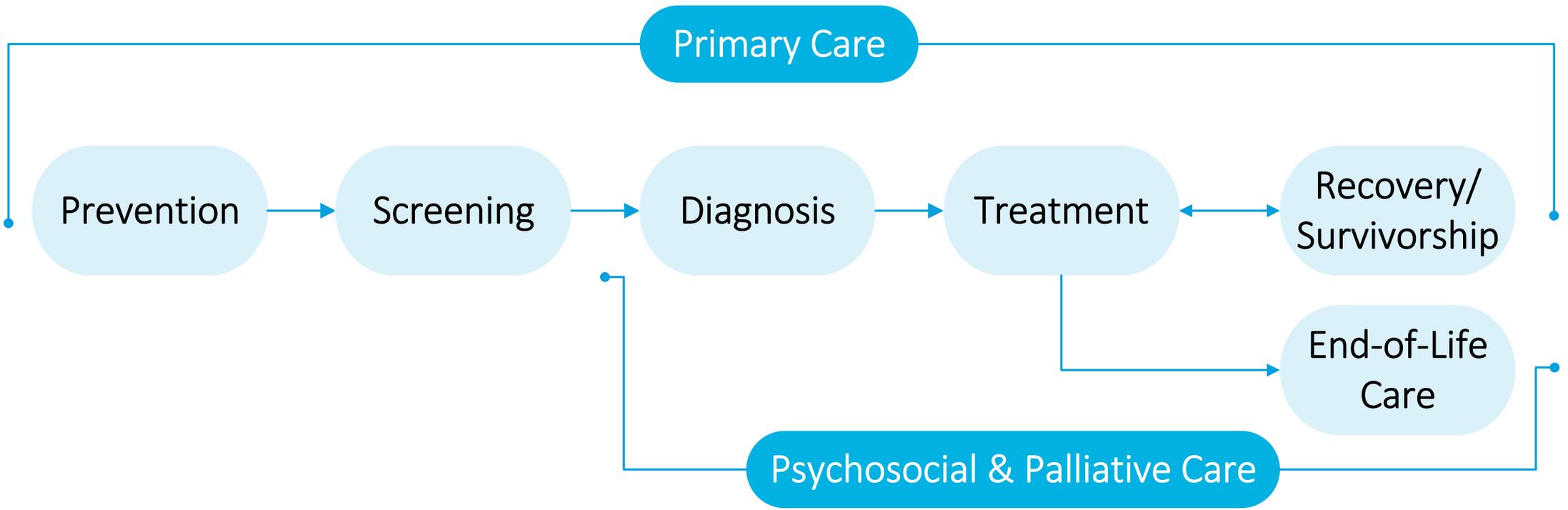
Glioma Reflexive Testing Algorithm

Version 2025.10



Ontario Health
Cancer Care Ontario

Target Population

CNS cancer patients who present with signs or symptoms suspicious of high or low grade gliomas.

Algorithm Considerations

- MGMT gene promoter methylation testing is recommended for all diffuse gliomas[1]
- Recommend a tiered approach with IHC first followed by sequencing if needed (e.g., BRAF fusions)[2]
- In a patient 55 years of age or older at diagnosis with a histologically classic glioblastoma not located in midline structures and with no history of a pre-existing lower-grade glioma, IDH1 R132H-Negative by immunohistochemistry is sufficient for diagnosis of "Glioblastoma, IDH-wildtype', without proceeding to *IDH1/2* sequencing[3]
- MMR IHC and H3G34 IHC is recommended in AYA patients with HGG (see page 4)
- In confirmed cases of MMRD, tumour mutational burden should be performed
- If the diagnosis is unconfirmed after following this molecular workup algorithm and neuropathologist opinion x2, consider genome-wide profiling of CpG methylation patterns[4]

[1]Kinslow CJ, Mercurio A, Kumar P, et al. Association of *MGMT* Promotor Methylation With Survival in Low-grade and Anaplastic Gliomas After Alkylating Chemotherapy. *JAMA Oncol.* Published online May 18, 2023. doi:10.1001/jamaoncol.2023.0990

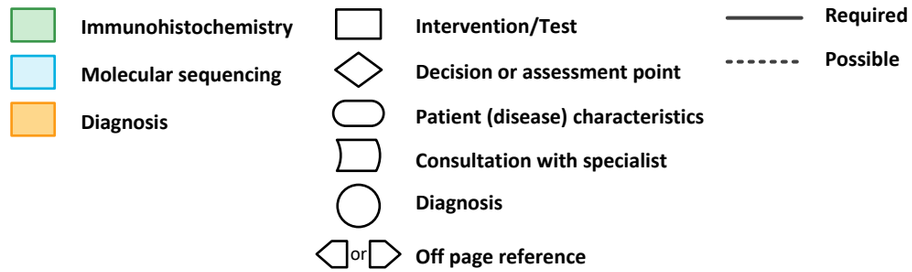
[2]Lim-Fat MJ, Macdonald M, Lapointe S, et al. Molecular testing for adolescent and young adult central nervous system tumors: A Canadian guideline. Front Oncol. 2022 Sep 23;12:960509. doi: 10.3389/fonc.2022.960509. PMID: 36249063; PMCID: PMC9559579.

[3]Louis DN, Aldape KD, Capper D, et al. Glioblastoma, IDH-wildtype, WHO Classification of Central Nervous System Tumours. 5th Edition. IARC; 2021, page 53.

[4]Capper D, Jones DTW, Sill M, et al. DNA methylation-based classification of central nervous system tumours. Nature. 2018 Mar 22;555(7697):469-474. doi: 10.1038/nature26000. Epub 2018 Mar 14. PMID: 29539639; PMCID: PMC6093218.

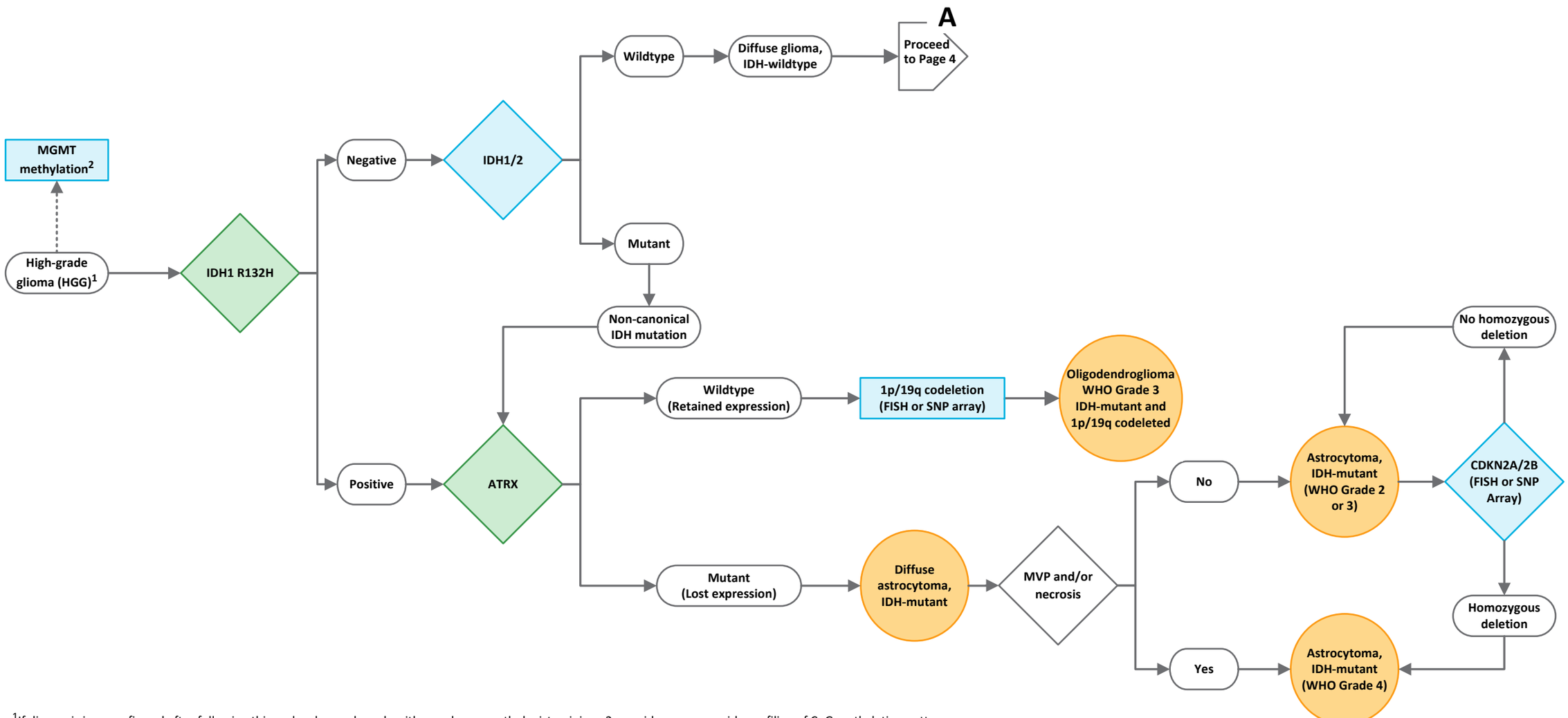
The following algorithms have been adapted from Lim-Fat MJ, Macdonald M, Lapointe S, et al. Molecular testing for adolescent and young adult central nervous system tumors: A Canadian guideline. Front Oncol. 2022 Sep 23;12:960509. doi: 10.3389/fonc.2022.960509. PMID: 36249063; PMCID: PMC9559579.

Algorithm Legend



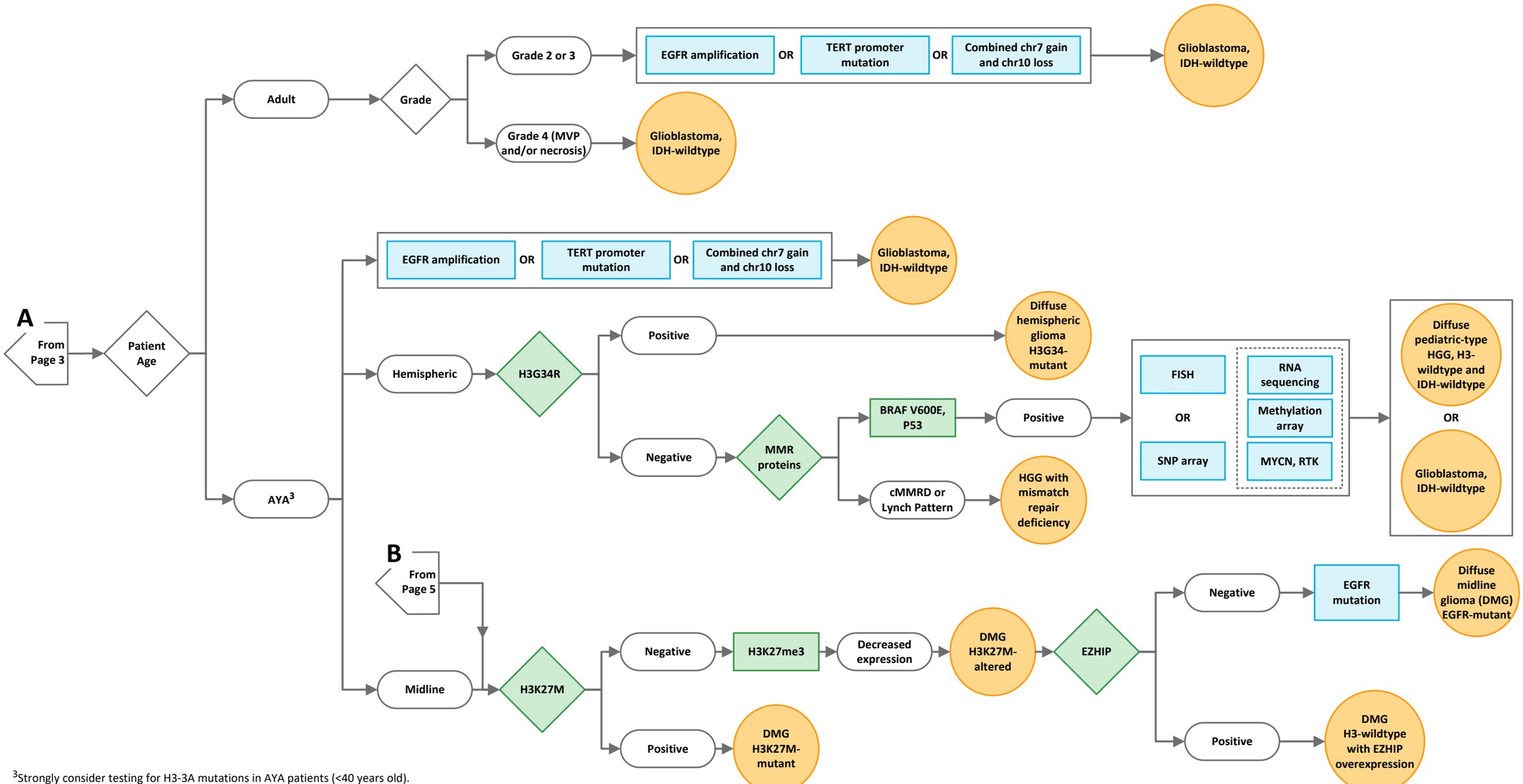
Abbreviations:

ATRX – alpha-thalassemia/mental retardation syndrome X-linked
AYA – adolescents and young adults
BRAF – B-Raf
CDKN – cyclin-dependent kinase inhibitor
cMMRD – constitutional mismatch repair deficiency
DMG – diffuse midline glioma
EGFR – epidermal growth factor receptor
EZHIP – EZH Inhibitory Protein
FGFR – fibroblast growth factor receptor
FISH – fluorescence in situ hybridization
HGG – high grade gliomas
IDH – isocitrate dehydrogenase
IHC – immunohistochemistry
LGG – low grade glioma
MAPK – mitogen-activated protein kinase
MGMT – O6-methylguanine-DNA methyl-transferase
MMR – mismatch repair
MMRD – mismatch repair deficiency
MYB – avian myelobalstosis viral oncogene
MYBL1 – MYB Proto-Oncogene Like 1
MYCN – N-myc proto oncogene
NTRK – neurotrophic tyrosine receptor kinase
PXA – pleomorphic xanthoastrocytoma
RNA – ribonucleic acid
RTK – receptor tyrosine kinase
SNP – single nucleotide polymorphism
TERT – telomerase reverse transcriptase
WHO – World Health Organization

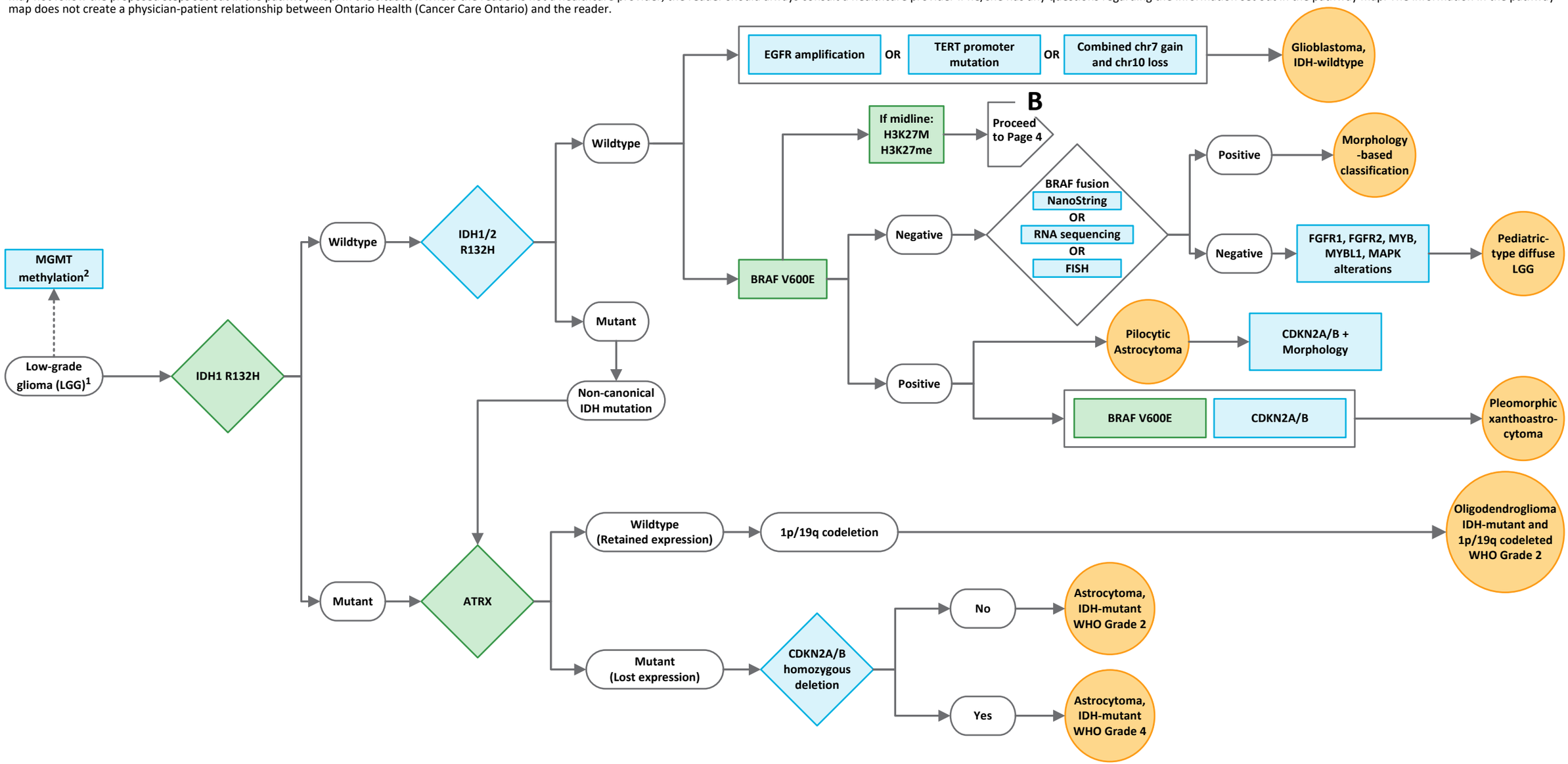


[1]If diagnosis is unconfirmed after following this molecular workup algorithm and neuropathologist opinion x2, consider genome-wide profiling of CpG methylation patterns.

[2]Testing for MGMT gene promoter methylation is encouraged in all diffuse gliomas.



[3]Strongly consider testing for H3-3A mutations in AYA patients (<40 years old).



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