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Original Research

The 'Survivorship Passport' for childhood cancer survivors

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Childhood cancer;
Survivorship;
Long-term care;
Long-term follow-up;
Late effects;
Cancer treatment summary

Abstract ***Background:*** Currently, there are between 300,000 and 500,000 childhood cancer survivors (CCSs) in Europe. A significant proportion is at high risk, and at least 60% of them develop adverse health-related outcomes that can appear several years after treatment completion. Many survivors are unaware of their personal risk, and there seems to be a general lack of information among healthcare providers about pathophysiology and natural history of treatment-related complications. This can generate incorrect or delayed diagnosis and treatments.

Method: The Survivorship Passport (SurPass) consists of electronic documents, which summarise the clinical history of the childhood or adolescent cancer survivor. It was developed by paediatric oncologists of the PanCare and SIOPE networks and IT experts of Cineca, together with parents, patients, and survivors' organisations within the European Union–funded European Network for Cancer research in Children and Adolescents. It consists of a template of a web-based, simply written document, translatable in all European languages, to be given to each CCS. The SurPass provides a summary of each survivor's clinical history, with detailed information about the original cancer and of treatments received, together with personalised follow-up and screening recommendations based on guidelines published by the International Guidelines Harmonization Group and PanCareSurFup.

Results: The SurPass data schema contains a maximum of 168 variables and uses internationally approved nomenclature, except for radiotherapy fields, where a new classification was defined by radiotherapy experts. The survivor-specific screening recommendations are mainly based on treatment received and are automatically suggested, thanks to built-in algorithms. These may be adapted and further individualised by the treating physician in case of special disease and survivor circumstances. The SurPass was tested at the Istituto Giannina Gaslini, Italy, and received positive feedback. It is now being integrated at the institutional, regional and national level.

Conclusions: The SurPass is potentially an essential tool for improved and more harmonised follow-up of CCS. It also has the potential to be a useful tool for empowering CCSs to be responsible for their own well-being and preventing adverse events whenever possible. With sufficient commitment on the European level, this solution should increase the capacity to respond more effectively to the needs of European CCS.

1. Introduction

Survival after childhood cancer has improved substantially over the past five decades, and currently, it is estimated that there are between 300,000 and 500,000 childhood cancer survivors (CCSs) in Europe [1–3], with a median age between 25 and 29 years, and approximately 8000 to 10,000 new survivors added every year [4].

Research has shown that certain subgroups of this growing population are more vulnerable and have a higher risk of experiencing adverse health-related and quality of life outcomes than their peers [1,5–7]. Some adverse effects can appear soon, but many develop several years or even decades after treatment completion [8,9].

Long-term follow-up (LTFU) is therefore crucial well beyond the end of the paediatric age, in particular during the critical transition period from childhood to adult care [10,11]. However, several reports [12–14] have shown that many survivors are unaware of their personal risk of developing specific late effects. In addition, there seems to be a general [15] lack of information among healthcare providers about the pathophysiology and natural history of treatment-related complications. This can result in incorrect or delayed diagnosis and treatments [9]. Moreover, information about anticancer treatment given many years earlier may have been forgotten or be insufficiently documented and thus unavailable to medical teams or the survivors themselves. There is particular difficulty when the survivor moves from paediatric to adult healthcare services or to a different region or country. In the latter case, a translation may be required to inform healthcare professionals accordingly.

We report here about the Survivorship Passport (SurPass) application developed as part of the European Union–funded (FP7-HEALTH-F2-2011 no. 261474) European Network for Cancer research in Children and Adolescents (ENCCA, www.encca.eu) project, the PanCare Childhood and Adolescent Cancer Survivor Care and Follow-up Studies project (PanCareSurFup, www.pancaresurfup.eu – HEALTH 2010 2.4.1-7, no. 257505-2), and the European Expert Paediatric

Oncology Reference Network for Diagnostics and Treatment (ExPO-r-Net project (Chafea Project Grant Nr: 2013 12 07), aiming to provide each CCS with an electronic treatment summary including individualised recommendations for follow-up as well as respective translations in European languages.

2. Methods

The SurPass concept aimed to define a common template of a document to be given to the individual patient after the elective end of treatment therapies. The document had to fulfil the following set of requirements: i) be available on paper and digitally; ii) be written in a simple way, containing cancer history and therapy information according to a common coding scheme whenever possible; iii) provide advice and guidance on patient-specific LTFU of possible late effects according to internationally accepted standard guidelines for follow-up and care, as available and iv) be translatable to all EU languages.

Major developments included the following: first, relevant stakeholders of various European institutions and communities actively participated, and paediatric oncology late effect experts (see acknowledgements), parents' and survivors' organisations (Childhood Cancer International (CCI) and the Pan-European Network for Care of Survivors after Childhood and Adolescent Cancer (PanCare)) were actively involved. The variables summarising the details about the original cancer and associated treatments were defined for the summary section of the SurPass document. When available, internationally approved nomenclature and coding schemes were adapted for each variable. Otherwise, a specific coding system was developed.

Second, Cineca IT experts designed the electronic infrastructure for the SurPass data collection and insertion, taking into consideration security and privacy issues, the possibility of data transfer from already available clinical datasets and multilanguage support. The resulting electronic platform had to be fully compliant with the latest national and international data privacy regulations.

Third, the screening recommendations for possible late complications of treatment were developed by PanCareSurFup in collaboration with the International Guideline Harmonization Group (IGHG) (www.ighg.org/international-guideline-harmonization-group/methods/process) [16].

Finally, these components were integrated to form the SurPass structure and ready-to-use tool.

During the phase of prototype development, institutions interested in the SurPass were given a personal password to test remote data entry and built-in algorithms for defining personal recommendations. Over 50 accounts were activated, and feedback from users was then considered for further implementation and improvements. Furthermore, the possibility of automatic download from databases of the clinical trial in which the survivor was previously enrolled was also tested.

When the first SurPass prototype had been developed, a test phase was carried out at one institution (Istituto Giannina Gaslini, Italy) after ethics committee approval was granted. In this test, after obtaining informed consent from the survivor or, for those underage or lacking capacity, their parents, the SurPass was handed out to survivors during a regular late effects follow-up consultation by the treating oncologist or the late effects expert in the presence of a nurse and a psychologist. A 27-question Likert questionnaire (Supplementary Table 1) was then sent by mail 3 months after the SurPass delivery to evaluate the psychological and emotional impact on the survivor and/or their relatives.

3. Results

3.1. Treatment summary template

The SurPass data schema (Fig. 1) contains a total of 168 variables, divided into five sections: i) demographic data; ii) tumour description and other concurrent diseases, either cancer predisposition syndromes (e.g. ataxia telangiectasia) or other clinical conditions not cancer associated (e.g. diabetes) if any; iii) front-line treatment for the primary main tumour and salvage treatment in case of progression/relapse before the first elective end of treatment, with details on iiia) chemotherapy, iiib) stem cell transplantation, iiic) radiation therapy, iiid) major surgery, iiie) other relevant clinical events that occurred during treatment and iiif) medical prescriptions at the time of elective end of treatment; iv) screening recommendations and v) follow-up. Variables were translated from English into several European languages, including Croatian, Czech, Dutch, French, German, Italian, Lithuanian and Spanish, within the scope of the European project ExPO-r-Net (www.expornet.eu).

In case of a relapse or of a subsequent malignant neoplasm (SMN) after the end of first-line treatment, the SurPass may be updated by the treating physician once the new information about site and type of relapse or SMN and related salvage treatments becomes available. Individualised screening recommendations may be affected by the additional salvage treatments. Therefore, updated and adapted new screening recommendations are generated and may be integrated into the updated SurPass. Because some survivors might become lost to follow-up, a statement that 'information is updated to the best of our knowledge at the date of this document issue/update' is included.

Tumour description is based on the International Classification of Diseases for Oncology 3rd edition, 1st

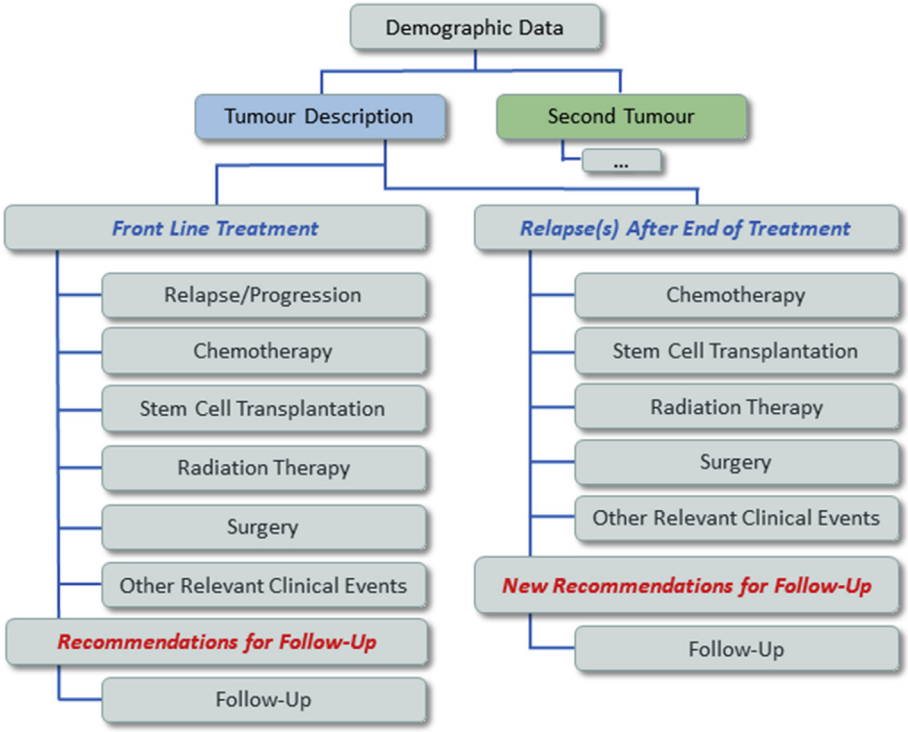

Fig. 1. Data schema of the Survivorship Passport.

version (ICD-O-3 morphology and topography), available in different languages, thanks to a licence agreement with the World Health Organization (English and French) or national groups (Spanish, Italian, German, Lithuanian and Hungarian), and the International Classification of Childhood Cancer (ICCC) 3rd edition. To facilitate understanding by survivors, an algorithm defines the most usual lay term to describe the specific tumour either using the main or extended classification table of ICCC-3. In the case of 'unspecified' or 'other' tumours in the ICCC-3 classification, the ICD-O-3 morphology term is used. Information can also be collected about somatic genetic or molecular markers of the tumour. ICD-9 or ORPHANET codes are used to identify other diseases and/or predisposing syndromes.

The Anatomical Therapeutic Chemical drug (www.atccode.com) classification has been used to identify each drug used to treat the cancer. Synonyms and/or commercial names for each compound have also been included into the system to assign drugs that might have been reported with different names (e.g. Endoxan, Cytoxan) to the same compound (cyclophosphamide).

For survivors having undergone stem cell transplantation, information on the date of the procedure, source of cells, conditioning regimen (to be included in the cumulative dose calculation of chemo-immune-radio-therapy), GVHD grade and type is included in the SurPass.

In the absence of a radiotherapy coding system, radiotherapy experts found it necessary to adapt the radiotherapy classification scheme as in use in North America (www.survivorshipguidelines.org), which is based on body regions rather than radiation fields. Because the level of detail on the treatment field varied greatly across decades, and continues to change, we drafted a three-tier scheme, where level one addresses large anatomical areas, level two whole organs, and level three defines parts of those organs. A special code was also generated for specific, commonly used large radiotherapy fields that include multiple anatomical sites (e.g. total body irradiation, mantle and inverted Y). For survivors treated many years ago, only level-one information might be available, but this is often sufficient for linkage with the current follow-up surveillance guidelines [16]. More patient-specific text, imaging or modern radiotherapy plans showing dose/volume histograms and organs at risk (OAR) can also be added as summary attachments, although such information cannot be incorporated in the standardised coding scheme at present. Details will be reported in a separate publication.

The variety and scope of surgical procedures is too complex for appropriate coding. Therefore, space (text field) for non-coded information to report about the surgical intervention and complications, if any occurred during the procedure, is provided. However, it is possible to identify organs either enucleated/amputated and/or prostheses insertion. In addition, there is space to

report on shunt application, colostomy, gastrostomy, insertion of a central venous catheter, and so on.

Information is also provided about supportive care with blood derivates (e.g. packed red cells) and date of last transfusion. In the section 'other relevant clinical events,' the SurPass allows reporting of events during treatment (e.g. seizures or admission to intensive care unit) that are considered to be important for general medical follow-up purposes.

3.2. Follow-up recommendations

Organ-specific surveillance recommendations implemented into the SurPass are based on guidelines developed by the IGHG and PanCareSurFup consortia [16]. Each organ-specific guideline defines the following: i) who needs surveillance; ii) what is the most appropriate test for screening; iii) when and at what frequency screening should be initiated and or ended and iv) what should be done if abnormalities are identified.

Subjects at risk for each outcome (e.g. cardiomyopathy, subsequent breast cancer, male or female gonadal toxicity and thyroid cancer) [17–21] are identified by using automated algorithms built into the system, which are based on the risk group definitions reported in the respective guidelines. The published LTFU care for childhood, adolescent and young adult cancer survivor guidelines can be found here http://www.ighg.org/guidelines/

The system provides the strength of the screening recommendation. According to IGHG criteria [16], four levels of strength of recommendations to enter a specific screening program are reported and highlighted with a colour code: strong (green), moderate (yellow) or weak (orange) or a recommendation not to do (red) because of the expectation of more harm than benefit of such testing. The treating physician can also assign other screening recommendations, based on survivor-specific medical history (e.g. complications during treatment). A shared decision to enter the screening program for each organ at risk identified by the system will be made by the treating physician together with the survivor and/or their parents based on the strength of recommendations, survivor's wishes, any other possible risk factor (e.g. family history) and local circumstances.

For each guideline, an organ-specific brochure has been prepared by paediatric oncologists of the PanCare network after approval by the respective guideline group (in paper and electronic format) to summarise the personal recommendations in lay language with a question-and-answer format (examples in online Figs. 1–4). A general description of the pathophysiology of the organ at risk is also included. The SurPass platform automatically suggests the recommendations to be delivered to the survivor according to the treatment received. The treating physician approves the personalised recommendations and issues the personalised SurPass, bearing the survivor's name and SurPass number. In addition, the organ-specific brochure with the survivor name and SurPass number can be printed. Each brochure is originally prepared in English and then translated into several European languages by native speakers in the affiliated consortia and/or translators of the UN Volunteers Programme (https://unv.org). The brochures are currently available in the following languages: Croatian, Czech, Dutch, English, French, German, Italian, Lithuanian and Spanish. Translations into Greek, Hungarian, Polish, Portuguese, Swedish and Hebrew are in progress.

Information regarding timing and results of screening tests performed after SurPass delivery can be uploaded by the treating physician or late-effects clinic staff into the follow-up form and stored. At each visit, the system reports the clinical summary of the previous evaluation and requests updated medical and socioeconomic history, results of physical examination and of other evaluations performed during the visit. A new summary will then be prepared by the physician, after evaluation of all new information. Any chronic condition (either newly or already diagnosed) can be reported and categorised through identification of i) system affected (e.g. cardiovascular); ii) organ or system affected (e.g. heart, vessels) and iii) details (e.g. cardiomyopathy, arrhythmia and hypertension).

3.3. IT infrastructure development

The web-based platform provides a secure online database that enables the collection and storage of all the data and images in a standard format, allowing the self-generation of the SurPass document (Fig. 2).

The web-based platform can be delivered from the Italian Cineca-certified data centre in SaaS (Software as a Service) mode or can be installed at any local data center that can guarantee compliance to security and quality standards if it is requested according to the country-related needs. In addition, personalisation can be done to activate the platform in a dedicated environment.

Fig. 3 summarises the SurPass data flow and access. Patient data can be either automatically imported from already existing electronic health records, using interoperability standards and data linkage procedures, or inserted and completed through remote data input. Personal data are encrypted, and the platform is compliant with the highest security standards (using HTTP and SSL encryption standards) and data quality procedures, according to ISO 270001 certification (https://www.cineca.it/en/content/certifications). Privacy is enforced with role-based user security (survivor, health professional and data manager), authentication, identification and authorisation mechanisms to share and store data.

Data ownership is regulated in compliance with the European Directive 2016/679, which went into effect on 25 May 2018 (GDPR): individual centres/survivors retain data ownership; the software provider must be

survivorship PASSPORT

GASLINI

encca

SIOP Europe the European Society for Paediatric Oncology

PanCareSurFup

SUMMARY OF CANCER TREATMENT

This Survivorship Passport is a short summary extracted from the information reported in the medical record. It describes the disease and its clinical course as well the treatments you received.This document does not replace the medical record that is always available at our center.

** ***** **Passport Number: IT12**509**85**

PERSONAL DATA

Date of birth	**/**/2002	**Sex**	Female

FIRST TUMOR

DIAGNOSIS

Date of diagnosis	20/09/2005
Institution	Istituto "Giannina Gaslini", Genova
Diagnosis	Nephroblastoma, NOS
Diagnosis description	Wilms' Tumor
Site	Kidney, NOS
Laterality	Left
Metastatic	No

OTHER DISEASES

Hereditary Cancer Predisposition Syndrome or medical condition cancer associated	No
Other medical conditions, not cancer associated	No

FRONT LINE TREATMENT

The treatment has been executed following	Trial/Protocol: AIEOP TW 2003	
Group/Arm/Randomization	1A	
Summary of major treatments	Chemotherapy	Yes
	Stem Cell transplantation	No
	Radiotherapy	No
	Major Surgery	Yes
Progression/relapse during frontline treatment	No	
Date of first elective end of treatment	04/11/2005	

RELAPSE AFTER FIRST ELECTIVE END OF TREATMENT

N. 1

Type of event	Relapse		
Date	08/02/2006		
Type	Local		
The salvage treatment has been executed following	Trial/Protocol: AIEOP TW 2003		
Summary of major treatments	Chemotherapy	Yes	
	Stem Cell transplantation	Yes	
	Radiotherapy	Yes	
	Major Surgery	No	
Date of end of treatment	13/06/2006		

CHEMOTHERAPY

CLINICAL COURSE

Start date	20/09/2005	**End date**	04/11/2005
	CLASSIC/TRADITIONAL ANTINEOPLASTIC AGENTS		
Drug name		**Total cumulative dose**	**Measure unit**
Vincristine		8.64 (Dose given)	mg/m2
Dactinomycin		3.9 (Dose given)	mg/m2
Intrathecal injections		No	
	OTHER ANTINEOPLASTIC AGENTS		
Hormones		No	
Immunotherapy		No	
	OTHER TREATMENTS		
Other treatments		No	

RELAPSE AFTER FIRST ELECTIVE END OF TREATMENT N. 1

N. 1

Start date	08/02/2006	**End date**	13/06/2006
	CLASSIC/TRADITIONAL ANTINEOPLASTIC AGENTS		
Drug name		**Total cumulative dose**	**Measure unit**
Etoposide		1161.29 (Dose given)	mg/m2

Fig. 2. Survivorship Passport layout and template of a hypothetical survivor.

Ifosfamide	11.61 (Dose given)	gr/m2	
Cyclophosphamide	1.29 (Dose given)	gr/m2	
Melphalan	129.03 (Dose given)	mg/m2	
Carboplatin	1725.81 (Dose given)	mg/m2	
Doxorubicin	111.29 (Dose given)	mg/m2	
Intrathecal injections	No		
OTHER ANTINEOPLASTIC AGENTS			
Hormones	No		
Immunotherapy	No		
OTHER TREATMENTS			
Other treatments	No		

STEM CELL TRANSPLANTATION

RELAPSE AFTER FIRST ELECTIVE END OF TREATMENT N. 1

N. 1

Date of transplant	27/04/2006
Type of donor	Autologous

RADIATION THERAPY EPISODE

RELAPSE AFTER FIRST ELECTIVE END OF TREATMENT N. 1

N. 1

Type of radiotherapy		External beam: Linac (Linear Accelerator) electrons			
Start date	29/05/2006	**End date**	13/06/2006		
Site (1)		Flank / hemiabdomen (top of diaphragm to iliac crest) (left)		**Dose**	20 Gy

MAJOR SURGERY

CLINICAL COURSE

N. 1

Date of surgery	20/09/2005
Surgery description	Left Nephrectomy

OTHER INFORMATION AND RELEVANT CLINICAL EVENTS DURING TREATMENT

RELAPSE AFTER FIRST ELECTIVE END OF TREATMENT N. 1

N. 1

CVC positioning	Yes
If yes, specify the site	Right jugular vein
Last transfusion date	05/05/2006

RECOMMENDATIONS FOR FOLLOW-UP

Because of the treatment you have had we have listed the tests recommended for you. This advice is because a few people who had the same treatment as you have developed problems which we hope can be picked up at an early and treatable stage.

Cardiomyopathy Screening

We think that you need regular checks on how your heart is working.

Premature Ovarian Insufficiency Surveillance

We think that you need regular checks to monitor your ovarian function.

Although the risk is greater with higher doses of treatment, it is still possible for lower doses to cause premature ovarian insufficiency in a few females.

Data are updated to the date of issue of the passport or the date of the last clinical examination certified by the physician.

GASLINI

Passport issued by ***Davide Saraceno***

Institution ***Istituto "Giannina Gaslini", Genova***

Date of issue ***28/02/2018***

Signature of the doctor in charge:

2/2

Fig. 2. (*continued*).

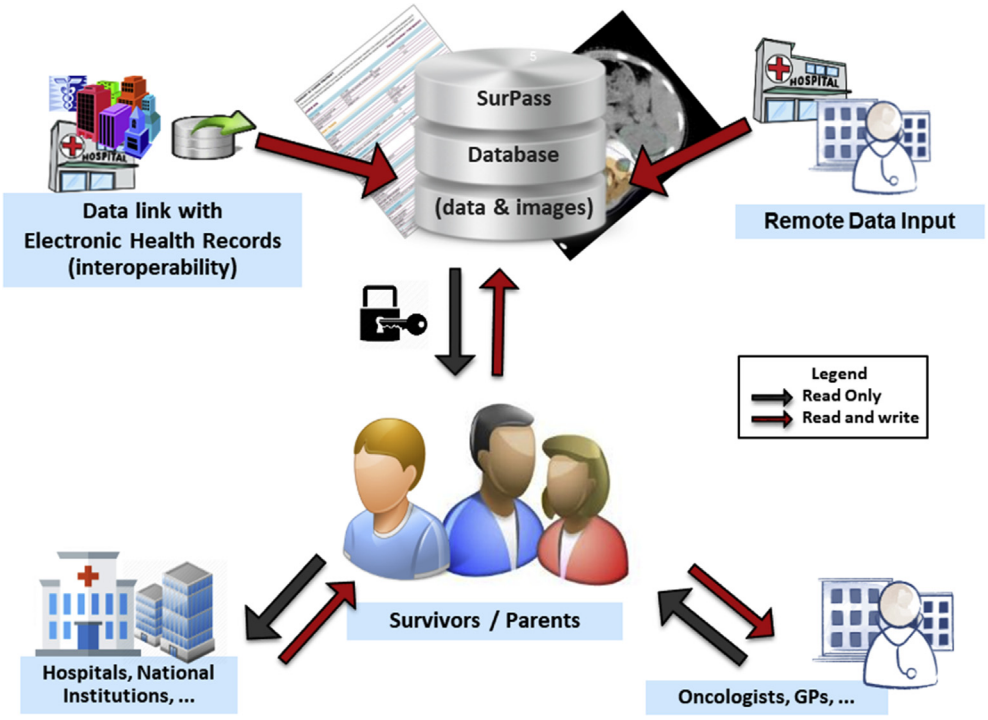

Fig. 3. Survivorship Passport data flow and access.

nominated as data processor and guarantees the correct management of the survivors' data.

When the treating physician issues the personalised SurPass and recommendations to the survivor or their parents, it is possible to activate a personal account to give the survivor access to view and/or print the electronic documents (summary treatment, brochures and any other documents uploaded on the platform such as radiotherapy files) in any of the available languages. Electronic documents can thus be shared at any time with the survivor's physicians or hospitals where they were admitted. The SurPass data can be modified only by the healthcare providers with the appropriate credentials (at this stage, only the treating physicians). It is however possible that survivors themselves can add some more information in a dedicated section of the online platform (e.g. visits, examinations, patient reported outcome measures and other tests).

3.4. Implementation and impact

The SurPass is being integrated in several paediatric cancer centres as well as in some EU Member States' National Cancer Plans. In 2015, it was included in the 5-year Austrian cancer plan for paediatrics. In 2017, the Italian Association of Paediatric Haematology and Oncology (AIEOP) approved the SurPass for use in all the AIEOP centres. Belgium, Croatia, Germany, Lithuania, Portugal and Spain are considering its implementation.

For each survivor, the treatment summary can be uploaded either manually by retrieving data from hardcopies of their clinical record or electronically by downloading data from databases used during the treatment period (e.g. electronic clinical records, databases of clinical trials in which the former patient was enrolled or cancer registries). The electronic download of data was tested in Italy, using the AIEOP-I-BFM ALL 2009 protocol. After mapping of the variables in common between the two databases, it was possible to download 61% of the requested data (72% if only mandatory fields were considered), thus reducing the average time of 1.5 h to just 30 min for preparing the SurPass for a standard risk leukemic patient.

A user manual is available either online or in paper format. The treating physicians and/or authorised personnel access the secured website (http://www.survivorshippassport.org): and login with their personal credentials. The first step is to insert the personal data of the survivor to create his or her personal record. Then, treatment data should be inserted following the predefined forms of the web-based platform. The online system performs automatic checks. After completion of the treatment summary, built-in algorithms suggest which recommendations should be given to the survivor. However, the clinician can take into account other circumstances when finalising the decision about recommendations and generating the electronic documents to be delivered to the survivor.

Between 2012 and 2015, 314 SurPass documents were delivered to CCS who had survived at least 5 years since

Table 1
Answers to selected items of the Likert questionnaire completed by 190 long-term survivors after having received the Survivorship Passport.

Question type and number	Disagree				Agree				Overall score	
	Strongly disagree N (%)	Disagree N (%)	Slightly disagree N (%)	Total disagree N (%)	Slightly agree N (%)	Agree N (%)	Strongly agree N (%)	Total agree N (%)	Mean (sd)	Median (IQ)
2. It has been useful to me to have a recapitulatory interview when I was given the Passport	0	2 (1.1)	1 (0.5)	3 (1.6)	6 (3.2)	77 (40.7)	103 (54.5)	186 (98.4)	5.5 (0.7)	6 (5–6)
3. It has been useful to me to have the possibility of talking about the disease for which I have been treated	2 (1.1)	1 (0.5)	1 (0.5)	4 (2.1)	11 (5.8)	88 (46.8)	85 (45.2)	184 (97.8)	5.3 (0.8)	5 (5–6)
6. I asked all questions in my mind because I was not embarrassed[a]	6 (3.3)	8 (4.4)	7 (3.8)	21 (11.5)	6 (3.3)	65 (35.5)	91 (49.7)	162 (88.5)	5.1 (1.3)	5 (5–6)
8. My knowledge about the possible consequences of the treatment I received has changed	22 (12.2)	61 (33.9)	8 (4.4)	91 (50.5)	26 (14.4)	43 (23.9)	20 (11.1)	89 (49.4)	3.4 (1.7)	3 (2–5)
9. My concerns about the possible complications related to the treatment I received have not increased[a]	13 (7.1)	18 (9.8)	24 (13.1)	55 (30.0)	15 (8.2)	65 (35.5)	48 (26.2)	128 (69.9)	4.3 (1.6)	5 (3–6)
11. It reassures me to know I have a personalised schedule of control examinations aimed at evaluating the possible complications of the treatment I received	0	2 (1.1)	2 (1.1)	4 (2.2)	7 (3.8)	75 (40.5)	99 (53.5)	181 (97.8)	5.4 (0.7)	6 (5–6)
13. The information I have been given prompted me to change some aspects of my life	16 (8.8)	29 (16.0)	15 (8.3)	60 (33.1)	27 (14.9)	60 (33.1)	34 (18.8)	121 (66.8)	4.1 (1.6)	5 (3–5)
14. After the examination and the interview with physicians, I do not have feelings of fear and/or anxiety that I had not before[a]	5 (2.8)	8 (4.5)	10 (5.6)	23 (12.9)	9 (5.1)	73 (41.1)	73 (41.1)	155 (87.3)	5.0 (1.2)	5 (5–6)
23. It is useful to have a written summary report on my underlying disease and on the treatment I received	0	3 (1.6)	0	3 (1.6)	1 (0.5)	54 (29.1)	128 (68.8)	183 (98.4)	5.6 (0.7)	6 (5–6)
24. The Passport has made me more aware of prevention aspects related to my health	6 (3.3)	11 (5.9)	12 (6.5)	29 (15.7)	31 (16.8)	73 (39.7)	51 (27.7)	155 (84.2)	4.7 (1.3)	5 (4–6)
27. The Passport has allowed a more effective communication with my family doctor or with physicians from other hospitals	2 (1.1)	7 (3.8)	6 (3.3)	15 (8.2)	27 (14.7)	85 (46.2)	57 (31.0)	169 (91.9)	4.9 (1.1)	5 (5–6)

[a] The original question has been reversed for ease of data reporting.

the end of treatment, were in regular follow-up and had attended the late effects clinic of Istituto Giannina Gaslini in Italy. All received the Likert questionnaire and 190 (61%) participated in the survey; details of the results will be published separately. In general (Supplemental Table 2), there were no differences in demographic, type of diagnosis and interval between SurPass delivery and date of diagnosis between those who responded and those who did not respond to the questionnaire. Respondents were 96 males and 94 females with a median age at follow-up of 17.1 years (Inter Quartile Range (IQR) 12.8–23.0) and a median follow-up since end of treatment of 9 years (IQR 6–15). The questionnaire was completed by the survivors themselves in 71 cases with a median age of 22.6 years (IQR 20.5–26.1), by the survivor and his/her parents in 56 cases with a median age of 15.6 years (IQR 13.2–18.6) and by parents in 49 cases with a median age of 11.92 years (IQR 8.1–13.1). Table 1 reports on results of selected answers to the questionnaire. Overall, 98.4% of survivors or their families agreed or strongly agreed on the benefit of receiving the SurPass. Increased awareness about their health status and need for follow-up was reported by 49.4% of the CCS, and 66.8% reported modifications in their lifestyle; 91.9% shared the SurPass with their family doctor. However, 30.1% of survivors reported some increase in anxiety related to possible health consequences [22].

4. Discussion

Evidence exists that if follow-up is extended up to early adulthood, as many as two-thirds of CCS may experience one or more chronic health condition that can be severe or life-threatening [5,1,6,23] and that the prevalence of these conditions among CCS is much higher than expected in the general population [7]. It is thus of great importance that paediatric oncologists ensure that the national health systems implement services and strategies to carefully monitor these patients well beyond the paediatric age. Primary and secondary prevention strategies need to be set up to try to avoid late effects, or at least aid their early diagnosis. These measures may improve quality of life for CCS and eventually reduce the financial burden that these chronic conditions cause for health services.

The experience of long-term survivors in Europe is extremely variable, both within a country but especially between countries [24,25]. Not all survivors, in particular those treated many years ago, are aware or have adequate information of possible late effects and of their risks. There is not enough knowledge about screening investigations (what, when and why are they necessary), and survivors report fewer contacts with experts in the field – 'don't know where to go', 'lost in follow-up' [25,26]. Nowadays, most paediatric oncologists ensure that adequate information on treatments, risks and prevention opportunities is provided to all CCS at the end of treatment and again at the time of transition to adult care [10,11]. It should, however, be recognised that the impact of the delivery of care plans in the post-treatment period still needs to be further assessed. A recent systematic review of studies addressing this issue [27] has shown only a minimal evidence of a beneficial effect that mainly refers to quality of life measures, but not on distal health outcomes. Further research is still needed since great variability was evident across the study's design as well as target population.

From this premise and with strong support of CCI members, the idea of providing a SurPass to each child and adolescent treated for cancer was developed. The initiative was further inspired by both the 'Passport for Care' (PFC) project developed by the Children's Oncology Group in the United States (www.cancersurvivor.passportforcare.org) [28] and by the Erice Statement [11], which specified that it is the responsibility of the paediatric cancer unit to provide the survivor and parents with a summary of the characteristics of the disease, of the treatments received and of the late complications that may occur.

While the PFC and SurPass are quite similar initiatives, they differ in that the SurPass has been developed to meet the needs of all European CCS and has therefore been made available in many European languages. The SurPass' strong link with the guidelines developed by the IGHG make it ideally suited for use in multiple countries. In addition, the SurPass has a built-in follow-up form, which may allow for the collection of information about the results of the screening tests during follow-up in a standardised format. This information could eventually provide statistics about the prevalence and/or incidence of chronic conditions or second malignant neoplasms in the long-term survivor population and could be used at the institutional level or shared with other national or international groups through cooperative projects.

The aim of developing the SurPass was to not only provide an online tool but also offer a personalised and integrated healthcare resource to improve the quality of life of former childhood cancer patients through more effective monitoring of their long-term health. They would be provided with guidance for their 'transition' into adult healthcare, empowering them to be responsible for their own well-being and preventing adverse events whenever possible. We hope that this tool will be appreciated in particular in this young and mobile population, which nowadays is much more likely to move either within but also between countries. Survivors own their SurPass and decide whether or not to share it with other people. In particular, we believe that the SurPass may also be a useful guide for those general practitioners who have less experience in, and knowledge about, possible late complications occurring in this relatively rare, new and growing population.

In our view, there is also some potential for the SurPass to be used for research purposes. In fact, if survivors also consent to the follow-up form, it might be possible, either at institutional or even larger level, to collect statistics about who has done what in terms of screening and the corresponding results. Statistics could then be provided about prevalence and/or incidence and analysis performed on risk factors of chronic conditions detected following evidence-based screening recommendations.

This tool has already been tested in a few institutions and has received mostly positive feedback from CCS. However, our 'customer satisfaction' questionnaire showed that although for most subjects the SurPass delivery had a positive impact, in some survivors it increased the level of anxiety related to possible side-effects. We believe that careful strategies to improve the communication of health risks are needed to avoid an unnecessary psychological burden on survivors. We plan to further build on the questionnaire and continue to evaluate the use and impact of the SurPass in each centre which will be issuing it. The SurPass should ideally not stand on its own but be an integrated part of a system of LTFU thereby assuring a point-of-contact for CCS in need of support. Communications should be tailored to each CCS taking into account their cultural, emotional, cognitive and psychological background [11]. While there is a need to communicate sensitive clinical aspects to a survivor of childhood cancer without generating unnecessary anxiety, there is also a need for clear and accurate medical language which can be understood by any healthcare professional who needs to access this information.

We recognise that the preparation of each SurPass might be quite time consuming. This is the case particularly if the treatment summary is entered manually by retrieving data from hard copies of the clinical record. However, we have shown that recovering data from databases used during the treatment period (e.g. electronic clinical records, databases of clinical trials in which the former patient was enrolled or cancer registries) is also feasible. This procedure requires that a mapping procedure be performed to associate variables between each clinical trial or institutional electronic clinical record database and the SurPass. This process may require some extra time but, once done, it can be useful for all former patients whose data are stored in that specific database.

Importantly, because of quality control issues, final data from clinical trials might not be available until several years after treatment completion. In addition, there may be data protection and informed consent issues to be considered when aiming to retrieve clinical trial data in retrospect other than initially planned. While historic radiotherapy requires manual review and entry, future developments should integrate modern electronic radiotherapy records.

International codes have been adopted wherever possible for homogeneity purposes to allow multi-language translation and to facilitate the preparation of built-in algorithms. The radiotherapy coding system we have devised is based on treatments given in the era before 1995–2000. Most longer term survivors now troubled by late effects were treated in this era at a time before it was possible to measure dose to individual organs. Similarly, current guidelines for follow-up are based on available evidence, also usually from older data. Information about the radiotherapy given to survivors treated several years ago can be imprecise, but even 'basic' information is important (e.g. to know that some radiotherapy to the chest was received). Current guidelines do not use the OAR dose to estimate the risk for a specific side-effect (e.g. secondary breast cancer) but mostly use broad areas of the body that received radiotherapy (e.g. chest). When more detailed information on exposures to certain OAR is available, this can already be uploaded into the SurPass platform. This information might be of interest in the future for clinical purposes, e.g. local tumour relapse or for new guideline-specific risk stratification and surveillance recommendations.

Another important issue we had to deal with was that the SurPass platform contains personal data that need protection according to national and international privacy regulations. Based on local/national circumstances, it is possible to have data stored in the Cineca data centre or in a local certified data centre in the country that wants to adopt the SurPass platform. Any data center should anyway guarantee the highest level standards of security and privacy according to the European Directive 2016/679. In addition, *ad hoc* solutions can be implemented in the case of constraints that are more stringent. During the ExPO-r-Net project, a pseudo-anonymisation service, called EUPID (European Patient Identity Management—https://eupid.eu), was developed by project partner Austrian Institute of Technology, and it has been integrated into the SurPass platform [29].

The European Society for Paediatric Oncology (SIOPE) has continuously supported the SurPass initiative since its inclusion in the ENCCA, ExPO-r-Net and PanCareSurFup projects and has included the SurPass in the SIOPE Strategic Plan 'A European Cancer Plan for Children and Adolescents' (https://www.siope.eu/SIOPE_StrategicPlan2015/) [30]. More importantly, SIOPE supports the European National Paediatric Haemato-Oncology Societies in liaising with health ministries to ensure that this model will be effectively adopted and introduced into national healthcare systems in Europe. The SurPass project has also been integrated in the European Reference Network for Paediatric Cancers (ERN PaedCan, paedcan.ern-net.eu) launched in December 2016. This ERN PaedCan will establish a clear framework for European healthcare providers to provide equal access to healthcare across borders and will include a virtual network of late effect experts. More recently, the SurPass initiative

was also included in the Joint Action on Rare Cancers (jointactionrarecancers.eu), which will consolidate further the guidelines on models of healthcare for survivors of childhood cancers developed by PanCare partners.

In conclusion, we believe that the implementation of this innovative tool, the SurPass, at the institutional, regional or national level will represent a sustainable solution for national healthcare systems to systematically organise LTFU care in a consistent and cost-effective way. This innovative tool can provide a more homogeneous follow-up and screening of all European CCS. This will result in more efficient use of health systems' economic resources by avoiding unnecessary examinations and possibly prevent or delay the occurrence of severe chronic conditions that might further increase the personal, socioeconomic and psychosocial burdens faced by CCS.

To obtain access to a test version of the Survivorship Passport, please contact passport@siope.eu.

Conflict of interest statement

None declared.

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The EU agencies that partially funded this project has no active role in its development but periodically supervised the progress of the project as from EU regulation.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ejca.2018.07.006.

Appendix

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