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Adolescent and Young Adult (AYA) Oncology research is steadily but perceptibly entering a more mature phase. Adolescent and Young Adult-specific services have existed for almost 30 years, embedded in England since the National Institute for Health and Care Excellence (NICE) published guidance in 2005 directing where and how AYA aged 16-24 years were to be treated and cared for. Similar progress is being made with services across the world, where the lower age is considered to be in the region of 13 years at diagnosis and the upper age ranging from 29-39 years depending on jurisdiction (Husson, Manten-Horst et al., 2016, Saloustros, Stark et al., 2017, Stark, Bielack et al., 2016). Somewhat later than the development of specialist services was the need to evaluate the outcomes associated with such services, subsequently there has been an increase in high quality, programmatic research to evaluate and guide services (Parsons, Harlan et al., 2015, Stark, Bielack et al., 2016, Whelan J, 2012, White, Daly et al., 2016).

We know what our current research priorities are.

The priorities that AYA research is specifically seeking to address for patients and professionals are increasingly defined. Of course AYA research teams must contribute to key themes across cancer care such as 'what is the best treatment for my cancer', 'how can we ensure fewer people develop cancer'. A US team has recently reviewed AYA specific research priorities for the coming years, including care as well as diagnosis and treatment (Smith, Seibel et al., 2016). Australian and Canadian colleagues have recently produced policy in AYA health service care which speak to research[1]. The UK have recently undertaken a research priority setting exercise[2], in collaboration with the James Lind Alliance (JLA). This included: creating a multidisciplinary steering group of all involved in AYA cancer care including young people at all stages. The project gathered potential research questions from young people, carers and professionals online; checked submitted questions to ensure they were unanswered; and 2 phases of prioritisation. Agreement was reached on the Top 10 research priorities (Table 1). To reach these a total of 855 potential questions were gathered from 292 respondents; refined into 208 unique questions. Seven were already answered and 16 were the focus of ongoing studies and very positively could be removed from our immediate future priorities. One hundred and seventy-four respondents prioritised these to 30 top questions. A final consensus workshop attended by 25 young people, carers, and professionals from a broad range of roles finalised the top 10.

----------------------------------Table 1 around here--

The central themes expressed here, along the AYA cancer timeline, have been known for many years(Lewis, 1996). There is clearly a need for AYA-specific biologically driven research. Examples include to improve early and late adverse effects specific to AYA (Henson, Reulen et al., 2016, Kremer, Mulder et al., 2013, Rugbjerg and Olsen, 2016); and to target treatments to the personal biology of the young person (Gaspar, Marshall et al., 2018, Hughes and Stark, 2018). However, the majority of the research priorities identified in the JLA priority setting exercise relate to improving care and support. Adolescent and young adult cancer research is therefore an excellent 'home' for the ambitious and talented cancer care researcher.

We should design and implement intervention studies in our priority areas

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[1] https://www.cosa.org.au/groups/adolescent-young-adult/activities/ accessed 29-AUG-2018; http://www.cancerview.ca/treatmentandsupport/ayacancer_ca/aboutus/ Accessed 29-AUG-2018

[2] http://www.jla.nihr.ac.uk/priority-setting-partnerships/teenage-and-young-adult-cancer/the-top-10-priorities.htm, accessed 07-SEP-2018

What is also apparent from comparing current programmatic AYA research with 'the JLA' is that much current research activity remains descriptive and observational. There is increasing pressure for interventional research and this is accompanied by an increasing desire from patients, funders and professionals for research to improve outcomes, rather than continuing to describe need, compare with others and call for action. We should now extend our work in these well described themes to *intervention*; to scientifically test changes that we rigorously assess have strong potential to improve care and its outcomes. This has indeed required detailed characterisation of the specific similarities and differences between AYA and older/younger patients, over and above merely highlighting them, but much of that is now in place. For example

- Specific barriers to AYA entering clinical trials are now characterised (Fern L A., 2014)
- Patient and health service organisational factors that underpin advanced disease at AYA cancer presentation are increasingly understood (Herbert, Lyratzopoulos et al., 2018)
- Biological differences between apparently similar cancers in AYA and other age groups are described in some areas (Tricoli, Blair et al., 2016)
- The specific healthcare professional competencies required for working with AYA are characterised (Taylor, Feltbower et al., 2016)
- The social difficulties of AYA with cancer are specifically and systematically described (Warner, Kent et al., 2016).
- The unmet needs of AYA have been frequently described and differ relatively little during the cancer trajectory (cite the Identifying the needs paper in this edition). In this edition, Darlington et al comprehensively describe how specific AYA needs can influence the quality of life (cite 'Does age matter' paper in this edition).

We need to remain specific in our research to the details of AYA cancer

Another key feature – true specificity to AYA issues- is steadily pervading cancer research. One way to achieve this in the 21st Century is large-scale population-based cohort studies, which can now widely be done with existing data. Once risks of adverse outcomes are described however, appropriate more detailed studies are essential to provide the AYA-specific characterisation of those risks and steer us to the most effective intervention. One biological example is that we now know after radiotherapy as an AYA for a brain tumour, by age 60 the risk of admission to hospital with a stroke is almost 10%, where the general population expected level is around 2.5%(Bright, Hawkins et al., 2017). Case-control studies with patients can now identify which treatment, genetic and lifestyle factors are leading to these substantially increased health problems. Then we can intervene specifically for AYA and expect our intervention to improve health.

We need to keep AYA with cancer at our centre

Core to the success of AYA oncology, and complex interventions in particular, has been placing young people at the heart of research, from the point of theoretical modelling to intervention development. One excellent feature of this special edition of the European Journal of Cancer Care is the specific focus upon young people. The studies here, in the main, have young people at their heart, characterising the specific similarities and differences between AYA and older or younger patients. The projects presented are contributing to the AYA cancer care research endeavour overall, such as the challenges of outcome measurement (cite Galen in this edition) and the impact upon families (cite Hsaolin this edition). This evidence also contributes to the development of interventions that are AYA-specific.

We need to use the specific methods for complex interventions in our AYA intervention research to improve outcomes in our priority areas

The focus of this edition of this journal is upon AYA cancer care specifically. Here our interventions often involve seeking to change the behaviour of clinicians (or any human) who provide or receive that care. This can be obviously, and technically, be described as 'complex' (Campbell, Fitzpatrick et al., 2000). The success of these interventions relies upon the development of an even closer collaboration between the research community, patients and clinical practice to ensure the scientific rigor with which the intervention is developed is not only specific and works, but is also in keeping with the way healthcare professionals work in practice or is acceptable to young people as a change in practice. The UK Medical Research Council (MRC) continue to provide updated and clear guidance on how such complex interventions should be developed[3].

We need to develop research on larger scale in and more varied collaborations

One very enjoyable way to accelerate intervention research is to embed formative studies within the infrastructure of an international clinical trial. One example would be the AYA-Hears study examining treatment-related hearing loss from multiple perspectives within the AGCT1531 germ cell tumour clinical trial[4]. Clinical care interventions in psychosocial wellbeing or survivorship could also proceed faster in this manner, recruit a larger and more representative patient group and on completion already be developed alongside clinical teams to enhance the subsequent intervention trial. Timely consideration of the priorities of healthcare providers, commissioners and policy is critical. This is largely achieved by embedding specific outcome variables that matter to them. Then, once we have shown interventions work, patients can receive them more equitably. If our research does not get converted into health services, sometimes that is because of our decisions during our research.

Another way to accelerate AYA cancer care research towards interventions is to ensure study designs are debated as proposals with multi-professional multi-centre research groups at the earliest possible stage. 'Dragon's den' sessions[5] and workshops at congresses[6] present excellent opportunities to do this, and are open to all.

Increasingly, collaborative groups tasked with study design and implementation for AYAs are gaining a foothold alongside site-specific groups, supportive care and psychosocial oncology groups[7]. Darlington et al in this edition delivered their AYA-specific study in the context of the pan-European EORTC Quality of Life group, harnessing huge expertise in the development of rigorous patient-reported outcomes instruments and their subsequent implementation as robust outcome variables in intervention trials.

The emergence of AYA oncology as a distinct clinical and research speciality is further evidenced by the recent formation of 'The AYA Global Accord'. Key worldwide charities in AYA oncology now meet regularly, and have recently offered pilot funding for projects that specifically build international collaboration in AYA psychosocial research[8]. As we mature as a speciality there are increasing

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[3] https://mrc.ukri.org/documents/pdf/complex-interventions-guidance/, accessed 05-SEP-2018

[4] https://clinicaltrials.gov/ct2/show/NCT03067181, accessed 31-AUG-2018

[5] http://www.ncri.org.uk/case-study/a-dragons-den-workshop-to-improve-research-through-consumer-involvement/ accessed 08-SEP-2018

[6] https://www.eiseverywhere.com/ehome/312967/758333/ accessed 08-SEP-2018

[7] http://csg.ncri.org.uk/about-the-csgs/clinical-studies-groups/tya-germ-cell-tumours/ accessed 07-SEP-2018

[8] https://med.unsw.edu.au/news/unsw-researcher-lead-global-initiative-develop-training-end-life-conversations accessed 30-AUG-2018

opportunities, enthusiasm, confidence and demand for wider cooperation and a reducing need for stand-alone smaller scale studies, which may not be designed with a vision of a future intervention, and not developed alongside research groups with the reach to deliver intervention trials. The AYA-specific charitable funders contribute hugely to the infrastructure of clinical AYA services, do not have the resources to fund such large-scale intervention trials that can fulfil the regulatory requirements for health service adoption. Coalescing our community's approach around the key set of issues through such as 'the JLA' has already begun to attract the attention of larger-scale funders. The building of even larger multi-professional, multi-centre, international research communities will be necessary to achieve intervention trial funding.

Conclusion

It is fabulous to have a special edition of the journal dedicated to bringing together AYA research into cancer care. This can only serve to further develop the relationships and academic collaborations required to develop and deliver large-scale intervention research and through that to improve the outcomes of AYA with cancer. To deliver for young people we must create ever more spaces where we can design and implement that research together; professionals whose focus is upon care, diagnosis, treatment; research methodologists, working with young people and the public, to develop faster and more effective research. We are closing in upon an era of mature research in AYA oncology, becoming evidenced in our services, and running AYA-specific interventional studies that make a real difference.

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