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Long-term morbidity and health care use in childhood cancer survivors

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THE DUTCH LATER PHYSICAL OUTCOMES SET FOR SELF-REPORTED DATA IN SURVIVORS OF CHILDHOOD CANCER.

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ABSTRACT

Purposes

Studies investigating self-reported long-term morbidity in childhood cancer survivors (CCS) are using heterogeneous outcome definitions, which compromises comparability and include (un)treated asymptomatic and symptomatic outcomes. We generated a Dutch LATER core set of clinically relevant physical outcomes based on self-reported data. Clinically relevant outcomes were defined as outcomes associated with clinical symptoms or requiring medical treatment.

Methods

First, we generated a draft outcomes set based on existing questionnaires embedded in the Childhood Cancer Survivor Study, British Childhood Cancer Survivor Study and Dutch LATER study. We added specific outcomes reported by survivors in the Dutch LATER questionnaire. Second, we selected a list of clinical relevant outcomes by agreement among a Dutch LATER experts team. Third, we compared the proposed clinically relevant outcomes to the severity grading of the Common Terminology Criteria of Adverse Events (CTCAE).

Results

A core set of 74 self-reported long-term clinically relevant physical morbidity outcomes was established. Comparison to the CTCAE showed that 36% of these clinically relevant outcomes were missing in the CTCAE.

Conclusions and implications for cancer survivors

This proposed core outcome set of clinical relevant outcomes for self-reported data will be used to investigate the self-reported morbidity in the Dutch LATER study. Furthermore, this Dutch LATER outcome set can be used as a starting point for international harmonization for long-term outcomes in survivors of childhood cancer.

INTRODUCTION

The vast majority of children diagnosed with cancer nowadays will achieve long-term survival.^{1,2} Those childhood cancer survivors (CCS) are a growing, vulnerable group of individuals who are at risk of developing long-term morbidity due to previous treatment for cancer in early stages of life. Knowledge on the burden of long-term morbidity in CCS, its underlying types of health conditions and its risk factors, has been presented in various studies during the past decades.³⁻⁵

In long-term morbidity research in CCS, a broad variety of outcome assessment methods is used. Long-term morbidity outcomes can be assessed by self-reporting via questionnaires,⁶⁻²⁴ by medical evaluation during outpatient clinic visits²⁵⁻³⁴ or by linkage with existing registries such as national hospital discharge registries.³⁵⁻³⁹ Authors often include different types and different numbers of organ systems in their calculations of physical long-term morbidity.^{6-23,25-40} Also, incidence or prevalence estimates are often reported without describing which health conditions or organ systems were included in these calculations. Definitions of long-term morbidity outcomes also vary, for example, authors reporting on cardiovascular conditions generally report on heart failure, myocardial infarction and hypertension, but some also include stroke as a cardiovascular condition.^{10,14,17,18,36} While many authors do not grade the severity of the reported long-term morbidity in CCS, others use the Common Terminology Criteria for Adverse Events (CTCAE);⁴¹ either in its original form or an adapted version incorporating specific additional outcomes that authors considered missing.⁴²⁻⁴⁴ This lack of uniformity in types of outcomes, outcome definitions and outcome grading – even among studies that use similar data ascertainment methods – limits interpretation, comparability and generalizability of studies investigating the burden of long-term morbidity in CCS. Furthermore, the described outcomes in current studies include asymptomatic and symptomatic outcomes with or without treatment. To get a better insight in the overall burden for survivors the Dutch LATER questionnaire study would like to evaluate only outcomes that are symptomatic and/or requiring medical treatment.

The aim of this study is to develop a set of self-reported long-term physical outcomes that are clinically relevant for CCS, defined as morbidities with clinical symptoms and/or requiring medical treatment, to investigate the burden of morbidity in the Dutch LATER questionnaire study.

METHODS

Development of draft outcomes set based on existing questionnaires and input from survivors

Three commonly used questionnaires addressing long-term morbidity in childhood cancer survivors were used for this article; the Dutch Childhood Oncology Group – Long-Term Effects After Childhood Cancer (Dutch LATER) study questionnaire which was used in the Dutch LATER research program,⁴⁵ the Northern American Childhood Cancer Survivor Study questionnaire⁴⁶ and the British Childhood Cancer Survivor Study questionnaire.⁴⁷ See Tables S1-S3 for the respective items. In long-term morbidity research, the Childhood Cancer Survivor Study questionnaire was used either in its original form^{6-8,10,12-15,18,20,22,24,48-53} or adapted by authors for their own specific study.^{9,21,54} The questionnaires covered multiple dimensions of late side effects. For this article, we focused on self-reported physical outcomes, covered by the questionnaire sections on medical history and health conditions.

The methods of comparing the three long-term morbidity questionnaires and selection of self-reported long-term physical outcomes for CCS, is summarized in Figure 1. We condensed all outcomes from the three questionnaires into 15 categories. All but two were defined per organ system, i.e. conditions of the eye, ear, speech, cardiac, vascular, pulmonary, gastro-intestinal, hepatic, renal and urinary tract, endocrine, musculoskeletal, neurologic conditions, other conditions. In addition, surgical procedures, and malignancies were considered (Supplementary Table S4). We listed the concordances and discordances in outcomes embedded in the three aforementioned questionnaires.

The draft outcome set consisted of a selection of (concordant and discordant) outcomes. Next, we reviewed all health conditions that were reported in the open text fields by CCS participating in the Dutch-LATER questionnaire study and added these outcomes to the draft outcome set by outcome category. Temporary or self-limiting morbidities, for example urinary tract infections, pneumonia and runner's knee, were not considered as potential outcomes due to their transient nature and were, therefore, removed from the draft outcome set. Childhood cancer directed surgeries impacting CCS in later life, for example limb amputation which results in a lifelong disability or removal of an eye which results in lifelong complications, were added to the draft outcome list. Also, obesity and underweight were added because they were no self-reported outcome in the aforementioned questionnaires.

Selection of self-reported long-term physical outcomes for CCS.

The draft outcome set was reviewed in detail by the Dutch LATER-experts team, which comprised a multidisciplinary team of late effects clinicians

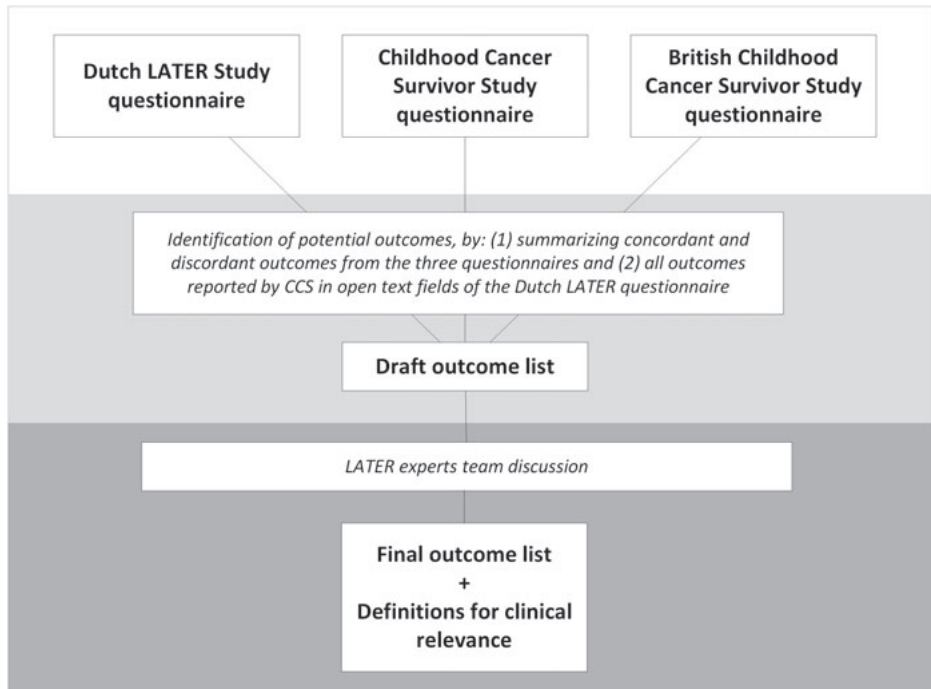


Figure 1. Overview steps followed in the process of development of patient reported outcome list for research for physical long-term morbidity in childhood cancer survivors.

(pediatric oncology and medical oncology), late effects researchers, a pediatric endocrinologist and a survivor representative, all of whom are involved in late effects research. The experts team focused on health conditions that were relevant for childhood cancer survivors; i.e. health conditions that influence their daily life, either by resulting in symptoms or by requiring medical treatment. A proposal for a core outcome set was established by agreement by two authors (N.S. and L.F.), which was discussed by the experts team in a phone meeting. During this meeting, agreement was established regarding a final core set, containing all outcomes deemed relevant for survivors.

Subsequently, for each outcome in the core set, definitions for clinical relevance were established by three authors (N.S., L.F. and L.K.), based on outcome-specific (potential) clinical symptoms and/or (potential) medical treatment. For obesity and underweight in adults, clinical relevance was defined according to the definitions used by the World Health Organization. These definitions were discussed by the experts team by e-mail, until agreement was reached for all clinical relevance criteria.

Comparison between CTCAE and the new Dutch LATER core outcome set

The CTCAE, originally developed to score acute treatment toxicities,^{41,55} is commonly used to grade the severity of outcomes in survivorship studies. This terminology comprises a five-point grading scale for many adverse events, which are defined as unfavorable and unintended signs, symptoms or disease, associated with the use of medical treatment. Severity grades rank from 1 (Mild: asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated) to 5 (Death related to adverse event).⁴¹ To gain insight in the agreement between our newly defined outcome set and CTCAE grading we added the CTCAE grade based on version 4.03 corresponding to our outcome definition for every proposed physical long-term morbidity outcome. Recently, researchers from the St. Jude Lifetime Cohort Study (SJLIFE) adjusted the CTCAE criteria to grade long-term morbidity in their cohort for which data was obtained during clinical assessment using multiple diagnostic modalities. To get insight in concordance between the CTCAE outcomes and the Dutch LATER core outcome set we compared the different lists of outcomes.

RESULTS

Selection of self-reported long-term physical outcomes of clinical relevance

The process of selection of self-reported clinically relevant physical long-term physical outcomes, as displayed in Figure 1, resulted in a core outcome set consisting of 74 proposed outcomes. The experts team decided on re-categorizing surgical procedures within their respective organ system, and did not consider conditions of speech as clinically relevant. Therefore, the 15 initial outcome categories were re-categorized into 13 proposed main organ system categories: conditions of the eye, ear, cardiac, vascular, respiratory, gastro-intestinal, hepatobiliary tract, renal and urinary tract, endocrine, musculoskeletal, nervous system conditions, other conditions, and neoplasms (see Table 1).

Agreement between the newly defined core outcome set and the CTCAE grading

For each outcome, the minimum CTCAE grades that correspond with our criteria for clinical relevance are shown in Supplementary Table S5. In all, 27 out of 74 (36%) outcomes cannot be graded according to CTCAE because they are not present in the CTCAE as a separate entity. This group of outcomes can be categorized into three subgroups. First, it comprised certain surgeries of which the LATER experts team agreed upon clinical relevance (n=18), because they influence CCS's daily life either by having medical consequences (for example splenectomy or organ transplantations) or by having cosmetic consequences (for example eye enucleation or limb amputation). Second, it comprised blindness and deafness, which are included in the CTCAE not as a specific outcome, but as grading scale for

several specific other eye and ear/nose/throat outcomes. The LATER experts team agreed that regardless of the underlying pathophysiological mechanism, blindness and deafness were both clinically relevant outcomes that should be included in the core outcome set. Third, specific outcomes that were not present as separate entities in the CTCAE were reported by CCS in the Dutch LATER questionnaire, and were perceived as clinically relevant by the experts team (n= 7): aortic aneurysm, liver cirrhosis, tubular dysfunction of the kidneys, prolactinoma, polycystic ovarian syndrome, underweight and pituitary dysfunction.

Of the remaining 48 conditions, 11 (15%) fulfilled the definition for conditions with a CTCAE grade 3, that is, severe or medically significant but not immediately life-threatening. For 27 (36%) conditions our criteria for clinical relevance corresponded with a CTCAE grade 2, moderate severity. For nine (12%) conditions (decreased pulmonary function, proteinuria, chronic kidney disease, precocious puberty, diabetes mellitus, ischemic cerebrovascular accident, transient ischemic attack, epilepsy and headache), it was not possible to define the corresponding CTCAE grade for our established clinical relevance criteria, because additional clinical information was needed for CTCAE-based grading. Comparison to the SJLIFE based grading, showed that 34 conditions from our core set were not present in SJLIFE (46%) and additional information was needed for grading of 5 conditions (7%). A total of 23 clinically relevant conditions corresponded with SJLIFE grade 2 (31%) and two clinically relevant conditions (adrenal insufficiency and growth hormone deficiency) corresponded with SJLIFE grade 1 (3%).

DISCUSSION

We present a proposal for a core set of 74 self-reported long-term physical outcomes of clinical relevance in survivors of childhood cancer. By comparison of existing survivorship questionnaires and by reviewing every specific morbidity reported by CCS in the open text fields in our Dutch nationwide questionnaire study, we followed an innovative method which focuses on outcomes that are clinically relevant for the survivor, due to the fact that its presence influences daily life. Our outcome set will be used for investigating the burden of long-term morbidity in the Dutch LATER questionnaire study. This set can also be used for international harmonization of a uniform core outcome set for long-term morbidity in CCS, to facilitate worldwide collaboration in late effects research.

Compared to other grading scales used for long-term morbidity research in CCS, the newly developed Dutch LATER core outcome set differs on three important key points. First, this core outcome set was designed with the single purpose of investigating self-reported long-term morbidity in childhood cancer survivors, by combining existing questionnaires and outcomes reported by survivors. Second,

we selected outcomes describing morbidity with clinical symptoms or requiring medical treatment, the so called clinically relevant outcomes. Third we included outcomes where the treatment for childhood cancer caused direct damage, that had persistent impact for the survivor also in later life, for example limb amputation which results in a lifelong disability or removal of an eye which results in lifelong complications. Because the CTCAE criteria were originally designed for grading acute adverse events during adult cancer trials⁵⁵ the current CTCAE version 4.03⁴¹ does not cover the complete spectrum of long-term morbidity that CCS might encounter.⁴³ Several authors have already stated that relevant outcomes were missing for CCS and use adapted versions.⁴²⁻⁴⁴ Comparison of our core set of long-term self-reported physical outcomes to the commonly used CTCAE showed that 36% of the outcomes were not present in the CTCAE. Moreover, CTCAE does not incorporate self-reported data to assess long-term morbidity.⁴³ For nine out of the 48 conditions that were present in the CTCAE, we could not perform severity grading because detailed additional clinical information was needed for appropriate grading, which was not available from current questionnaires and is often too complicated to directly ask patients in a questionnaire. Although often only health conditions grade 3 and higher are included when studying severe physical long-term morbidity in CCS, our results show that many grade 2 conditions will have consequences for a survivor because of symptoms or needed treatment. From our core outcome set, up to 27 clinically relevant outcomes corresponded with CTCAE grade 2, for example several endocrine deficiencies that require chronic medication use, and would have been missed in such studies. Comparison to the SJLIFE adapted CTCAE for grading of clinically ascertained data showed that more of our core outcomes were missing, and that 24 clinically relevant conditions corresponded to grade 2 or even grade 1. Hence, our results support previous authors, concluding that the CTCAE in its current form is not optimal to grade severity of (self-reported) long-term physical morbidity outcomes for CCS.⁴²⁻⁴⁴ To our knowledge, this is the first comprehensive proposal to define a core outcome set for self-reported long-term physical outcomes in CCS. A strength of this study is that we focused on clinical relevance for CCS. A limitation is that we were not yet able to incorporate the prioritization of outcomes by survivors. This can be the focus of future research. Also, because the purpose of this core outcome set was facilitating the investigation of physical long-term morbidity in the Dutch LATER cohort, the proposed outcome definitions reflect the agreement among the Dutch LATER experts team only. To overcome any subjectivity in outcomes used by various childhood cancer survivorship research groups, we advocate international harmonization of a core outcome set for physical long-term morbidity in childhood cancer survivors. A uniform global core outcome set is highly needed to enable comparison of future long-term morbidity studies, to uniformly evaluate survivorship care and to facilitate collaboration within survivorship research. The International Guideline Harmonization Group⁵⁶ started an initiative to develop

a harmonized outcome set by A Delphi method. This will facilitate international collaboration and data pooling.

In conclusion, we propose a Dutch LATER core set of self-reported long-term physical outcomes of clinical relevance for CCS that will be used to investigate the burden of long-term morbidity in childhood cancer survivors from the Dutch LATER questionnaire study. We advocate to start international discussion and research to harmonize long-term physical morbidity outcomes that are clinically relevant for CCS.

Table 1. Core set of self-reported long-term physical outcomes of clinical relevance for childhood cancer survivors

	Self-reported long-term physical outcome	Definition of clinical relevance
Eye disorders	Cataract	Cataract of at least one eye treated with surgery.
	Blindness	Blindness of at least one eye.
	Eye removal	Status after removal of at least one eye.
Ear conditions	Hearing loss	Hearing loss of at least one ear, requiring a hearing aid.
	Deafness	Deafness of at least one ear.
Cardiac conditions	Heart failure	Heart failure with clinical symptoms, with at least one of the following criteria: 1. requiring medication (ACE inhibitors, beta-blockers, mineralocorticoid receptor antagonists, aldosterone receptor antagonists, diuretics, angiotensine II blockers, digoxin), or 2. requiring devices (CRT-P or CRT-D, Pacemaker, ICD, LVAP, cardiac reduction surgery).
	Ischemia	Cardiac ischemia with clinical symptoms requiring intervention (angioplasty, stent, coronary bypass graft).
	Periarditis	Pericarditis with clinical symptoms, with at least one of the following criteria: 1. life-threatening consequences (haemodynamic compromise, tamponade), or 2. requiring surgical intervention (pericardectomy).
	Valvular disease	Valvular disease with clinical symptoms, with at least one of the following criteria: 1. requiring medication (ACE inhibitors, calcium channel blockers, beta-blockers, enalapril, diuretics, digoxin), or 2. requiring valve replacement or valvuloplasty.
	Arrhythmia	Arrhythmia with clinical symptoms, with at least one of the following criteria: 1. requiring medication (Beta-blockers, digoxin, calcium channel blockers, amiodarone, sotalol, flecainide, propafenone, electrolytes, anti-thrombines, anti-platelets, N-3 fatty acid and lipids), or 2. requiring device or surgical intervention (ICD, pacemaker, CRT-P, CRT-D, ablation, antiarrhythmic surgery, cardioversion).
	Heart transplantation	Status after heart transplantation.
Vascular conditions	Hypertension	Hypertension, requiring antihypertensive medication (ACE inhibitors, beta blockers, diuretics, calcium antagonists, angiotensin II antagonists, alfa blockers).
	Thrombosis	Thrombosis or a thrombo-embolic event, with at least one of the following criteria: 1. requiring chronic treatment with anti thrombotic agents, or 2. requiring surgical intervention.
	Aneurysm	The presence of an aneurysm (confirmed by medical imaging), requiring surgical intervention.

Table 1. *Continued.*

	Self-reported long-term physical outcome	Definition of clinical relevance
Respiratory conditions	Obstructive pulmonary disease	<p>Pulmonary obstructive disease (i.e. Asthma, COPD, Chronic bronchitis), with clinical symptoms, with at least one of the following criteria:</p> <ol style="list-style-type: none"> 1. requiring chronic medication (beclometason, fluticason propionate, ciclesonide, salmeterol, beclomethason/formoterol, budesonide/formoterol, Salmeterol/estril, montelukast), or; 2. requiring chronic oxygen treatment. <p>* Only intermittent therapy with acute bronchodilators is not defined as clinically relevant</p>
	Decreased pulmonary function	<p>Decreased pulmonary function confirmed by spirometry function, which results in limitations in daily life on participation level (i.e. due to the pulmonary condition unable to function in work, hobbies, household or social circumstances).</p> <p>* Asymptomatic decreased lung function without symptoms detected during routine screening is not defined as clinically relevant.</p>
	Pulmonary resection	<p>Status after surgery to remove (part of a) lung after which symptoms of decreased pulmonary function are present.</p>
	Pulmonary transplantation	<p>Transplantation of one or more lungs after which symptoms of decreased pulmonary function are present.</p>
	Other pulmonary conditions	<p>Other pulmonary conditions (including: bullae, pulmonary edema, pleuritis) with clinical symptoms, confirmed by clinical evaluation, with at least one of the following criteria:</p> <ol style="list-style-type: none"> 1. requiring medical treatment with medication or surgery, or; 2. resulting in limitations in daily life on participation level (due to the pulmonary condition unable to function in work, hobbies, household or social circumstances).
Gastro-intestinal	Gastroesophageal reflux disease	<p>Gastroesophageal reflux disease, with clinical symptoms, requiring anti acid medication.</p>
	Inflammatory bowel disease	<p>Inflammatory bowel disease (i.e. Crohn and Colitis Ulcerosa) with clinical symptoms, with at least one of the following criteria:</p> <ol style="list-style-type: none"> 1. requiring treatment with immunosuppressive medication, or; 2. Requiring surgical intervention.
	Other gastrointestinal conditions	<p>Gastro-intestinal health conditions, not otherwise specified, with clinical symptoms, causing mechanical problems (i.e. adhesions, ileus, stenosis, stoma), with at least one of the following criteria:</p> <ol style="list-style-type: none"> 1. requiring chronic tube feeding, or; 2. requiring chronic total parenteral feeding, or; 3. requiring surgical intervention, or; 4. the presence of a stoma, or; 5. the removal of (part of) the jaw.

Table 1. *Continued.*

	Self-reported long-term physical outcome	Definition of clinical relevance
Hepatobiliary conditions	Hepatitis	Chronic infection with Hepatitis B or C, with at least one of the following criteria: 1. requiring at least one of the listed medication (interferon or antiviral medication), or: 2. resulting in liver cirrhosis.
	Hemochromatosis	Hemochromatosis (iron overload), with clinical symptoms, with at least one of the following criteria: 1. requiring treatment with flebotomy or erythrocytapheresis, or: 2. requiring iron lowering medication.
	Liver cirrhosis	Cirrhosis of the liver with clinical symptoms.
	Liver transplantation	Status after liver transplantation.
	Cholecystectomy	Status after cholecystectomy.
Renal and urinary tract conditions	Tubular dysfunction	The presence of renal tubular dysfunction with clinical symptoms, resulting in electrolyte imbalance requiring medication.
	Proteinuria	Proteinuria confirmed by urine analysis, requiring treatment with medication (ACE inhibitors, thiazide diuretics).
	Chronic kidney disease	Renal insufficiency with clinical symptoms, requiring medical treatment with at least one of the following: 1. antihypertensive drugs (ACE inhibitors, Angiotensin II antagonists, diuretics), or: 2. medication for proteinuria (ACE inhibitors or thiazide diuretics), or: 3. medication for the prevention of cardiovascular complications (statins), or: 4. medication for anemia (EPO), or: 5. medication for osteodystrophia (phosphate binding medicine, active vitamin D), or: 6. medication for electrolyte deficiencies/tubular dysfunction, or: 7. dialysis, or: 8. renal transplantation.
	Urinary tract obstruction	Urinary tract obstruction with clinical symptoms, requiring surgical intervention.
	Nephrectomy	Status after the removal of at least one kidney.
	Renal transplantation	Status after transplantation of one (or more) kidney(s).
	Other conditions of kidney and urinary tract	Other conditions of kidney and urinary tract with clinical symptoms, including: 1. the presence of an urine stoma, or: 2. incontinence, requiring surgical intervention, or: 3. the need for structural catheterization, or: 4. dialysis, or: 5. removal of bladder, or: 6. elevated uric acid treated with chronic medication.
Endocrine conditions	Adrenal insufficiency ^B	Adrenal insufficiency with clinical symptoms and confirmed by laboratory testing, requiring hormonal treatment (glucocorticoids, mineralocorticoids).

Table 1. Continued.

Self-reported long-term physical outcome	Definition of clinical relevance
Hypercortisolism	Hypercortisolism (Cushings disease) with clinical symptoms and confirmed by laboratory testing, with at least one of the following criteria: 1. requiring surgical intervention, or: 2. requiring radiation therapy, or: 3. requiring post-treatment substitution therapy (hydrocortison).
Hypothyroidism ^B	Hypothyroidism with clinical symptoms and confirmed by laboratory testing requiring treatment with chronic medication (levothyroxine).
Hyperthyroidism	Hyperthyroidism with clinical symptoms and confirmed by laboratory testing, with at least one of the following criteria: 1. requiring iodine treatment (radioactive), or: 2. requiring surgical intervention (i.e. (hemi) thyroidectomy), or: 3. requiring medication (i.e. thyreostatics or thyroid suppletion therapy for iatrogenic hypothyroidism).
Estrogen deficiency ^B	Estrogen deficiency with clinical symptoms and confirmed by laboratory testing, with at least one of the following criteria: : 1. requiring treatment with transdermal estrogen, or: 2. requiring chronic medication (oral estrogen).
Testosterone deficiency ^B	Testosterone deficiency with clinical symptoms and confirmed by laboratory testing, requiring treatment with testosterone
Growth hormone deficiency ^B	Growth hormone deficiency with clinical symptoms and confirmed by laboratory testing, with at least one of the following criteria: 1. requiring medical treatment with growth hormone, or: 2. for which growth hormone treatment was indicated, but the treating physician and/or parents decided not to start this treatment because of medical contra-indications.
Hypoparathyroidism	Hypoparathyroidism with clinical symptoms and confirmed by laboratory testing, with at least one of the following criteria: 1. requiring calcium suppletion, or: 2. requiring active vitamin D3 (calcitrol or etalpa).
Hyperparathyroidism	Hyperparathyroidism with clinical symptoms and confirmed by laboratory testing, requiring surgical intervention.
Prolactinoma	Prolactinoma with clinical symptoms and confirmed by laboratory testing, with at least one of the following criteria: 1. requiring treatment with dopamine agonists, or: 2. requiring surgical treatment
Polycystic ovarian syndrome	The presence of polycystic ovarian syndrome with clinical symptoms, confirmed by imaging.

Table 1. Continued.

Self-reported long-term physical outcome	Definition of clinical relevance
Precocious puberty	Early puberty, that has been, or is currently treated with medication (puberty inhibiting medicine, i.e. GnRH analogues).
Pubertas tarda	Late puberty, that has been or is currently treated with medication (sex steroids).
Pituitary deficiency	Pituitary deficiency, with clinical symptoms and confirmed by laboratory testing, with at least one of the following criteria: 1. requiring growth hormone treatment, or: 2. requiring thyroid hormone treatment, or: 3. requiring hydrocortisone treatment, or: 4. requiring sex hormone treatment, or: 5. requiring desmopressine treatment.
Pituitary surgery	Status after surgery to the pituitary gland
Obesity	The presence of obesity according to the World Health Organization's standardized definition of obesity for adults: BMI >30, or for children > + 2 SDS in corrected for age and sex according to Dutch normative data. ^A
Underweight	The presence of underweight according to the World Health Organization's standardized definition of underweight for adults: BMI <18.5, or for children < -2 SDS corrected for age and sex according to Dutch normative data. ^A
Diabetes mellitus	Diabetes mellitus with confirmed by laboratory testing with at least one of the following criteria: 1. requiring treatment with oral antidiabetic agents, or: 2. requiring treatment with intramuscular or intravenous insulin.
Diabetes insipidus ^B	Diabetes insipidus with clinical symptoms and confirmed by laboratory testing, requiring treatment with medication (desmopressin).
Thyroidectomy	Status after (partial) thyroidectomy, after which medication use (levothyroxine) is required.
Adrenal gland removal	Status after the removal of one or two adrenal gland(s).
Ovariectomy	Status after the removal of one or more ovaria.
Orchidectomy	Status after the removal of one or more testes.
Nervous system conditions	Cerebrovascular accident – hemorrhagic
	Cerebrovascular accident – ischemic

Table 1. Continued.

	Self-reported long-term physical outcome	Definition of clinical relevance
	Transient ischemic attack	The presence of a transient ischemic attack (duration <24 hours) with clinical symptoms, requiring treatment with medication (acetylsalicylic acid, dipyridamol, statins or antihypertensive agents).
	Epilepsy	Epilepsy with clinical symptoms and confirmed by electro-encephalography, requiring treatment with medication (carbamazepine, lamotrigine, levetiracetam, oxacarbezepine, valproate, clobazepam, fenytoin, gabapentin, lacosamide, perampanel, pregabalin, topiramate, zonisamid, clonazepam).
	Headache	Headache (migraine, cluster headache) resulting in clinical symptoms treated with at least one of the following criteria: 1. requiring treatment with beta blockers, anti-epileptic medication, flunarizine, pizotifene, methysergide or candesartan (migraine), or: 2. requiring treatment with verapamil, lithuim carbonate, methysergide, pizotifene, ergotamine or prednisone (cluster headache).
	Hydrocephalus	The presence of hydrocephalus, requiring surgical intervention.
	Other neurological conditions	The presence of other neurologic conditions, with clinical symptoms, including facialis paresis, spinal cord injury, (spastic) paresis, loss of strength, disturbance of equilibrium, coordination problems, vertigo, acquired brain injury, tremor, parkinsonism, ataxia).
Muculo-skeletal conditions	Amputation	Status after the amputation of a (part of a) limb, excluding fingers and toes
	Deformities	The presence of at least one of the following major deformities (scoliosis, kyohosis, lordosis or spondylolisthesis) with clinical symptoms.
	Osteoporosis	Osteoporosis confirmed with a DEXA scan, requiring treatment with chronic medication (bisphosphanates, estrogen receptor modulators or parathyroid hormone).
	Other musculoskeletal conditions	At least one of the following conditions with clinical symptoms: arthritis (bacterial, gout, reactive, rheumatoid arthritis), arthrosis, osteonecrosis, epiphysiolysis, with at least one of the following criteria: 1. requiring medication (allopurinol, benzbromaron, leflunomide, methotrexate, sulfasalazine, infliximab, adalimumab, ethanercept, certolizumab, anti-IL1, anti-CD80, anti-CD86, aurothiomalaat, ciclosporin, hydroxychloroquinine, cyclophosphamide), or: 2. requiring therapy using intra-articular injection(s), or: 3. requiring joint replacement surgery, or: 4. requiring arthrodesis surgery.
Neoplasms	Malignant neoplasms	Malignant neoplasms of any kind.

Table 1. *Continued.*

	Self-reported long-term physical outcome	Definition of clinical relevance
Other conditions	Dermatological conditions	Dermatological conditions with clinical symptoms and that require systematic treatment.
	Hysterectomy	Status after the removal of the uterus.
	Prostatectomy	Status after the removal of the prostate.
	Mastectomy	Status after the removal of one or more breast(s).
	Splenectomy	Status after splenectomy.

^A In this study we used Dutch population based normative data for children below 18 years. For international harmonization we recommend using Child Growth Standards from the World Health Organization.

^B When this hormonal deficiency is the result of pituitary dysfunction, it is categorized separately as "Pituitary deficiency".

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Supplementary Table S1. Translation of the DCOG-LATER questionnaire section on medical information

Question	Answer options
B1. You have been treated in childhood for childhood cancer or a related condition. Did you afterwards get another form of cancer, leukemia or a tumor, or are you currently diagnosed with it?	
	Yes/No
- Yes/No	Yes/No
B2. If yes, please report the organ/body part, type of tumor and age at diagnosis or year of diagnosis.	
- Organ/Body part	Open text field
- Type of tumor	Open text field
- Age at diagnosis or year of diagnosis	Open text field
B3. Please fill in in the diagram below whether you have had one of the following conditions	
If yes, please note age at diagnosis or year of diagnosis and whether you use medication for this condition at the moment.	
<i>If you currently use medication for this condition, please note the name of the medication and the age or year in which you started using it in question B4.</i>	
a. Myocardial infarction	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
b. Angina pectoris (during exercise or in rest)	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
c. Valvular condition	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
d. Pericarditis	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
e. Cardiomyopathy	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
f. Heart failure	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No

Supplementary Table S1. *Continued.*

Question	Answer options
g. Arrhythmia	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
h. Congenital heart disease	
- Have you had this condition or do you currently have this condition?	Yes/No
- Open text field for reporting the specific condition	Open text field
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
i. Other heart disease	
- Have you had this condition or do you currently have this condition?	Yes/No
- Open text field for reporting the specific condition	Open text field
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
k. Stroke (cerebrovascular accident/cerebral infarction/cerebral hemorrhage)	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
l. Transient ischemic attack	
- Have you had this condition or do you currently have this condition?	Yes/No
- Open text field for reporting the specific condition	Open text field
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
m. Vascular conditions	
- Have you had this condition or do you currently have this condition?	Yes/No
- Open text field for reporting the specific condition	Open text field
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
n. Conditions leading to enhanced coagulation (thrombosis)	
- Have you had this condition or do you currently have this condition?	Yes/No
If yes: which condition?	
■ Protein C deficiency	Tick box
● What was the age at diagnosis or year of diagnosis?	Open text field
● Are you currently using medication for this condition?	Yes/No
■ Protein S deficiency	Tick box
● What was the age at diagnosis or year of diagnosis?	Open text field
● Are you currently using medication for this condition?	Yes/No

Supplementary Table S1. *Continued.*

Question	Answer options
<ul style="list-style-type: none"> ■ Factor V Leiden mutation 	Tick box
<ul style="list-style-type: none"> ● What was the age at diagnosis or year of diagnosis? 	Open text field
<ul style="list-style-type: none"> ● Are you currently using medication for this condition? 	Yes/No
<ul style="list-style-type: none"> ■ Other 	Tick box
<ul style="list-style-type: none"> ● Open text field for reporting the specific condition 	Open text field
<ul style="list-style-type: none"> ● What was the age at diagnosis or year of diagnosis? 	Open text field
<ul style="list-style-type: none"> ● Are you currently using medication for this condition? 	Yes/No
<hr/>	
n. Hypertension	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
<hr/>	
o. Hypercholesterolemia	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
<hr/>	
p. Gastro-intestinal problems	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
<hr/>	
q. Pulmonary conditions	
- Have you had this condition or do you currently have this condition?	Yes/No
- Open text field for reporting the specific condition	Open text field
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
<hr/>	
r. Period of cough with a duration of over 6 weeks	
- Have you had this condition or do you currently have this condition?	Yes/No
- Are you currently using medication for this condition?	Yes/No
<hr/>	
s. Infections of the respiratory tract over 3 times a year	
- Have you had this condition or do you currently have this condition?	Yes/No
- Are you currently using medication for this condition?	Yes/No
<hr/>	
t. Urinary tract infections, accompanied by fever (pyelonephritis)	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- If yes: how often?	
<ul style="list-style-type: none"> ■ 1 time 	Tick box
<ul style="list-style-type: none"> ■ 2-5 times 	Tick box
<ul style="list-style-type: none"> ■ Over 5 times 	Tick box

Supplementary Table S1. *Continued.*

Question	Answer options
u. Other kidney problems (for example malfunction of kidneys, kidney stones, proteinuria, cysts)	
- Have you had this condition or do you currently have this condition?	Yes/No
- Open text field for reporting the specific condition	Open text field
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
v. Adrenal problems	
- Have you had this condition or do you currently have this condition?	Yes/No
- Open text field for reporting the specific condition	Open text field
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
w. Liver problems, specified:.....	
- Have you had this condition or do you currently have this condition?	Yes/No
- Open text field for reporting the specific condition	Open text field
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
x. Musculoskeletal problems (for example arm/leg/elbow/knee)	
- Have you had this condition or do you currently have this condition?	Yes/No
- Open text field for reporting the specific condition	Open text field
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
y. Diabetes Mellitus	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
z. Seizures	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
aa. Diagnosed with cataract	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
bb. Using a hearing aid	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No

Supplementary Table S1. *Continued.*

Question	Answer options
cc. Ringing in the ears	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
dd. Experiencing (or experienced) reduced growth (short stature)	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
ee. Impaired thyroid function (hypothyroidism)	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
ff. Increased thyroid function (hyperthyroidism)	
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
gg. Thyroid nodule	Yes/No
- Have you had this condition or do you currently have this condition?	Yes/No
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
hh. Other thyroid condition	
- Have you had this condition or do you currently have this condition?	Yes/No
- Open text field for reporting the specific condition	Open text field
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
ii. Other problem with hormonal regulation	
- Have you had this condition or do you currently have this condition?	Yes/No
- Open text field for reporting the specific condition	Open text field
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No
jj. Other health condition	
- Have you had this condition or do you currently have this condition?	Yes/No
- Open text field for reporting the specific condition	Open text field
- What was the age at diagnosis or year of diagnosis?	Open text field
- Are you currently using medication for this condition?	Yes/No

Supplementary Table S1. *Continued.*

Question	Answer options
B4. Please note which medicines you are currently using for the conditions listed in question B3 and at what age or in which year you started taking them? <i>If you do not know the name of the medicine, please enter the name of the disorder from B3 followed by “don’t know”.</i>	
- Medication name (room for multiple answers)	Open text field
- For which health condition	Open text field
- Start use: age or year	Open text field
B5. Are you currently using other medicines or injections in addition to the medicines that you may have mentioned above? For example, painkillers that you use more than once a week (eg aspirin, paracetamol, Ibuprofen) or hormones.	
- Yes/No	Yes/No
B6. If yes, which medication do you use and at what age or in which year did you start taking them?	
- Medication name	Open text field
- Start use: age or year	Open text field
B7. Have you ever undergone one or more of the following treatment(s) or surgical procedure(s)?	
- Did you ever undergo a replacement of a heart valve?	Yes/No
- Did you undergo this surgery?	Yes/No
- What was the age at surgery or year of surgery?	Open text field
- Did you ever undergo any other heart surgery (including heart catheterization)?	
- Did you undergo this surgery?	Yes/No
- Open text field for reporting the specific type of surgery	Open text field
- What was the age at surgery or year of surgery?	Open text field
- Did you ever have a pacemaker/ICD?	
- Did you undergo this surgery?	Yes/No
- What was the age at surgery or year of surgery?	Open text field
- Have you ever had an organ transplantation?	
- Did you undergo this surgery?	Yes/No
- Open text field for reporting which organ	Open text field
- What was the age at surgery or year of surgery?	Open text field
- Have you ever had an organ/arm/leg removed?	
- Did you undergo this surgery?	Yes/No
- Open text field for reporting the organ/limb	Open text field
- What was the age at surgery or year of surgery?	Open text field

This table provides an English translation of all the questions in the DCOG-LATER questionnaire, addressing physical long-term morbidity (question B1 – B7).

Supplementary Table S2. Other questionnaires addressing long-term morbidity in childhood cancer survivors: the Childhood Cancer Survivor Study questionnaire.

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
7. We would like to know all of the drugs and medications that you have taken during THE LAST 2 YEARS, THAT IS SINCE THE DATE EXACTLY 2 YEARS AGO. We are interested in only those tablets, pills, syrups, injections, patches and creams that were prescribed by a doctor, and which you took regularly for MORE THAN ONE MONTH, or for a total of 30 DAYS OR MORE IN A YEAR.	
7a. Antibiotics such as amoxicillin, penicillin, erythromycin, cephalixin or others	Yes/No/Not sure
Names of drugs	Open text field
7b. Testosterone (male hormones) such as Sustanon or others	Yes/No/Not sure
Names of drugs	Open text field
7c. Thyroid medications such as Thyroxine or others	Yes/No/Not sure
Names of drugs	Open text field
7d. Other medications to replace body hormones such as growth hormone, steroid hormones (hydrocortisone), DDAVP or others	Yes/No/Not sure
Names of drugs	Open text field
7e. Medication for Diabetes such as insulin, metformin (Glucophage), glibenclamide, gliclazide or others	Yes/No/Not sure
Names of drugs	Open text field
7f. Muscle relaxants such as baclofen (Lioresal), dantrolene (Dantrium) or others	Yes/No/Not sure
Names of drugs	Open text field
7g. Prescribed pain killers such as Solpadol, Tylex, diclofenac, naproxen, dihydrocodeine, morphine or others	Yes/No/Not sure
Names of drugs	Open text field
7h. Prescribed nutritional supplements such as iron tablets, magnesium, potassium, sodium bicarbonate, vitamin D or others	Yes/No/Not sure
Names of drugs	Open text field
7i. Anti-epileptic (anti-seizure) drugs such as phenytoin (Epanutin), carbamazepine (Tegretol), sodium valproate (Epilem), lamotrigine (Lamictal), ethosuximide (Zarontin), phenobarbitone or others	Yes/No/Not sure
Names of drugs	Open text field
7j. Drugs for high blood pressure or for your heart such as atenolol, captopril, enalapril, digoxin, frusemide or others	Yes/No/Not sure
Names of drugs	Open text field
7k. Prescribed antacids (for excess stomach acid or ulcers) such as cimetidine (Tagamet), ranitidine (Zantac),omeprazole (Losec) or others	Yes/No/Not sure
Names of drugs	Open text field

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
7l. Chemotherapy or Immune suppressants such as prednisolone, azathioprine, cyclosporin or others	Yes/No/Not sure
Names of drugs	Open text field
7m. Antidepressants or other prescribed drugs for depression or other mood disorders such as dothiepin (Prothiaden), amitriptyline, fluoxetine (Prozac), lithium or others	Yes/No/Not sure
Names of drugs	Open text field
7n. Other prescribed drugs	Yes/No/Not sure
Names of drugs	Open text field
The questions in this section ask about medical conditions you might have had which were confirmed by a doctor, nurse or other medical professional.	
Has a doctor, nurse or other medical professional ever confirmed you have, or have had:	
8. Brain and nervous system	
8a. Cerebral palsy?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8b. Paralysis of any kind?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
8c. Mental retardation?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8d. Epilepsy?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8e. Repeated seizures, fits, convulsions, or blackouts?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8f. Migraine?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8g. Other frequent headaches?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
8h. Problems with balance, equilibrium or ability to reach for, or manipulate, objects?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8i. Tremors or problems with movements?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8j. Weakness or inability to move your arm(s)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8k. Weakness or inability to move your leg(s)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8l. Decreased sense of touch or feeling in your hands, fingers, arms or legs?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8m. Prolonged pain or abnormal sensation in arms, legs or back?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8n. Problems chewing or swallowing solids or liquids?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8o. Any other brain or nervous system problems?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
9. Kidneys, bladder and other urinary tract conditions	
9a. Kidney stones?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
9b. REPEATED kidney infections?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
9c. REPEATED bladder infections?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
9d. Dialysis?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
9e. Any other kind of kidney or urinary tract disorder?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
10. Digestive system	
10a. Gallstones?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10b. Any other gallbladder trouble?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
10c. Cirrhosis of the liver?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10d. Hepatitis?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10e. Jaundice?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10f. Any other liver trouble?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
10g. An ulcer?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10h. Any disease of the oesophagus?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
10i. FREQUENT indigestion?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10j. FREQUENT heartburn?	
Yes/No/Not sure	Yes/No/Not sure
IF yes: did you take medication for it for more than once a month?	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10k. Any other stomach trouble?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
10l. Intestinal polyps?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10m. Diverticular disease?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10n. Colitis?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10o. FREQUENT constipation?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10p. Chronic diarrhoea?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10q. Rectal or anal fistula?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10r. Rectal or anal stricture (narrowing or scarring)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10s. Any other digestive problems?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
11. Hormonal system	
11a. An <u>over</u> active thyroid gland (hyperthyroid)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11b. An <u>under</u> active thyroid gland (hypothyroid)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11c. Thyroid nodules?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11d. Other thyroid enlargements?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11d. Diabetes - controlled with diet? ^A	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11e. Diabetes - controlled with pills or tablets?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11f. Diabetes - controlled with insulin injections?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11g. Lack of growth hormone?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11h. Have you ever received injections of growth hormone?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11i. Osteoporosis, brittle, weak or fragile bones?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11j. Did you need medication to go into puberty?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
11k. Any other hormonal problems?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
12. Lungs and breathing	
12a. Bronchitis?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12b. Hay fever?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12c. Recurrent sinus infections?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12d. Tonsillitis or enlargement of the tonsils or adenoids?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12e. Pleurisy (inflammation of the lining of the lung)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12f. Asthma?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12g. Abnormal chest wall?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12h. Chronic cough or shortness of breath for more than a month?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12i. Have you ever had a need for extra oxygen?	
Yes/No/Not sure	Yes/No/Not sure
IF yes: are you currently using extra oxygen?	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12j. Pneumonia 3 or more times in the past 2 years?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
12k. Emphysema?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12l. Lung fibrosis or "scarring" of the lung?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12m. Any other breathing or lung problems?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
13. Heart and circulatory system	
13a. Rheumatic heart disease?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13b. Hardening of the arteries or arteriosclerosis?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13c. Irregular heart beat or palpitations, (Arrhythmia) requiring medication or follow-up by a doctor?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13d. Congestive heart failure or cardiomyopathy (weak heart muscle)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13e. A myocardial infarction (heart attack)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13f. Coronary heart disease?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13g. A heart murmur?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13h. Hypertension (high blood pressure) <u>not</u> requiring medication?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
13i. Hypertension (high blood pressure) requiring medication?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13j. A stroke or a cerebrovascular accident?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13k. Angina pectoris (chest pains due to lack of oxygen to heart requiring medication such as Glyceryl Trinitrate sometimes known as GTN)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13l. Pericarditis or fluid around the heart?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13m. Pericardial constriction (scarring or tightness of the sac around the heart)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13n. Stiff or leaking heart valves?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13o. Heart catheterisation?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13p. Biopsy of the heart muscle?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13q. Blood clot in head, lung, arm, leg or pelvis?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13r. Does exercise cause severe chest pain, shortness of breath, or irregular heart beat?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13s. Have you seen a cardiologist (heart specialist)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
13t. Has anyone in your immediate family (biological mother, father, brothers, sisters) had a heart attack before the age of 55?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13u. Any other heart or circulatory problems?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
14. Hearing, vision, speech and taste	
14a. Hearing loss requiring a hearing aid?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14b. Deafness in one or both ears not completely corrected by a hearing aid?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14c. Complete deafness in either ear?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14d. Tinnitus or ringing in the ears?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14e. Persistent dizziness or vertigo?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14f. Problems hearing sounds, words, or language in crowds?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14g. Any other hearing problems?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
14h. Registered as blind?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14i. Cataracts?	
Yes/No/Not sure	Yes/No/Not sure

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
Please give age when it started (in years)	Open text field
14j. Glaucoma (excess pressure in the eyeball)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14k. Problems with double vision?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14l. A detached retina or any other condition of the retina?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
14m. Any other trouble seeing with one or both eyes even when wearing glasses?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14n. Very dry eyes requiring eye drops or ointment?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14o. Short-sightedness (Myopia)	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14p. Long-sightedness (Hypermetropia)	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14q. Any other eye problems?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
14r. Stammering or stuttering?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14s. Any other speech defects?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
14t. Abnormal sense of taste?	
Yes/No/Not sure	Yes/No/Not sure

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
Please give age when it started (in years)	Open text field
14u. Loss of taste or smell which lasted for 3 months or more?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
15. It is important to know whether some forms of medical treatment in childhood affect a man's potential to father a child.	
15a. Has a doctor ever told you that you might have problems fathering a child?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
15b. Have you ever had medical tests (such as a blood test, ultrasound or sperm count) to see whether or not you might have problems fathering a child?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
15c. Have you ever been told that you have a low sperm count?	
16. please indicate if you have ever had any of the following types of surgery and give your approximate age when you first had each type of operation. Please also indicate which types of surgery you never had by ticking the no box.	
16a. Amputation of an arm, leg, hand, foot, finger or toe?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
16b. Scoliosis surgery (insertion of rods or other methods to straighten the spine)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16c. Other surgery of your spinal cord or spine?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
16d. Leg lengthening or shortening operations?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16e. Joint replacement operations?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
16f. Other bone surgery?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16g. Coronary artery bypass surgery?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16h. Pericardiectomy (stripping of the sac around the heart)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16i. Angioplasty (enlarging a heart vessel using a balloon)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16j. Other heart surgery?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
16k. Surgery for intestinal obstruction (blocked intestines)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16l. Colostomy or ileostomy (stool going into a bag)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16m. Reconnection after a colostomy or ileostomy?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16n. Surgery to remove a blood clot in an artery or vein?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
16o. Removal of the thyroid gland in your neck?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16p. Removal of your spleen?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
16q. Ventriculoperitoneal shunt (tube from the brain to the abdomen, under the skin, which removes excess spinal fluid)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16r. Breast surgery for removal or biopsy of a suspicious lump?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16s. A bronchoscopy since your therapy stopped?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16t. Other lung surgery?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
16u. A liver biopsy since your therapy stopped?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16v. Reconstructive surgery (surgery to repair damage due to an accident or medical therapy or other surgery)?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
16w. A heart transplant?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16x. A lung transplant?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16y. A kidney transplant?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16z. A bone marrow transplant?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S2. *Continued.*

Childhood Cancer Survivor Study questionnaire	
Question	Answer options
17a. Other organ transplant?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
17b. Cataract surgery?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
17c. Sinus surgery?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
17d. Surgery on your jaw?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
17e. Any other surgery?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
18a. Did your childhood cancer, leukaemia, tumour or similar illness ever come back (recur or relapse) after it was first treated?	
Yes/No	Yes/No
If yes, please give details of the first time it came back after the first treatment	
- Date doctor confirmed illness has come back	DD/MM/YYYY
- Doctor's name	Open text field
- Hospital name	Open text field
- Hospital address	Open text field
18b. Apart from your original childhood cancer, leukaemia, tumour or similar illness, have you ever been diagnosed with any OTHER cancer, leukaemia or tumour?	
Yes/No	Yes/No
If yes, please give details of the first time it came back after the first treatment	
- Date doctor confirmed illness has come back	Open text field
- Illness diagnosed	DD/MM/YYYY
- Doctor's name	Open text field
- Hospital name	Open text field
- Hospital address	Open text field

^A Question no. 11.b was numbered twice in the original Childhood Cancer Survivor Study questionnaire.

Supplementary Table S3. Other questionnaires addressing long-term morbidity in childhood cancer survivors: the British Childhood Cancer Survivor Study questionnaire.

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
7. We would like to know all of the drugs and medications that you have taken during THE LAST 2 YEARS, THAT IS SINCE THE DATE EXACTLY 2 YEARS AGO. We are interested in only those tablets, pills, syrups, injections, patches and creams that were prescribed by a doctor, and which you took regularly for MORE THAN ONE MONTH, or for a total of 30 DAYS OR MORE IN A YEAR.	
7a. Antibiotics such as amoxicillin, penicillin, erythromycin, cephalixin or others	Yes/No/Not sure
Names of drugs	Open tekst field
7b. Testosterone (male hormones) such as Sustanon or others	Yes/No/Not sure
Names of drugs	Open tekst field
7c. Thyroid medications such as Thyroxine or others	Yes/No/Not sure
Names of drugs	Open tekst field
7d. Other medications to replace body hormones such as growth hormone, steroid hormones (hydrocortisone), DDAVP or others	Yes/No/Not sure
Names of drugs	Open tekst field
7e. Medication for Diabetes such as insulin, metformin (Glucophage), glibenclamide, gliclazide or others	Yes/No/Not sure
Names of drugs	Open tekst field
7f. Muscle relaxants such as baclofen (Lioresal), dantrolene (Dantrium) or others	Yes/No/Not sure
Names of drugs	Open tekst field
7g. Prescribed pain killers such as Solpadol, Tylex, diclofenac, naproxen, dihydrocodeine, morphine or others	Yes/No/Not sure
Names of drugs	Open tekst field
7h. Prescribed nutritional supplements such as iron tablets, magnesium, potassium, sodium bicarbonate, vitamin D or others	Yes/No/Not sure
Names of drugs	Open tekst field
7i. Anti-epileptic (anti-seizure) drugs such as phenytoin (Epanutin), carbamazepine (Tegretol), sodium valproate (Epilim), lamotrigine (Lamictal), ethosuximide (Zarontin), phenobarbitone or others	Yes/No/Not sure
Names of drugs	Open tekst field
7j. Drugs for high blood pressure or for your heart such as atenolol, captopril, enalapril, digoxin, furosemide or others	Yes/No/Not sure
Names of drugs	Open tekst field
7k. Prescribed antacids (for excess stomach acid or ulcers) such as cimetidine (Tagamet), ranitidine (Zantac),omeprazole (Losec) or others	Yes/No/Not sure
Names of drugs	Open tekst field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
7l. Chemotherapy or Immune suppressants such as prednisolone, azathioprine, cyclosporin or others	Yes/No/Not sure
Names of drugs	Open tekst field
7m. Antidepressants or other prescribed drugs for depression or other mood disorders such as dothiepin (Prothiaden), amitriptyline, fluoxetine (Prozac), lithium or others	Yes/No/Not sure
Names of drugs	Open tekst field
7n. Other prescribed drugs	Yes/No/Not sure
Names of drugs	Open tekst field
The questions in this section ask about medical conditions you might have had which were confirmed by a doctor, nurse or other medical professional.	
Has a doctor, nurse or other medical professional ever confirmed you have, or have had:	
Brain and nervous system	
8a. Cerebral palsy?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8b. Paralysis of any kind?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
8c. Mental retardation?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8d. Epilepsy?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8e. Repeated seizures, fits, convulsions, or blackouts?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8f. Migraine?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8g. Other frequent headaches?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
8h. Problems with balance, equilibrium or ability to reach for, or manipulate, objects?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8i. Tremors or problems with movements?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8j. Weakness or inability to move your arm(s)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8k. Weakness or inability to move your leg(s)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8l. Decreased sense of touch or feeling in your hands, fingers, arms or legs?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8m. Prolonged pain or abnormal sensation in arms, legs or back?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8n. Problems chewing or swallowing solids or liquids?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
8o. Any other brain or nervous system problems?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
Kidneys, bladder and other urinary tract conditions	
9a. Kidney stones?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
9b. REPEATED kidney infections?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
9c. REPEATED bladder infections?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
9d. Dialysis?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
9e. Any other kind of kidney or urinary tract disorder?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
Digestive system	
10a. Gallstones?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10b. Any other gallbladder trouble?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
10c. Cirrhosis of the liver?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10d. Hepatitis?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10e. Jaundice?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10f. Any other liver trouble?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
10g. An ulcer?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
10h. Any disease of the oesophagus?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
10i. FREQUENT indigestion?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10j. FREQUENT heartburn?	
Yes/No/Not sure	Yes/No/Not sure
IF yes: did you take medication for it for more than once a month?	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10k. Any other stomach trouble?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
10l. Intestinal polyps?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10m. Diverticular disease?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10n. Colitis?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10o. FREQUENT constipation?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10p. Chronic diarrhoea?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10q. Rectal or anal fistula?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
10r. Rectal or anal stricture (narrowing or scarring)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
10s. Any other digestive problems?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
Hormonal system	
11a. An <u>over</u> active thyroid gland (hyperthyroid)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11b. An <u>under</u> active thyroid gland (hypothyroid)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11c. Thyroid nodules?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11e. Other thyroid enlargements?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11d. Diabetes - controlled with diet? ^A	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11e. Diabetes - controlled with pills or tablets?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11f. Diabetes - controlled with insulin injections?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11g. Lack of growth hormone?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11h. Have you ever received injections of growth hormone?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11i. Osteoporosis, brittle, weak or fragile bones?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
11j. Did you need medication to go into puberty?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
11k. Any other hormonal problems?	
Yes/No/Not sure	Yes/No/Not sure
Please describe:	Open text field
Please give age when it started (in years)	Open text field
Lungs and breathing	
12a. Bronchitis?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12b. Hay fever?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12c. Recurrent sinus infections?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12d. Tonsillitis or enlargement of the tonsils or adenoids?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12e. Pleurisy (inflammation of the lining of the lung)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12f. Asthma?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12g. Abnormal chest wall?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12h. Chronic cough or shortness of breath for more than a month?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12i. Have you ever had a need for extra oxygen?	
Yes/No/Not sure	Yes/No/Not sure
IF yes: are you currently using extra oxygen?	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
12j. Pneumonia 3 or more times in the past 2 years?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12k. Emphysema?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12l. Lung fibrosis or "scarring" of the lung?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
12m. Any other breathing or lung problems?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
Heart and circulatory system	
13a. Rheumatic heart disease?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13b. Hardening of the arteries or arteriosclerosis?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13c. Irregular heart beat or palpitations, (Arrhythmia) requiring medication or follow-up by a doctor?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13d. Congestive heart failure or cardiomyopathy (weak heart muscle)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13e. A myocardial infarction (heart attack)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13f. Coronary heart disease?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13g. A heart murmur?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
13h. Hypertension (high blood pressure) <u>not</u> requiring medication?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13i. Hypertension (high blood pressure) requiring medication?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13j. A stroke or a cerebrovascular accident?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13k. Angina pectoris (chest pains due to lack of oxygen to heart requiring medication such as Glyceryl Trinitrate sometimes known as GTN)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13l. Pericarditis or fluid around the heart?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13m. Pericardial constriction (scarring or tightness of the sac around the heart)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13n. Stiff or leaking heart valves?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13o. Heart catheterisation?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13p. Biopsy of the heart muscle?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13q. Blood clot in head, lung, arm, leg or pelvis?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13r. Does exercise cause severe chest pain, shortness of breath, or irregular heart beat?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
13s. Have you seen a cardiologist (heart specialist)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13t. Has anyone in your immediate family (biological mother, father, brothers, sisters) had a heart attack before the age of 55?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
13u. Any other heart or circulatory problems?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
Hearing, vision, speech and taste	
14a. Hearing loss requiring a hearing aid?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14b. Deafness in one or both ears not completely corrected by a hearing aid?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14c. Complete deafness in either ear?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14d. Tinnitus or ringing in the ears?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14e. Persistent dizziness or vertigo?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14f. Problems hearing sounds, words, or language in crowds?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14g. Any other hearing problems?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
14h. Registered as blind?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
14i. Cataracts?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14j. Glaucoma (excess pressure in the eyeball)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14k. Problems with double vision?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14l. A detached retina or any other condition of the retina?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
14m. Any other trouble seeing with one or both eyes even when wearing glasses?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14n. Very dry eyes requiring eye drops or ointment?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14o. Short-sightedness (Myopia)	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14p. Long-sightedness (Hypermetropia)	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14q. Any other eye problems?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
14r. Stammering or stuttering?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14s. Any other speech defects?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
14t. Abnormal sense of taste?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
14u. Loss of taste or smell which lasted for 3 months or more?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
It is important to know whether some forms of medical treatment in childhood affect a man's potential to father a child.	
15a. Has a doctor ever told you that you might have problems fathering a child?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
15b. Have you ever had medical tests (such as a blood test, ultrasound or sperm count) to see whether or not you might have problems fathering a child?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
15c. Have you ever been told that you have a low sperm count?	
16. please indicate if you have ever had any of the following types of surgery and give your approximate age when you first had each type of operation. Please also indicate which types of surgery you never had by ticking the no box.	
16a. Amputation of an arm, leg, hand, foot, finger or toe?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
16b. Scoliosis surgery (insertion of rods or other methods to straighten the spine)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16c. Other surgery of your spinal cord or spine?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
16d. Leg lengthening or shortening operations?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16e. Joint replacement operations?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
16f. Other bone surgery?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16g. Coronary artery bypass surgery?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16h. Pericardiectomy (stripping of the sac around the heart)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16i. Angioplasty (enlarging a heart vessel using a balloon)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16j. Other heart surgery?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
16k. Surgery for intestinal obstruction (blocked intestines)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16l. Colostomy or ileostomy (stool going into a bag)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16m. Reconnection after a colostomy or ileostomy?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16n. Surgery to remove a blood clot in an artery or vein?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
16o. Removal of the thyroid gland in your neck?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16p. Removal of your spleen?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
16q. Ventriculoperitoneal shunt (tube from the brain to the abdomen, under the skin, which removes excess spinal fluid)?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16r. Breast surgery for removal or biopsy of a suspicious lump?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16s. A bronchoscopy since your therapy stopped?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16t. Other lung surgery?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
16u. A liver biopsy since your therapy stopped?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16v. Reconstructive surgery (surgery to repair damage due to an accident or medical therapy or other surgery)?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
16w. A heart transplant?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16x. A lung transplant?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16y. A kidney transplant?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
16z. A bone marrow transplant?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field

Supplementary Table S3. *Continued.*

British Childhood Cancer Survivor Study questionnaire	
Question	Answer options
17a. Other organ transplant?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
17b. Cataract surgery?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
17c. Sinus surgery?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
17d. Surgery on your jaw?	
Yes/No/Not sure	Yes/No/Not sure
Please give age when it started (in years)	Open text field
17e. Any other surgery?	
Yes/No/Not sure	Yes/No/Not sure
If yes: please describe	Open text field
Please give age when it started (in years)	Open text field
18a. Did your childhood cancer, leukaemia, tumour or similar illness ever come back (recur or relapse) after it was first treated?	
Yes/No	Yes/No
If yes, please give details of the first time it came back after the first treatment	
- Date doctor confirmed illness has come back	DD/MM/YYYY
- Doctor's name	Open text field
- Hospital name	Open text field
- Hospital address	Open text field
18b. Apart from your original childhood cancer, leukaemia, tumour or similar illness, have you ever been diagnosed with any OTHER cancer, leukaemia or tumour?	
Yes/No	Yes/No
If yes, please give details of the first time it came back after the first treatment	
- Date doctor confirmed illness has come back	Open text field
- Illness diagnosed	DD/MM/YYYY
- Doctor's name	Open text field
- Hospital name	Open text field
- Hospital address	Open text field

^A Question no. 11.b was numbered twice in the original British Childhood Cancer Survivor Study questionnaire.

Supplementary Table S4. Summary of all outcomes embedded in the three selected questionnaires

	DCOG LATER	CCSS	BCSS	Concordant discordant	Present in the draft outcome list (yes/no) ^A
Eye					
Cataract	X	X	X	Concordant	Yes
Blind		X (registered as blind)	X (registered as blind)	Discordant	Yes
Glaucoma		X	X	Discordant	No
Double vision		X	X	Discordant	No
Detached retina		X	X	Discordant	No
Other retina condition		X	X	Discordant	No
(very) Dry eyes		X	X	Discordant	No
Other trouble seeing with one or both eyes		X	X	Discordant	No
Myopia		X	X	Discordant	No
Hypermetropia		X	X	Discordant	No
Other eye problems		X	X	Discordant	No
Ear					
Hearing loss		X (requiring hearing aid)	X (requiring hearing aid)	Discordant	Yes
Hearing aid	X			Discordant	No
Deafness		X	X	Discordant	Yes
Tinnitus	X	X	X	Concordant	No
Dizziness		X	X	Discordant	No
Problems hearing sounds/words/language in crowds		X	X	Discordant	No
Speech					
Stammering/stuttering		X	X	Discordant	No
Other speech defects		X	X	Discordant	No
Abnormal sense of taste		X	X	Discordant	No
Loss of taste for 3 months or more		X	X	Discordant	No

Supplementary Table S4. *Continued.*

	DCOG LATER	CCSS	BCSS	Concordant discordant	Present in the draft outcome list (yes/no) ^A
Cardiac					
Myocardial infarction	X	X	X	Concordant	Yes (Cardiac ischemia)
Coronary heart disease		X	X	Discordant	No
Angina pectoris	X	X	X	Concordant	Yes (Cardiac ischemia)
Valvular condition	X	X (stiff or leaking valves)	X (stiff or leaking valves)	Concordant	No
Pericarditis	X	X	X	Concordant	No
Pericardial constriction		X	X		No
Cardiomyopathy	X	X (congestive heart failure or cardiomyopathy)	X	Concordant	No
Heart failure	X	X (congestive heart failure or cardiomyopathy)		Concordant	Yes
Arrhythmia	X	X	X	Concordant	Yes
Congenital heart disease	X			Discordant	No
Rheumatic heart disease		X	X	Discordant	No
Arteriosclerosis		X	X	Discordant	No
Murmur		X	X	Discordant	No
Heart catheterisation		X	X	Discordant	No
Biopsy of heart muscle		X	X	Discordant	No
Heart failure during pregnancy or after delivery (females)		X		Discordant	No
Other heart disease	X	X	X	Concordant	No
Does exercise cause chest pain/shortness of breath/irregular heartbeat		X	X	Discordant	No
Have you seen a cardiologist		X	X	Discordant	No
Has anyone in your family had a heart attack before age of 55		X	X	Discordant	No

Supplementary Table S4. Continued.

	DCOG LATER	CCSS	BCSS	Concordant discordant	Present in the draft outcome list (yes/no) ^A
Vascular					
Vascular conditions in general	X			Discordant	No
Blood clot in lung/arm/leg/pelvis		X	X	Discordant	Yes (thrombosis)
Hypertension	X	X	X	Concordant	Yes
Conditions leading to enhanced coagulation	X			Discordant	No
Hypercholesterolemia	X			Discordant	No
Pulmonary					
Pulmonary conditions in general	X			Discordant	No
Cough	X	X (chronic cough or shortness of breath for greater than one month)	X (chronic cough or shortness of breath for greater than one month)	Concordant	No
Respiratory tract infections over 3 times a year	X			Discordant	No
Recurrent sinus infections		X	X	Discordant	No
Tonsillitis or enlargement of tonsils or adenoids		X	X	Discordant	No
Bronchitis		X	X	Discordant	No
Pneumonia 3 or more times past 2 years		X	X	Discordant	No
Hay Fever		X	X	Discordant	No
Pleurisy		X	X	Discordant	No
Asthma		X	X	Discordant	Yes (obstructive pulmonary disease)
Abnormal chest wall		X	X	Discordant	No
Need for extra oxygen		X	X	Discordant	No
Emphysema		X	X	Discordant	No
Lung fibrosis		X	X	Discordant	No
Other breathing problems		X	X	Discordant	No

Supplementary Table S4. *Continued.*

	DCOG LATER	CCSS	BCSS	Concordant discordant	Present in the draft outcome list (yes/no) ^A
Gastro-intestinal					
Gastro-intestinal conditions in general	X			Discordant	No
Ulcer		X	X	Discordant	No
Disease of esophagus		X	X	Discordant	No
Frequent indigestion		X	X	Discordant	No
Frequent heartburn (medication)		X	X	Discordant	Yes (gastro-intestinal reflux)
Other stomach trouble		X	X	Discordant	No
Intestinal polyps		X	X	Discordant	No
Diverticular disease		X	X	Discordant	No
Colitis		X	X	Discordant	No
Drequent constipation		X	X	Discordant	No
Chronic diarrhea		X	X	Discordant	No
Rectal or anal fistula		X	X	Discordant	No
Rectal stricture		X	X	Discordant	No
Other digestive problems			X	Discordant	Yes
Liver					
Conditions of the liver in general	X			Discordant	No
Gallstones		X	X	Discordant	No
Other gallbladder trouble		X	X	Discordant	No
Cirrhosis of the liver		X	X	Discordant	Yes
Hepatitis		X	X	Discordant	Yes
Jaundice		X	X	Discordant	No
Other liver trouble		X	X	Discordant	No

Supplementary Table S4. Continued.

	DCOG LATER	CCSS	BCSS	Concordant discordant	Present in the draft outcome list (yes/no) ^A
Renal and urinary tract					
Renal and urinary tract conditions in general	X			Discordant	No
Pyelonephritis	X	X (repeated kidney infections)	X (repeated kidney infections)	Concordant	No
Repeated bladder infections		X	X	Discordant	No
Kidney stones		X	X	Discordant	No
Dialysis		X	X	Discordant	No
Other kind of kidney or urinary tract disorder		X	X	Discordant	No
Endocrine					
Adrenal problems	X			Discordant	Yes
Diabetes mellitus	X	X (diet/pills/insulin injections)	X (diet/pills/insulin injections)	Concordant	Yes
Lack of growth hormone		X	X	Discordant	Yes
Injections of growth hormone		X	X	Discordant	No
Short stature	X			Discordant	No
Hypothyroidism	X	X	X	Concordant	Yes
Hyperthyroidism	X	X	X	Concordant	Yes
Thyroid nodule	X	X	X	Concordant	No
Other thyroid Enlargement		X	X	Discordant	No
Other thyroid problem	X			Discordant	No
Osteoporosis		X	X	Discordant	No
Medication to go into puberty		X	X	Discordant	Yes
Problems with fertility		X	X	Discordant	No
Has a doctor told you might have trouble having children		X	X	Discordant	No
Have you ever had medical tests to see whether you might have trouble having children		X	X	Discordant	No

Supplementary Table S4. *Continued.*

	DCOG LATER	CCSS	BCSS	Concordant discordant	Present in the draft outcome list (yes/no) ^A
Have you ever been told you have a low sperm count (males)		X	X	Discordant	No
Have you ever had a menstrual period (female)		X	^A	Discordant	No
Are you currently having menstrual periods (female)		X	^A	Discordant	No
Have you ever taken female hormones including birth control pills to have your period (female)		X	^A	Discordant	No
Other problem with hormonal regulation	X	X	X	Concordant	No
Musculoskeletal					
Musculoskeletal problems in general	X			Discordant	Yes
Neurological					
Stroke	X (Cerebrovascular accident, Cerebral infarction)	X (classified as heart and circulatory system)	X (classified as heart and circulatory system)	Concordant	Yes
Transient Ischemic Attack	X			Discordant	Yes
Seizures	X	X	X	Concordant	No
Epilepsy		X	X	Discordant	Yes
Cerebral palsy		X	X	Discordant	No
Paralysis of any kind		X	X	Discordant	No
Mental retardation		X	X	Discordant	No
Migraine		X	X	Discordant	No
Headache		X	X	Discordant	Yes
Problems with balance		X	X	Discordant	No
Tremors		X	X	Discordant	No
Weakness		X	X	Discordant	No
.....					

Supplementary Table S4. *Continued.*

	DCOG LATER	CCSS	BCSS	Concordant discordant	Present in the draft outcome list (yes/no) ^A
Decreased sense/touch	X		X	Discordant	No
Prolonged pain	X		X	Discordant	No
Problems chewing/swallowing	X		X	Discordant	No
Other brain or nervous system problem	X		X	Discordant	No
Nervousness	X			Discordant	No
Faintness or dizziness	X			Discordant	No
Pains in heart or chest	X			Discordant	No
Thoughts on ending your life	X			Discordant	No
Suddenly scared for no reason	X			Discordant	No
Feeling lonely	X			Discordant	No
Feeling blue	X			Discordant	No
Feeling to interest in things	X			Discordant	No
Feeling fearful	X			Discordant	No
Feelings being easily hurt	X			Discordant	No
Nausea or upset stomach	X			Discordant	No
Trouble getting your breath	X			Discordant	No
Hot or cold spells	X			Discordant	No
Numbness or tingling in parts of your body	X			Discordant	No
Feeling hopeless about the future	X			Discordant	No
Feeling weak in parts of your body	X			Discordant	No
Feeling tense or keyed up	X			Discordant	No
Spells of terror or panic	X			Discordant	No
Feeling so restless you couldn't sit at all	X			Discordant	No
Feelings of worthlessness	X			Discordant	No
Pain	X			Discordant	No
Anxieties	X			Discordant	No

Supplementary Table S4. *Continued.*

	DCOG LATER	CCSS	BCSS	Concordant discordant	Present in the draft outcome list (yes/no) ^A
Surgical procedures					
Coronary artery bypass surgery		X	X	Discordant	No
Pericardectomy		X	X	Discordant	No
Angioplasty		X	X	Discordant	No
Replacement of heart valve	X			Discordant	No
Surgery to remove a blood clot in an artery or vein		X	X	Discordant	No
Pacemaker/ICD	X			Discordant	No
Other heart surgery	X	X	X	Concordant	No
Removal of organ	X			Discordant	Yes
Removal of arm/leg	X	X (also only hand/foot)	X (also only hand/foot/finger/toe)	Concordant	Yes
Scoliosis surgery		X	X	Discordant	No
Other surgery to the spinal cord or spine			X	Discordant	No
Leg lengthening or shortening procedures		X	X	Discordant	No
Joint replacement		X	X	Discordant	No
Other bone surgery		X	X	Discordant	No
Surgery for intestinal obstruction		X	X	Discordant	No
Colostomy		X	X (or ileostomy)	Discordant	No
Takedown of the colostomy or ileostomy		X	X	Discordant	No
Removal of the thyroid gland in the neck		X	X	Discordant	No
Removal of the spleen		X	X	Discordant	Yes
Ventriculoperitoneal shunt		X	X	Discordant	No
Breast surgery		X	X	Discordant	No
Bronchoscopy		X	X	Discordant	No
Other lung surgery		X	X	Discordant	No

Supplementary Table S4. Continued.

	DCOG LATER	CCSS	BCSS	Concordant discordant	Present in the draft outcome list (yes/no) ^A
Liver biopsy		X	X	Discordant	No
Reconstructive surgery		X	X	Discordant	No
Heart transplant		X	X	Discordant	Yes
Lung transplant		X	X	Discordant	Yes
Kidney transplant		X	X	Discordant	Yes
Bone marrow transplant		X	X	Discordant	No
Organ transplantation (other)	X	X	X	Concordant	No
Cataract surgery		X	X	Discordant	No
Sinus surgery		X	X	Discordant	No
Surgery on the jaw		X	X	Discordant	No
Other surgery		X	X	Discordant	No
Other					
Other conditions in general	X			Discordant	No
Cancer, leukemia or tumors					
Cancer, leukemia or tumors	X	X	X	Concordant	Yes

^A only male list available online.

Supplementary Table S5. Core set of long-term self-reported physical outcomes that are clinically relevant for CCS, and correspondence to Common Terminology Criteria of Adverse Events (CTCAE) severity grading.

	Long-term self-reported physical outcome	Minimum corresponding CTCAE grade	Minimum corresponding SJLIFE grade
Eye conditions	Cataract	3 (max 4) ^A	3 (max 4)
	Blindness	^B Listed as outcome (grade 4) of multiple "Eye disorders"	^B
	Eye removal	^B	^B
Ear conditions	Hearing loss	3	^C
	Deafness	^B	^B
Cardiac conditions	Heart failure	3	3
	Ischemia	3 Listed as "Acute coronary syndrome"	3 Listed as "Coronary artery disease"
	Periarteritis	3	3
	Valvular disease	3	3
	Arrhythmia	2	2
	Heart transplantation	^B	^B
Vascular conditions	Hypertension	2	2
	Thrombosis	2	2
	Aneurysm	^B	3-4
Respiratory conditions	Obstructive pulmonary disease	2 Listed as "Bronchospasm"	2 (for COPD) 3 (for asthma)
	Decreased pulmonary function	^C (max 3) Listed under "Investigations" as "Carbon monoxide diffusing capacity decreased", grading based on carbon monoxide diffusing capacity, all grades are asymptomatic	^C
	Pulmonary resection	^B	^B
	Pulmonary transplantation	^B	^B
	Other pulmonary conditions	2	^B
	Gastro-intestinal conditions	Gastroesophageal reflux disease	2 (max 3) ^A
Inflammatory bowel disease		4 Listed as "Enterocolitis"	4 Listed as "Enterocolitis"
Other gastrointestinal conditions		2	^B
Hepato-biliary conditions	Hepatitis	3 Listed under "Infections"	2 Listed under "Infections"
	Hemochromatosis	3 Listed under "Metabolism and nutrition disorders" as "Iron overload"	2 Listed under "Hematologic"
	Liver cirrhosis	^B Listed as outcome (grade 3) of "Viral hepatitis"	^C
	Liver transplantation	^B	^B
	Cholecystectomy	^B	^B

Supplementary Table S5. *Continued.*

	Long-term self-reported physical outcome	Minimum corresponding CTCAE grade	Minimum corresponding SJLIFE grade
Renal and urinary tract conditions	Tubular dysfunction	^B	^B
	Proteinuria	^C (max 3) ^A Grading based on urinary protein level, no separate grade for treatment required	^B
	Chronic kidney disease	^C Grading based on eGFR or CrCl, no separate grade for treatment required	2
	Urinary tract obstruction	2	2
	Nephrectomy	^B	^B
	Renal transplantation	^B Listed as outcome of chronic kidney disease (grade 4)	^B Listed as outcome of chronic kidney disease (grade 4)
	Other conditions of kidney and urinary tract	2	^B
	Endocrine conditions	Adrenal insufficiency ^X	2
Hypercortisolism		2 (max 3) ^A	^B
Hypothyroidism ^X		2	2
Hyperthyroidism		2	2
Estrogen deficiency ^X		2 Not listed as a separate condition; "other endocrine conditions"	^B
Testosterone deficiency ^X		2 Not listed as a separate condition; "other endocrine conditions"	^B
Growth hormone deficiency ^X		2 (max 2) ^A Listed under "Investigations" as "Growth hormone abnormal"	1 (max 2)
Hypoparathyroidism		2	2
Hyperparathyroidism		2 (max 2) ^A	2 (max 2)
Prolactinoma		^B	2 Listed as "hyperprolactinemia"
Polycystic ovarian syndrome		^B	2
Pubertas praecox		^C Grading based on biochemical markers and age, not a separate grade for treatment required (max 2)	^C Grading based on biochemical markers and age, not a separate grade for treatment required (max 2)
Pubertas tarda		3 (max 3)	^B
Pituitary deficiency		^B	^B
Pituitary surgery		^B	^B
Obesity		3 (max 4) Listed under "Metabolism and nutrition disorders"	3 (max 4)
Underweight	^B	2 (max 2)	

Supplementary Table S5. *Continued.*

	Long-term self-reported physical outcome	Minimum corresponding CTCAE grade	Minimum corresponding SJLIFE grade
	Diabetes mellitus	^c "Hyperglycaemia" listed under "Metabolism and nutrition disorders". Grading based on fasting glucose levels and hospitalization indication, no separate grade for treatment required	2
	Diabetes insipidus ^x	2 Not listed as a separate condition; "other endocrine conditions"	2
	Thyroidectomy	^b	^b
	Adrenal gland removal	^b	^b
	Ovariectomy	^b	^b
	Orchidectomy	^b	^b
Nervous system conditions	Cerebrovascular accident – hemorrhagic	2 Listed under "Nervous system disorders" as "Intracranial hemorrhage". Also listed under "Nervous system disorders" as "Stroke", grading based on neurologic deficit with no separate grade for treatment required	2
	Cerebrovascular accident – ischemic	^c Listed under "Nervous system disorders" as "Stroke" or as "Cerebrovascular ischemia" (max 2), grading based on neurologic deficit with no separate grade for treatment required	2
	Transient ischemic attack	^c (max 2) Grading based on neurologic deficit and imaging, no separate grade for treatment required	^b
	Epilepsy	2-3 ^c Listed as "Seizure", grade 2 is brief generalized seizure and grade 3 is multiple seizures despite medical intervention	2
	Headache	^c (max 3) Grading based on intensity of pain and ADL, no separate grade for treatment required	3
	Hydrocephalus	3	3
	Other neurological conditions	2	^b

Supplementary Table S5. *Continued.*

	Long-term self-reported physical outcome	Minimum corresponding CTCAE grade	Minimum corresponding SJLIFE grade
Musculoskeletal conditions	Amputation	^B	2 (max 3)
	Deformities	2 (max 3) ^A	2 (max 3)
	Osteoporosis	2 (max 3) ^A	^C
	Other musculoskeletal conditions	2	^B
Neoplasms	Malignant neoplasms	2	^B
Other conditions	Dermatological conditions	2-3	^B
	Hysterectomy	^B	^B
	Prostatectomy	^B	^B
	Mastectomy	^B	^B
	Splenectomy	^B	^B

^A: (max) is stated when the maximum possible CTCAE grade is below grade 5. In this case, the number at (max) represents the maximum possible CTCAE grade for that condition is shown.

^B: We could not perform CTCAE grading, because the condition was not present in the CTCAE as a separate entity.

^C: It was not possible to define the corresponding CTCAE grade for our established clinical relevance criteria, because additional clinical information was needed for CTCAE-based grading.

^X: When this hormonal deficiency is the result of pituitary dysfunction, it is categorized separately as "Pituitary deficiency".