Pancreatic Cancer UK

#SummitPanc20

Virtual

ANNUAL SUMMIT 2020

IMPROVING OUTCOMES NOW

Improving the Pathway from Diagnosis to Treatment, 29th Sept 2020, 9 – 11am

Supported by erytech oncosil angiodynamics

The Latest in the Pathway from Diagnosis to Treatment

Dr Andrew Millar, Consultant Gastroenterologist and Hepatologist,
North Middlesex University Hospital and Joint NCL Cancer Alliance
Clinical Lead for Rapid Diagnostic Centres

NHS
North Central London
Cancer Alliance

The Latest in the Pathway from Diagnosis to Treatment

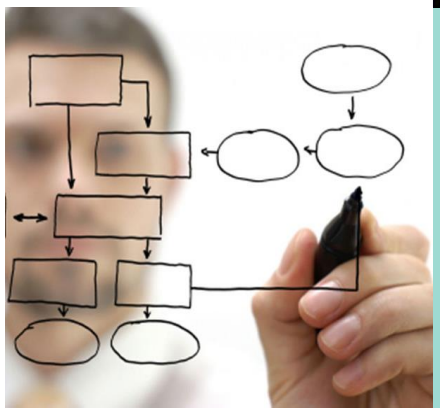
Dr Andrew Millar

Gastroenterologist and Hepatologist,

North Middlesex University Hospital

Clinical Lead RDC Project, NCL Cancer Alliance

- Funding - Gilead/Janssen/Norgine/Astra Zeneca
- Shareholder Medefer Ltd
- Director GI Diagnostics Ltd
- PCUK Advisory Board



We have two problems

North Central London Cancer Alliance

1) **To speed and coordinate diagnosis for symptomatic patients.. and those with incidental findings**
2) **To identify patients at higher risk of pancreatic cancer and safely prevent or cure their cancer**

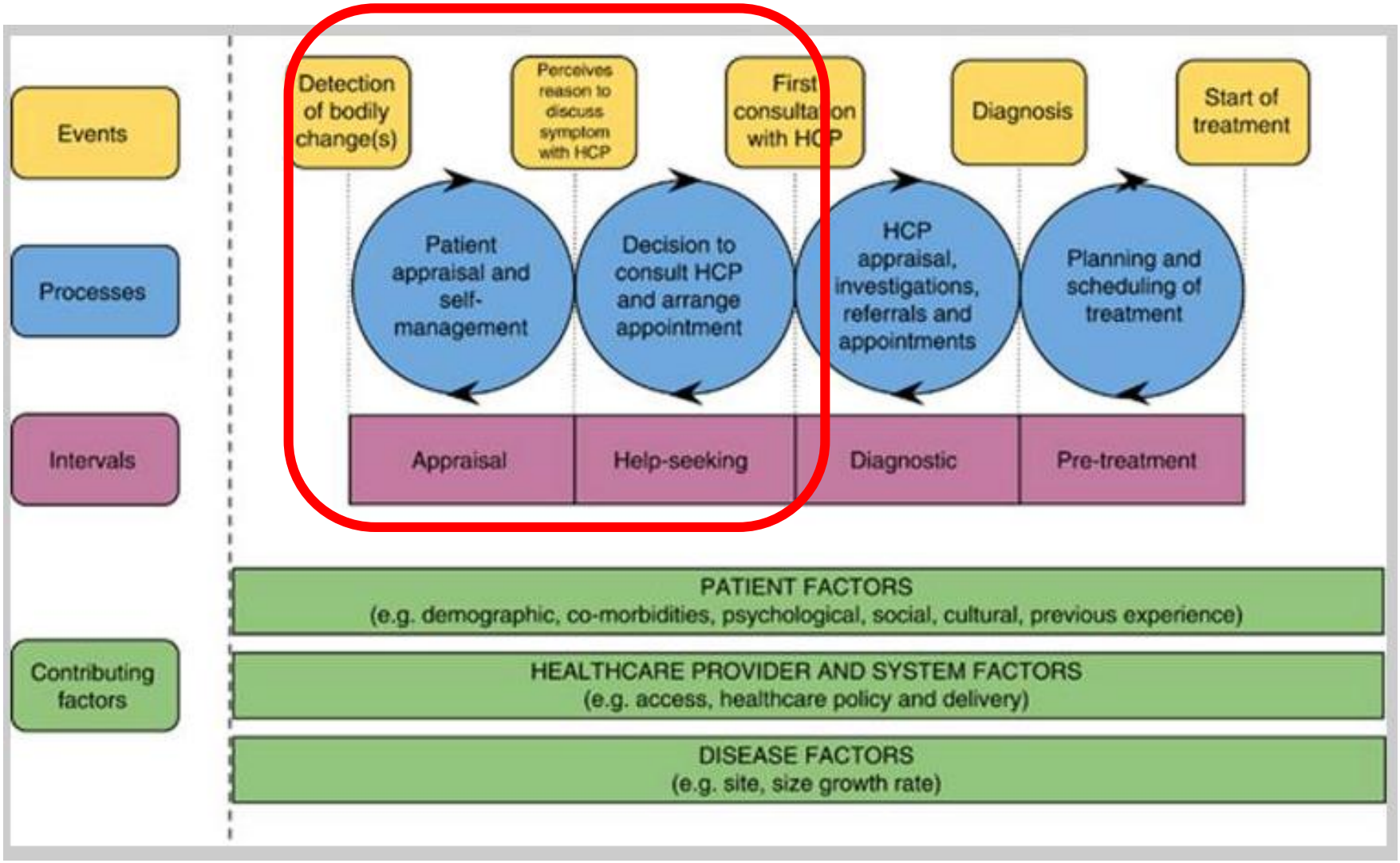
What will be discussed today

- Where is action needed in the symptomatic pathway?
- How to improve patients access to services?
- What is being done to improve referral to specialists?
  - Can RDCs support better referral pathways?
- What research is being done in this area?

Not discussing biomarkers - but much research in progress

Action by the Patient

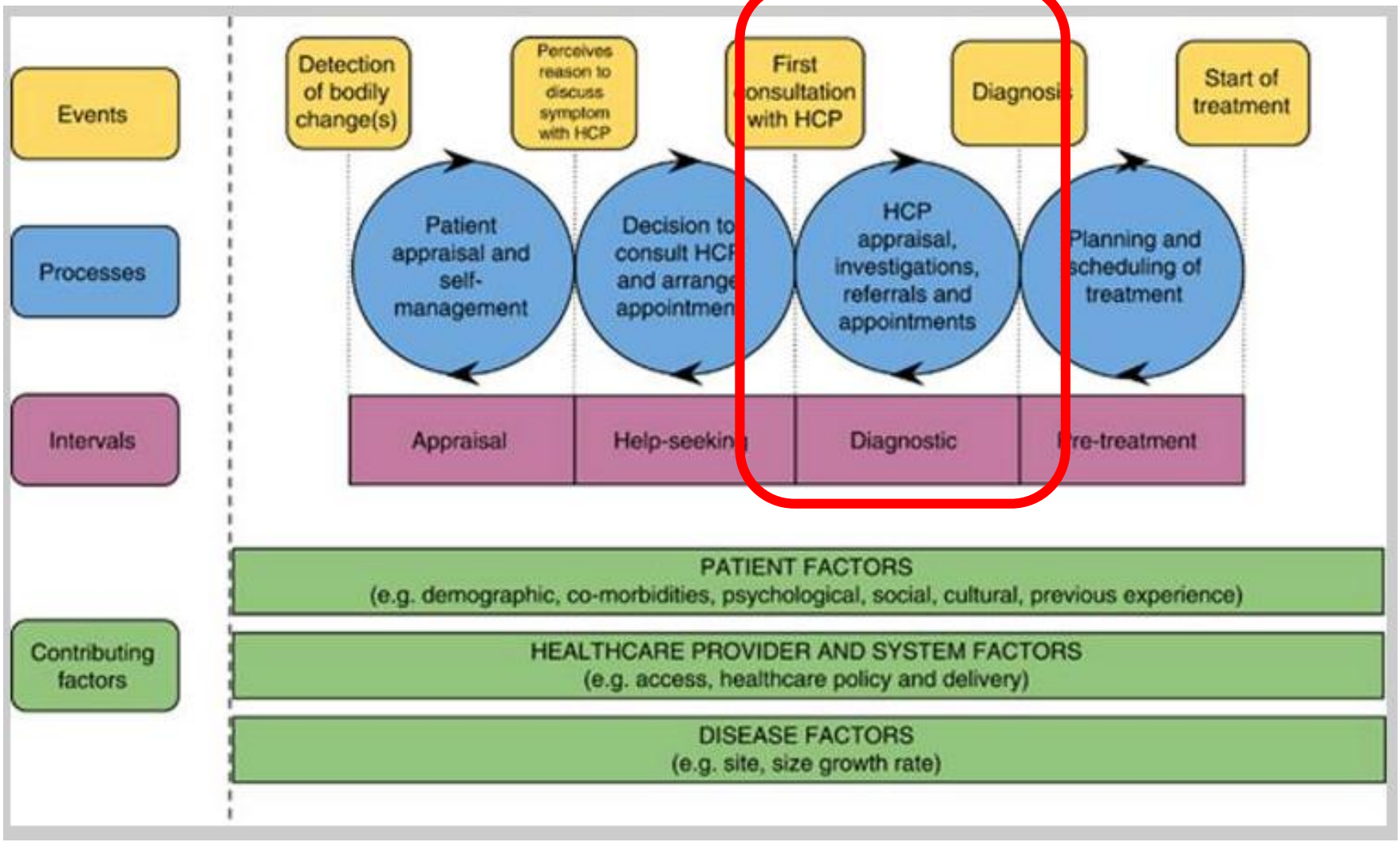
North Central London Cancer Alliance



Walter et al J Health Serv Res Policy Vol 17 No 2 April 2012

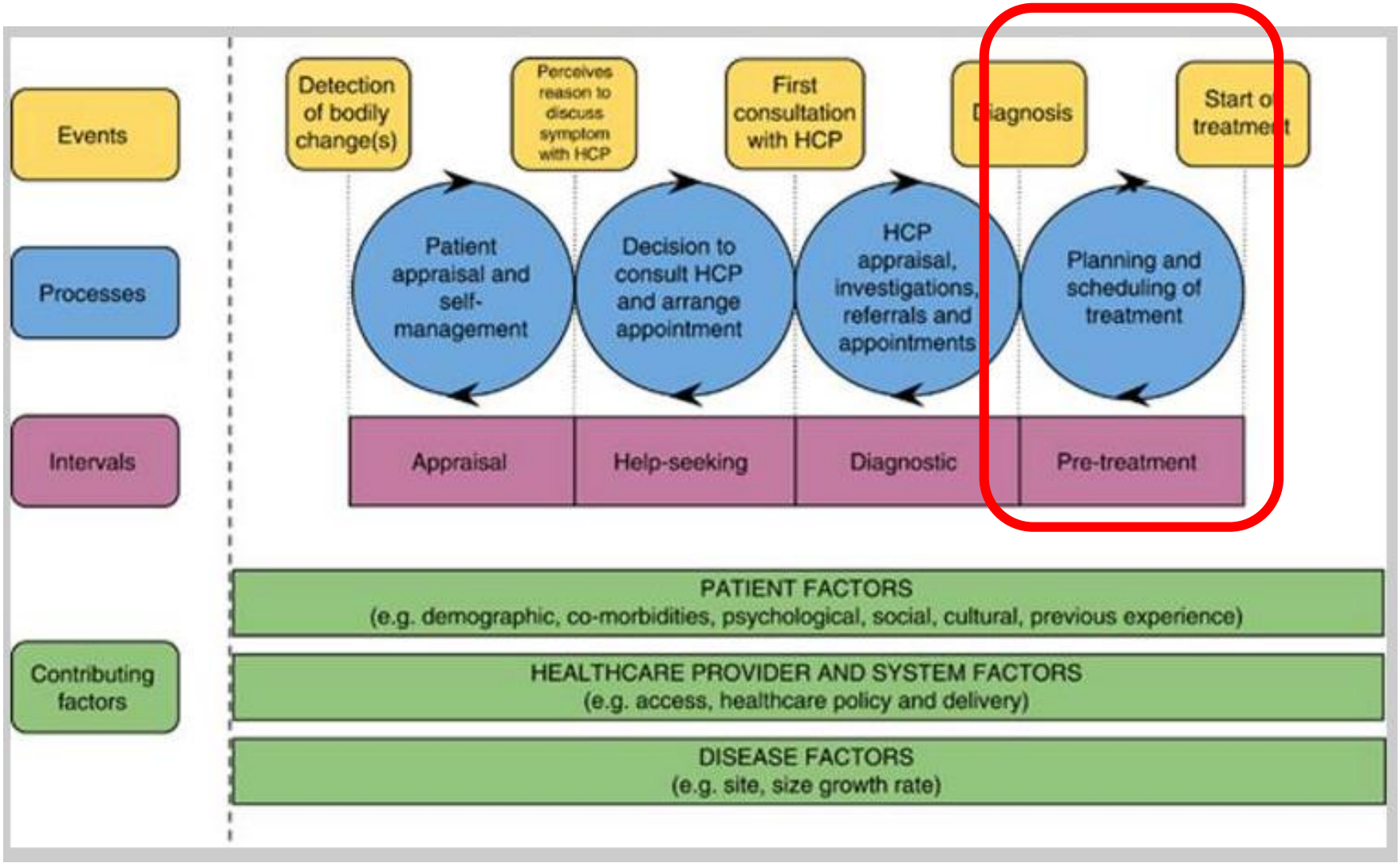
Action by Diagnosticians in Primary and Secondary Care

North Central London Cancer Alliance



Walter et al J Health Serv Res Policy Vol 17 No 2 April 2012

Action by the Treatment Team



Walter et al J Health Serv Res Policy Vol 17 No 2 April 2012

Open Access Research

BMJ Open

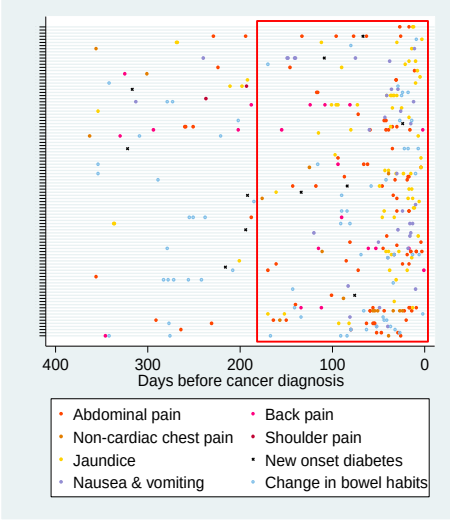
A case–control study comparing the incidence of early symptoms in pancreatic and biliary tract cancer

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

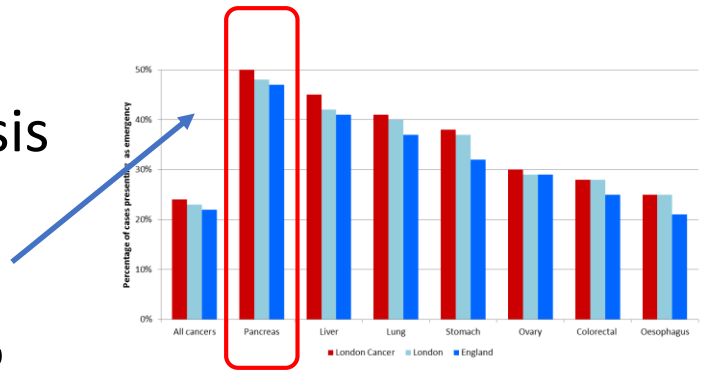


Slide courtesy of Prof S Pereira, UCLH

Why diagnose symptomatic pancreatic cancer early?

North Central London Cancer Alliance

- Progression time from stage T1 to T4 is just over 1 year [1]
- Tumours >2 cm to mets in mean of 3.5 (1.2–8.4) months [2]
- Tumour growth is exponential – later growth is faster
- Early diagnosis increases survival[3]
- Psychological effects of late diagnosis
- Healthcare costs of late diagnosis
- Avoid emergency admissions – 50%



Source: PHE Route to Diagnosis 2006-2013 (2016)

[1]Yu J, Blackford AL, Dal Molin M, et al. Gut. 2015;64(11):gutjnl-2014-308653
[2]J Gastrointest Cancer. 2017;48(2):164–169. doi:10.1007/s12029-016-9876
[3]Poruk KE et al. Ann Surg. 2013; 257: 17-26
[3]Neoptolemos JP et al. Nat Rev Gastroenterol Hepatol. 2018; 15: 333-348

Symptom Appraisal and Help-Seeking

NHS North Central London Cancer Alliance

- Promoted by charities and NHS
- No consistent NHS ‘Be Clear on Cancer’ for Pancreatic Cancer

CANCER RESEARCH UK

Pancreatic Cancer UK

PANCREATIC CANCER ACTION NETWORK

PCS PANCREATIC CANCER SCOTLAND

APPG on Pancreatic Cancer

pancreatic cancer research fund

What is being done now to improve the referral pathway?

North Central London Cancer Alliance

- Pancreatic Cancer in NICE guidelines from 2015
- GP systems 50% - integrate Q score decision tool*
- The ACE programme has led to RDCs mandated for all Alliances
- Increasing primary care access to diagnostics – future for Community Diagnostic Hubs
- RCGP Cancer Training Toolkits and E-Learning modules
  - Primary Care Cancer toolkit
  - Consequences of Cancer toolkit
  - Early Diagnosis of Cancer Significant Event Analysis toolkit
  - Early Diagnosis eLearning module
- Biomarkers on the horizon!

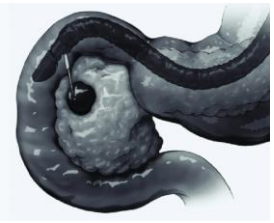
* Hippisley-Cox et al Br J Gen Pract. 2012 Jan; 62(594): e38–e45

Who should be investigated?

North Central London Cancer Alliance

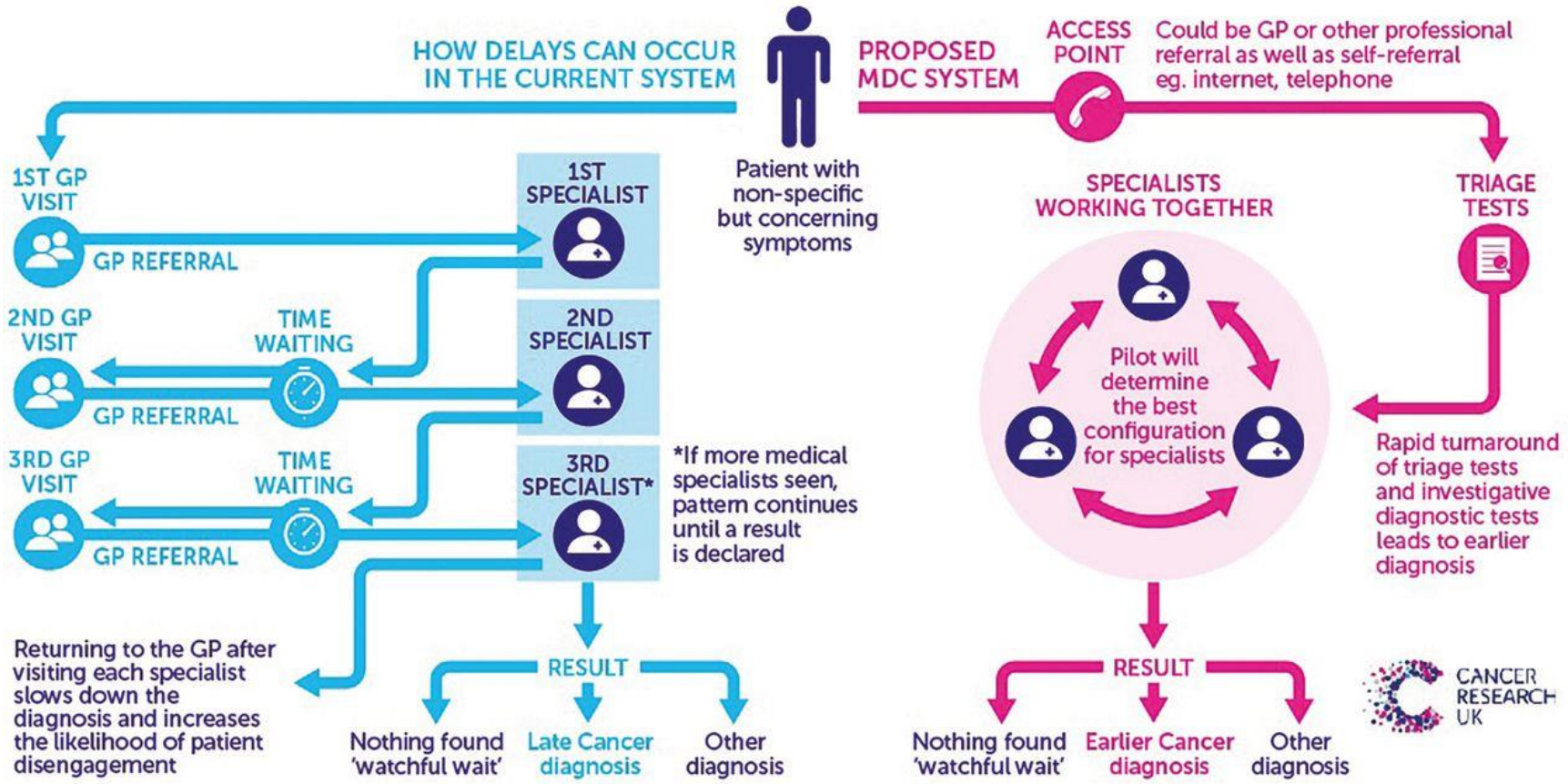
- SYMPTOMATIC
- NICE Guidance - ? Too restrictive better DSTs needed
  - Aged >40 and with jaundice
  - Aged >60 with weight loss **and** any of diarrhoea / back pain / abdominal pain / nausea / vomiting / constipation / **new diabetes**
- Future – refer to Rapid Diagnostic Centre (RDC)

- SCREENING/SURVEILLANCE – Pancreatic cancer risk > 5%
- Cancer Syndromes that include pancreatic cancer
- Familial Pancreatic Cancer
- Pre-malignant cystic lesions – IPMN, MCN
  - Why is there no national cancer surveillance system for pre-malignant lesions?



RDCs offer avoidance of multiple pathways - serial or in parallel

North Central London Cancer Alliance



Edmund Fuller et al. Br J Gen Pract 2016;66:176-177

Nationally - 10 ACE MDCs across England

NHS North Central London Cancer Alliance

Airedale, Wharfdale & Craven
MDC site: Airedale General Hospital

Greater Manchester
MDC sites: Manchester University NHS Foundation Trust (Wythenshawe Hospital) and The Northern Care Alliance (Royal Oldham Hospital)

Oxford
MDC site: Oxford University Hospital Trust (Specialist Cancer Centre)

Leeds
MDC site: St James University Hospital (Specialist Cancer Centre)

London
MDC sites: North Middlesex University Hospital, University College London Hospital (Specialist Cancer Centre), Southend University Hospital, Queens (BHRUT) and the Royal Free Hospital

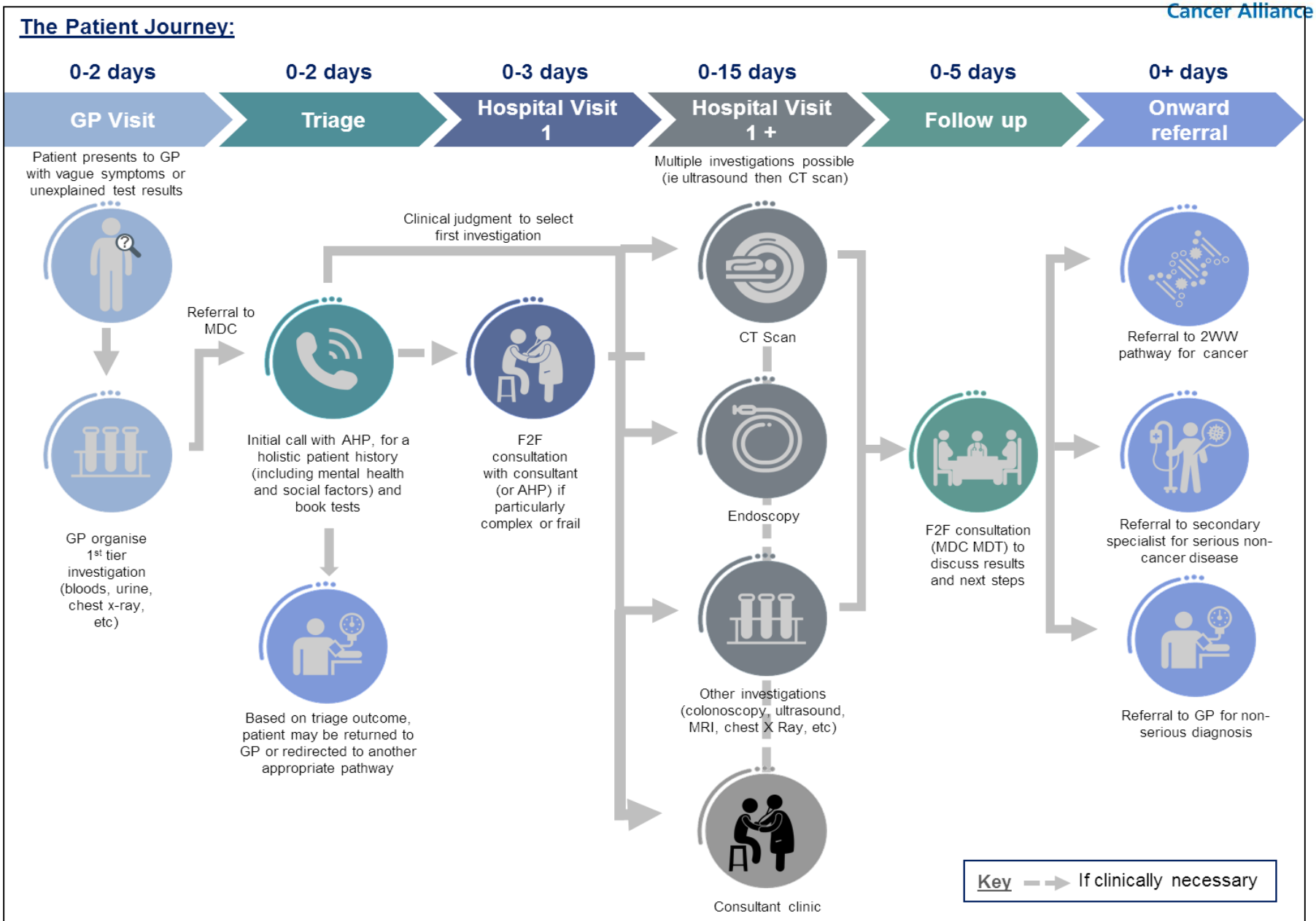
- A common dataset and reporting framework agreed across the projects
- National Cancer Diagnosis Audit used to create a 'proxy comparator pathway' for NSCS patient cohort
- Different approaches taken

A national approach allows different NHS settings to be explored and creates a larger MDC referral data set for analysis

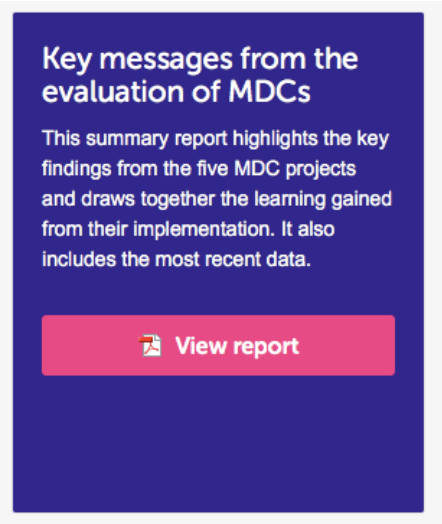
CANCER RESEARCH UK

RDCs – The patient journey

North Central London Cancer Alliance



CRUK ACE Program



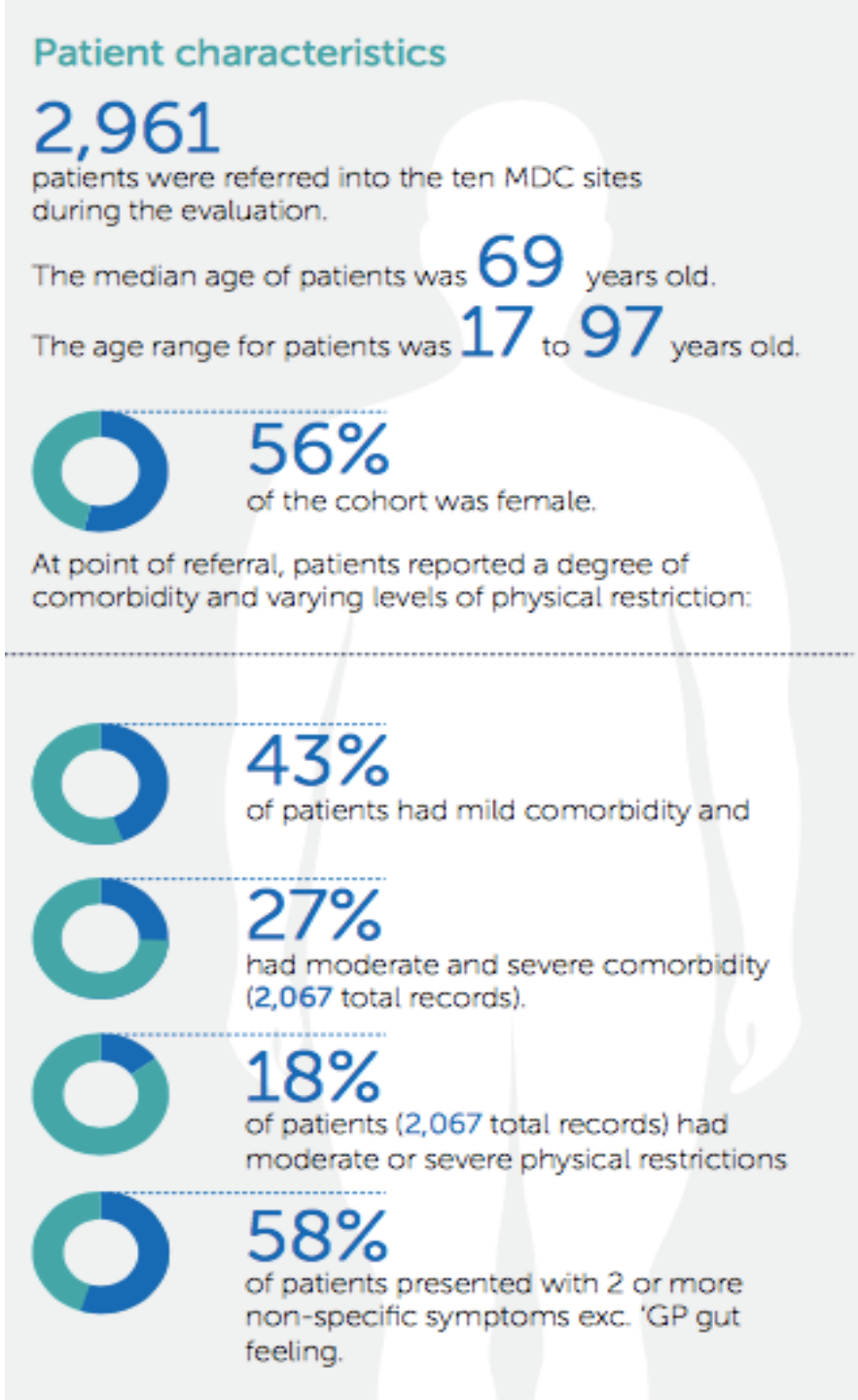
CANCER RESEARCH UK

https://www.cancerresearchuk.org/health-professional/diagnosis/accelerate-coordinate-evaluate-ace-programme

First results from five multidisciplinary diagnostic centre (MDC) projects for non-specific but concerning symptoms, possibly indicative of cancer

D. Chapman, V. Poirier, D. Vulkan, K. Fitzgerald, G. Rubin, W. Hamilton, S. W. Duffy

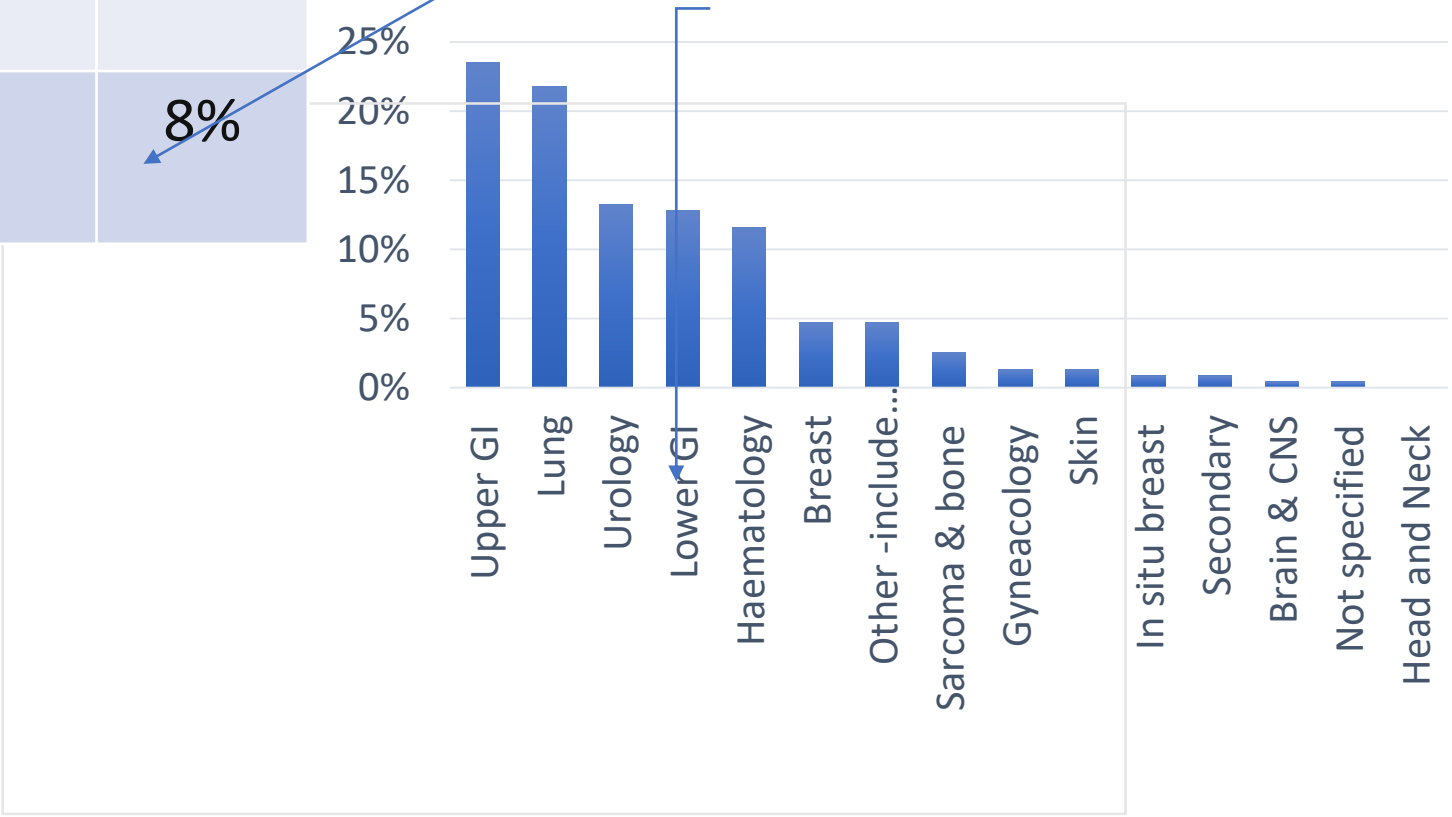
British Journal of Cancer 123, 722–729(2020)



ACE MDCs - Cancer diagnoses distribution (July 2018)

Total MDC referrals*	2,873
Number of cancers	234
Cancer conversion	8%

Pancreatic cancer (10.6%) **n=25**

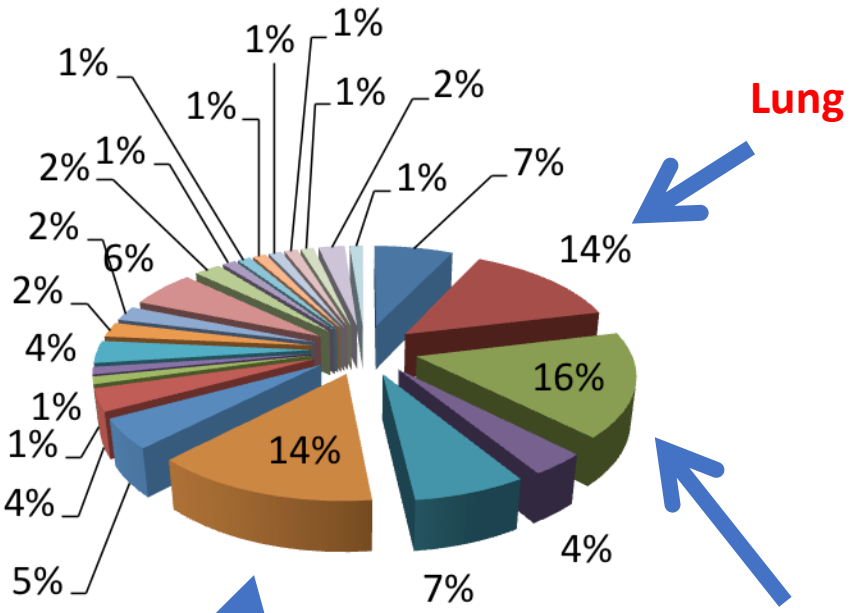


NCEL Cancer Alliance MDC
Cancer types

North Central London Cancer Alliance

Cancer types in 1903 patients
(Apr 17 – Apr 19)

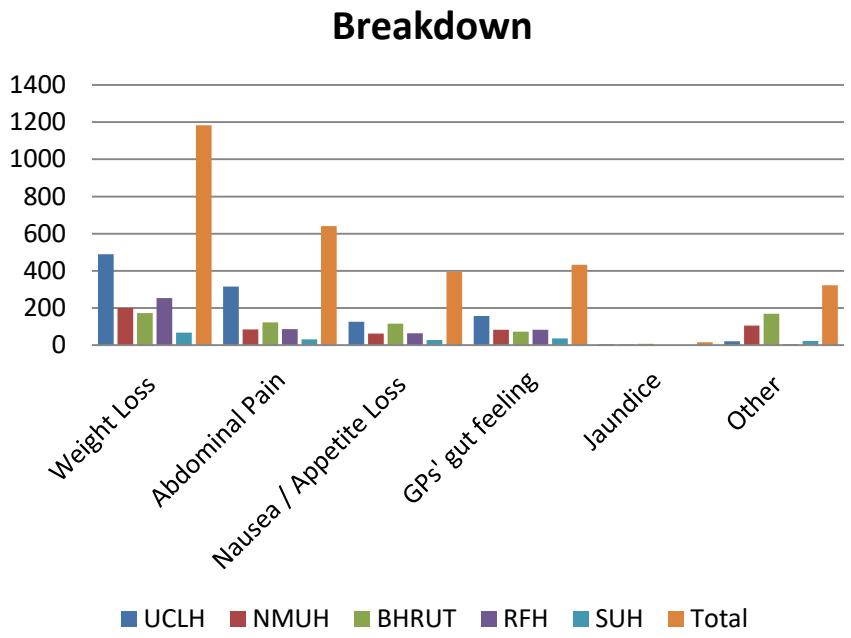
- Breast
- Lung
- Pancreas
- Oesophagus
- Stomach
- Colon
- Rectosigmoid
- Gallbladder
- Unspecified Female Genital Organs
- Peripheral & Cutaneous T-cell lymphomas

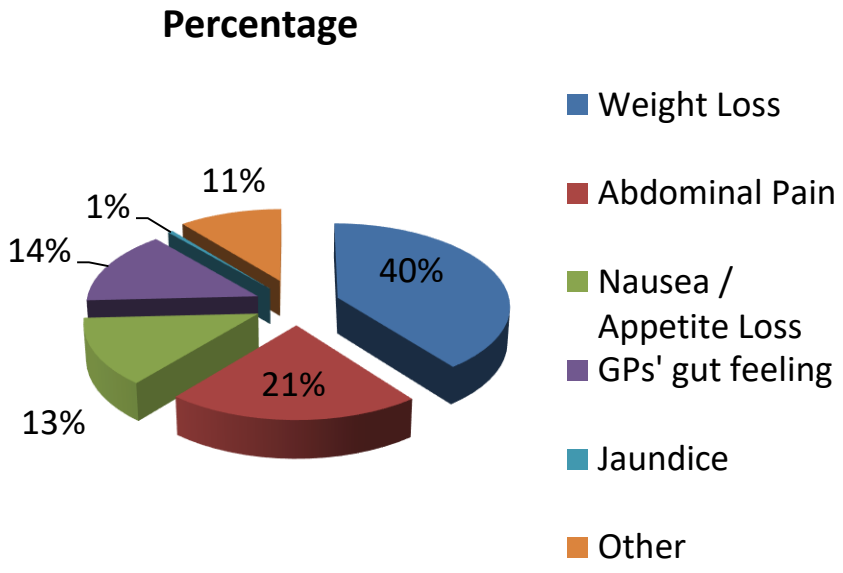


Source: UCLH, NMUH, RFH, BHRUT and SUH data

NECL Cancer Alliance MDC

Referral reasons patients (Apr 17 – Apr 19)





- Weight loss 40%
- Abdominal pain 21%

Source: UCLH, NMUH,RFH, BHRUT and SUH data

NCEL Cancer Alliance
MDC Cancer Conversion and Challenges

NHS North Central London Cancer Alliance

Site	Number of referrals	No. of Cancers	Cancer conversion rate	Time to cancer diagnosis (mean)
UCLH	814	40	4.91%	31
NMUH	327	13	3.98%	33.5
SUH	129	10	7.75%	41.7
BHRUT	295	20	6.78%	39.1
RFH	338	7	2.07%	47.7
Total	**1903**	**90**	4.73%	**38.6**

- Considerable challenge in clinic availability and radiology and endoscopy waiting times in all sites
- National RDC specification and resource allocation help to resolve this
- Key learning from Covid-19 moving to more virtual and agile services with remote consultations and utilising external diagnostic sites

Source: UCLH, NMUH, RFH, BHRUT and SUH data

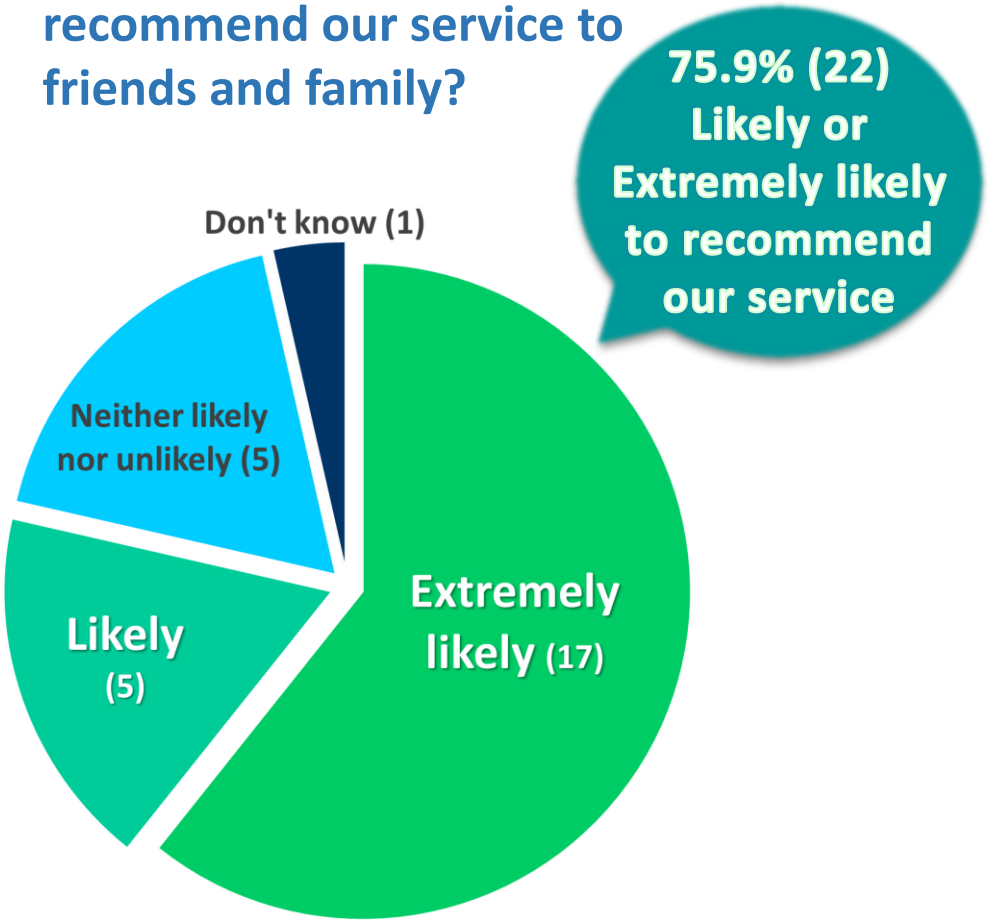
Patient Experience

(50 patients)

NHS North Central London Cancer Alliance

- 82.8 % felt they received their first hospital appointment as soon as was necessary
- 89.3% felt their test results were explained in a way they could understand
- 78.6% felt they waited a reasonable amount of time while attending clinics and appointments

How likely are you to recommend our service to friends and family?



Will RDCs improve the Pancreatic Cancer Pathway?

NHS North Central London Cancer Alliance

Now

- Improve the speed of diagnosis
  - Welsh study - 84.2 to 40.8 days if investigations booked - 5.9 days if at first appointment[1]
- Improve patient experience
- Improve primary-secondary care communication
- Potential route for ALL suspected pancreatic cancer

Future

- Improve efficiency of site specific pathways
- Support research
  - Biomarkers
  - CDST/Self-referral tools
  - Population awareness of non-specific symptoms
- Rapid access will support stage shift at diagnosis and thus improve survival

[1]Rapid cancer diagnosis for patients with vague symptoms: a cost-effectiveness study Sewell et al British Journal of General Practice 2020; 70 (692): e186-e192

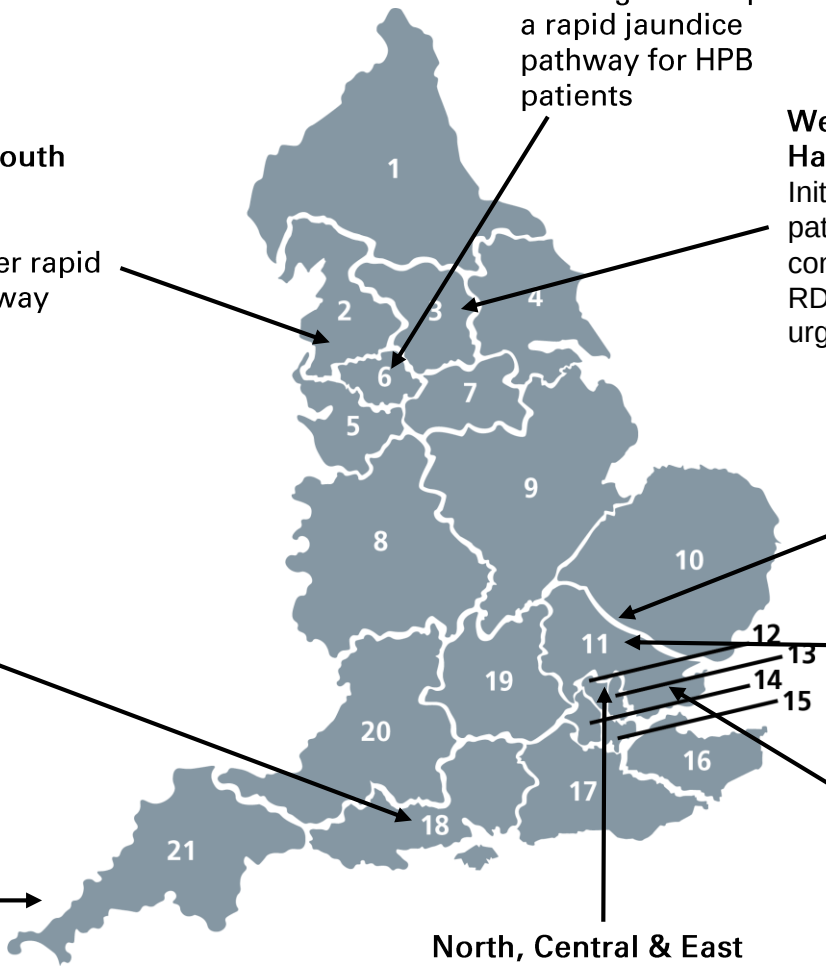
Pancreatic Cancer UK

- Currently **7 Cancer Alliances** are implementing or planning a rapid diagnostic pathway/centre for pancreatic cancer (Lancashire & South Cumbria, West Yorkshire & Harrogate, Wessex, Peninsula, Greater Manchester, East of England, North Central & East London).

Greater Manchester:
Looking to incorporate a rapid jaundice pathway for HPB patients

Lancashire & South Cumbria:
Alliance wide pancreatic cancer rapid diagnostic pathway

West Yorkshire & Harrogate:
Initiated a HPB optimal pathway group which will consider a pancreatic cancer RDC pathway, with a possible urgent jaundice pathway.



East of England:
Setting up a pancreatic cancer rapid diagnostic pathway

Suffolk & North East Essex:
Accepting GP referrals for pancreatic cancer and self-referral. RDC will also incorporate upper GI referrals.

Wessex:
Will consider wider review of the current upper GI 2WW referral to separate the pancreatic cancer referrals and redirect to the rapid diagnostic service

Peninsula:
Rolling out a rapid jaundice clinic – with CT available to patients with rapid onset jaundice within 48 hours

North, Central & East London:

Mid & South Essex:
RDC will include GP referrals for pancreatic cancer and referrals from A&E and radiology. RDC will also incorporate upper GI referrals as well as lower GI and NSS

Future RDC Research – Pan London Consortium

ADEPTS study

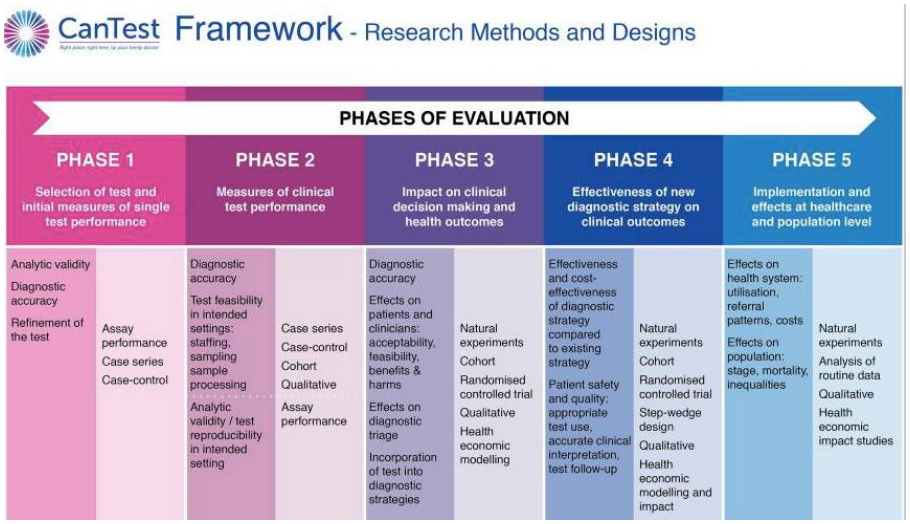
Pancreatic Cancer UK

- Accelerated Diagnosis of neuroEndocrine and Pancreatic TumourS
- Aim to develop new tests to diagnose PDAC and PNETs at an early stage; less invasive diagnosis.
- Benefits of earlier diagnosis: more treatment options, expectation of a better life and greater survival.
- Launched Nov 2018

Slide courtesy of Prof S Pereira, UCLH

Can detailed patient reported symptoms drive DSTs for NSCS?

- Symptom Pattern In the Nonspecific Presentation of Cancer (SPIN-PC)
  - Collect patient reported symptoms
  - Combine with outcome data
  - AI to develop DST to guide diagnostic testing

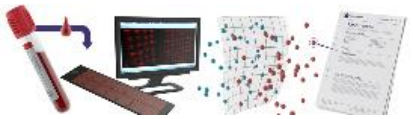


Evaluating diagnostic strategies for early detection of cancer: the CanTest framework Fiona M. Walter BMC Cancer. 2019; 19: 586

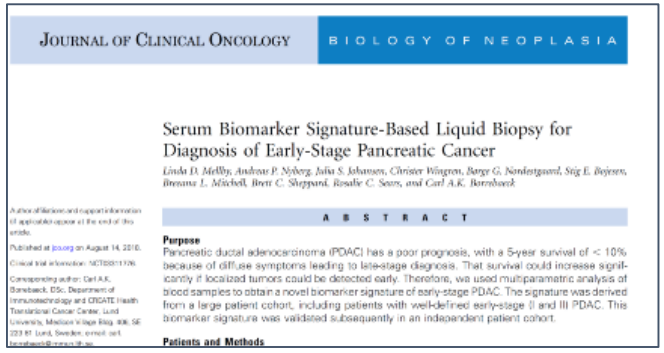
Combining multiple immune system and tumor biomarkers from a single blood sample can reliably detect early stage PDAC

immunovia

Immunovia AB



August 2018 Retrospective Scandinavian study, validated with US cohort



JOURNAL OF CLINICAL ONCOLOGY | BIOLOGY OF NEOPLASIA

Serum Biomarker Signature-Based Liquid Biopsy for Diagnosis of Early-Stage Pancreatic Cancer

Linda D. Mellby, Andreas P. Nyberg, Julia S. Johansen, Christer Wingren, Børge G. Nordestgaard, Stig E. Bojesen, Breanna L. Mitchell, Brett C. Sheppard, Rosalie C. Sears, and Carl A.K. Borrebaeck

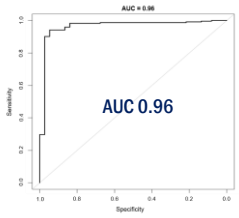
ABSTRACT

Purpose

Pancreatic ductal adenocarcinoma (PDAC) has a poor prognosis, with a 5-year survival of < 10% because of diffuse symptoms leading to late-stage diagnosis. That survival could increase significantly if localized tumors could be detected early. Therefore, we used multiparametric analysis of blood samples to obtain a novel biomarker signature of early-stage PDAC. The signature was derived from a large patient cohort, including patients with well-defined early-stage II and III PDAC. This biomarker signature was validated subsequently in an independent patient cohort.

Patients and Methods

Diagnosis	Stage	# Cases
PDAC	IA	15
	IB	16
	IIA	59
	IIB	148
	III	80
	IV	268
IPMN	Benign	13
	Borderline	5
	Malignant	10
Chronic Pancreatitis		57
Controls		1107

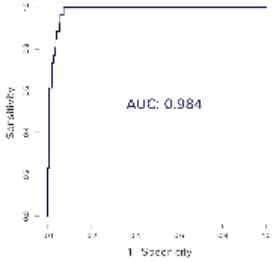


PDAC Stage I and II vs healthy controls

June 2019 Collaborative study with UCL
PDAC vs non PDAC symptomatic controls

	PDAC				Controls		
	Stage I	Stage II	Stage III	Stage IV	Healthy controls	Symptomatic controls (without diabetes)	Diabetes controls
No.	20	34	21	61	277	480	90

Results combining IMMray™ PanCan-d and CA19-9



PDAC Stage I and II vs symptomatic and healthy controls

2017 Prospective validation studies covering UK, US, Sweden, Canada, Spain

26 sites from Europe and USA part of

3 large pancreatic cancer clinical studies: PanFAM-1, PanSYM-1 and PanDIA-1

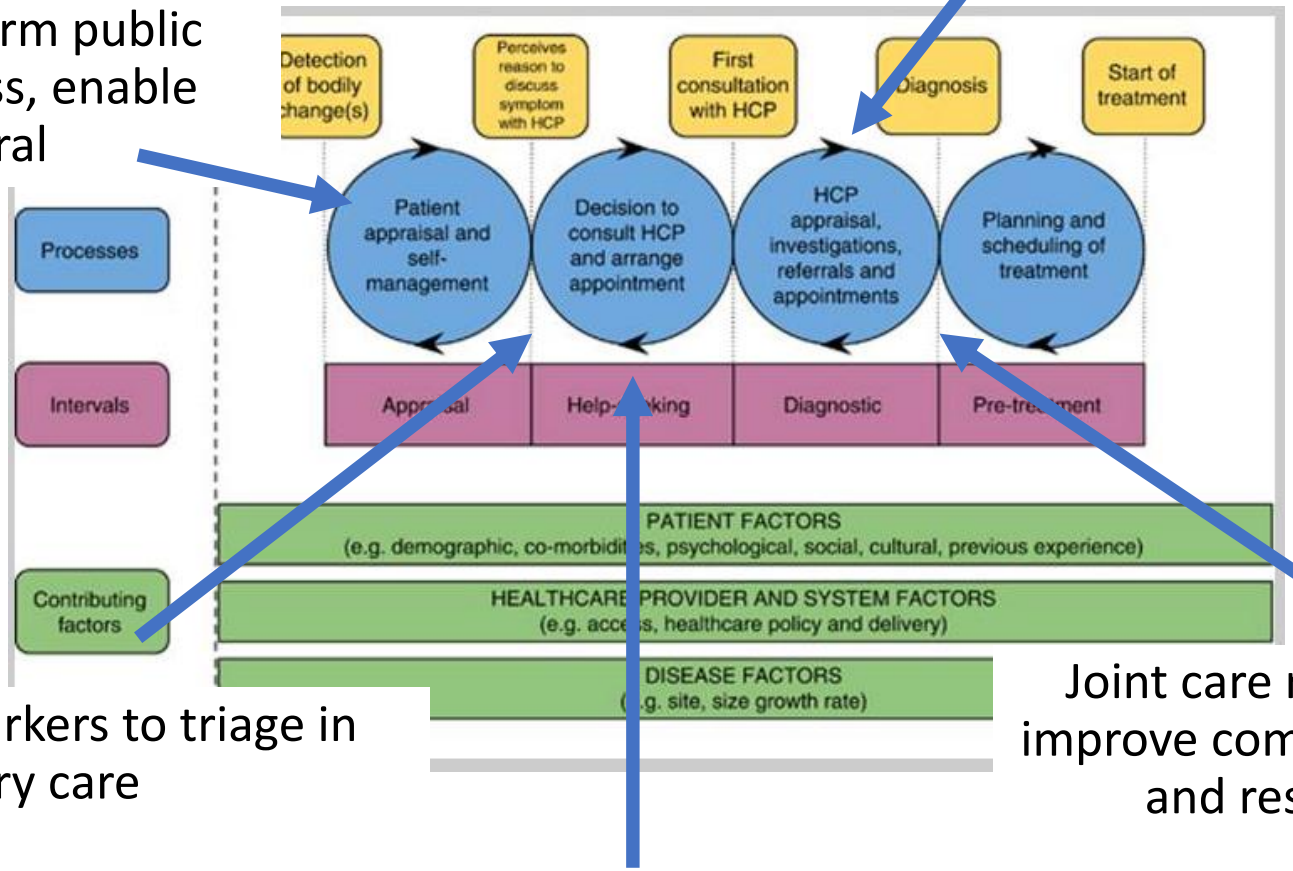
Totally covering **>10 000 high risk subjects**

Slide courtesy of Prof S Pereira, UCLH

The Future

RDCs for rapid and earlier diagnosis

Decision support tools inform public awareness, enable self-referral



Biomarkers to triage in primary care

Joint care records to improve communication and research

National surveillance for pre-malignant lesions

Acknowledgments

NCEL Cancer Alliance MDC project

- Sara Taiyari
- Mairead Lyons
- Michelle Cairns
- Janet Jugdeese
- Kathy Pritchard-jones
- Derralynn Hughes
- Eleanor Knights
- Elizabeth Parsons
- Mushleh Ahmed
- David Khoo
- Alara Bailey
- Asif Daroge
- David Graham
- Isobel Mason
- Lindsay Steward
- Karen Bramble
- Pollock Sallie
- Krishnaswamy Madhavan
- Nitika SILHI
- Kate REES, Kate
- Lucy McLaughlin
- Tommy LAY
- Rosemary Wilson
- Dylan Smiley
- Debasis Majumdar
- Hasmita Shivji
- Helga Laszlo

Thank you

MDC project leads

- Rebecca Hewitt
- Karen Blackburn
- Susan Sykes
- Helen Ryan
- Zoe Kaveney

ACE Project clinical teams from

- Airedale General Hospital
- Manchester University NHS Foundation Trust (Wythenshawe Hospital) & The Northern Care Alliance (Royal Oldham Hospital)
- Leeds St James University Hospital
- Oxford University Hospitals Trust

ACE/CRUK Team

- Dave Chapman
- Véronique Poirier
- Clare Pearson
- Karen Fitzgerald
- Sarah Hiom

Policy Research Unit cancer evaluation team

- Stephen Duffy
- Daniel Vulkan

Pancreatic Cancer UK

#SummitPanc20

Rapid Diagnostic Centres (RDCs)

Pancreatic Cancer UK are keen to work further with any Cancer Alliances and health professionals that are implementing rapid diagnostic pathways for pancreatic cancer, to share learning and innovations between centres and to optimise the rapid diagnostic pathway model for pancreatic cancer.

If you are working on a pancreatic cancer rapid diagnostic pathway/centre or want any more information please contact andrewmillar@nhs.net or peter@pancreaticcancer.org.uk

RDC at NMUH
Pancreatic Pathway – Nov 2020

All referrals sent via ERS or direct from ED / Radiology

1. Daily vetting by consultant – triage – tests/TC/F2F
2. CNS/navigator call patient and arranges (jaundiced patients always seen <48 hours by consultant)
3. The Navigator / RDC CNS coordinate tests – PET-CT, EUS, ERCP if needed, anaesthetic work up, psychological support, dietician, HNA
4. Twice weekly MDT review by team of progress
5. Patient admitted only if pain / debility
6. Patients with resectable tumours referred directly - MDT to agree surgical plan