Cancer Research UK response to AMS review: How does society use evidence to judge the risks and benefits of medicines?'

October 2015

Cancer Research UK believes that all cancer patients across the UK should have access to the best, evidence based interventions for their disease. The UK has a long tradition of excellence in developing medicines, along with the developing trial design to create better evidence; this has transformed outcomes for cancer patients.

As our understanding of medical science evolves and new types of medicines emerge, the medical research community needs to ensure that the evidence being produced and evaluated remain relevant and useful. We want to see the main users of evidence in society, whether in the healthcare service or the public, have a better understanding the types of evidence research produces. We also want to ensure how it relates to policy and regulatory decisions.

We believe the community should consider the following to support evidence based medicines:

- Commissioners, regulators and payers should be considering new forms of evidence such as stratified trials to inform decision making on interventions.
- Strict and transparent agreements should cover partnerships between industry and academia to ensure that evidence produced is accurate and trustworthy.
- Researchers and scientific funders should establish a clear set of guidelines for making information understandable and available to the public.

1. **The overarching aim of the workstream is to better understand how society uses evidence to judge the risks and benefits of medicinal products. In your view, what are the key factors underpinning this process that the Academy should consider?**

Cancer Research UK recently held a workshop looking at the barriers to innovation and the adoption of new treatments in the NHS. The workshop went back to first principles and was designed to consider the identification of thresholds and standards of evidence to support innovation in radiotherapy, surgery and service redesign, a previously unexplored or underexplored area.

Some of the recommendations looked specifically at evidence generation and the ways in which the healthcare system should consider using evidence to inform practice. The report made the following recommendations:

- **Commissioners and health technology appraisers should consider and evaluate new forms of evidence demonstrating that new technologies work for patients and are cost effective**

  New models of evidence collection for drug interventions are emerging as stratified medicines require smaller and more specialised trials which focus on select groups. This means that models need to change away from the large datasets produced by phase III trials and to consider how evidence produced.

- **Both commissioners and medical research funders should seek ways to evaluate and implement innovations using existing evidence and cost effective improvements**

  There is a need to better reflect the value of innovations that represent step changes over existing practice; however the system should not operate on the principle that 'new is necessarily better.'

- **Health Technology Assessments and commissioning decisions need to better reflect how innovations are used in the real world, looking at the combination of technologies and the benefits that are derived from this. There should be a move towards delivering real world data to inform decision making in this area.**

  A whole system approach needs to be taken to innovation, based on treatment and care pathways rather than technologies in isolation. More consideration needs to be given to the method for evaluating multiple innovations together (beyond pharmaceuticals) and their impact on the health service and its budgets as a whole. There is also a need to better understand the potential for disinvestment in treatments that may not be effective.

Cancer Drugs Fund

Using the example of the Cancer Drugs Fund we can see the disadvantages of the healthcare system not embracing evidence collection and the problems that this can cause in making informed decisions. The Cancer Drugs Fund was formed to allow patients access to treatments that otherwise were not funded through the NHS. When the fund was created no data collection mechanisms were put in place to evaluate how medicines provided by the fund had affected patients.

It has meant that following five years of the fund operating we currently only know the number of patients who have accessed treatments through the fund, as opposed to the benefits in terms of increased survival the fund has brought. This is a significant missed opportunity to gather real world evidence on the use of medicines that could have informed future decisions about how they are used on the NHS.

2. **When evaluating the risks and benefits of medicinal products, what are the *strengths* of evidence that originates from different sources?**
3. **When evaluating the risks and benefits of medicinal products, what are the *limitations* of evidence that originates from different sources?**

Different sources of evidence all contribute to informing our understanding of both the risks and benefits of medicinal products. A range of different sources need to be acknowledged as valid and appropriate depending on the type of research question is being asked.

A well established pathway for drug development has traditionally provided a stable model for developing an evidence base that supports getting new drugs to patients. However, it is clear that new models for gathering evidence need to emerge, as genetic testing and biomarkers make targeting populations much easier.

Lung matrix trial
The recent launch of the multi-arm Lung Matrix trial is an example of new trial design and mean to collect evidence. Each individual Lung Matrix trial arm will recruit small numbers of patients to try drugs based on their genetic profile which will produce much less data on effectiveness and value than traditional Phase III trials, but the size of the overall trial will produce data on which different treatments are effective. The trial is similar to other trials being run in the UK for prostate and breast cancer; it allows companies to trial new treatments on smaller treatment arms of the trial on a rolling basis. This both gives patients access to new innovative treatments while also making the NHS more ready for stratified medicine once the treatment has been approved.

This approach could address issues of providing sufficient statistical power to trials in small patient populations by designing statistical analysis setting out realistic and clear endpoints. Such an approach will target specific sub-populations of patients to maximise efficacy and reduce unnecessary side effects.

4. **Please provide details of any further examples or case studies that it would be useful for the project to consider.**

5. **Please highlight any broadly applicable principles that should govern the presentation, interpretation and weighting of evidence about medicinal products.**

6. **Concerns have been raised about how industry funding impacts on the validity, or the perception of validity, of evidence. For example, the ability of academic researchers funded by industry to remain impartial when evaluating evidence has come into question. How should conflicts of interest be addressed? How important is industry funding in generating and analysing evidence? Other than industry sponsorship, what are other potential sources of conflicts of interest?**

Cancer Research UK does not directly receive money from pharmaceutical companies to deliver clinical research. We do however partner on several programmes of work and pharmaceutical companies also make contributions to trials by, for example, offering free drugs.

Our technology transfer arm Cancer Research Technology licenses the intellectual property (IP) associated with our research to support the development of treatments. As part of the contractual process we ensure that all research that is funded will be published, we also ensure that quality of the publications through internal oversight throughout the process guaranteeing academic freedom for the investigators that we fund. Where possible in the IP arrangements we also look to ensure non-exclusivity arrangements with the datasets produced from these partnerships to ensure that evidence generated reaches as wide an audience as possible. It is also critical to our work and improving patient outcomes that evidence is reported in a timely way.

While industry studies are often most cited in terms of conflict of interest, similar issues can arise around academic researchers and their pressure to publish, and bias in the community towards

"positive" results and new findings. In order to ensure a robust evidence base we also support transparency across all forms of clinical research in order to improve the practice of evidence based medicine which ultimately benefits patients. Transparency for example publishing results via open access routes also ensures that public will have access to the research they have funded.

We welcome efforts to improve transparency in research, especially the publication of negative data from all sectors involved in clinical studies, this is currently being reviewed by the European Medicines Agency. When defining the rules for public disclosure of clinical trial information, it is important that the European Medicines Agency strikes the correct balance between promoting transparency and protecting commercially confidential information. This balance is crucial to support research in Europe and ensure that our patients can access innovative treatments through trials.

7. Please outline any past, current or planned initiatives to examine how patients, citizens and healthcare professionals (and those who seek to inform them) evaluate scientific evidence about medicinal products.

Cancer Research UK has policies in place to support transparency in research studies. We require that trials funded through our Clinical Trials Awards and Advisory Committee undertake clinical trial registration and we monitor when these trials publish their results. Cancer Research UK runs the CancerHelp UK clinical trials database which aims to list all cancer studies recruiting in the UK - not just those supported by Cancer Research UK.[1]

CancerHelp UK works with trial teams to produce summaries of studies to provide useful, easily understandable information for the public. This helps patients with cancer identify which studies they could potentially participate in as well as giving information on studies that have been completed, both the positive and negative findings. The database currently includes details of approximately 500 studies recruiting people in UK, and more than 400 summaries of study results. In 2012 we added 83 results summaries, including 25 from studies that had received funding from Cancer Research UK and 15 that were sponsored by pharmaceutical companies.

8. What are the most effective ways of communicating evidence to various stakeholders and engaging with them about such evidence?

Communicating evidence to the wider population

Cancer Research UK provides public information on all aspects of cancer including prevention, detection, treatment and clinical trials. Specialist teams use a range of peer reviewed evidence to create this content. Sources include major randomised controlled trials, systematic reviews, NICE guidance and Cochrane reviews – the full editorial policy is described on our website http://www.cancerresearchuk.org/about-cancer/utilities/cancers-in-generalhelp-uk/cancerhelp-uk-policies/editorial-policy/

We also check all our written copy and visuals with clinical experts to ensure accuracy and to gain a better understanding of the clinical context and patient experience. Our trials database is compiled

[1] http://www.cancerresearchuk.org/cancer-help/trials/

using trials protocols obtained from academic centres, funding bodies and pharmaceutical companies and has its own editorial policy. All content is checked by patient reviewers to ensure ease of understanding and we are accredited by the Information Standard reflecting the high standards we work to ensure both accuracy and comprehension.

Communicating scientific evidence with different audiences

Cancer Research UK's science blog receives about 200,000 unique visitors per month. The purpose of the blog is to provide a selection of the latest news and findings related to cancer in an interesting and understandable way. Presenting evidence in the blog faces its own challenges as it is written for a diverse audience ranging from patients to doctors to politicians. Therefore our team has devised a series of recommendations on how best to provide informative content to many audiences at once these including: keeping sentences short, removing jargon or using plain English descriptions first, and dealing with a single concept per paragraph.

These principles for good and clear writing support the communications of evidence with the public. Of our 200,000 monthly visitors roughly 10,700 headed for deeper evidence. We know that following initial access to information visitors, go on to:

- 3,500 of them visited a peer reviewed journal
- 6,000 of them visited another medical information site (CRUK/about cancer, NHS, Clinicaltrials.gov)
- a further 1,200 headed over to Wikipedia.

Scientific papers are become more freely available to the public due to the rise of open-access publishing and online journals. Journals and authors need to consider how articles are written so that the public can understand the concepts and conclusions in the paper. Recent studies have found that the use of jargon in scientific literature has made it impenetrable even to experts within the same field.[2] Better standards of writing will also support the spread and adoption of ideas throughout the scientific community.

About Cancer Research UK

Cancer Research UK is the world's largest independent cancer charity dedicated to saving lives through research. In 2014/15, Cancer Research UK spent £434 million on research in institutes, hospitals and universities across the UK.

We are a leading funder of clinical research in the UK, supporting around 250 clinical studies. This includes early diagnosis, prevention and epidemiological research, as well as clinical trials of investigational medicinal products. In 2013/14, over 27,000 cancer patients were enrolled onto Cancer Research UK supported trials.

[2] Experts' ideas get lost in a fog of impenetrable jargon, The Times, 5 September http://www.thetimes.co.uk/tto/science/article4548298.ece