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
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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

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

- Detection of bodily change(s)
- Perceives reason to discuss symptom with HCP
- First consultation with HCP
- Diagnosis
- Start of treatment

**Events**

- Patient appraisal and self-management
- Decision to consult HCP and arrange appointment
- HCP appraisal, investigations, referrals and appointments
- Planning and scheduling of treatment

**Processes**

- Appraisal
- Help-seeking
- Diagnostic
- Pre-treatment

**Intervals**

**Contributing factors**

**Patient factors**
- (e.g. demographic, co-morbidities, psychological, social, cultural, previous experience)

**Healthcare provider and system factors**
- (e.g. access, healthcare policy and delivery)

**Disease factors**
- (e.g. site, size growth rate)
Symptomatic Cancer - Anderson Model of Total Patient Delay

Action by Diagnosticians in Primary and Secondary Care
Symptomatic Cancer - Anderson Model of Total Patient Delay

Action by the Treatment Team

- Detection of bodily change(s)
- Perceives reason to discuss symptom with HCP
- First consultation with HCP
- Diagnosis
- Start of treatment

Events

Processes

Intervals

Contributing factors

PATIENT FACTORS
(e.g. demographic, co-morbidities, psychological, social, cultural, previous experience)

HEALTHCARE PROVIDER AND SYSTEM FACTORS
(e.g. access, healthcare policy and delivery)

DISEASE FACTORS
(e.g. site, size growth rate)
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
Why diagnose symptomatic pancreatic cancer early?

• 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)
Symptom Appraisal and Help-Seeking

- Promoted by charities and NHS
- No consistent NHS ‘Be Clear on Cancer’ for Pancreatic Cancer
What is being done now to improve the referral pathway?

- 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!

Who should be investigated?

- **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

©2016 by British Journal of General Practice
A national approach allows different NHS settings to be explored and creates a larger MDC referral data set for analysis.
RDCs – The patient journey

**The Patient Journey:**

0-2 days
- **GP Visit**
  - Patient presents to GP with vague symptoms or unexplained test results
  - Referral to MDC
  - GP organise 1st tier investigation (bloods, urine, chest x-ray, etc)

0-2 days
- **Triage**
  - Initial call with AHP, for a holistic patient history (including mental health and social factors) and book tests

0-3 days
- **Hospital Visit 1**
  - F2F consultation with consultant (or AHP) if particularly complex or frail
  - Based on triage outcome, patient may be returned to GP or redirected to another appropriate pathway

0-15 days
- **Hospital Visit 1+**
  - Multiple investigations possible (e.g. ultrasound then CT scan)
  - Clinical judgment to select first investigation
  - CT Scan

0-5 days
- **Follow up**
  - F2F consultation (MDC MDT) to discuss results and next steps
  - Endoscopy
  - Other investigations (colonoscopy, ultrasound, MRI, chest x-ray, etc)

0+ days
- **Onward referral**
  - Referral to 2WW pathway for cancer
  - Referral to secondary specialist for serious non-cancer disease
  - Referral to GP for non-serious diagnosis

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


ACE MDCs - Cancer diagnoses distribution (July 2018)

<table>
<thead>
<tr>
<th>Total MDC referrals*</th>
<th>2,873</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cancers</td>
<td>234</td>
</tr>
<tr>
<td>Cancer conversion</td>
<td>8%</td>
</tr>
</tbody>
</table>

Pancreatic cancer (10.6%)  

n=25

- Upper GI
- Lung
- Urology
- Lower GI
- Haematology
- Breast
- Other - include...
- Sarcoma & bone
- Gynaeology
- Skin
- In situ breast
- Secondary
- Brain & CNS
- Not specified
- Head and Neck

Pancreatic cancer referrals: 25

Total MDC referrals: 2,873

Cancer conversion: 8%
NCEL Cancer Alliance MDC
Cancer types

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

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

- 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)

- 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?

- Extremely likely: 75.9% (22)
- Likely: 17 (5)
- Neither likely nor unlikely: 5
- Don't know: 1

6 October 2016
Will RDCs improve the Pancreatic Cancer Pathway?

Now

- Improve the speed of diagnosis
  - Welsh study - 84.2 to 40.8 days if investigations booked - 5.9 days if at first appointment
- 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
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).

- 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.
- 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
- 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.
- 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

Peninsula: Rolling out a rapid jaundice clinic – with CT available to patients with rapid onset jaundice within 48 hours
Future RDC Research – Pan London Consortium

- **North Central London**
  - Approximately 1.5 million residents
  - Five CCGs
  - Five local authorities

- **North West London**
  - Approximately 2.1 million residents
  - Eight CCGs
  - Eight local authorities

- **North East London**
  - Approximately 2 million residents
  - Seven CCGs
  - Eight local authorities

- **South East London**
  - Approximately 1.8 million residents
  - Six CCGs
  - Six local authorities

- **South West London**
  - Approximately 1.5 million residents
  - Six CCGs
  - Six local authorities
ADEPTS study

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

**Immunovia AB**

**August 2018 Retrospective Scandinavian study, validated with US cohort**

**Journal of Clinical Oncology**

**Purpose**

Pancreatic ductal adenocarcinoma (PDAC) has a poor prognosis, with a 5-year survival of <10%, because of silent symptoms leading to late diagnosis. This survival could increase significantly if a circulating biomarker could be detected early. Therefore, we used multiparametric analysis of blood samples obtained from a novel biomarker signature of early-stage PDAC. This signature was derived from a large patient cohort, including patients with well-known stage I-III PDAC. This biomarker signature was evaluated subsequently in an independent patient cohort.

**June 2019 Collaborative study with UCL**

**PDAC vs non PDAC symptomatic controls**

<table>
<thead>
<tr>
<th></th>
<th>PDAC</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>5</td>
<td>0.96</td>
</tr>
<tr>
<td>Stage II</td>
<td>10</td>
<td>0.96</td>
</tr>
<tr>
<td>Stage III</td>
<td>15</td>
<td>0.96</td>
</tr>
<tr>
<td>Stage IV</td>
<td>20</td>
<td>0.96</td>
</tr>
</tbody>
</table>

**Results combining IMMray™ PanCan-d and CA19-9**

**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**

PDAC Stage I and II vs healthy controls

**Slide courtesy of Prof S Pereira, UCLH**
The Future

Decision support tools inform public awareness, enable self-referral

RDCs for rapid and earlier diagnosis

Biomarkers to triage in primary care

Joint care records to improve communication and research

National surveillance for pre-malignant lesions
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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
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