CUP – THE PROBLEM

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CUP – THE PROBLEM

Agenda

I The size of the *problem*
(epidemiology)

II The unique *problems* facing patients
(patient experience research and peer review)

III Critical issues in ending the *problem*

A challenging diagnosis for oncologists

'Malignancy of undefined primary origin' (MUO).
Patients who present with metastatic malignancy identified on clinical examination or by imaging, without an obvious primary site.

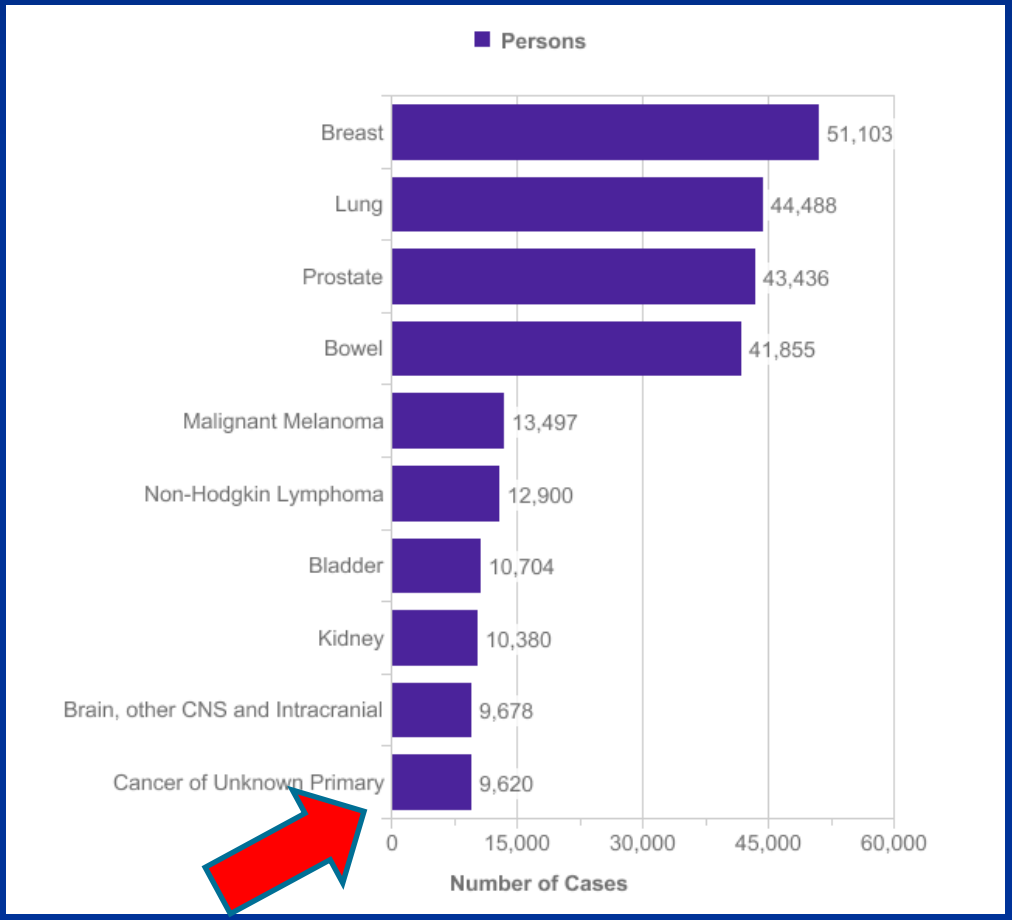
'Provisional carcinoma of unknown primary origin' (pCUP)
Patients with metastatic malignancy of proven epithelial, neuro-endocrine or undifferentiated lineage, after initial, but not exhaustive investigations.

'Confirmed CUP' (cCup)
After the results of all tests are complete and no primary site is found.

A 'double agony' for patients and families

CUP Incidence UK, 2012

(C77-80)



CUP has the 10th highest number of new cancer cases each year in the UK

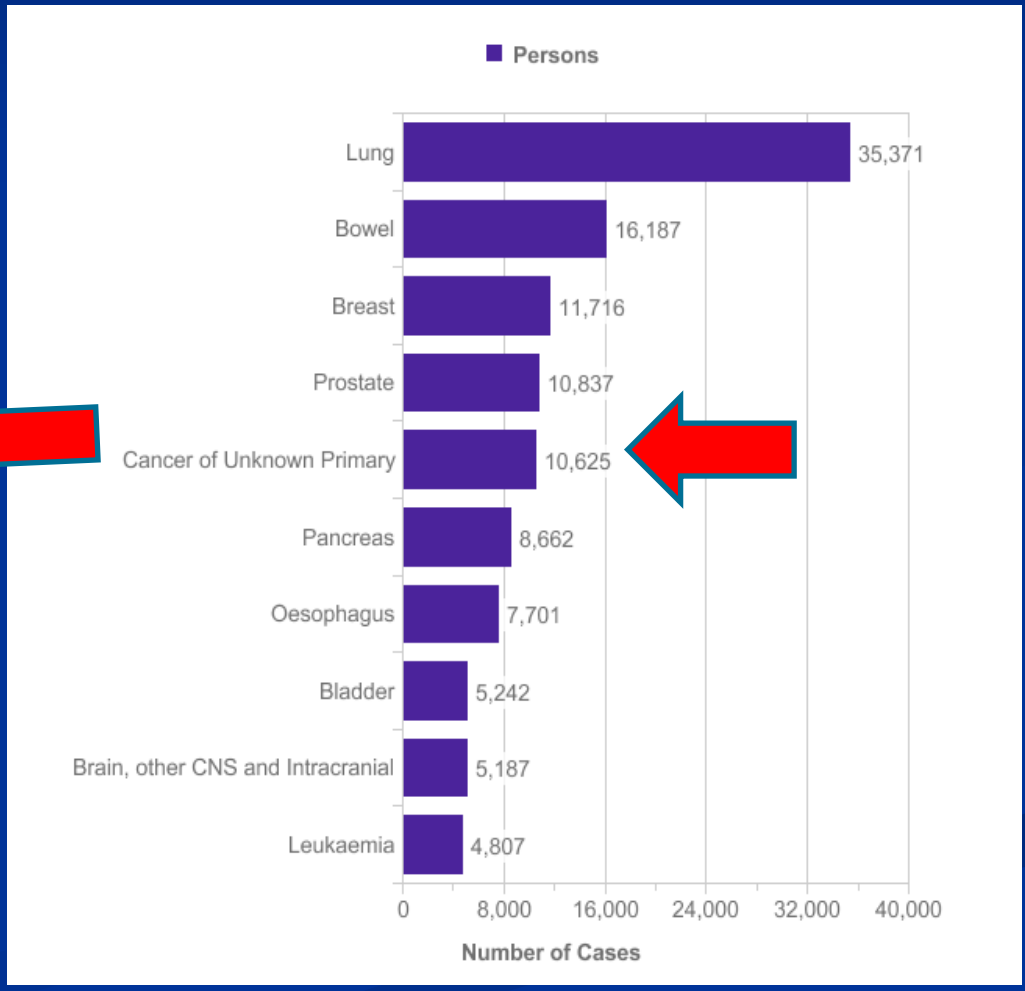
	England	Wales	Scotland	N Ireland	UK
Male	3,730	259	402	95	4,486
Female	4,235	311	463	125	5,134
Persons	7,965	570	865	220	**9,620**

Data source: CRUK 5/2015

CUP Mortality UK, 2012

(C77-80)

	England	Wales	Scotland	N Ireland	UK
Male	4,189	291	367	111	4,958
Female	4,687	392	454	134	5,667
Persons	8,876	683	821	245	**10,625**



CUP is the 5th highest cause of cancer death in the UK

Data source: CRUK 5/2015

UK (ICD-10 C77-80)					
	Incidence			*Mortality*	
Year	No. of new cases	Rate* per 100,000		No. of deaths	Rate* per 100,000
1996	15,838	20.4		15,024	19.4
1998	14,972	19.0		15,259	19.3
2000	14,013	17.3		14,559	18
2002	13,428	16.1		14,058	16.7
2004	12,640	14.8		13,288	15.4
2006	11,566	13.1		12,267	13.7
2008	10,752	11.9		11,228	12.0
2010	9,585			10,472	10.7
2012	9,620			10,625	

**Age-standardised to the European Population.*
Source: NCIN & CRUK

- 40% drop in *incidence* over 16 years (28% in last 10 yrs)
- 30% drop in *mortality* over 16 years (23% in last 10 yrs)

UK CUP Incidence by ICD code C77-80		
ICD Code:	**2009**	2008
C77: Secondary and unspecified malignant neoplasm of lymph nodes	**972**	854
C78: Secondary malignant neoplasm of respiratory and digestive organs	**3,163**	3,388
C79: Secondary malignant neoplasm of other sites	**1,230**	2,189
C80: Malignant neoplasm without specification of site	**5,105**	4,321
Total (C77-80)	**10,470**	**10,752**

Not counted as CUP:
C76 (*Malignant neoplasm of other & ill-defined sites*),
C26 (*Malignant neoplasm of other & ill-defined digestive organs*),
C39 (*Malignant neoplasm of other & ill-defined sites in the respiratory system and intrathoracic organs*)

Routes to Diagnosis

NCIN 2006-2010

- **57% of patients diagnosed with CUP presented as an emergency**, compared with 23% for all cancers.
  (Reflecting the non-specific symptoms experienced by MUO patients?)
- 45% were aged 80 and over; 4% were aged under 50.
- Ratio of 1 male to 1.2 females
- 21% in the most deprived socio-economic group.

There are damned lies .....and statistics

- 7,000 men admitted to hospital for obstetric services
- 8,000 men were seen by a gynaecologist
- 20,000 men were referred to a midwife
- 3,000 children required geriatric services

BMJ/ Imperial College Healthcare NHS Trust on 2009 -2010 data. (Reported in D/Telegraph)

...and then there are data users!

"It isn't pollution that's harming the environment. It's the impurities in our air and water that are doing it.." --Al Gore

Coding issues

CRUK-NCIN Partnership Project

Registries:	
Australia	8
Ireland	1
England	8
Scotland	1
Wales	1
N Ireland	1

- **No consistent national or international coding guidance** for registering and reporting CUP resulting in varied cancer registration practices.
- Reporting practices vary with some registries using ICDO3 codes and others using different ICD10 codes to represent CUP.
- Differing interpretations of: ICDO3 and ICD10 codes, the investigation of death certificate only notifications, electronic notifications, consideration of prior registrations of site-specific cancers, and the types of notifiers for additional information.
- Variation in coding practices for tumours with non-epithelial morphologies such as melanoma and sarcoma, and the use of ill-defined primary site codes such as 'gastrointestinal' cancer.

II - Patient experience

"Because someone is in a white coat and using big medical instruments [it] doesn't necessarily mean they are right".

Kylie Minogue on Cancer Diagnosis (Apr. 2007)

"Until the pathology results came through for me, I felt quite lost and pretty hopeless, with no control over my situation, no clues regarding treatment – one [oncologist] seemed to give up, the other suggested it would be possible to hit me with up to 3 chemo agents, given that I was fairly young and fit".

CUP patient (2008, subsequently diagnosed as Breast, now deceased)

Patient experience research
Boyland & Davis, 2008 themes

- Poor understanding of CUP/ causality
- Struggling with uncertainty
- Multiple investigations
- Unable to treat
- Healthcare professionals not knowing the answers
- Difficulty of explaining CUP to others

University of Southampton and CUP Foundation patient experience research (2009 - 2013)

- Numbers. Women: 10, Men: 7. Age Mean: 60.6 years, Range: 41–78 years
- Recruitment sources: University Hospital Southampton; Portsmouth Hospitals; Isle of Wight NHS Primary Care Trust ; CUP Foundation
- Triangulation. Professional carers (nominated by patients): Oncologist (n=5) ; Surgeon (n=2) ; CNS (n=2) ; GP (n=2) ; Dietician (n=1) ; Radiographer (n=1)
- Sites of mets: Lung , neck, liver, pelvis, lymph nodes, adrenal glands, spine, pancreas, ovaries, mediastinum, appendix, mesentera, peritoneum
- Treatment history: Chemotherapy only ; Chemotherapy + radiotherapy; Radiotherapy only; Surgery, chemotherapy + radiotherapy; Surgery + radiotherapy ; Surgery + chemotherapy

Findings – A disrupted patient journey

- **Medical professionals experienced difficulty communicating uncertainty to patients**
- **Ambiguity** in deciding optimal treatment plans
- **Test or treat dilemma:** when to discontinue chasing the primary/start treatment/ BSC.
- The remit of MDTs often excluded CUP, leading to '**MDT tennis**'.
- In the absence of a primary diagnosis, patients and informal carers experienced **uncertainty** regarding prognosis, possible recurrence and the primary's hereditary potential.
- Common problems with care continuity were amplified for CUP patients relating to **coordination, accountability and timeliness of care.**

CANCER OF UNKNOWN PRIMARY (C77-80) PATIENT EXPERIENCE PERSPECTIVES COMPARED WITH ALL CANCERS IN THE NATIONAL CANCER PATIENT EXPERIENCE SURVEY (2012).

- **CUP patients responses were generally more negative than the national 'all'.** Using the DoH's benchmark of less than or equal to70% as being 'less positive' there are 23 'less positives' for CUP versus 16 for 'all'. (There is a significant variation between the 'big 4' collectively and the less common tumour sites.)

- **Information and support, confidence and trust, and effective communication by doctors and nurses in relation to CUP patients are perceived to be significantly lower than the national 'all'.**

- **There are some 'less positives' that are easily rectified. Such things as: the lack of patient information and information about support groups.**

Analysis of CUP patients in the 2010, 2011-12 & 2013 Cancer Patient Experience Surveys (CPES) England. Soton Uni, Jun 15

- **Positive comments regarding CNSs predominated over negative comments** (negatives about access/ contact)
- **Lack of communication** between different health sectors (e.g. primary and secondary), different providers (e.g. trusts), and between different hospital departments and health professionals within the same trust
- **GPs.** Respondent's comments regarding their interactions with GPs were predominantly negative.
- **Delays by GPs to diagnosis and referrals** for investigations and secondary referrals; **Delays to receiving the results of investigations**

'It can take 2 weeks for information to cross a corridor to the other department because of bureaucracy.' (4178 2011-12)

- **Manner of communication between health professionals and patients/relatives**

'When I was told I had cancer in my local hospital, I was told in an open ward, without the curtains being drawn, by a consultant who was rude, with his large group of other doctors/trainees. He then left me without any info apart from 'This is very serious'. 2022 2010

[Note: ratios of negative to positive comments remained relatively constant over the three time-points]

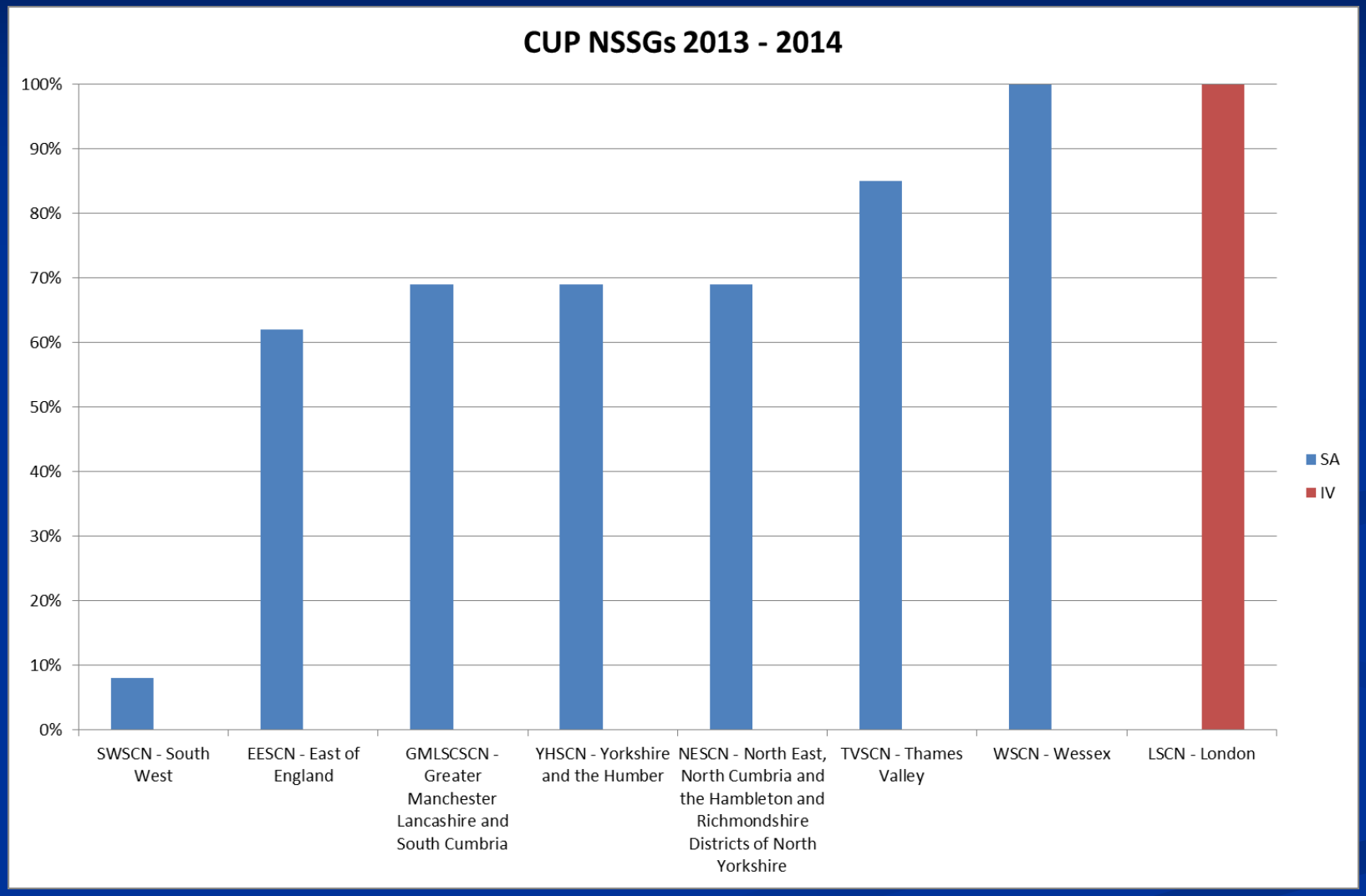
Peer Review 2013/14 CUP Services

2 on SA and 142 on IV

- 144 teams reviewed
- Maidstone Hospital =100% compliance; the lowest: S****** & ****Hospitals = 4%
- 8 Immediate risks; 41 Serious concerns (from no functional MDT to lack of: cover, robust pathways, good practice)
- Lead clinician and core team in place = 30%
- Patients experience exercise = 23%
- Patient written info = 60%

Peer Review – Network Compliance

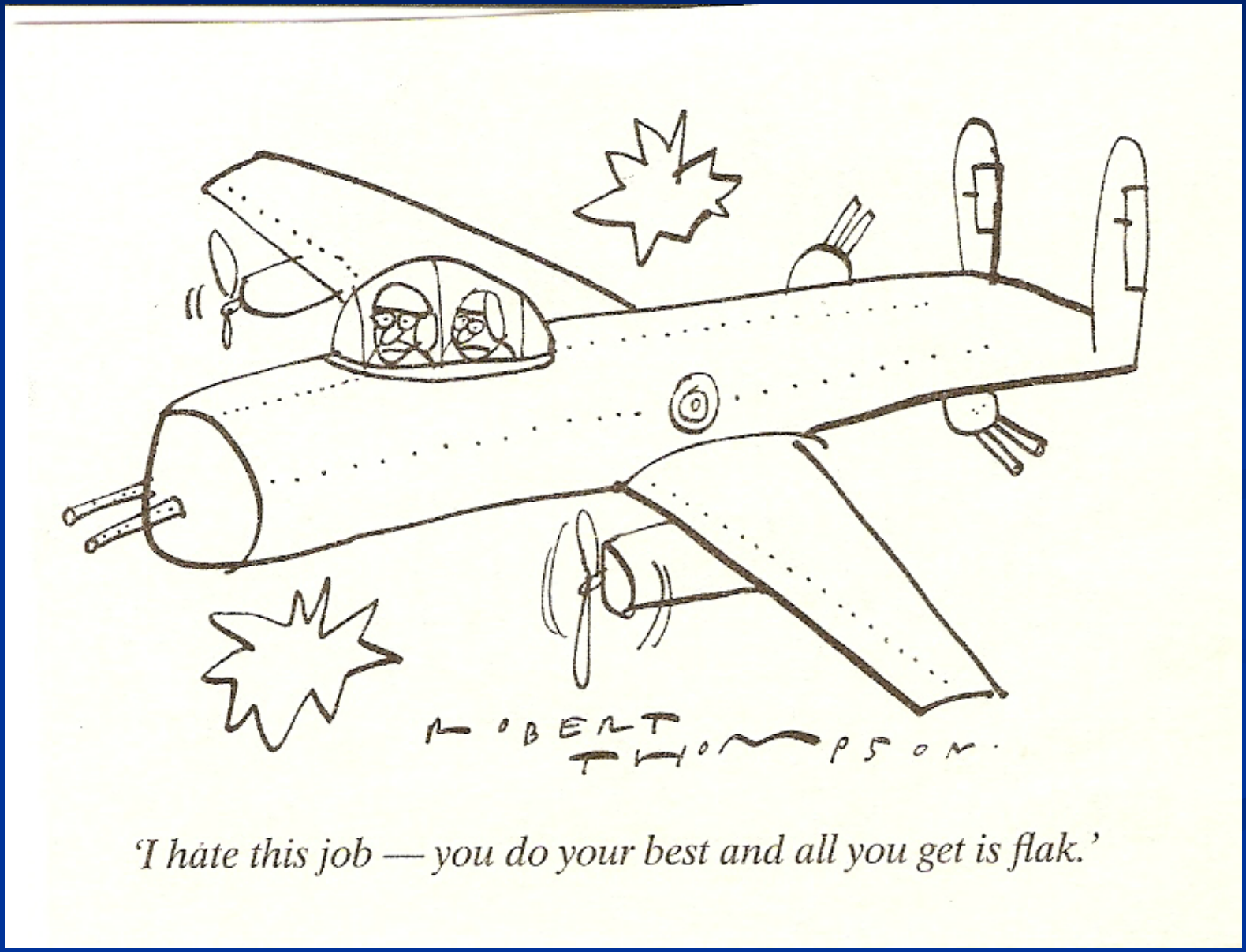
(PHE - Quality Surveillance Team - formerly Peer Review Programme)



South West

Wessex & London

What patients say to us



'I hate this job — you do your best and all you get is flak.'

Late referral and CUP not diagnosed

- ..my husband was suffering … back and forth to his GP on many occasions was fobbed off with him being a hypocondriact [sic] and referred to a counsellor. …. we were finally sent for an ultrasound and diagnosed with terminal abdominal cancer. … He then died 5 weeks later aged 52 of abdominal carcinoma, primary unknown.
- She has been misdiagnosed for 5 months now. …..Once Jake was born there was no improvement and she was admitted to hospital with what we were told was pneumonia.

Patient info and pathway guidance failures

- I have no idea what is going to happen to me and have not even been offered info on CUP (the nurse today hadn't even heard of it!!). I feel too scared to ask if this is killing me.
- This year has been the most horrendous & traumatic experience that I could only have dreamt about in my worst nightmares. We were given very little information on the condition & I feel very let down by both the oncologist and our local GP

Professionals not knowing, not understanding, not communicating

- My wife has CUP and the frustration of not knowing the cause has been the worst bit for us.
- It was the psychological trauma of professionals and services not knowing and not understanding her cancer that really took its toll on her.
- How will we know if the treatment has worked when we don't know where to look.
- I find it so hard to believe that no one could do anything to help and he was just left to pass away. His death certificate says : Carcinomatosis and Occult Primary. Would you say this is CUP? It is heartbreaking enough to loose my husband but not to know why is even more devastating….

Impact on family

- My sister is 42 and has just been diagnosed with CUP....My family are devastated and children frightened.
- I am caring for him, my partner who has Parkinsons disease and my mum who is showing early signs of Alzheimers Disease. I feel that I am sinking and need to be strong as I have my own son to care for and have to work full time

Patients on oncologists

- "You can choose to do nothing, or wait-and-see, but when something does go wrong it may be too late to react. However, you have to understand; as a physician, I have no option but to recommend that you take the standard chemotherapy…If you wish, I can do some research …. [surely, it can't be that I know more about some aspects of this disease and its treatment than the oncologist!]"

The oncologist was doing nothing more than reading the standard procedures from her computer - while we sat there. ..scary situation of sitting in front of an experienced consultant who says we don't know what to do next and she's done that two weeks running now. I feel as if I need somewhere else to turn.

[Oncology consultant on our forum] has now posted a helpful comment which has renewed my confidence in what's being planned for me and clarified what I need to ask in my next appointment. Just what I needed.

Filling the gap to help patients, carers & clinicians

- I really do appreciate your massive part in part in helping us to come to understand and not be afraid of questioning the illness and treatments.
- You and this site are really what I have used as a support measure, the best educational tools possible and this knowledge has helped me to adjust to a level of calm acceptance of CUP, more so than any other form of educational literature or professionals involved in my care
- Wow thank you for telling me about Dr Oien, what a fascinating talk. Please keep me updated about any further CUP seminars that are happening
- Thanks for your help , my family, son is also a doctor, have found it an invaluable resource from day one [UK GP]
- I've been practicing medicine since my early 20s and I had never heard of it [A US doctor on CUP].

III - Overcoming the problems – Moving towards a solution?

1500BC - Record of cauterisation to destroy tumours, *the fire drill*, in Egypt. Distinction made between benign and malignant disease

1700s - Cancer hospital established in France

1899 - Radiation first used for cancer treatment

1907 - William Halstead paper on 'non demonstrable cancer' published in *Annals of Surgery*

1926 - Nobel prize for discovering the cause of cancer (a worm!)

1940s - Chemo first used

1953 - Crick & Watson publish on DNA structure

1970s – CUP definition & autopsy data

1980s – CUP prognostic factors, Australian Guideline

2010s

- ESMO (2011) and NICE (2010) Guidelines

- 'CUP One' recruitment (2010 – 2014)

2004 - Osborne starts lobbying NICE

2008-2010 - GDG

2011-2012 - Peer Review Measures Group

2020

95% of 'CUP' patients in the UK treated with specific therapies based on a confident determination of tissue of origin .

Balance sheet - Positives

Management & Treatment Guidelines

England, Wales & N. Ireland
- NICE Guideline (2010)
- Peer Review Measures England (2012)

USA
- 2014. Cancer of Unknown Primary Site.
F Anthony Greco & John D Hainsworth in
Cancer: Principles & Practice of Oncology 10th ed.
- 2012. NCCN Guideline

Europe
- 2011 ESMO Guideline

Reduction in nihilism in the medical profession

Increased knowledge of CUP amongst oncologists

Local protocols on the treatment of CUP

Research CUP-One

Local research

MUO/ CUP patient under the care of a CUP team – CNSs highly valued

METASTATIC SITE

Liver (14)

cCUP 71% (10)

Small Bowel 7% (1)

Pancreas 21% (3)

Metastatic Site at final diagnosis.

From POOLE HOSPITAL Annual Report 2014

Bone (13)

cCUP 25% (3)

Lung 25% (3)

Pancreas 17% (2)

Renal 17% (2)

Ovarian 8% (1)

Prostate 8% (1)

Haem 8% (1)

Peritoneal (9)

cCUP 67% (6)

Lung 11% (1)

Ovarian 22% (2)

What do we need?

Patient with non specific cancer symptoms needs:

- Rapid referral by GP to MUO/CUP team
- Rapid identification – site specific MDT/ pCUP (Do not 'lose' the patient between MDTs!)

pCUP patient needs:

- Rapid, expert, assessment
- Rapid, expert-led, and *appropriate* investigation (CNS pathway guidance) with MDT review
- Concurrent holistic support

Palliative care early in the Pathway

Increased Measures compliance

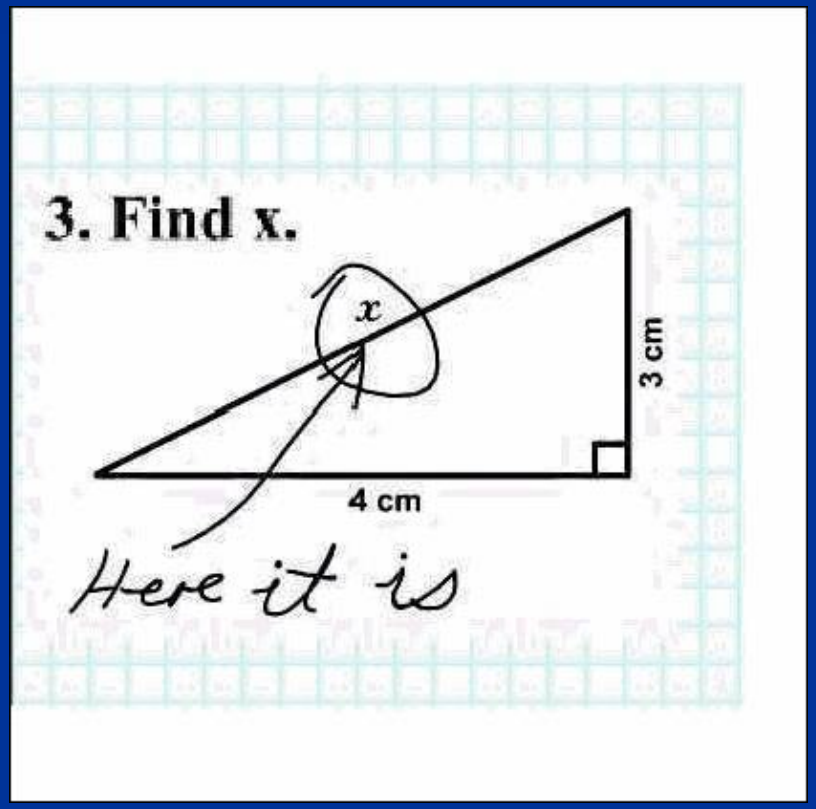
Research, & more research

Greater knowledge/ understanding amongst oncologists

Pathologists & oncologists & NHS to recognise the value of molecular profiling!

Bottom line in 2015: Management is improving but not outcomes

To improve outcomes and to end CUP we need clever scientists to…



…and then we need the knowledge applied

Hear from **leading CUP researchers** (US, Australia, Greece and the UK); and look at how **CUP MDTs** are really working, in

London

on

24 September