Pancreatic Cancer UK

PCUK National Study Day Birmingham 7th Oct 2019

Early Diagnosis

Steve Pereira

Professor of Hepatology & Gastroenterology

Institute for Liver & Digestive Health, UCL

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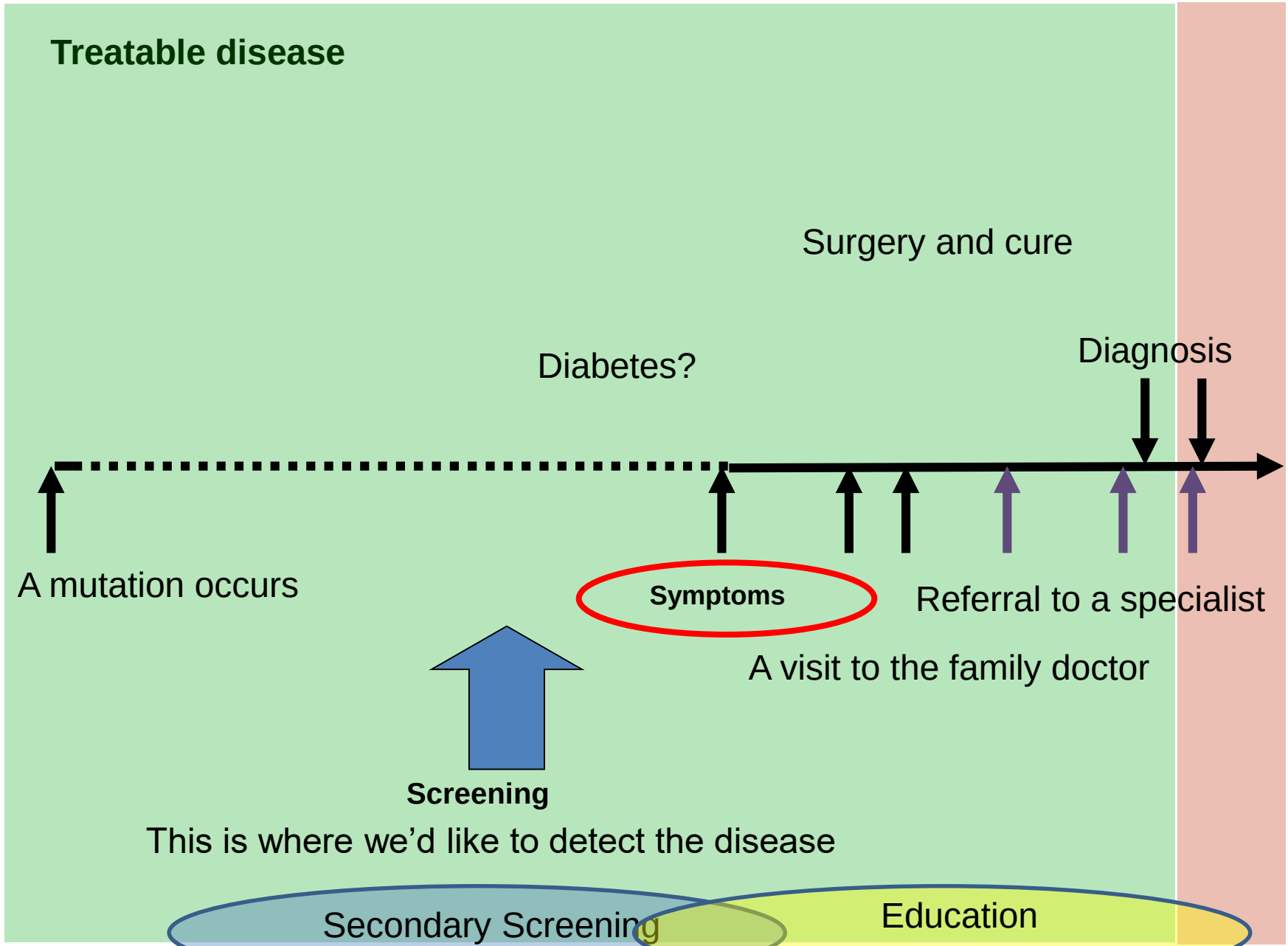
@PereiraGroup

Biomarkers for early diagnosis

Overview

- Identifying symptoms earlier
- Screening high-risk groups
- Emerging diagnostics
- The practicalities

Windows of opportunity for diagnosis of pancreatic cancer



Identifying symptoms earlier

- Existing cancer referral pathways are not very effective
  - ~90% do not yield a cancer diagnosis
  - 1/3 cancers diagnosed through this route
- Symptoms and signs are often too late
- 50% cancers present without recognised alarm symptoms

QCancer

Hippisley-Cox et al, 2013

Information Technology for GPs

- Cancer Decision support tools – risk factors + symptoms

ClinRisk

Welcome to the QCancer®-2016 risk calculator for women: http://qcancer.org/female

Reset | For men | Information | Publications | About | Copyright | Contact Us | Algorithm | Software

Calculate risk

About you

Age (25-89): 68

UK postcode: leave blank if unknown

Postcode: B40 1PP

Clinical information

Smoking status: non-smoker

Alcohol status: non-drinker

Do you have...

- a family history of gastrointestinal cancer?
- a family history of breast cancer?
- a family history of ovarian cancer?
- type 2 diabetes?
- chronic obstructive airways disease (COPD)?
- endometrial hyperplasia or polyp?
- chronic pancreatitis?

Do you currently have...

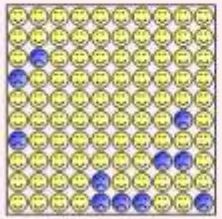
- loss of appetite?
- unintentional weight loss?
- abdominal pain?
- abdominal swelling?
- difficulty swallowing?
- heartburn or indigestion: indigestion
- rectal bleeding?
- blood in your urine?
- blood when you vomit?
- blood when you cough?

Your risk of having one of the following cancers, as yet undiagnosed is:

Cancer	Type	Risk
No cancer		89.05%
Any cancer		10.95%
	pancreatic	3.79%
	ovarian	2.12%
	other	1.67%
	colorectal	1.12%
	gastro-oesophageal	1%
	breast	0.46%
	renal tract	0.27%
	lung	0.2%
	blood	0.2%
	uterine	0.09%
	cervical	0.03%

You have a 10.95% risk of having a cancer as yet undiagnosed, and correspondingly, a 89.05% chance that you are clear.

In other words, in a crowd of 100 people with the same risk factors as you, 11 are likely to have a cancer as yet undiagnosed and 89 will not, as shown by the chart below.



Risk of a cancer as yet undiagnosed

Research

Identifying patients with undetected pancreatic cancer in primary care:

an independent and external validation of QCancer® (Pancreas)

Open Access Research

BMJ Open

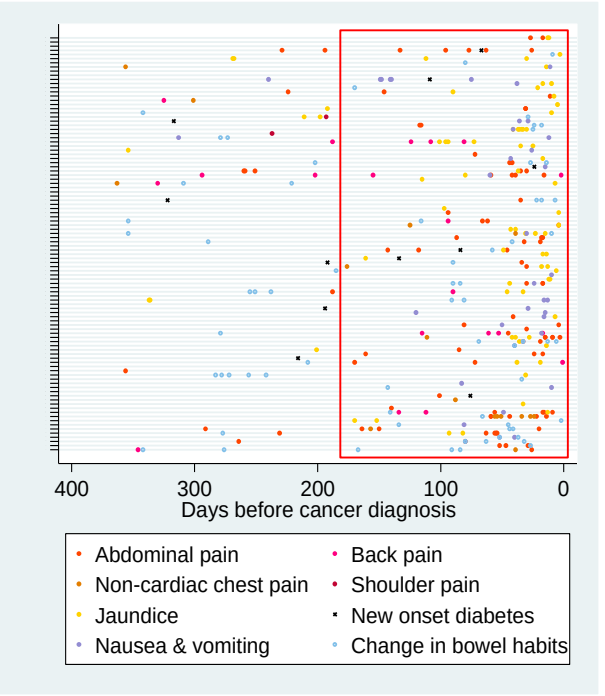
A case–control study comparing the incidence of early symptoms in pancreatic and biliary tract cancer

M G Keane,[1] L Horsfall,[2] G Rait,[2] S P Pereira[1]

BMJ Open 2014;**4**:e005720.

- Anonymised data on > 8 million patients: 3,400 cases of PDAC (matched 6:1 with controls)
- 93% had relevant symptoms in the 2 years prior to diagnosis
- Patients attended their GP with relevant symptoms on average 3 (0-19) times

	Biliary Tract cancer	Pancreatic cancer	Controls	Pancreatic cancer vs. Control		
Symptom (%)	n=829	n=2790	n=17,192	OR*	95% CI	p-value
Weight loss	46 (5.5)	294 (10.5)	302 (1.8)	6.6	5.54,7.86	<0.001
Abdominal pain	309 (37.3)	1225 (43.9)	1946 (11.3)	6.38	5.81,7.02	<0.001
Nausea and vomiting	126 (15.2)	463 (16.6)	978 (5.7)	3.43	3.00,3.91	<0.001
Bloating	27 (3.3)	113 (4.1)	229 (1.3)	3.1	2.48,3.89	<0.001
Dyspepsia	118 (14.2)	559 (20)	1597 (9.3)	2.56	2.30,2.85	<0.001
New onset diabetes	48 (5.8)	380 (13.6)	1037 (6)	2.46	2.16,2.80	<0.001
Change in bowel habit	194 (23.4)	764 (27.4)	2557 (14.9)	2.17	1.98,2.39	<0.001
Pruritus	91 (11)	147 (5.3)	526 (3.1)	1.73	1.43,2.10	<0.001
Lethargy	71 (8.6)	293 (10.5)	1308 (7.6)	1.42	1.25,1.61	<0.001
Back pain	111 (13.4)	446 (16)	2111 (12.3)	1.33	1.18,1.49	<0.001
Dysphagia	10 (1.2)	51 (1.8)	254 (1.5)	1.21	0.90,1.64	0.206
Non-cardiac chest pain	114 (13.8)	335 (12)	2055 (12)	1.02	0.91,1.16	0.699
Shoulder pain	47 (5.7)	137 (4.9)	1052 (6.1)	0.78	0.65,0.93	0.006
Jaundice *	358 (43.2)	860 (30.8)	36 (0.2)	246.	172,351	<0.001



Identifying risk factors and symptoms for pancreatic cancer

- UCL Farr institute (HDR UK)
  - CPRD data from participating NHS GP surgeries (15M)
  - Data from
    - Primary care
    - Hospital Episode Statistics
    - ONS death registration data
    - Cancer registry
- QResearch (40M)
- CanTest Collaborative

Biomarkers for early diagnosis

Overview

- Identifying symptoms earlier
- **Screening high-risk groups**
- Emerging diagnostics
- The practicalities

UNIVERSITY OF LIVERPOOL

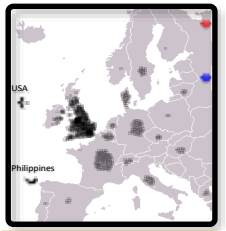
Liverpool Cancer Research UK Centre

Who should undergo surveillance?

‘High-risk’ cohorts: patients without symptoms

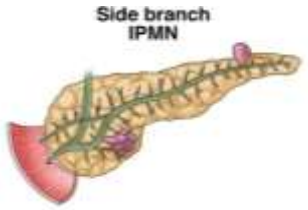
EUROPAC

The European Registry of Hereditary Pancreatitis and Familial Pancreatic Cancer



John Neoptolemos, Bill Greenhalf

- **Pancreatic cancer families (currently CT/MR, EUS)**
  - at least two relatives with pancreatic cancer
  - associated cancer syndromes with a case of pancreatic cancer



- **Cystic tumours of the pancreas (currently MRI, EUS)**
  ~1-13% of the population, increased pancreatic cancer risk

- **Pancreatic cancer-associated diabetes mellitus**

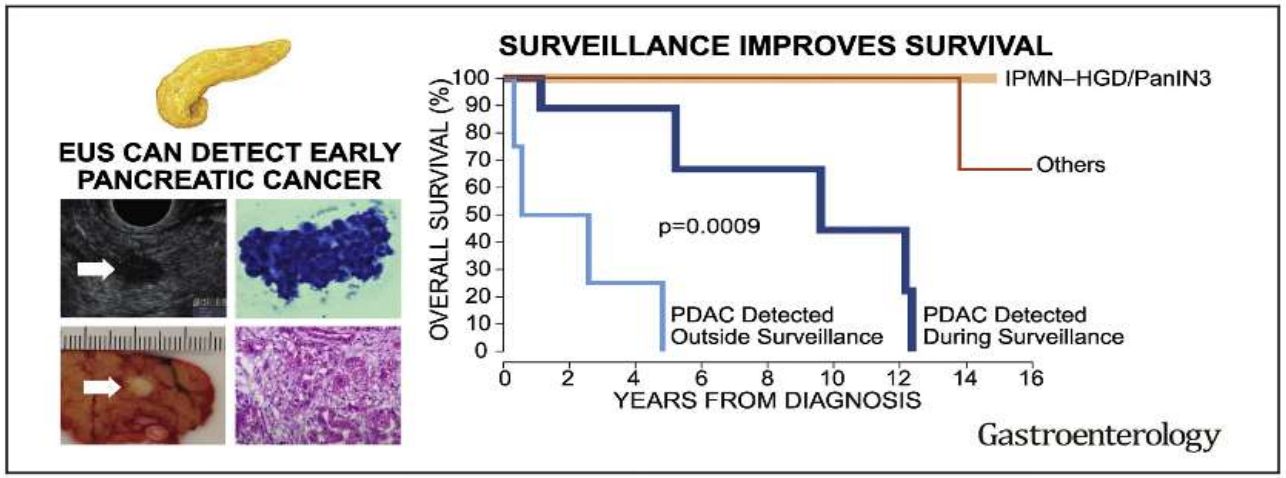
Gastroenterology

Risk of Neoplastic Progression in Individuals at High Risk for Pancreatic Cancer Undergoing Long-term Surveillance

Marcia Irene Canto,[1,2,*] **Jose Alejandro Almario,**[1,3,*] Richard D. Schulick,[4] Charles J. Yeo,[5] Alison Klein,[2] Amanda Blackford,[2] Eun Ji Shin,[1] Abanti Sanyal,[6] Gayane Yenokyan,[6] Anne Marie Lennon,[1] Ihab R. Kamel,[7] Elliot K. Fishman,[7] Christopher Wolfgang,[8] Matthew Weiss,[8] Ralph H. Hruban,[3] and Michael Goggins[1,3]

Gastroenterology 2018;155:740–751

- 354 High risk individuals for familial PDAC
- EUS/MRI and/or CT annual follow-up
- 16 year program. Median follow-up 5.6 years.
- Primary endpoint: cumulative incidence of PDAC, PANIN3, IPMN with HGD.



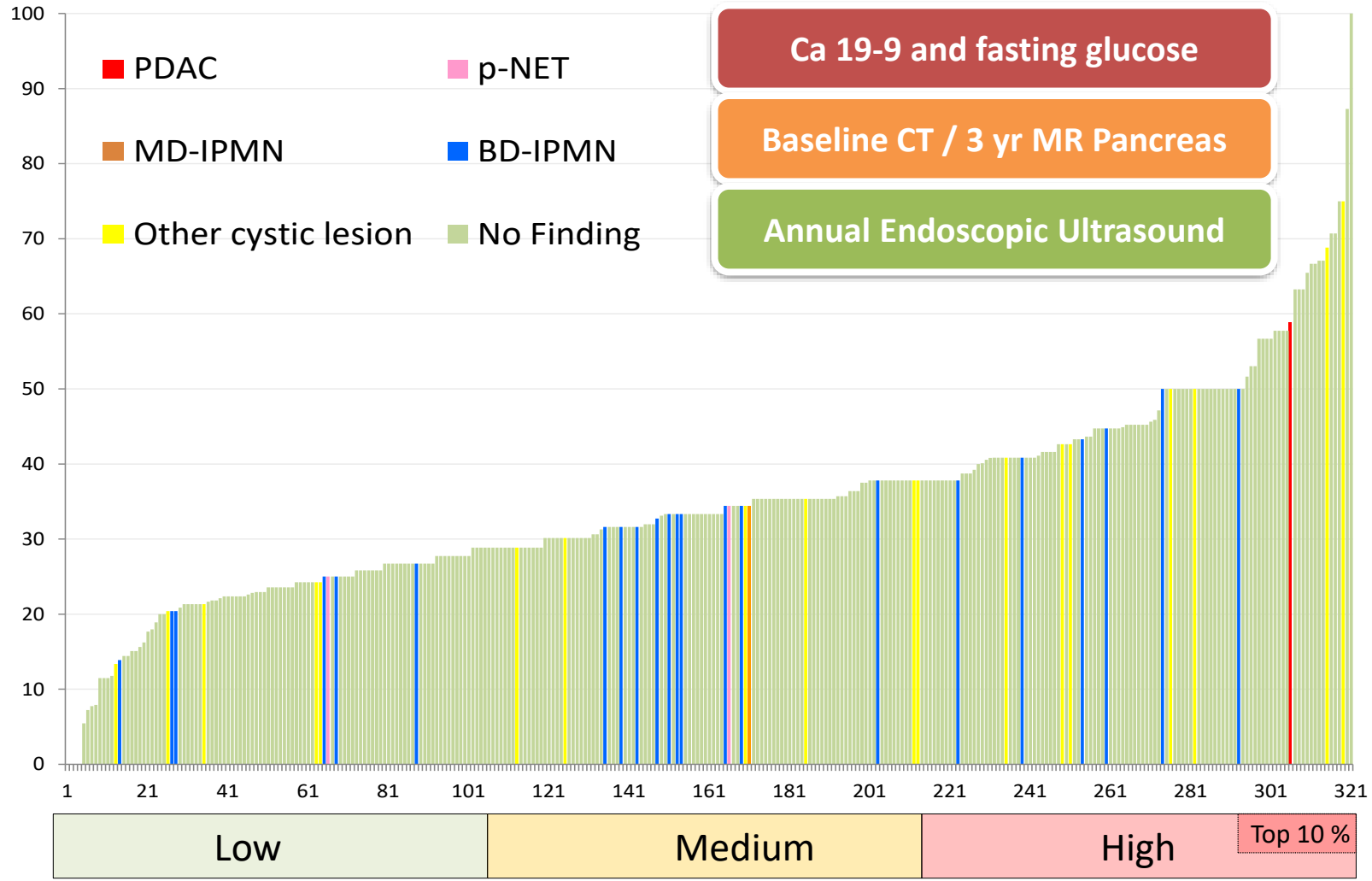
After initial screening:

- **7%** cumulative incidence of high risk pancreatic lesions (24/354)
- **3 yr survival of HRI with PDAC > other PDAC pts (57% vs. 8.9%)**
- Annual rate of malignant progression **1.6%**

Identification of Cystic Lesions by Secondary Screening of Familial Pancreatic Cancer (FPC) Kindreds Is Not Associated with the Stratified Risk of Cancer

A. R. G Sheel, BSc, MBChB, MRCS[1], S. Harrison, BSc, MSc[1], I Sarantitis, MBBS, MSc, MRCS[1], J. A. Nicholson, MBChB, MRCS, PhD[1], T. Hanna, MBChB, MRCS[1], C. Grocock, MD[1], M. Raraty, MBChB, MRCS, PhD[1], J. Ramesh, MBBS[2], A. Farooq, MBBS, MRCP, FRCR[3], E. Costello, PhD[1], R. Jackson, PhD[1], M. Chapman, MBBS, PhD, MRCP[4], A. Smith, MBBS, BSc, FRCS[5], R. Carter, MBChB, FRCS, FRCS, MD[6], C. Mckay, MBChB, MD, FRCS[6], Z. Hamady, MBChB, PhD, FRCS[7], G. P. Aithal, MBBS, MD, FRCP, PhD[8], R. Mountford, PhD[9], P. Ghaneh, MBChB, FRCS, MD[1], P. Hammel, MD, PhD[10], M. M. Lerch, MD, FRCP[11], C. Halloran, BSc MBChB MD FRCS[1], S. P. Pereira, BSc, PhD, FRCP[4] and W. Greenhalf, BSc, PhD[1] on behalf of EUROPAC collaborators

Am J Gastro 2018



Biology of Human Tumors

Clinical Cancer Research

August 2015

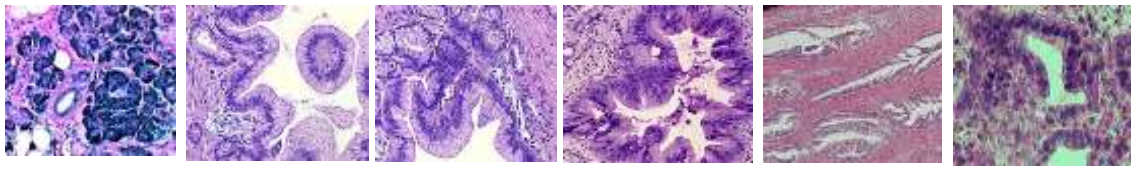
Identification of a Three-Biomarker Panel in Urine for Early Detection of Pancreatic Adenocarcinoma

Tomasz P. Radon[1], Nathalie J. Massat[2], Richard Jones[3], Wasfi Alrawashdeh[1], Laurent Dumartin[1], Darren Ennis[1], Stephen W. Duffy[2], Hemant M. Kocher[4], Stephen P. Pereira[5], Luisa Guarner (posthumous)[6], Cristiane Murta-Nascimento[7], Francisco X. Real[8], Núria Malats[8], John Neoptolemos[9], Eithne Costello[9], William Greenhalf[9], Nick R. Lemoine[1], and Tatjana Crnogorac-Jurcevic[1]

IMAGE: THIS IS DR. TATJANA CRNOGORAC-JURCEVIC, BARTS CANCER INSTITUTE, QUEEN MARY UNIVERSITY OF LONDON. view more ›

CREDIT: PANCREATIC CANCER RESEARCH FUND

REG1A, TFF1 and LYVE1



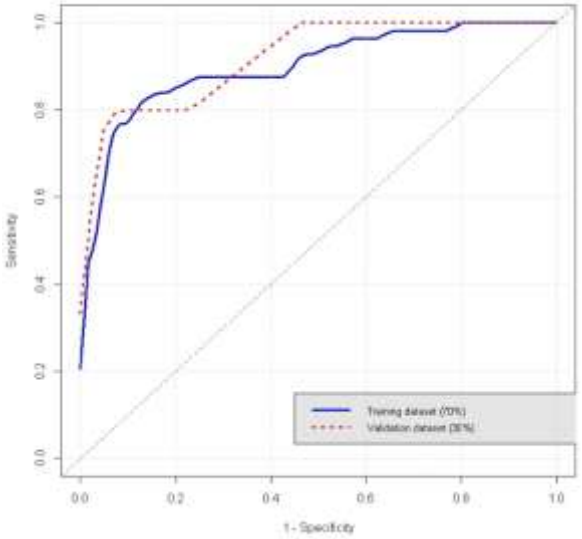
Normal | Hyperplasia | Dysplasia | Carcinoma in situ | Invasion | Metastasis

12 ± 3 years | 7 ± 3 years | 3 ± 1 years

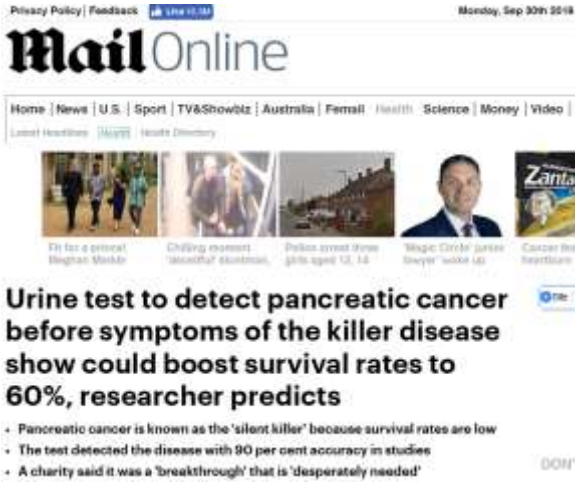
'window of opportunity'

Multicentre validation:

Healthy vs PDAC Stage I/II



Training dataset (70%); AUC = 0.90
Validation dataset (30%); AUC = 0.93



Mail Online

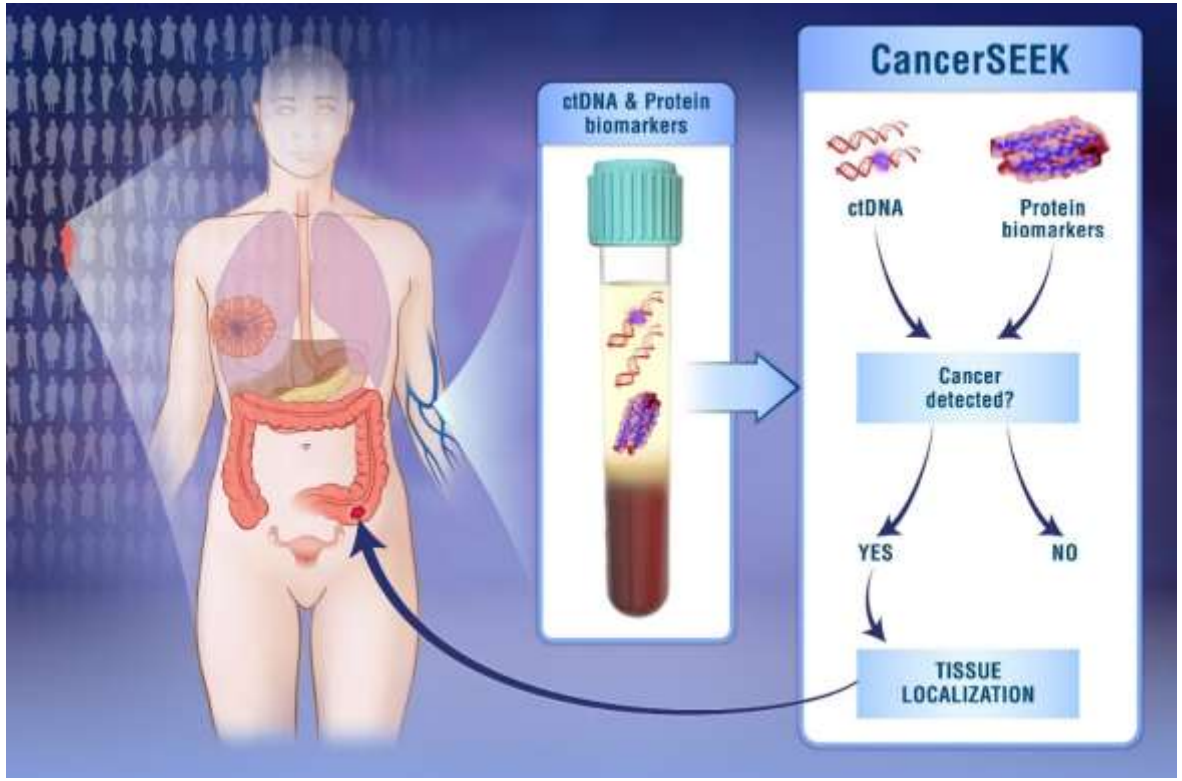
Urine test to detect pancreatic cancer before symptoms of the killer disease show could boost survival rates to 60%, researcher predicts

- Pancreatic cancer is known as the 'silent killer' because survival rates are low
- The test detected the disease with 90 per cent accuracy in studies
- A charity said it was a 'breakthrough' that is 'desperately needed'

Science
18 January 2018

Detection and localization of surgically resectable cancers with a multi-analyte blood test

Joshua D. Cohen,[1,2,3,4,5] Lu Li,[6] Yuxuan Wang,[1,2,3,4] Christopher Thoburn,[3] Bahman Afsari,[7] Ludmila Danilova,[7] Christopher Douville,[1,2,3,4] Ammar A. Javed,[8] Fay Wong,[1,2,3,4] Austin Mattox,[1,2,3,4] Ralph. H. Hruban,[3,4,9] Christopher L. Wolfgang,[8] Michael G. Goggins,[3,4,9,10,11] Marco Dal Molin,[4] Tian-Li Wang,[3,9] Richard Roden,[3,9] Alison P. Klein,[3,4,12] Janine Ptak,[1,2,3,4] Lisa Dobbyn,[1,2,3,4] Joy Schaefer,[1,2,3,4] Natalie Silliman,[1,2,3,4] Maria Popoli,[1,2,3,4] Joshua T. Vogelstein,[13] James D. Browne,[14] Robert E. Schoen,[15,16] Randall E. Brand,[15] Jeanne Tie,[17,18,19,20] Peter Gibbs,[17,18,19,20] Hui-Li Wong,[17] Aaron S. Mansfield,[21] Jin Jen,[22] Samir M. Hanash,[23] Massimo Falconi,[24] Peter J. Allen,[25] Shibin Zhou,[1,3,4] Chetan Bettegowda,[1,2,3,4] Luis Diaz,[1,3,4] Cristian Tomasetti,[3,6,7*] Kenneth W. Kinzler,[1,3,4*] Bert Vogelstein,[1,2,3,4*] Anne Marie Lennon,[3,4,8,10,11*] Nickolas Papadopoulos[1,3,4*]



Tumor Detection

- ctDNA
- 8 Protein Markers
  - CA-125
  - CEA
  - CA19-9
  - PRL
  - HGF
  - OPN
  - MPO
  - TIMP-1

- 1,005 cancer patients (93 PDAC)
  - No distant metastasis (20% Stage I, 49% Stage II, 31% Stage III)
- 812 healthy controls

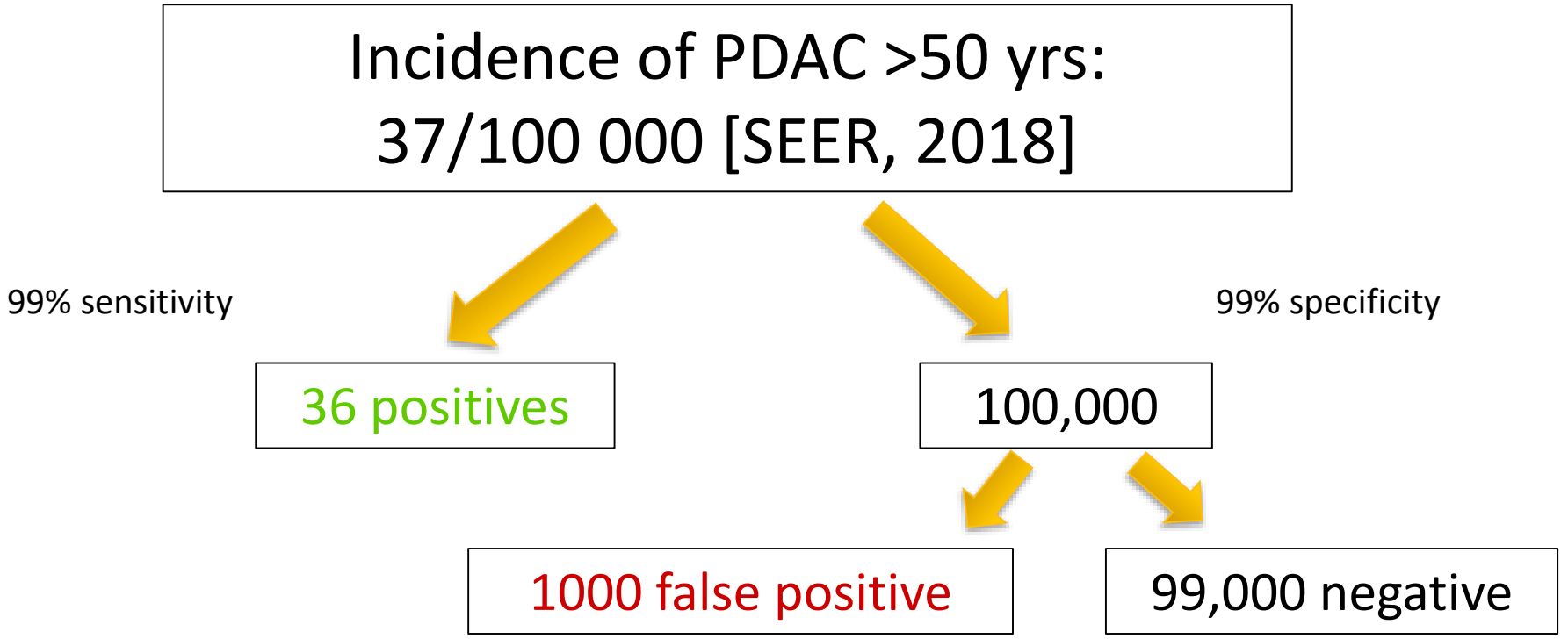
Biomarkers for early diagnosis

Overview

- Identifying symptoms earlier
- Surveillance of ‘high-risk’ groups
- Emerging diagnostics
- **The practicalities**

Population screening for PDAC is not feasible

- Screening for PDAC in average risk persons will fail due to low cancer prevalence
- Use of an “almost perfect test” with a 99% sensitivity and a 99% specificity for PDAC



Hart & Chari *Clin Gastro Hep* 2018 Sep 27.

uclh

News

- Latest news
- Media

New biomarker trials to detect upper gastrointestinal cancers earlier

17 Aug 2017

UCLH Cancer Collaborative has launched two new biomarker trials with the aim of developing simple and affordable tests that can detect upper gastrointestinal cancers earlier to improve survival.

The trials are for cancer of the pancreas – a large gland behind the stomach and next to the small intestine, and cancer of the oesophagus – the tube that connects the throat to the stomach.

Latest news

- Is it a bird? Is it a plane? No, it's our surgical superhero!
- May the force be with you...
- A message for the future
- UCLH joins World's Biggest Coffee Morning
- New theatres and wards at National Hospital for Neurology and Neurosurgery

Contact details

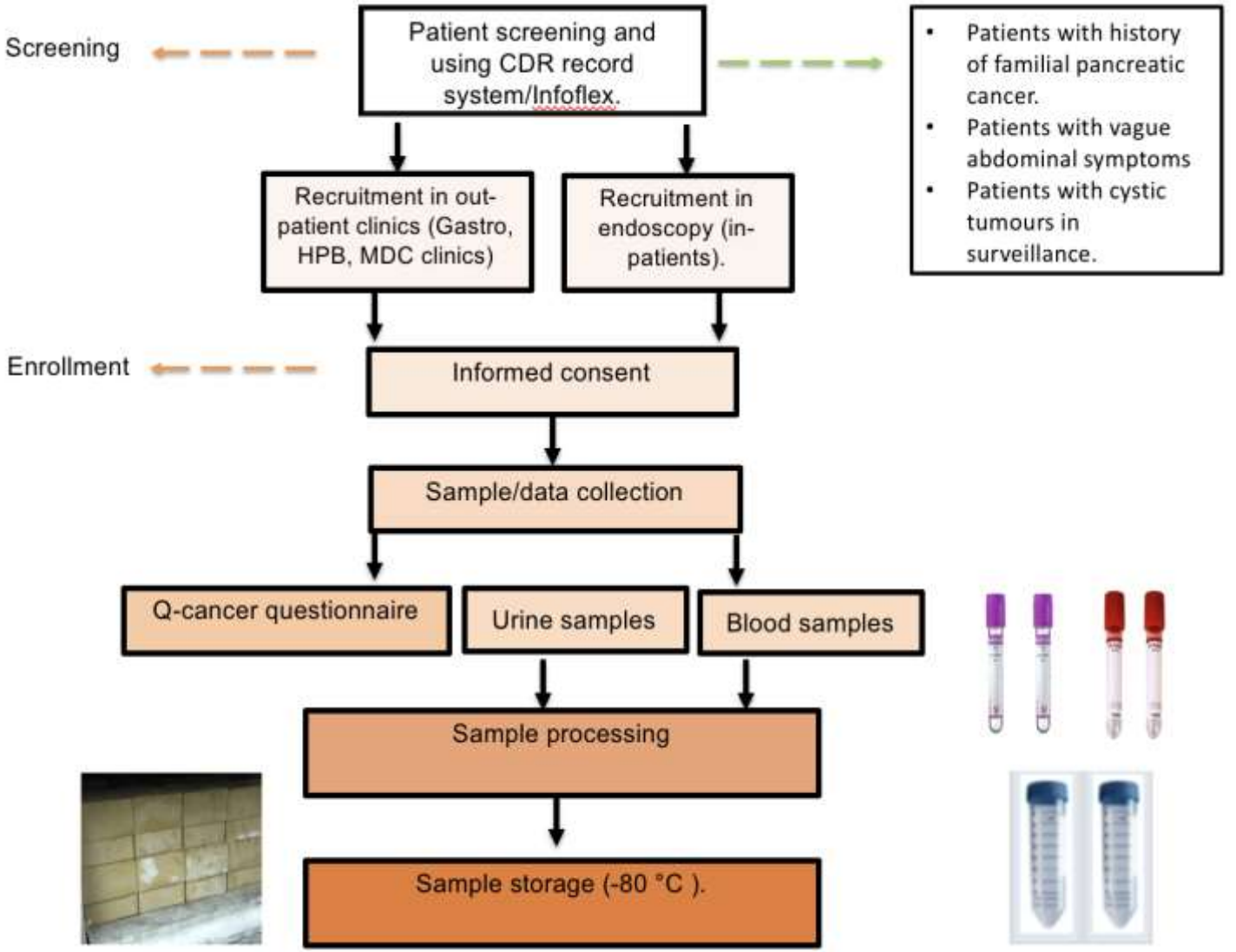
Communications unit
2nd floor central
250 Euston Road
London NW1 2PG

Media enquiries

Switchboard: 020 3456 7890
Media enquiries: 020 3447 7542 / 020 3447 9506
Email: media.enquiries@uclh.nhs.uk

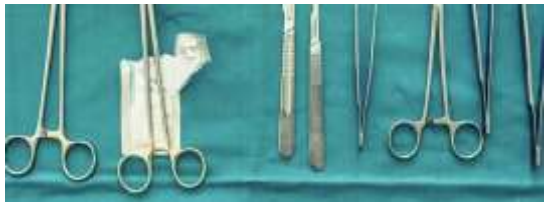
Out of hours

Recruitment Process



SURGICAL & INTERVENTIONAL TRIALS UNIT (SITU)
UCL DIVISION OF SURGERY & INTERVENTIONAL SCIENCE
Faculty of Medical Sciences

From Patient to Freezer



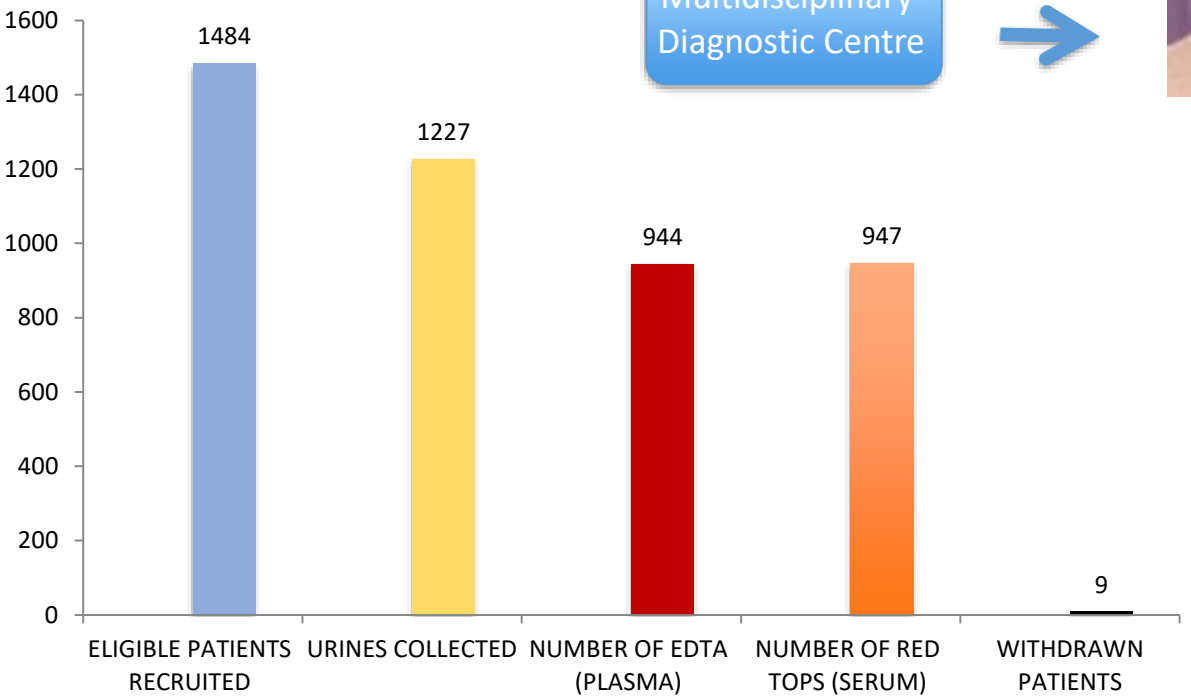
Gastro/HPB clinics

Endoscopy

Multidisciplinary Diagnostic Centre

Blood, urine

Processing in lab
NIH SOPs



Tuesdays and Wednesday PM

Royal Free Hospital

Wednesdays & Thursdays

University College London Hospital

Clinical Research team

Andrés García

October 2018

Shahida Islam

January 2019

Freya Luling Feilding

May 2019

Jade Hue

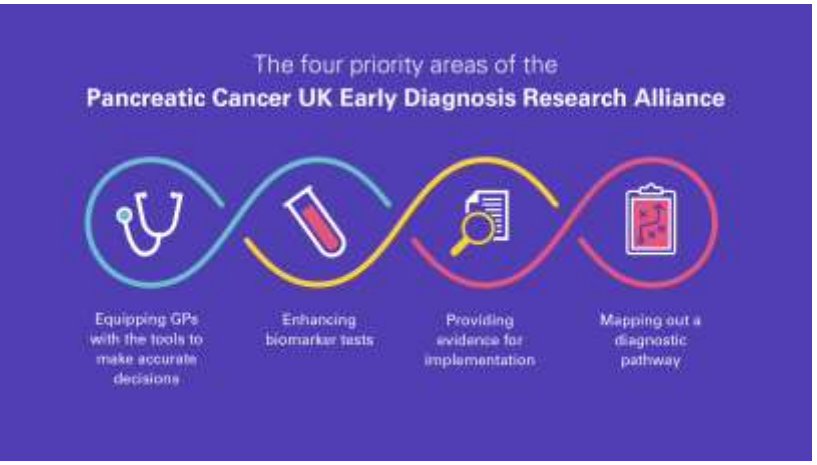
July 2019

Iulia Munteanu

Pilar Acedo Núñez – Biobank Manager

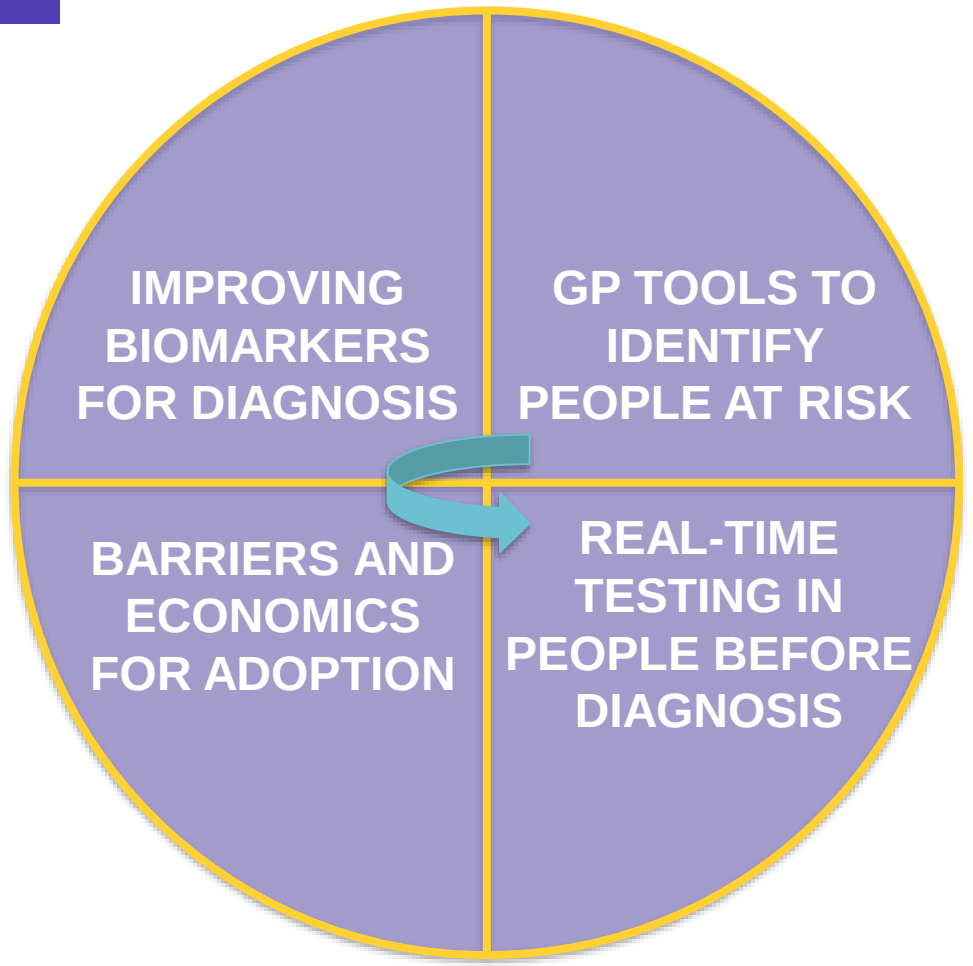
Alexander Ney – Clinical Research Fellow

Harry Martin – Clinical Research Fellow



Accelerating diagnosis of pancreatic cancer: a 360° approach






Please note the deadline for the submission of proposals is **Monday 14th October at 5pm.**

NCRI Screening, Prevention & Early Diagnosis (SPED) Workshop

Call for proposal ideas for studies in Screening, Prevention or Early Diagnosis

NCRI National Cancer Research Institute

Current National Pancreatic Cancer Clinical Research SPED Studies Portolio:

stephen.pereira@ucl.ac.uk **(deadline 14 Oct 2019)**

- **EUROPAC**: The European Registry of Hereditary Pancreatitis and Familial Pancreatic Cancer
- **ADEPTS**: Accelerated Diagnosis of neuroEndocrine and Pancreatic TumourS
- **UroPanc**: Urinary bioamarker panel for early detection of Pancreatic cancer
- **UK-EDI**: UK Early Detection Initiative for Pancreatic Cancer

Non-commercial Open

Non-commercial Planned

Commercial Open

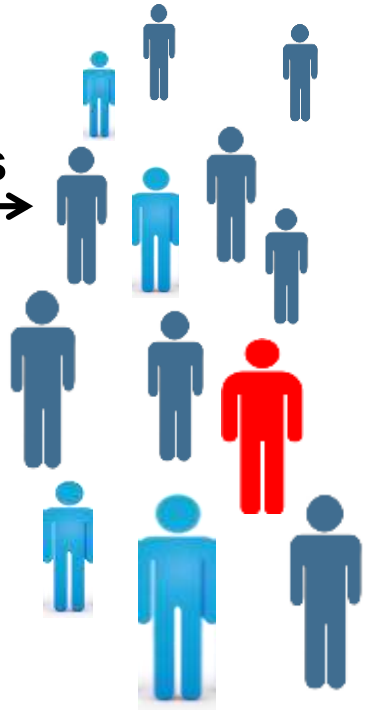
Aim of the UK Early Detection Initiative (UK-EDI)

To develop a test that will select a sub-population of new-onset diabetes individuals (which contains those with pancreatic cancer)

High risk group for pancreatic cancer

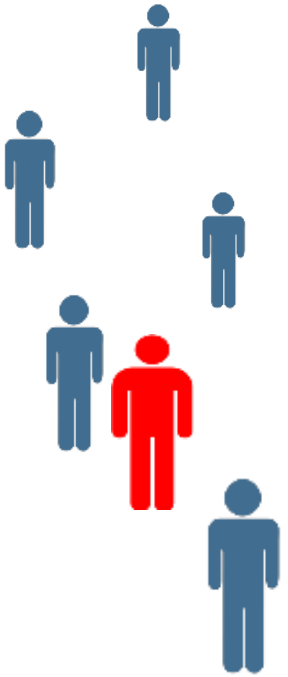
Biomarker(s) that enrich for type 3c diabetes

Higher risk group for pancreatic cancer

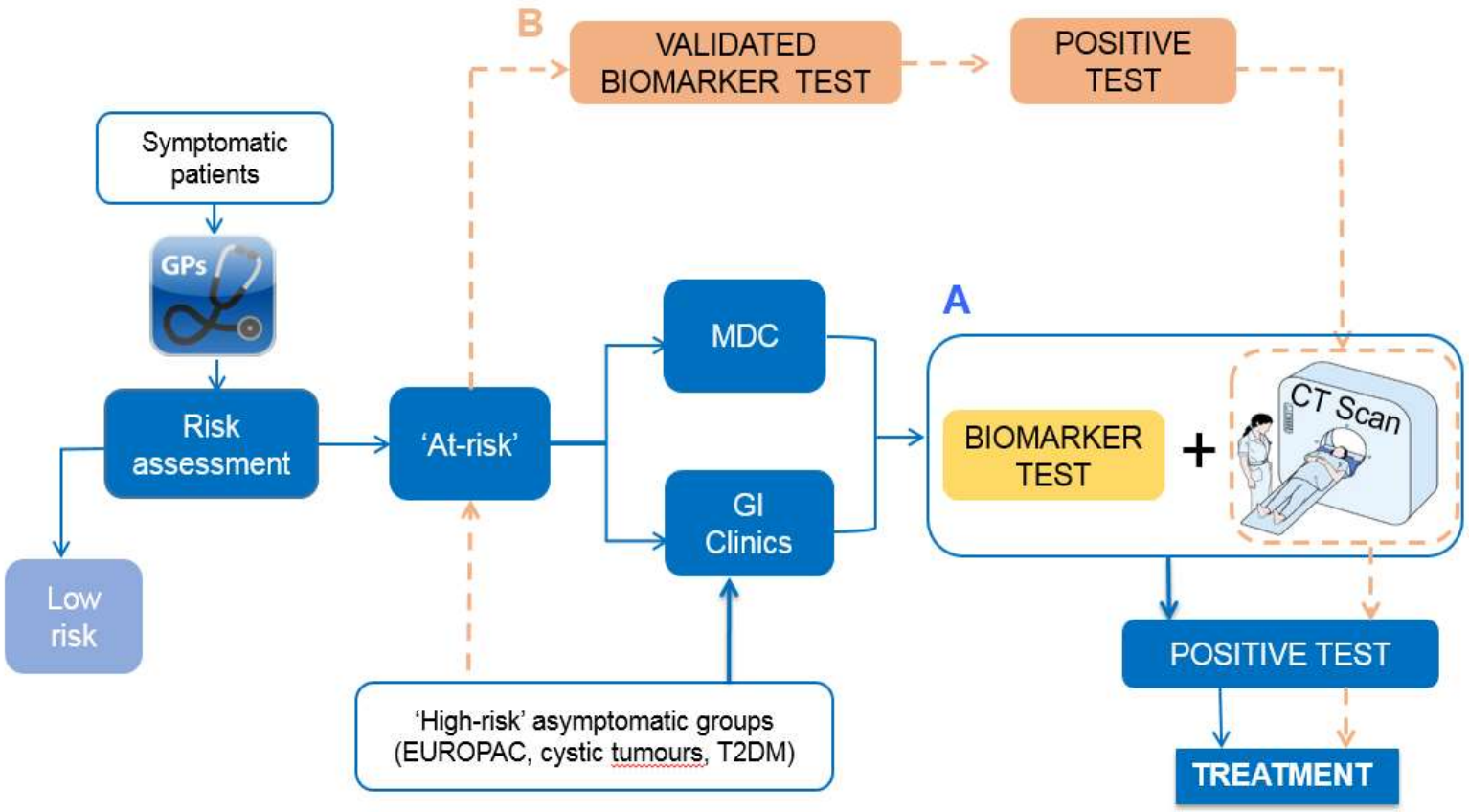


Future Screening

Imaging,
Biochemistry,
CA19-9,
Full blood counts



Accelerating diagnosis of pancreatic cancer



A Biomarker test panel added to 'standard' diagnostic pathway – for validation against CT result

B Validated biomarker test incorporated into 'new' diagnostic pathway

Accelerating early diagnosis research

2020 -

- Big data on risk factors and symptoms - decision support tools
- PCUK Early Diagnosis Research Alliance
- National sample collection
  - early stage pancreatic cancers
  - non-specific but concerning symptoms
  - familial PDAC, cystic tumours, T2DM, PSC
- Looking for new centres!