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ICR The Institute of Cancer Research

CANCER RESEARCH UK

The Annabel Evans Memorial Fund

The ROYAL MARSDEN NHS Foundation Trust

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The SIGNIFY Study

Magnetic ReSonance ImaGing screeNing In Li Fraumeni SYndrome: An exploratory whole body MRI study

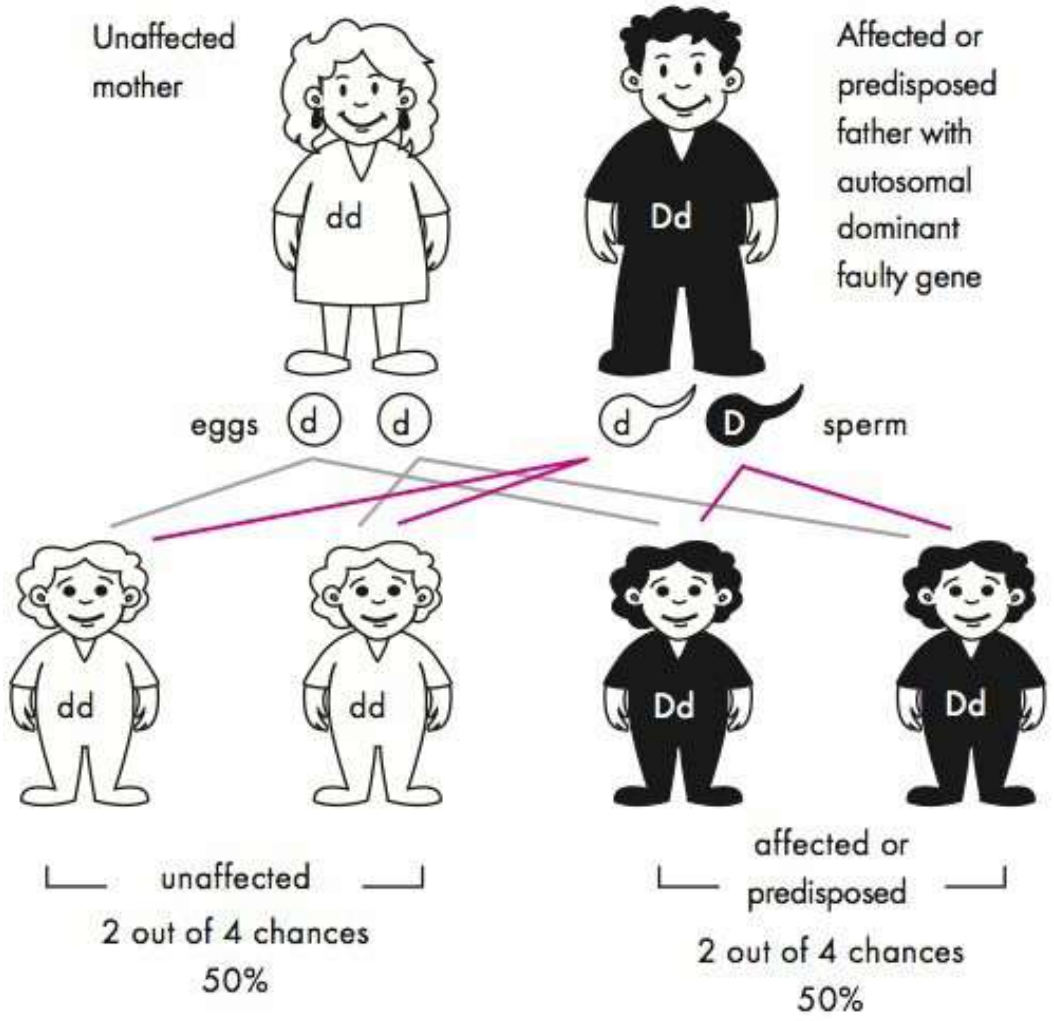
Professor Ros Eeles

Li Fraumeni Syndrome

- Majority of families who meet the criteria for Li Fraumeni Syndrome harbour a mutation in the gene *TP53* (aka p53)
- Mutations are inherited in an autosomal dominant fashion
- Mutation carriers are predisposed to a range of cancers:
  - Including sarcoma, breast cancer, brain tumours, adrenocortical carcinoma, leukaemia
- Typically age of cancers can be 20 – 30 years younger than the general population
- Carriers can get more than one cancer each
- Estimates of the chance of carriers getting ≥1 cancer vary
  - This chance could be up to 93% in women and 68% in men by age 50
  - The actual risk likely varies depending on family history and specific mutation

Autosomal Dominant Inheritance

- A person can carry only one copy with a mutation, other copy is normal
- 50% chance of passing on mutated copy to children
- Inheritance is not linked to gender – but implications of being a carrier are different



Centre for Genetics Education

Management of LFS (Pan-Thames Guidelines)

- Open door policy
- Female breast cancer risk:
  - Practice breast awareness and self-examination
  - Annual breast MRI age 20 – 50
  - Annual mammography from age 40 in some centres and some countries (not all)
  - Discussion regarding risk-reducing mastectomy
- No other targeted screening is recommended as there is no proven benefit
- Cancer treatment should be optimal: radiotherapy only avoided where another type of treatment is of at least equal benefit
- Predictive genetic testing after appropriate counselling can be done at any age

Whole body MRI screening in LFS

- A Brazilian study screened 57 carriers with two cancers found (1 kidney cancer and 1 breast DCIS) (Paixao et al. 2015)
    - Most of these patients carry a Brazilian ‘founder’ mutation which has a slightly lower rate of cancer
- A paediatric WB-MRI study scanned 24 children on average twice each (Anupindi et al. 2015)
    - 9 suspicious lesions were found and one was confirmed to be cancer (thyroid)
- Toronto study employed a very thorough screening program which showed better outcomes in those who had the screening (Villani et al, 2011)
- Currently there are several screening studies at different centres (USA, UK, Australia, Netherlands) looking at whether whole-body MRI is an effective method of screening
- Results from these studies will be collated to ensure the most useful information results

Whole body MRI screening in LFS

- Advantages:
  - Can detect malignant lesions
  - Most incidental lesions can be evaluated on the WBMRI
  - Wide availability
  - No need for special software
  - No need for IV contrast
  - Lack of radiation
- Disadvantages:
  - Many incidental lesions
  - Extra investigations needed to assess uncertain lesions
    - May include invasive or radiation modalities
  - Inter-scanner variability
  - Lack of optimised protocol
  - Long acquisition time
  - Patient tolerability

The SIGNIFY Study

- Aims to assess:
  - incidence of malignancies diagnosed in asymptomatic *TP53* mutation carriers using whole body MRI technique against general population controls
  - incidence of non-malignant relevant disease
  - incidence of irrelevant findings and the investigations required to determine relevance of MRI findings
  - the psychological impact of whole body MRI screening in *TP53* mutation carriers
- 44 full-body MRI scans for *TP53* mutation carriers
- 44 matched population controls

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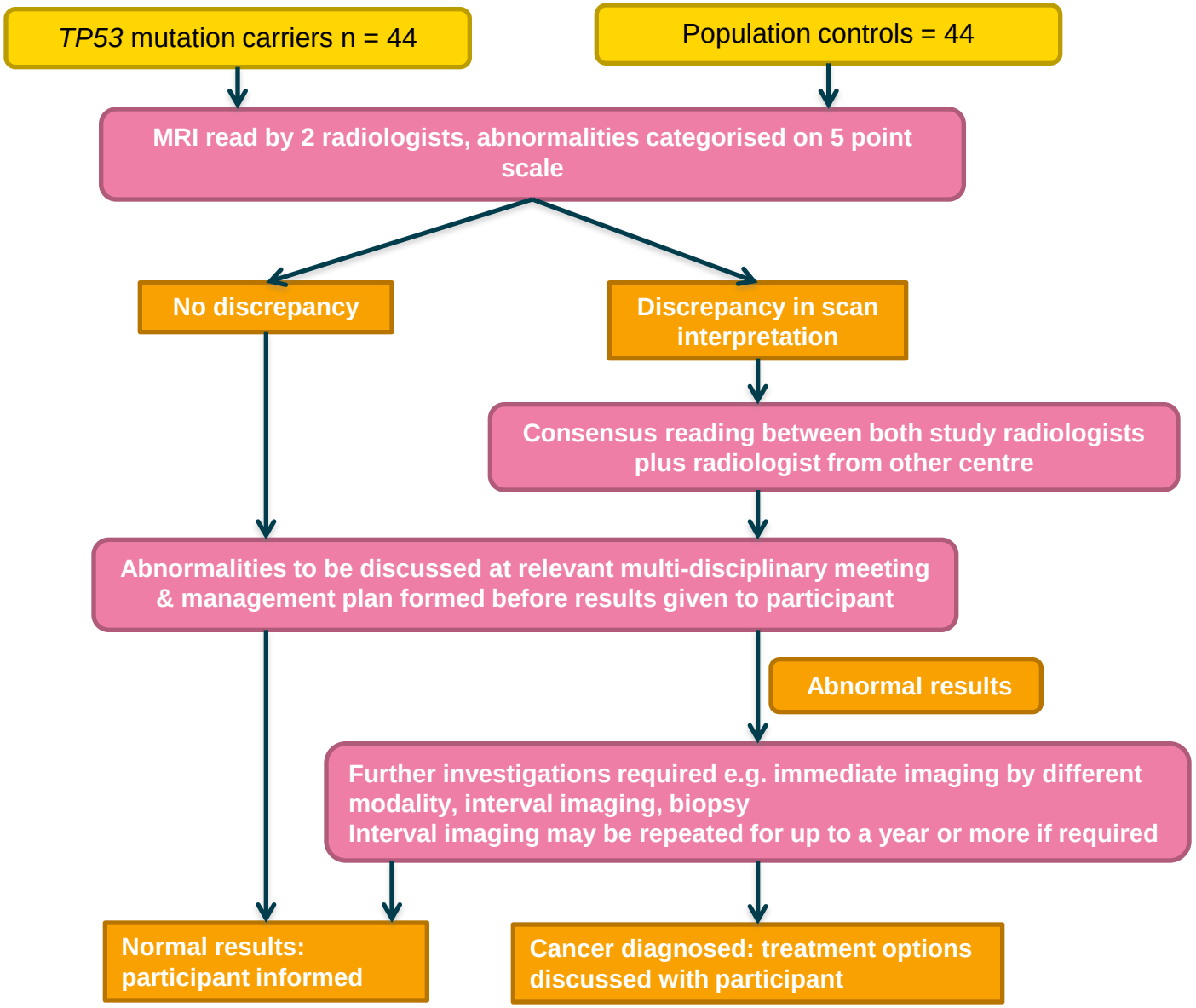
Imaging Algorithm



Conclusions

- Study is not yet complete

- Psychosocial impact on carriers is also not yet complete
- Final publication expected in early 2018
- International effort underway to find the best way to find cancers early in this group of people

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Many thanks to all the participants for volunteering their time

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