

John Symons

Director

CUP Foundation - Jo's friends

IMPROVING (?) PATIENT MANAGEMENT & OUTCOMES

30 people in the UK die *each day* from CUP. CUP is the **5th** highest cause of cancer death in the UK

CRUK 2012 data

57% of patients diagnosed with CUP in the UK (**9%** of all cancer cases) present as an emergency

50% of UK CUP patients are aged 50-80 (**45%** aged 80 and over). Ratio of 1 male to 1.2 females. **21%** from the most deprived socio-economic group

NCIN 2006-2010

Year	UK new cases	UK deaths
1996	15,838	15,024
1998	14,972	15,259
2000	14,013	14,559
2002	13,428	14,058
2004	12,640	13,288
2006	11,566	12,267
2008	10,752	11,228
2010	9,585	10,472
2012	9,620	10,625
ICD 10 C77-80		

10th highest number of new cancer cases in the UK are CUP

CRUK 2012 data

40% drop in UK *incidence* over last 16 years

30% drop in UK mortality over last 16 years

NCIN/CRUK data

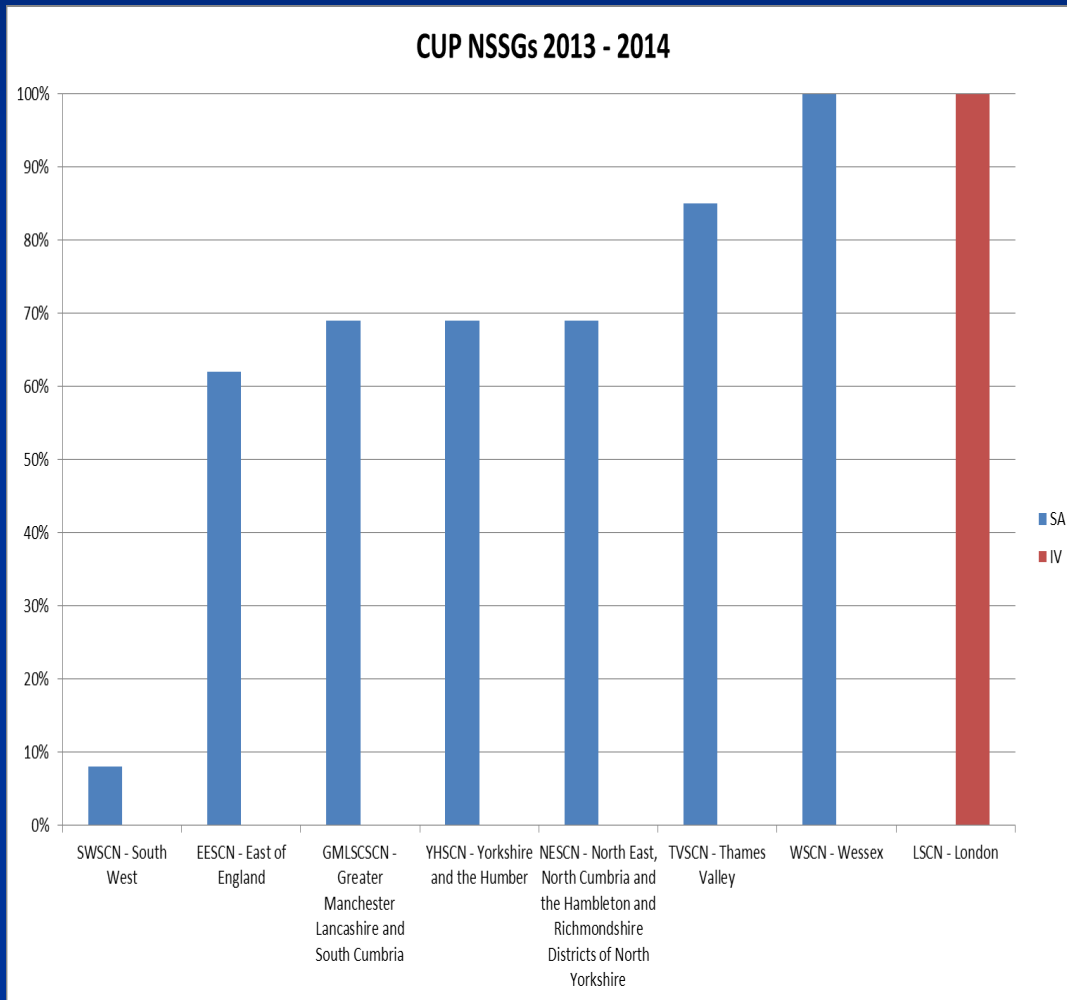
144 CUP teams peer reviewed in 2013/14

PHE - Quality Surveillance Team

CUP Foundation

Peer Review 2013/14 CUP Service – 144 teams

Network Compliance



South
West

Wessex &
London

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

A challenging diagnosis for oncologists



A 'double agony' for patients and families

Digest of CUP patient experience research including NCPES (2010, 2011-12 & 2013)

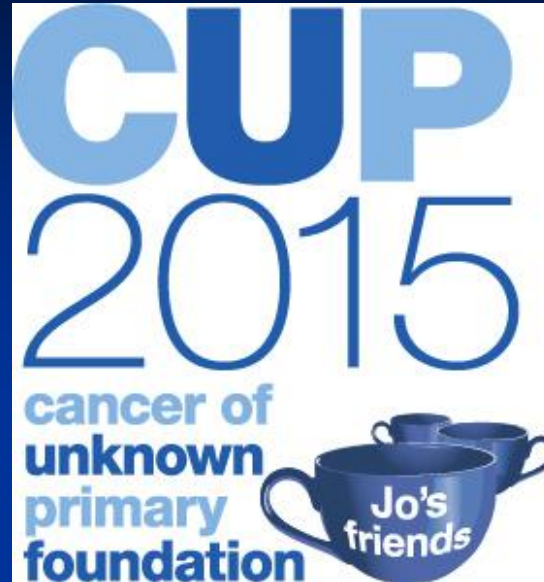
- Multiple investigations
- Uncertainty/ CUP not diagnosed
- Pathway guidance failures
'MDT tennis', Delays & Disruption
- Lack of communication & Poor patient information
- Poor accountability
- Poor understanding of CUP/
Poor explanation of causality
- Healthcare professionals not knowing, not communicating, not able to treat (issue of trust)
- Impact on family & friends
- Difficulty of explaining CUP to others
- CNSs highly valued

IMPROVING PATIENT *MANAGEMENT & OUTCOMES* - 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' 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 & associated autopsy data**
- 1980s**
 - Australian Guideline
 - Recognition of Prognostic factors & favourable clinicopathologic subsets
- 1990s Era of CUP empiric chemotherapy**
- 2005s Improved, evolving immunohistochemistry and use of molecular profiling**
- 2010s**
 - ESMO (2011) and NICE (2010) Guidelines
 - 'CUP One' recruitment in the UK (2010 – 2014)
 - Data accumulating to support accurate cancer type diagnosis, site specific therapy with potential of improved outcome for large number of CUP patients

2020

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



Dr. F. Anthony Greco

Co-Founder, Sarah Cannon Research Institute
&

Chairman CUP 2015

CUP History

- Recognized for decades; where is the primary tumor?
- Very few clinical investigators had any interest in the study and understanding of CUP.
- Essentially no new insights until late 1970's except autopsy studies revealed very small clinically undetectable primary sites in most patients (75%).
- Empiric chemotherapy
 - 1970's → Present

CUP History

- Recognition of treatable/favorable subsets of patients within the heterogeneous CUP group
 - Late 1970's □ Present
- Diagnosis of anatomical primary tumor site or tissue of origin NOT possible. Medical imaging and endoscopies find some small primaries (Not CUP).
 - Decades ago □ 2007

Improving Diagnosis and Patient Management

- Development and improving immunohistochemistry
 - 1970's → Present
- Development and improving gene expression profiling
 - 2007 → Present
- Diagnosis of the cancer type or tissue of origin now possible in the majority of patients
- Site-specific therapy based on diagnosis of the cancer type in CUP improves the outcome for many patients

Introductory Remarks

- CUP – Not one cancer, but one constant feature – anatomical primary site not detected.
- Autopsy Data – About 75% of CUP patients have very small primary tumor sites found and these are the source of metastasis

Primary Sites Determined at Autopsy in 884 Patients with Unknown Primary Cancer

Cancer Treatment Rev. 2009 May, 35 (3) 221-227

Autopsy-found primaries, 644 of 884 (73%)

Lung 27%

Pancreas 24%

Liver/Bile duct 8%

Kidney/Adrenal 8%

Bowel 7%

Genital System 7%

Stomach 6%

Bladder 0.5%

Breast 0.5%

Other 10%

Introductory Remarks

- Does the size of the known primary cancer site change the therapeutic plan?
- Lung – 1.1 cm spiculated lesion in right lung apex with large mediastinal mass, bone and adrenal metastasis
- Breast – 0.7 cm lesion found by breast MRI with metastasis to liver and bone

Introductory Remarks

- CUP – Most have clinically undetectable very small primary cancers but give rise to detectable metastasis
- Cancer type in CUP defined by immunohistochemistry and molecular assay of a metastatic site in about 95%+ of patients
- These diagnostic tests not universally applied to CUP-Why?
- The aim of “make the unknown, known” has been accomplished.