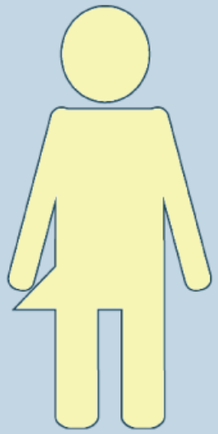
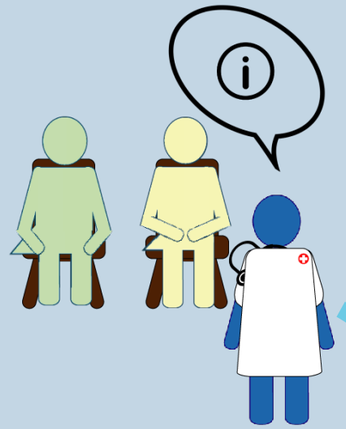
ERN GENTURIS patient journey: Birt-Hogg-Dubé (BHD) syndrome

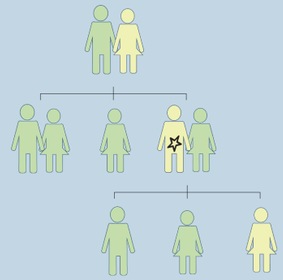
Affected person with unknown genetic status



Genetic counselling



Cascade testing (testing of blood relatives)

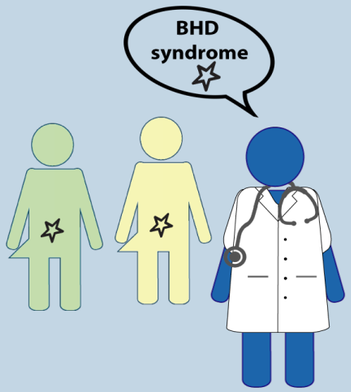


Baseline assessment and surveillance

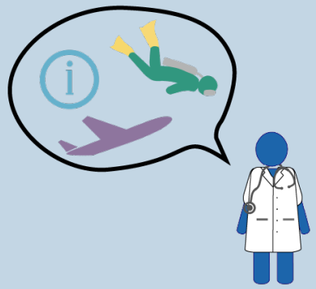
Eligible for germline genetic testing for BHD syndrome

Germline genetic testing

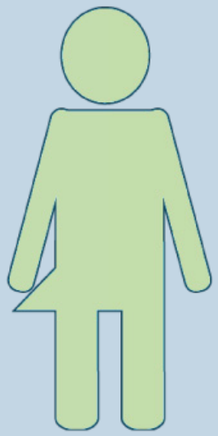
Disclosure of the results



Cautions

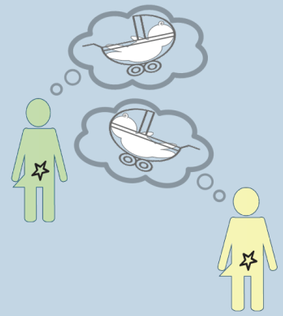


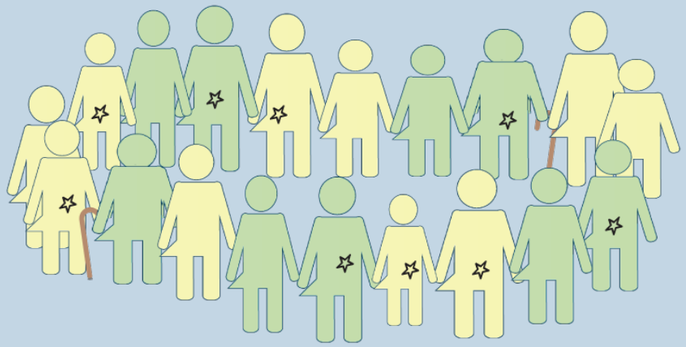
Unaffected person with unknown genetic status



Personalised therapy

Family planning





Peer support and emotional support

European Reference Network

Genetic Tumour Risk Syndromes (ERN GENTURIS)

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Disclaimer: This patient journey is intended as a general overview of the clinical and diagnostic pathway for BHD syndrome or its suspicion. It should not replace an individual clinical and genetic counselling at an expertise centre. It also does not intend to address all specific challenges of the complex condition of BHD syndrome. Specific clinical guidelines, diagnostic criteria and nomenclature may change at short notice and therefore are only referred to in this patient journey.

Affected person with unknown genetic status

A person diagnosed with a common manifestation of BHD syndrome (kidney cancer, fibrofolliculomas, pneumothorax), who has not yet had genetic testing.

Unaffected person with unknown genetic status

BHD syndrome known in the family or family history consistent with BHD syndrome.

Eligible for germline genetic testing for BHD syndrome

BHD syndrome should be considered for a person having one or more of the following conditions:

- lung collapse (pneumothorax), especially if recurrent or familiall
- multiple pulmonary cysts
- kidney tumour, specifically if multiple and/or bilateral
- multiple skin bumps (fibrofolliculomas / trichodiscomas) on the face and neck.

Testing for BHD syndrome in an adult unaffected person can be relevant if:

- known BHD syndrome in the family
- family history of a combination of previously mentioned manifestations (see above).

See also "Cascade testing".

Genetic counselling

Persons eligible for germline genetic testing need thorough information before and after testing regarding:

- clinical manifestations and natural history of BHD syndrome
- surveillance, cautions and follow-up
- treatment for specific complications
- process of genetic counselling
- implications of genetic test results at an individual level and for family members
- legal, social, insurance and financial aspects of diagnosis
- emotional support including peer support: www.genturis.eu, section patient-area.

Germline genetic testing and disclosure of the results

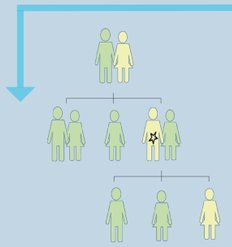
General information regarding germline genetic testing can be found on:

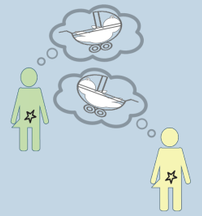
https://www.coe.int/en/web/bioethics/information-brochure-on-genetic-tests-for-health-purposes

Germline genetic testing should at least consider the *FLCN* gene. This is commonly included in wider panels used for hereditary kidney cancers.

Disclosure of the testing results should be accompanied by genetic counselling.

To make a diagnosis of BHD syndrome an individual must have a disease-causing variant in the *FLCN* gene. Alternatively, if no alteration is detected by the germline genetic test, a clinical diagnosis can be made on clinical criteria (one major criterion or two minor criteria, see guideline). The most recent diagnostic criteria for BHD syndrome can be found on the ERN GENTURIS website (www.genturis.eu, section BHD syndrome guideline).





Cascade testing (testing of blood relatives)

Cascade testing is the process of providing genetic counselling and germline genetic testing for relevant family members at risk of inheriting BHD syndrome. Based on the family history the clinical geneticist will decide for which family members germline genetic testing would be relevant. The clinical geneticist will provide guidance on how relevant family members pursue genetic counselling. **Testing of these family members and follow up with appropriate clinical measures where needed may save lives and improve quality of life.**

BHD syndrome is inherited in an autosomal dominant manner:
A person with BHD syndrome has a 50% probability of passing the condition on to their child.

Minors are in principle not eligible for cascade testing as BHD syndrome seldom manifests in childhood and surveillance is not recommended before the age of 20 years.Testing is postponed until the minor is old enough to make an informed choice themselves.

Baseline assessment and surveillance

A formal dermatologic assessment should be considered at diagnosis.

A baseline lung scan by high resolution computed tomography (HRCT) can be considered after age 20 years.

Surveillance for kidney cancer by MRI with intravenous contrast where possible (or ultrasound if MRI not possible) should start at age 20 years and continue lifelong every 1-2 years. More frequent screening should be considered if a new small lesion is identified to ascertain growth rate.

Cautions

Patients should be informed on potential risks associated with specific exposures (e.g., potential relation of pneumothorax with rapid changes in air pressure, for instance diving or air travel).

Patients should be aware of the symptoms of a pneumothorax: chest pain and shortness of breath.

Personalised therapy

Personalised therapy for BHD syndrome is always related to the decision of surgery versus watchful waiting (surveillance).

Surgical removal of kidney tumours is usually considered, depending on size and location. In general, treatment protocols should follow standard oncologic practice.

Removal of skin lesions using standard approaches should be considered, which may require a referral to a dermatologist. Removal of skin lesions should be considered when a patient feels that quality of life is affected but should be warned that lesions are likely to recur.

Patients should be reassured that BHD syndrome does not affect lung function in the long term. Lung function is only temporarily affected during an acute episode of a lung collapse.

Family planning

BHD syndrome is an inherited condition. For some this has implications for family planning. When relevant a referral for reproductive counselling should be offered early in the patient journey.

Depending on the country there might be options for prenatal testing and preimplantation genetic testing. Financial resources for reproductive options in the public healthcare system and the legal framework differ per country.

Peer support and emotional support

Patients and their family might seek peer and emotional support repeatedly, at different times, for example: at diagnosis of a new cancer, in case of family planning , when deciding on kidney surgery.

Peer support and emotional support on:

-how to cope with stress related to diagnostic delay - in ongoing cancer therapy - how to decide about genetic testing - how to inform family members on their genetic risk
-how to cope with anxiety about the status of untested children or sense of guilt if children are affected - how to cope with risk of cancer and other clinical manifestations
-how to cope with body image related to skin lesion - how to deal with social consequences such as mortgage or potential restriction on specific jobs (i.e. airplane pilot) or leisure activities (i.e. diving).

Patient organisation can be found on:
https:/://www.genturis.eu/l=eng/patient-area/patient-associations.html

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