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### Screening for tumor predisposition syndromes in childhood cancer

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# CHAPTER 4

## **Consequences of diagnosing a tumor predisposition syndrome in children with cancer: A literature review**

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## **ABSTRACT**

Up to 8.5% of children with cancer have a genetic cause for their cancer: a tumor predisposition syndrome (TPS). Diagnosing a TPS is of great importance, as it may have major consequences for clinical care. Patients with TPSs require specific monitoring and management. We present an overview of the cancer related and non-cancer related consequences for the 36 most common TPSs.

## INTRODUCTION

A tumor predisposition syndrome (TPS) is a syndrome in which there is an increased susceptibility (typically  $\geq 5\%$ ) to develop cancer.<sup>1</sup> In at least 8.5% of all patients who develop cancer as a child, a TPS is the underlying cause of this cancer.<sup>2,3</sup> It is of great importance to recognize a TPS, not only for the understanding of the cause of the cancer, but also because of its clinical consequences. In some TPSs, a modification in therapy for the cancer is needed, for example when radiotherapy is contraindicated or when an adjustment of chemotherapy dose is advised. Furthermore, for several TPSs a surveillance program is indicated for the early recognition of other malignancies. The diagnosis of a TPS can also lead to the recognition and treatment of signs and symptoms unrelated to the cancer, such as neurological or immunological problems. Lastly, the diagnosis of a TPS can ensure proper genetic counselling for family members.

A TPS can be suggested by several factors, such as the family history and the tumor type. Some tumor types are highly associated with a TPS, e.g. adrenocortical tumors and choroid plexus carcinomas in Li-Fraumeni syndrome. Nevertheless, the recognition of a TPS remains a challenging issue. It is proposed that the presence of a TPS should be evaluated in every child with cancer, preferably by consultation of a clinical geneticist.<sup>4,5</sup> However, research shows that not all children with cancer are referred to the clinical geneticist by the pediatric oncologist, and half of the TPSs in children with cancer are missed.<sup>6</sup>

Here we provide an overview of the consequences of diagnosing the most common TPSs. Knowledge of consequences of a TPS may lead to a more frequent referral to a clinical geneticist and should ensure optimal care for each child with cancer.

## MATERIALS AND METHODS

### Tumor Predisposition Syndromes identification

For the identification of the TPSs with dysmorphic features, we searched the Winter-Baraitser Dysmorphology Database (WBDD)<sup>7</sup> and the textbook Gorlin's Syndromes of the Head and Neck,<sup>8</sup> as described previously.<sup>9</sup> In addition, we performed a literature search using PubMed, to also include TPSs without dysmorphic features. This methodology is described in detail elsewhere<sup>10</sup>.

We included syndromes with a described cancer incidence of at least 5% and a minimum of 100 affected individuals reported in literature.<sup>1</sup> In addition, we included syndromes

with 50 to 100 affected individuals described in literature, in order to allow inclusion of recently described TPSs as well. To avoid the inclusion of syndromes in which causality between the cancer and the syndrome was still uncertain, we included the latter group of syndromes with 50-100 reported individuals only if cancer incidence was 10% or higher, which admittedly was an arbitrary choice. In addition, the tumor should have been described occurring between 0-18 years at least once.

### **Consequences of TPSs**

We searched the WBDD and Gorlin's Syndromes of the Head and Neck for relevant information regarding the consequences of each TPS. Furthermore we searched in GeneReviews<sup>®</sup>,<sup>11</sup> the textbook Management of Genetic Syndromes,<sup>12</sup> and the Orphanet database.<sup>13</sup> In addition we searched the Dutch Foundation Detection of Hereditary Tumors ([www.stoet.nl](http://www.stoet.nl)), the Dutch website for guidelines for oncological care in The Netherlands ([www.oncoline.nl](http://www.oncoline.nl)) and the National Comprehensive Cancer Network ([www.nccn.org](http://www.nccn.org)) and PubMed for suggestions for cancer surveillance and follow-up in children.

### **Data Selection**

For each syndrome we collected the most common associated pediatric cancers and the management and recommendations schedules. We selected all data regarding consequences which might be missed if the TPS would not have been diagnosed or for which monitoring and/or treatment are necessary.

These consequences were divided in cancer related and in non-cancer related. Cancer related consequences are the recommendations for therapy and surveillance to ensure early recognition of recurrences or additional malignancies. The non-cancer related consequences are recommendations regarding development, organ anomalies and dysfunctions, and immunologic, metabolic, and neurologic functioning.

## **RESULTS**

### **Identification of TPSs**

In total 33 syndromes were selected in which more than 100 individuals have been described, and in which cancer occurs in 5% or more of affected individuals. Three additional syndromes were described in 50-100 individuals, with a cancer incidence of 10% or more (Supplementary Table S1). We provide an overview of all cancer and non-cancer related consequences in Table 1.

**TABLE 1.** Consequences of TPs subdivided into cancer and non-cancer related issues

SYNDROME	CANCER RELATED			NON- CANCER RELATED			Management and recommendations
	Cancer type	Cancer surveillance (main refe-rences)	Therapy adjustment	Developmental	Organ anomalies	Immunologic (I) Metabolic (M) Neurologic (N)	
Ataxia telangiectasia	ALL, Lym		+	+		I, N	Physical therapy, monitoring immune status
Beckwith-Wiedemann syndrome	WT, Hbl, ACC, RMS, NBl	14-16			+		Speech therapy, management asymmetric body growth, monitoring organ anomalies
Bloom syndrome	ALL, AML, Lym, CRT, BC		+	+	+	I, M	Nutritional supplementation, avoid excessive sun exposure
Cardiofaciocutaneous syndrome	ALL			+	+	N	Management growth and cognitive development, monitoring neurologic and organ anomalies
Congenital central hypoventilation syndrome	NBl	17			+	N	Ventilation support optimization, monitoring organ anomalies, avoid swimming and alcohol
Const. Mismatch Repair-Deficiency syndrome*	AML, ALL, BrT, CRT, Lym	18,19			+		Monitoring organ anomalies
Costello syndrome	RMS, NBl, BlaC	20-22		+	+	N	Monitoring growth, monitoring developmental and organ anomalies, physical therapy, management facial papillomata
DICER 1 syndrome	PPB, RMS, SLCT, PihBl, PihBl, ThyCa, WT, CN				+		Management nasal chondro-mesenchymal hamartoma, monitoring organ anomalies
Down syndrome	AML, ALL		+	+	+		Physical, psychomotor and speech therapy, monitoring organ anomalies
Dyskeratosis congenita	MDS, AML, SCC			+	+		Pulmonary function tests; routine dental screening
Familial adenomatous polyposis**	CRT, Desm, HBl, ThyCa	23,24			+		Sigmoidoscopy, colonoscopy
Familial isolated pituitary adenoma	PitAd						Monitoring pituitary function
Familial neuroblastoma	NBl	25			+		Monitoring organ anomalies
Familial or isolated WT1 mutations***	WT, GoBl	26			+		Monitoring organ anomalies

TABLE 1. (continued)

SYNDROME	CANCER RELATED		NON-CANCER RELATED				Management and recommendations
	Cancer type	Cancer surveillance (main references)	Therapy adjustment	Developmental anomalies	Immunologic (I) Metabolic (M) Neurologic (N)		
Familial pheochromocytoma/paragangliocytoma	Pheo, PGL	27					Avoid tobacco products
Familial retinoblastoma	RB, OS		+	+			Monitoring by ophthalmologist
Fanconi anemia	AML, MDS, SCC			+			Monitoring of growth and pubertal development, monitoring BMF and organ anomalies
Gorlin syndrome	BCC, MB	28		+			Routine orthopantomograms, monitoring skin, avoid sun exposure
Lateralized overgrowth	WT	14			+		Management asymmetric body growth
Li-Fraumeni syndrome	RMS, OS, BrT, ACC, BC, ThyCa	29,30		+			Avoid excessive sun exposure
Multiple endocrine neoplasia type 2	Medullary ThyCa, Pheo, PTA	31,32			+		Prophylactic thyroidectomy for individuals with an identified germline RET pathogenic variant.
Neurofibromatosis type 1	ONG, MPNST, BrT	33,34		+			Ophthalmologic evaluation, management neurofibromas
Neurofibromatosis type 2	Men, Ep	35,36		+		N	Hearing evaluation, ophthalmologic evaluation
Nijmegen Breakage syndrome	Lym, MB, glioma, RMS			+		I	Management growth and development, monitoring organ anomalies
Peutz-Jeghers syndrome	GIC, SLCT testis, BC, PC, Gyc	37			+		Management polyps
PTEN hamartoma tumor syndrome****	CDG, non-medullary ThyCa, BC, ECa, RCC	38,39		+			Monitoring skin, monitoring organ and developmental anomalies
Rhabdoid tumor predisposition syndrome	RhT, CPC, MB	40					
Rothmund-Thomson syndrome	OS, BCC, SCC				+		Monitoring of skin, use sunscreen with UVA and UVB protection, avoid excessive sun exposure

**TABLE 1. (continued)**

SYNDROME	CANCER RELATED		NON- CANCER RELATED			Management and recommendations
	Cancer type	Cancer surveillance (main references)	Therapy adjustment CT RT	Developmental anomalies	Immunologic (I) Metabolic (M) Neurologic (N)	
Rubinstein-Taybi syndrome	RMS, Pheo, Men, BRT			+		Management developmental disabilities, monitoring growth, senses and organ anomalies, dental examination
Shwachman-Diamond syndrome	MDS, AML	41		+	I	Monitoring orthopedic complications, monitoring organ anomalies
Simpson Golabi Behmel syndrome	WT, HBl, NBl, GoBl, HCC	42,43	+	+		Monitoring organ anomalies, neurodevelopmental assessment
Turner syndrome	GoBl			+	M	Monitoring organ anomalies, growth hormone therapy, psychotherapy
Von Hippel-Lindau syndrome	HB, RCC, Pheo, PGL, ELST	44				Avoid tobacco products
WAGR syndrome	WT, GoBl	26,45	+	+	N	Early developmental assessment, monitoring organ anomalies
Werner syndrome	STS, OS, Mel, ThyrcA			+	M	Monitoring organ anomalies, screening DM2
Xeroderma pigmentosa	BCC, SCC, Mel			+		Skin examinations, avoid total sun exposure, vitamin D supplementation, monitoring eye anomalies

Abbreviations: ACC, adrenocortical carcinoma; ALL, acute lymphoblastic leukemia; AML, acute myeloblastic leukemia; BC, breast cancer; BCC, basal cell carcinoma; Blac, bladder carcinoma; BMF, bone marrow failure; BRT, brain tumor; CDG, cerebellar dysplastic gangliocytoma; CN, cystic nephroma; cons, constitutional; CPC, choroid plexus carcinoma; CRT, colorectal tumor; CT, chemotherapy; Desm, desmoid tumor; DM2, Diabetes Mellitus Type 2; Eca, endometrial carcinoma; ELST, endolymphatic sac tumor; Ep, ependymoma; Glc, gastrointestinal cancer; GoBl, gonadoblastoma; GYC, gynecologic cancer; HB, hemangioblastoma; HBl, hepatoblastoma; HCC, hepatocellular carcinoma; Lym, lymphoma; MB, medulloblastoma; MDS, myelodysplastic syndrome; Mel, melanoma; Men, meningioma; MPNST, malignant peripheral nerve sheath tumor; NBl, neuroblastoma; Od, odontoma; ODG, oligodendroglioma; ONG, optic nerve glioma; OS, osteosarcoma; PC, pancreas cancer; PGL, paraganglioma; Pheo, pheochromocytoma; PinBl, pineoblastoma; PitAd, pituitary adenoma; PitBl, pituitary blastoma; PPB, pleuropulmonary blastoma; PSG, presacral ganglioma; PTA, parathyroid adenoma; RB, retinoblastoma; RCC, renal cell carcinoma; RMS, rhabdomyosarcoma; RT, radiotherapy; RHT, rhabdoid tumor; SCC, squamous cell carcinoma; SLC1, Sertoli-Leydig cell tumor; STS, soft tissue sarcoma; TestCa, testicular carcinoma; ThyrcA, thyroid carcinoma; WT, Wilms tumor; \*Including Turcot syndrome, Bi-allelic Lynch syndrome; \*\* Including Gardner syndrome; \*\*\* Including Denys Drash syndrome, Frasier syndrome, and isolated WT1 germline mutations; \*\*\*\* Including Cowden syndrome



### **Surveillance**

For 21 of the 36 TPSs, cancer surveillance schemes have been suggested.<sup>14-45</sup> Especially in TPSs with a high risk of developing embryonal tumors, such as Wilms tumor or hepatoblastoma, close imaging surveillance has been recommended.<sup>46</sup> For several syndromes differences of opinion regarding surveillance do exist.

### **Therapy adjustment**

In 8 of the 36 syndromes, patients are known to be hypersensitive for ionizing radiation.<sup>28,29,33,35,47-50</sup> In 4 out of the 36 syndromes, caution is advised when administrating chemotherapy.<sup>12,47-49</sup>

### **Development**

In almost half of the TPSs (15/36) developmental problems may arise. Frequently detailed information regarding the nature and severity of the developmental problems was missing, and therefore we refrained from specifying these problems for each TPS.

### **Immunologic functioning**

In three TPSs immunodeficiency is a frequent complicating problem: Ataxia Telangiectasia, Bloom syndrome, and Nijmegen Breakage syndrome.<sup>47,48,50</sup> Neutropenia is a common complication in Shwachman-Diamond syndrome.<sup>41</sup>

### **Metabolism**

Diabetes mellitus type 2 (DM2) is a serious metabolic complication common in patients with Bloom syndrome (18%) and Werner syndrome (71%).<sup>48,51</sup> Approximately one third of individuals with Turner syndrome suffer from hypothyroidism.<sup>52</sup>

### **Neurologic functioning**

Nearly 50% of patients with cardiofaciocutaneous (CFC) syndrome have a seizure disorder, mostly beginning in infancy or early childhood.<sup>53</sup> In up to one third of patients with WAGR syndrome neurologic abnormalities such as hypertonia or hypotonia and epilepsy occur.<sup>54</sup> Hypotonia is also seen in patients with Costello syndrome.<sup>20</sup> Ataxia-Telangiectasia is characterized by progressive cerebellar ataxia beginning between one and four years of age,<sup>47</sup> and children are typically wheelchair bound by the age of 10 years. Patients with congenital central hypoventilation syndrome suffer from autonomic nervous system dysregulation, which can range from mild to life-threatening.<sup>17</sup> A neurologic feature of neurofibromatosis type 2 is a mononeuropathy occurring particularly in childhood and

frequently presenting as a facial nerve palsy, a squint (third cranial nerve palsy), or a foot or hand drop.<sup>35</sup>

### **Organ anomalies and dysfunctions**

Organ anomalies and dysfunctions are common in TPSs, occurring in more than 80% of the TPSs (29/36) (Table 2). Anomalies in the cardio-vascular system, digestive system, integumentary system, sensory organs and in the urinary system, were the most frequently reported. Infertility is a serious problem in patients with Bloom syndrome and Fanconi Anemia, specifically for men.<sup>48,55</sup> Most women with Turner syndrome are infertile due to gonadal dysgenesis.<sup>56</sup> Anomalies in the kidney are just as common in syndromes which are associated with kidney tumors such as Wilms tumor as in syndromes not associated with these tumors.

### **Management and recommendations**

In Bloom syndrome, Gorlin syndrome, Li-Fraumeni syndrome, Rothmund-Thomson syndrome and xeroderma pigmentosa (XP) excessive sun exposure should be avoided, due to a high risk of skin damage and skin malignancies.<sup>28,29,48,57,58</sup> Patients with XP should try to completely avoid sun exposure, not only due to increased skin cancer risk, but also because of the severe sunburns that can develop even after only minutes of sun exposure.<sup>58</sup> The syndrome specific issues (Table 1) typically require a physician or multidisciplinary team with expertise in the syndrome involved.

## **DISCUSSION**

The consequences of a TPS in a child with cancer are widespread and pediatric oncologists may wish to be aware of those consequences, in deciding whether or not a patient should be referred to a clinical geneticist. For instance in a two-year-old child with a hepatoblastoma, the pediatric oncologist will focus on adequate treatment of the malignancy first, so that evaluating the presence of a TPS has lower priority. However, a hepatoblastoma might be associated with a TPS as Beckwith Wiedemann syndrome (BWS), Familial Adenomatous Polyposis (FAP) and Simpson-Golabi-Behmel syndrome (SGBS). Morphological facial features as seen in BWS and SGBS may be present, but the signs may be too subtle to be recognized by pediatricians without specific experience in dysmorphology. However, the hepatoblastoma might be the first noticeable feature of the syndrome. In FAP morphological features are not common. BWS and SGBS go along with organ anomalies which can be monitored and in patients with FAP sigmoidoscopy and colonoscopy are required to monitor polyps. Also, sometimes preventive surgery might be advised. When the pediatric oncologist is aware of the possible consequences of a TPS, he or she will more easily refer to a clinical geneticist.

**TABLE 2.** Organ anomalies and dysfunctions occurring in TPSS

	Cardio-vascular system	Central nervous system	Digestive system	Endocrine system	Integumentary system	Lymphatic system	Musculo-skeletal system	Reproductive system	Respiratory system	Sensory organs	Urinary system
Beckwith-Wiedemann syndrome	H	L, P	A	LO		S					K
Bloom syndrome				SC			I	Lu			
Cardiofaciocutaneous syndrome	H			SC			M		Ey		K
Congenital central hypoventilation syndrome	H	B	G					Lu			
Cons. Mismatch Repair-Deficiency syndrome			G	CAL							
Costello syndrome	H, V			SC			M		Ey		
DICER1 syndrome				NG							K
Down syndrome	H		G							Ea, Ey	
Dyskeratosis congenita				ND		BM		Lu			
Familial adenomatous polyposis			G								
Familial neuroblastoma			G								
Familial or isolated WT1 mutations								PH			K
Fanconi anemia	H		G	SC		BM		I			K, U
Gorlin syndrome	H	B		SC				O		Ey	
Lateralized overgrowth	H	L, P	A			S	LO				K
Multiple endocrine neoplasia type 2		G									
Neurofibromatosis type 1				CAL, NF							
Neurofibromatosis type 2				CAL							Ea, Ey

**TABLE 2.** (continued)

	Cardio-vascular system	Central nervous system	Digestive system	Endocrine system	Integumentary system	Lymphatic system	Musculo-skeletal system	Reproductive system	Respiratory system	Sensory organs	Urinary system
Nijmegen Breakage syndrome					SC			O			K
Peutz-Jeghers syndrome			G		MP						
PTEN hamartoma tumor syndrome			G		T					Ey	
Rothmund-Thomson syndrome			G		PD, SC		Sk				
Rubinstein-Taybi syndrome	H				ke			C		Ea, Ey	K
Shwachman-Diamond syndrome			L, P				Sk				
Simpson Golabi Behmel syndrome	H						M				K
Turner syndrome	H, V							I		Ea	
WAGR syndrome			P							Ey	K, U
Werner syndrome	V				SC		Sk			Ey	
Xeroderma pigmentosa					SC					Ey	

Abbreviations: A, adrenals; B, brain; BM, bone marrow; C, cryptorchidism; CAL, café au lait macules; Ea, ear; Ey, eye; G, gastrointestinal; H, heart; I, infertility; K, kidneys; Ke, keloids; L, liver; LO, lateralized overgrowth; Lu, lungs; NF, neurofibromas; M, musculoskeletal; MP, mucocutaneous pigmentation; ND, nail dysplasia; NG, nodular goiter; O, ovarian; P, pancreas; PD, poikiloderma; PH, pseudohermaphroditism; S, spleen; SC, skin conditions; Sk, skeletal; T, trichilemmomas; U, urinary tract; V, vascular.

Diagnosing a TPS in a child with cancer is of extreme importance as it may intervene with the cancer therapy protocol. The use of high resolution CT scans and radiotherapy may increase the chance to develop a second primary cancer in patients, and radiation is advised to be reduced or, if possible, avoided. Patients with Down syndrome are very susceptible to the side effects of chemotherapy, requiring chemotherapy dose reduction.<sup>12</sup> For this reason, evaluation whether or not a TPS is present should preferably take place shortly after the cancer diagnosis.

The non-cancer related problems may have consequences as well. Knowing what signs and symptoms to expect in children might ensure the recognition of problems for which early intervention can be provided. Irrespective of nature and severity of the problems, the development is entitled to adequate support. For example, patients with WAGR syndrome can be affected by behavioral problems, including depression, anxiety, attention deficit disorder, obsessive-compulsive disorder, or autism spectrum disorders.<sup>54</sup>

In patients with a TPS in which immunodeficiency is a common problem, treating physicians should be aware of their increased susceptibility for infections. Intravenous immunoglobulin replacement therapy or prophylactic antibiotics can be considered when infections are frequent or may have a severe course.<sup>47,50</sup> For patients with a TPS in which DM2 frequently occurs, screening should be standard and at least annually to diagnose the potential disease in an early stage and prevent further complications. When a TPS is diagnosed, a patient can be checked for the associated organ anomalies and dysfunctions. If such anomaly or dysfunction is present, monitoring may be necessary and if indicated it should be further managed.

Establishing the diagnosis of a TPS and starting surveillances when appropriate can make patients and their families feel more secure. It can be helpful to know that they will be closely monitored by a physician, including routine visits with full physical examination and/or additional imaging studies, monitoring growth and development, and to receive psychological support. However, these surveillances may also have downsides: it might increase medicalization of patients, and surveillances might cause anxieties and may lead to false positive or false negative results.<sup>15</sup> Any surveillance should be well discussed with parents and patient, to match surveillance with their individual needs.

Scott et al. proposed that a chance of 5% or more of developing a malignancy in a TPS should be reason for surveillance.<sup>59</sup> In the present study a surveillance program for 21 of the 36 TPSs is summarized. There is no global consensus on surveillance for every TPS.

For BWS patients for example abdominal ultrasound has been proposed at various ages and intervals.<sup>14-16,60</sup> Maas et al. provided an overview of existing literature summarizing data on 2,000 BWS individuals, and suggested surveillance in BWS patients depending on molecular subgroups.<sup>15</sup> We refrain from providing a detailed evaluation of each of the suggested surveillance schemes.

Diagnosing a TPS might influence family planning and reproductive choices. Parents and children with a TPS, when grown up, may consider preimplantation genetic testing or prenatal diagnosis when appropriate. All available options should be carefully discussed.

We have focused the present overview on consequences of TPSs during childhood. In adults different surveillance programs should be advised, such as prophylactic therapy and screening for colon and breast cancer for Bloom Syndrome patients.<sup>48</sup> These issues are beyond the scope of the present study, and should be discussed separately.

Recognizing a TPS in a child with cancer is of extreme importance, as it has clinical consequences which require specific monitoring and management. We provided an overview of those cancer and non-cancer related consequences. Knowledge of these consequences and their importance to optimal care may facilitate early referral to a clinical geneticist and ensure optimal care for each patient with childhood cancer.

## REFERENCES

1. Bleeker FE, Hopman SM, Merks JH, et al. Brain tumors and syndromes in children. *Neuropediatrics* 2014;45:137-61.
2. Merks JH, Caron HN, Hennekam RC. High incidence of malformation syndromes in a series of 1,073 children with cancer. *Am J Med Genet Part A* 2005;134a:132-43.
3. Zhang J, Walsh MF, Wu G, et al. Germline Mutations in Predisposition Genes in Pediatric Cancer. *N Engl J Med* 2015;373:2336-46.
4. Mehes K. Malformations in children with cancer. *Am J Med Genet Part A* 2006;140:932.
5. Orellana C. Malformation syndromes during cancer in childhood. *Lancet Oncol* 2005;6:198.
6. Merks JH, Caron HN, Hennekam RC. High incidence of malformation syndromes in a series of 1,073 children with cancer. *Am J Med Genet A* 2005;134A:132-43.
7. Winter RM, Baraitser M. The London Dysmorphology Database. *J Med Genet* 1987;24:509-10.
8. Hennekam RCM, Krantz ID, Allanson JE. *Gorlin's syndromes of the head and neck*. 5th ed. New York, USA Oxford University Press Inc.; 2010.
9. Hopman SM, Merks JH, de Borgie CA, et al. The development of a clinical screening instrument for tumor predisposition syndromes in childhood cancer patients. *Eur J Cancer* 2013;49:3247-54.
10. Postema FA, Hopman SM, Aalfs CM, et al. Childhood tumors with a high probability of being part of a tumor predisposition syndrome; reason for referral for genetic consultation. *Eur J Cancer* 2017; accepted
11. Pagon RA, Adam MP, Ardinger HH, et al. *GeneReviews*®. 2017.
12. Cassidy SB, Allanson JE. *Management of genetic syndromes*: John Wiley & Sons; 2010.
13. Ayme S. The importance of review articles in making the voice of rare diseases heard: OJRD's 10th anniversary. *Orphanet J Rare Dis* 2016;11:71.
14. Clericuzio CL, Martin RA. Diagnostic criteria and tumor screening for individuals with isolated hemihyperplasia. *Genet Med* 2009;11:220-2.
15. Maas SM, Vansenne F, Kadouch DJ, et al. Phenotype, cancer risk, and surveillance in Beckwith-Wiedemann syndrome depending on molecular genetic subgroups. *Am J Med Genet Part A* 2016;170(9):2248-60.
16. Mussa A, Di Candia S, Russo S, et al. Recommendations of the Scientific Committee of the Italian Beckwith-Wiedemann Syndrome Association on the diagnosis, management and follow-up of the syndrome. *Eur J Med Genet* 2016;59:52-64.
17. Weese-Mayer DE, Marazita ML, Rand CM, Berry-Kravis EM. Congenital Central Hypoventilation Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews*(R). University of Washington, Seattle; 1993 (updated 2014).
18. Jongmans MC, Gidding CE, Loeffen J, et al. [Constitutional mismatch repair deficiency syndrome]. *Nederlands tijdschrift voor geneeskunde* 2015;159:A8602.
19. Vasen HF, Ghorbanoghli Z, Bourdeaut F, et al. Guidelines for surveillance of individuals with constitutional mismatch repair-deficiency proposed by the European Consortium "Care for CMMR-D" (C4CMMR-D). *J Med Genet* 2014;51:283-93.

20. Gripp KW, Lin AE. Costello Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. GeneReviews 1993 (updated 2012).
21. Gripp KW, Scott CI, Jr., Nicholson L, et al. Five additional Costello syndrome patients with rhabdomyosarcoma: proposal for a tumor screening protocol. *Am J Med Genet Part A* 2002;108:80-7.
22. Gripp KW. Tumor predisposition in Costello syndrome. *Am J Med Genet C Med Genet* 2005;137c:72-7.
23. Jasperson KW, Burt RW. APC-Associated Polyposis Conditions. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. GeneReviews 1993 (updated 2017).
24. Provenzale D, Gupta S, Ahnen DJ, et al. Genetic/Familial High-Risk Assessment: Colorectal Version 1.2016, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2016;14:1010-30.
25. Greengard EG, Park JR. ALK-Related Neuroblastic Tumor Susceptibility. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. GeneReviews 1993 (updated 2015).
26. Dome JS, Huff V. Wilms Tumor Predisposition. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. GeneReviews(R). University of Washington, Seattle; 1993 (updated 2016).
27. Benn DE, Gimenez-Roqueplo AP, Reilly JR, et al. Clinical presentation and penetrance of pheochromocytoma/paraganglioma syndromes. *J Clin Endocrinol Metab*. 2006;91:827-36.
28. Evans DG, Farndon PA. Nevoid Basal Cell Carcinoma Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. GeneReviews(R). University of Washington, Seattle; 1993 (updated 2015).
29. Schneider K, Zolley K, Nichols KE, Garber J. Li-Fraumeni Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. GeneReviews(R). University of Washington, Seattle; 1993 (updated 2013).
30. Villani A, Tabori U, Schiffman J, et al. Biochemical and imaging surveillance in germline TP53 mutation carriers with Li-Fraumeni syndrome: a prospective observational study. *Lancet Oncol* 2011;12:559-67.
31. Marquard J, Eng C. Multiple Endocrine Neoplasia Type 2. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. GeneReviews(R). University of Washington, Seattle; 1993 (updated 2015).
32. Moline J, Eng C. Multiple endocrine neoplasia type 2: an overview. *Genet Med*. 2011;13:755-64.
33. Friedman JM. Neurofibromatosis 1. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. GeneReviews(R). University of Washington, Seattle; 1993 (updated 2014).
34. Hersh JH. Health supervision for children with neurofibromatosis. *Pediatrics* 2008;121:633-42.
35. Evans DG. Neurofibromatosis 2. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. GeneReviews(R). University of Washington, Seattle; 1993 (updated 2011).
36. Ardern-Holmes S, Fisher G, North K. Neurofibromatosis Type 2. *J Child Neurol*. 2017;32:9-22.
37. Syngal S, Brand RE, Church JM, et al. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am J Gastroenterol*. 2015;110:223-62; quiz 63.
38. Eng C. PTEN Hamartoma Tumor Syndrome (PHTS). In: Pagon RA, Adam MP, Ardinger HH, et al., eds. GeneReviews(R). University of Washington, Seattle; 1993 (updated 2016).
39. Heaney RM, Farrell M, Stokes M, et al. Cowden Syndrome: Serendipitous Diagnosis in Patients with Significant Breast Disease. Case Series and Literature Review. *Breast J*. 2017;23:90-4.



40. Teplick A, Kowalski M, Biegel JA, et al. Educational paper: screening in cancer predisposition syndromes: guidelines for the general pediatrician. *Eur J Pediatr.* 2011;170:285-94.
41. Myers K. Shwachman-Diamond Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews(R)*. University of Washington, Seattle; 1993 (updated 2014).
42. Golabi M, Leung A, Lopez C. Simpson-Golabi-Behmel Syndrome Type 1. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews(R)*. University of Washington, Seattle; 1993 (updated 2011).
43. Lapunzina P. Risk of tumorigenesis in overgrowth syndromes: a comprehensive review. *Am J Med Genet C Semin Med Genet.* 2005;137c:53-71.
44. Frantzen C, Klasson TD, Links TP, et al. Von Hippel-Lindau Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews(R)*. University of Washington, Seattle; 1993 (updated 2007).
45. Halim A, Elashry R, Soliman O, et al. Bilateral Wilms' tumor: Mansoura multi-centers 15 years experience. *J Oncol Pharm Pract.* 2012;18:115-21.
46. Kalish JM, Doros L, Helman LJ, et al. Surveillance Recommendations for Children with Overgrowth Syndromes and Predisposition to Wilms Tumors and Hepatoblastoma. *Clin Cancer Res.* 2017 Jul 1;23(13):e1115-e122.
47. Gatti R. Ataxia-Telangiectasia. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews* 1993 (updated 2016).
48. Sanz MM, German J, Cunniff C. Bloom's Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews* 1993 (updated 2016).
49. Lohmann DR, Gallie BL. Retinoblastoma. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews(R)*. University of Washington, Seattle; 1993 (updated 2015).
50. Varon R, Demuth I, Digweed M. Nijmegen Breakage Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews* 1993 (updated 2017).
51. Oshima J, Martin GM, Hisama FM. Werner Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews* 1993 (updated 2016).
52. Lichiardopol C, Mota M. Hypothyroidism in Turner syndrome. *Rom J Intern Med* 2007;45:177-82.
53. Rauen KA. Cardiofaciocutaneous Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews* 1993 (updated 2016).
54. Hingorani M, Moore A. Aniridia. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews* 1993 (updated 2013).
55. Mehta PA, Tolar J. Fanconi Anemia. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews* 1993 (updated 2016).
56. Abir R, Fisch B, Nahum R, Orvieto R, Nitke S, Ben Rafael Z. Turner's syndrome and fertility: current status and possible putative prospects. *Hum Reprod Update* 2001;7:603-10.
57. Wang LL, Plon SE. Rothmund-Thomson Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews* 1993 (updated 2016).
58. Kraemer KH, DiGiovanna JJ. Xeroderma Pigmentosum. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews* 1993 (updated 2016).
59. Scott RH, Walker L, Olsen OE, et al. Surveillance for Wilms tumor in at-risk children: pragmatic recommendations for best practice. *Arch Dis Child* 2006;91:995-9.
60. Shuman C, Beckwith JB, Smith AC, et al. Beckwith-Wiedemann Syndrome. In: Pagon RA, Adam MP, Ardinger HH, et al., eds. *GeneReviews* 1993 (updated 2016).

**SUPPLEMENTARY MATERIAL****Supplementary TABLE S1a.**

Syndromes described in  $\geq 100$  individuals, and of whom  $\geq 5\%$  were reported to have cancer

<i>Syndrome</i>	Syndrome described in $\geq 100$ individuals [References]	Cancer reported in $\geq 5\%$ [References]
Ataxia telangiectasia	[1]	[1]
Beckwith-Wiedemann syndrome	[2]	[2]
Bloom syndrome	[3]	[3]
Cardiofaciocutaneous syndrome	[4]	[5]
Congenital central hypoventilation syndrome	[6]	[6]
Cons. Mismatch Repair-Deficiency Syndrome	[7-11]	[7-11]
Costello syndrome	[12]	[12]
Down syndrome	[13]	[13]
Dyskeratosis congenita	[14]	[14]
Familial adenomatous polyposis	[15]	[15]
Familial isolated pituitary adenoma	[16]	[16]
Familial or isolated WT1 mutations	[17-20]	[21]
Familial pheochromocytoma/paragangliocytoma	[22]	[22]
Familial retinoblastoma	[23]	[23]
Fanconi anaemia	[24]	[24]
Gorlin syndrome	[25]	[25]
Lateralized overgrowth	[26-28]	[21, 26, 27]
Li-Fraumeni syndrome	[29]	[29]
Multiple endocrine neoplasia type 2	[30]	[30]
Neurofibromatosis type 1	[31]	[31]
Neurofibromatosis type 2	[32]	[32]
Nijmegen Breakage syndrome	[33]	[33]
Peutz-Jeghers syndrome	[34]	[34]
PTEN hamartoma tumour syndrome	[35]	[35]
Rothmund-Thomson syndrome	[36]	[36]
Rubinstein-Taybi syndrome	[37]	[38]
Shwachman-Diamond syndrome	[39-43]	[43]
Simpson Golabi Behmel syndrome	[44]	[45]
Turner syndrome	[46]	[46]
Von Hippel-Lindau syndrome	[47]	[47]
WAGR syndrome	[48, 49]	[21]
Werner syndrome	[50, 51]	[50, 51]
Xeroderma pigmentosa	[52, 53]	[52, 53]

**Supplementary TABLE S1b.**

Syndromes described in 50-100 individuals, and of whom  $\geq 10\%$  were reported to have cancer

<i>Syndrome</i>	Syndrome described in 50-100 individuals [References]	Cancer reported in $\geq 10\%$ [References]
DICER1 syndrome	[54-56]	[54-56]
Familial neuroblastoma	[57, 58]	[57, 58]
Rhabdoid tumour predisposition syndrome	[59-62]	[59-62]

**SUPPLEMENTAL REFERENCES**

1. Gatti, R., Ataxia-Telangiectasia, in GeneReviews(R), R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
2. Shuman, C., et al., Beckwith-Wiedemann Syndrome, in GeneReviews(R), R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
3. Sanz, M.M., J. German, and C. Cunniff, Bloom's Syndrome, in GeneReviews(R), R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
4. Rauen, K.A., Cardiofaciocutaneous Syndrome, in GeneReviews(R), R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
5. Kratz, C.P., et al., Cancer in Noonan, Costello, cardiofaciocutaneous and LEOPARD syndromes. *Am J Med Genet C Semin Med Genet*, 2011. 157c(2): p. 83-9.
6. Weese-Mayer, D.E., et al., Congenital Central Hypoventilation Syndrome, in GeneReviews(R), R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
7. Attarbaschi, A., et al., Non-Hodgkin's lymphoma and pre-existing conditions: spectrum, clinical characteristics and outcome in 213 children and adolescents. *Haematologica*, 2016.
8. Bakry, D., et al., Genetic and clinical determinants of constitutional mismatch repair deficiency syndrome: report from the constitutional mismatch repair deficiency consortium. *Eur J Cancer*, 2014. 50(5): p. 987-96.
9. van der Klift, H.M., et al., Comprehensive Mutation Analysis of PMS2 in a Large Cohort of Probands Suspected of Lynch Syndrome or Constitutional Mismatch Repair Deficiency Syndrome. *Hum Mutat*, 2016.
10. Vasen, H.F., et al., Guidelines for surveillance of individuals with constitutional mismatch repair-deficiency proposed by the European Consortium "Care for CMMR-D" (C4CMMR-D). *J Med Genet*, 2014. 51(5): p. 283-93.
11. Wimmer, K. and C.P. Kratz, Constitutional mismatch repair-deficiency syndrome. *Haematologica*, 2010. 95(5): p. 699-701.
12. Gripp, K.W. and A.E. Lin, Costello Syndrome, in GeneReviews(R), R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
13. Bhatnagar, N., et al., Transient Abnormal Myelopoiesis and AML in Down Syndrome: an Update. *Curr Hematol Malig Rep*, 2016. 11(5): p. 333-41.
14. Savage, S.A., Dyskeratosis Congenita, in GeneReviews(R), R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
15. Jasperson, K.W. and R.W. Burt, APC-Associated Polyposis Conditions, in GeneReviews(R), R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
16. Korbonits, M. and A.V. Kumar, AIP-Related Familial Isolated Pituitary Adenomas, in GeneReviews(R), R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
17. Mueller, R.F., The Denys-Drash syndrome. *J Med Genet*, 1994. 31(6): p. 471-7.
18. Ezaki, J., et al., Gonadal tumor in Frasier syndrome: a review and classification. *Cancer Prev Res (Phila)*, 2015. 8(4): p. 271-6.

19. Guaragna, M.S., et al., Frasier syndrome: four new cases with unusual presentations. *Arq Bras Endocrinol Metabol*, 2012. 56(8): p. 525-32.
20. Gwin, K., et al., Expanding the clinical spectrum of Frasier syndrome. *Pediatr Dev Pathol*, 2008. 11(2): p. 122-7.
21. Dome, J.S. and V. Huff, Wilms Tumor Overview, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
22. Kirmani, S. and W.F. Young, Hereditary Paraganglioma-Pheochromocytoma Syndromes, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
23. Lohmann, D.R. and B.L. Gallie, Retinoblastoma, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
24. Mehta, P.A. and J. Tolar, Fanconi Anemia, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
25. Evans, D.G. and P.A. Farndon, Nevoid Basal Cell Carcinoma Syndrome, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
26. Atik, T., O. Cogulu, and F. Ozkinay, Results of fifteen-year follow-up from a single center: findings and risks for tumor development in isolated hemihyperplasia cases. *Genet Couns*, 2014. 25(4): p. 417-21.
27. Dempsey-Robertson, M., et al., Incidence of abdominal tumors in syndromic and idiopathic hemihypertrophy/isolated hemihyperplasia. *J Pediatr Orthop*, 2012. 32(3): p. 322-6.
28. Bliet, J., et al., Epigenotype, phenotype, and tumors in patients with isolated hemihyperplasia. *J Pediatr*, 2008. 153(1): p. 95-100.
29. Schneider, K., et al., Li-Fraumeni Syndrome, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
30. Marquard, J. and C. Eng, Multiple Endocrine Neoplasia Type 2, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
31. Friedman, J.M., Neurofibromatosis 1, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
32. Evans, D.G., Neurofibromatosis 2, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
33. Varon, R., I. Demuth, and M. Digweed, Nijmegen Breakage Syndrome, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
34. McGarrity, T.J., C.I. Amos, and M.J. Baker, Peutz-Jeghers Syndrome, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
35. Eng, C., PTEN Hamartoma Tumor Syndrome (PHTS), in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
36. Wang, L.L. and S.E. Plon, Rothmund-Thomson Syndrome, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
37. Stevens, C.A., Rubinstein-Taybi Syndrome, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.

38. Milani, D., et al., Hepatoblastoma in Rubinstein-Taybi Syndrome: A Case Report. *Pediatr Blood Cancer*, 2016. 63(3): p. 572-3.
39. Minelli, A., et al., Incidence of Shwachman-Diamond syndrome. *Pediatr Blood Cancer*, 2012. 59(7): p. 1334-5.
40. Myers, K.C., et al., Variable clinical presentation of Shwachman-Diamond syndrome: update from the North American Shwachman-Diamond Syndrome Registry. *J Pediatr*, 2014. 164(4): p. 866-70.
41. Myers, K.C., S.M. Davies, and A. Shimamura, Clinical and molecular pathophysiology of Shwachman-Diamond syndrome: an update. *Hematol Oncol Clin North Am*, 2013. 27(1): p. 117-28, ix.
42. Pichler, J., et al., Nutritional status in children with Shwachman-diamond syndrome. *Pancreas*, 2015. 44(4): p. 590-5.
43. Myers, K., Shwachman-Diamond Syndrome, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
44. Tenorio, J., et al., Simpson-Golabi-Behmel syndrome types I and II. *Orphanet J Rare Dis*, 2014. 9: p. 138.
45. Golabi, M., A. Leung, and C. Lopez, Simpson-Golabi-Behmel Syndrome Type 1, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
46. Cassidy, S.B. and J.E. Allanson, Management of genetic syndromes. 2010: John Wiley & Sons.
47. Frantzen, C., et al., Von Hippel-Lindau Syndrome, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
48. Fischbach, B.V., et al., WAGR syndrome: a clinical review of 54 cases. *Pediatrics*, 2005. 116(4): p. 984-8.
49. Breslow, N.E., et al., Characteristics and outcomes of children with the Wilms tumor-Aniridia syndrome: a report from the National Wilms Tumor Study Group. *J Clin Oncol*, 2003. 21(24): p. 4579-85.
50. Oshima, J., G.M. Martin, and F.M. Hisama, Werner Syndrome, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
51. Onishi, S., et al., Japanese diabetic patients with Werner syndrome exhibit high incidence of cancer. *Acta Diabetol*, 2012. 49 Suppl 1: p. S259-60.
52. Kraemer, K.H. and J.J. DiGiovanna, Xeroderma Pigmentosum, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
53. Kleijer, W.J., et al., Incidence of DNA repair deficiency disorders in western Europe: Xeroderma pigmentosum, Cockayne syndrome and trichothiodystrophy. *DNA Repair (Amst)*, 2008. 7(5): p. 744-50.
54. Doros, L., et al., DICER1-Related Disorders, in *GeneReviews(R)*, R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
55. Slade, I., et al., DICER1 syndrome: clarifying the diagnosis, clinical features and management implications of a pleiotropic tumour predisposition syndrome. *J Med Genet*, 2011. 48(4): p. 273-8.
56. Khan, N.E., et al., Macrocephaly associated with the DICER1 syndrome. *Genet Med*, 2016.
57. Eng, C., Cancer: A ringleader identified. *Nature*, 2008. 455(7215): p. 883-4.

58. Greengard, E.G. and J.R. Park, ALK-Related Neuroblastic Tumor Susceptibility, in GeneReviews(R), R.A. Pagon, et al., Editors. 1993, University of Washington, Seattle.
59. Eaton, K.W., et al., Spectrum of SMARCB1/INI1 mutations in familial and sporadic rhabdoid tumors. *Pediatr Blood Cancer*, 2011. 56(1): p. 7-15.
60. Bourdeaut, F., et al., Frequent hSNF5/INI1 germline mutations in patients with rhabdoid tumor. *Clin Cancer Res*, 2011. 17(1): p. 31-8.
61. Kordes, U., et al., Favorable outcome of patients affected by rhabdoid tumors due to rhabdoid tumor predisposition syndrome (RTPS). *Pediatr Blood Cancer*, 2014. 61(5): p. 919-21.
62. Bruggers, C.S., et al., Clinicopathologic comparison of familial versus sporadic atypical teratoid/rhabdoid tumors (AT/RT) of the central nervous system. *Pediatr Blood Cancer*, 2011. 56(7): p. 1026-31.