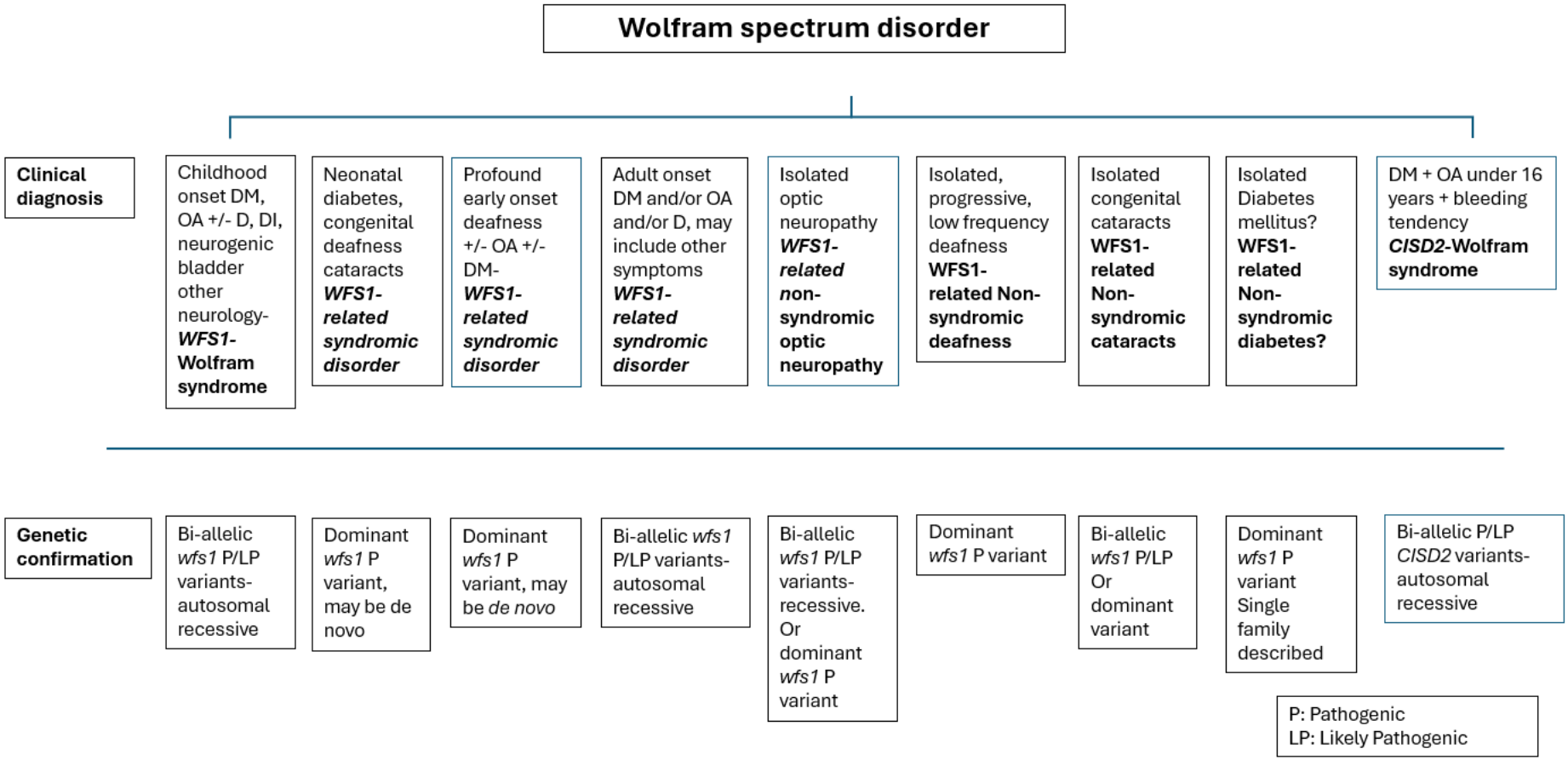

Wolfram spectrum disorder
Clinical diagnosis
Childhood onset DM, OA +/- D, DI, neurogenic bladder other neurology- WFS1-Wolfram syndrome
Neonatal diabetes, congenital deafness cataracts WFS1-related syndromic disorder
Profound early onset deafness +/- OA +/- DM- WFS1-related syndromic disorder
Adult onset DM and/or OA and/or D, may include other symptoms WFS1-related syndromic disorder
Isolated optic neuropathy WFS1-related non-syndromic optic neuropathy
Isolated, progressive, low frequency deafness WFS1-related Non-syndromic deafness
Isolated congenital cataracts WFS1-related Non-syndromic cataracts
Isolated Diabetes mellitus? WFS1-related Non-syndromic diabetes?
DM + OA under 16 years + bleeding tendency CISD2-Wolfram syndrome
Genetic confirmation
Bi-allelic wfs1 P/LP variants- autosomal recessive
Dominant wfs1 P variant, may be de novo
Dominant wfs1 P variant, may be de novo
Bi-allelic wfs1 P/LP variants- autosomal recessive
Bi-allelic wfs1 P/LP variants- recessive. Or dominant wfs1 P variant
Dominant wfs1 P variant
Bi-allelic wfs1 P/LP Or dominant variant
Dominant wfs1 P variant Single family described
Bi-allelic P/LP CISD2 variants- autosomal recessive
P: Pathogenic
LP: Likely Pathogenic
Wide spectrum of severity