

There are many rare genetic conditions which are associated with an increased risk of cancer, and they may involve multiple systems. This table includes general and cancer genetic conditions with “well-established” evidence of cancer risk (>1%) in children, adolescents, and young adults (age <21 years). Genetic conditions with a few case reports with cancer but no evidence for increased risk have been excluded. Any adult-onset cancer predisposition conditions that may be rarely associated with paediatric presentations have been included.

The table lists the conditions and associated genes, inheritance, mechanism of disease, and links to information about the condition (including management and cancer surveillance). It is to be used by clinical geneticists, genetic counsellors, general paediatricians, and paediatric oncologists. It aims to raise awareness of the potential paediatric cancer risk in general and cancer genetic conditions, and to assist interpretation of variants detected on genetic testing (as diagnostic or incidental findings).

The cancer risk estimation may vary within the same genetic condition due to genotype/phenotype correlations (i.e. different risk with different genes). Specific tumour risks for each condition are not documented as these may change rapidly with evolving knowledge. It is beyond the scope of the eviQ paediatric cancer genetics reference committee to develop risk management protocols for every condition in this table. This table is not intended to be comprehensive, and inclusion in the table does not indicate endorsement of the resource as accurate. Clinical judgement should be used when accessing information from these resources. The table should not be used for predictive testing or referrals.

If a clinician would like to request an addition or amendment of a genetic condition in the table, please contact feedback@eviq.org.au

Genetic conditions with established paediatric cancer risk

Genetic condition	Gene(s)	Inheritance	Mechanism of disease	Links to guidelines and/or additional information
<i>ALK</i> -related neuroblastoma tumour susceptibility	<i>ALK</i>	Dominant	Gain of function	https://www.ncbi.nlm.nih.gov/books/NBK24599/ https://www.eviq.org.au/p/3735
Ataxia-pancytopenia syndrome	<i>SAMD9L</i>	Dominant	Gain of function	https://www.ncbi.nlm.nih.gov/books/NBK435692/
Ataxia-telangiectasia	<i>ATM</i>	Recessive	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK26468/ https://pubmed.ncbi.nlm.nih.gov/26621971/
Beckwith–Wiedemann syndrome	<i>CDKN1C</i> 11p15.5 methylation defect	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1394/ https://www.eviq.org.au/p/3700
Bloom syndrome	<i>BLM</i>	Recessive	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1398/ https://pubmed.ncbi.nlm.nih.gov/30055079/
Bohring-Opitz syndrome	<i>ASXL1</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK481833/ https://pubmed.ncbi.nlm.nih.gov/28674120/ https://www.eviq.org.au/p/3702
Carney complex	<i>PRKAR1A</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1286/
<i>CEBPA</i> -associated familial acute myeloid leukaemia	<i>CEBPA</i>	Dominant	Dominant negative	https://www.ncbi.nlm.nih.gov/books/NBK47457/

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Congenital central hypoventilation syndrome	<i>PHOX2B</i> (non-polyalanine repeat mutation)	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1427/ https://www.eviq.org.au/p/3735
Constitutional mismatch repair deficiency	<i>MLH1</i> <i>MSH2</i> <i>MSH6</i> <i>PMS2</i>	Recessive	Loss of function	https://www.eviq.org.au/p/3655
Costello syndrome	<i>HRAS</i>	Monoallelic	Gain of function	https://www.ncbi.nlm.nih.gov/books/NBK1507/ https://pubmed.ncbi.nlm.nih.gov/35677617/
<i>CTR9</i> -related Wilms tumour	<i>CTR9</i>	Dominant	Unclear	https://pubmed.ncbi.nlm.nih.gov/25099282/ https://www.eviq.org.au/p/3702
Denys-Drash / Frasier syndrome	<i>WT1</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK556455/ https://pubmed.ncbi.nlm.nih.gov/28674120/ https://www.eviq.org.au/p/3702
Diamond-Blackfan anaemia	Multiple	Dominant & X-linked	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK7047/ https://pubmed.ncbi.nlm.nih.gov/18671700/
<i>DICER1</i> -related cancer predisposition syndrome	<i>DICER1</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK196157/ https://www.eviq.org.au/p/3653

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Down syndrome	<i>Trisomy 21</i>	N/A	N/A	https://www.downsyndrome.org.au/wp-content/uploads/2021/08/DSA_Health-tool_web_March-2021.pdf
Dyskeratosis congenita and related telomere biology disorders	Multiple	X-linked, Recessive, & Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK22301/ https://teamtelomere.org/telomere-biology-disorders-diagnosis-and-management-guidelines-downloads/
<i>ELP1</i> -related medulloblastoma susceptibility	<i>ELP1</i>	Dominant	Loss of function	https://pubmed.ncbi.nlm.nih.gov/32296180/
<i>ETV6</i> -related thrombocytopenia and predisposition to leukemia	<i>ETV6</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK564234/
Familial adenomatous polyposis	<i>APC</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1345/ https://www.eviq.org.au/p/178
Familial isolated pituitary adenoma	<i>AIP</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK97965/ https://www.eviq.org.au/p/4188
Familial platelet disorder with associated myeloid malignancy	<i>RUNX1</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK568319/ https://www.eviq.org.au/p/3905
Fanconi anaemia	Multiple	Recessive, X-linked, & Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1401/ https://www.fanconi.org/explore/clinical-care-guidelines
<i>GATA2</i> deficiency syndrome	<i>GATA2</i>	Dominant	Loss of function	https://www.eviq.org.au/p/4054

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Gorlin syndrome (Nevoid basal cell carcinoma syndrome)	<i>PTCH1</i> <i>SUFU</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1151/ https://www.eviq.org.au/p/748
<i>GPR161</i> -related medulloblastoma susceptibility	<i>GPR161</i>	Dominant	Loss of function	https://pubmed.ncbi.nlm.nih.gov/31609649/
Hereditary paraganglioma / pheochromocytoma syndrome	<i>MAX</i> <i>SDHA</i> <i>SDHB</i> <i>SDHC</i> <i>SDHD</i> <i>SDHAF2</i> <i>TMEM127</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1548/ https://www.eviq.org.au/p/4062 https://www.eviq.org.au/p/4066
Hyperparathyroidism-jaw tumour syndrome	<i>CDC73</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK3789/ https://www.eviq.org.au/p/3575
Juvenile polyposis syndrome	<i>BMPR1A</i> <i>SMAD4</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1469/ https://www.eviq.org.au/p/751
Juvenile polyposis of infancy	<i>Contiguous deletion of PTEN + BMPR1A</i>	Dominant	Loss of function	https://www.eviq.org.au/p/4306
Ligase 4 syndrome	<i>LIG4</i>	Recessive	Loss of function	https://pubmed.ncbi.nlm.nih.gov/30719430/

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Li–Fraumeni syndrome	<i>TP53</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1311/ https://www.eviq.org.au/p/1349
Mirage syndrome	<i>SAMD9</i>	Dominant	Gain of function	https://www.ncbi.nlm.nih.gov/books/NBK564655/
Mosaic variegated aneuploidy	<i>BUB1B</i> <i>TRIP13</i>	Recessive	Loss of function	https://pubmed.ncbi.nlm.nih.gov/28674120/ https://www.eviq.org.au/p/3702
Mulibrey nanism	<i>TRIM37</i>	Recessive	Loss of function	https://pubmed.ncbi.nlm.nih.gov/28674120/ https://www.eviq.org.au/p/3702
Multiple endocrine neoplasia type 1	<i>MEN1</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1538/ https://www.eviq.org.au/p/192
Multiple endocrine neoplasia type 2	<i>RET</i>	Dominant	Gain of function	https://www.ncbi.nlm.nih.gov/books/NBK1257/ https://www.eviq.org.au/p/1526
Multiple endocrine neoplasia type 4	<i>CDKN1B</i>	Dominant	Loss of function	https://www.eviq.org.au/p/192
Neurofibromatosis type 1	<i>NF1</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1109/ https://www.eviq.org.au/p/752
Neurofibromatosis type 2	<i>NF2</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1201/ https://www.eviq.org.au/p/1910

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Nijmegen breakage syndrome	<i>NBN</i>	Recessive	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1176/
Noonan syndrome	Multiple	Dominant & Recessive	Gain of function (monoallelic) Loss of function (Recessive)	https://www.ncbi.nlm.nih.gov/books/NBK1124/ https://rasopathiesnet.org/wp-content/uploads/2014/01/265_Noonan_Guidelines.pdf
Perlman syndrome	<i>DIS3L2</i>	Recessive	Loss of function	https://pubmed.ncbi.nlm.nih.gov/23613427/ https://pubmed.ncbi.nlm.nih.gov/28674120/ https://www.eviq.org.au/p/3702
Peutz–Jeghers syndrome	<i>STK11</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1266/ https://www.eviq.org.au/p/395
<i>PTEN</i> hamartoma syndrome (Cowden syndrome)	<i>PTEN</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1488/ https://www.eviq.org.au/p/546
<i>REST</i> -related Wilms tumour	<i>REST</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1294/ https://www.eviq.org.au/p/3702
Retinoblastoma	<i>RB1</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1452/ https://www.eviq.org.au/p/3704

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Rhabdoid tumour predisposition syndrome	<i>SMARCA4</i> <i>SMARCB1</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK469816/ https://www.eviq.org.au/p/3742 https://www.eviq.org.au/p/3743
Rothmund–Thomson syndrome	<i>ANAPC1</i> <i>RECQL4</i>	Recessive	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1237/
Schwannomatosis	<i>LZTR1</i> <i>SMARCB1</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK487394/ https://pubmed.ncbi.nlm.nih.gov/28620005/
Schinz-Giedion syndrome	<i>SETBP1</i>	Dominant	Gain of function	https://pubmed.ncbi.nlm.nih.gov/28346496/ https://pubmed.ncbi.nlm.nih.gov/28620009/
Shwachman-Diamond syndrome	<i>DNAJC21</i> <i>EFL1</i> <i>SBDS</i> <i>SRP54</i>	Recessive & Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1756/ https://pubmed.ncbi.nlm.nih.gov/22191555/
Simpson–Golabi–Behmel syndrome	<i>GPC3</i>	X-linked	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1219/ https://pubmed.ncbi.nlm.nih.gov/28674120/ https://www.eviq.org.au/p/3702
Sotos syndrome	<i>NSD1</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1479/
Tatton-Brown-Rahman syndrome	<i>DNMT3A</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK581652/

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<i>TRIM28</i> -related Wilms tumour	<i>TRIM28</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1294/ https://www.eviq.org.au/p/3702
Tuberous sclerosis complex	<i>TSC1</i> <i>TSC2</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1220/ https://pubmed.ncbi.nlm.nih.gov/34399110/
Von Hippel–Lindau syndrome	<i>VHL</i>	Dominant	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1463/ https://www.eviq.org.au/p/397
WAGR syndrome	<i>11p13 deletion</i> (<i>WT1</i> + <i>PAX6</i>)	Dominant	Loss of function	https://pubmed.ncbi.nlm.nih.gov/28674120/ https://www.eviq.org.au/p/3702
Weaver syndrome	<i>EZH2</i>	Dominant	Unknown	https://www.ncbi.nlm.nih.gov/books/NBK148820/
Werner syndrome	<i>WRN</i>	Recessive	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1514/
Xeroderma pigmentosa	Multiple	Recessive	Loss of function	https://www.ncbi.nlm.nih.gov/books/NBK1397/

The information contained in this document is based on the highest level of available evidence and consensus of the eviQ reference committee regarding their views of currently accepted approaches to care or treatment. Any clinician seeking to apply or consult this document is expected to use independent clinical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use is subject to eviQ's disclaimer available at www.eviq.org.au