

Isolated lateralized overgrowth and the need for tumor screening: A clinical practice resource of the American College of Medical Genetics and Genomics (ACMG).

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1 Article Isolated lateralized overgrowth and the need for tumor screening: A clinical practice resource of the American College of Medical Genetics and Genomics (ACMG) Erwin Angelika L. 1
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27 10 494125 101480 101480 09 06 2025 22 07 2026 25 09 2025 14 04 2026 Purpose: To provide
diagnostic guidance for individuals with lateralized overgrowth (LO) and implement appropriate
screening protocols. LO without a syndromic presentation is considered idiopathic isolated lateralized overgrowth (ILO).

We performed a literature search of LO syndromes and malignancy risk, reviewed existing guidelines and expert input.

We integrated 940 unique articles to form recommendations. We defined LO as significantly larger length and/or girth of aspect(s) of one side of the body compared to its contralateral side. It can be associated with somatic overgrowth syndromes. ILO was previously defined based on clinical features and deemed idiopathic by absence of molecular findings. Much of the tumor risk is likely due to specific LO syndromic causes now identified through improved diagnostic technologies, and therefore the tumor risk in idiopathic ILO is likely lower than previously accepted.

Mosaicism complicates molecular diagnosis for children with LO. However, conditions such as Beckwith-Wiedemann spectrum and PTEN -related hamartoma tumor syndrome necessitate routine tumor screening. Establishing a specific diagnosis via comprehensive molecular testing on affected tissue will guide screening and management. In cases of idiopathic ILO, location of the overgrowth, estimation of tumor risk, regional practice approaches and family concerns all play roles in determining tumor screening.