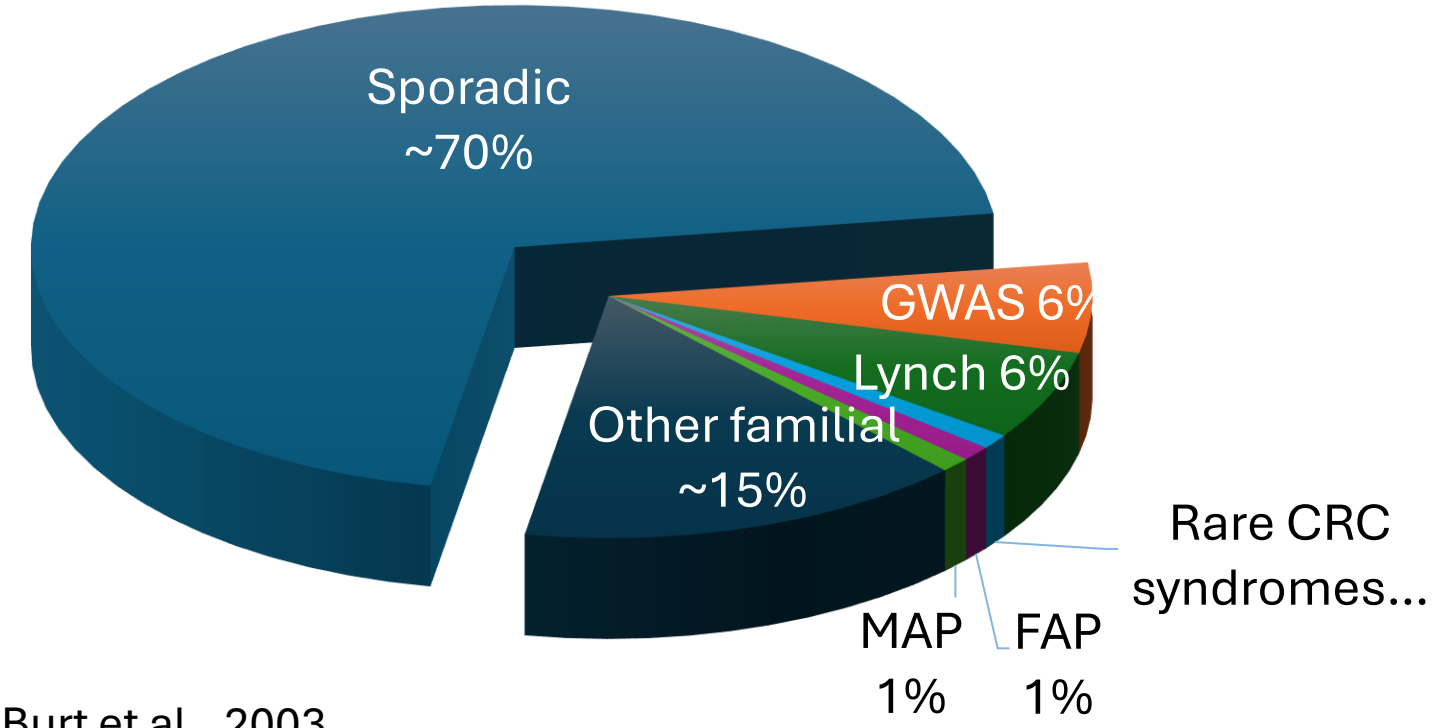
Duodenal involvement in MUTYH-associated polyposis: findings from an international prospective study and implications for endoscopic surveillance.

Imogen Bennett
PhD Student

Wales Rare Disease Research Network Event

Sporadic vs Familial Causes of Colorectal Cancer (CRC)



Burt et al., 2003

- Familial Adenomatous Polyposis
  - 1000s adenomas
  - APC mutation
  - Up to 100% lifetime risk of CRC
- MUTYH Associated Polyposis
  - 10-100 adenomas
  - MUTYH mutation

Colectomy

Duodenal disease

Duodenal Disease in FAP and MAP

	FAP	MAP
Polyposis	up to 90%	>25%
Cancer	~5%	>2%

Spigelman Staging (Modified Vienna)

		Score	
Factor	**1 Point**	**2 Points**	**3 Points**
No. of polyps	1-4	5-20	>20
Polyp size (mm)	1-4	5-10	>10
Histology	Tubulous	Tubulovillous	Villous
Dysplasia	Low Grade		High Grade

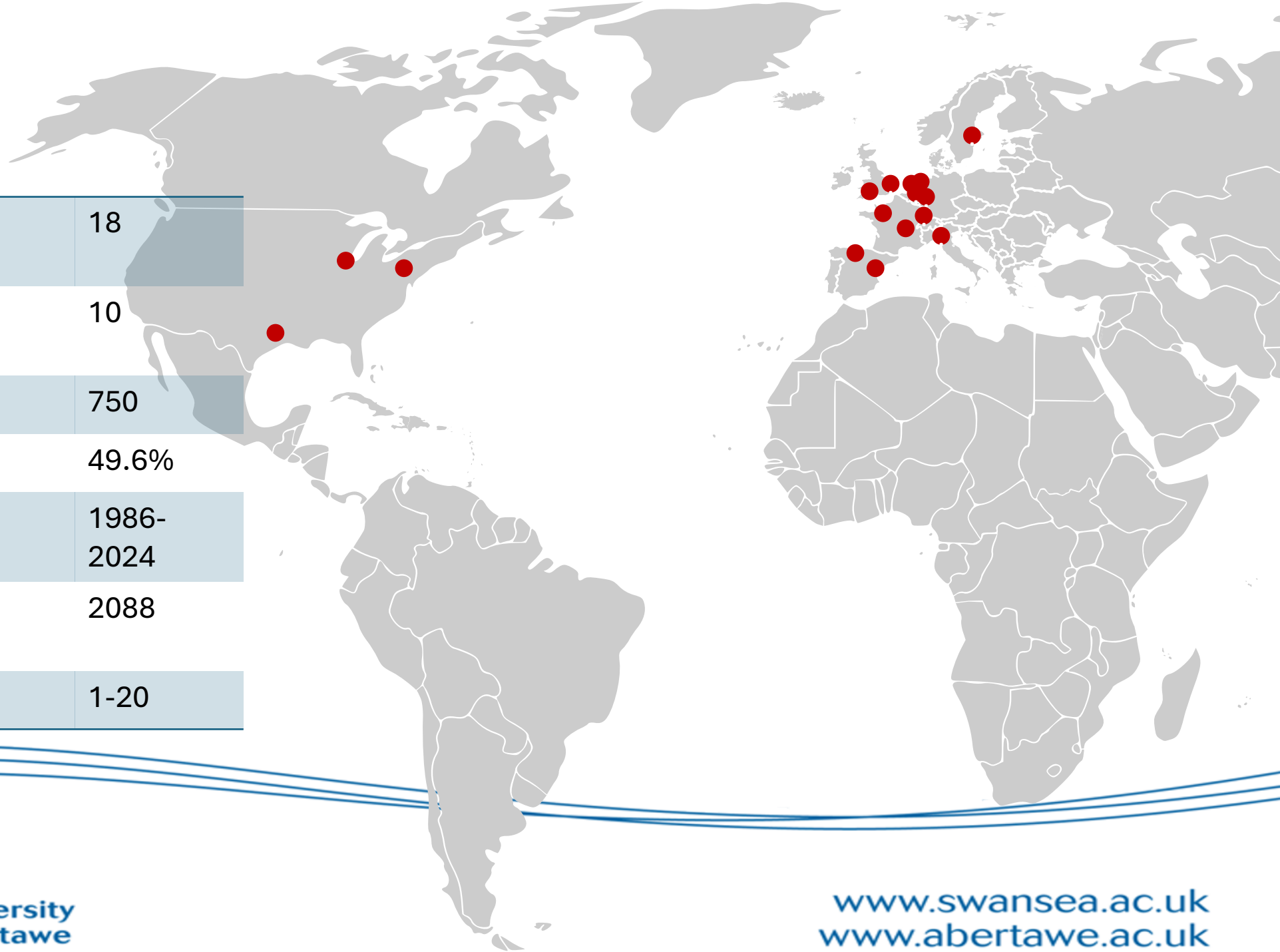
Score	Stage	Frequency of Surveillance Endoscopy
0	0	Every 5 years
1-4	I	Every 4 years
5-6	II	Every 3 years
7-8	III	1-2 years
9-12	IV	6 months, Consider resection

Mallorca Group (Vasen et al, 2008)

Aims

1. To explore the natural history of duodenal disease in MAP using upper GI surveillance endoscopy data from MAP patients
2. To determine if current management for duodenal disease in MAP is effective

Number of study sites	18
Number of countries	10
Number of subjects	750
Sex (males)	49.6%
Study period	1986-2024
Number of endoscopies	2088
Range	1-20



Methods - Data Collection

Baseline Data

- DOB, Sex, etc.
- *MUTYH* Mutations (diagnosis confirmation)

Duodenal Disease

- Endoscopy details: date, Number of polyps, location, histology, size
- Spigelman staging and progression
- Duodenal cancer
- Treatments for duodenal disease (biopsy, surgery, etc.)

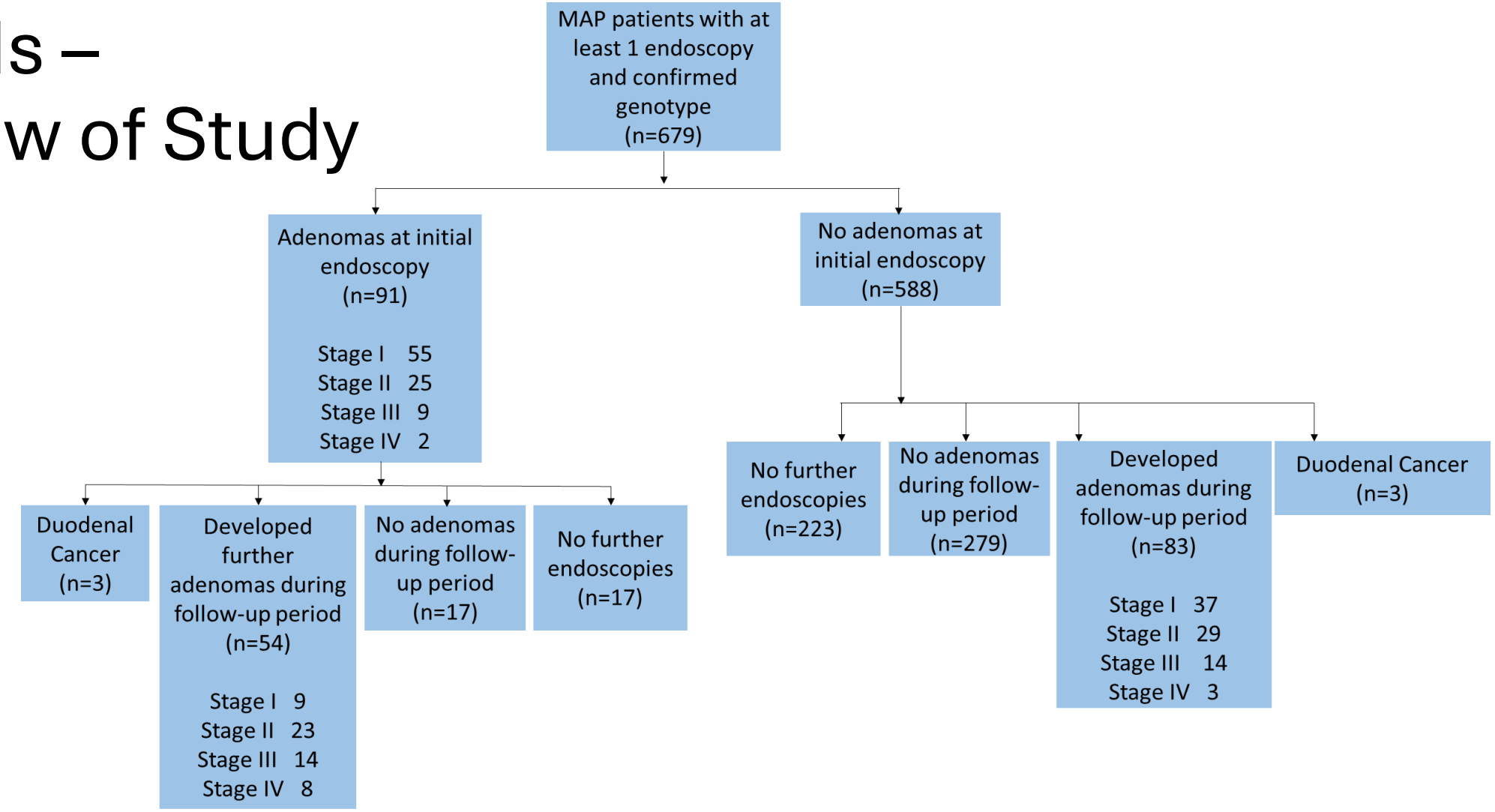
Colorectal Disease

- Date and result of first colonoscopy
- Colorectal surgery
- Colorectal cancer

Miscellaneous

- Additional cancer types
- Date of death and reason (if applicable)

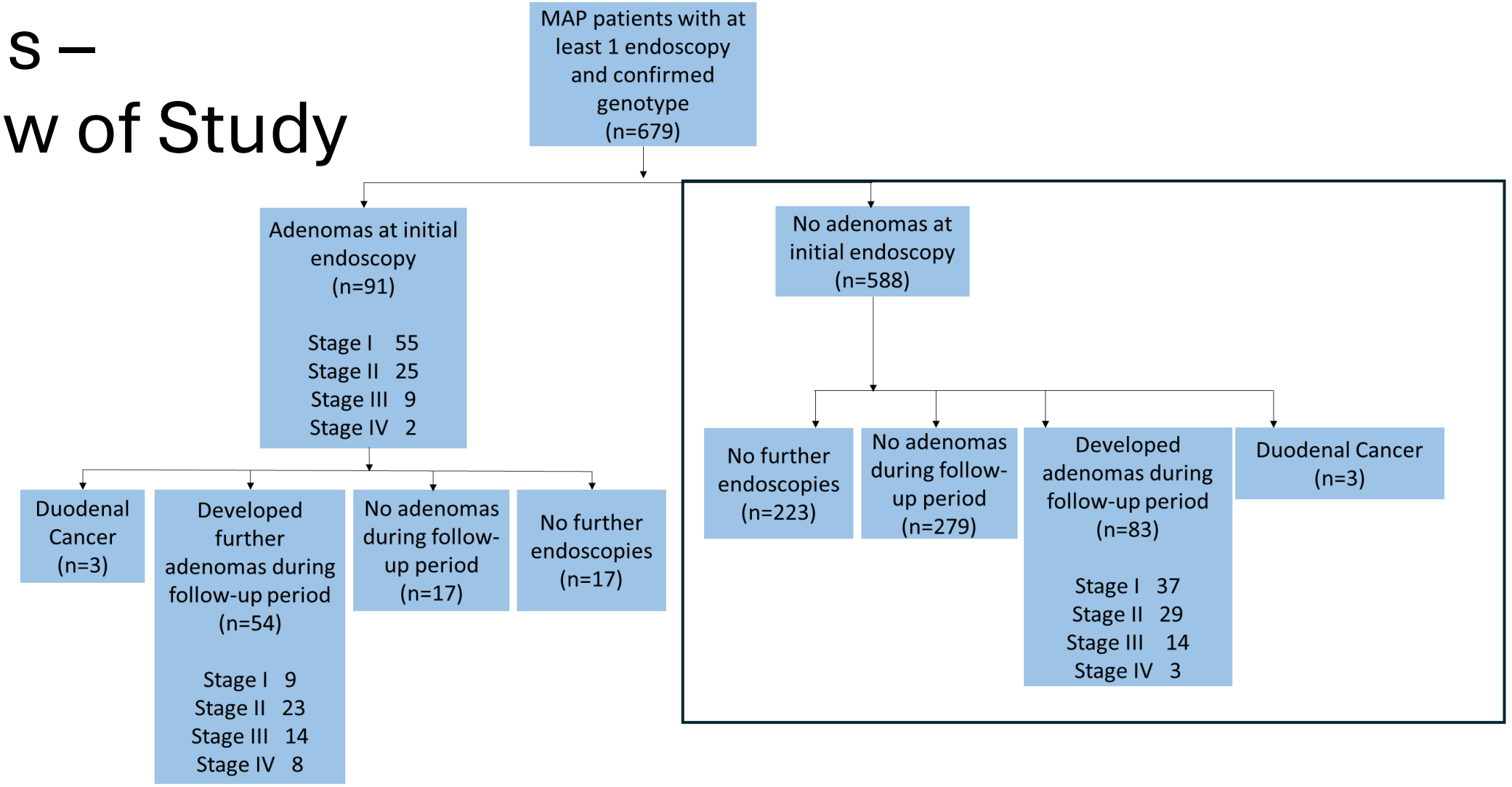
Methods – Overview of Study



Duodenal Cancer Incidence

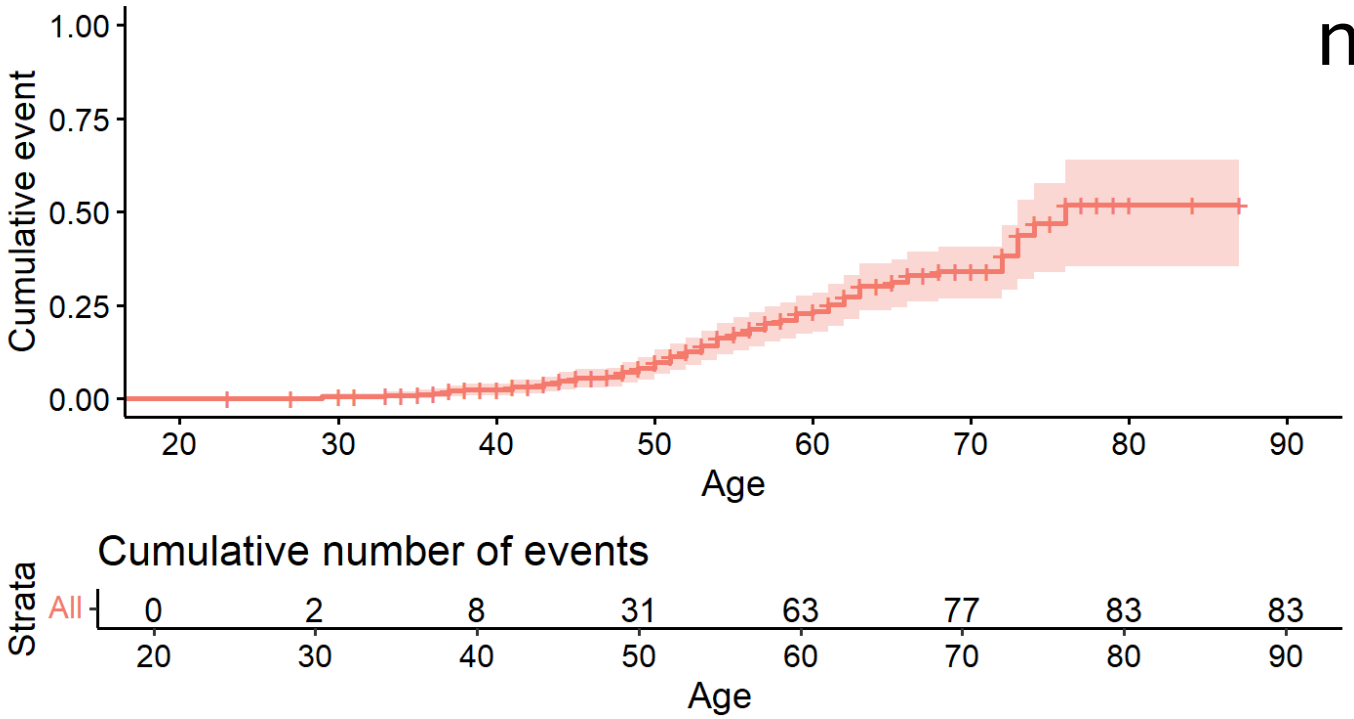
Patient	Genotype	Age at cancer development	Location of Cancer	Number of years follow up before cancer development	Spigelman stage at initial endoscopy	Prior Spigelman stage before Cancer	Spigelman stage characteristics at last OGD prior to cancer development					Spigelman progression
							Histology	Location	Dysplasia	Size (mm)	Number	
1	Y179C (HOM)	47	ND - 'Distally located'	1	III(8)	II(6)	TVA	D2	LGD	4	10	III(8)-II(6)-ca-ca
2	G396D/ R245H	61	Unknown	9 months	0	0	-	-	-	-	-	0-ca
3	Y179C (HOM)	65	duodenal – jejunal transition (Ligament of Treitz)	2	0	0	-	-	-	-	-	0-ca
4	G396D/ P405L	64		12	I(4)	0	-	-	-	-	-	I(4)-0-I(4)-I(4)-I(4)-I(4)-I(4)-I(4)-I(4)-0-Ca
5	G396D/ 933+3A>C	67	Ligament of Treitz	8 months	I(4)	I(4)	Fragments of TA	Unknown	Unknown	1-3mm	Random biopsy	I(4)-ca-0-0-0-1(4)-0
6	G396D/ E480X	83	D2/D3	1	0	0	-	-	-	-	-	0-ca

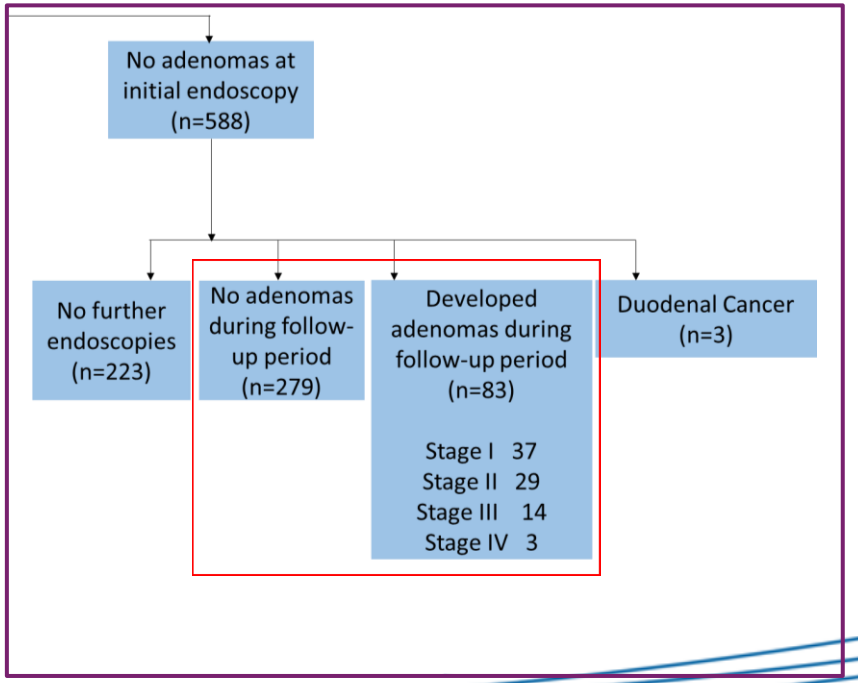
Methods – Overview of Study



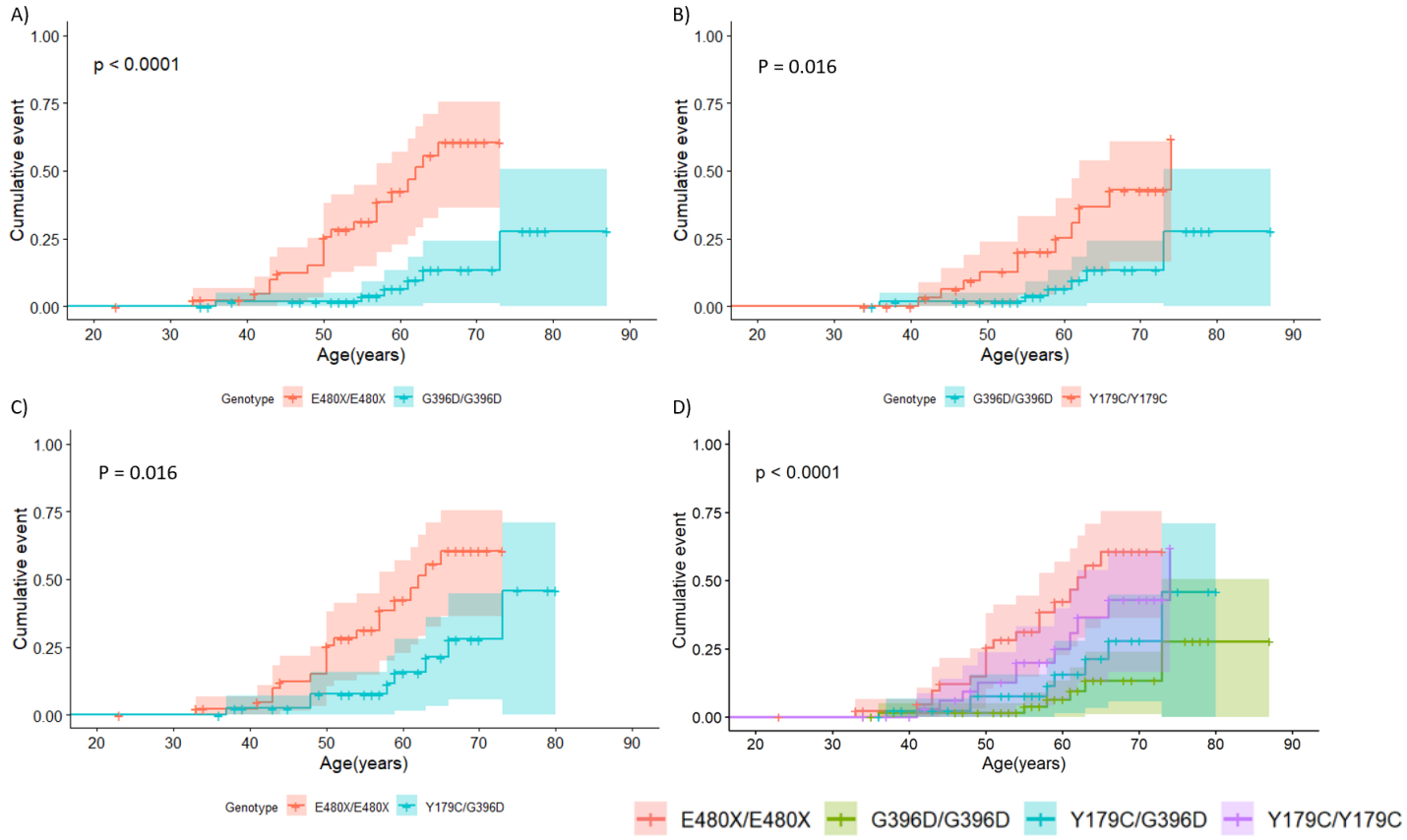
Incidence of Duodenal Adenomas During Prospective Follow Up

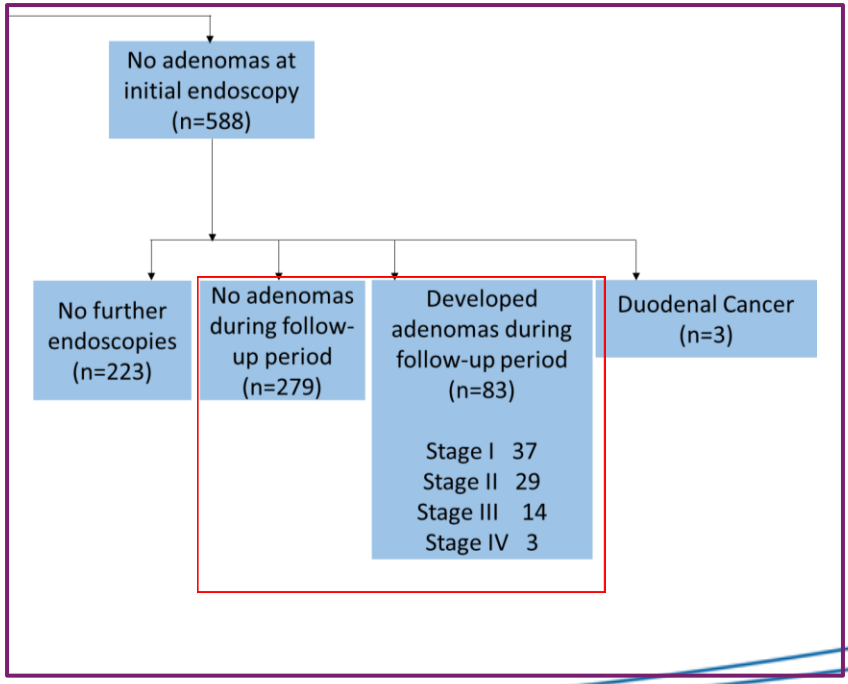
22.7%, Median age: 53 years, median follow up: 10.3 years





Incidence of Adenomas During Follow Up: Genotype/Phenotype Correlation





Conclusions

Swansea University
Prifysgol Abertawe
Faculty of Medicine, Health & Life Science
Y Gyfadran Meddygaeth, Gwyddor Iechyd a Bywyd

- Duodenal disease in patients with MAP is a growing cause for concern
- Duodenal cancer in MAP is rarer than in FAP, and not preceded by stage IV disease
- Duodenal adenomas develop less frequently, and later in MAP than FAP
- Small adenomas with HGD are relatively common, earlier polypectomy should be considered
- Genotype specific guidelines could be considered
- MAP specific guidelines for duodenal disease should be developed.

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Laura Thomas: Laura.E.Thomas@swansea.ac.uk

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Swansea University
Prifysgol Abertawe
Faculty of Medicine, Health & Life Science
Y Gyfadran Meddygaeth, Gwyddor Iechyd a Bywyd

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Rhiannon Owen
Laura Baker
Laura Butlin

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Julian Sampson
Becky Truscott
Hannah West