# CANCER OF UNKNOWN PRIMARY (CUP): A STUDY OF DATA INEQUALITY

**Jo's friends**

Cancer of
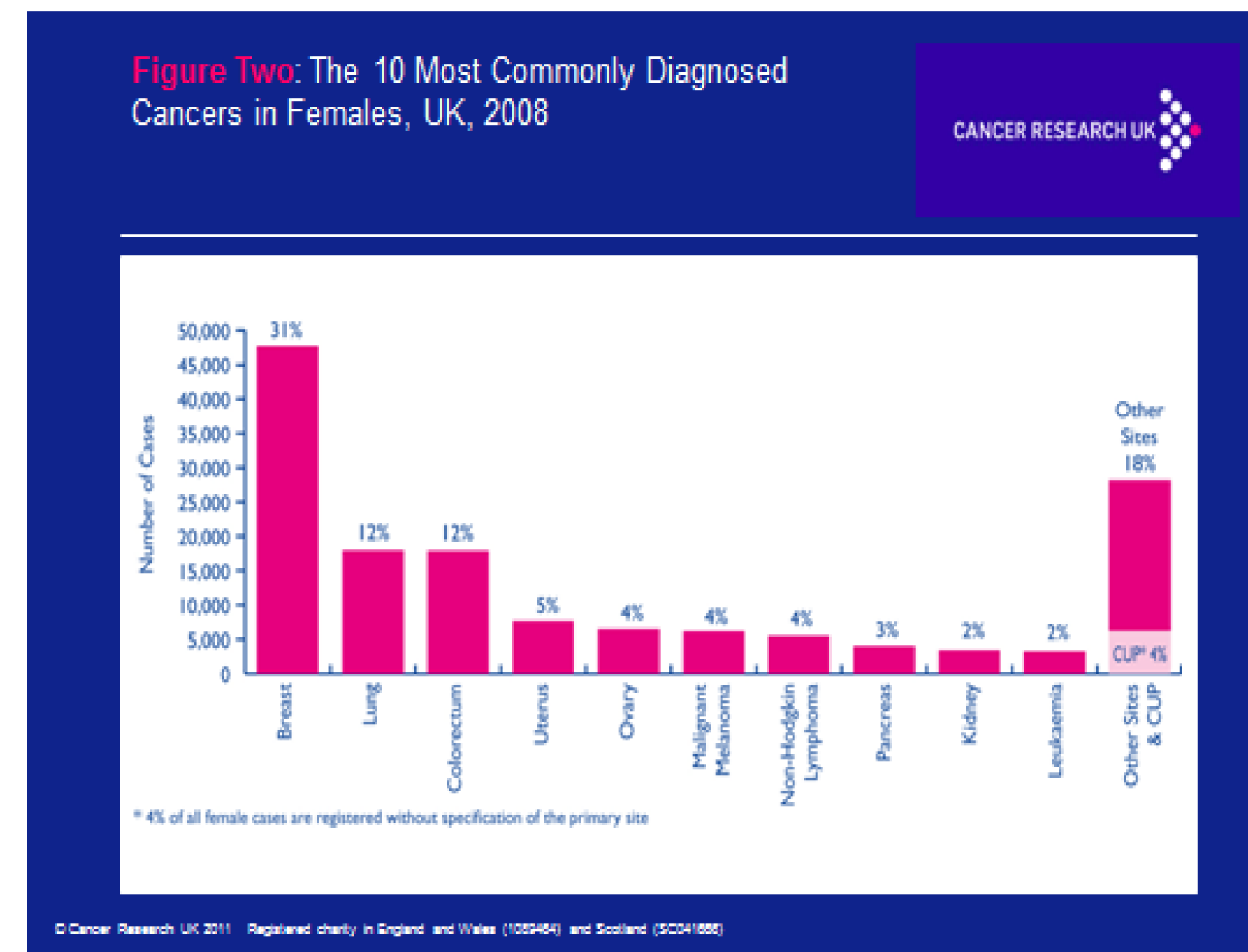Unknown Primary
(CUP) Foundation

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### INTRODUCTION – CUP NIHILISM

**CUP is not just a hidden cancer in the body but has been, for too long, a hidden cancer in the representation of the UK's cancer picture. Until April 2011 you would not have seen Cancer of Unknown Primary (CUP) included in the top 10 cancers in Cancer Research UK (CRUK) or National Cancer Intelligence Network (NCIN) presentations: yet CUP is within the top 10 for incidence and mortality. Without representation it is difficult to argue for funding and patient support on the basis of national statistics. For example, CRUK data for 2007, showing Research spend versus Mortality and Incidence by cancer site, omits CUP. Cancer Australia, by comparison, includes CUP in equivalent presentations (AIHW, 2008a).**

CUP patients and their relations do not believe they are being treated equally: they believe they are a neglected group where the lack of interest in their condition can often lead to sub-optimal treatment and care. It is difficult to dispute a causal link between data representation and data poverty or uncertainty, and limited research leading to poor patient outcomes.

**Aim**. The aim of this poster is to use published evidence to represent the CUP picture and explore the problems associated with classifying CUP and the historical failure to *liberate information,* without which it is impossible to *improve outcomes* for CUP patients.
**Methodology**. Meta-analysis of ONS, CRUK, NCIN incidence and mortality data compared with Cancer Australia, supplemented by recommendations made by the NICE CUP Guideline Group. This is augmented by empirical research findings on how CUP data is handled by Registries (*Binysh, Osborne & Symons, 2011).*

#### Table 1: CUP Incidence and Mortality. 2008

| (C77 - 80) | No. of cases | | | No. of deaths | | |
|---|---|---|---|---|---|---|
| | Male | Female | Persons | Male | Female | Persons |
| England | | | 9166 | | | |
| Wales | | | 546 | | | |
| Scotland | | | 934 | | | |
| N. Ireland | | | 305 | | | |
| CUP | 5028 | 5923 | 10,951 | 5248 | 6002 | 11,250 |
| (% of Total) | (3.2%) | (3.8%) | (3.54%) | | | (7.2%) |

Source: Extracted from Cancer Research UK.
info.cancerresearchuk.org/cancerstats. Apr 2011.

### EPIDEMIOLOGY

**The NICE *Guideline (NICE, 2010)* represented CUP as the 4th commonest cause of cancer mortality in England and Wales based on 2006 data. Following its publication, CRUK included CUP in their incidence data for 2007. For 2007 Cancer Research UK figures (using ICD-10 - C77-80 codes) showed CUP as the 6th most common cancer for women (4.4% of new cases) and the 8th most common for men (3.5% of new cases). (CRUK, 2011).**

At 4% of cancer diagnoses, CUP incidence is the same as, or more than, many known cancers such as Kidney, Stomach, Leukaemia, Pancreas, Ovary, and Malignant Melanoma.

Recent figures released by CRUK for 2008 – Table 1 above - *(CRUK, 2011)* show an improved picture but the reporting of the data is recognised as problematic and we would anticipate an increase in future years as the syndrome is captured more fully following the recommendations of the NICE Guidelines. The 2008 data show CUP in the 10 most commonly diagnosed cancers as "other sites & CUP" - CRUK Figure 2.

The Australian Institute of Health and Welfare is not shy in representing CUP. CUP incidence in 2005 stood at 3% for males and 3.5% for females (ranking 7th commonest for both sexes). Mortality at 8.8% made CUP the 3rd commonest cause of cancer death (sexes combined) in Australia. *(AIHW, 2008b).*

#### Table 2: Incidence by ICD 10 Code C77-C80. United Kingdom. 2008

| ICD Code: | Persons | Males | Females |
|---|---|---|---|
| **C77:** Secondary and unspecified malignant neoplasm of lymph nodes | 854 | 437 | 417 |
| **C78:** Secondary malignant neoplasm of respiratory and digestive organs | 3,388 | 1,463 | 1,925 |
| **C79:** Secondary malignant neoplasm of other sites | 2,189 | 1,066 | 1,123 |
| **C80:** Malignant neoplasm without specification of site | 4,321 | 1,949 | 2,372 |
| **Total (C77-80)** | 10,752 | 4,915 | 5,837 |

Source: National Cancer Intelligence Network (NCIN), UK Cancer
Information Service (UKCIS)

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**Figure Two**: The 10 Most Commonly Diagnosed Cancers in Females, UK, 2008

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* 4% of all female cases are registered without specification of the primary site

### WHAT CONSTITUTES CUP?

**CUP does not have a discrete classification within the International Classification of Disease (ICD) nomenclature. The WHO ICD codes, which capture registrations of CUP in the UK, are usually ICD-10 C77 to C80. See Table 2.**

However, there is no international agreement. The Australian CUP data are based on C26 (*Malignant neoplasm of other and ill-defined digestive organs),* C39 (*Malignant neoplasm of other and ill-defined sites in the respiratory system and intrathoracic organs),* C76, and C80. (WHO embrace C76-80 in a group defined as *Malignant neoplasms of ill-defined, secondary and unspecified sites. WHO, 2007).*

Research amongst UK Registries in 2011 indicates that there is a lack of clarity in defining CUP. *(Binysh, Osborne & Symons, 2011).* Responses indicate also that Hospital Episode Statistics (HES) data input from MDTs is inconsistent. This is likely to be caused by the lack of rules for recording CUP leading to variability between MDTs in terms of the precision of the diagnosis recorded. MDTs are likely to have different thresholds for attributing a probable site-specific diagnosis when further investigation is needed. Anecdotal evidence suggests also that CUP patients reviewed at MDTs are often classified as having a probable primary tumour which corresponds to the site-specialty of the MDT.

There is no universal agreement on recording CUP and this, in part, reflects the lack of a universally agreed definition of CUP and the nature of the WHO codes.

If we assume that existing data capture, to some extent, pCUP and cCUP – see NICE definitions - the addition of MUO, were it to be added to the overall CUP picture, is likely to increase incidence figures significantly.

#### Table 3: ICD-10 C77-80. UK. 1993-2008

| Year | Incidence | | Mortality | |
|---|---|---|---|---|
| | No. of new cases | Rate* per 100,000 | No. of deaths | Rate per 100,000* |
| **1993** | 14,693 | 19.6 | 14,420 | 19.3 |
| **1994** | 15,097 | 19.9 | 14,449 | 19.1 |
| **1995** | 15,118 | 19.7 | 14,654 | 19.0 |
| **1996** | 15,838 | 20.4 | 15,024 | 19.4 |
| **1997** | 15,777 | 20.1 | 14,949 | 19.1 |
| **1998** | 14,972 | 19.0 | 15,259 | 19.3 |
| **1999** | 14,373 | 18.1 | 14,666 | 18.4 |
| **2000** | 14,013 | 17.3 | 14,559 | 18 |
| **2001** | 13,824 | 16.8 | 14,252 | 17.1 |
| **2002** | 13,428 | 16.1 | 14,058 | 16.7 |
| **2003** | 12,875 | 15.3 | 13,625 | 16.0 |
| **2004** | 12,640 | 14.8 | 13,288 | 15.4 |
| **2005** | 12,011 | 13.9 | 12,801 | 14.5 |
| **2006** | 11,566 | 13.1 | 12,267 | 13.7 |
| **2007** | 11,120 | 12.4 | 11,970 | 13.0 |
| **2008** | 10,752 | 11.9 | 11,228 | 12.0 |

*Age-standardised to the European Population
Source: National Cancer Intelligence Network (NCIN), UK Cancer Information Service (UKCIS)

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### CONCLUSION

**Patients with CUP face the double agony of a cancer diagnosis and the recognition that it is a condition that is little understood. Initiatives, such as the evidence-based NICE Guideline of 2010, encourage CUP to be tackled consistently and for it to appear fully on the canvas of the national cancer picture.** The nihilistic approach to CUP where practiced by clinicians and statisticians - the hope that the "too difficult" problem will be solved by chance or disappear - is unethical, unscientific and an insult to patients. Uncertainty in medicine is often seen as failure; and a CUP diagnosis as a failure of diagnosis rather than a diagnosis in its own right. It is only by capturing the data and presenting CUP fully and fairly that action, in particular research, can be encouraged.

- **Even by existing measures, CUP falls firmly within the "top 10" of cancers for incidence and mortality.** CRUK recognises in the latest data presentation that the full burden of disease may not be captured *(CRUK, 2011).* Diagnoses may be included within other ICD codes. Qualification of the data may be necessary because of the unique features of the disease and its progression.

- **The incidence and mortality of CUP is falling** (Table 3) and there is an increase in one year survival (data not presented in this poster but UK 1 year relative survival for 2004-2008 stands at 16% , male and female). This has been achieved partly through improved diagnosis and improving treatment regimen.

- **The UK has lagged behind other countries**, **such as Australia, in representing the problem of CUP**. Historically, CUP may have been relegated because of the difficulties of achieving a simple definition or classification of a disease spectrum; but this argument is specious if it is accepted that CUP is captured by identified ICD codes.

- **There are new initiatives presently underway in the UK that should encourage greater recognition of CUP in national statistics**: the introduction of Peer Review Measures with regard to the CUP Guideline; the review of NICE's Referral Guidelines for suspected cancer; and the data emerging from Acute Oncology practice about CUP.

- **Echoing the recommendations of the NICE Guideline, data and coding definitions for MUO and CUP should be developed** and agreed nationally. A national audit should be established for MUO and CUP patients based on the agreed minimum data set. *(NICE, 2010).*

- **The introduction of the NICE CUP classification and the move to a single IT system** within registries present an opportunity to bring about greater consistency in the recording of CUP including MUO.

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