Considerations for HLRCC

Skin

~50–80
in 100 people with HLRCC **get skin leiomyomas**

YES IF

Cutaneous leiomyomas: firm, biopsy-confirmed (even one). Often painful; sensitive to touch or cold; paresthesias. Mean onset ~25 (10–47).

Uterus

~85
in 100 females with HLRCC **get fibroids (to ~100)**

YES IF

Uterine fibroids (leiomyomas):

- Median ~28–30 (vs ~38 FH-negative)
- Heavy/irregular bleeding; pelvic pain

Kidney

~15
in 100 people with HLRCC **get kidney cancer**

YES IF

FH-deficient RCC, especially before 40.

Skin GeneReviews Table 2 (Kamihara et al. 2025). Uterus ~85–100; up to 98–100% with cutaneous leiomyomas (Stewart et al. 2008). Kidney ~15 (Menko et al. 2014). **Most people with HLRCC do not get kidney cancer.**

When to consider germline FH testing

- RCC — especially early-onset or papillary; FH-deficient RCC on IHC (FH loss, 2SC positive); RCC at age 46 or under
- Cutaneous piloleiomyomas / skin leiomyomas; multiple, early, or recurrent uterine fibroids
- Family history of RCC; FH-deficient fibroids on pathology; a relative with a known FH variant

If yes to any of the above: consider germline FH testing.

How: see back ›

Kidney surveillance

Kidney MRI every year, for life

starting at age 8–10



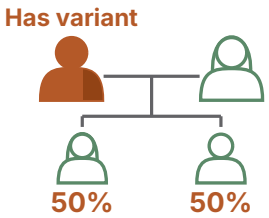
MRI with contrast, 1–3 mm slices through the kidneys. **Ultrasound alone: not enough.**

Identifying HLRCC early can save lives: screening finds early-stage RCC; stage 1–2 lived longer than stage 3–4 (Forde et al. 2020).

⚠ No wait for 3 cm

Can spread under 1 cm. NCI (Grubb et al. 2007): nearly half had nodal or distant mets at presentation. **Solid lesion or suspected cancer: prompt wide-margin surgery** by an HLRCC-experienced team; partial if a wide margin is feasible, else radical; consider RPLND. No ablation.

Passing it on



Each child: 1 in 2 (50%)

Test relatives for the known variant.

OTHER CARE

- Dermatologist every 1–2 years
- Gynecologist who knows HLRCC

Criteria, imaging, how to test: see back ›

Diagnose

Not prospectively validated. A P/LP germline FH variant establishes the diagnosis.

SMIT 2011 / MENKO 2014: LIKELY HLRCC

1. **Histologically confirmed multiple cutaneous piloleiomyomas**

— OR —

2. **At least 2 of:**
   - Surgery for symptomatic uterine leiomyomas before age 40
   - Type 2 papillary renal cell carcinoma before age 40
   - First-degree relative who meets one of these criteria

SCHMIDT & LINEHAN 2014

MAJOR (high likelihood)

- Multiple cutaneous leiomyomata, at least one biopsy proven

MINOR (suspicious)

- Solitary cutaneous leiomyoma + family history of HLRCC
- Early onset renal tumors of type 2 papillary histology
- Multiple early-onset (<40) symptomatic uterine fibroids

DEFINITIVE

- Positive germline FH-mutation test

Pathology: FH-deficient RCC/fibroids often show loss of FH staining and positive 2SC staining.

Kidney MRI findings

	MRI FINDING	BOSNIAK 2019	IN HLRCC
	Simple or minimally complicated cyst: smooth thin (≤2 mm) wall, no or few (1–3) thin septa, no enhancing nodule	**I–II**	**Keep annual MRI.** Exception: benign-looking cysts can be or become cancer.
	Many (≥4) thin enhancing septa, or minimally thickened (3 mm) enhancing wall/septa	**IIF**	**Follow closely:** prompt follow-up MRI, same modality; review by an HLRCC expert.
	Thick (≥4 mm)/irregular enhancing wall or septa	**III (~50%*)**	**Concerning:** low threshold for surgery.
	Enhancing nodule	**IV (~90%*)**	**Remove promptly**, wide margins.
	Solid enhancing mass, any size	**not a cyst**	**Remove promptly**, wide margins, even under 1 cm. No 3 cm wait.
	New lesion, change in a known cyst, or diffusion restriction in a solid part	**–**	**Expert review.** Diffusion restriction strongly linked to cancer (Sheikhy et al. 2026); in 83% of HLRCC RCCs (Paschall et al. 2020).

*Malignant rates (Silverman et al. 2019). Sheikhy et al. 2026: 44/76 benign; Paschall et al. 2020: mean growth ~1.1 cm/year.

Real HLRCC MRI examples: Paschall et al. 2020: DWI+ solid areas (HLRCC RCC). Sheikhy et al. 2026: 5.8 cm cyst, enhancing solid component → malignant; 4.0 cm, DWI+, no enhancement → benign.

Germline *FH* testing: how (3 steps)

When: see front

1 COUNSEL

Counseling before and after testing.

2 ORDER

Blood or saliva. *FH* sequencing plus deletion/duplication analysis, by a CLIA-certified lab.

3 RESULTS, THEN RELATIVES

P/LP: confirms HLRCC in most cases. **VUS:** does not confirm or rule it out; follow personal and family history; it can be updated later. Cascade testing.

Learn more

REFER Counselor
findageneticcounselor.nsgc.org
FIND Specialist
hlrcc.org/hlrcc-map
SHARE Handbook
hlrcc.org/hlrcc-handbook

TRIALS Trials
hlrcc.org/clinical-trials
NIH NIH study
hlrcc.org/nih-enrollment
JOIN Join
hlrcc.org/join-us

References and sources: hlrcc.org/clinician-references

Scan for references

Scan for the Handbook