

cancer of  
unknown  
primary   
foundation

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***Annual Report  
and Accounts***  
*for the year ended  
31 December 2023*

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Registered Charity Number: 1119380  
[www.cupfoundjo.org](http://www.cupfoundjo.org)

The Fold, Lower End, Daglingworth, Cirencester GL7 7AH

## CANCER OF UNKNOWN PRIMARY (CUP) FOUNDATION – JO’S FRIENDS

ANNUAL REPORT FOR THE YEAR ENDED 31 DECEMBER 2023

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### INTRODUCTION

The Trustees are pleased to present their report, together with the financial accounts of the charity, for the year ending 31 December 2023. **This is the 16th and final report of Cancer of Unknown Primary (CUP) Foundation *Jo’s friends*** since it became a registered charity on 27 May 2007.

**We ceased to be an *active* charity with effect from 1 January 2024.**

As a private venture, without seeking funds from the public, we will continue to maintain our highly valued website, for the time being, as a source of information and support for patients, carers, researchers and clinicians.

CUP research is at a tipping point and the trustees have resolved to capitalise on the leading edge CUP research and treatment centred on the *Christie NHS Foundation Trust* in Manchester, transferring our funds to a ring-fenced CUP account with *The Christie Charity* and dissolving *CUP Foundation - Jo’s friends*.

Today, the CUP environment is markedly different to that of 2007. Patients have a managed pathway following the introduction of the NICE CUP Guideline in 2010. The Guideline has had the effect of making CUP a diagnosis in its own right, rather than a failure of diagnosis. This may seem a pedantic philosophical distinction but its tacit acceptance led to the formation of MUO/ CUP<sup>1</sup> teams and, for patients, expert led assessment and appropriate investigation. Importantly, there followed the recording of CUP as a distinct entity in national statistics.

Each NHS Trust<sup>2</sup> is mandated to have a multi-disciplinary clinical CUP Group (which may now be accessed via one of the new Rapid Diagnostic Centres or even, in some cases, by direct GP referral). Clinical expertise, coupled with scientific advances, particularly in imaging and genomics, is transforming the ability to place patients on a more treatable pathway. Awareness of the disease amongst the medical profession since 2007 has risen exponentially. Research, which has in recent decades led to changes in *treatment* has now reached a point where it is impacting *outcomes*. This is explored further on page 8 in the section ‘Making the unknown, known’.

In short, CUP management and treatment in the UK is being transformed through the growing interest of researchers and oncologists coupled with scientific advances. Almost gone, are the days of patients being bounced around different Multi Disciplinary Teams (MDTs) like a tennis ball with clinicians ‘chasing the primary’, looking for ideas, with treatment options limited to empiric or palliative chemotherapy.

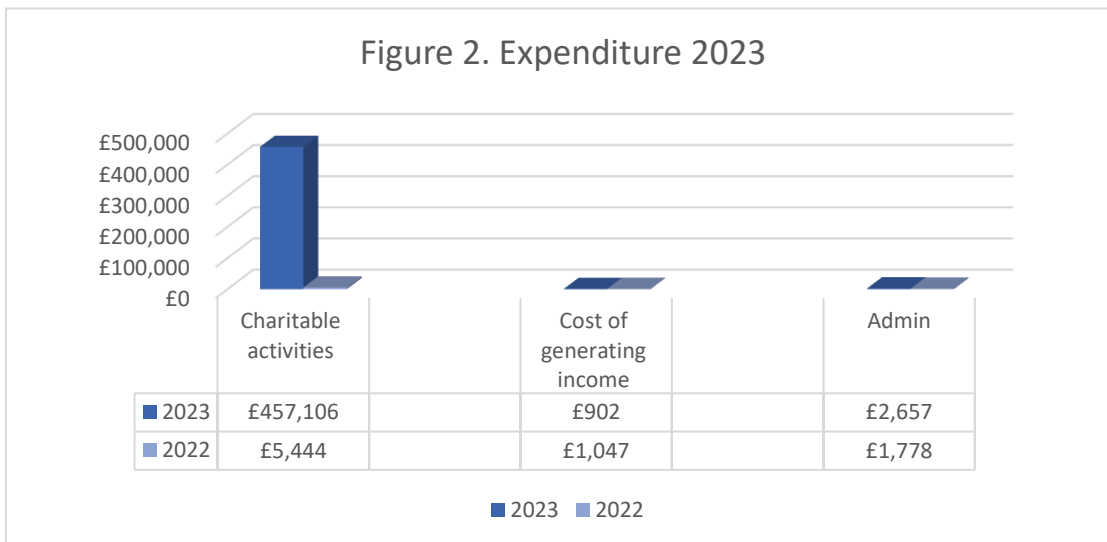
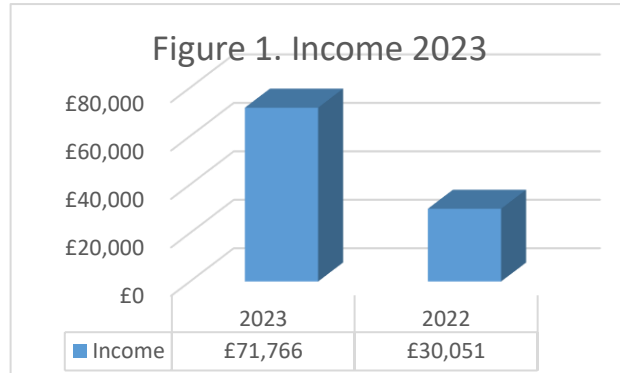
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<sup>1</sup> MUO is *metastatic malignant disease of unknown primary origin* - an initial diagnostic stage of limited clinical investigations. CUP is further divided into *provisional CUP* (pCUP) involving further and more complex investigations and *confirmed CUP* (cCUP) at a point when further investigations are inappropriate. If the patient is fit for treatment, the aim is to gain sufficient evidence as early as possible to place the patient on a treatable pathway with confidence.

<sup>2</sup> Scotland is not bound by the NICE CUP Guideline but has chosen to adopt it in practice.

## Financial summary

Income for this financial year is £71,766.21. In anticipation of dissolution, we extended the financial year from 1 October to 31 December. Thus, the income and expenditure shown in Figures 1 and 2 represent 12 months for 2022 and 15 months for 2023. In this financial year we have transferred £450,997.61 to the ring-fenced CUP account with the Christie Charitable Fund in preparation for dissolution and this is included within the graphic in Figure 2 as part of our charitable activities for the year. Also included in the figure is a direct research grant of £1,000 made to the Christie Hospital and £3,000 spent on conferences. **The accounts are shown on page 11.**



## Spending to achieve our charitable objectives 2007-2023

### We have spent approximately:

- **£700,000** to support CUP research
- **£90,000** on our international conferences and training events for CUP clinicians and researchers
- **£90,000** to provide information and support for patients and carers and to achieve our other charitable objects.

Funding to achieve our charitable objects has been made possible through generous donations, often from funeral memorials, and challenge events undertaken by those affected by CUP<sup>3</sup>.

We have maintained administrative spending throughout at around 7% of annual income. We have received no Government support.

<sup>3</sup> £307,260 of income (including Gift Aid) have been processed through *Just Giving*.

# ORGANISATIONAL STRUCTURE, GOVERNANCE AND MANAGEMENT

## Trustees<sup>4</sup>

**Barry Hamilton** B Soc Sc MBA.  
(*Chairman*)

**John Symons** MBE TD MA MSc MEd PhD.  
(*Director*)

**Rosemary Bates** BA (Hons), PG Dip OCGD.

**Kate Fulton** BSc (Hons).

**Philippa McEwan** BA (Hons).

## Advisory Board

### Medical

**Dr Natalie Cook** MBChB, MRCP, PhD is a Senior Clinical Lecturer in Experimental Cancer Medicine and Honorary Consultant in Medical Oncology at the University of Manchester and the Christie NHS Foundation Trust. She is the medical lead for the Experimental Cancer Medicine Team at the Christie with a research interest in liquid biomarkers in CUP; Chief Investigator for the CUP-COMP trial; and a Principal Investigator on CUPISCO.

**Dr F. Anthony Greco** MD is Director of the Sarah Cannon Cancer Center located in Nashville, USA. Dr Greco's principal professional interest has been clinical cancer research and he specialises in cancers of unknown primary origin, lung cancer and germ cell tumors. He has helped to define the complex group of patients with unknown primary cancer recognizing many subsets of patients requiring specific therapy. He has developed, or helped develop, new and improved therapies for patients with several types of neoplastic diseases, including CUP.

**Dr Sarah Ngan** BMedSci MBBS PhD MRCP is an oncologist specialising in caring for patients with upper gastro-intestinal cancers and CUP. She is presently the clinical lead for acute oncology and CUP at Guys and St Thomas's (GSTT) and the network CUP lead for the London Cancer Alliance. She chairs a specialist MDM at GSTT for patients with CUP which is video-linked to units across SE London and is passionate about improving the patient pathway for CUP patients.

**Professor Penelope Schofield** BSc (Hons) PhD MAPS is Professor of Health Psychology, Swinburne University of Technology. She is also Honorary Principal Research Fellow, Department of Cancer Experiences Research, Peter MacCallum Cancer Centre, Melbourne, Australia, where she is leading the 'SUPER' research on CUP.

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<sup>4</sup> The trustee board has remained unchanged since the charity's inception.

**Dr Harpreet S. Wasan** MD MBBS PhD FRCP is a Consultant and Reader in Medical Oncology at Imperial College London, and the Department of Cancer Medicine, Hammersmith Hospital. Dr Wasan leads the CUP-One trial and has recently instigated the CUPem trial.

#### Non-Medical

**Malcolm J. Glenn** – *Communications, Advertising and Marketing*

Malcolm Glenn has been an advertising creative director for more than 30 years, overseeing the development of creative products for clients. He is a lecturer and consultant business adviser for local colleges and the Young Enterprise charity.

**J. Roger Newnham** FCA. – *Finance and Accounting*

Roger Newnham is a recently retired Chartered Accountant with 40 years experience, including considerable involvement with charities as a part of his practice.

#### Emeritus Board Members

**Dr Maurice L. Slevin** MD FRCP. Founding Director of The London Oncology Clinic (now Leaders in Oncology Care); co-founder CancerBackup, (now merged with Macmillan Cancer Support).

**Dr Richard J. Osborne** MD FRCP FRACP. Lead Clinician for the development of the NICE Guideline for CUP.

Volunteers. We are most grateful for the support of those who volunteer their services for a particular project or, like **Malcolm Glenn**, our graphic designer, **Roger Newnham** with financial advice and **Jill Foulds**, our Conference and Administration Manager, help us throughout the year.

## **HISTORY**

Cancer of Unknown Primary (CUP) Foundation – *Jo's friends* is a Charitable Trust governed by its deed dated 27 April 2007. It was registered by the Charity Commission with number 1119380 on 24 May 2007. The charity was established in memory of Jo Symons who died with CUP in September 2006 a few days after her 46th birthday. To her family and friends, it seemed incomprehensible that, in the 21<sup>st</sup> century, it was not possible to make a diagnosis and that little was being done to promote awareness and research; or to offer information and support to CUP patients and carers. The charity became extant in 2007 after 'proof of concept' was established.

## **OBJECTIVES AND ACTIVITIES**

Our mission is to *Make the Unknown, Known* by:

- Providing information and support to CUP patients and those who care for them
- Raising awareness of CUP
- Promoting improved diagnosis and treatment
- Undertaking, encouraging or supporting CUP research to achieve the objectives above with the ultimate goal of seeing the end of CUP

## WHAT IS CANCER OF UNKNOWN PRIMARY (CUP)?

CUP is where a patient has been diagnosed as having cancer that has spread but the origin of the cancer cannot be determined in assessment before treatment; and it may remain hidden throughout the patient's life and at *post mortem*. Incidence is now some 2 - 3% of cancer diagnoses in the UK (the 15<sup>th</sup> commonest). It has been estimated by CRUK that 1 in 64 people will be diagnosed with CUP during their lifetime.

### Why is the cancer occult (hidden)? - Hypotheses:

- Metastasis (cancer spread) occurs very early when the primary is unusually small – too small to be identifiable - and the primary remains dormant
- The primary shrinks (regresses) or disappears. Cancer growth is diverted to the seeding cells with the primary starved of nutrients, or the primary may be pushed out of the body if, for example, it is hanging perilously to part of the digestive system after it has spread
- The primary is successfully attacked by the immune system as it tries to get a toehold but has already shed cells that migrate through the body to find 'sanctuary sites' (confusing or hiding from the immune system while thriving.)

CUP is a heterogeneous disease unified by a challenging diagnosis. The biology of the disease is not understood. Usually, the most important step in a cancer diagnosis is the biopsy because this allows a general cancer categorisation of carcinoma, sarcoma, lymphoma or melanoma. Most CUP definitions are of metastatic *carcinoma* of unknown primary where (unlike sarcoma, lymphoma and melanoma) further definitions are needed to achieve effective treatment.

- Clinical presentations are usually non-specific and may involve metastasis in more than one organ.
- Some further classifications are often possible from the biopsy sample which will help determine likely treatment. But in the case of CUP, because the cells have lost their unique features in the cancer spread, identifying the original cancer cells (the target of chemotherapy) is difficult.
- The biology of CUP is not understood, other than that the primary, which may originate in any epithelial cells in the body, spreads unpredictably when very small. The primary tumour may even disappear after it has spread. This makes it a challenging diagnosis for the oncologist as well as the patient.
- The key diagnostic aim is to gain sufficient evidence of the disease's genetic 'fingerprints' to be able to treat it as a site-specific cancer; or to identify and treat the primary's molecular profile or 'actionable mutations'.
- CUP patients who present as an emergency – the majority and considerably more than for any other cancer type - have the lowest survival of all the routes to diagnosis. The nature of CUP is that the symptoms are usually non-specific.
- Until the advent of the NICE Guideline in July 2010 there had been no NHS guidance for the treatment and management of CUP patients in England, Wales and N. Ireland (Scotland is not officially covered by the NICE Guideline). Informed by the Guideline and mandated by Peer Review (England only), patient management in England and Wales has improved markedly where there has been an introduction of clinical CUP teams managing and treating patients.

## CUP NUMBERS

*CUP incidence and mortality rates have decreased by about a third (35%) in the UK in the period 2007 [when the charity was formed] to 2017. CUP, along with stomach cancer, has shown the fastest decrease in incidence in both males and females of all cancer types over this period. (CRUK)*

As a cancer charity, we have always been focused on numbers related to CUP because, to quote management guru Peter Drucker ‘*If you can’t measure it, you can’t improve it.*’ In the early years of the charity we worked with CRUK and others such as the National Cancer Intelligence Network to report on CUP using ICD10 codes 77-80. There had been reluctance to include CUP data in national reporting as, being of unknown origins, it did not fit the reporting of site specific cancers.

CUP is the 15<sup>th</sup> most frequent cancer diagnosis and the 6<sup>th</sup> commonest cause of cancer death in the UK (measured by ICD-10 codes C77-80). Broken down by gender, it is the 4<sup>th</sup> commonest cause of death for females and 6<sup>th</sup> for males. However, in the period since the charity was formed in 2007 CUP incidence and mortality rates have decreased by about a third in the UK. CUP data, kindly provided by CRUK has undergone a change of format making yearly comparison more complicated.

**Table 1. UK CUP incidence and mortality (ICD-10 C77-80).**

Data from NCIN/ NCRAS & CRUK distilled from ONS

Year	Incidence (No. of new cases)	Mortality (No. of deaths)
2019	c. 8,100	c. 9,500
2018	8,589	9,775
2016	8,899	9,410
2014	8,930	10,142
2012	9,620	10,625
2010	9,585	10,472
2008	10,752	11,228
2006	11,566	12,267

### Patient information and support via the website

Using Google Analytics we monitor the hits on our website and other information such as the route to access, the country, the means of access such as laptop, mobile, tablet etc. Our website is designed to work well on different platforms and we have found that people increasingly use portable devices. 50% of access to our website is by tablet or mobile and the same has been roughly true for access to our eNews. Website hits are very imperfect measures of performance, and it is difficult to interpret variations, but they give some indication of our reach. The data show that every year we receive some 10-20,000 hits. No reliance should be put on the number of overall hits as it is likely that a considerable number are spurious. But there is no doubt that we have a worldwide reach and people from many different countries make direct contact with the charity. **For examples of patient and carer endorsements of our work see Appendix 1.**

**Table 2: Average UK CUP Incidence & Mortality (ICD-10 C77-80).** Data source: CRUK @ Feb 2024

<b>CUP incidence UK (average 2016-2018) – 8,589 persons</b>			
England	Scotland	Wales	N. Ireland
7063	788	541	197
<b>CUP mortality UK (average 2017-2019) – 9,495 persons</b>			
7877	801	589	228

## MAKING THE UNKNOWN, KNOWN

Looking back to the ‘proof of concept’ stage of establishing a new cancer charity in 2006/7, two comments stood out which have influenced our strategy and motivation. The first was: *is there really a need for yet another cancer charity?* And the second, from a very high profile oncologist: *You are wasting your time, it [a CUP charity] will never take off.*

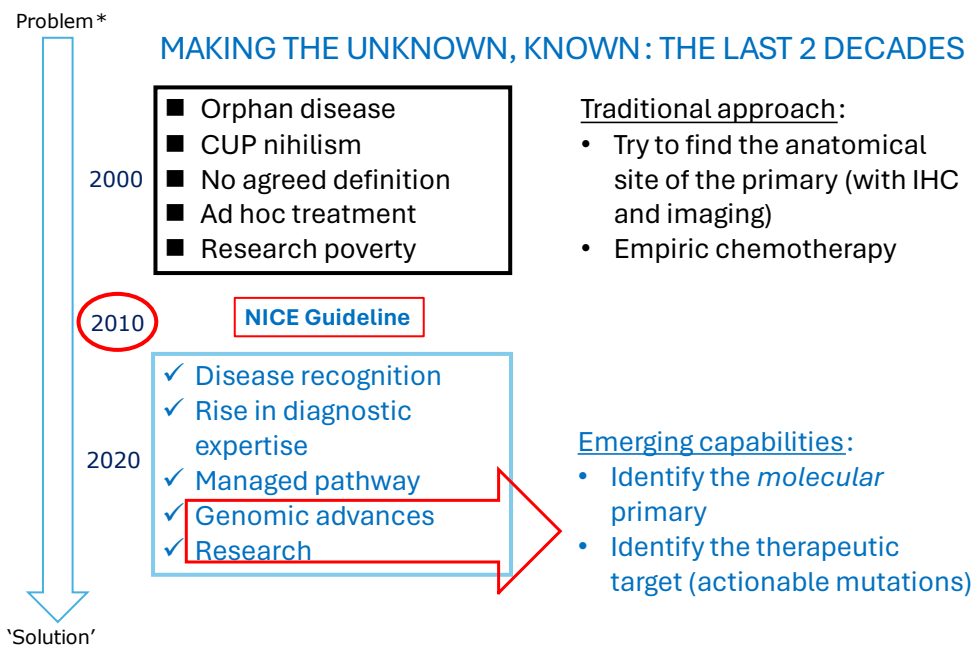
The founders were convinced of the need in the absence of any other charity with a focus on CUP in the UK, or worldwide. Patients and carers faced a nihilistic approach from much of the medical profession; and CUP research was almost non-existent outside the US. The intention was formed to put a time limit on the charity. The trustees ‘2020 vision’ was influenced by Dr Tony Greco, the world-leading authority on CUP in relation to anticipated scientific advances. The advances have taken place and as Greco wrote in 2017 (eMail Greco/Symons 10 Apr 2017) the primary site can usually now be determined:

### CUP biology remains unknown

CUP presentations with their bizarre pathological mutational features remain mysterious. But CUP oncologists, enabled by improved diagnostic techniques, and the growing weight of research evidence, are justifiably now able to put increasing numbers of patients on more treatable pathways.

‘With IHC [ immunohistochemistry] and molecular cancer classifier assays [determining the type of cancer] is now possible in about 95% of CUP patients. If they have a responsive cancer type then these specific treatments should be given and in essence the puzzle for that patient is solved.’

Figure 3: Making the Unknown, Known – the Last Two Decades (Slide: Symons)



For examples of our impact in achieving our charitable objects see Appendix 2



## **Making the unknown, known: reasons to be cheerful**

There have been many advances, particularly since 2017, in ‘making the unknown, known’ – many of which we have been involved with and supported – that have started to impact, or have the potential to impact, management and treatment of CUP patients in 2023. We would highlight:

**CUPISCO.** This international Phase II trial covered 33 countries with 10 UK centres and reported in October 2023. It has proven the value of genetic testing and its relevance in identifying appropriate chemotherapy and immunotherapy drugs. Sponsored and delivered by Roche, this is the largest CUP trial ever attempted and has demonstrated the value of including comprehensive genomic profiling early in the diagnostic work-up to inform treatment decisions. It is to be hoped that the evidence from this trial will encourage NICE to update the CUP Guideline (CG 104) which currently does not permit the use of gene expression based profiling in patients with provisional CUP other than for research (which is at odds with NHS England’s availability of Whole Genome Sequencing (WGS) for CUP patients through Genomic Laboratory Hubs).

**CUP-One.** This major study, to which we contributed funds and support 17 years ago, has suffered from issues with commercial partners and data analysis problems which have delayed the findings. It was the first significant major UK study to prospectively validate molecular profiling, in comparison with an immunohistochemistry (IHC) classifier. It sought also to establish the efficacy of the ECX chemo regimen (ECX stands for the drugs: Epirubicin, Cisplatin and Capecitabine) with and without Vandetanib (an inhibitor of different intracellular signaling pathways involved in tumour growth, progression, and angiogenesis). The study led by Dr Wasan reported in October 2023 that the molecular profile assay used was as effective as IHC and proved significantly better at differentiating Cholangiocarcinoma (now known to be 25-40% of CUPs).

**Circulating tumour cell research.** We have given financial support to oncologist Dr Alicia-Marie Conway at the Manchester Biomedical Research Centre for research focused on multi-modal blood-based circulating free DNA (cfDNA) profiling in patients with CUP. She has demonstrated the clinical feasibility of predicting tissue-of-origin and identifying targetable molecular alterations from a single blood draw in patients with CUP. This approach overcomes the challenge of the scarcity of tissue in patients with CUP and could potentially negate the need for repeat biopsies. Using liquid as well as tissue biopsies enable more treatment options for patients.


**Discriminating between presentations to improve treatment options.** MUO teams expertise, developed since the introduction of the NICE Guideline<sup>5</sup>, have diverted many patients from a CUP pathway or put them onto a site specific pathway. For example, of 1225 patients presenting at the Edinburgh Cancer Centre with radiological MUO (i.e. based on imaging alone) 897 (73%) were classified as provisional CUP after investigation and biopsy. Those 897 patients faced further investigations and specialist review. 97 (8%) were found not to have cancer, 443 (36%) had a primary cancer identified putting them onto a site specific pathway, and 301 (25%) were confirmed as CUP.

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<sup>5</sup> Scotland is not bound by the NICE CUP Guideline but clinicians have chosen to adopt it.

CUP researchers at the Christie Hospital in Manchester have made the interesting finding that a third of patients with liver-involved CUP (Intrahepatic cholangiocarcinoma) could have been reclassified as bile duct cancer patients thus putting them on a site specific pathway with increased treatment options.

**Prognostic biomarkers.** Research at the Edinburgh Cancer Centre has shown the value of prognostic biomarkers demonstrating that biomarkers of systemic inflammation reliably predict likely outcomes for CUP patients.



Prognostic biomarker scores

Glasgow Prognostic Score (GPS)			Scottish Inflammatory Prognostic Score (SIPS)		
mGPS	CRP	Albumin	SIPS	Neuts	Albumin
0	≤ 10	any	0	≤ 7.5	>35
1	> 10	≥35	1	> 7.5	≥35
2	> 10	<35	2	> 7.5	<35

Simple tools based on routine blood tests  
 Validated in >1000 MUO/CUP patients  
 Patients with GPS 2 or SIPS 2 do worse in all CUPs irrespective of type

Figure 4. Prognostic Biomarkers (slide: Dr Sally Clive)

**Comparison of different diagnostic approaches.** CUP- COMP has been a comparative study across tissue and liquid biomarkers for CUP examining genetic changes in CUP tumours alongside blood-based biomarkers, which can help reveal the origins of a person’s cancer and predict responses to existing or new treatments. The study is led by Dr Natalie Cook of our Advisory Board and has 7 UK centres.

**CUP Intratumoural Microbiome.** Work in progress. In 2021 we made a research grant to Imperial College, London to analyse the Intratumoural Microbiome in CUP and explore diagnostic and biomarker utility. The researchers are collaborating with the Weizmann Institute to characterise the tumour specific bacteria present in an expanded range of different cancer types. By correlating the microbiome signature with therapy outcomes, it is hoped to identify the effect that intratumoural bacteria may have on therapy efficacy as well as identifying whether CUP has a distinct intratumoural signature. (This work links to a project on the use of the intratumoural microbiome to predict response to immune checkpoint inhibitors.)

**CUPem.** This is a three year Phase II trial looking at the potential benefits of immunotherapy treatment at three London centres. The trial, led by Dr Wasan, investigates whether using the immunotherapy drug *Pembrolizumab* will help the immune system to detect and fight cancer cells and work better than chemotherapy.

**Genomic sequencing as standard of care in English hospitals.** NHS patients in England are starting to benefit from the scientific advances in genomic medicine and the introduction of genetic sequencing of patients and their tissue for certain conditions. We have promoted the use of genomic profiling for CUP patients to identify the cancer’s ‘fingerprints’, thereby improving diagnosis and tailored treatment options, since the charity’s inception. Starting from 31 October 2022 NHS Genomic Laboratory Hubs (GLHs) were commissioned and funded by NHS England to deliver Whole Genome Sequencing (WGS) for CUP patients. The value of this is not in WGS *per se*, which is of questionable appropriateness and cost effectiveness (in comparison with NGS) for CUP patients; but by its introduction it is allowing oncologists access to the *NHS National Genomic Medicine Service*. Many CUP oncology leads are starting to work with their local GLH to tailor a more appropriate targeted gene panel. It is hoped that NICE will shortly adjust their guidance to reflect practice.

**Patient experience research.** Of equal importance to clinical research is patient experience research. It may be less glamorous, but it is of significance in terms of patient management and the patient experience. Over the past decades we have worked with the University of Southampton and others', including Professor Penny Schofield in Australia, to represent accurately through research the CUP patient's experience. In summary CUP patients experience anxiety, uncertainty, and pathway management problems relating to co-ordination, communication, accountability and the timeliness of care. Whilst some of these characteristics would not be uncommon for any cancer group, research has shown that CUP patients in comparison with other patients with metastatic cancer suffer: higher depression and anxiety; worse physical, emotional, role and cognitive functioning due to the 'unknown' nature of their cancer.

## **FINANCIAL STATEMENTS AND PERFORMANCE**

### **Statement of Principles and Financial Management Policies Adopted**

It has been the policy of the charity to maintain effective financial management systems and programmes, to continually improve financial operations and systems and to identify more efficient methods of operations regarding accounting and financial reporting. In the reporting period there were no contracts from central or local government to deliver services, nor grants from central or local government. All funds in this financial year are unrestricted. The Charity is staffed by volunteers and no payments were made to staff or trustees other than the reimbursement of expenses.

Whilst *CUP Foundation - Jo's friends* is not unique in the small charity sector, it is unusual in that it is run without salaries, office expenses etc. The Trustees take the view that sound administration is a vital foundation of an effective organisation. Whilst administrative expenses have always been kept as low as possible, this has not been to the detriment of achieving the Charity's objectives. However, it should be noted that the overall administrative costs are artificially low as the charity is run from the volunteer Director's house and no charge is made for rent, heat, telephone, light, etc.

The Financial Statements comply with the requirements of the Statement of Recommended Practice, Accounting and reporting for charities issued by the Charities Commission and are prepared on a *receipts and payments* basis. The Trustees reviewed the Charity's financial controls in August 2023.

### **Independent Examiner**

Roger Newnham FCA kindly agreed to continue as the Independent Examiner and he was formally re-appointed at the August 2023 Trustees meeting.

Barry Hamilton  
Chairman

John Symons  
Director

**Cancer of Unknown Primary (CUP) Foundation - Jo's friends  
Receipts & Payments Account for the period ended 31 December 2023**

	<b>31 December 2023</b>	<b>1 October 2022</b>
	£	£
<b>INCOMING RESOURCES</b>		
Voluntary income	35,827.15	26,846.16
Activities for generating funds	8,213.76	2,055.15
Investment income and gain	27,725.30	1,149.34
	<u>71,766.21</u>	<u>30,050.65</u>
<b>RESOURCES EXPENDED</b>		
Costs of generating voluntary income	902.15	1,047.11
Charitable activities	6108.26	5,443.85
Transfer of funds to the Christie Charity	450,997.61	0
Governance costs	1260.79	904.64
Computer costs, printing and stationery	1395.82	873.3
	<u>460,664.63</u>	<u>8,268.90</u>
Net payments (2022 receipts)	(388,898.42)	21,781.75
Bank balances at 2 October 2022	388,898.42	367,116.67
Bank balances at 31 December 2023	<u>0.00</u>	<u>388,898.42</u>
 Statement of assets and liabilities at 31 December 2023		
<b>Monetary Assets</b>		
Bank balance	0.00	18,898.42
COIF Charities Deposit Fund	0.00	237,000.00
COIF Charities Global Equity Income Fund	0.00	133,000.00
Net assets	<u>0.00</u>	<u>388,898.42</u>

**INDEPENDENT EXAMINER'S REPORT TO THE TRUSTEES OF  
THE CANCER OF UNKNOWN PRIMARY (CUP) FOUNDATION – JO'S FRIENDS  
Charity number 1119380**

I report on the Receipts and Payments Account and the Statement of Assets and Liabilities of the Trust for the year ended 31 December 2023 shown on page 11.

**Respective responsibilities of the trustees and the examiner**

The charity's trustees are responsible for the preparation of the accounts.

The charity's trustees consider that an audit is not required for this year under section 144(2) of the Charities Act 2011 and that an independent examination is needed.

It is my responsibility to:

- examine the accounts under section 145 of the 2011 Act,
- to follow the procedures laid down in the general Directions given by the Charity Commission (under section 145(5)(b) of the 2011 Act, and
- to state whether particular matters have come to my attention.

**Basis of independent examiner's report**

My examination was carried out in accordance with General Directions given by the Charity Commission. An examination includes a review of the accounting records kept by the charity and a comparison of the accounts presented with those records. It also includes consideration of any unusual items or disclosures in the accounts and seeking explanations from the trustees concerning any such matters. The procedures undertaken do not provide all the evidence that would be required in an audit, and consequently no opinion is given as to whether the accounts present a "true and fair" view and the report is limited to those matters set out in the statement below.

**Independent examiner's statement**

In connection with my examination, no matter has come to my attention

1. which gives me reasonable cause to believe that in, any material respect, the requirements:
  - to keep proper accounting records in accordance with section 130 of the 2011 Act; and
  - to prepare accounts which accord with the accounting records and comply with the accounting requirements of the 2011 Act have not been met; or
2. to which, in my opinion, attention should be drawn in order to enable a proper understanding of the accounts to be reached.

J.R. Newnham F.C.A.  
Lawn Cottage, Portsmouth Road,  
Milford, Surrey.  
GU8 5HZ

## Appendix 1: Endorsements

### **Making a Difference: A Selection of Endorsements Received Since 2007**

*(patients and carers if not attributed)*

The landscape for CUP patients has changed beyond all recognition compared with 10 years ago....the CUP Foundation has been behind the vast majority of these steps. *Dr Richard Osborne, Lead Clinician for the NICE CUP Guideline at the time of our 10 year anniversary.*

I think there are probably hundreds, if not thousands of people out there for whom the CUP Foundation has absolutely made a difference to those affected by the disease and to those, like me, who supported them/ cared for them during their illness.

Soon after my diagnosis my daughter contacted you and you were kind and gave her hope.

Not only is the website an essential resource but the Foundation has been instrumental in bringing together experts from across the world and encouraging the development of research to improve the outcomes of patients with CUP. *Dr Andrew Fowell (Macmillan Consultant in Palliative Medicine)*

Thanks for your help. My family, son is also a doctor, have found it an invaluable resource from day one [of my husband's CUP diagnosis]. *(UK GP)*

What a brilliant site, it provides a light in the grey world of CUP.

...a good balance of accessible information, but not too much to overwhelm the patient/carer.... I'm very impressed and will continue to direct my patients, relatives and colleagues to it.

*Dr Simon Grumett, Consultant & Honorary Senior Lecturer in Medical Oncology*

We as a family needed you at the worst time in our lives and found the support for the short time we needed it so helpful.

This is the loneliest diagnosis one can receive. Thank God [for] this website.

At first I was tired of answering the questions about CUP to friends and some doctors but this website has helped me realize that the world needs to know about us.

Thank you from the bottom of my heart for your wonderful site.

The information here is the most comprehensive and timely data regarding CUP in the world. In my view this is an invaluable resource. *Dr Tony Greco, Sarah Cannon Cancer Center, USA*

I have only recently found your website which is very informative & only wish I had found it sooner.....This year has been the most horrendous & traumatic experience that I could only have dreamt about in my worst nightmares..... It is very much the "unspoken" cancer.

Thank God for this forum! I cried when I found it!

The immense relief that I have obtained so far from just reading everyone's stories on this site is incredible. Up to this point I have felt so very alone as no one could give me any advice, nothing to read, nothing to comfort me as I flounder.

When we received the diagnosis, the Foundation's resources were crucial in helping us build an informed understanding ..... I hope you know that your work is helping many.

Your slogan 'making the unknown known' could not be more true.

You have [opened] a "scientific door" to this neglected syndrome in terms of education, research and public awareness. I would like to reassure you that I will remain a supporter of your endeavour for ever.  
*Dr Nicolas Pavlidis. ESMO Guideline lead clinician.*

Am so glad to have found this site!!!! Since diagnosis I have felt like I'm on a raft in the middle of the ocean and no one knows I'm there or can rescue me.... I started to cry at the thought that I found people who have experienced the frustration of dealing with this illness and can understand my frustration.

Your site is so great. I have a hard road ahead but feel calmer now that I've started a targeted chemo treatment. I fully understand the importance of your website and help. It has really helped me to lose that sense of fear and dread, and I feel much more positive and in control.

Thank you for replying to me, because the diagnosis and passing was so quick it's hard for me to understand but thank you for explaining.

Thank you so much for your help....You really did something good for me today.

You've done a brilliant job at mobilising the front line community to improve care options for patients.  
*(Health Care Professional)*

Firstly, I must say what a fantastic website this is, a great balance of information and support. I am a cancer nurse who is interested in the complex care needs of patients with unknown primary....

I am a junior doctor who recently cared for and lost a patient with CUP who was a lovely woman. I was motivated to read about the diagnosis and management. I came across your website and found it very inspirational.

As an oncologist treating numerous patients with the diagnosis of CUP and as a lead clinician of CUP MDT and CUP network group, I greatly value the work of Jo's friends for this group of patients and your personal effort in setting up the CUP meetings. I am also very impressed by the Jo's friends website which is a very useful resource for patients, carers and health professionals.

...please continue to represent the patients and their families with so much passion.

Beyond your very thoughtful and kind advice, I want to extend my and my friends' gratitude for the work you do at the CUP Foundation and the excellent resources on your website. When we received the diagnosis, the Foundation's resources were crucial in helping us build an informed understanding of [the] condition and prognosis. .... I hope you know that your work is helping many.

I can't remember a conference that I learnt more from in a day and that was so enjoyable. *(Health Care Professional)*

Things certainly do seem to be advancing in the CUP world, and there's no doubt that you have played a major role in helping to achieve this. *(UK Oncologist)*

## Appendix 2 - Impact

### **Making a Difference since 2007**

*CUP Foundation – Jo’s friends was the first national, and probably international, CUP charity. We have achieved a worldwide reach and reputation and are the ‘Go to’ charity for clinicians, researchers and pharma as well as patients and carers.*

Summary examples of how we have achieved our objectives of **providing information and support for patients and carers, supporting research, raising awareness, and promoting change** are shown below:

- ❖ Website. Our website [www.cupfoundjo.org](http://www.cupfoundjo.org) has been at the heart of our public facing information, support and awareness. Accessed from countries around the world with a thousand or more hits each month, it is a source of information for clinicians and researchers as well as patients and carers. Oncologists advise patients to look at our website. We have run a closed Face Book page for interaction by patients and carers. (A more comprehensive interactive service on our website had to be closed following malicious ‘spam bots’ attacks and we also suffered a ‘denial of service’ attack.)
- ❖ International conferences Training and development. We have developed and run four international CUP conferences - the first held in the world - drawing together the world’s CUP experts, practicing clinicians and researchers. Conference papers have been published retrospectively e.g. in *Annals of Oncology*. We developed a Europe wide event in conjunction with the European Society for Medical Oncology (ESMO) for junior doctors involved in CUP. The Director speaks regularly at conferences and we have held a number of webinars mainly for UK clinicians. We have run face to face training for MUO/CUP team members in conjunction with conference organisers SBK in Manchester, Bristol, London, and Birmingham. A useful measure of peer recognition came in 2013 when the Director was invited to chair the plenary session of the National Cancer Intelligence Network conference in Brighton.
- ❖ Written materials and publications. We have developed Patient Decision Aids (PDAs) in conjunction with Sue Ryder and the *Gloucestershire Hospitals NHS Foundation Trust* to help patients decide treatment options for this complex condition. CUP Foundation leaflets for patients and carers have been distributed by hospitals to help patients and carers understand CUP. We initiated and helped write the ‘Understanding CUP’ booklet with *Cancer Backup* which was subsequently taken-up by *Macmillan Cancer Support* (reviewed every 3 years). The Director has written or co-authored some 20 articles (in popular and peer reviewed clinical journals), conference papers, and posters.
- ❖ What’s in a name? We fought successfully for the disease title in the UK to be *Cancer* (or more specifically *Carcinoma*) of *Unknown Primary*. Partly to align with our charity name, partly to get closer to the nomenclature in the USA where there was active research, and partly for national data presentation reasons. Before the NICE Guideline, patients were disoriented by an incomprehensible diagnosis that might be different in different hospitals e.g. ‘occult cancer’, ‘metastatic disease of unknown origin’ which emphasised the impression of a failure of diagnosis.



- ❖ Media. Where there have been opportunities, we have worked to explain CUP and raise awareness. There have been articles in Nationals e.g. the Observer, the Daily Mail, the New York Times and many local UK papers. Broadcast interviews have taken place with CNN, Radio 4 (Case Notes), BBC Radio Oxford and BBC Radio Berkshire. We have sent out our eNewsletter quarterly to subscribers.
- ❖ Research. We have been involved in most national, and some international, research trials testing diagnostic approaches and treatment e.g. CUP-One, CUPem, CUP-COMP, CUPISCO. CUPISCO is the largest international research trial ever undertaken on CUP and the Director was involved initially in the development of the trial protocol by Roche. We have made patients aware of current trials availability worldwide. We have made grants to researchers researching topics including: the benefits of immunotherapy; molecular profiling; the CUP microbiome; and diagnostic comparators working with hospitals and universities e.g. Manchester, Imperial and Southampton. Funds to support a PhD researcher on groundbreaking research into circulating tumour cells in CUP, obtained through liquid biopsies, has shown significant potential. Patient experience research is important and we have worked, mostly with Southampton University and the Peter MacCallum Cancer Centre in Australia, to use the outcomes to inform clinical practice.
- ❖ Working with others. The Director was a member of the NICE Guideline Development Group for 3 years which led to the 2010 Guideline: *Diagnosis and Management of the metastatic malignant disease of unknown primary origin* (leading the sub group on Molecular Profiling). He was later part of the expert group developing Peer Review Guidelines for the National Cancer Action Team (2012). This resulted in inspections of the 135 CUP hospital MDTs (there had been no CUP MDTs before 2010!). The Director was a founder member of the umbrella organisation for rare and less common cancers, *Cancer 52*, in 2008 and a Board member until 2020. We have worked with other charities such as *CRUK*, *Macmillan Cancer Support*, and *Cancer BackUp*. (Other charities have reproduced our ideas and content – usually without reference – and we take this as a compliment and a way of spreading our message!) The charity pushed successfully for inclusion of CUP in the ground-breaking 100,000 Genome Project. The Director served on three clinical studies groups of the National Cancer Research Institute from 2010 until it closed in 2023. We have given support and encouragement to embryo CUP charities in Australia, America, Ireland, and the Netherlands (of which only the Irish and Dutch are thriving presently.)
- ❖ CUP data/ codifying. The key to any discussion with government, health services and funders is to be able to present the epidemiology of CUP as it affects UK decision makers. We persuaded the National Cancer Intelligence Network and Cancer Research UK that national incidence and mortality for CUP as a discrete condition should be included in the UK reporting of cancer where the disease had previously been ignored. We initiated a comparative codifying project to identify gaps in knowledge and inconsistencies in reporting which involved Public Health England, CRUK, and colleagues in Australia and Ireland (2011).
- ❖ Policy, Advocacy and Awareness. The Director has presented to a teach-in at the Royal College of Physicians on CUP epidemiology and diagnosis and has made multiple presentations to clinical audiences e.g. Sheffield Hospital Trust as well as presenting to opinion formers e.g. the European

Parliamentary Cancer Select Committee in Brussels. National political influencing has been sought through meetings with MPs, Parliamentary Questions and joining with Westminster's 'Britain Against Cancer'. The Director has presented at pharma events e.g. Roche's global conference in Amsterdam in 2017. We have promoted the use of molecular profiling and with the 2022 introduction of Whole Genome Sequencing in England we have argued successfully for CUP to be included and offered early in the patient pathway. We have worked with organisations such as the Royal College of Pathologists on their first, and revised, CUP datasets (similar to a Guideline) and with NHS England in the development of the Long Term Strategy for cancer, promoting particularly Genomics and the new Rapid Diagnostic Centres.

### **Examples of feedback following the announcement that the charity is dissolving**

This progress on to the next stage seems to me to represent CUP's terrific achievements, and a positive consequence of doing what it set out to do- to make the unknown known. ....That's incredible from where it came from as a group of Jo's friends and something of which to be very proud....what a marvellous legacy...

*Deborah Wilson. (supporter)*

I think this is a very good ending for an important chapter in improving cancer care. We did a good job, catalysed by you, and the testimonials you have amassed confirm this. The further significant boost to CUP research that will arise from the financial support you are injecting will cement the foundations we laid.

*Dr Richard Osborne (NICE Guideline clinical lead)*

I just wanted to express my gratitude to you for all the work you have done for patients and families with cancer of unknown primary. Personally, my family and I are so grateful to you for all the information we received from Jo's friends when Sarah was diagnosed. You were the light at the end of our tunnel, and we'll be forever grateful to you for empowering us with so much knowledge. You were also the inspiration behind my setting up of the Sarah Jennifer Knott Foundation and thank you for all the advice. You were the first person I spoke to when I first considered it. I don't know if there words enough to describe the impact you have had not only in the UK but around the world as the first and for a long time the only charity advocating for the needs of patients with CUP.

*Tanya Knott (SJK Foundation- Ireland)*

I just wanted to write and thank you for all that you and your family have done for CUP over many, many years. It was an incredible help to Paul as he was navigating his illness and treatment plan and gave us, his family and friends something positive to focus on as we came to terms with our loss. ....

*Frances McIntyre (supporter)*

I just wanted to take this opportunity to thank you and your team for the amazing work you have done through the CUP foundation. The fact that you have reached a point where you are able to close as a charity and focus instead on being a hub for information speaks for itself as to how much the management of CUP has improved since the CUP Foundation was established. You have played an important part in making this happen.

*Helen Rickards (CUP CNS Sheffield Teaching Hospitals NHS Foundation Trust)*