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Abstract

Over 14,000 patients aged 15-24 are estimated to be diagnosed with cancer in the EU each year. Teenagers and Young Adults (TYA) often fall down gaps between children's and adults cancer services. The specific challenges of providing optimal care to them are described, but we present a summary of recent progress. Progress to overcome these challenges is happening at different rates across Europe. We summarise the European national projects in this field but more recently we have seen the beginnings of European co-ordination. Within the EU FP7 European Network for Cancer Research in Children and Adolescents program (ENCCA) a specific European Network for Teenagers and Young Adults with Cancer (ENTYAC) has held a series of scientific meetings, including professionals, patients and caregivers. This group has proposed unanswered research questions and agreed key features of a high quality service that can improve outcomes for TYA with cancer, including the primacy of collaboration between adult and pediatric services to eliminate the gap in the management of TYA with cancer.

Keywords: Teenagers, Adolescents, Cancer.

Background

The estimated population of teenagers and young adults (TYAs) in the European Union is 58 million in the age range between 15 and 24 years (EUROSTAT, 2013); approximately 14,000 new cases of cancer are diagnosed in TYAs annually (Steliarova-Foucher et al., 2014)). In this age group, cancer is for the second greatest overall cause of loss of life, even though over 80% of TYAs diagnosed are long-term survivors (Gatta et al., 2009). TYAs with cancer are established to be a unique group, with special characteristics (Leonard et al., 1995, Hollis and Morgan, 2001)). Being in an age of transition, they are known to inhabit a “no man’s land”, neither the focus of pediatric nor of adult oncology (Albritton and Bleyer, 2003, Michelagnoli et al., 2003). The transition to TYA arises at different ages in different illnesses, as biology evolves from childhood to adulthood (Bleyer et al., 2008).

This paper aims to update these previous observations with current clinical evidence, challenges for designing cancer services and unanswered clinical and translational research questions for TYA cancer. It then describes the current evolution from developing local and national projects to improve TYA cancer outcomes, to international collaboration through the EU FP7 European Network for Cancer Research in Children and Adolescents (ENCCA) program, to bring these efforts together and define the characteristics of comprehensive high quality European services.

What makes TYAs different?

There is substantial evidence of specific clinical and psychosocial features which mark out being a TYA with cancer (listed and referenced in Table 1). They are already identified to develop specific clinical cancer types, but their specific host biology, pharmacology and specific late effects are more recently characterised. Even recently the observation persists that TYA survival remains poorer than that of children with the same tumor type (Wilhelm et al., 2014, Hunger et al., 2012)). The amount of current biological cancer biology data remains disappointing due to poor clinical trial entry, but the reasons why clinical trial recruitment remains poor have recently been characterized in detail (Fern L A., 2014).

Health services still face challenges to manage TYA cancer well (listed and referenced in Table 2). Neither a pediatric nor an adult clinical group can manage this group of patients properly and consistently without the active collaboration of the other (Ferrari et al., 2010): an integrated specifically-trained multi-professional team and dedicated projects are needed. Even recently, healthcare professionals may not consider cancer in TYA presenting with symptoms, making the diagnostic pathways complex (Dommett et al., 2013). TYAs specific clinical needs may be unnoticed or misinterpreted without specific professional training, which has been recently defined (Smith, 2013).

National TYA cancer care projects in Europe

Though the clinical culture, investment and networks for TYA remain less mature than those for children or adults, various specific programs involving organizations, healthcare providers, academic societies, and governments have developed across Europe.

The UK pioneered a model in the 1990s with the charity Teenage Cancer Trust (TCT), with the aim of building dedicated TYA units jointly funded with the National Healthcare System (NHS) (Whiteson, 2003, Carr et al., 2013). The NHS has service guidance on care for TYA (NICE(UK), 2005), that mandate joint pediatric-adult case-review for every TYA diagnosis. A pathway from symptoms to treatment is defined. The facilities, staff and training undergo annual peer-review. Lead clinicians lead regional specialist networks including adult and pediatric-trained senior staff. The UK National Cancer Research Institute (NCRI) includes a TYA Clinical Studies Group to develop and deliver research, and works alongside TYA living with and after cancer (Fern L A., 2014, Whelan J, 2012). A UK professional membership organization (www.tyac.org.uk) provides

multi-professional education, supports and disseminates service developments. More recently shared medical training curricula and clinical outreach services to smaller hospitals have developed.

In Germany, the provision of TYA oncology has been characterized by distinct and separated infrastructures for pediatric and adult oncology and a usually quite strict age barrier of 18 years between them. The provision of healthcare to adolescents is generally within pediatric oncology, organized in the German Society for Pediatric Oncology and Hematology (GPOH). In healthcare policy inpatient treatment of cancer patients < 18 years is only reimbursed if carried out in certified pediatric oncology units. Medical oncology has long-established nationwide cooperative infrastructures for leukemia and lymphoma and selected solid tumors of young adults. Patients being managed from before to after their 18th birthday remain challenging outside of experienced centres. Recently, Germany is adapting its approach and an active collaboration between the pediatric and the adult medical oncology national societies has been initiated, and some centers have initiated TYA-specific interdisciplinary programs.

In Italy, the first specific programs for TYAs arose in pediatric oncology. In 2010 a national Committee on Adolescents was founded by the Associazione Italiana Ematologia Oncologia Pediatrica (AIEOP), with the mission of ensuring that Italian adolescents with cancer have prompt, adequate, and equitable access to the best care to optimize their treatment outcome and quality of life (Ferrari et al., 2009, Ferrari et al., 2012). A formal cooperation was established with the federation of parents organizations. Two TYA units have developed, one arising from a medical oncology and one from a pediatric oncology perspective, with a common denominator of cooperation between pediatric and adult medical oncologists (Ferrari et al., 2009). In 2013, a more ambitious comprehensive national program was defined and a national broad-based task-force dedicated to adolescents and young adults has developed, as a cooperation between adult and pediatric cooperative groups: SIAMO (Società Italiana Adolescenti Malati Onco-ematologici, www.progettosiamo.it)(Ferrari, 2014). The newborn association has finally achieved a formal support from national health services and governments.

TYA care in France is structured as an integrated cooperative program with pediatric and adult oncologists within a cross-cutting field. After a study indicated that 82% of 15-18 year-old patients were treated in an adult environment, and that only a minority were included in clinical studies (Desandes et al., 2012), an improvement plan for the pathway to care and for research for TYA has been included in successive national Cancer Plans since 2004. The Institut National du Cancer (INCa) selected 8 French TYA centres, and a further 3 specialist units since, that include a cross-cutting clinical team (at least one pediatric and one adult oncologist, coordinating nurse, psychologists, social worker), the systematic inclusion in a programme of disease-focused clinical trials, and a specific psycho-social program. INCa is now planning to organize an optimal pathway of care for TYA in each region, and to define a national framework and criteria for specialist TYA teams. A national association – called Groupe Onco-hématologie Adolescents et Jeunes Adultes (Go-AJA) - has been funded, focusing on patients aged 15 to 25. Go-AJA includes patients and their representatives (Jeunes Solidarité et Cancer).

In Spain, the Adolescents with Cancer Committee was established by the Spanish Society of Pediatric Hemato-Oncology (SEHOP) in 2011. A survey indicated that over 14 year-olds are generally treated in adult oncology wards (Lassaletta, 2013). Recently, a co-operation between TYA oncologists, patients and charities founded the charity AAA - 'Spanish Association of Adolescents and Young Adult with Cancer' (www.aacancer.org) to raise awareness and create a community of patients and organized activities (www.adolescentesyjovenesconcancer.com/).

In the Netherlands, in 2013 health professionals from university medical centers and large regional

centers started a national cooperative TYA project, initiated mainly by medical oncologists and nurses, dedicated to 18-35 year-old patients, involving patients through their own national digital community and focused on quality of life, fertility, and late effects of treatment (Aben et al., 2012). In Denmark, a TYA nurse-initiated project started in 2000, in the adult oncology department at Aarhus University Hospital (Olsen and Harder, 2011). The Danish Cancer Society is currently developing a national initiative to identify young people's views, centralise and specialise the treatment of TYAs, and establish TYA units in three university hospitals with charitable investment.

In Portugal, there is no national cooperative project but in Lisbon a project to create a TYA unit has begun, with medical and nursing staff from the pediatric and adult settings, and joint therapeutic protocols for patients aged 16 to 25.

In other countries (e.g. Belgium, Bulgaria, Czech Republic, Eire, Greece, Hungary, Lithuania, Norway, Poland, Rumania, Slovenia, Sweden) there is no national coordinated project for TYA with cancer, although there are some individual projects such as the Canteen charity in Ireland, guideline development in Scandinavia, a joint professional training scheme for adolescent care in the Czech Republic and a charity-funded inventory of TYA needs in the Southern Swedish Health Care Region. Table 3 summarises these different European national projects, to highlight the differences, similarities, achievements and next plans.

A joint European project

The European Network for Cancer in Children and Adolescents ('ENCCA') is a network of research institutes and clinical organizations recognized for their excellence in pediatric oncology, developed within the European Seventh Framework Programme for Research (FP7, 2011-2014). This network aims to integrate all stakeholders involved in the pediatric oncology field in an effort to facilitate access to novel therapy and raise standards of care across Europe, reducing the existing gaps and limitations in pediatric oncology. Among the 18 projects and activities, one work package (number 17) of ENCCA is completely dedicated to TYAs: "Improving Outcomes for Teenagers and Young Adults with Cancer". The ENCCA TYA project includes 6 tasks: 1) create a European multidisciplinary framework, i.e. the European Network for Teenagers and Young Adults with Cancer (ENTYAC) and develop specific practice guidance relevant to TYA cancer; 2) promote TYA multi-professional cancer care education; 3) improve access to clinical trials; 4) develop a specific TYA research initiative (e.g. tissue collection and biologic research; promote links between cancer registries to establish Europe-wide comprehensive epidemiology); 5) promote healthy lifestyles in TYA population and cancer survivors (e.g. fertility preservation, secondary prevention); 6) embed patient and support organizations into all that we do.

Many European national projects have been involved in growing ENTYAC and delivering its work. The ENCCA project was pediatric-led, but ENTYAC leadership includes adult oncologists. A major goal of this venture is to see pediatric and adult oncologists working together, pooling their resources and expertise in a synergistic process for TYAs, notably training, tumor biology, epidemiology and clinical care. Concerning clinical trial development, for example, an effective meeting of requirements may combine the pediatric oncologists' experience of establishing international networks and multidisciplinary cooperative protocols in rare diseases and delivering high recruitment, with the experience of adult oncologists in novel therapies. This can enable pooling enough cases across age groups to plan randomized studies even for rare tumors with particular ages at onset.

A key feature of ENTYAC is the central involvement of many stakeholders; patients themselves, caregivers and charities. Our patient's voice is of major importance: young people guide us in the

optimal delivery of services, influence politicians differently from professionals, and achieve improvements at many levels of local, national/and European Parliament policy. The role of charities is currently fundamental; funding some services, research, and service development projects. This includes coordinating patient involvement, engaging clinicians and researchers, stimulation with ideas and actions from outside healthcare, and advocating in community and government the development of dedicated TYA oncology professionals and services as a standard of care. Large professional organizations across wide geographies are developing shared initiatives in trial recruitment and professional training, i.e. International Society of Pediatric Oncology (SIOP)-Europe, European Society of Medical Oncology (ESMO) and European Organisation for Research and Treatment of Cancer (EORTC).

ENCCA has agreed specific practice guidance relevant to TYA cancer, defining the specific criteria and required facilities to ensure hospitals that treat TYA with cancer (whether they began as pediatric or adult units, or collaborations between the two) have the optimal structure, trained staff and facilities.

These guidelines are as follows: TYA centres will:

- not have restrictive age cut-offs, but treat according to need in the community they serve
- provide an environment where TYAs feel supported, to complete their treatment successfully, and tailor-make supportive care to each TYA and their family/carers
- include a) multidisciplinary staff who embody an active cooperation between pediatric and adult oncologists, or alternatively, a dedicated TYA team co-ordinating the two specialities, b) a specialist team dedicated to providing age-appropriate TYA care (e.g. dedicated nurses, social workers, psychologists, teachers, activity organizers), adequately trained c) dedicated adequate physical spaces alongside other young people, d) a fertility preservation program, e) a transition program, to welcome TYA who have had cancer in childhood who still need care, and to help older TYA patients thrive when receiving adult care later in life, f) comprehensive clinical trial availability and demonstrable excellence in recruiting TYA, in the different tumor types arising in adolescence and young adulthood

Cancer care for TYA in Europe – the way forward.

The organization of specific TYA cancer care is in development towards an integrated pediatric-adult multidisciplinary model in several of the larger European countries, but this needs further strengthening. Many countries are lacking a specific focus on this challenge and need to develop their services in the integrated direction outlined here. There is also a need for further public and political awareness of the needs of this particular group of patients. ENCCA WP 17 projects will come to a conclusion in 2015, but we plan ENTYAC to continue as a dedicated pan-European multi-level program. ENTYAC may represent the European structure to be accessed by regulatory authorities, organizations, healthcare providers, academic societies and international oncology cooperative groups, as well as patient and parent groups.

Ethics Statement

Ethical approval was not sought, as it is not appropriate for this form of work.

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