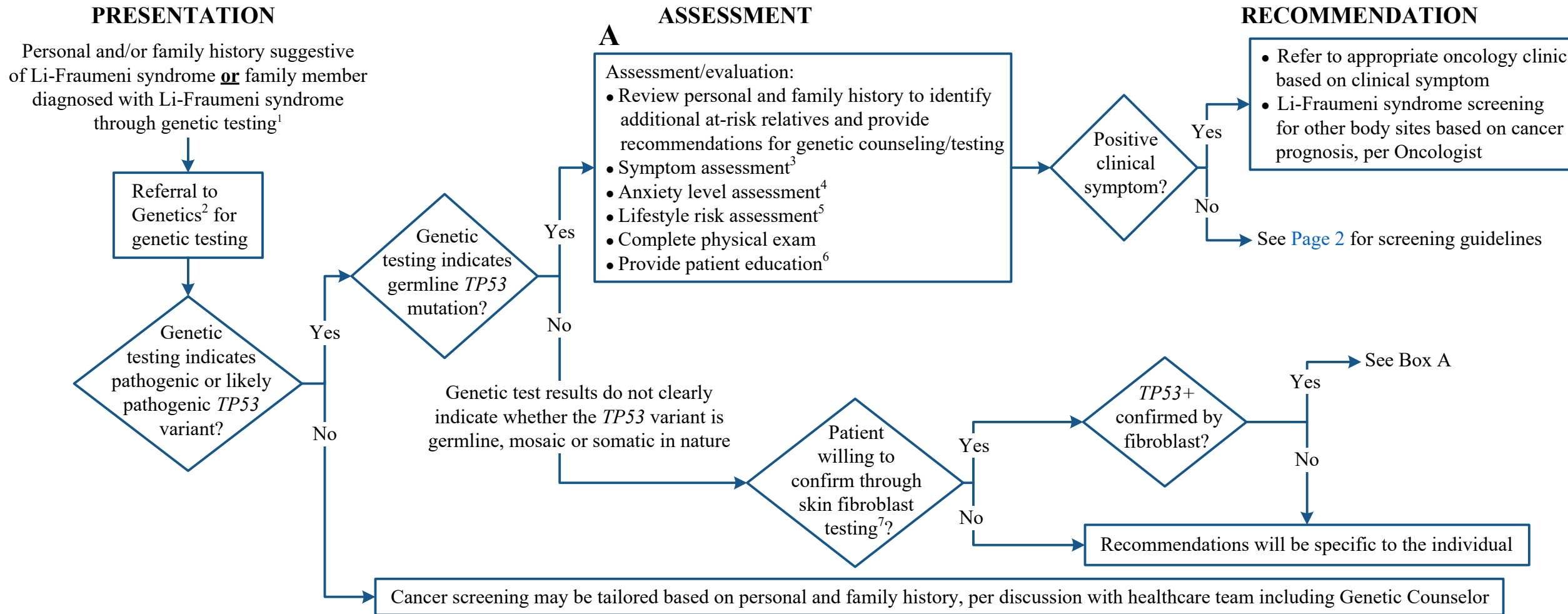Disclaimer: *This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care.*

Note: Screening is only intended for asymptomatic individuals. Individuals undergoing Li-Fraumeni Syndrome screening should have a 10-year life expectancy and no co-morbidities that would limit the diagnostic evaluation or treatment of any identified problem. The screening technique should be performed with a consistent technique and process.

PRESENTATION

Personal and/or family history suggestive of Li-Fraumeni syndrome **or** family member diagnosed with Li-Fraumeni syndrome through genetic testing[1]

↓

Referral to Genetics[2] for genetic testing

↓

Genetic testing indicates pathogenic or likely pathogenic *TP53* variant?

- **Yes** → Genetic testing indicates germline *TP53* mutation?
- **No** → Cancer screening may be tailored based on personal and family history, per discussion with healthcare team including Genetic Counselor

Genetic testing indicates germline *TP53* mutation?
- **Yes** → (Box A)
- **No** → Genetic test results do not clearly indicate whether the *TP53* variant is germline, mosaic or somatic in nature → Patient willing to confirm through skin fibroblast testing[7]?
  - **Yes** → *TP53+* confirmed by fibroblast?
    - **Yes** → See Box A
    - **No** → Recommendations will be specific to the individual
  - **No** → Recommendations will be specific to the individual

ASSESSMENT

A

Assessment/evaluation:
- Review personal and family history to identify additional at-risk relatives and provide recommendations for genetic counseling/testing
- Symptom assessment[3]
- Anxiety level assessment[4]
- Lifestyle risk assessment[5]
- Complete physical exam
- Provide patient education[6]

→ Positive clinical symptom?

RECOMMENDATION

Positive clinical symptom?
- **Yes** →
  - Refer to appropriate oncology clinic based on clinical symptom
  - Li-Fraumeni syndrome screening for other body sites based on cancer prognosis, per Oncologist
- **No** → See Page 2 for screening guidelines

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[1] Personal and/or family history of LFS-associated cancers including adrenocortical carcinomas, breast cancer, central nervous system tumors, osteosarcomas, and soft-tissue sarcomas. Additional LFS-associated cancers include leukemia, lymphoma, gastrointestinal cancers, cancers of head and neck, kidney, larynx, lung, skin (*e.g.,* melanoma), ovary, pancreas, prostate, testis, and thyroid. See CRIT-7 LFS testing criteria within the NCCN guidelines.

[2] Patients will be referred to Genetics within their home center. If the patient is new or does not have a genetics counselor assigned to their home center, they can be referred through any home center.

[3] Refer to Patient Education - Li-Fraumeni Syndrome Education and Early Detection Program (LEAD) - Adult Screening Program

[4] If moderate to severe anxiety related to Li-Fraumeni syndrome screening is identified, refer for psychiatric evaluation and/or counseling

[5] See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

[6] Patient Education - Li-Fraumeni Syndrome Education and Early Detection (LEAD) - Adult Screening Guidelines

[7] Skin fibroblast testing requires a skin punch biopsy

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Li-Fraumeni Syndrome Education and Early Detection (LEAD) - Adult Screening Guidelines

Cancer	Exams and Tests	Frequency
General	Complete physical exam	Every 6 months
Adrenocortical Tumor (ACT)	• MRI[1] whole body Assess for clinical signs/symptoms: Females only: • Hirsutism • New changes in menstrual cycle regularity Males and females: • New onset or newly uncontrolled hypertension, new onset or newly uncontrolled diabetes mellitus, unexplained weight gain, new lower extremity edema, new hypokalemia, new acne **If patient reports any of the above order the following ACT screening labs: DHEA-S, ACTH, total testosterone, total cortisol, BMP and referral/discussion with Endocrinology, as needed**	Annually
Brain	MRI[1,2] brain	Annually
Breast (begin at age 20-25 years old)	Clinical breast exam (begin at age 20 years old)	Every 6-12 months
	• Breast awareness (begin at age 18 years old) • Mammogram (begin at age 30 years old) • MRI[1] breast with and without contrast (begin at age 20 years old)	Annually (alternating every 6 months)
	Consider surgical removal of both breasts to prevent cancer (bilateral prophylactic mastectomy). For women treated for breast cancer, screening of remaining breast tissue should continue.	Age and patient appropriate
Colon (begin at age 25 or 5 years before earliest known colon/gastric cancer diagnosis in family history, whichever comes first)	• Colonoscopy • Esophagogastroduodenoscopy (EGD)	Every 2-5 years
Leukemia/Lymphoma	CBC with differential	Annually
Melanoma	Skin exam – see Skin Cancer Screening algorithm	Annually
Pancreas[3]	• CA 19-9 • Amylase • HgbA1c • Lipase • MRI whole body • Fasting glucose	Annually
Sarcoma	MRI whole body	Annually

DHEA-S = dehydroepiandrosterone sulfate   ACTH = adrenocorticotropic hormone   BMP = basic metabolic panel

[1] MRI of the whole body and brain are both performed on an annual basis, staggered with a six month interval in between. MRI breast with and without contrast should be performed at the same time as the MRI brain (but on different days due to the contrast dose).

[2] The first MRI brain should be performed with and without contrast; if normal, MRI brain without contrast should be performed thereafter. If patient has a history of malignancy, all brain MRIs should be performed with and without contrast.

[3] For patients with a family history of pancreatic ductal adenocarcinoma (PDAC) on affected side [1 first-degree relative (FDR) or 1 second-degree relative (SDR)]: See Pancreatic Cancer Screening algorithm

SUGGESTED READINGS

Kratz, C., Achatz, M., Brugières, L., Frebourg, T., Garber, J., Greer, M., . . . Kratz, C. (2017). Cancer screening recommendations for individuals with li-fraumeni syndrome. *Clinical Cancer Research*, *23*(11), e38-e45. https://doi.org/10.1158/1078-0432.CCR-17-0408

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DEVELOPMENT CREDITS

This screening algorithm is based on majority expert opinion of the Li-Fraumeni Syndrome work group at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

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