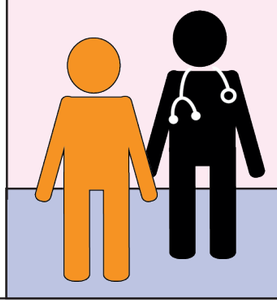
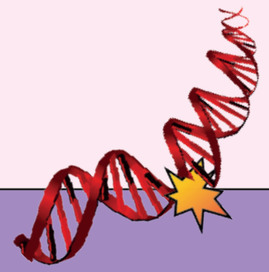
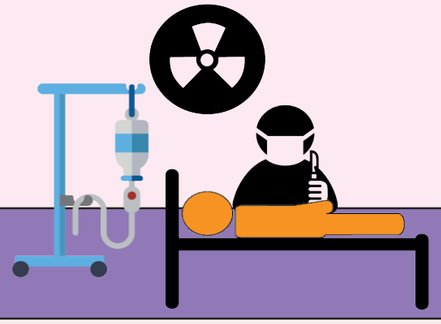
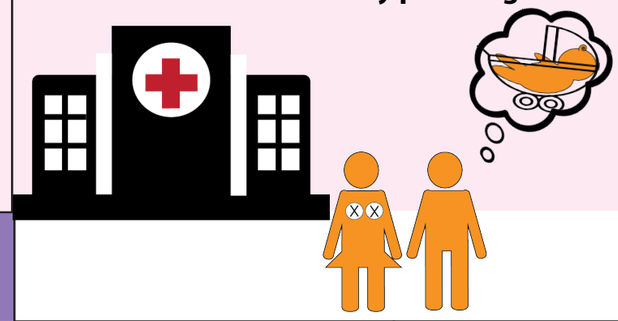
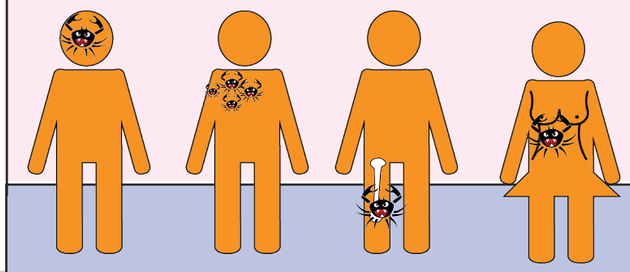
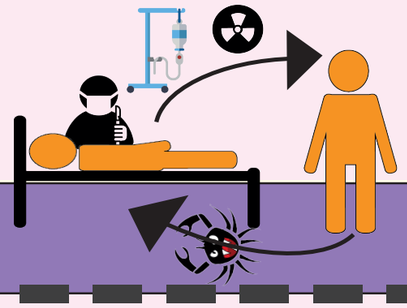
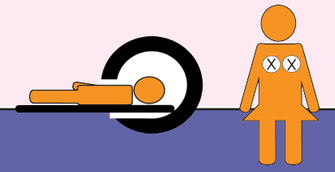
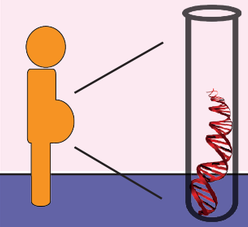
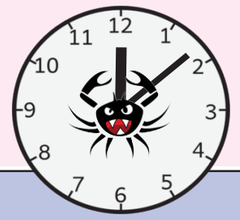
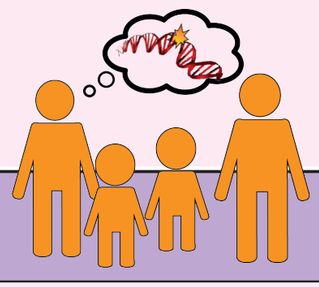
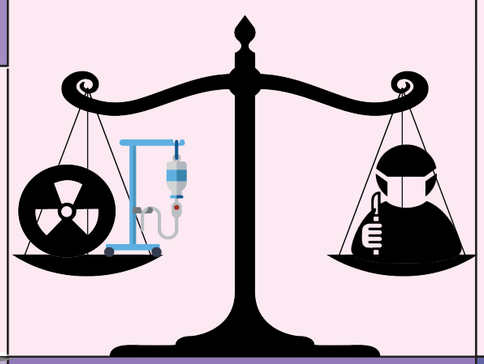
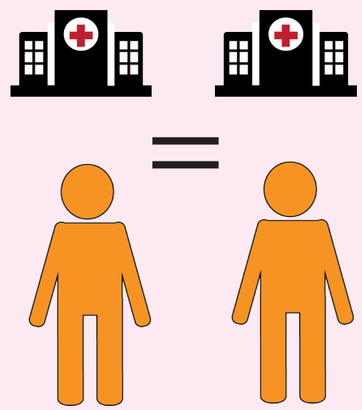
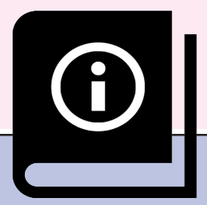
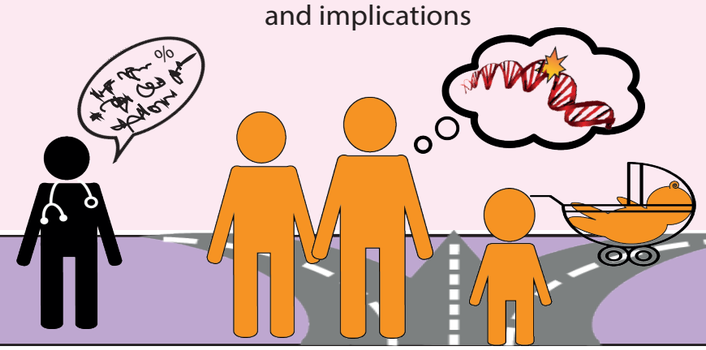
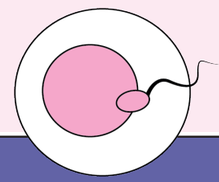
Patient Journey heritable *TP53*-related cancer (h*TP53*rc) syndrome / Li Fraumeni Syndrome

	1st symptoms	Cancer diagnosis	Genetic diagnosis	Cancer treatment	Follow-up and family planning
Disease					
Clinic	Wide range of (rare) cancers at an early age 	Involvement of broad multidisciplinary team 	Extensive and repeated treatment due to relapses and recurrences 	Screening and optional preventive surgery 	Prenatal diagnosis 
Challenge	Early detection 	Implications for family members 	Quick genetic diagnosis 	Personalised treatment and counselling on treatment decisions Tailored clinical handling 	International guidlines to provide equal follow-up for all h*TP53*rc patients 	Psychological support 
Goal	Awareness and education for GPs and other clinicians 	Informed decision making on genetic testing and implications 				IVF and PGT should be discussed with every h*TP53*rc patient 

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Genetic Tumour Risk Syndromes (ERN GENTURIS)

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07-05-2019 Version 3.0
textual update 2023

Patient Journey heritable *TP53*-related cancer (h*TP53*rc) syndrome / Li Fraumeni Syndrome

Disease

1st symptoms

No phenotypic features other than tumour

Cancer diagnosis

Sarcoma the sentinel tumour
Glioma
Breast cancer
Adrenocortical
Lung
Many others

Genetic diagnosis

This is conformed by identification of a pathogenic variant in *TP53* in a blood or other constitutional sample.

Cancer treatment

Decisions on type of chemotherapy and try to avoid radiotherapy unless essential.

Follow-up and family planning

Surveillance:
- Breast (women): yearly MRI from 20 years of age
- Dedicated brain MRI annually
- Whole body MRI annually
- Ultrasound adrenals 0-16 years every 3-4 month

Clinic

Wide range of (rare) cancers at an early age

In particular embryonal rhabdomyosarcoma, osteosarcoma, glioma, medulloblastoma, choroid plexus carcinoma and adrenocortical carcinoma in childhood and beyond.

Addition of breast, lung and other common cancers in adulthood.

Involvement of broad multidisciplinary team

Multiple specialist have to work together, e.g:
- Geneticist
- Oncologist
- Surgeon
- Radiologist
- Psychologist
- Paediatrician

Extensive and repeated treatment due to relapses and recurrences

Try to detect tumours early to avoid need for DNA damaging treatments in particular radiotherapy.

Screening and optional preventive surgery

Whole body MRI,
Dedicated brain and breast (women) MRI

Risk reducing mastectomy should be discussed with all women under 45 years as well as contralateral mastectomy at time of first breast cancer diagnosis

Prenatal diagnosis

Counselling on options for family planning:
- Prenatal diagnostics
- Preimplantation genetic diagnosis

Challenge

Early detection

High grade glioma and sarcoma may present as interval cancers despite brain and whole body MRI.

Implication for family members

50% likelihood for offspring unless mosaic. May need to test parents to assess risk to siblings unless clear h*TP53*rc pattern.

Rapid genetic diagnosis

Vital at relevant cancer diagnosis to drive treatment choices .

Personalised treatment and counselling on treatment decisions

Consider new trials to assess preventive treatments.

International guidelines to provide equal follow-up for all h*TP53*rc patients

Psycholigical support

Important to offer and assess impact annually in particular in adolescence and in young adults.

Goal

Awareness and education for GPs and clinicians

GPs and cancer treating clinicians are aware of:
- Existence of h*TP53*rc and the associated tumours.

Informed decision making on genetic testing and implications

Genetic counselling a prerequisite.

Support for h*TP53*rc patients and their relatives.

Counselling on consequences of genetic testing for relatives.

Tailored clinical handling

Adjusted treatment and subsequent follow-up and lifelong surveillance after cancer treatment.

IVF and PGT should be discussed with every h*TP53*rc patient

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