

What is already available?

Raoul CM Hennekam

Department of Paediatrics, Amsterdam UMC,
Amsterdam, Netherlands



Topics

- 100 syndromes
- literature
- physical problems
- cognitive / behavioural problems
- consensus guidelines
- updates
- differences between countries



Most common syndromes

- no existing list
- unreliable incidence / prevalence data
- differences between countries / ethnicities



- estimate
- ID part but not necessarily always

ps small additional list without ID (n=20)

- 1995 Max Muenke / update 2018 Alain Verloes



Most common syndromes

Aarskog	Del 5p	Lymphedema-lymphangiectasia-ID	Roberts
Alagile	Del 16p11.2	Malan	Robinow
Albright	Del 22q11.2	Mandibuloacral	Rothmund-Thomson
Alström	Del 22q13	Marshall-Smith	Rubinstein-Taybi
Angelman	DOOR	Meier-Gorlin	Saethre-Chotzen
Apert	Down	Menkes	Sanfilippo
ATR-X	Dup17p11.2	Mowat-Wilson	SHORT
Baraitser-Winter	Dyskeratosis congenita	Muenke	Silver-Russel
Bardet-Biedl	Fanconi	Myotonic dystrophy	Simpson-Golabi-Behmel
Beckwith-Wiedemann	Fetal Alcohol	Neurofibromatosis I	Smith-Lemli-Opitz
Bloom	Fetal anticonvulsant	Nicolaides-Baraitser	Smith-Magenis
Borjeson-Forssman-Lehmann	FG	Noonan	Sotos
CFC	Floating-Harbor	Opitz G/BBB	Trisomy 8
CHARGE	FraX	Osteoplastic primordial dwarfism	Trisomy 13
Cleidocranial	Goltz-Gorlin	Otopalatodigital	Trisomy 18
Cockayne	Gorlin	Pallister-Hall	TrichoRhinoPhalangeal
Coffin-Lowry	Greig	Pallister-Kilian	Tuberous sclerosis
Coffin-Siris	Holoprosencephaly	Peters plus	Turner
Cohen	Incontinentia pigmenti	PIK3CA related	UPD 14
Cornelia de Lange	Idic 15	Pitt-Hopkins	Waardenburg
Costello	Kabuki	PKU	Weaver
Crouzon	Kleefstra	Prader-Willi	Werner
Cutis laxa	Klinefelter	Proteus	Wiedemann-Rautenstrauch
Del 1p36	Koolen-DeVries	PTEN hamartome tumor	Wiedemann-Steiner
Del 4p	Loeys-Dietz	Rett	Williams



Literature

A International

- PubMed
- MeSH term syndrome
- if >100 publications: “guideline(s)”; “management”
- pdf
- >2000 (often >2010); molecularly confirmed

B National

- national guidelines
- through support groups
- 2021

searches



Literature

bias!

ps available site Ithaca



Overview

Publications

Total	981
physical aspects	818
cognition / behaviour	125
consensus	38



Physical

	<i>Publications</i>	<i>Entities</i>
- general review	171	98
- molecular	74	57
- senses	38	21
- internal organs	108	57
- neurology	29	22
- immunology	9	8
- cancer	57	31



Senses

	<i>Publications</i>	<i>Entities</i>
- eye	17	15
- ENT/hearing	21	15



Internal organs

	<i>Publications</i>	<i>Entities</i>
- cardiovascular	47	22
- lung	12	10
- gastro-intestinal	13	10
- liver	5	3
- kidney	10	8
- gynaecology / fertility	21	11



Neurology(-related)

	<i>Publications</i>	<i>Entities</i>
- neurology	29	22
- speech	7	7
- sleep	27	19
- anaesthesia	19	18



Bone / Growth / Skin

	<i>Publications</i>	<i>Entities</i>
- bone / integumentum	63	38
- growth	30	23
- diet	11	9
- oral / dental	40	29
- skin	19	16



Behaviour / Cognition

	<i>Publications</i>	<i>Entities</i>
- cognition	24	21
- behaviour	59	30
- QoL / parental stress	42	23



Consensus

	<i>Publications</i>	<i>Entities</i>
- consensus	22	15
update	2	2
- diagnostic criteria	16	14



Consensus

achondroplasia

NF1

Albright

Noonan

Beckwith-Wiedemann

Pitt-Hopkins

CFC

PKU

Cornelia de Lange

PTEN hamartoma

Down

Silver-Russell

Fetal anticonvulsivant

Williams

Kabuki



Consensus

General

- methods sometimes not mentioned ↔ sometimes detailed
- input support groups not existing ↔ co-author
- reliability not mentioned ↔ detailed and defined
- info for adults often limited
- one in two languages (Engl + Fr)
- no version in lay persons language



Consensus

Differences among countries for guidelines on same topics

- detailedness
- defensive
- national resources

ps once comparison between guidelines

Smerdel, Eur J Med Genet 2020;63:103873



Consensus

Updates

- Down 2001 - 2011
- earlier guidelines not mentioned

AAP cee, Pediatrics 2001;107:442

Bull, Pediatrics 2011;128:393



Consensus

Updates

- Achondroplasia 1995 – 2005 - 2020
- adaptations of recommendations not visible
- added:
 - treatment options
 - monitoring complications in adults

AAP cie, Pediatrics 1995;95:443

Trotter, Pediatrics 2005;116:771

Hoover, Pediatrics 2020;146:e2020 1010



Conclusions

- still limited publications on cognition / behaviour
- general / molecular reviews well available
- especially immuno / speech limited
- consensus increasing
- defined methodology needed for (ultra-)rare disorders
- input support groups