Analysis of UK blood cancer research spend from 2002 - 2020

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NCRI Partners

NCRI is a UK-wide partnership between research funders working together to maximise the value and benefits of cancer research for the benefit of patients and the public. A key strength of the NCRI is our broad membership with representation across both charity and government funders as well as across all four nations in the United Kingdom.

Summary

Blood cancers are the 3rd highest cause of cancer related death in the UK and the most common type of childhood cancer. Blood cancer data sits on a historically generated backdrop of complexity, with our understanding of these cancers increasing dramatically in recent years. Yet most commonly they are simply reported by broad grouping of leukaemia, Hodgkin lymphoma, non-Hodgkin lymphoma and myeloma. Using the National Cancer Research Institute (NCRI) Cancer Research Database (CaRD), in partnership with Blood Cancer UK, the blood cancer funding landscape was assessed at a more granular level to assess the value of research spend and to avoid duplication of work. Improvements in national level data collection are required, along with a greater understanding of these cancers.

Introduction

Haematological malignancies, more commonly known as blood cancers, are the 5th most commonly occurring cancer group in the UK. In men they are the 4th most commonly occurring (after prostate, lung and bowel) and in women the 4th (after breast, lung and bowel).[1] They are the 3rd highest cause of cancer related death in the UK.[2]

There are over 100 different types of blood cancer and related conditions.[3] Most commonly they are grouped by the location they were first detected: in blood (leukaemias), lymph nodes (lymphomas) or bone (myelomas). But our understanding of haematological malignancies and precursor conditions has changed significantly in recent years, with updates made to how they are classified. Today we have a far better understanding of the interlinking nature of these conditions, better connected by factors such as the 'cell of origin' of the disease.[4] For example; chronic lymphocytic leukaemia (CLL) is more closely related to lymphoma than its other leukaemia counterparts, with both affecting B lymphocytes. This has created added complexity and inconsistencies, as most organisations have struggled to capture the new level of detail, and continue to group blood cancers under the broad grouping of leukaemia, Hodgkin lymphoma, non-Hodgkin lymphoma and myeloma.

Blood Cancer UK is a UK medical research charity, funding blood cancer research and supporting people affected by blood cancer. To drive progress in blood cancer research, Blood Cancer UK wanted to understand the blood cancer funding landscape, to identify gaps in funding and avoid duplication. To do this Blood Cancer UK worked with the National Cancer Research Institute (NCRI), a partnership of 21 of the largest funders of cancer research in the UK, including both charity and government research funding organisations. Each year, the NCRI collects research funding data from all of its funding partners and collates it into the NCRI Cancer Research Database (CaRD) to create a detailed repository of their research funding data. This data has been collected since NCRI's inception in 2001 and contains detailed records of over 20,000 individual cancer research projects funded in the UK.

At present, the NCRI CaRD codes blood cancer research funding into projects that focus on leukaemia, Hodgkin lymphoma, non-Hodgkin lymphoma and myeloma. Using this dataset, a more granular analysis of blood cancer research spend was carried out to better reflect the complexity of this group of diseases and provide insight into potential gaps in the current blood cancer research funding landscape in the UK.

Materials and Methods

NCRI Cancer Research Database (CaRD)

The NCRI CaRD is a comprehensive repository of over 20,000 research projects funded by NCRI partner members since 2001. Those partners are Biotechnology and Biological Sciences Research Council (BBSRC); Blood Cancer UK; Brain Tumour Research; Breast Cancer Now; Cancer Research UK; Cancer Research Wales; Children's Cancer and Leukaemia Group; Children with Cancer UK; Health and Care Research Wales (Welsh Government); Macmillan Cancer Support; Marie Curie; Medical Research Council (MRC); Myeloma UK; National Institute for Health Research (NIHR); Northern Ireland Health and Social Care Public Health Agency (Research & Development Department); Pancreatic Cancer Research Fund; Pancreatic Cancer UK; Prostate Cancer Research; Prostate Cancer UK; Scottish Government Health Directorates (Chief Scientist Office), and Yorkshire Cancer Research.

The NCRI CaRD records direct spend on cancer research, and resources and infrastructure that directly support or enable specific areas of cancer research. This excludes the purchase of land or buildings for the purposes of research, the building or refurbishment of laboratories, the costs of attending or holding scientific meetings, conferences or training courses, and projects focussed on policy or advocacy which do not have a research component.

Each project record includes name of the research funder, award value, start and end date, details of the principal investigator(s) and host institution(s), project title and abstract. Using this information each project undergoes coding into cancer type and research theme using the internationally recognised Common Scientific Outline (CSO) classification system developed by the International Cancer Research Partnership (ICRP).[5] Coding is carried out by an independent manual coder and an automated coding tool developed by UberResearch. Once coded by both, a second independent manual coder reviews and finalises the coding.

Re-coding by type of blood cancer

Data covering all live and completed projects was extracted from a relational database management system (RDBMS) called Microsoft SQL Server. To help filter results, a SQL script was developed to extract all projects associated with blood cancers.

Each project was re-coded based on the title and abstract of the award and re-categorised into 16 specific types of leukaemia as well as other blood cancers such as MPN and MDS, which are not usually represented. The categories were; Rare blood cancers, Bone Marrow Transplantation, Multiple leukaemia's, Multiple blood cancers, Other cancers (inc. blood cancer), Cancer and other diseases, Myeloma, Hodgkin Disease, Non-Hodgkin Lymphoma, Primary CNS Lymphoma, MPN (Myeloproliferative neoplasms) and MDS (Myelodysplastic syndromes). Furthermore, projects where leukaemia was originally assigned were re-coded by the main subtypes; ALL (Acute lymphoblastic leukaemia), AML (Acute myeloid leukaemia), CLL (Chronic lymphocytic leukaemia) and CML (Chronic myeloid leukaemia) and allocated here or to other relevant groups. Each project was given a maximum of two disease site codes and totalled to 100%, with the most relevant codes selected.

'Other Cancers (inc. blood cancers)' was assigned to projects which focus on common cancer mechanisms. 'Cancer and other diseases' included grants where the projects focus on research looking beyond just cancer (for example autoimmune diseases).

Further categorisation took place to help compare research spend between adults vs. childhood, young adult and adolescent (CYA) blood cancers. Each grant was categorised into 3 main groups: Adult, Partially and Wholly. Grants focused only on adults were assigned as 'Adult', grants focused on both adults and CYA where classed as 'Partially' and those involving only CYA was assigned as 'Wholly'.

Research spend was calculated based on fiscal year (i.e. 1st April to 31st March) for consistency and comparison. Adjustments for inflation were not applied, funding analysis is based on the actual cash value in pounds sterling (£) at time of the funding award.

Results

Funding landscape before re-coding (original CaRD data)

Before the data was re-coded into more specific types of blood cancer, the CaRD data was analysed based on the current blood cancer groupings used by the NCRI. This showed that the majority of funding in blood cancer research has been in leukaemia, compared to myeloma, Hodgkin disease and non-Hodgkin lymphoma. Due to the significant amount of funding received, it was decided that leukaemia would be broken down further into its most common sub-types, to understand more of the granularity sitting within this group.

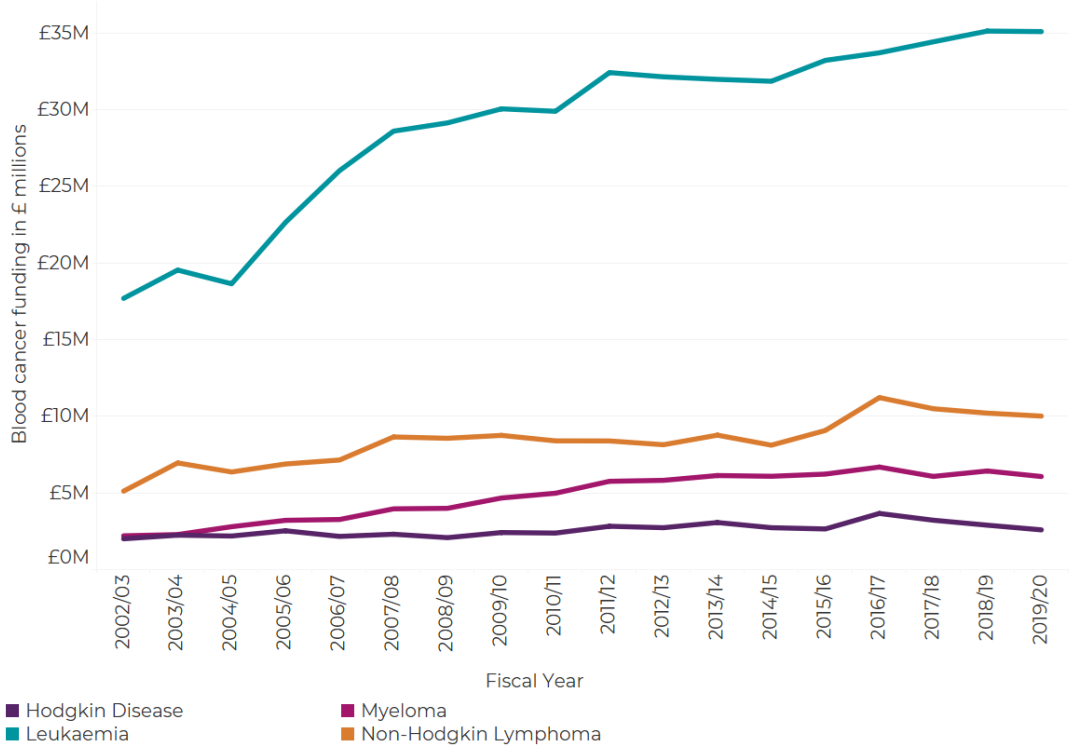

Figure 1: Blood cancer research funding over time, by the four classical blood cancer groupings. Using the original CaRD database, all research spend in blood cancer across all NCRI partners was plotted over time, from FY 2002/3 to 2019/20, and split according to the four main blood cancer groupings (leukaemia, Hodgkin lymphoma, non-Hodgkin lymphoma and myeloma).

There has been a significant increase in funding for leukaemia over the 18 years of data collection, in particular between FY 2004/05 and 2007/8. There is also a small increase in funding for myeloma and non-Hodgkin lymphoma grants, but funding for Hodgkin lymphoma indicates very little growth over the period shown.

Funding landscape post re-coding

Following the initial analysis (Figure 1), the re-coded data was used for the remainder of the analysis (Figure 2, 3 & 4). In Figure 2, the original data was re-coded (see Materials and Methods) and plotted according to ICRP CSO codes: 1) Biology, 2) Aetiology, 3) Prevention, 4) Early Detection, Diagnosis and Prognosis, 5) Treatment and 6) Cancer Control, Survivorship and Outcomes Research.

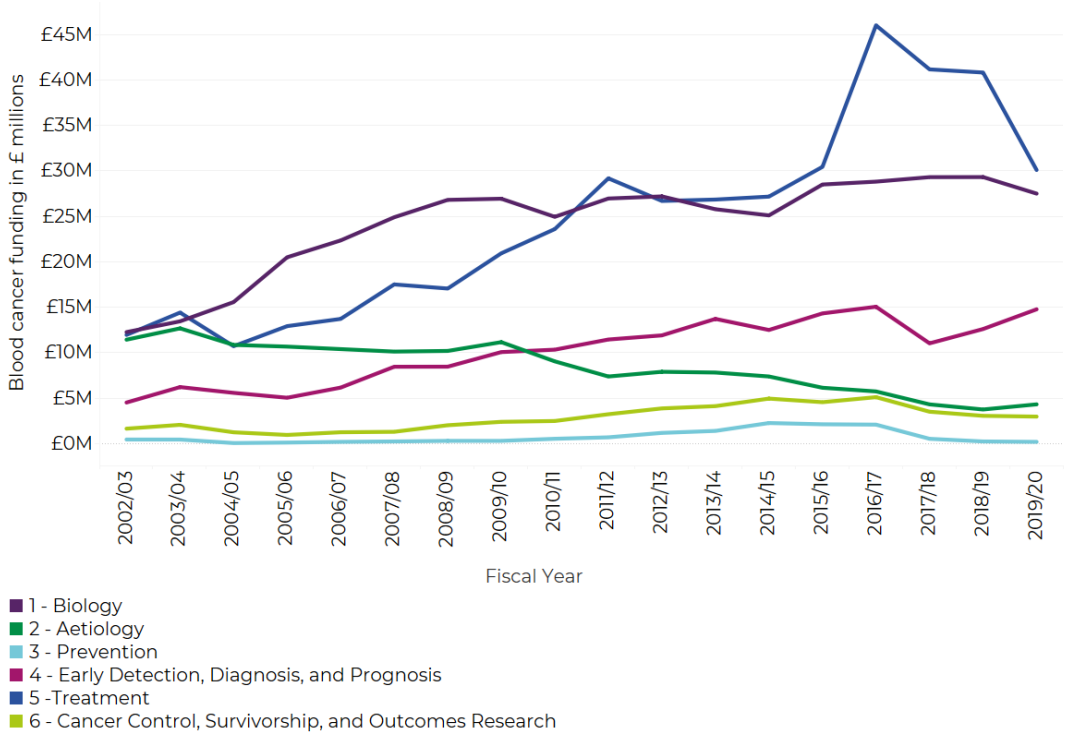

Figure 2: Blood cancer re-coded research funding over time, split by CSO code. Using the re-coded dataset all research spend in blood cancer across all NCRI Partners was plotted over time, from FY 2002/03 to 2019/20 and split according to CSO code.

Most spend in blood cancer research has been focused in 'Biology' and 'Treatment', with the smallest amount of funding going into 'Prevention'. 'Cancer control, survivorship and outcome research' also has had comparatively less funding, compared with the other CSO groups. There has been an overall increase in spend in the most funded areas 'Early detection, diagnosis and prognosis', 'Biology' and 'Treatment'. However, spend in 'Prevention' and 'Cancer control, survivorship and outcome research' has remained relatively stagnant over the last 18 years, with a decline in 'Aetiology'. There was a spike in 'Treatment' related grant spend from 2015/16 to 2016/17, with spend in this area declining in 2019/20 to similar levels as before the sharp increase.

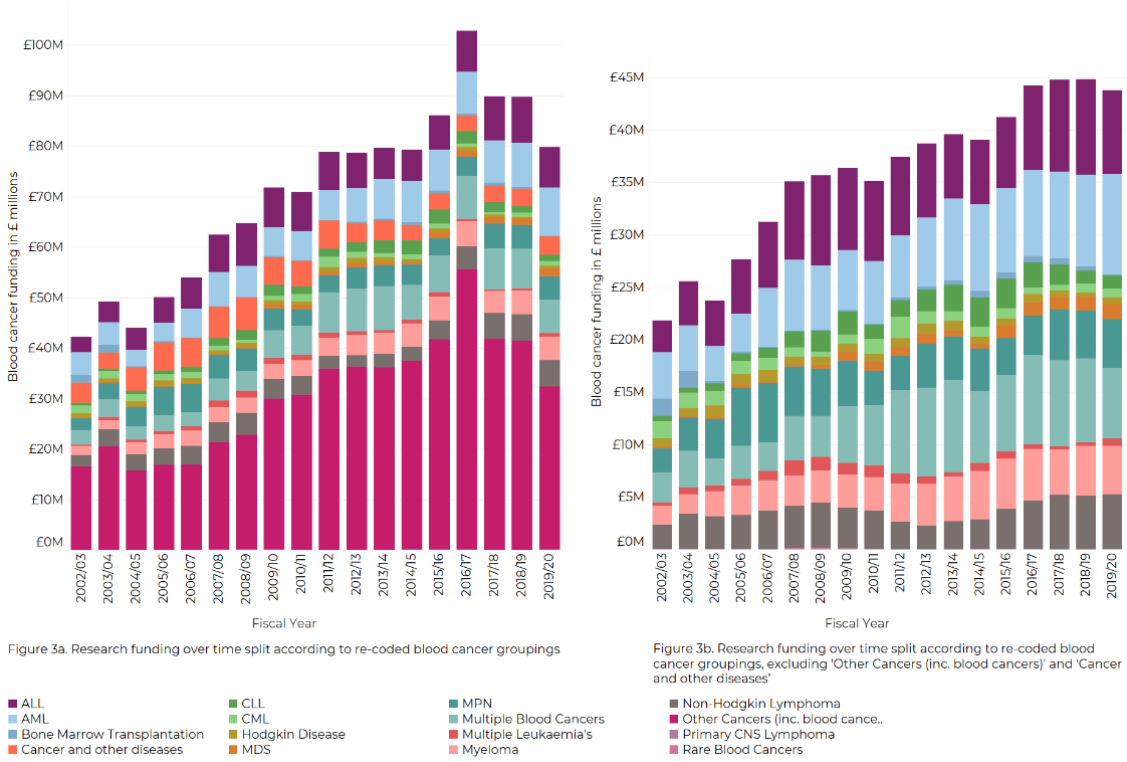

Figure 3a. Research funding over time split according to re-coded blood cancer groupings

Figure 3b. Research funding over time split according to re-coded blood cancer groupings, excluding 'Other Cancers (inc. blood cancers)' and 'Cancer and other diseases'

Figure 3: NCRI partners blood cancer research funding over time split according to re-coded blood cancer groupings, including (left, 3a) and excluding (right. 3b) 'Other Cancers (inc. blood cancers)' and 'Cancer and other diseases'. Using the re-coded data set all research spend in blood cancer across all NCRI partners was plotted over time, from FY 2002/03 to 2019/20 and split according to blood cancer groups defined within the project.

The re-coded data highlighted that a large proportion of the data was grouped under 'Other Cancers (inc. blood cancers)', where grants were for research in areas with the potential to have an impact on a number of different types of cancer (e.g. lung, bowl, breast ...etc) including blood cancer, as one of these cancers. This group was excluded from Figure 3b and Figure 4 because it skewed the data and made comparison challenging for the other groups. 'Cancer and other diseases' was also excluded from Figure 3b and Figure 4 because this group was not 'blood cancer' specific. In Figure 3, you can comparatively see the data where these two categories are included (left, 3a) and excluded (right, 3b).

Overall blood cancer research spend has increased over the 18 years of data collection. Most research funding is allocated to 'Other Cancers (inc. blood cancers)', where projects focus on work that has the potential to impact several different cancers. When this category is excluded, a clearer picture is provided for the other groups.

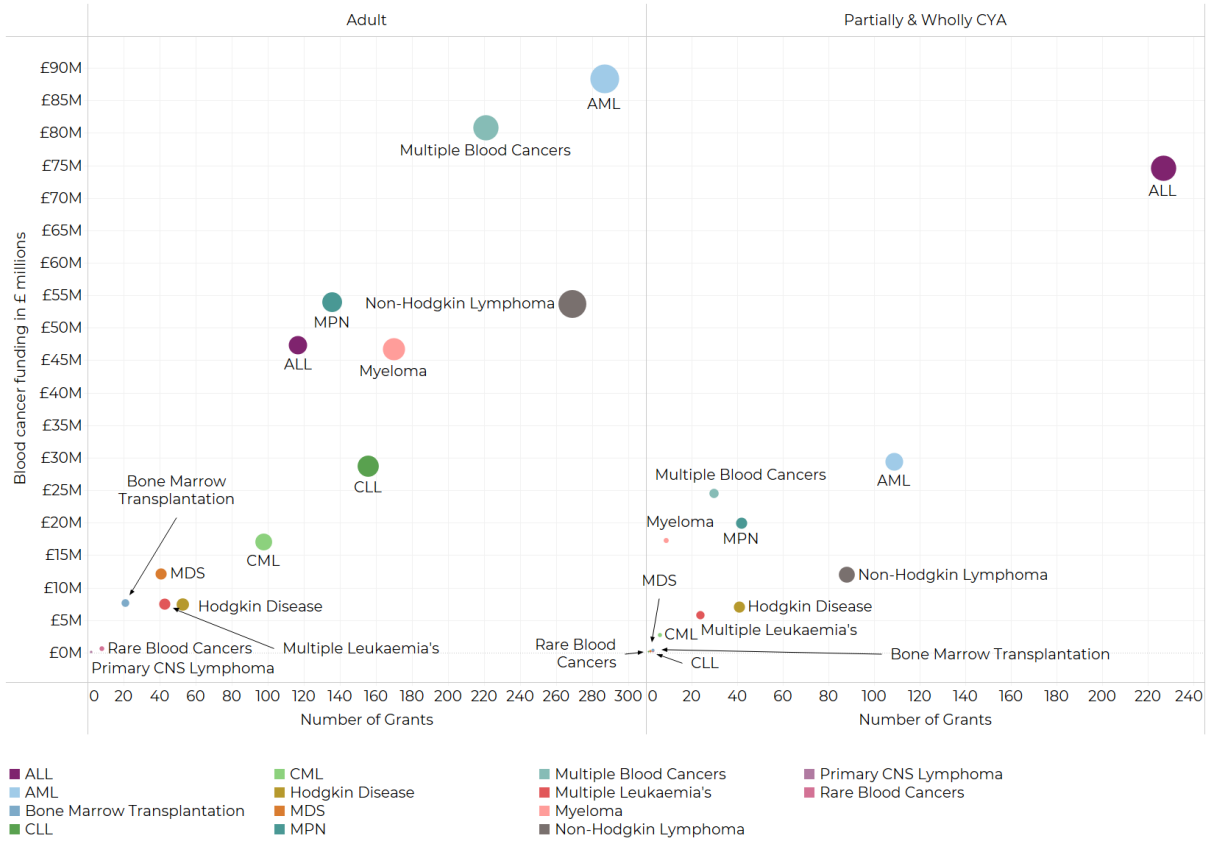

Figure 4: Blood cancer research spend by adult vs. childhood, young adult and adolescent (CYA) grants. Grants assigned as 'partially' CYA were grouped with grants assigned as 'wholly' CYA cancer projects. The size of the dot is based on the total number of grants per blood cancer group. The data excludes 'Cancer and other diseases' and 'Other cancers (inc. blood cancer)'.

Grants were further assessed and grouped as being either 'adult' or 'childhood, young adult and adolescent (CYA)'. Those grants that were 'partially' CYA were grouped with those that were 'wholly' CYA due the similarities in the funding pattern of these categories. Some cancers are not found (or are incredibly rare) in the CYA group, so there is less of a spread across the subtypes for partially and wholly CYA grants.

Of the total spend, leukaemia has historically received the most funding compared with myeloma and lymphoma (Figure 1). Specifically, acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL) have received the most funding overall, with ALL receiving the most funding in CYA projects and AML receiving the most in adult projects (Figure 4). Across both age groups there has also been significant investment in grants which target 'multiple blood cancers', and 'non-Hodgkin lymphoma' have received comparatively high funding. Less funding has been invested in Hodgkin lymphoma, MPN, MDS and rare blood cancers.

Discussion

Through trying to understand the funding landscape of blood cancer research across the UK, using the NCRI CaRD database as a proxy for this, several complications of blood cancer data and the coding of blood cancer research grants were highlighted. Blood cancer data sits against a historical backdrop of complexity, but there is also lots of research that has the potential to impact a large number of cancers and other disease (including for example autoimmune diseases) which adds additional questions about how they are grouped and classified.

The data only serves as a proxy for the UK blood cancer research landscape because it excludes some smaller blood cancer research funders (who are not NCRI partners) and does not include larger infrastructure grants, given to or generated by institutions to support research in many areas, of which cancer may only be one research topic.

Complexity in project classification

Following the re-coding of the leukaemia grant data, where the originally coded leukaemia portfolio was split into leukaemia subtypes, some additional complexity was highlighted. In the original database, one project may be subdivided and the funds allocated to various cancers, including blood cancers such as leukaemia. While these projects may potentially impact blood cancer, often the focus of the project was far broader than any one specific cancer. In this case, the whole grant was allocated to 'Other Cancers (inc. blood cancer)'. We found that the grants coded as 'Other Cancers (inc. blood cancer)' made up a significant proportion of grants associated with blood cancers and as a result this group was excluded in much of the analysis (except Figure 2 and 3a) because it overshadowed the other nuances in the data, which were then hard to separate. The group 'Cancer and other diseases' was also excluded because of the broad remit of the research of these grants and a feeling that while the research might potentially impact blood cancer at arm's length, the original intent of the work was not to make improvements specifically for blood cancer patients.

In terms of groups, some additional categories were needed to indicate where projects covered 'Multiple Leukaemia's', 'Multiple Blood Cancers' and were broader than cancer ('Cancer and other diseases'). In all other cases grant funding was either allocated 50:50 between two blood cancer types or 100% to a cancer type which the research most closely focused on. Most 'Cancer and other diseases' projects were autoimmune disease or immune system focused, which makes sense considering that blood cells are a key part of the immune system. Again, this group was excluded from some analysis (Figure 3b and 4) as it was felt that this research is further removed from that specifically on blood cancer.

Funding by CSO codes

Most spend in blood cancer research has been focused in 'Biology' and 'Treatment', with the smallest amount of funding going into 'Prevention' (Figure 2). Currently our understanding of what causes blood cancers is in its infancy[6] and for most blood cancers we do not know why they occur, so little money can currently be spent in 'Prevention' as we do not know what to prevent and so how to prevent them. Overall NCRI partner spend across all cancer areas shows there is little funding into 'Prevention',[7] with this not a specific pattern for blood cancer research spend. Similarly, as for blood cancer, the most amount of funding across all NCRI partners is in 'Biology' and 'Treatment'.

The spike in funding for 'treatment' between 2015/16 – 2016/17 was due to two significant clinical research grants funded in 2016/17 where both grants focused on systemic therapies under discovery and development. Together, these two grants represent 35% of total spend in treatment alone. Further investigation showed both grants are assigned as 'Other cancers (inc. blood cancers)' which explains the overall increased spend in 2016/17 (Figure 3) when comparing against 'Other cancers (inc. blood cancers)' in other fiscal years.

Significance of acute leukaemia's in adults and CYA

Leukaemia grants have had the most significant amount of funding (Figure 1), but specifically acute leukaemia's (Figure 4). This makes sense because acute leukaemia's have historically been the most 'quickly deadly' and resulted in the most rapid death. Within Childhood, Young Adult and Adolescent (CYA) blood cancer funding the most funding has been invested in acute lymphoblastic leukaemia (ALL) (Figure 4). Not all

blood cancers occur in the CYA group, with the median age of diagnosis across all blood cancers being 71 years and most cases happening in older individuals. However, the most commonly occurring blood cancer in those aged 0-14 years is ALL, which accounts for nearly 70% of all blood cancer diagnoses in this age group[8] and explains why the corresponding funding is so high in this leukaemia subgroup for CYA.

In adult blood cancers, AML has historically received the most significant funding, yet relative five-year survival rates remain some of the lowest across blood cancers.[8] However, we know that because acute leukaemia's cause rapid death, and AML is more common than ALL, AML has been more intensively studied for longer and so has more well-developed scientific models often used across research.[9] AML was the first cancer genome to be sequenced, meaning that there has been far greater available data for AML compared with other blood cancers. AML is an incredibly complex cancer, resulting from multiple mutations. In fact, there are over 100 genes which can be mutated in AML, and these can have individual effects.[10]

The progress made from the funds put into AML research may also not yet have translated into survival statistics. Before 2017 only one drug had received Federal Drug Association (FDA) approval to treat AML and treatments options for people were mainly limited to cytotoxic chemotherapy. However, in the last 4 years eight new drugs have received FDA approval. Examples include FLT3 inhibitors and show promising new ways to treat AML,[11] hopefully resulting in noticeable improvements in survival rates in the future. While overall AML survival rates remain poor, there is one key success story for one subtype of AML; acute promyelocytic leukaemia (APML). Today APML has a 65% 5-year relative survival rate compared with the other AML subtypes which have an overall 5-year relative survival rate of 15.3%.[8]

This is contrasted with CYA ALL, in recent years we have seen significant improvements in childhood ALL survival rates, with 9/10 children now surviving ALL.[8] In this case, the significant amount of funding correlates with changes in survival. On the other hand, despite the smaller amount of funding in chronic leukaemia's these have shown the biggest step changes in treatment, with CML for example being the poster child for targeted therapies across oncology. Today CML can often be managed by a one/ twice a day oral medication, and while there still remains much work to be done, in particular around the side effects of being on long terms treatment, this shows a great step forward in blood cancer treatment approaches.[12] Ultimately, it appears that amount of funds spent does not always correlate with changes in survival.

Conclusion

Overall greater consistency is required in the recording and subdividing of blood cancer research data, both funding data and broader blood cancer data sets. However, this will require a national approach and robust and consistent classification methods. One of the key challenges continues to be whether it is feasible for organisations to gather greater detail than the four key blood cancer grouping of; leukaemia, Hodgkin lymphoma, non-Hodgkin lymphoma and myeloma. There are also disadvantages to subdividing blood cancers ever further, as when considered individually they become ever more insignificant, when compared with the other common cancer types and are likely to continue to not get the attention or funding required and deserved.

While significant investment has been made into acute leukaemia, especially AML, this is likely to continue until significant changes are seen in the currently poor survival outcomes for this group. Investment in childhood leukaemia is also likely to continue due to the number of quality-adjusted life-years (QALYs) which might be achieved with improvements in treatment, despite the majority of blood cancers occurring in more elderly people (median age of diagnosis is 71 years). There are also a huge number of areas and subtypes that continue to require funding, with improvements needed across blood cancers. In respect of this, categorising research spend by condition, while helpful in some scenarios, does not necessarily capture that some research in a specific blood

cancer will have broader value across multiple blood cancer types and may be the start of a breakthrough that has an impact on a much wider field.

Like in many other cancer areas, patients want research to move towards 'prevention' as opposed to 'treatment', however for blood cancer we still do not have enough knowledge to be able to 'prevent' them. In the meantime, we need to deepen our understanding of fundamental disease processes and focus of how we can improve treatment options for individuals, in the hope that in the future we might be able to prevent these diseases. With many different cancer research funders (including government organisations), there continues to be need for a strategic approach which puts people affected by blood cancer first, to ensure that collectively we focus on areas of valued most by this group and minimise duplication of efforts across the sector.

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