Care of adolescents and young adults with cancer in Asia: results of an ESMO/SIOPE/SIOP Asia survey

Chi Kong Li,1 Rashmi Dalvi,2 Kan Yonemori,3 Hany Ariffin,4 Chuhl Joo Lyu,5 Mohamad Farid,6 Julieta Rita N Gonzales-Santos,7 Qing Zhou,8 Stefan Bielack,9 Laurence Brugieres,10 Anne Blondeel,11 Samira Essiaf,11 Fedro Alessandro Peccatori,12 Svetlana Jezdic,13 Daniel P Stark,14 Jean-Yves Douillard,13 Emmanouil Saloustros,15 Giannis Mountzios16

ABSTRACT

Background Adolescents and young adults (AYAs) with cancer require dedicated management encompassing both adult and paediatric cancer services. Following a European survey, the European Society for Medical Oncology, the European Society for Paediatric Oncology and the Asian continental branch of International Society of Paediatric Oncology undertook a similar survey to assess AYA cancer care across Asia.

Methods A link to the online survey was sent to healthcare professionals (HCPs) in Asia interested in AYA cancer care. Questions covered the demographics and training of HCPs, their understanding of AYA definition, availability and access to specialised AYA services, the support and advice offered during and after treatment, and factors of treatment non-compliance.

Results We received 268 responses from 22 Asian countries. There was a striking variation in the definition of AYA (median lower age 15 years, median higher age 29 years). The majority of the respondents (78%) did not have access to specialised cancer services and 73% were not aware of any research initiatives for AYA. Over two-thirds (69%) had the option to refer their patients for psychological and/or nutritional support and most advised their patients on a healthy lifestyle. Even so, 46% did not ask about smokeless tobacco habits and only half referred smokers to a smoking cessation service. Furthermore, 29% did not promote human papillomavirus vaccination for girls and 17% did not promote hepatitis B virus vaccination for high-risk individuals. In terms of funding, 69% reported governmental insurance coverage, although 65% reported that patients self-paid, at least partially. Almost half (47%) reported treatment non-compliance or abandonment as an issue, attributed to financial and family problems (72%), loss of follow-up (74%) and seeking of alternative treatments (77%).

Conclusions Lack of access to and suboptimal delivery of AYA-specialised cancer care services across Asia pose major challenges and require specific interventions.

INTRODUCTION

Cancer is not uncommon as a cause of morbidity and mortality among adolescents and young adults (AYAs) worldwide. The definition of AYA differs across countries and clinicians, but a recent authoritative review of epidemiology defined this group as patients aged between 15 and 39 years.1 Cancer in this age group is less common than in older people; however, it is more common than in childhood: almost three times as many cancers occur in people aged 15–30 years compared with younger individuals2; and a 2016 estimate suggested that around a million cases of cancer occurred globally in people aged 15–39.3

AYAs with cancer require dedicated care that encompasses aspects of both adult and
paediatric services. Given improvements in survival in the AYA patients with cancer and the relative low comorbidities, a rapidly growing number of people have survived cancer diagnosed in adolescence and young adulthood. However, it is disturbing to note that survival rates in AYA with cancer have not improved to the same extent as in childhood cancer and in older adults.1 Paucity of clinical trials recruiting patients in this age group is one cause of this distressing situation.

The leading cancer types among AYAs differ from that in younger and older patients, and there are also differences both geographically and ethnologically. In a recent European series, the most frequent diagnoses were breast carcinoma (which accounts for 18% of cases), cutaneous melanoma (14%), germ cell tumours (13%), brain tumours (12%), carcinomas of the female genital tract (11%), thyroid cancer (7%), Hodgkin’s lymphoma (also 7%) and non-Hodgkin’s lymphoma (6%). However, data from Cancer Incidence in Five Continents and SEER registries show that the incidence of testicular cancer in AYAs is markedly higher in Europe (137 cases per million) than in Asia (27 per million), with intermediate rates in North America (95 per million) and South and Central America (67 per million).4 It is likely that the incidence of other relevant tumours is also highly variable according to geography.

Moreover, differences in healthcare systems, AYA-dedicated infrastructure, as well as cultural and social issues, lead to significant differences in AYA cancer care across the five continents. Hence, there is a need to collect data from individual regions and countries.

In 2016, the European Society for Medical Oncology (ESMO) and the European Society for Paediatric Oncology (SIOPE) conducted a European survey among clinicians with an interest in AYA oncology. Its results, published in 2017, revealed substantial under-provision of specialised services for AYA patients across Europe and marked differences in provision between geographical areas, with lack of access to those services being more pronounced in Eastern and Southeastern Europe than in Western and Northern regions.5

Following the successful paradigm of the European survey, ESMO and SIOPE in collaboration with the Asian continental branch of International Society of Paediatric Oncology (SIOP), SIOP Asia, conducted a similar survey in Asia. Through this survey, the three societies aimed to increase professional and social awareness on AYA-related issues across the multicultural and diverse Asian continent. Herein, we present the results of this survey emphasising on the special needs of young people with cancer across Asia.

METHODS
An online survey of 35 questions was conducted by the ESMO/SIOPE/SIOP Asia steering committee. Healthcare professionals (HCPs) who had declared a specific interest for AYA with cancer were identified through their national registries and/or the membership lists of the three societies and were invited via email to complete an online questionnaire on a voluntary and anonymous basis. The questionnaire obtained data on respondents’ demographic characteristics, their perception of the age definition of AYA, the services and clinical management they could provide, efforts to maintain the health of AYA survivors after cancer treatment, cancer risk assessment and management, educational activities available to HCPs interested in the AYA field, and means of raising awareness and improving care and outcome. The questionnaire was based largely on that used in the prior European survey but was adapted to take into account of issues that are relevant to some Asian countries, including the healthcare setting (urban vs rural), routine performance of pretreatment counselling of the patient and her/his family regarding adverse/late side effects of treatment and especially fertility, particular habits (ie, smokeless tobacco chewing), promotion of hepatitis B vaccination for AYA patients with high risk of exposure to hepatitis B virus, access to nutritionist/dietician and treatment non-compliance or abandonment for a variety of reasons. A section on the availability of health insurance or other means of payment for care and reasons for treatment discontinuation was also included. The full questionnaire was available online at www.esmo.org and provided in online supplementary file 1.

RESULTS
Characteristics of respondents
There were a total of 268 respondents: 39% female and 61% male.

The age distribution was as follows: 20–29 years, 5%; 30–39 years, 38%; 40–49 years, 32%; 50–59 years, 19%; 60 years and over 7%. Altogether, 22 countries were represented (figure 1). The great majority of respondents were from the South and the Southeast Asia; only 5% of respondents were from the Middle East. In country of origin, the largest proportion (19%) came from Japan, followed by India (17%), China (14%) and the Republic of Korea (10%). Given the non-proportional distribution of respondents, we have not analysed data by country or geographical subregion.

The majority (93%) of respondents serve in urban areas and only 7% in rural areas. Half were medical oncologists and 26% paediatric oncologists, with 7% being radiation oncologists, 3% haematologists and 3% surgical oncologists. Four per cent were in training. Very few responses from nurses (0.4%) were received.

The majority of respondents to the Asian survey (52%) worked in general academic centres, with 21% in specialised cancer hospitals, 18% in general hospitals and 10% in paediatric or children’s hospitals.

Fifty per cent had been trained to treat adult patients with cancer, 28% to treat paediatric cases and 22% both. In Europe, 60% had been trained to treat adults, 25% paediatric patients and 15% both.
There were wide differences in the number of patients aged 15–39 years Asian respondents had treated over the past year. Thirty-five per cent had treated between 1 and 10 such patients, 23% had treated 11–20, 18% had treated between 21 and 50 cases, and 19% more than fifty. Six per cent had treated none.

Management of AYA patients and access to services
Respondents were asked about their perception of the AYA age range. The mean lower age limit was reported to be 15 years (median 15; range 10–25) and the mean upper limit 29 years (median 30; range 15–39).

Respondents were presented with three hypothetical patients (all aged 17 years)—who had metastatic soft-tissue sarcoma, acute lymphoblastic leukaemia (ALL) or embryonal carcinoma of the testis—and asked whether (in their country) the doctor leading patient management would be trained in adult oncology, paediatric oncology or both (figure 2). In sarcoma, it was thought the physician would be more likely to have adult rather than paediatric training (39% vs 23%). With testicular carcinoma, 44% thought the responsible physician would be adult trained versus 24% paediatric trained. Only with ALL, did the more respondents think the treating physician should be paediatric rather than adult trained (34% vs 31%).

When asked if their patients could access specialised services for AYA with cancer in which adult and paediatric specialists worked together, or if such services were in development, 78% of respondents said they cannot. Fifteen (15%) of respondents reported that such services were available.

Respondents were asked whether AYAs whom they treated had access to a range of professionals with experience in AYA cancer (figure 3). The majority (>60%) reported that their patients had access to the support of a professional psychologist, social worker, physiotherapist or occupational therapist and nutritionist or dietician. However, less than half had access to a mentor to guide their education or training (37%) and to a support group of other young people (43%). Finally, 28% had access to age-specific specialised nursing.

When respondents were asked whether they were aware of the trends in outcome for AYAs compared with those for children or older adults with cancer, 63% said they were not. Seventy-three per cent were not aware of research initiatives, clinical trials or studies (near them or further afield) focused on the specific clinical, epidemiological or psychosocial features of AYAs with cancer.

Promoting well-being and preventing disease among AYA cancer survivors
Asked if they routinely undertook pretreatment counselling of the patient and her/his family regarding adverse and late effects of treatment, and especially fertility, 69% said they do it regularly. Less than half (42%) reported that their institutions offer consultation with a fertility specialist to help meet their wish to children after treatment.

Seventy-seven per cent reported that patients who had had potentially cardiotoxic treatment were evaluated for modifiable cardiovascular risk factors such as high blood pressure, high cholesterol and obesity.
Figure 2  Responses to the question 'What is the most likely training background for the doctor leading the treatment of a 17-year-old patient with soft-tissue sarcoma, acute lymphoblastic leukaemia and metastatic embryonal carcinoma of testis in your country?'
The majority of patients (approximately 80%) were advised on the importance of a healthy approach to body weight, eating healthily and remaining active. Sixty-seven per cent of respondents advised patients to cut back on alcohol consumption and 52% gave advice on limiting exposure to the sun (figure 4). Advice on tobacco-related habits is considered in table 1, which provides a summary of situation where we received an answer from the respondents.

Respondents were also asked if they had access to a specialised service to advise AYA patients some years after treatment on late effects. Fifty-nine per cent did not. Fewer than a third of respondents overall (27%) had access to a specialised service to which they could refer patients some years after completion of cancer treatment. This service was envisaged as providing education and minimising the risk of late effects or enhancing their management.

In relation to vaccination in general, respondents were asked how often they reviewed the status of AYA patients after cancer to ensure they complied with national standards. Seventeen per cent admitted that they never did this. Nine per cent reviewed vaccination status at each visit, 43% occasionally and 18% annually. More specifically, 58% of respondents promoted human papillomavirus (HPV) vaccination for young female patients, though 29% did not. Fourteen per cent recommended HPV vaccination for young male patients with cancer. Seventy per cent promoted vaccination against hepatitis B for those patients at risk while 17% did not.

**Family history**
Sixty-five per cent of respondents said they felt competent to evaluate family history and to screen AYA patients for the more frequent hereditary syndromes that predispose to cancer. In total, 56% had access to a genetics service for AYA patients with a family history that suggested a hereditary cancer syndrome.

**Improving the AYA cancer care service**
Thirty-five per cent of respondents said that their unit, hospital, region or country asked AYA patients about the quality of their care as part of an effort to improve services. Forty-seven per cent said their patients were not consulted in this way.

Only 12% of respondents said they had access to education and training courses (online or face to face) that were focused on the management of AYAs with cancer. Sixty-nine per cent said that they did not. In relation to educational activities that ESMO/SIOPE Joint Working Group on AYA in Cancer might undertake in the future, respondents were asked to prioritise four options. Cancer treatment services and their quality improvement for AYA was given top priority by 47% of respondents. Survivorship health for AYA after cancer was prioritised by 28%; basic science and clinical research about AYA cancer by
SURVIVORSHIP HEALTH LIFESTYLE FACTORS

Figure 4  Responses to the question “Do you choose to discuss with AYA patients the issues related to each of the following lifestyle factors after their cancer treatment?” AYA, adolescents and young adult.

Table 1  Health advice in relation to tobacco use: proportion of respondents

<table>
<thead>
<tr>
<th>Activity</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asking patients about smoking habit at every visit</td>
<td>33%</td>
<td>54%</td>
</tr>
<tr>
<td>Advising patients who smoke to stop</td>
<td>6%</td>
<td>81%</td>
</tr>
<tr>
<td>Suggesting referral to a smoking cessation service</td>
<td>38%</td>
<td>49%</td>
</tr>
<tr>
<td>Planning follow-up in regard to tobacco use</td>
<td>52%</td>
<td>35%</td>
</tr>
<tr>
<td>Asking about use of smokeless (eg, chewing) tobacco</td>
<td>46%</td>
<td>40%</td>
</tr>
</tbody>
</table>

27%; and cancer risk assessment and cancer prevention in AYA by 22%.

Funding for and compliance with treatment
The Asian survey, unlike the survey conducted earlier in Europe, asked about the sources of funding for care in AYA cancer. It seems that several funding sources are involved (figure 5). Around two-thirds of respondents acknowledged government-based social insurance, as well as patient self-funding. Private insurance plays a part for around 56%. Fifty per cent of respondents said charities are a source and 20% industry. In response to a further question, 56% said that they did not experience particular difficulties in terms of insurance for their AYA patients while 26% said that they did.

Respondents were asked whether lack of compliance or treatment discontinuation was an issue for their patients. Almost half of the respondents (47%) said that it was. These respondents were then asked a further question, about the proportion of their patients at risk. Almost half (47%) said that it was an issue for 10% or fewer of their patients, and a further 30% that it was an issue in 10%–30%. However, 9% of respondents who thought that failure to comply with or complete treatment was an issue in AYA cancer reported that it affected more than half of their patients.

Financial problems and/or lack of insurance coverage, family issues and lack of belief in the benefits of treatment (possibly accompanied by seeking alternative treatments) were all thought to play a substantial role in this failure to adhere to or complete treatment (table 2). Religious beliefs were thought relevant by 27% of respondents. Notably, three-quarters of respondents thought that loss to follow-up was an important issue for their patients.
TREATMENT FUNDING FOR ADOLESCENT PATIENTS

Figure 5  Responses to the question ‘where does the insurance cover for your patients come from?’

Finally, gender discrimination was an issue in a family’s decision to treat the AYA patient, for one out of four respondents (24%).

DISCUSSION

There is increasing recognition that the needs of patients with cancer differ according to the site of the primary tumour, extent of spread and molecular biology, and according to the individual patient characteristics. One major such factor is age at diagnosis.

The care of elderly patients is likely to be complicated by frailty, comorbidities and polypharmacy—and that it needs to be modulated according to competing causes of mortality and life expectancy. The care of AYAs with cancer is in many respects the other side of the coin: setting the cancer to one side, AYAs are likely to be in good health, with robust physiological reserves, and have a long life expectancy. But they also face particular issues relating to social, psychological and cognitive function, maintenance of fertility, and the possibility of long-term adverse events associated with treatment. For example, Keegan et al found that AYAs with a second malignant tumour—Hodgkin lymphoma, sarcoma, breast, thyroid or testicular cancer—were more than twice as likely to die of their disease than those with the same tumour but no prior cancer.6 This may explain why survival in AYAs with cancer has not improved as much as survival in older people with the same tumours. Other potential contributing factors include different tumour biology, including genomic risk, histopathology and response to chemotherapy.7 However, it is also possible that the relatively poor outcome is due at least in part to the fact that AYAs fall into the age group that is neither paediatric nor mainstream adult oncology and may, as a result, have received services that are not adapted to their needs, along with insufficient clinical trial inclusion. Both these problems

| Table 2  Reasons for lack of compliance with or abandoning treatment |
|----------------------------------|------------------|
| Financial problems/lack of insurance cover | 28% | 72% |
| Family problems | 28% | 72% |
| Disbelief in treatment benefit-seeking alternatives | 23% | 77% |
| Religious reasons | 73% | 27% |
| Loss to follow-up | 26% | 74% |
may explain the poor improvement in survival. Relevant to the latter point, it is striking that in many countries the AYA age group is an increasingly large proportion of the total population. In Bangladesh, for example, it accounts for 44% of the nation.9

It is in this context that the ESMO/SIOPEN/SIOP Asia survey was conducted. It had the aim not only of obtaining information about access to specialised services for AYA patients, but to raise awareness for research and education. Overall, respondents from Asia had considerably less access to specialised AYA services combining paediatric and adult oncology expertise than their European counterparts: 15% had such access, compared with 33% in Europe. That said, the majority were able to refer patients for specialised psychological support and had access to social workers—both professions being important to patients in whom the psychosocial impact of cancer is enormous. However, AYA patients in Asia had considerably less access to other specialised services, including genetic counselling, nutritional support, smoking cessation services and fertility preservation counselling compared with their European counterparts.

The survey revealed some particular aspects that need to draw our attention especially to Asian AYA patients: First, there is a striking underprovision of care in rural areas; second, AYAs with ‘paediatric type’ malignancies (ie, rhabdomyosarcoma) tend to be treated by adult oncologists, perhaps due to the relative paucity of paediatric oncologists in Asian countries; third, hazardous habits, like chewing smokeless tobacco, are popular in some Asian countries; fourth, consultation regarding late effects, vaccination and healthy lifestyle is lagging behind to that in Europe; and finally and perhaps more strikingly, the levels of treatment non-compliance and abandonment due to financial, social and cultural issues, including gender discrimination are worrisome and call for specific, cause-related interventions, including proper education and information for the family and the caregivers.

What are the needs of the HCPs taking care of AYAs with cancer in Asia? Respondents identified monitoring post-treatment, communication with professionals, preservation of fertility and return to work and school as priorities in care, similar to the European survey.9 In relation to the scope for future initiatives, only 12% of respondents said they currently had access to education and training focused on AYA cancer management, and almost half gave a top priority to courses that could potentially improve the quality of care for their AYA patients. There is clearly an urgent need to provide education and training to these HCPs and this gives a clear lead to professional bodies willing and able to provide such material and services. International collaborations among societies like ESMO, SIOPEN and SIOP Asia set the example for such fruitful collaboration.

We noticed a range of differences in terms of our previously conducted European landscape in AYA cancer care. The high proportion of male respondents in the Asian survey contrasts with that in European one where the majority of those who completed the questionnaire were female. The proportion of European respondents who reported they could access the specialised services for AYA with cancer is at some extent better: 33% overall, arising to 60% in Northern Europe. The figures about access to a range of different professionals with experience in AYA cancers are around 10% lower in Asia than that reported in earlier European survey. There are also considerable differences among Asian and European respondents in terms of whether their institutions offer consultation with a fertility specialist to help meet their wish to children after treatment (42% vs 62%) or evaluation for modifiable cardiovascular risk factors in patients who had had potentially cardiotoxic treatment (77% vs 91%). Finally, the access to a genetics service for AYA patients with a family history that suggested a hereditary cancer syndrome is substantially less in Asia (56%) than that among respondents from both Northern Europe (95%) and Southern Europe (81%).

The Asian survey was not a random sample of Asian clinicians who treat AYA cancer patients. The majority of respondents came from only four countries: Japan, India, China and the Republic of Korea. This represents one of the major limitations of the survey when consider the great heterogeneity across Asian countries, and therefore, the results cannot be interpreted as representative of the whole Asian continent. Importantly, all but 7% practised in urban areas, meaning that in the current survey, there is an under-representation of the AYA cancer care in rural Asia. Further limitations are the relatively small number of overall responses (although we are not aware of current Asian workforce in the AYA oncology field) and that respondents were drawn from a wide range of age groups and a spread of specialties and training backgrounds. Moreover, the fact that the respondents were self-selected introduces an inherent and largely unavoidable bias to our survey, since respondents had declared a personal interest in AYA cancer care and were thus more likely to reply to the questionnaire.

Nevertheless, our survey represents a starting point to better understand the current situation in AYA cancer care in Asia. More importantly, we hope that our results will increase professional and social awareness on issues like prevention, vaccination, early diagnosis and maintaining a healthy lifestyle among AYA cancer survivors. Last but not least, raising the issue of treatment incompliance and abandonment will help HCPs to identify potential causes and ways to tackle the problem. Ultimately, we hope that surveys like this will contribute to focus more on AYA and improve cancer care for this fragile and rather neglected patient group.

In conclusion, our survey among Asian HCPs providing care to AYA patients with cancer revealed a substantial lack of access and suboptimal delivery of AYA-dedicated cancer care across Asian countries. Lack
of infrastructure and specialised services for AYA, as well as of AYA-orientated education and training pose major challenges and worrisome levels of treatment non-compliance and abandonment call for cause-specific interventions.

Author affiliations
1Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong SAR, Hong Kong
2Department of Pediatrics and Hematology-Oncology, Bombay Hospital Institute of Medical Sciences and SRCC Children’s Hospital, Mumbai, India
3Department of Breast and Medical Oncology, National Cancer Center Hospital, Tokyo, Japan
4Department of Paediatrics, University of Malaya Medical Centre, Kuala Lumpur, Malaysia
5Department of Paediatrics, Yonsei University College of Medicine, Seoul, Korea
6Division of Medical Oncology, National Cancer Centre Singapore, Singapore, Singapore
7Department of Paediatrics, De La Salle University Medical and Health Sciences Institute, Dasmarias, Cavite, Philippines
8Guangdong Lung Cancer Institute, Guangdong General Hospital & Guangdong Academy of Medical Sciences, Guangzhou, China
9Zentrum für Kinder, Jugend und Frauenmedizin Pädiatrie 5, KlinikumStuttgart – Olgahospital, Stuttgart, Germany
10Children and Adolescent Oncology Department, Gustave Roussy Cancer Campus, Villejuif, France
11Department of Scientific Programme Coordination, European Society for Paediatric Oncology (SIOPE), Brussels, Belgium
12Gynecologic Oncology, European Institute of Oncology, Milan, Italy
13Scientific and Medical Division, European Society for Medical Oncology (ESMO), Lugano, Switzerland
14Department of Oncology, Leeds Institute of Medical Research at St James's, and Leeds Teaching Hospitals NHS Trust, Leeds, UK
15Department of Oncology, University Hospital of Larissa, Larissa, Greece
162nd Department of Oncology, Henry Dunant Hospital Center, Athens, Greece

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Contributors All authors conceived the idea, drafted the survey, analysed the data, drafted the manuscript, collected the data and assisted in the preparation of the manuscript. All authors edited and approved the manuscript.

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