

Oncology Webinar series

PART 1: COLORECTAL CANCER | PART 2: PANCREATIC CANCER | PART 3: LUNG CANCER





BMJ Masterclasses provide busy doctors with essential updates on the latest evidence, important advances and current issues that are relevant to their daily practice.

In March and April 2023 we held a series of three webinar on oncology. The sessions were introduced by Dr Kieran Walsh, Clinical Director at BMJ and Henry Spilberg, Senior Publisher at BMJ.

The webinars provided generalist and trainee oncology healthcare professionals with the knowledge to treat and diagnose patients according to the latest updates and best practices.

The key learning points from the discussions are presented in this document. Recordings of the webinars can be [watched online](#).

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Part 1: Colorectal cancer

Presentation 1: Colorectal cancer: a primary care/generalist perspective – the challenges of diagnosing early and managing late effects of treatment

Dr Anthony Cunliffe, National Lead Medical Adviser, Macmillan Cancer Support; Joint Clinical Director for the South East London Cancer Alliance; and Oncology Lead at ORCHA.

Introduction

This presentation focuses on the challenges of diagnosing colorectal cancer early in primary care, the rise in colorectal cancers in younger people, and managing patients living with treatment impacts.

Key points

- Fourth most common cancer in the UK (11% of cancers)
- Second most common cause of cancer death in the UK (10% of cancer deaths)
- Mostly occurs older people but younger cases are rising
- Late-stage diagnosis has a 58.4% five-year survival rate compared with 92% for earlier diagnosis

Route to diagnosis

Patients diagnosed via the National Screening Programme or GP referral on average have better outcomes than those diagnosed in an emergency.

National Screening Programme

- A FIT (faecal immunochemical test) every 2 years for people aged 60-74.
- People 75 and over can opt in.
- NHS England plans to expand to over 50s.
- Lower take-up in lower socioeconomic quintiles, and people living in areas of high ethnic diversity.
- GPs must make sure that refusal is an informed decision.

Presentations to GP surgery

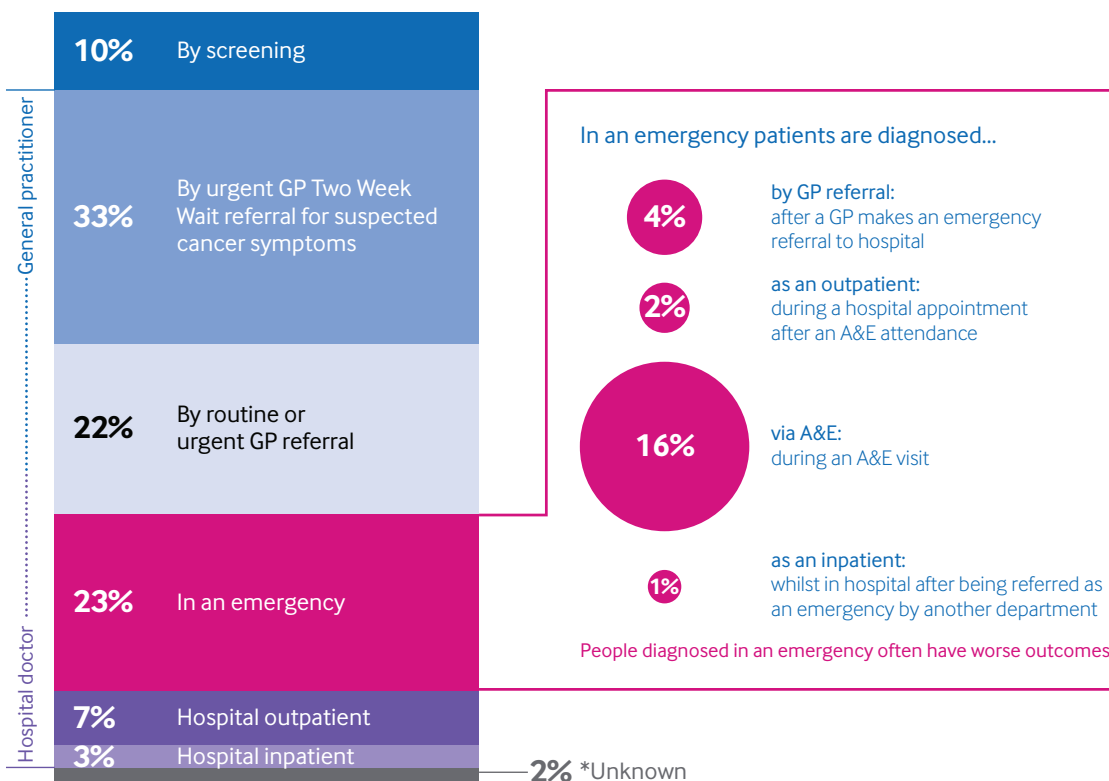
GPs diagnose very few cancers per year (8-9 on average). Most of the common symptoms (abdominal pain, constipation, diarrhoea, rectal bleeding, weight loss) that GPs see will be benign.

The UK has low referral rates. We have a responsibility as gatekeepers to not refer too many patients in.

Who to investigate and how quickly is based on:

- Symptoms (duration and severity).
- Past medical history.
- Recurrent presentation (relies on appropriate coding).
- Patient age.
- Family history.

Routes to diagnosis



*Incomplete data Source: PHE, Routes to Diagnosis, 2016

Need to be familiar with the urgent suspected cancer referral guidelines, introduced in 2015, though you can refer outside guidelines with a 'GP hunch'.

People often present multiple times while primary care investigations are carried out to strengthen confidence in referral.

FIT

FIT should be done for most suspected patients, including urgent referrals, to help make referral decisions and help triage in secondary care.

Patients should understand that FIT picks up different levels of haemoglobin within stool.

- Symptomatic patients: 10 micrograms per gram.
- Screening programs: 80 - 150 micrograms.

Full blood count

Anyone over 60 with iron-deficient anaemia should be referred. Under 60 with iron-deficient anaemia, we would do a FIT and refer if positive.

Watch and wait

Guidelines are to watch and wait patients with new symptoms but negative FIT with a safety net. Can also access advice from a secondary care clinician or refer to pathways such as Rapid Access Diagnostic Clinics.

Cases in younger people

Consider other conditions requiring urgent referral such as inflammatory bowel disease (IBD).

FIT is encouraged in younger people. If somebody's younger, no family history, negative FIT, their chances of having colorectal cancer are very low.

Lynch Syndrome

- Genetic condition with 80% lifetime risk of colorectal cancer.
- Affects an estimated 200,000 people in the UK, most unaware.
- Genetic testing available for colorectal cancer diagnosis, but significant variation in implementation.
- Primary care clinicians may be asking for testing by patients diagnosed with colorectal cancer or if a family member is diagnosed with Lynch Syndrome.

Post-treatment consequences

Significant increases in five- and 10-year survival means more cured patients in primary care. We need to understand the negative impacts of cancer treatment on quality of life.

Patients often do not report effects, or effects may not be linked to a previous cancer if it hasn't been coded correctly.

We need improved communication between primary and secondary care: summaries of treatments; correct coding etc.

Presentation 2: Endoscopic early detection and minimally-invasive endoscopic management of colorectal lesions – the state of the art

Edward J. Despott, Consultant Gastroenterologist & Interventional Endoscopist, The Royal Free Hospital & The Wellington Hospital

Introduction

This presentation looks at how endoscopy is used as a treatment for colorectal cancers and pre-cancers.

Benefits of colonoscopy

- Removing polyps/lesions removes the cancer or potential cancer.
- Reduces incidence of colorectal cancer by 53% and mortality from colorectal cancer by 63%.
- Up to 95% of precancerous lesions can be detected and removed.

Quality of colonoscopy

Primary care doctors should communicate to patients the importance of following bowel preparation guidance—the best technology will miss lesions in a poorly prepared bowel.

Good quality visualisation in colonoscopy requires removal of mucus from bowel wall; insufflation of the bowel and/or positioning the patient; and high-definition cameras to detect and characterise even subtle lesions.

AI and colonoscopy

The use of AI is beginning to revolutionise colonoscopy, detecting small and subtle lesions which humans can miss. It can also help to characterise lesions.

Understanding the lesion

Characterising lesions influences the type of procedure. We also discuss the patient as a whole eg age, comorbidities or medications at MDT meetings to tailor each procedure.

Lesions are optically assessed during colonoscopy using blue light laser imaging to look at the granularity of the lesion (Kudo pit pattern). The more irregular, the more dangerous.

Lesions are also graded by SM1 to SM3 depending on their level of invasion into the submucosa. These correlate with lymph node metastasis. We won't resect lesions that are more than SM1.

The SMSA score (size, morphology, site, access) tells us how difficult the procedure will be.

Minimally invasive removal techniques

Cold snaring

A thinly braided metal snare is used to grab and cut the lesion once it has been injected to lift it away from the bowel wall. No diathermic current is used, making this a safer technique in terms of perforation risk.

Polypectomy (pedunculated)

A diathermic snare is used to cut through the stalk of a pedunculated lesion. Heat can be used to cauterise the blood vessels. A detachable snare can be used to act as a ligature if the stalk is particularly large to reduce the risk of delayed bleeding.

EMR (endoscopic mucosal resection)

A diathermic snare is used to remove large, flat (sessile) lesions which have not penetrated deeply, either in one piece (en bloc) or in a piecemeal process for larger lesions. Tissue adjacent to the lesion is also removed to reduce the chance of recurrence and the margins of the lesion are cauterised.

There is a 7% risk of delayed bleeding with EMR, usually in elderly people or more difficult resections. There is also a risk of perforation, which requires closing the bowel wall, antibiotics and admission for the patient. In cases of delayed perforation, the patient is treated with antibiotics, pain relief and surgery.

If a lesion is removed piecemeal, a scope is done three months later because of the high risk of recurrence (36%).

Endoscopic submucosal dissection (ESD)

Only available in a handful of specialised centres/hubs in the UK. It is a long procedure, 2-4hrs, so not suited to elderly patients.

This specialised technique is used for around 5% of lesions where we're worried about high-grade dysplasia or submucosal invasion/early cancer, or else if a lesion is fibrosed and can't be resected with a snare. ESD can help to avoid surgery for this type of lesion.

We use the pocket method, where a knife is used to undermine a lesion and bring it out in one piece.

We follow up after a year with ESD because there is less chance of recurrence.

Part 2: Pancreatic cancer

Presentation 1: Pancreatic cancer: diagnosis and biomarkers

Hemant Kocher, Professor of Liver and Pancreas Surgery, Centre for Tumour Biology, Co-Lead, Cancer Screening & Early Diagnosis, Barts Cancer Institute

Introduction

This presentation focuses on the diagnosis of pancreatic cancer, and research aiming to improve early diagnosis.

Key facts

- One person is diagnosed with, and one person dies from, pancreatic cancer every hour.
- Lowest cancer survival rate.
- 12th most common cancer, but the fourth commonest killer.
- Will be the second most common cancer killer by 2035 due to the aging population and lack of effective treatments.

Early diagnosis

Most pancreatic cancer diagnoses are late stage and therefore have poor survival rates:

- Stage 1-2b (operable): 32-65% 5-year survival. Accounts for just 10% of diagnoses.
- Stage 3 (locally advanced): 10-12% 5-year survival. Accounts for 30-35% of diagnoses.
- Stage 4 (metastatic): 3% 5-year survival. 55-60% of diagnoses.

Early diagnosis starts with awareness. Unfortunately, the symptoms of pancreatic cancer are vague and common.

Main symptoms: jaundice and unexplained weight loss (particularly over aged 50).

Other symptoms:

- Nausea and vomiting.
- Loss of appetite.
- Indigestion.
- Diabetes (type 3: recent and not weight related).
- Mid-back pain.
- Changes in stool.

Common misdiagnoses: gallstones, peptic ulcer, IBS, GORD, musculoskeletal pain, pancreatitis and hepatitis.

Anyone over 40 with jaundice should be referred onto the suspected cancer pathway.

Anyone over 60 with weight loss and any other symptom should be referred for an urgent CT.

There are tools available help GPs diagnose/refer eg the Qcancer risk calculator. AI will help to refine these further in the future.

Screening

For screening to impact survival rates it must be able to detect cancer in asymptomatic patients.

The prevalence of pancreatic cancer is less than 1/10,000—mass screening isn't appropriate for something so uncommon.

We a 'sieve' to enrich the population to a prevalence of 1/1000. We then need a biomarker with more than 99% sensitivity and specificity to screen the enriched population and not get too many false positives or negatives.

This first sieve could be: age, presence of chronic/heredity diseases, familial pancreatic cancer, pancreatic cyst, new onset diabetes. The biomarker could then be something detectable in: blood, urine, saliva, breath, scan or endoscopy.

There are six studies currently underway for screening an enriched population:

EUROPAC: registry of people with family history (two or more close relatives), a gene mutation (and a least one family member case), Peutz-Jeghers Syndrome, or hereditary pancreatitis.

UK-EDI: aims to develop a biomarker for early detection of type 3 diabetes. Aims to recruit 2500 people with new onset diabetes and follow them for 3 years.

UroPanc: development of a 3-biomarker panel in urine. Will screen 3500 people with symptoms and aim to uncover about 50 pancreatic cancer cases at four centres in the UK.

ADEPTS: an electronic tool to refine the population, followed by urine and serum biomarkers to diagnose neuroendocrine and pancreatic ductal adenocarcinoma. Aims to recruit 2500 people.

PANC-CYS-GAN: using an artificial intelligence tool to discriminate which cysts are pre-malignant.

CAN-DETECT: aims to accelerate detection of pancreatic and gastro-oesophageal cancer in primary care.

Future research

Scans don't have high enough sensitivity and specificity, and there are issues with access, expense etc.

There are lots of studies into biomarkers and some show promise but improvements are needed to reach the >99% target.

We need more research, which relies on availability of cases and controls, clinical data and well-controlled and well-stored samples.

The Pancreatic Cancer Research Fund tissue bank is a new, open-access UK tissue bank that aims to ultimately help patients with new diagnostic tests and therapies. Seventy-three projects have been initiated using samples from the bank and have led to 23 publications.

Presentation 2: Pancreatic cancer treatment

Fieke E M Froeling, Clinical Senior Lecturer and Consultant Medical Oncologist, Wolfson Wohl Cancer Research Centre; and Beatson West of Scotland Cancer Centre, School of Cancer Sciences, University of Glasgow

Introduction

This presentation covers the current treatment of pancreatic cancer and the potential of precision medicine.

Treatment for locally advanced or metastatic pancreatic cancer

Pancreatic tumours are in a fibrotic microenvironment which is immune evasive and tumour supporting. Pancreatic cancer patients haven't benefited from the immunotherapy drugs that have transformed care of other cancers.

Though the statistics around pancreatic cancer survival are poor, there is hope. Treatment can work if it is right for the patient.

Locally advanced or metastatic pancreatic cancer is treated with either:

- Triple agent combination chemotherapy (FOLFIRINOX) or
- Combined gemcitabine and Nab-paclitaxel.

Survival remains less than a year for most patients on both regimens.

Treatment is based largely on physician choice due to differing logistics, side effects, drug availability and state of patient's health.

Patients with the gBRCA1/2 gene mutation may also be treated with Olaparib, but it doesn't change overall survival.

Second line treatment options have minimal impact on survival.

Functional decline is challenging and contributes to poor survival statistics: many patients are too unwell to start chemotherapy.

Symptom control is key to keeping patients well enough to receive chemotherapy.

The same regimens are currently used for all patients, we need methods to predict which treatment patients should receive.

Treatment of localised pancreatic cancer

Surgery is the only cure for pancreatic cancer and is generally only possible in resectable or borderline resectable cases.

The standard of care has been surgical resection and six months of post-operative chemotherapy.

What we learn about chemotherapy in advanced cancer we can apply to earlier cancers.

The FOLFIRINOX regimen was a significant change in 2018 bringing near five-year survival rates, but with challenging side effects (largely neutropenia and diarrhoea).

But surgery and six months of chemotherapy is tough on patients. There may be complications from surgery, or some patients die from neutropenic sepsis while on chemotherapy, for example.

Clinical trials in this area have found that giving neo-adjuvant or peri-operative chemotherapy leads to fewer surgeries, but the patients you operate on do better and can complete chemotherapy.

But how do we make sure that we operate on the 'right' patients and impact on survival outcomes?

Tailoring treatments

The priority is trying to predict the best first line treatment for a patient, as patients deteriorate so quickly. Using available treatments in the most effective way leads to better tumour control, symptom improvement and avoidance of rapid functional decline.

The genetic variation of tumours within pancreatic cancer is particularly high, so we haven't had the success of, say, breast cancer, where large group of patients share the same genetic mutation.

But the KRAS mutation is present in almost all pancreatic cancer patients and there is a lot of research targeting it.

There is some evidence emerging that patients with mutations in the DNA damage repair machinery do better with platinum-based therapies, and those without do better with gemcitabine-based.

If we group patients by gene transcription, two populations emerge: a 'classical' subtype (which responds more to current treatments) and a squamous subtype, which has tumours which look very different.

Loss of SMAD4 could also be a negative prognostic factor.

The UK therapeutic development platform, Precision Panc, biopsies patients for molecular profiling and then assigns clinical trials based on disease profile.

Treatment is by clinical trial where possible. There are multiple exciting agents in development.

Part 3: Lung cancer

Presentation 1: Radiotherapy and Systemic Treatment of Lung Cancer

Dr Kathryn Banfill, Clinical Oncology Consultant,
the Christie NHS Foundation Trust

Introduction

This presentation covers curative and palliative radiotherapy for lung cancer, adjunctive systemic treatment and molecular profiling in lung cancer.

Lung cancer key stats

- 48,000 people diagnosed each year.
- 21% of all cancer deaths.
- Five-year survival rate of just 16.2%.
- Lots more treatment options available than 10 years ago.

Screening

UK recommendation to screen patients between 50 and 75 with a smoking history.

Trials have found 12-20% reduction in lung cancer mortality in screened populations (earlier diagnosis means access to potentially curative treatment). But the overdiagnosis rate is 38%, and the capacity isn't there to roll out nationally.

Stage 1 treatment

Stage 1 (less than 5cm with no nodal involvement) – 20% cases (potential to increase with screening).

1. Surgery
2. Stereotactic, ablative radiotherapy (SABR, high precision, high dose)

Radiotherapy damages cancer cells, mostly via formation of hydroxy radicals within the cells. Measured in Gray and divided into fractions to allow normal tissue recovery.

There hasn't been a head-to-head trial of surgery and SABR so research data is often retrospective. Overall survival is better with surgery than radiotherapy, but cancer-specific survival is roughly the same (fitter patients tend to go for surgery).

Side effects of SABR include: dysphagia; red, itchy skin; and lung scarring leading to shortness of breath and chronic respiratory infection.

Stage 3 treatment

- Heterogenous group of cancers and patients.
- Rapidly changing treatment options.
- Ideal is concurrent chemoradiotherapy – platinum-based chemo alongside 4-6 weeks of radiotherapy.
- People who can't have chemotherapy (due to age, comorbidities) have 3-4 weeks of radiotherapy.
- Less fit patients may also do chemo first and then radiotherapy.
- Concurrent therapy is 8% more effective.

Molecular markers for lung cancer

Immunotherapy has been a game changer in other cancers. Beginning to have an impact in lung cancer.

PDL-1

PD-L1 is a protein found on tumour cells which helps evade the immune system. PD-1 inhibitor drugs reveal the tumour cells and activate the immune system against them.

One year of durvalumab following concurrent chemoradiotherapy in stage 3 PD-L1 positive patients: 42.9% five-year survival (historically 15%). Immunotherapy is having an impact in stage 4 cancer too.

Recent trial in stage 1b to 3a lung cancer patients of neo-adjuvant chemoimmunotherapy (three cycles of nivolumab and platinum-based chemotherapy) prior to surgery led to 31 months survival rather than 20 months in fit patients.

EGFR

EGFR is a cell surface marker. Drugs such as osimertinib bind to the extracellular domain and prevent EGFR from keeping lung cancer cells alive.

Three years of adjuvant Osimertinib in stage 1b – 3a NSCLC patients with an EGFR mutation following surgery or chemotherapy. Huge difference in disease-free survival (65 months to 28) and may also impact overall survival.

Only around 10-15% of patients have EGFR mutation and there are side effects. Mainly acne rash plus diarrhoea, pneumatosis, mouth ulcers, URTIs, low platelets/neutrophils.

Kras

Kras is downstream of EGFR. Was thought to be undruggable in lung cancer. Now sotorasib (for Kras G12C mutations) has had a modest impact vs docetaxel. Will hear more in the Kras space.

Small cell lung cancer

15% of lung cancer patients, generally smokers, with median overall survival of one year. No recent advances – ideal treatment is concurrent combination chemotherapy and radiotherapy, or chemoimmunotherapy in stage 4. SMLC goes to the brain, so some patients receive prophylactical cranial radiation.

Palliative radiotherapy

Carried out for conditions such as malignant spinal cord compression, superior vena cava obstruction, tumour-induced breathlessness, brain metastases or chest/bone pain. Also consolidation chest radiotherapy following chemotherapy.

The benefit takes a few weeks so expected survival needs to be beyond a few weeks.

Presentation 2: Lung Cancer and Acute Cancer Care

Dr Ashling Lillis, Consultant in Acute Medicine,
Whittington Health NHS Trust; National Clinical Adviser,
Macmillan Cancer Support

Introduction

This presentation covers the care of acutely unwell cancer patients – many of whom have lung cancer.

Acute cancer care

Caring for people living with cancer who become acutely unwell, round the clock. It encompasses primary and community care, acute generalists, as well as oncology and specialist cancer services.

Presentations:

Type 1: emergency cancer diagnosis – advanced disease, often health inequalities and comorbidities.

Type 2: complications of anticancer treatment: neutropenic sepsis, complications of novel treatments, chemotherapy issues.

Type 3: progressive disease or age/frailty/comorbidities interacting with cancer (50% of presentations).

Scale of challenge

- People living with cancer for longer, with more comorbidities etc.
- 110,000 with treatable but not curable cancer in 2017, will rise to 200,000 by 2030.
- Complexity now the norm for people with cancer – acute illness will happen.
- Acute care provided by a broad range of oncology and generalist healthcare professionals.
- People with cancer make up a significant proportion of emergency presentations.

Study in Merseyside:

- 5% of presentations to emergency department, 15% of ED admissions (80% admission rate).
- 10% of paramedic activity and 60% of conveyance to hospital.
- Follow up: 20% died within 30 days, 70% had died within 12 months.

Acute care and lung cancer

Huge proportion of people living with lung cancer are in the last 12 months of life. The need for acute care is part of the transition to end of life. It costs a lot of money and is a poor experience for patients.

Risk factors for lung cancers are also risk factors for comorbidities – 10% of people with lung cancer are living with three or more comorbidities.

Optimising from the start of a cancer journey, with prehab and other treatments for comorbidities, means we might be able to avoid some of this acute care.

In one study, lung cancer made up 25% of emergency cancer admissions. If we can get this right for lung cancer, we can get it right for others.

Out of hours

Too many cancer patients, particularly older people, are being admitted to hospital after an out of hours GP consultation – we need alternative ways of getting people help that isn't acute care in hospitals.

Most emergency presentations of cancer don't happen in 9-5 working hours but oncology clinics run within working hours.

As professionals we need to get better at screening, triaging and seeking expert advice.

Sources:

- UKONS Acute oncology initial management guidance. One page per common cancer-related presentations and tells you what you should do.
- In the UK most oncology hotlines are staffed 24/7, and we should use these as healthcare professionals.
- UKONS Macmillan AO triage tool – useful for stratifying patients.

End-of-life care

How can we make sure that we aren't prolonging care and making life worse when we could make it more comfortable?

If we don't identify that someone is making a transition, we won't be able to optimise their care and make the end of their life what they wish.

We don't talk to people about that risk of death. Just 27% of acutely unwell cancer patients had an end-of-life conversation recorded in one study.

The conversation

We've normalised acute admissions, but they are extremely traumatic for patients. We often can't avoid the first admission but we might be able to prevent the second, third or fourth.

All health professionals should have the confidence to have these conversations – they don't have to be delivered by an oncologist. You can call a patient's oncologist if you need to, and the 24hr hotline is for everyone to use, including health professionals.

If you have the conversation, write it down and share it.