

Cancer in people with intellectual disabilities

epidemiology and genetics

Cancer in people with severe and profound intellectual disability

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Cancers in people with intellectual disability (PWIDS)

- Are globally **as frequent** as in the general population
Incidence (Patja et al 2001, Sullivan et al 2004).
Mortality data: cancer is frequently the second or third cause of death (Hosking et al 2016, Oppewal et al 2018).
- Have a **particular distribution** different from that in the general population: more digestive tract cancer, less lung and ENT cancer.

Cancer incidence and distribution vary with ID level

Mild ID (80% of persons with ID)	IQ 70-50
Moderate ID (15% of PWIDs)	IQ 50-35
Severe/profound ID (5% of PWIDs)	IQ <35 <20

Values for the whole group of PWIDs are not similar to those of people with severe/profound intellectual disability (SPID)

Cancer incidence in SPID, old studies

Before 1971 (USA) 4 cancer deaths among 660 deaths (0,006%) in persons with SPID

Years 1973-6 (USA) deeper the ID, rarer the cancer deaths. At these times life expectancy was around 19,8 years for persons with SPID vs 71 years in the general population USA.

These values are true for this period, however not currently

Cancer incidence and mortality in persons with SPID recent data

Incidence 1967-1997 (Finland) **similar** for severe ID (SIR 0.95) and for deep ID (SIR 1) compared to the whole group of PWIDs (SIR 0.9) (Patja et al 2001).

Mortality 1976-1984 standardized mortality ration (SMR 0.84 M, 1.35 F) (Denmark) (Dupont and Mortensen 1990). Cancer death 4% in SPIDs versus 11% in moderate ID and 16% in mild ID (Patja et al 2001).

Age at cancer diagnosis in PWIDs

0 – 20 years risk x 2-3 compared to the general population (GP)

20 – 60 years risk around 1

60 and + risk 0.60 – 0.80

(Sullivan et al 2004, Satgé et al 2020)

For persons with SPID no value stratified on age are available currently.

The differences between old and recent studies are due to:

- An **increase in life expectancy** of people with SPID which has greatly progressed.
- A **better medical follow-up** of persons with SPID

Distribution of cancer in persons with severe/profound ID compared to persons with mild/moderate ID

(Patja et al 2001 Finland 1967–1997)

	Severe and profound ID (30 patients) (SIR)	Mild and moderate ID (87 patients) (SIR)
Digestive tract	1.4	1.1
Esophagus	2.5	2
Gallbladder	10.3	1.4
Lung	0.0	0.8
Prostate	0.4	0.2
Testis	9.9	2.1
Urinary tract	0.9	0.2
CNS	3.5	0.6
Thyroid	3.1	2.1
Lymphoma	1.2	1.5

Differences in cancer incidence between mild/moderate and severe/deep ID (Patja et al 2001)

140 patients with mild/moderate ID

32 patients with severe/deep ID

↑ CNS x 6 in persons with SPID

↑ Testis x 5

↑ Gallbladder x 7

↓ Lung cancer

No indication for feminine cancer: breast, ovary, uterus

Environmental cancer risk factors in people with SPID

Reduced risk:

- ↓ Tobacco (lung cancer, bladder cancer...)
- ↓ Alcohol (ENT cancer, liver cancer)
- ↓ Sun exposure (skin cancer)

Unknown:

Diet? (fruits, vegetables / red meat, cooked meat)

Increased risk:

Reduced physical activity (breast cancer, colon cancer and many other cancers)

Environmental cancer risk factors in people with SPID

Infectious agents:

↓ HPV infections (↓ cervix uterine and ENT cancer)

↑ *Helicobacter pylori* (chronic gastritis → ↑ gastric cancer)

↑ C and B hepatitis (↑ liver cancer)

Comorbidities and life events favoring cancer in people with SPID

- **Gastrointestinal reflux** which affects nearly half of persons with SPID (IQ<35) and more if there are motor disabilities, scoliosis and antiepileptic treatment → ↑ esophagus cancer
- **Neurologic bladder** with chronic inflammation → ↑ urinary bladder cancer
- **Nulliparity and no breast feeding** ↑ breast cancer

SPID, genetic anomalies and cancer

- **More than 50% of SPID are due to a genetic disease** vs 20% in mild ID.
- Genetic conditions may enhance cancer risk. These cancers occur more frequently in early life, mainly in children, adolescences and young adults.
- Cancer are more frequent in children with SPID, but the exact incidence is unknown. In the general population nearly 1/400 child under 15 develops a cancer.

Genetic syndromes with ID and cancer risk

- Increased cancer risk seen mainly in childhood
- genetic syndromes often show a particular tumor profile, some cancers being more frequent, and other unexpectedly rare.

Trisomy 21 in childhood

↑ leukemia, germ cell tumors

↓ Solid tumors medulloblastoma, neuroblastoma, nephroblastoma, hepatoblastoma (except retinoblastoma)

Trisomy 18

↑ hepatoblastoma, nephroblastoma

↓ Brain tumors, leukemia, lymphoma

Organs more at risk for cancer in children with SPID

In particular **genetic conditions**

Leukemia: Down S.

Kidney cancer: WAGR S., trisomy 18, tuberous sclerosis

Brain tumors: tuberous sclerosis, Rubinstein-Taybi S.

Liver cancer: trisomy 18, Wolff-Hirschhorn S.

Neuroblastoma: Costello S., Rubinstein-Taybi S.

and many others...

Organs more at risk for cancers in adults with SPID

Digestive tract: +++ esophagus, ++ colon, stomach, gallbladder

Urinary tract: urinary bladder

Breast

brain

Some cancers are less frequent

Ear – nose – throat cancers

Oral cavity cancers

Lung cancers

Any organ may develop cancers, even if exceptionally

Cancer screening in people with SPID

Breast cancer: mammography every two years (or ultrasonography if mammography is not possible)

Colon cancer: fecal occult blood test (FOT) every two years

Cervix uterine cancer: in case of sexual relationship. Cervix cancer is very rare in women with SPID

In particular countries,

Malignant melanoma, (Australia)

Gastric cancer (China, Korea)

Age at screening beginning remains to be evaluated

Cancer surveillance in people with SPID

Esophagus, in case of gastro-intestinal reflux disease

Stomach, in case of *helicobacter pylori* chronic gastritis

Urinary bladder, in case of neurological bladder

Testis, 15-40 years even in absence of cryptorchidism

Other organs in case of **familial context** of cancer predisposition

There is a lower participation of persons with SPID to screening programs

Many cancers are discovered late

Therapeutic success is observed (sometimes with a modified treatment due to comorbidities and particular vulnerabilities) in children (Meazza et al 2020), and adults when the tumor is not discovered too late

Adults with SPID should be included in cancer screening programs, taking into account their life expectancy

A particular group, **people with profound and multiple disabilities (PMD)**

- Have important motor disabilities associated with severe ID
- Are more prone to cancer related to comorbidities favoring malignancies: gastrointestinal reflux disease, neurological bladder, cryptorchidism.
- Cancer **may occur earlier** than in the general population (particularly esophageal cancer and colon cancer)

Conclusions



Cancer risk in people with SPID **remains to be evaluated** more precisely, and is more frequent than previously estimated.

- Cancer screening and medical surveillance should be **adapted**
- Cancer surveillance should take into account the genetic condition responsible for ID.
- Surveillance of particular organs is important in case of familial context of cancer predisposition.

Data are needed on 1) cancer incidence, 2) cancer distribution, 3) age at diagnosis for cancer screening, and 4) cancer treatment.

Thank you for your attention



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