



LEIDS UNIVERSITAIR MEDISCH CENTRUM

Clinical manifestations in 40 Dutch MUTYH associated Polyposis (MAP) patients

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Background

2002: discovery MUTYH associated polyposis (MAP)

Since then 126 biallelic patients described in detail, natural history?

Aims

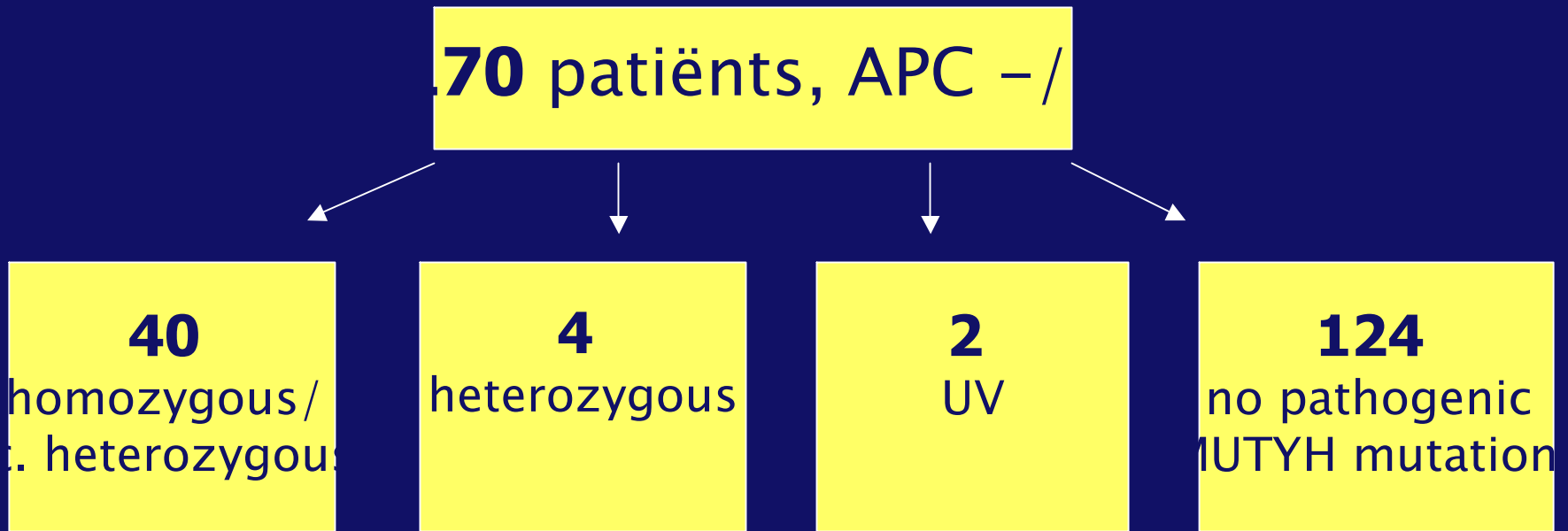
1. Assess the clinical features of MUTYH associated Polyposis (MAP)
2. Develop guidelines for surveillance

Patients and Methods

- 170 (A)FAP families, APC negative
 - Referred from clinical centres and polyposis registry
 - Data collection (polyp count, crc, pathology, age, extra colonic manifestations)

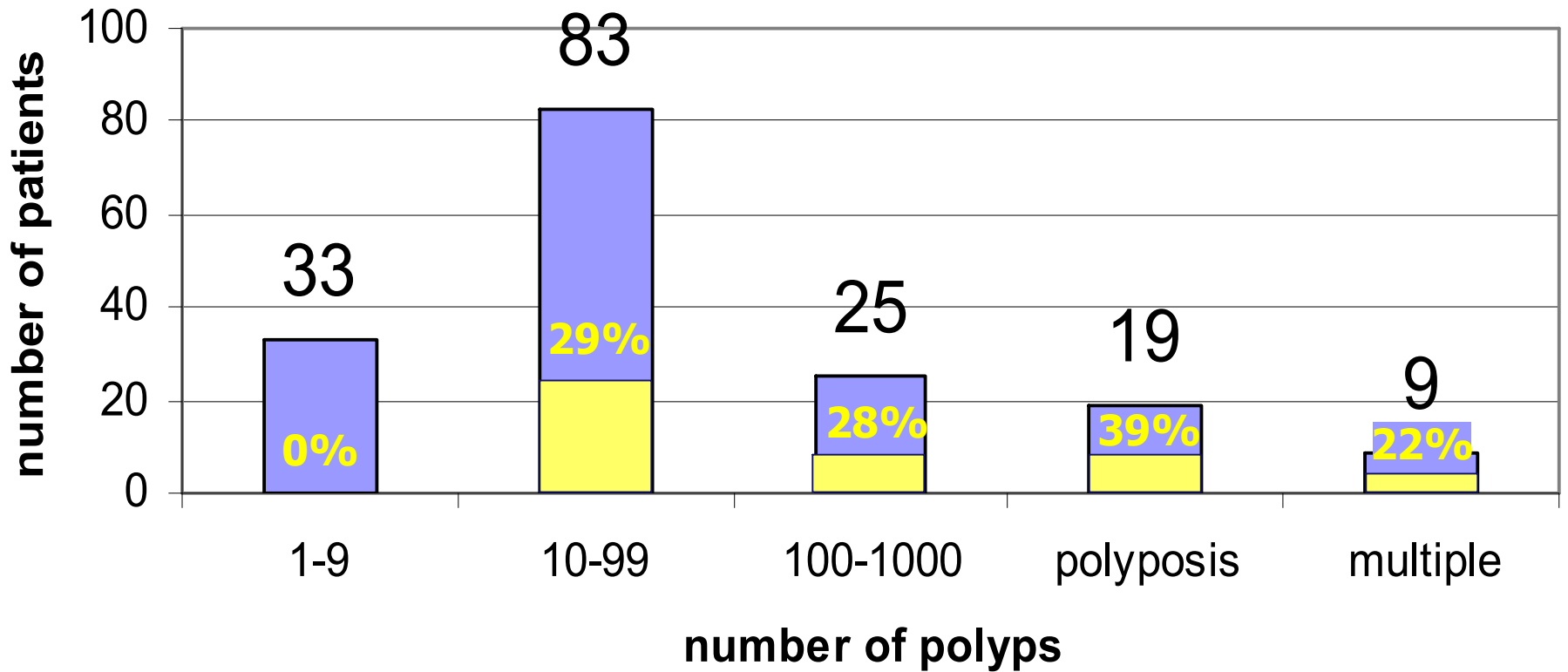
- MUTYH Mutation analysis
 - DGGE (exon 2, 7, 8 and 10)
 - MUTYH sequence analysis (exons 1, 3 - 6, 9, 11-16)

Results



Polyp count

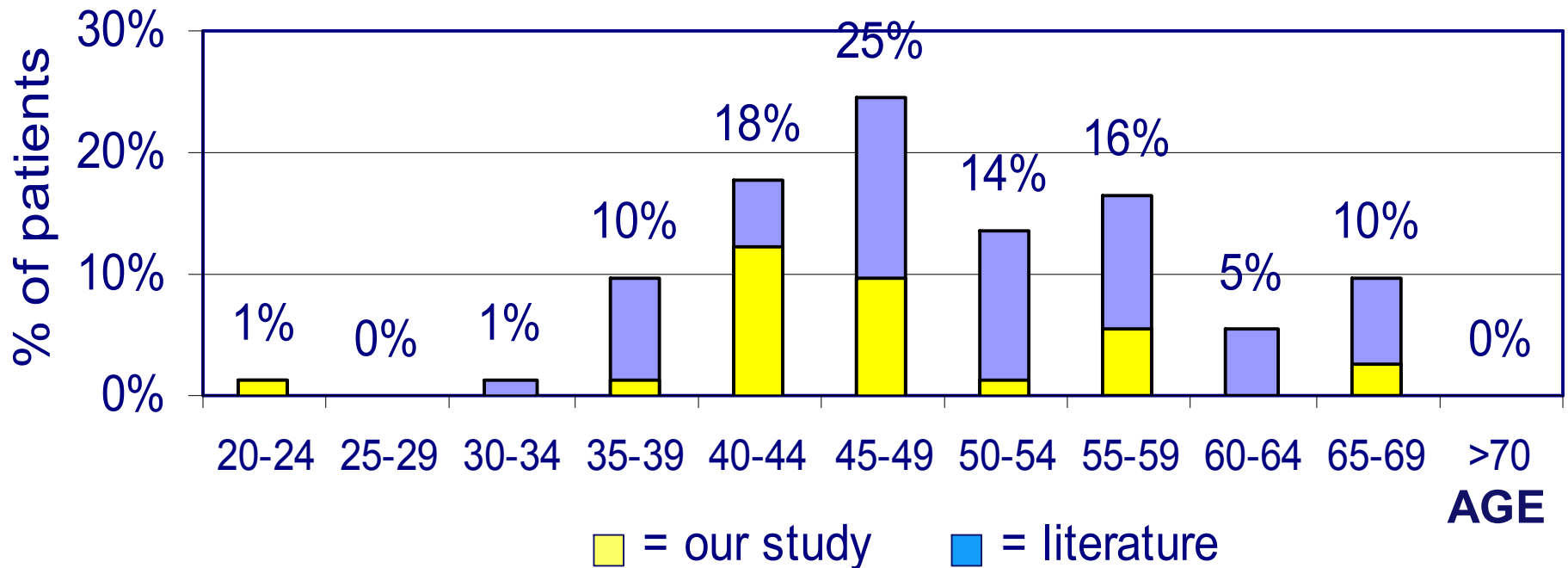
Cumulative polyp counts & MUTYH mutations



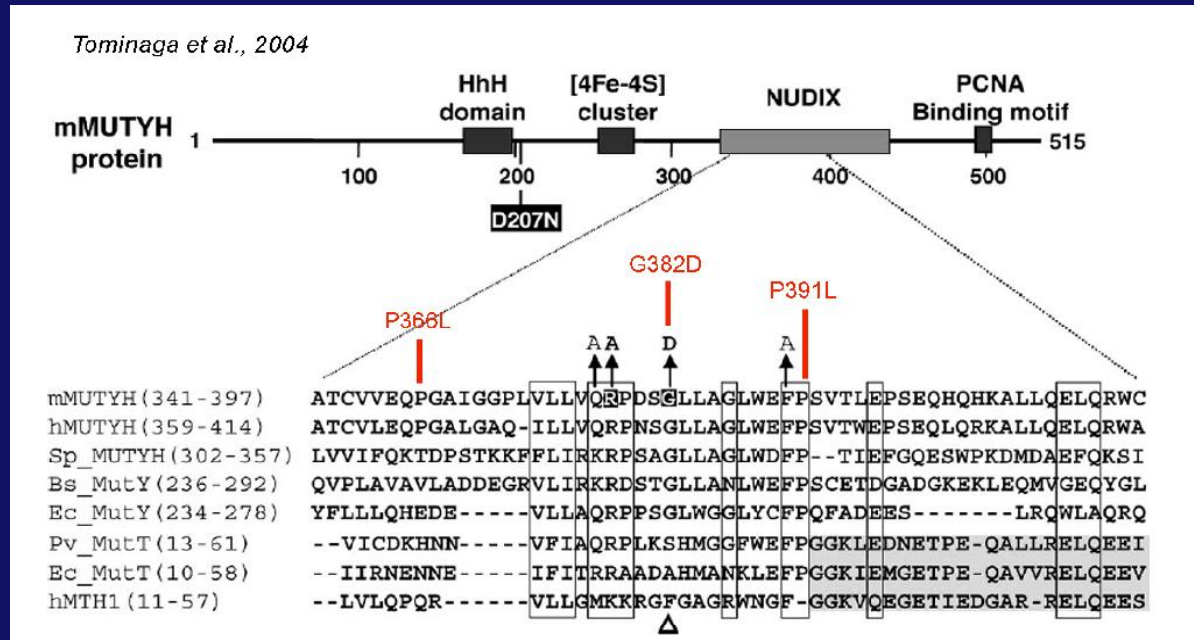
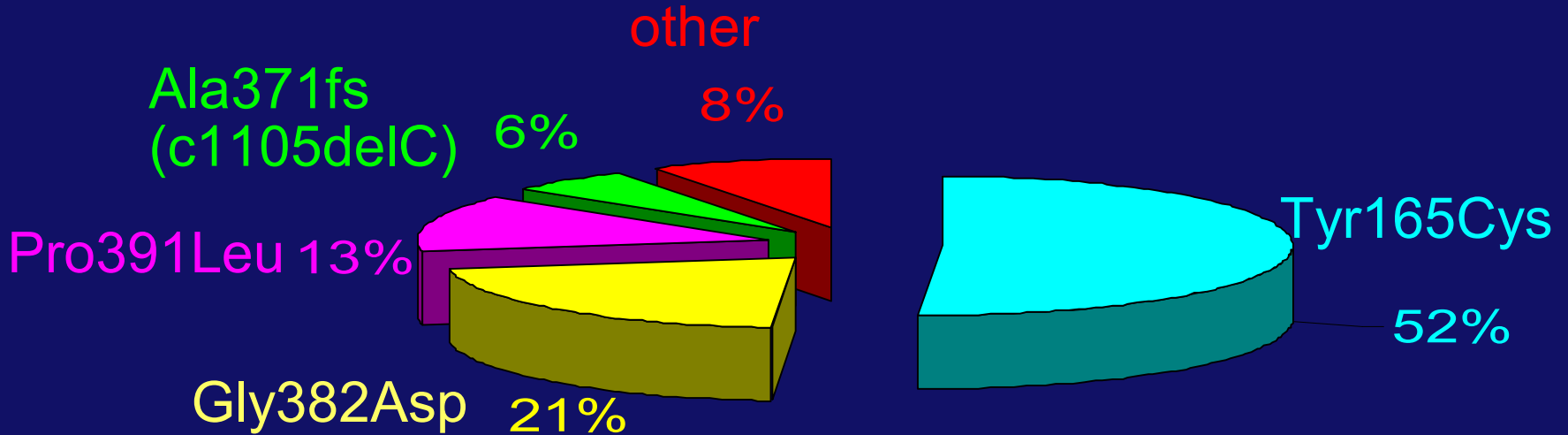
MAP and CRC

- 26/40 (66%) CRC mean age 47 yrs
- 62% rightsided

age of diagnosis of CRC in 73 MAP patients

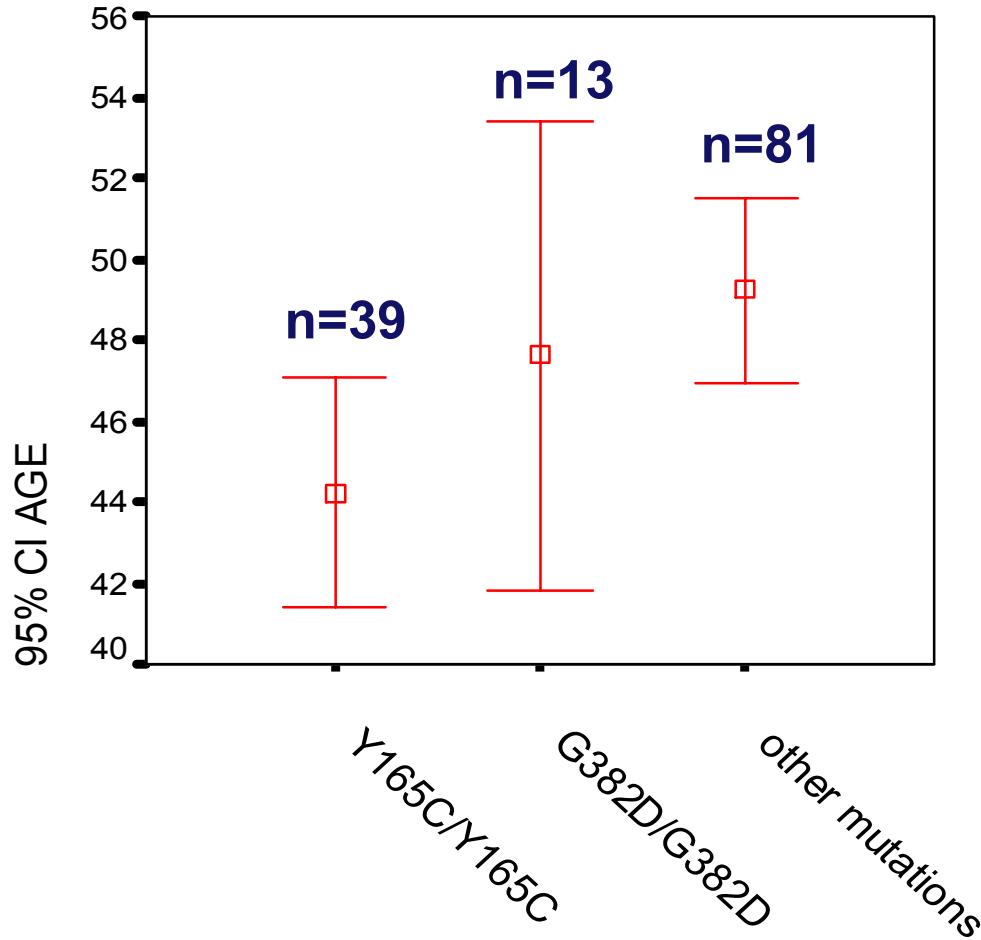


Mutations



Genotype-Phenotype

mean age of diagnose in 133 MAP patients



MAP and extra colonic manifestations

➤ 5/16 (31%) gastro-duodenal polyps

- 3 duodenal adenomas
- 1 duodenal adenomas & carcinoma
- 1 fundic gland polyposis



➤ 4/21 (18%) females had breast cancer

- Standardised Morbidity Ratio = 3,75

MUTYH and breast cancer

	Total	MUTYH Bi-allelic	MUTYH Heterozygotes	MUTYH mutations
Braest & Colon cancer Families	148	1 (0,7%)	4 (3%)	3x G382D/- Y165C/- G382D/Y165C
Controls*	593	0	8 (1,3%)	4x G382D/- 4x Y165C/-

Conclusions/ Recommendations

- MAP associated with attenuated and classic forms of polyposis coli
- ~Two third CRC and one third upper GI lesions
- Colonoscopy: every 2-3 years starting; > 25-30 years
- Upper GI endoscopy: every 1-5 years; > 25-30 years (?)
- Relation MUTYH and breast cancer still needs further research

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