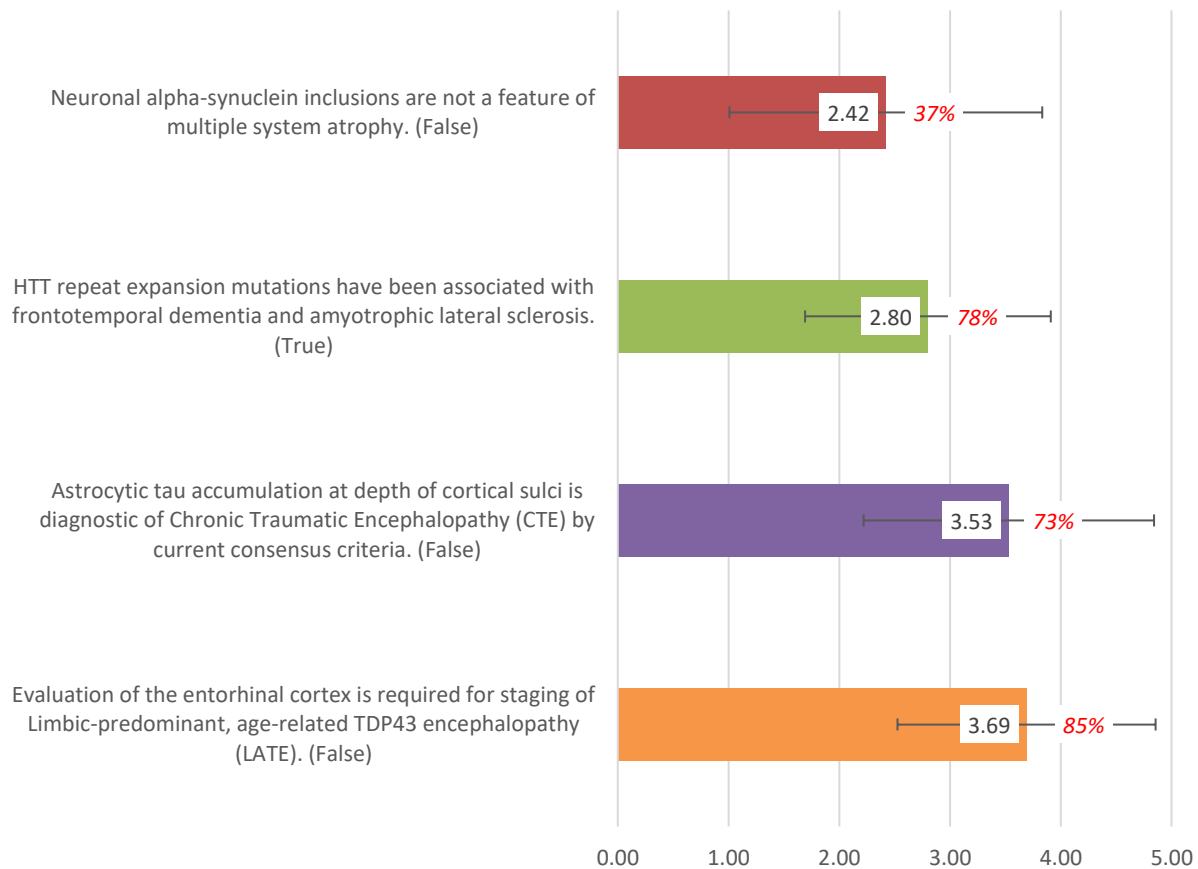


Figure 7

Figure 7 provides the results for the four questions evaluating knowledge in the area of **neurodegenerative diseases and age-associated brain changes**. Statements one, three and four are false, while statement two is true. Members selected responses in the desired direction for statement one. Statements two, three and four had a mean score on the incorrect side of the scale indicating additional education is appropriate:

- HTT repeat expansion mutations have been associated with frontotemporal dementia and amyotrophic lateral sclerosis. (True)
- Astrocytic tau accumulation at depth of cortical sulci is diagnostic of Chronic Traumatic Encephalopathy (CTE) by current consensus criteria. (False)
- Evaluation of the entorhinal cortex is required for staging of Limbic-predominant, age-related TDP43 encephalopathy (LATE). (False)

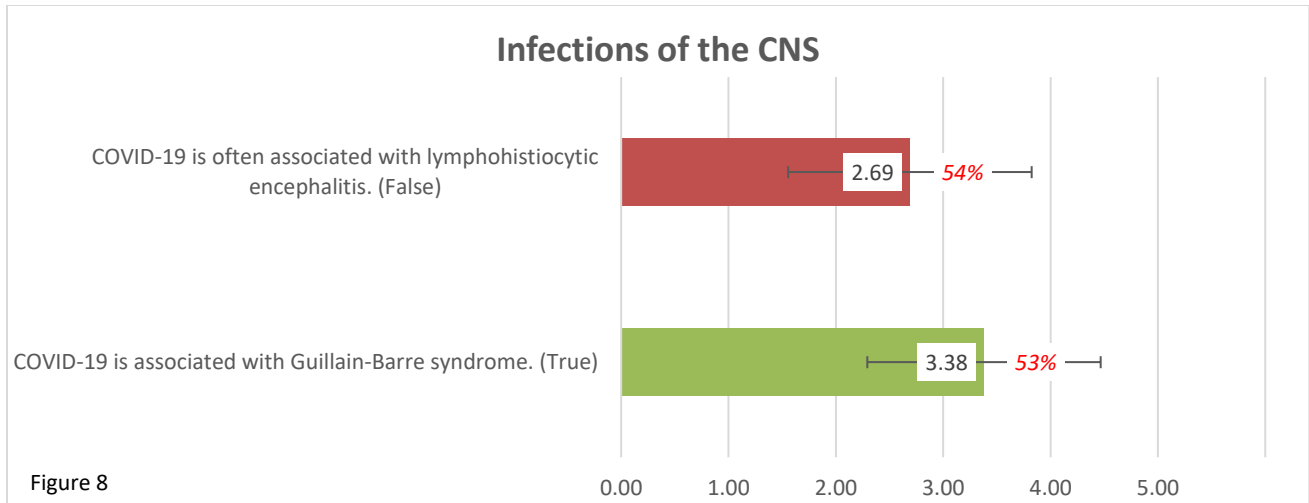


Figure 8 provides the results for the two questions evaluating knowledge in the area of **infections of the central nervous system**. Statement one is false and statement two is true. Statements one had a mean score in the desired direction, however 54% of responses were incorrect or neutral. Additionally, statement two had 53% of respondents answer either incorrectly or in the neutral position, indicating that education may be appropriate. In sum, areas of appropriate additional education include:

- COVID-19 is associated with Guillain-Barre syndrome. (True)
- COVID-19 is often associated with lymphohistiocytic encephalitis. (False)

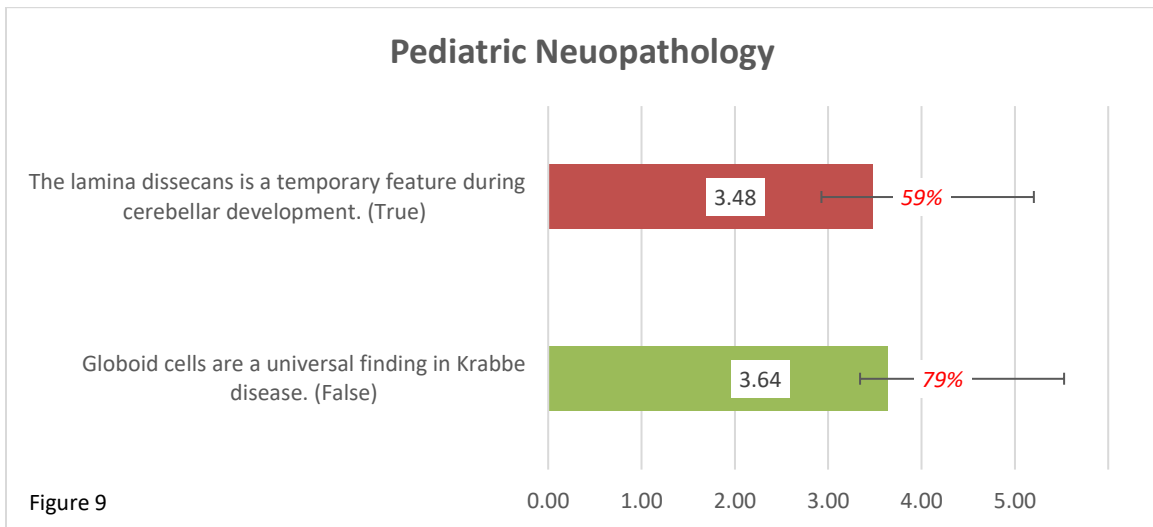


Figure 9 provides the results for the two questions evaluating knowledge in the area of **pediatric neuropathology**. Statement one is true and statement two is false. Statements one and two had mean scores close to the neutral position, and, 59% and 79%, respectively, of respondents answer in the incorrect or neutral position, indicating education is appropriate. In sum, areas of appropriate additional education include:

- Globoid cells are a universal finding in Krabbe disease. (False)
- The lamina dissecans is a temporary feature during cerebellar development. (True)

Muscle, Nerve and Forensic Neuropathology

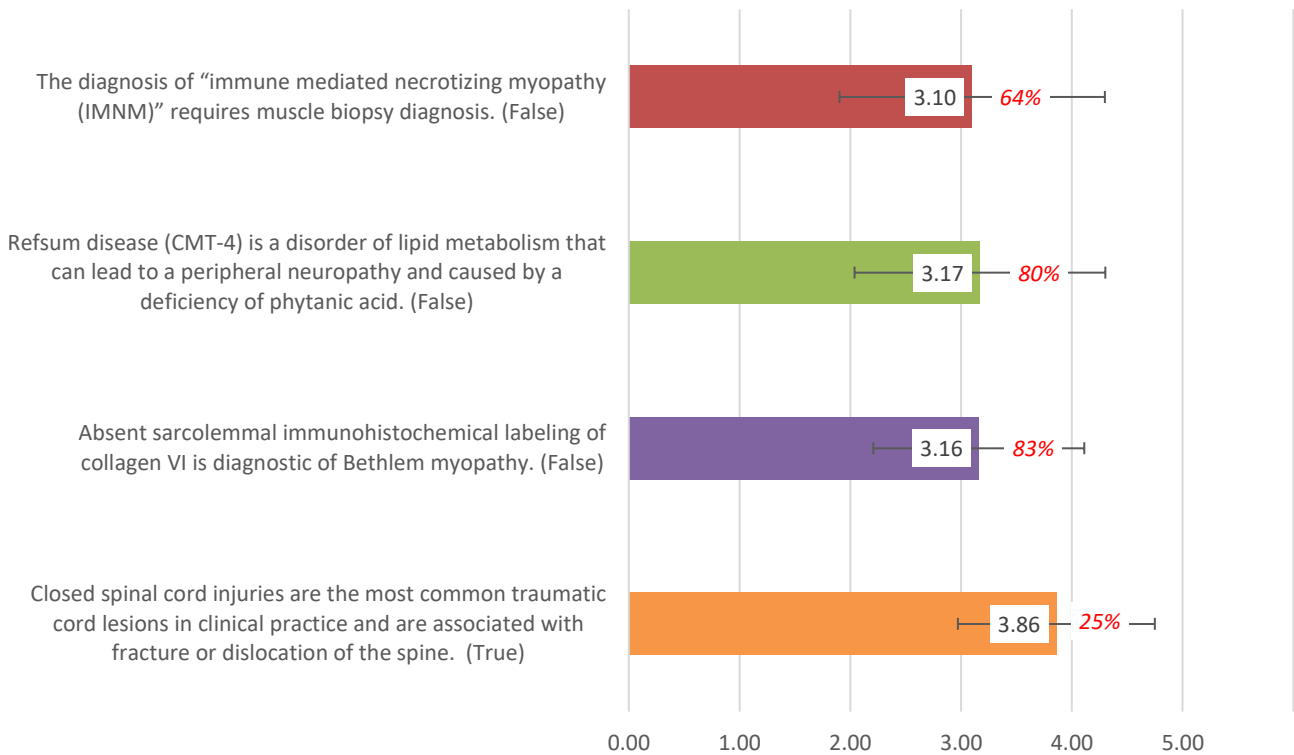


Figure 10

Figure 10 provides the results for the four questions evaluating knowledge in the areas of muscle, nerve and **forensic neuropathology**. Statement one through three are false, while statement four is true. Statements one through three had mean scores in the neutral position, additionally, 64%, 80% and 83%, respectively, of respondents answer in the incorrect or neutral position, indicating education is appropriate. Statement four had a mean in the desired direction. In sum, areas of appropriate additional education include:

- The diagnosis of "immune mediated necrotizing myopathy (IMNM)" requires muscle biopsy diagnosis. (False)
- Refsum disease (CMT-4) is a disorder of lipid metabolism that can lead to a peripheral neuropathy and caused by a deficiency of phytanic acid. (False)
- Absent sarcolemmal immunohistochemical labeling of collagen VI is diagnostic of Bethlem myopathy. (False)

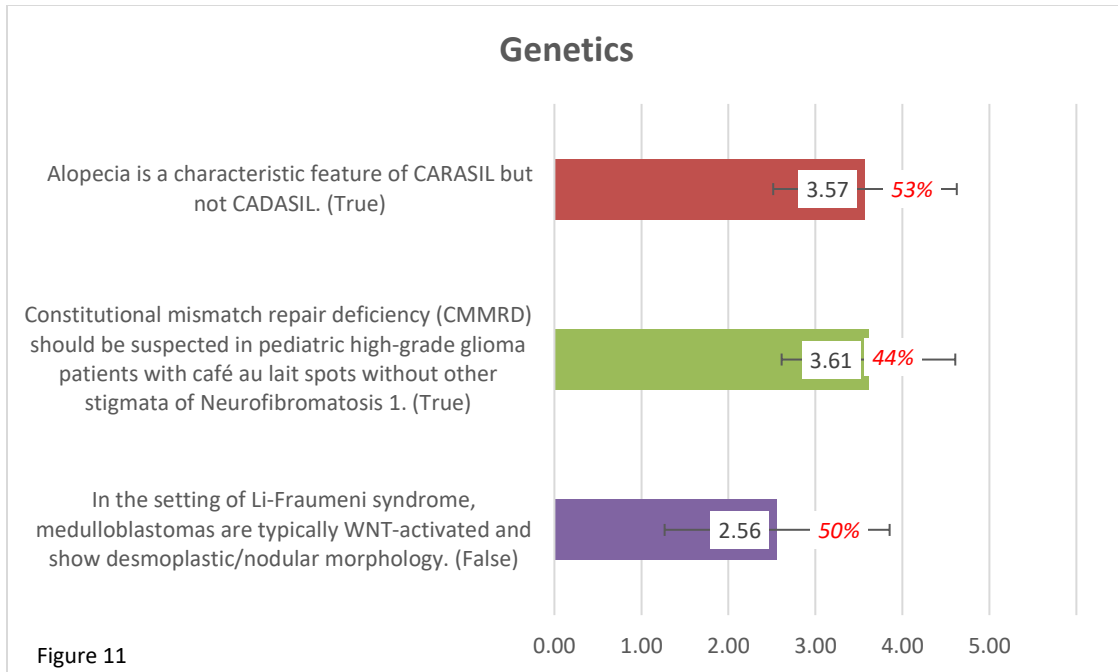


Figure 11 provides the results for the three questions evaluating knowledge in the area of **genetics**. Statement one and two are true, while statement three is false. All three statements had mean scores in the desired direction, however, statement one and three had 53% and 50%, respectively, of respondents answer in the neutral or incorrect position, indicating education is appropriate. In sum, areas of appropriate additional education include:

- Alopecia is a characteristic feature of CARASIL but not CADASIL. (True)
- In the setting of Li-Fraumeni syndrome, medulloblastomas are typically WNT-activated and show desmoplastic/nodular morphology. (False)

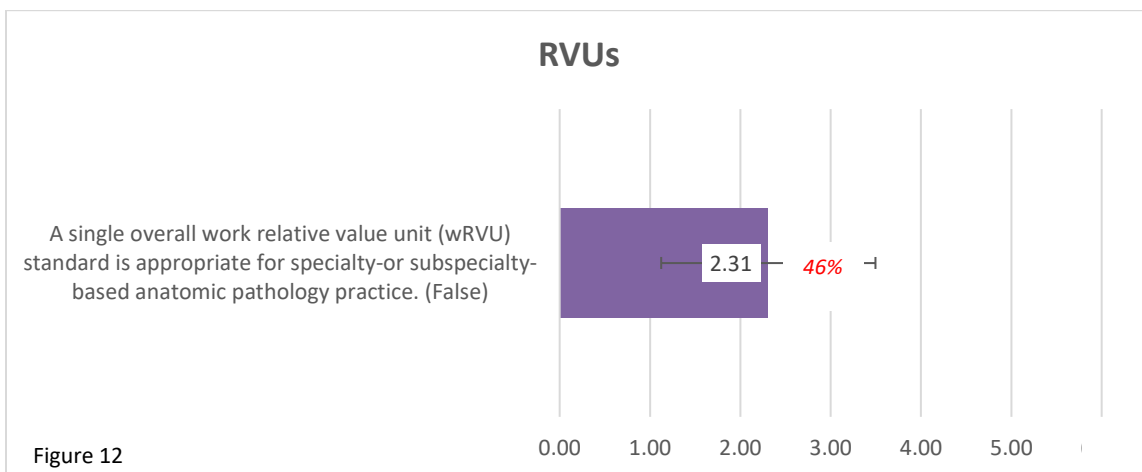


Figure 12 provides the results for the one question evaluating knowledge in the area of **relative value units (RVUs)**. The statement is false. This statement had mean scores in the desired direction, therefore no additional education is needed.

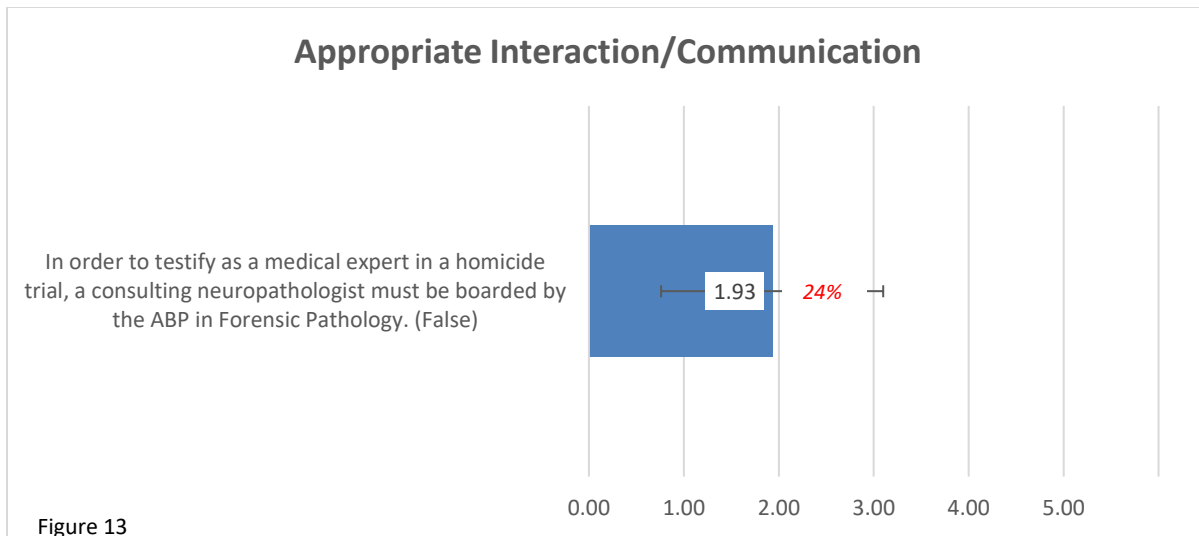


Figure 13 provides the results for the one question evaluating knowledge in the area of **communication**. The statement is false. This statement had a mean score in the desired direction.

Conclusion:

Based on the analysis of the 2020 Membership Survey, there were some statements where responses were close to neutral and many respondents answered in the neutral position which provides areas where there may be need for additional education. Further, several scores were on the opposite/wrong side of the scale. Both situations indicate that the following are areas of need for additional education:

- **Sudden Unexpected Death**
 - A personal or family history of febrile seizures in a toddler found unexpectedly dead changes the diagnosis from SUDC to SUDEP. (False statement, 58% unknown/incorrect responses)
- **Pituitary and Sellar Region Tumors**
 - Spindle cell oncocytomas show ultrastructural features suggestive of pituitary folliculo-stellate cells. (False statement, 82% unknown/incorrect responses)
 - Pituitary blastoma, part of the DICER1 syndrome, most likely presents with signs and symptoms of hyperprolactinemia. (False statement, 63% unknown/incorrect responses)
 - USP8 mutations are the most common genetic alterations in sporadic corticotroph adenomas. (True statement, 58% unknown/incorrect responses)
- **Neoplastic Diseases**
 - The clivus is the most common location for chordomas. (False statement, 67% unknown/incorrect responses)
 - IDH wild type/H3F3A wild type pediatric diffuse gliomas behave aggressively. (False statement, 59% unknown/incorrect responses)
- **Neurodegenerative Diseases and Age-associate Brain Changes**
 - Evaluation of the entorhinal cortex is required for staging of Limbic-predominant, age-related TDP43 encephalopathy (LATE). (False statement, 85% unknown/incorrect responses)
 - HTT repeat expansion mutations have been associated with frontotemporal dementia and amyotrophic lateral sclerosis. (True statement, 78% unknown/incorrect responses)

- Astrocytic tau accumulation at depth of cortical sulci is diagnostic of Chronic Traumatic Encephalopathy (CTE) by current consensus criteria. (False statement, 73% unknown/incorrect responses)
- **Infections of the CNS**
 - COVID-19 is often associated with lymphohistiocytic encephalitis. (False statement, 54% unknown/incorrect responses)
 - COVID-19 is associated with Guillain-Barre syndrome. (True statement, 53% unknown/incorrect responses)
- **Pediatric Neuropathology**
 - Globoid cells are a universal finding in Krabbe disease. (False statement, 79% unknown/incorrect responses)
 - The lamina dissecans is a temporary feature during cerebellar development. (True statement, 59% unknown/incorrect responses)
- **Muscle, Nerve and Forensic Neuropathology**
 - Absent sarcolemmal immunohistochemical labeling of collagen VI is diagnostic of Bethlem myopathy. (False statement, 83% unknown/incorrect responses)
 - Refsum disease (CMT-4) is a disorder of lipid metabolism that can lead to a peripheral neuropathy and caused by a deficiency of phytanic acid. (False statement, 80% unknown/incorrect responses)
 - The diagnosis of “immune mediated necrotizing myopathy (IMNM)” requires muscle biopsy diagnosis. (False statement, 64% unknown/incorrect responses)
- **Genetics**
 - Alopecia is a characteristic feature of CARASIL but not CADASIL. (True statement, 53% unknown/incorrect response)
 - In the setting of Li-Fraumeni syndrome, medulloblastomas are typically WNT-activated and show desmoplastic/nodular morphology. (False statement, 50% unknown/incorrect response)

Additional Survey Questions

The following data regarding prion disease and molecular testing for glioma diagnosis was collected in order for the AANP to gather data that may help the organization achieve *Accreditation with Commendation* through the Accreditation Council for Continuing Medical Education (ACCME) during its next reaccreditation cycle.

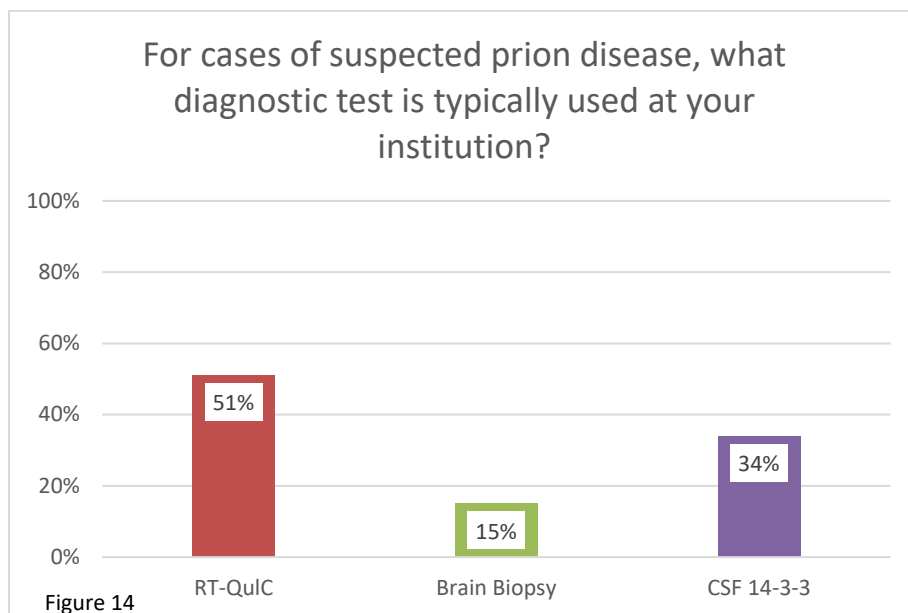


Figure 14 provides the results for the type of diagnostic tests used in cases of suspected prion disease at members' institutions. Most members, 51%, use Real-time quaking-induced conversion (RT-QulC) testing to determine the presence of prion disease.

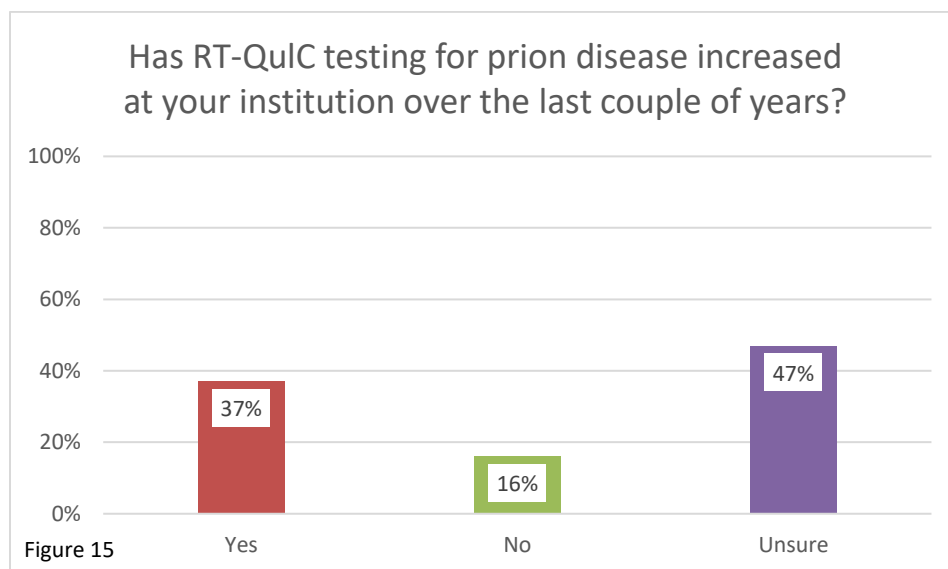


Figure 15 provides the results assessing the frequency of use of RT-QulC in members' institutions in recent years. Many members (47%) are unsure if there has been a change, while 37% do report an increase use of RT-QulC to test for suspected prion disease.

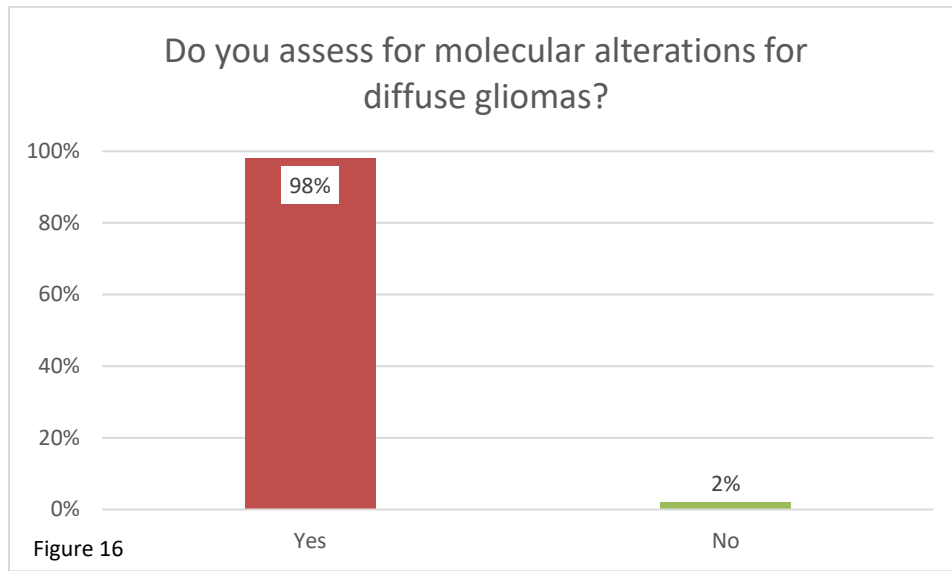


Figure 16 provides the results assessing the frequency of testing for molecular changes of diffuse gliomas at members' institutions. Testing can occur in-house or can be sent out to another lab. The overwhelming majority of members, 98%, indicated that this type of testing was used at their institution.

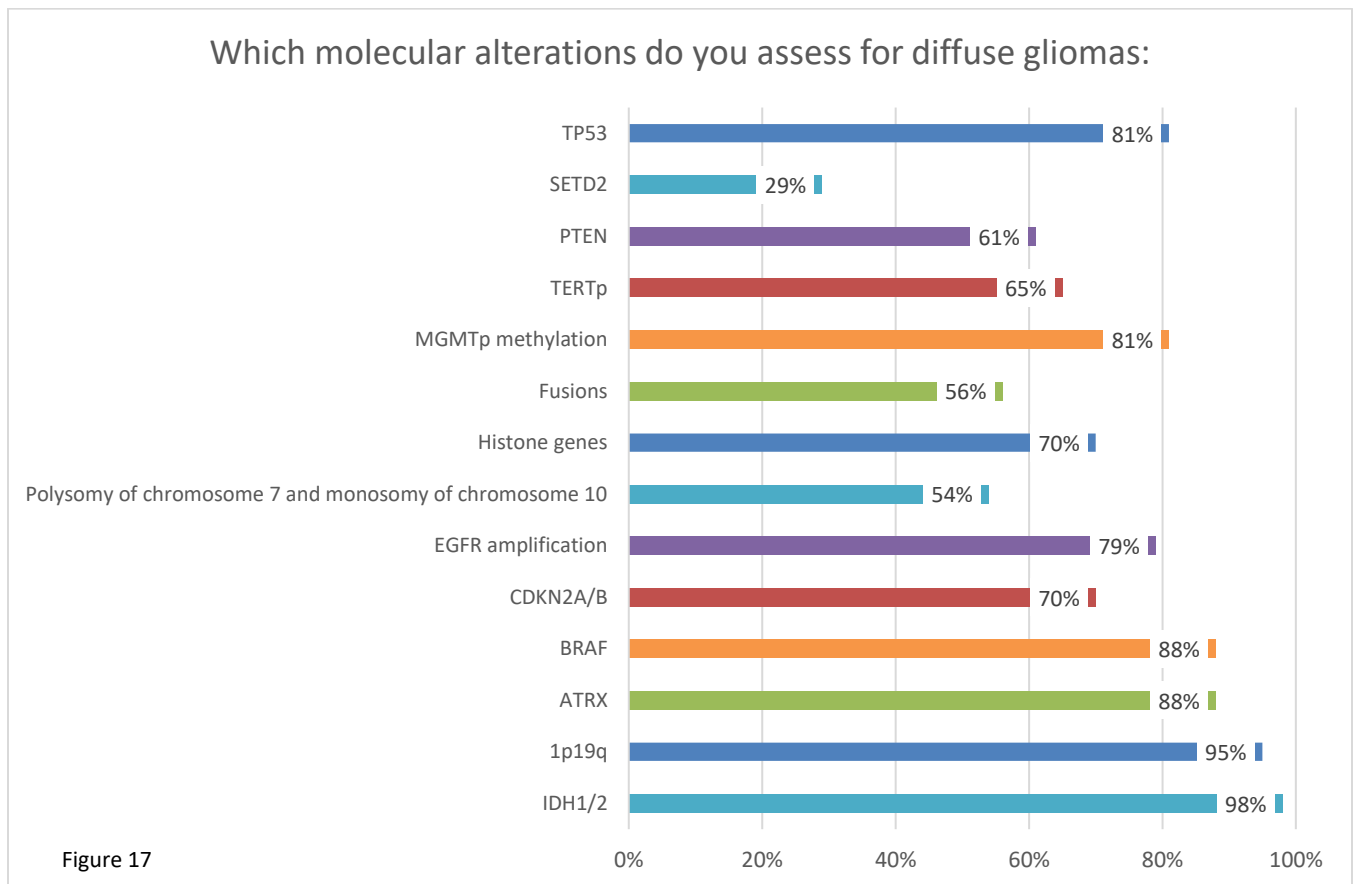


Figure 17 provides the results of which molecular markers members use to assess diffuse gliomas for molecular alterations. Testing can occur in-house or can be sent out to another lab. The most frequently used, with a response rate at >75% are: TP53, MGMTp methylation, EGFR amplification, BRAF, ATRX, 1p19q and IDH1/2.

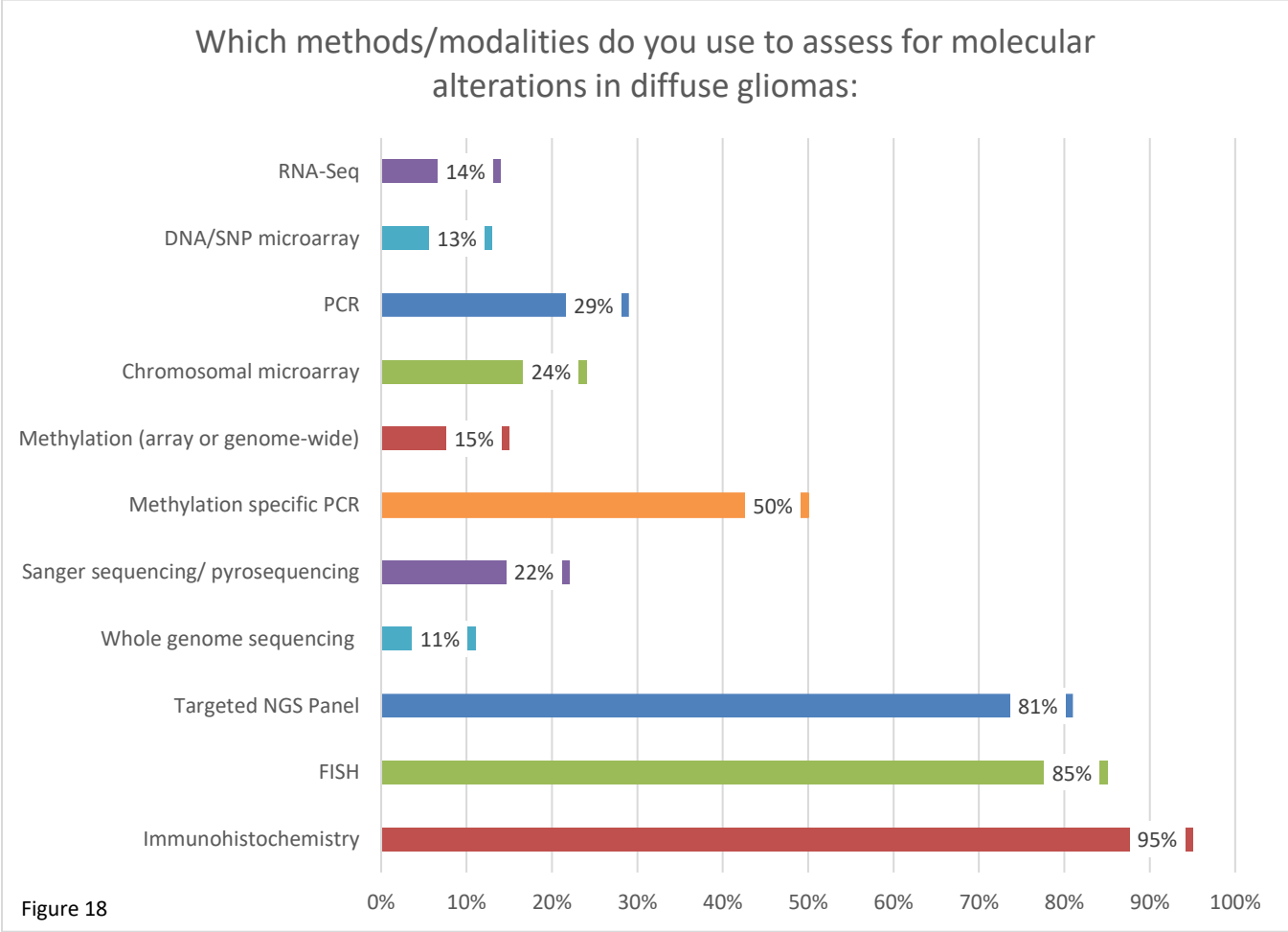


Figure 18

Figure 18 provides the results of type of testing members use to assess diffuse gliomas for molecular alterations. Testing can occur in-house or can be sent out to another lab. The most frequently used, with a response rate at >75% are: Targeted NGS panel, FISH and Immunohistochemistry.