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Original Research

# European PanCareFollowUp Recommendations for surveillance of late effects of childhood, adolescent, and young adult cancer

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**Abstract** ***Background:*** Long-term follow-up (LTFU) care for childhood, adolescent, and young adult (CAYA) cancer survivors is essential to preserve health and quality of life (QoL). Evidence-based guidelines are needed to inform optimal surveillance strategies, but many topics are yet to be addressed by the International Late Effects of Childhood Cancer Guideline Harmonization Group (IGHG). Therefore, the PanCareFollowUp Recommendations Working Group collaborated with stakeholders to develop European harmonised recommendations in anticipation of evidence-based IGHG guidelines.
***Methods:*** The PanCareFollowUp Recommendations Working Group, consisting of 23 late effects specialists, researchers, and survivor representatives from nine countries, collaborated in the first Europe-wide effort to provide unified recommendations in anticipation of evidence-based guidelines. A pragmatic methodology was used to define recommendations for topics where no evidence-based IGHG recommendations exist. The objective was to describe the surveillance requirements for high-quality care while balancing the different infrastructures and resources across European health care systems. The process included two face-to-face meetings and an external consultation round involving 18 experts from 14 countries.
***Results:*** Twenty-five harmonised recommendations for LTFU care were developed collaboratively and address topics requiring awareness only (n = 6), awareness, history and/or physical examination (n = 9), or additional surveillance tests (n = 10).
***Conclusions:*** The PanCareFollowUp Recommendations, representing a unique agreement across European stakeholders, emphasise awareness among survivors and health care providers in addition to tailored clinical evaluation and/or surveillance tests. They include existing IGHG guidelines and additional recommendations developed by a pragmatic methodology and will be used in the Horizon 2020–funded PanCareFollowUp project to improve health and QoL of CAYA cancer survivors.


## 1. Introduction

Five-year survival rates of childhood, adolescent, and young adult (CAYA) cancer have increased considerably and currently exceed 80% in the majority of European countries [1,2]. The population of CAYA cancer survivors in Europe is estimated at nearly half a million and continues to increase by approximately 12,000 per year [3]. Because of their essential, but potentially toxic cancer therapies, survivors are at substantial risk for developing severe chronic health conditions, even at a young age [4–7]. The burden of these physical and psychosocial late effects on the quality of life (QoL) of survivors and their families, as well as on health care and societal resources, is significant [8–10]. Long-term follow-up (LTFU) care, including prevention, surveillance for early detection of treatable disease, and timely initiation of interventions, is fundamental to preserve health, improve QoL, and mitigate the impact of late effects on survivors and their families.

Clinical practice guidelines (CPGs) are powerful instruments that facilitate consistent, efficient, and high-quality clinical care for defined patient groups, including CAYA cancer survivors [11]. However, large variations are observed in the recommendations for survivorship care across different national and local CPG working

groups [12–15]. Over the last decade, members of the International Late Effects of Childhood Cancer Guideline Harmonization Group (IGHG) have collaborated in the development of harmonised evidence-based surveillance strategies. So far, nine IGHG guidelines for early detection and management of asymptomatic cardiomyopathy, ototoxicity, subsequent thyroid cancer, subsequent female breast cancer, subsequent central nervous system neoplasms, premature ovarian insufficiency, male gonadotoxicity, fatigue, and obstetric care have been published in peer-reviewed journals [16–24]. Furthermore, structural components of LTFU care, such as transition from paediatric to adult health care settings or models of care, have been addressed with evidence-based methods on a European level by the PanCareSurFup project [25,26] (Table 1).

At present, harmonised evidence-based recommendations are not yet available for many of the late effects, even including several of those prioritised in a Delphi consensus process among survivorship experts [11]. The lack of CPGs for many clinically relevant late effects is a potential barrier to optimal survivorship care [26]. The Pan-European Network for Care of Survivors after Childhood and Adolescent Cancer (PanCare) established the PanCareFollowUp project (www.pancarefollowup.eu/) in 2019 [27]. This is a European Horizon 2020–funded project, including the development and implementation of a person-centred model for survivorship care for adult survivors of CAYA cancer: the PanCareFollowUp Care Intervention. This intervention will be evaluated in a prospective cohort study across four European countries: the PanCareFollowUp Care Study (Table 1). Surveillance recommendations are, together with person-centred care, the cornerstones of this PanCareFollowUp Care Intervention. Therefore, one of the aims within the European PanCareFollowUp project was to complete harmonised recommendations for surveillance of late effects and survivorship care for topics that are not yet covered within IGHG, using a pragmatic methodology.

Table 1
Overview of relevant concepts, projects and organisations.

| | |
|---|---|
| International Late Effects of Childhood Cancer Guideline Harmonization Group (IGHG) | International and multidisciplinary collaboration with the aim to develop harmonised evidence-based surveillance guidelines for survivors of childhood, adolescent, and young adult cancer. |
| Pan-European Network for Care of Survivors after Childhood and Adolescent Cancer (PanCare) | European multidisciplinary network with the aim of reducing the frequency, severity, and impact of late adverse effects by establishing high-quality and sustainable survivorship care for all survivors in Europe, among others by establishing various European Union–funded research projects. |
| PanCareFollowUp project | PanCare project funded by the European Union under the Horizon 2020 framework (ongoing), with the overall aim to improve the health and quality of life of adult survivors of childhood cancer by facilitating person-centred survivorship care. |
| PanCareFollowUp Care Intervention | Person-centred model of survivorship care including surveillance recommendations, developed within the PanCareFollowUp project. |
| PanCareFollowUp Care Study | Prospective cohort study in four European countries, evaluating the PanCareFollowUp Care Intervention. |
| PanCareFollowUp Recommendations Working Group | Collaboration to develop surveillance recommendations for topics not yet addressed by the IGHG. |
| PanCareSurFup project | PanCare project funded by the European Commission under the Seventh Framework Programme (2011–2017), among others including the development of surveillance guidelines. |

## 2. Methods

### 2.1. PanCareFollowUp Recommendations Working Group

To achieve the goal of completing harmonised LTFU care recommendations for the PanCareFollowUp Care Intervention, a PanCareFollowUp Recommendations Working Group was assembled. It included 23 stakeholders (late effects specialists, researchers, and survivor representatives) representing nine European countries. It was supported by a core group (HP, LK, RK, RM, and RS) whose main tasks included drafting a methodology to identify clinically relevant topics not yet addressed by the IGHG and guiding the development of harmonised CPGs for these topics using a pragmatic approach.

### 2.2. Selection of topics

The process of topic selection is described in detail in Fig. 1. At the outset, a total of 55 late effects were identified that require LTFU strategies. Of these topics, 16 were already addressed in IGHG guidelines that are published or awaiting publication. The remaining 39 topics were included in ongoing IGHG (bone abnormalities, diabetes mellitus, dyslipidaemia, hypertension, pulmonary dysfunction, mental health disorders, overweight, renal toxicity, neurocognitive deficits, psychosocial disorders, thyroid dysfunction) or PanCareSurFup (health promotion) projects that were not expected to be finished at the start of the PanCareFollowUp Care Intervention cohort study (Care

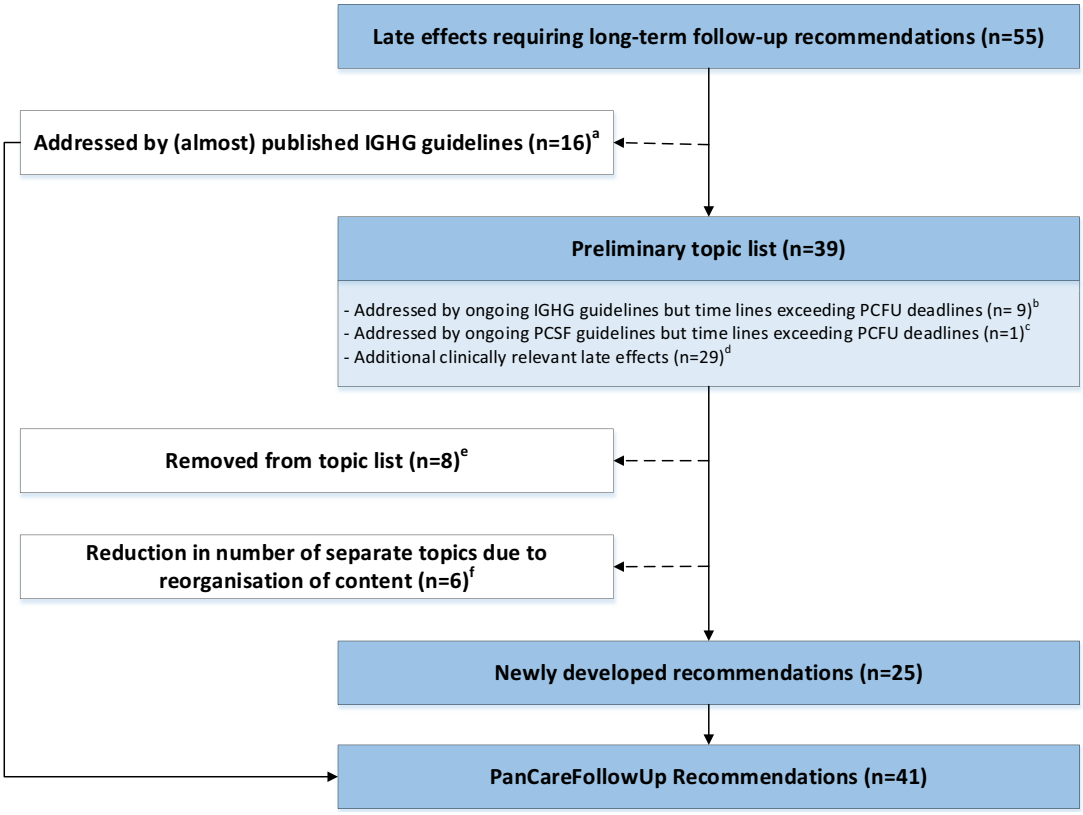


Fig. 1. **Flow chart of topic selection for the PanCareFollowUp Recommendations.** IGHG, International Late Effects of Childhood Cancer Guideline Harmonization Group; PCFU, PanCareFollowUp; PCSF, PanCareSurFup. [a]Includes the topics cardiomyopathy, breast cancer, cancer-related fatigue, central precocious puberty, coronary artery disease, CNS neoplasms, late liver injury, iron overload, hypothalamic-pituitary dysfunction, male gonadotoxicity, mental health problems, obstetric risks, ototoxicity, premature ovarian failure, psychosocial problems, and thyroid cancer. [b]Includes the topics bone abnormalities, pulmonary dysfunction, metabolic syndrome (including overweight, hypertension, diabetes and dyslipidaemia), renal toxicity, neurocognitive deficits, and thyroid dysfunction. [c]Includes the topic health promotion. [d]Includes the topics acute myeloid leukaemia or myelodysplasia, alopecia, primary adrenal insufficiency, arrhythmia, bladder cancer, bone cancer, cerebrovascular problems, cervical cancer, chronic pain, colorectal cancer, craniofacial growth disturbance, dental and oral problems, endometrial cancer, epilepsy, gastrointestinal abnormalities, lower urinary tract abnormalities, lung cancer, melanoma and non-melanoma skin cancer, oesophageal cancer, oral cancer, pericardial disease, peripheral neuropathy, prostate cancer, scoliosis, spleen problems, stomach cancer, testicular cancer, visual abnormalities, valvular disease. [e]Included in other guideline (CNS neoplasms): epilepsy. Not (sufficiently) addressed in existing guidelines: Primary adrenal insufficiency, oesophageal cancer, and stomach cancer. Existing guidelines similar to general population recommendations: endometrial cancer, cervical cancer, testicular cancer, and prostate cancer. [f]The topic cardiac problems now includes arrhythmia, valvular disease, and pericardial disease; the topic subsequent neoplasms now includes acute myeloid leukaemia or myeloid dysplasia, bladder cancer, bone cancer, lung cancer, and oral cancer.

Study) or were not yet assigned to guideline development groups. During the recommendation development process, it was decided to remove eight topics from the list because of inclusion in another guideline (n = 1), absence of recommendations regarding the topics in existing guidelines (n = 3), or recommendations that were similar to general population guidelines (n = 4). A further reduction of six topics was achieved by reorganisation of topics.

### *2.3. Pragmatic methodology for developing recommendations*

For topics where no evidence-based recommendations exist yet, an appropriate pragmatic methodology was drafted to define recommendations in anticipation of the future development of evidence-based CPGs.

First, for each of the designated topics, the recommendations of the four existing LTFU guidelines (from the North American Children's Oncology Group (COG), the Dutch Childhood Oncology Group (DCOG), the Scottish Intercollegiate Guidelines Network (SIGN), and the UK Children's Cancer and Leukaemia Group (UKCCLG)) were reviewed and compared for the following issues: (1) Who needs surveillance? (2) What surveillance modality should be used? (3) At what age or time should surveillance be initiated? (4) At what frequency should surveillance be performed? (5) When should surveillance be discontinued? and (6) What should be done when

abnormalities are identified? For late effects, which might benefit from prevention, an additional question was reviewed: (7) What standard recommendations should be given to survivors at risk? The core group drafted a PanCareFollowUp Recommendation based on the extracted information. For each recommendation, the objective was to describe the surveillance requirements for high-quality care while balancing the distinct infrastructures and resources across different European health care systems. If at least three of the existing guidelines agreed on a certain approach, it was adopted in the PanCareFollowUp Recommendations. If not all guidelines covered the late effect or if fewer than three guidelines had concordant recommendations, inclusion of the recommendation was scheduled for discussion within the Recommendations Working Group to reach consensus. To avoid bias and acknowledging the pragmatic concept, the Working Group refrained as much as possible from adding new recommendations, considering recent experiences or using single studies.

### 2.4. Internal and external consultation rounds

From June to October 2019, the Recommendations Working Group collaborated to formulate the recommendations. A 2-day face-to-face Guideline Workshop in Amsterdam, the Netherlands, was attended by 16 Working Group Members near the end of the process to review the recommendations and other overarching themes and discuss more complex topics. This was followed by an internal e-mail consultation round, a 2-day face-to-face core group meeting, and an external e-mail consultation round. Eighteen European late effects experts working in research and/or clinical care representing 14 European countries reviewed the recommendations. After revision and complementing the harmonised recommendations with existing IGHG guidelines [16–23], the PanCareFollowUp Recommendations were endorsed by all PanCareFollowUp project partners in February 2020 for use in the PanCareFollowUp project. The process of developing these recommendations is depicted in Fig. 2.

### 2.5. Considerations of the PanCareFollowUp Recommendations Working Group

Certain late effects require surveillance strategies, including diagnostic tests, but in other cases, it might be more appropriate to provide guidance by awareness only or to perform a medical history or physical examination. All these types of recommendations are included in the PanCareFollowUp Recommendations.

Several consensus decisions were made during the recommendation development process. First, the occurrence of several late effects is known or suspected to be influenced by lifestyle factors or familial risk in addition to treatment-related risk factors. Furthermore, certain late effects occur more often if the survivor was exposed at a younger age, but the four existing guidelines were often inconclusive or did not mention a specific age threshold. Both for lifestyle and hereditary risk factors as well as age thresholds, more systematic evidence-based approaches were deemed necessary before informing the surveillance recommendations. Therefore, these risk factors and specific age limits were not included in the recommendations but may nevertheless be taken into account when determining whether a survivor is at risk for a certain late effect. Second, dose effects are often assumed, but if no threshold was defined in the four existing guidelines, no new threshold was defined on consensus or single studies. Larger studies or systematic reviews are needed to appropriately address the question of above which dose threshold surveillance is needed to improve health and QoL of survivors at risk. Third, corticosteroid exposure is usually not documented in cumulative doses in clinics. A pragmatic consensus definition of relevant corticosteroid use was agreed to be "corticosteroids as anti-cancer treatment, at least 4 weeks

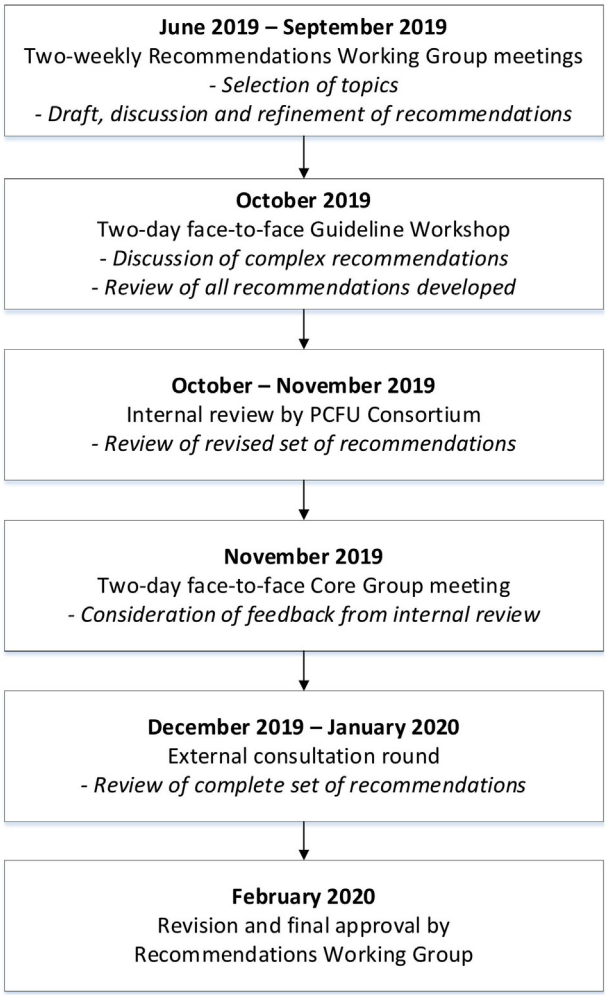


Fig. 2. Process of developing PanCareFollowUp Recommendations for topics not yet addressed by the IGHG. PCFU, PanCareFollowUp.

Table 2
Overview of harmonised recommendations developed by a pragmatic methodology and IGHG evidence-based recommendations including surveillance tests included in the PanCareFollowUp Recommendations.

| PanCareFollowUp Recommendation for surveillance of: | Who is at risk? CAYA cancer survivors treated with or with a history of … | What surveillance test should be used and at what frequency?[a] (Positive recommendations only[b]) |
|---|---|---|
| Bone problems (reduced bone mineral density)<br>*Pragmatic methodology* | - Prolonged corticosteroids as anticancer treatment, at least 4 weeks continuously<br>- Methotrexate<br>- HSCT, especially with any history of cGvHD<br>- TBI<br>- Cranial and/or spinal radiotherapy<br>- Gonadal failure<br>- GHD | - DXA scan once, if possible, and thereafter as clinically indicated<br><br>Note: It might be considered to postpone the DXA-scan in prepubertal and pubertal survivors. |
| Breast cancer (female)<br>*Updated evidence-based IGHG guideline* | - Radiotherapy ≥10 Gy to a volume exposing the breasts<br>- Upper abdominal field radiation that can extend above the diaphragm likely exposing breast tissue at a young age[c] | - Mammography and breast MRI every year if ≥25 years of age or ≥8 years from radiation, whichever occurs last |
| Cardiac problems (arrhythmia)<br>*Pragmatic methodology* | - Radiotherapy ≥15 Gy to a volume exposing the heart<br>- Anthracyclines, including doxorubicin, daunorubicin, epirubicin, idarubicin, and mitoxantrone[d] | - ECG once at entry into LTFU<br>- Repeat ECG once after the age of 18 years if entry into LTFU was at a younger age |
| Cardiac problems (cardiomyopathy)<br>*Evidence-based IGHG guideline* | - Radiotherapy to a volume exposing the heart<br>- Anthracyclines, including doxorubicin, daunorubicin, epirubicin, idarubicin, and mitoxantrone[d] | - Echocardiogram with specific attention to left ventricular systolic function, starting 2 years after treatment<br>*If treated with a total cumulative anthracycline dose[d] ≥250 mg/m², or radiotherapy ≥ 35 Gy to a volume exposing the heart, or a combination of a total cumulative anthracycline dose[d] ≥100–250 mg/m² and radiotherapy ≥15 Gy: at least every 2–3 years*<br>*If treated with a total cumulative anthracycline dose[d] ≥100–250 mg/m² or radiotherapy ≥15 Gy to a volume exposing the heart: at least every 5 years*<br>- Echocardiogram with specific attention to left ventricular function, before pregnancy or in the first trimester, if female and treated with anthracyclines and/or radiotherapy to a volume exposing the heart<br>- Screening for modifiable cardiovascular risk factors (hypertension, diabetes, dyslipidaemia, obesity, smoking, and low levels of physical activity) |
| Cardiac problems (pericardial disease)<br>*Pragmatic methodology* | - Radiotherapy ≥15 Gy to a volume exposing the heart | - Echocardiogram with specific attention to the pericardium, at least every 5 years, starting 2 years after radiotherapy |
| Cardiac problems (valvular heart disease)<br>*Pragmatic methodology* | - Radiotherapy ≥15 Gy to a volume exposing the heart | - Echocardiogram with specific attention to valvular structure and function, at least every 5 years, starting 2 years after radiotherapy |
| CNS neoplasms<br>*Evidence-based IGHG guideline; to be published* (including meningiomas, (high-grade) gliomas and other CNS neoplasms) | - Radiotherapy to a volume exposing the head or brain, including TBI | - No recommendation can be formulated for routine MRI surveillance for asymptomatic survivors; the decision to undertake MRI surveillance should be made by the CAYA cancer survivor and HCP after careful consideration of the potential harms and benefits of MRI surveillance |

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Table 2 (*continued*)

| PanCareFollowUp Recommendation for surveillance of: | Who is at risk? CAYA cancer survivors treated with or with a history of … | What surveillance test should be used and at what frequency?[a] (Positive recommendations only[b]) |
|---|---|---|
| Colorectal cancer<br>*Pragmatic methodology* | - Radiotherapy to a volume exposing the colon and rectum, including TBI | - FOBT every 3 years<br>- As an alternative surveillance method, colonoscopy might be considered every 5 years starting 5 years after radiation or at the age of 30 years, whichever occurs last |
| Coronary artery disease (asymptomatic)<br>*Evidence-based IGHG guideline; to be published* | - Radiotherapy to a volume exposing the heart | - Surveillance for modifiable cardiovascular disease risk factors (hypertension, dyslipidaemia, diabetes, overweight or obesity, smoking and low levels of physical activity) according to local or national guidelines, starting no later than the age of 40 years, and at least every 5 years subsequently[e] |
| Dyslipidaemia<br>*Pragmatic methodology* | - TBI<br>- HSCT | - Fasting lipid profile starting no later than at the age of 40 years and at least every 5 years subsequently[e] |
| Ear problems<br>*Evidence-based IGHG guideline*<br>(including hearing loss and tinnitus) | - Cisplatin (with or without carboplatin >1500 mg/m$^2$)<br>- Radiotherapy ≥ 30 Gy to a volume exposing the head or brain | *Survivors < 6 years of age at risk:*<br>- Extensive testing by audiologist every year, to begin no later than the end of treatment<br><br>*Survivors ≥ 6 years of age at risk:*<br>- Pure tone conventional audiometry testing at 1000–8000 Hz<br>- Additional testing with high frequency audiometry >8000 Hz (whenever equipment is available), to begin no later than the end of treatment<br>- Every other year if 6–12 years of age<br>- Every 5 years for adolescents and young adults ≥ 12 years of age |
| Fertility problems and sexual dysfunction (male)<br>*Evidence-based IGHG guideline*<br>(including impaired fertility, impaired spermatogenesis, testosterone deficiency, and physical sexual dysfunction) | - Alkylating agents<br>- Radiotherapy to a volume exposing the testes, including TBI<br>- Surgery to the spinal cord, sympathetic nerves, or pelvis<br>- Hypogonadism | *Postpubertal survivors treated with radiotherapy ≥ 12 Gy to a volume exposing the testes, including TBI:*<br>- Early morning testosterone at clinically appropriate time intervals<br>- LH in addition to (early morning) testosterone if clinical signs of hypogonadism, previous low or borderline testosterone concentrations, or if an early morning testosterone sample cannot be obtained at least every 2–3 years<br><br>*Postpubertal survivors at risk that desire assessment of potential for future fertility:*<br>- Semen analysis |
| HP axis problems<br>*Evidence-based IGHG guideline; to be published*<br>(including GHD, TSHD, LH/FSHD, and ACTHD) | - Radiotherapy to a volume exposing the HP region, including TBI (if ≥30 Gy, refer directly to (paediatric) endocrinologist or see in multidisciplinary team)<br>- Surgery near or within the HP region (refer directly to (paediatric) endocrinologist or see in multidisciplinary team)<br>- A CNS tumour near or within the HP region (refer directly to (paediatric) endocrinologist or see in multidisciplinary team)<br>- Hydrocephalus or CSF shunt (at risk for GHD) | *Prepubertal and peripubertal survivors at risk:*<br>- fT4, TSH, morning cortisol every year, starting 6–12 months after completion of radiotherapy or directly after hydrocephalus or CSF shunt occurrence<br><br>*Postpubertal survivors at risk:*<br>- fT4, TSH, morning cortisol, IGF-1<br>- Morning testosterone or free testosterone in survivors with overweight and LH (males)<br>- Estradiol, FSH, and LH (females) every year, starting 6–12 months after completion of radiotherapy or directly after hydrocephalus or CSF shunt occurrence |

Table 2 (*continued*)

| PanCareFollowUp Recommendation for surveillance of: | Who is at risk? CAYA cancer survivors treated with or with a history of … | What surveillance test should be used and at what frequency?[a] (Positive recommendations only[b]) |
|---|---|---|
| | | Note: an IGF-1 level even as high as 0 SDS does not rule out GHD.<br>Note: continue surveillance at least 15 years from exposure. Continuation of surveillance should be a shared decision between survivor and HCP considering available health care resources. If surveillance is terminated, the survivor should be educated about possible signs and symptoms of HP axis problems. |
| Hypertension<br>*Pragmatic methodology* | - Radiotherapy to a volume exposing the kidneys or to a volume exposing the heart and associated large vessels, including TBI<br>- Nephrectomy<br>- Ifosfamide<br>- Platinum-based chemotherapy<br>- Nitrosoureas<br>- Immunosuppressives, e.g., ciclosporin, tacrolimus, and prolonged corticosteroids as anticancer treatment (at least 4 weeks continuously) | - Blood pressure measurement at least every 2 years and at every LTFU visit |
| Impaired glucose metabolism and diabetes mellitus<br>*Pragmatic methodology* | - Radiotherapy to a volume exposing the pancreas, including TBI | - Fasting blood glucose with or without HbA1c at least every 5 years |
| Iron overload<br>*Evidence-based IGHG guideline; to be published* | - HSCT<br>- Multiple red blood cell transfusions | - Serum ferritin once at entry into LTFU |
| Late liver injury<br>*Evidence-based IGHG guideline; to be published* (including liver fibrosis or cirrhosis, hepatocellular liver injury, hepatobiliary dysfunction, biliary tract injury, or liver synthetic dysfunction) | - Radiotherapy to a volume exposing the liver, including TBI<br>- HSCT<br>- Methotrexate<br>- Mercaptopurine<br>- Thioguanine<br>- Dactinomycin<br>- Busulfan<br>- Sinusoidal obstruction syndrome<br>- cGvHD<br>- Liver surgery<br>- Chronic viral hepatitis (it is assumed that these survivors are followed by an appropriate specialist, e.g., hepatologist or infectious disease specialist, according to local or national hepatitis CPGs) | - Serum liver enzyme concentrations (ALT, AST, gGT, and ALP) once at entry into LTFU |
| Overweight and obesity<br>*Pragmatic methodology* | - A CNS tumour near or within the HP region<br>- Radiotherapy to a volume exposing the HP region, including TBI<br>- Surgery near or within the HP region | - Height, weight, and BMI at least every 2 years and at every LTFU visit |
| Precocious puberty (central)<br>*Evidence-based IGHG guideline; to be published* | - Radiotherapy to a volume exposing the HP region, including TBI (if ≥30 Gy, refer directly to [paediatric] endocrinologist or see in multidisciplinary team)<br>- Surgery near or within the HP region (refer directly to [paediatric] endocrinologist or see in multidisciplinary team)<br>- A CNS tumour near or within the HP region (refer directly to [paediatric] endocrinologist or see in multidisciplinary team)<br>- Hydrocephalus or CSF shunt | *Pre- and peri-pubertal survivors at risk:*<br>- Height velocity in relation to parental height<br>- Tanner stage every 6 months, starting 6–12 months after completion of radiotherapy or directly after hydrocephalus or CSF shunt occurrence<br><br>Note: Continue surveillance until the age of 8 years (girls) and 9 years (boys). Boys exposed to radiotherapy to the testes may have testes small for pubertal stage while in puberty. |

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Table 2 (*continued*)

| PanCareFollowUp Recommendation for surveillance of: | Who is at risk? CAYA cancer survivors treated with or with a history of … | What surveillance test should be used and at what frequency?[a] (Positive recommendations only[b]) |
|---|---|---|
| | | Instead, morning testosterone (before 10:00 AM) should be used as screening modality as testicular volume may be unreliable. |
| Premature ovarian insufficiency (female)<br>*Evidence-based IGHG guideline* (including impaired fertility, amenorrhoea, and premature menopause) | - Alkylating agents<br>- Radiotherapy to a volume exposing the ovaries, including TBI | *Pre- and peri-pubertal survivors at risk:*<br>- FSH and oestradiol[f] in case of failure to initiate or progress through puberty at least for girls aged ≥11 years and for girls with primary amenorrhoea (aged 16 years)<br><br>*Postpubertal survivors at risk:*<br>- FSH and oestradiol[f,g] in case of menstrual cycle dysfunction suggesting premature ovarian insufficiency or if assessment of potential for future fertility is desired |
| Pulmonary problems<br>*Pragmatic methodology* (including pulmonary dysfunction and worsening pulmonary fibrosis after high oxygen exposure in survivors treated with bleomycin who already have evidence of pulmonary fibrosis) | - Carmustine (BCNU)<br>- Lomustine (CCNU)<br>- Busulfan<br>- Bleomycin<br>- Radiotherapy to a volume exposing the lungs, including TBI<br>- Allogeneic HSCT<br>- Thoracic surgery | - Pulmonary function tests, including spirometry and diffusing capacity for carbon monoxide (DLCO), once at entry into LTFU |
| Renal problems<br>*Pragmatic methodology* (including glomerular and tubular dysfunction) | - Ifosfamide<br>- Cisplatin<br>- Carboplatin<br>- Radiotherapy to a volume exposing the kidney or urinary tract, including TBI<br>- Nephrectomy<br>- HSCT | *All survivors at risk:*<br>- Glomerular function testing including blood testing (creatinine), urine testing (creatinine and proteinuria), eGFR calculation, at least every 5 years<br><br>*Survivors treated with ifosfamide, cisplatin, or carboplatin:*<br>- Additional tubular function testing including blood testing (Na, K, Mg, P, Ca, phosphate, and albumin) and urine testing (glucose, phosphate) at least every 5 years<br><br>*Other advice:*<br>- Education about caution in the use of NSAIDs<br>- Counselling about single kidney-related health risks |
| Thyroid cancer<br>*Evidence-based IGHG guideline* | - Radiotherapy to a volume exposing the thyroid gland, including TBI<br>- MIBG therapy (I-131 MIBG therapy) | - Counselling regarding options for differentiated thyroid carcinoma surveillance, at least every 5 years<br><br>*If the decision to commence surveillance is made, make a shared decision for one of these two surveillance modalities*[h]:<br>- Neck palpation, every 1–2 years, starting 5 years after radiotherapy, or thyroid ultrasonography[i], every 3–5 years, starting 5 years after radiotherapy |

Table 2 (*continued*)

| PanCareFollowUp Recommendation for surveillance of: | Who is at risk? CAYA cancer survivors treated with or with a history of … | What surveillance test should be used and at what frequency?[a] (Positive recommendations only[b]) |
|---|---|---|
| Thyroid function problems<br>*Pragmatic methodology*<br>(including hypothyroidism and hyperthyroidism[j]) | - Radiotherapy to a volume exposing the thyroid gland, including TBI<br>- Radioiodine therapy (I-131 ablation therapy)<br>- MIBG therapy (I-131 MIBG therapy)[k]<br>- Allogeneic HSCT<br>- Total thyroidectomy (follow-up by an endocrinologist starting directly after surgery) | - TSH and fT4 measurement − every year in survivors aged ≤18 years and at least every 2–3 years in survivors aged >18 years<br><br>*Female survivors at risk for hypothyroidism:*<br>- Measure TSH and fT4 before attempting pregnancy and periodically during pregnancy |

Note that only the green (strong recommendation to do), yellow (moderate recommendation to do) and red (recommendation not to do) IGHG recommendations were included in the PanCareFollowUp recommendations.

ACTHD, adrenocorticotropic hormone deficiency; CAYA, childhood, adolescent, and young adult; cGvHD, chronic graft versus host disease; CPG, clinical practice guideline; CSF, cerebrospinal fluid; DXA, dual-energy X-ray absorptiometry; FOBT, faecal occult blood testing; GHD, growth hormone deficiency; HBV, hepatitis B virus; HCP, health care provider; HCV, hepatitis C virus; HP, hypothalamic-pituitary; HSCT, haematopoietic stem cell transplantation; LTFU, long-term follow-up; LH/FSHD, luteinising hormone/follicle-stimulating hormone deficiency; NSAIDs, non-steroidal anti-inflammatory drugs; RBC, red blood cell; TBI, total body irradiation; TSHD, thyroid-stimulating hormone deficiency; ULN, upper limit of normal.

[a] Surveillance should be initiated no later than 5 years after treatment or 5 years from diagnosis, depending on the individual health care systems, and surveillance should be continued life-long, unless specified otherwise.

[b] Because of a lack of benefit or insufficient evidence, certain surveillance strategies were not recommended or recommendations could not be formulated and were not included in this table. Appendix A presents the complete recommendations.

[c] For survivors treated with upper abdominal field radiation that can extend above the diaphragm likely exposing breast tissue at a young age, the surveillance decision should be an individual one, taking into account additional risk factors (patient age, family history, menopausal status, and other previous cancer treatment) and personal values regarding the potential advantages and disadvantages of surveillance.

[d] Use the following formulas to convert to doxorubicin isotoxic equivalents before calculating total cumulative anthracycline dose. Doxorubicin: multiply total dose × 1; Daunorubicin: multiply total dose × 0.6 (Feijen, 2019); Epirubicin: multiply total dose × 0.8 (Feijen, 2019); Idarubicin: multiply total dose × 5 (COG guideline); Mitoxantrone: multiply total dose × 10 (Feijen, 2019).References: EAM Feijen, WM Leisenring, KL Stratton *et al.* Derivation of anthracycline and anthraquinone equivalence ratios to doxorubicin for late-onset cardiotoxicity. JAMA Oncology. 2019; 5(6):864–871.EAM Feijen, A Font-Gonzalez, HJH van der Pal *et al.* Risk and temporal changes of heart failure among 5-year childhood cancer survivors: a DCOG-LATER study. J Am Heart Assoc. 2019; 8(1):e009122.

[e] Timing of initiation and frequency should be based on the intensity of treatment exposure, family history, presence of comorbid conditions associated with disease risk or by general risk management guidelines.

[f] If amenorrhoea, measure FSH and oestradiol randomly; if oligomenorrhoea, measure during early follicular phase (Days 2–5).

[g] This assessment should be performed after ending oral contraceptive pill/sex steroid replacement therapy use, if applicable, ideally after 2 months discontinuation.

[h] The decision to commence surveillance and which modality to use should be made by the HCP in consultation with the survivor after careful consideration of the advantages and disadvantages of differentiated thyroid carcinoma surveillance in the context of the survivor's individual preferences, practice setting, the HCP's experience and expertise of local diagnosticians (radiology). HCPs should be aware that both diagnostic tests have advantages and disadvantages and can identify benign as well as malignant nodules resulting in need for invasive procedures.

[i] Ultrasound, FNA, and/or biopsy should be performed in centres where there is experience in assessment of thyroid cancers so that appropriate interpretation of radiographic features and clinical risk factors can minimise the number of unnecessary invasive and additional diagnostic procedures. When ultrasound is used for surveillance, the cervical lymph node stations should always be visualised.

[j] Risk of hypothyroidism for all mentioned exposures. Risk of hyperthyroidism after radiotherapy to a volume exposing the thyroid gland, including TBI, or allogeneic HSCT.

[k] MIBG used for diagnostic purposes (e.g. MIBG scanning) does not put patients at risk for hypothyroidism if adequate preventive measures were used.

continuously." Professional expertise may inform whether the exposure in the individual survivor is relevant in order to use the corresponding recommendation. Finally, for some of the recommendations, especially the surveillance tests, the frequency of surveillance is well defined. For others, a more general description of frequency (e.g. "at least every 5 years," which allows for a range of yearly to 5-yearly LTFU clinic appointments) was used to accommodate the wide range of survivorship care models and customs across Europe.

When merging the existing evidence-based IGHG guidelines with the newly developed recommendations resulting in the PanCareFollowUp Recommendations, a consensus decision was made to adopt the surveillance scheme for the strong (green) and moderate (yellow) IGHG recommendations, but not the weak (orange) recommendations. The strong recommendations not to do surveillance investigations (red) were also adopted. All recommendations were coloured light blue to clarify their adapted methodological background.

## 3. Results

### 3.1. Overview of the PanCareFollowUp Recommendations

A total number of 25 recommendations were developed to complement the 16 existing IGHG evidence-based guidelines. The PanCareFollowUp Recommendations were structured according to the type of guidance or surveillance needed: awareness only (n = 5); awareness, history, and/or physical examination (n = 13); and awareness, history, and/or physical examination with surveillance tests (n = 23). An overview of those PanCareFollowUp Recommendations that include surveillance tests is presented in Table 2. The complete list of PanCareFollowUp Recommendations is provided in Appendix A.

In addition to regular surveillance, ongoing awareness and prompt reporting of new symptoms or signs were considered of the utmost importance for the early detection and timely treatment of late effects. To support the knowledge about relevant alarm symptoms, a symptom list specifying important alarm symptoms was provided in an appendix to the recommendations. Many of the recommendations therefore relied primarily on awareness, detailed history taking, and careful physical examination. In addition, a health promotion recommendation for all survivors was developed because a healthy lifestyle is an effective measure in preventing chronic health conditions and lessening the burden of both mental and physical late morbidity.

## 4. Discussion

Harmonised LTFU recommendations are urgently needed to guide optimal care for survivors of CAYA cancer. Despite ongoing international evidence-based efforts, many relevant issues are not yet addressed by an integrated approach. The recommendations developed within the PanCareFollowUp project address this gap through the first Europe-wide effort to provide unified recommendations in anticipation of evidence-based guidelines. They represent a unique agreement across European LTFU expert groups. Moreover, these recommendations have been co-developed with CAYA cancer survivor representatives from start to finish to ensure a survivor-centred approach in the recommended strategies.

The PanCareFollowUp Recommendations guide health care providers (HCPs) in providing education or surveillance to allow early detection of, and timely intervention for, adverse health effects. Importantly, they are central to the guideline-based PanCareFollowUp Care Intervention, which aims to implement person-centred survivorship care across Europe. Aside from surveillance, these PanCareFollowUp Recommendations emphasise the importance of awareness and survivor education. Knowledge about their treatment history and related risks may empower survivors to adopt a lifestyle that reduces the risk of chronic health conditions [28]. Within the PanCareFollowUp Care Intervention, the survivor-specific recommendations are translated to plain, understandable language in their individual Survivorship Care Plans. Survivors can share this information with their HCP, if desired, and consult it at a time of their own convenience.

Our pragmatic methodology does not provide the power needed to draw definitive conclusions about optimum LTFU care. Ongoing and upcoming evidence-based guidelines, as well as innovative research, are awaited to provide more informed insights into the best strategies of surveillance. Another limitation of any CPG is that they can be quickly outdated with emerging evidence. Therefore, the development of a living guideline tool that enables real-time updating of recommendations based on new evidence is included in the PanCareFollowUp project, facilitated by a platform, which will be constructed to continuously search for newly published studies. IGHG topic working groups will be regularly updated with the search results. As such, they can efficiently review new findings and decide whether adaptation of the existing recommendations is required.

Considering the fact that two-thirds of European CAYA cancer survivors currently do not have access to LTFU care [3], these recommendations already require a substantial investment of logistics and resources and may be expected to have an impressive impact on survivor's health and well-being. CPGs alone are not enough to change health care – they need to be implemented and consistently used. The PanCareFollowUp Care Study will provide deeper insight into the barriers and facilitators of guideline-based person-centred survivorship care in different European countries. This will include the evaluation of the digital Survivorship Passport tool to facilitate the process of creating a personal care plan and sharing it with a survivor's HCPs [29]. Experience with these PanCareFollowUp Recommendations in the Care Study will elucidate both effectiveness and feasibility of screening as well as potential areas of improvement.

In conclusion, the PanCareFollowUp Recommendations for LTFU care fill an important gap of current European survivorship care. Through a highly collaborative effort involving 41 late effects specialists, researchers, and survivor representatives a total of 25 harmonised recommendations were developed, with a large emphasis on awareness among survivors and HCPs, in addition to surveillance tests in those at risk. Early recognition of late effects as well as effective surveillance and treatment strategies will help alleviate the burden on survivors and their families as well as their

health care and societal resources. By providing suitable, comprehensive, and easily accessible information, survivors are supported and empowered in the self-management of their health and care. Whilst awaiting the development of internationally harmonised evidence-based CPGs, these recommendations can bridge the gap and improve survivorship care for issues relevant to survivor's health and well-being.

## Disclaimer

The material presented and views expressed here are the responsibility of the author(s) only. The EU Commission takes no responsibility for any use made of the information set out.

## Authors' contributions

R.J.v.K. contributed to writing the article, visualisation, and project administration. H.J.H.v.d.P., L.C.M.K., R.S., and R.L.M. contributed to writing the article, visualisation, project administration, and funding acquisition. All authors contributed to conceptualisation, methodology, and reviewing and editing the article.

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## Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

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## References

[1] Gatta G, Botta L, Rossi S, Aareleid T, Bielska-Lasota M, Clavel J, et al. Childhood cancer survival in Europe 1999-2007: results of EUROCARE-5–a population-based study. Lancet Oncol 2014;15(1):35–47.
[2] Trama A, Botta L, Foschi R, Ferrari A, Stiller C, Desandes E, et al. Survival of European adolescents and young adults diagnosed with cancer in 2000-07: population-based data from EUROCARE-5. Lancet Oncol 2016;17(7):896–906.
[3] Vassal G, Schrappe M, Pritchard-Jones K, Arnold F, Bassete L, Biondi A, et al. The SIOPE strategic plan: a European cancer plan for children and adolescents. J Cancer Policy 2016;8:17–32.
[4] Oeffinger KC, Mertens AC, Sklar CA, Kawashima T, Hudson MM, Meadows AT, et al. Chronic health conditions in adult survivors of childhood cancer. N Engl J Med 2006;355(15):1572–82.
[5] Geenen MM, Cardous-Ubbink MC, Kremer LC, van den Bos C, van der Pal HJ, Heinen RC, et al. Medical assessment of adverse health outcomes in long-term survivors of childhood cancer. J Am Med Assoc 2007;297(24):2705–15.
[6] Bhakta N, Liu Q, Ness KK, Baassiri M, Eissa H, Yeo F, et al. The cumulative burden of surviving childhood cancer: an initial report from the St Jude Lifetime Cohort Study (SJLIFE). Lancet 2017;390(10112):2569–82.
[7] Suh E, Stratton KL, Leisenring WM, Nathan PC, Ford JS, Freyer DR, et al. Late mortality and chronic health conditions in long-term survivors of early-adolescent and young adult cancers: a retrospective cohort analysis from the Childhood Cancer Survivor Study. Lancet Oncol 2020;21(3):421–35.
[8] Yeh JM, Hanmer J, Ward ZJ, Leisenring WM, Armstrong GT, Hudson MM, et al. Chronic conditions and utility-based health-related quality of life in adult childhood cancer survivors. J Natl Cancer Inst 2016;108(9).
[9] Frederiksen LE, Mader L, Feychting M, Mogensen H, Madanat-Harjuoja L, Malila N, et al. Surviving childhood cancer: a systematic review of studies on risk and determinants of adverse socioeconomic outcomes. Int J Cancer 2019;144(8):1796–823.
[10] Mader L, Michel G, Roser K. Unemployment following childhood cancer. Dtsch Arztebl Int 2017;114(47):805–12.
[11] Kremer LC, Mulder RL, Oeffinger KC, Bhatia S, Landier W, Levitt G, et al. A worldwide collaboration to harmonize guidelines for the long-term follow-up of childhood and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group. Pediatr Blood Cancer 2013;60(4):543–9.
[12] Dutch Childhood Oncology Group. Guidelines for follow-up in survivors of childhood cancer 5 years after diagnosis. 2010. Available at: https://www.skion.nl/workspace/uploads/richtlijn_follow-up_na_kinderkanker_deel_1_1.pdf. [Accessed 22 March 2021].
[13] UK Children's Cancer Study Group Late Effects Group. Therapy based on long-term follow up practice statement. 2005. Available at: https://www.uhb.nhs.uk/Downloads/pdf/

CancerPbTherapyBasedLongTermFollowUp.pdf. [Accessed 22 March 2021].
[14] Scottish Intercollegiate Guidelines Network. Long term follow up of survivors of childhood cancer. A national clinical guideline. 2013. Available at: https://www.sign.ac.uk/media/1070/sign132.pdf. [Accessed 22 March 2021].
[15] Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent and young adult cancers. 2019. Available at:, Version 5.0. http://www.survivorshipguidelines.org/pdf/2018/COG_LTFU_Guidelines_v5.pdf. [Accessed 22 March 2021].
[16] Armenian SH, Hudson MM, Mulder RL, Chen MH, Constine LS, Dwyer M, et al. Recommendations for cardiomyopathy surveillance for survivors of childhood cancer: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Oncol 2015;16(3):e123–36.
[17] van Dorp W, Mulder RL, Kremer LC, Hudson MM, van den Heuvel-Eibrink MM, van den Berg MH, et al. Recommendations for premature ovarian insufficiency surveillance for female survivors of childhood, adolescent, and young adult cancer: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCareSurFup Consortium. J Clin Oncol 2016;34(28):3440–50.
[18] Skinner R, Mulder RL, Kremer LC, Hudson MM, Constine LS, Bardi E, et al. Recommendations for gonadotoxicity surveillance in male childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCareSurFup Consortium. Lancet Oncol 2017;18(2):e75–90.
[19] Clement SC, Kremer LCM, Verburg FA, Simmons JH, Goldfarb M, Peeters RP, et al. Balancing the benefits and harms of thyroid cancer surveillance in survivors of childhood, adolescent and young adult cancer: recommendations from the international Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCareSurFup Consortium. Cancer Treat Rev 2018;63:28–39.
[20] Clemens E, van den Heuvel-Eibrink MM, Mulder RL, Kremer LCM, Hudson MM, Skinner R, et al. Recommendations for ototoxicity surveillance for childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCare Consortium. Lancet Oncol 2019;20(1):e29–41.
[21] van der Kooi ALF, Mulder RL, Hudson MM, Kremer LCM, Skinner R, Constine LS, et al. Counseling and surveillance of obstetrical risks for female childhood, adolescent, and young adult cancer survivors: recommendations from the International Late Effects of Childhood Cancer Guideline Harmonization Group. Am J Obstet Gynecol 2021;224(1):3–15.
[22] Christen S, Roser K, Mulder RL, Ilic A, Lie HC, Loonen JJ, et al. Recommendations for the surveillance of cancer-related fatigue in childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group. J Cancer Surviv 2020;14:923–38.
[23] Mulder RL, Hudson MM, Bhatia S, Landier W, Levitt G, Constine LS, et al. Updated breast cancer surveillance recommendations for female survivors of childhood, adolescent, and young adult cancer from the International Guideline Harmonization Group. J Clin Oncol 2020:JCO2000562.
[24] Bowers DC, Verbruggen LC, Kremer LCM, Hudson MM, Skinner R, Constine LS, et al. Surveillance for subsequent neoplasms of the CNS for childhood, adolescent, and young adult cancer survivors: a systematic review and recommendations from the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Oncol 2021;22(5):e196–206.
[25] Mulder RL, van der Pal HJH, Levitt GA, Skinner R, Kremer LCM, Brown MC, et al. Transition guidelines: an important step in the future care for childhood cancer survivors. A comprehensive definition as groundwork. Eur J Cancer 2016;54:64–8.
[26] Michel G, Mulder RL, van der Pal HJH, Skinner R, Bardi E, Brown MC, et al. Evidence-based recommendations for the organization of long-term follow-up care for childhood and adolescent cancer survivors: a report from the PanCareSurFup Guidelines Working Group. J Cancer Surviv 2019;13(5):759–72.
[27] Van Kalsbeek RJ, Van der Pal HJH, Hjorth L, Falck Winther J, Michel G, Haupt R, et al. The European multistakeholder PanCareFollowUp project: novel, person-centred survivorship care to improve care quality, effectiveness, cost-effectiveness and accessibility for cancer survivors and caregivers. Eur J Cancer 20 May 2021;153:74–85.
[28] Landier W, Skinner R, Wallace WH, Hjorth L, Mulder RL, Wong FL, et al. Surveillance for late effects in childhood cancer survivors. J Clin Oncol 2018;36(21):2216–22.
[29] Haupt R, Essiaf S, Dellacasa C, Ronckers CM, Caruso S, Sugden E, et al. The 'Survivorship Passport' for childhood cancer survivors. Eur J Cancer 2018;102:69–81.