strong aya

A new, interdisciplinary, multi-stakeholder European network to improve healthcare services, research and outcomes for Adolescents and Young Adults with cancer.

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EORTC
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The future of cancer therapy

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STRONG AYA COS DATA COLLECTION RESOURCES

The following document contains the following essential parts of data collection in STRONG AYA, namely:

- An overview of the Core Outcome Set itself
- The Core Measurement Set
- Case-mix variables
- A study protocol
- The questionnaires for on- and off-treatment participants (*please note that due to copyright we have not reproduced EORTC QLQ C30, EORTC QLQ AYA and HADS questions in this document and one question derived from the EORTC QLQ SURV100 for off-treatment participants*)

This document should be seen as the scientific companion to the technical requirements documentation and the necessary legal documentation to run a study within the STRONG AYA federated data infrastructure. In particular:

D3.1 – Data Management Plan

D3.3 – Technical Blueprint

A template of our Data Access Agreement

The Core Outcome Set

The STRONG AYA Core Outcome Set consists of 15 core outcomes, with two additional on treatment and three additional off treatment domains

Outcome	Category
Overall survival Cancer progression Quality of life Pain Fatigue Access to mental health support Fertility or infertility Functional ability Psychological distress Cognitive issues caused by cancer or treatment Receipt of age-appropriate care Ability to do work/schoolwork Social activity or interaction Organ function Financial toxicity	Core outcomes
Participation in clinical trials Life-threatening infections	On treatment only
Fear of cancer recurrence Survivorship support Changes to life goals	Off treatment only

The development of this COS is fully outlined in a recent *Lancet Oncology* publication.

The Measurement set

Outcome	***Clinical or patient reported outcome***	***Explanation***	***How is it collected in STRONG AYA***
Overall survival	*Clinical*	*Length of time from date of diagnosis to last follow-up or death*	Time interval from date of diagnosis to last follow up/death
Cancer progression	*Clinical*	*Cancer worsening and cancer prognosis*	Expert opinion of clinician or TMN staging information
Quality of life	*Patient reported*	*Patient's age-specific quality of life*	EORTC QLQ C30 EORTC QLQ AYA
Pain	*Patient reported*	*Experience of pain*	EORTC QLQ C30

Fatigue	*Patient reported*	*Experience of fatigue and tiredness*	EORTC QLQ C30
Access to mental health support	*Clinical & patient reported*	Available access to psychological support (independently found or hospital referrals) and satisfaction with psychological support received	*Clinical: referral codes for mental health support* *PRO: Bespoke question*
Fertility or infertility	*Clinical & patient reported*	*Patient's fertility or infertility status, and whether patient had the opportunity for fertility preservation*	*Clinical: referral for fertility preservation or support or mention of pregnancy* *PRO: Bespoke question*
Functional ability	*Patient reported*	*Impact on day-to-day life and ability to carry out self-care*	EORTC QLQ C30
Psychological distress	*Patient reported*	*The experience of post-traumatic stress disorder, post-traumatic stress syndrome, anxiety, or depression*	*HADS*
Participation in clinical trials (on-treatment only)	*Clinical & patient reported*	*Whether patients have been offered or accepted (or both) to take part in a clinical trial*	*Clinical: EPR mentions of clinical trial enrolment* *PRO: bespoke question*
Cognitive issues caused by cancer or treatment	*Clinical & patient reported*	*Cognitive decline in patient due to cancer or its treatment directly*	*Clinical: mention of cognitive issues in EPR* *PRO: bespoke question and cognitive function in EORTC QLQ C30*
Fear of cancer recurrence (off-treatment only)	*Patient reported*	*Patient's worry about the possibility of cancer returning or worsening in the same place or another part of the body*	*Fear of Cancer Recurrence questionnaire*
Survivorship support (off-treatment only)	*Patient reported*	*Available access to survivorship support and satisfaction with survivorship support received*	*Bespoke question*
Receipt of age-appropriate care	*Patient reported*	*Satisfaction with care received and feeling heard by health-care professionals*	*Bespoke question*
Life-threatening infections (on-treatment only)	*Clinical & patient reported*	Occurrence of hospitalisation due to infection after cancer diagnosis	*Clinical: hospitalisation codes and CTCAE* *PRO: Bespoke question*
Ability to do work or schoolwork	*Patient reported*	Changes to work or schoolwork situation, actual job or school status, and ability to take	EORTC QLQ C30 EORTC QLQ AYA

		complete work or school-related tasks	
Social activity and interaction	*Patient reported*	Interactions with family, friends, and partner, effect on romantic life (including intimacy), and issues or concerns around taking part in social activities	EORTC QLQ AYA
Changes to life goals (off-treatment only)	*Patient reported*	Motivation to achieve personal goals, ability to distinguish between important and non-important things in life, and perceptions of control over life	*Bespoke question*
Organ function	*Clinical & patient reported*	Any abnormal organ function caused by cancer or its treatment	*Clinical: EPR* *PRO: bespoke questions regarding organ function*
Financial toxicity	*Patient reported*	Medical expenses, current financial situation, and worry for financial safety in later years	*Bespoke question*

Put another way, the final core measurement set resulted in the following measurements:

- Bespoke clinical domains questions loosely modelled on the St Jude's Childhood Cancer Survivorship Survey
- Limiting focused collection of life-threatening infections (given the extensive nature of the CTCAE) to the most common and serious issues, namely:
    - Left ventricular systolic dysfunction
    - Cardiac disorders - Other, specify
    - Hearing impaired
    - Diarrhea
    - Hepatic failure
    - Creatinine increased
    - Chronic kidney disease
    - Wound complication
    - Alanine aminotransferase increased
    - Aspartate aminotransferase increased
    - Blood bilirubin increased

    - Ejection fraction decreased
    - Lymphocyte count decreased
    - Platelet count decreased
    - Proteinuria
    - Amenorrhea
    - Azoospermia
    - Dyspnea
    - Hypertension
    - Thromboembolic event
- EORTC-QLQ-C30
- EORTC-QLQ-AYA
- HADS
- A mix of bespoke and borrowed questions on fear of cancer recurrence
- bespoke questions on domains such as fertility or access to age-specific care

Case mix variables

Case mix variables based on the literature review are ranked in order or importance below. Comorbidities are yellow for optional as these are difficult to collect information on in many instances, especially for those on treatment or those who are <5 years survival.

rank #	Case mix factors *(examples)*	EPR?	PRO	Measurement
1	**Age** *(age at diagnosis; age at study participation)*	X		EPR – in years for both: age at diagnosis Age at study participation
2	**Sex** *(sex; gender)*	X		M/F/X – refer to biological sex assigned at birth (including intersex where relevant/where this is recorded); gender identity is partially recorded via the PRO questionnaire

3	**Malignant (sub)types** *(tumor types; histological subtypes; date of diagnosis)*	X		EPR: ICD-10 codes C00-D44.5 Information related to COS domains: overall survival
4	**Treatment** *(type of treatment; number of treatments; treatment dosage; type of drugs (where relevant); date(s) of treatment)*	X		Includes chemotherapy, radiotherapy, targeted therapies, surgery, and hormone therapy Include type of protocol followed if relevant
5	**Stage** *(stage; TNM classification; tumor size; metastasis; prognosis)*	X		EPR - TNM Staging System, with T, N and M stage specified where possible COS Domains: prognosis
6	**Ethnicity** *(race; migration background; ethnicity)*		X	Socio-demographical information, Measured via the PRO questionnaire (Not legal/will not be approved for collection in all countries i.e. FR and NL)
7	**Socioeconomic status (SES)** *(socio-economic position; median income)*		X	Measured via the PRO questionnaire (income)
8	**Education** *(educational level; current or highest grade in school; change in school life)*		X	PRO questionnaire using local levels corresponding to ISCED 2011 classification
9	**Partner** *(partner status; marital status)*		X	Measured via the PRO questionnaire (relationship status)
10	**Delivery of care** *(type of treatment center; location of center; patient provider communication; healthcare access; unmet service needs)*	X	X	EPR: Location of care (name of centre and type i.e. pediatric or medical oncology); number of visits to centre and dates; specialist referrals (type of referral and dates); access to age-specific care question in PRO questionnaire Relates to COS domains: cancer progression; damage to brain caused by cancer; access to

				mental health support; receipt of age appropriate care; Life-threating infection resulting in hospitalization; receipt of survivorship care
11	**Comorbidities (preexisting and not effects of treatment)** *(comorbidities; pre-treatment mental health diagnosis)*	X		EPR – ICD codes corresponding to Charlson Comorbidity Index domains: Myocardial infarction Congestive heart failure (CHF) Peripheral vascular disease Cerebrovascular accident (CVA) or Transient ischemic attack (TIA) Dementia Chronic pulmonary disease Connective tissue disease Peptic ulcer disease Liver disease Diabetes mellitus Hemiplegia Moderate to severe chronic kidney disease (CKD) AIDS COS domains: Quality of life; functional ability; organ function
12	**Symptoms** *(symptoms, complaints; duration of symptoms; complications; late effects)*		X	PROs (C30; HADS, etc) COS domains: Quality of life, Pain, Fatigue, Functional ability; organ function; fertility/infertility; psychological stress
13	**Tumor markers** *(white blood cell count; serum levels; expression of tumor markers)*	X		EPR

14	**Location (of tumor)** *(primary tumor site; tumor location)*	X		EPR
15	**Employment** *(being employed, type of work; change in work life)*		X	PRO questionnaire COS domains: ability to do work/school; financial toxicity
16	**Health status** *(health status; performance status; functional status)*		X	PRO questionnaire C30 functioning questions COS domains: functional ability; quality of life
17	**Maternity/fertility characteristics** *(ever been pregnant; maternal age; infertility; menarche status)*	X	X	PRO questionnaire: Standalone questions about fertility preservation COS domains: fertility/infertility
18	**Psychological mechanisms** *(anxiety, depression; psychological outcomes; coping)*	(Maybe)	X	EPR (referrals to specific mental health support, i.e. psychologist/psychiatrist, including date of referral) PRO questionnaire: HADS questions COS domains: psychological stress; quality of life
19	**Secondary malignancies** *(second malignancies; history of cancer; stage of second malignancy)*	X		EPR COS domains: prognosis; progression
20	**Recurrence/relapse** *(recurrence; relapse; site of recurrence; time since relapse, date of relapse)*	X		EPR – recurrent malignancies PRO – fear of recurrence questions COS domains: recurrence
21	**Social support** *(social support; social factors; social desirability)*	X		PRO – AYA questionnaire and C30 have questions on social functioning COS domains: social activity interaction

22	**Trial participation** *(clinical/study trial participation; clinical trial enrollment)*	X	X	EPR PRO questionnaire as well COS domain: Clinical trial participation

However the *minimum variables* to collect clinically are:

Category of information	Variable
Patient	Sex
Patient	Age at diagnosis
Patient	Date of death / last contact
Tumor	Topography (ICD-O)
Tumor	Morphology
Tumor	Clinical TNM stage
Tumor	Pathological TNM stage
Treatment	Surgery
Treatment	Radiotherapy
Treatment	Systemic therapy
Treatment	Immunotherapy
Treatment	Targeted therapy
Treatment	Hormonal therapy
Follow-up	Recurrence/progression (*some centres do not make the distinction in their records*)

Note that a minimum set is the bare minimum; if studies are able to collect more information or more detailed information, they should do so.

The protocol

SSYNOPSIS – PROTOCOL N° (CSET)

EU CT number		**Version and Date**	v 1.0	29/10/2024
Title	**STRONG-AYA: Implementing a Core Outcome Set (COS) for adolescents and Young Adults (AYA) with cancer utilizing federated learning**			
Abbreviated title	STRONG AYA			
Sponsor				
Coordinating Investigator				
Number of centers	7 in total to collect data: 1. Netherlands Cancer Institute – Antoni van Leeuwenhoek Hopsital (Amsterdam, NL) – Principal Investigator: 2. University of Manchester/Christie NHS Foundation Trust (Manchester, UK) – Principal Investigator 3. University of Leeds and Leeds Teaching Hospitals NHS Trust (Leeds, UK) – Principal Investigator: 4. Institute Gustave Roussy (Villejuif, FR) – Principal Investiagator - 5. Centre de Lutte Contre le Cancer Leon Berard (Lyon, FR) – Principal Investigator: 6. Fondazione IRCCS Instituto Nazionale dei Tumori (Milan, IT) – Principal Investigator: 7. Maria Sklodowska-Curie National Research Institute of Oncology (Warsaw, PL) – Principal Investigator: Iwona Ługowska, MD, PhD, MBA			
Indication				
Context	*STRONG-AYA is an interdisciplinary, multi-stakeholder European network to improve healthcare services, research and outcomes for Adolescents and Young Adults (AYA) with cancer, defined as individuals aged 15-39 years at primary cancer diagnosis. AYAs with cancer form a unique group; they face age-specific issues (e.g. infertility, unemployment, financial problems) and decreased quality of life due to cancer and its treatment. Unlike dedicated healthcare and trials for paediatric cancer patients, AYA-specific healthcare services are scarce and vary across Europe. AYAs who are at the core of society and economy need access to age-adjusted and high-quality healthcare. AYA-care and research will benefit from the collection,* secure access, and integrative analysis of a large volume and highly inclusive *pool of patient-centred data and collaboration among all stakeholders: patients, healthcare professionals, scientists, and policymakers.*			

	*Within STRONG-AYA we will set up a value-based healthcare research ecosystem to develop data-driven, interactive policy and visualization tools that bring, in co-creation with all stakeholders including patients, novel insights into AYA healthcare. This will entail meeting the **overall project objectives**:* (1) *The development of an age-specific Core Outcome Set (COS) for AYAs with cancer* (2) *The Implementation of the COS in 5 national healthcare systems (France, Italy, Netherlands, United Kingdom, Poland) and establishment of data infrastructure ecosystems for the collection and management of outcome data (both prospective and retrospective);* (3) *3) The enactment of a pan-European STRONG-AYA ecosystem, including a privacy-preserving federated learning infrastructure;* (4) *4) The dissemination of the COS and its insights gleaned from the development of bespoke analytical tools to a wide range of local and pan-European stakeholders to use real world insight to develop data driven, value-based care and research across the continent.*
Primary objective	This protocol primarily concerns meeting objectives 2 and 4 listed above. As such the primary objectives of this study are: 1) To build a pan-European dataset of outcomes relevant to AYAs with cancer through the creation of local/national and pan-European federated learning data infrastructure ecosystems. and 2) Garner insights from this data, which includes, but is not limited to, the development of outcome prediction models (prevalence/incidence of, risk factors for and mechanisms of poor outcomes) for AYAs with cancer, which will be analyzed through the use of the federated learning data ecosystems using privacy preserving federated analysis. To do so, it will implement a **core outcome set (COS)** of clinical and patient-reported outcomes (13 core, 3 on-treatment, 3 off-treatment) for AYAs in seven clinical settings. This COS will be *implemented as a research instrument to gain real-world insight from AYA data (retrospective and prospective clinical and registry data, where relevant) and into clinical practice (prospective). In doing so, it aims to build a European healthcare research ecosystem for AYAs with cancer.* *More specifically, we aim to develop outcome prediction models (prevalence/incidence of, risk factors for and mechanisms of poor outcomes) for AYA with cancer through the*

	*method of Federated Learning (FL) (see Methodology below). These models mean that analysis is based on data from patients aged 15-39 years at primary cancer diagnosis across multiple international centres, **<u>without</u>** any individual level patient data leaving the institution it originates from, therefore preserving patient data privacy.*
Secondary Objectives	To refine the COS based on the views of AYAs with cancer To investigate the value of COS data collection To explore the views of AYAs with cancer and health professionals about the COS data collection process
Hypothesis	We hypothesise that robust and generalisable FL can be developed across centres, and that this method will provide statistical models that explain the data, and demonstrate clinically useful risk factors for good and bad cancer outcomes. By linking multiple international centres, the FL models can be developed using the largest available cohort of AYA cancer patients to further develop research into AYA cancer and to better inform the care of this underserved cancer population. This has previously and recently been successful done for lung cancer patients (NKI IRBd21-026_29-01-2021 – ARGOS project) and anal cancer patients (NKI IRBd21-166_06-08-2021 – atomCAT project)
Methodology	Implementation phase in a limited number of centers **Data collected by the patient** Patient Reported Outcome Measures (PROMS) data collecting will use an electronic / online or hardcopy version of the questionnaire, adapted to either on treatment or off treatment patients (on treatment refers to a cancer patient receiving curative treatment, including maintenance treatment, who is not believed to be disease-free; within 1 calendar year of diagnosis, off treatment refers to a cancer patient receiving curative treatment, including maintenance treatment, who is not believed to be disease-free). . PROMS consists of specific patient-reported outcomes, that were classified by patients, researchers, and healthcare professional as important to the provision of appropriate support for AYAs with cancer. Outcomes relate to treatment and toxicities (functional ability, pain, fertility, quality of life; QoL), psychological distress (emotional distress, fear of cancer recurrence), adverse social late affects (ability to engage with work or school financial burden, cognitive after-effects of cancer / treatment), receipt of support services (e.g., age appropriate care or other relevant referrals such as survivorship support), as well as demographic questions (age, gender, ethnicity, relationship status, income, work / school status, and disability status). The PROMS list will be patient-reported information and is comprised from a variety of validated measurement instruments, including the Hospital Anxiety and Depression Scale; (HADS; a 14 item questionnaire measuring anxiety and depression; Zigmond, A. S., & Snaith, R. P. (1983)), the EORTC QLQ C30 (a 30 item questionnaire measuring QoL; Aaronson et al., 1993), and the EORTC QLQ-AYA (a 29 item questionnaire measuring QoL; EORTC, 2024a). Additionally, 17 single item questions, and 7 demographic questions (generated from existing literature and validated measurement instruments, including, the EORTC item library (EORTC, 2023), the EORTC QLQ-FERT (EORTC, 2024b), the Impact of cancer—childhood survivors (Zebrack, 2009), the EORTC PATSAT32 (EORTC, 2018), and the COST (Facit, 2024) make up the PROMS list, resulting in a total

	on 98 questions (including all ON and OFF treatment domain questions). See Appendix XXX for the full PROMS list. **Data collected by the professional from electronic health records** As this study focuses on outcomes related to a cancer diagnosis, specific and relevant clinical information about patients is important.. Clinical information to be extracted include patients clinical diagnosis and its features (e.g., tumour stage), date of diagnosis, type of treatment, time since diagnosis / treatment, potential cancer progression, cognitive issues caused by cancer / treatment, organ function, referrals to support services, participation in clinical trials, events of hospitalization due to infections, and potential co-morbidities. See Appendix XXX for specifies on how clinical outcomes will be measured. This information will be updated, as needed for each participant, across the several iterations of the COS. **Evaluation interviews** Two sets of semi-structured evaluation interview will take place at each centre. The first set of evaluation interviews will be held within the first year of the study with a subsample of 5-10 AYAs per centre, to explore patients' perspectives of the outcomes included in the COS with patients on treatment (see "Study" section for more information). The second set of evaluation interviews will be held after 12 months of data collection and will be with AYAs with cancer and Health Care Professionals (HCPs) / researchers, to explore their views of the experience of data collection (see "Study" section for more information).
Inclusion Criteria	- Patients aged between 15-39 at primary diagnosis. For patients aged 15, consent will be gained with patients parent/guardian - Minimum of 10 weeks post-diagnosis and up to a year from diagnosis at the start of study enrolment for patients on-treatment - cancer survivors, treated with curative intent, who are at least 1 year post-treatment (with the exception of maintenance treatment), and believed to be disease-free (i.e. have no evidence of active disease) - Treated/under the care of XX hospital(s) - Able and willing to give informed consent (themselves or if aged 15 or lacking capacity, their parent/guardian) - Able to read and understand [NAME of LANGUAGE] or translated equivalent patient-facing materials
NON-Inclusion Criteria	- Low to no level of [Name of Language] comprehension, even when supported - Low to no ability of providing informed written consent, even when supported - Patients with a cancer diagnosis outside ICD-10 codes C00-D44.5. - Life expectancy less than 6 months based on the opinion of treating physician

Study	**COS data collection** Once participants have been invited to the study, they will be asked to provide informed consent (or assent / parental consent for patients aged 15 years old). The PROMS list will then be made available to the patient to view and complete either at home or in the hospital. The PROMS list can be delivered a) electronically; b) in paper format (either in clinic or returned via post); or c) verbally (face-to-face in clinic or via telephone / video chat). Once the patient has been provided with the PROMS list, they will have one month to complete and return this. In the case of incomplete / not returned PROMS lists, reminder emails will be sent 2 and 4 weeks after the one-month deadline. Both reminders will include the link to the PROMS list, additionally, if communication with patient takes place via post, the 4-week reminder will include a copy of the PROMS list in paper format. Subsequent iterations of the PROMS list will be administrated in the same ways as the initial survey. Administrating the PROMS list takes no longer than 30 minutes. Each participant will be issued a unique identification code. As well as this, any participants accessing the PROMS list electronically will be provided with a unique username and password. A recruitment monitoring form will be kept at each recruitment centre to monitor the recruitment progress, record specific procedures used to administrator the survey (including accessibility requests, mode of competition e.g., online, paper, verbal etc; location of completion e.g., clinic or remote, etc), and log of communication with the patients (e.g., when PROMS list was sent, when PROMS list was received by the centre, dates of any reminder emails sent etc) where possible. <u>Refining the COS: qualitative interviews</u> **Aims:** 1) To evaluate the outcomes included in the COS with patients on treatment. **Participants:** A subsample of 5-10 participants per centre who have completed the PROMS list and provided consent to be re-contacted. Participants will be aged 15-39 at diagnosis, be a minimum of 10 weeks post diagnosis, and within one year from diagnosis. **Procedure:** In the first year of the study a subsample of 5-10 participants per centre will be invited to a semi-structured evaluation interview, taking no more than 30 minutes. Patients will be shown a 20-item list of outcomes which make up the COS and asked to evaluate whether there are any domains are missing / if any domains should be removed, and if so, why patients feel these missing domains should be included / excluded. Participants will also be shown a second list of outcomes not included in the current COS (but have been identified by AYAs as important, but have not reached consensus agreement to be included in the final COS), and asked whether they believe any of these outcomes should be included in a 'core' outcome set for AYAs. These

	interviews will be conducted in each centre's native language, audio recorded, and summaries of the interviews written up in English. These interview summaries will then be sent to the University of Southampton for analysis, where outcomes may be added / removed from the COS as a result of patient feedback. **Analysis:** Interview summaries will be sent to the University of Southampton to be analysed with the aim of identifying any outcomes that are commonly suggested to be added / removed by patients, along with reasons why these suggestions have been made. <u>Evaluating data collection: qualitative interviews</u> **Aims**: 1) To investigate the value of COS data collection; 2) To explore the views of AYAs with cancer and health professionals about the COS data collection process. **Participants:** Additional evaluation work will be undertaken throughout the study where 10-15 patients (who have completed the PROMS list and provided consent to be re-contacted) and HCPs / researchers (who have been involved in the delivery of the CMS to patients) per centre will be asked to reflect on their experience with the process of completing / distributing the PROMS list. **Procedure**: Qualitative interviews with AYAs with cancer and Health Care Professionals (HCPs). AYAs and HCPs will be invited for an interview, after 12 months of data collection, to explore views of the experience of data collection. AYAs will be asked about 1) experiences of being asked to be part of the study, 2) experiences of completing the COS, 3) any changes that should be made to the COS, 4) understanding of the use of the data, and 5) any aspects that should be clarified or changed in the future. HCPs will be asked about 1) experiences of inviting AYAs into the study, 2) reasons of AYAs for declining or accepting participation, 3) their perception of the experiences of AYAs in participating in the study, and 4) views on the value of the collection of COS data and the overarching aims of STRONG-AYA. These interviews will be conducted in each centre's native language, audio recorded, and summaries of the interviews written up in English. These interview summaries will then be sent to the University of Southampton for analysis, where data collection experiences will be analysed. **Analysis:** Interview summaries will be sent to the University of Southampton to be analysed with the aim of exploring patients and HCPs / researchers perception of the COS data collection process. A list of recommendations / changes to be made during data collection will be generated, and this will then inform possible changes to the data collection process in subsequent years of PROMS list distribution.

Primary evaluation criterion		
Secondary evaluation criteria		
Sample size determination		
Statistical analysis		
Number of patients		
Duration of the trial	**Inclusion**	01 January 2025 – 30 September 2027
	Study	01 January 2025 – 30 September 2027
	Duration of the study	Grant/whole project: 01 October 2022-30 September 2027 Data collection: 01 January 2025 – 30 September 2027

Context:

In any healthcare system it is essential that patients have access to high-quality care and to deliver tangible improvements in outcomes encompassing survival, health-related quality of life (HRQoL), the ability to attend school or work, get and raise children and actively participate in society [1]. This is particularly important for adolescents and young adults (AYA) with cancer, defined as 15 to 39 years at initial cancer diagnosis [2]. Their annual cancer incidence is 42.2/100.000, with 156.431 cases in Europe and 1.231.007 cases worldwide reported in 2018 (together 6.8% of all cancers) [3]. Advances in cancer treatment have led to increased survival rates and in AYA's even over 80% will survive long-term (>5 years) [4], **However, despite the relatively favourable cancer prognosis, AYA cancer patients are at risk of treatment related development of medical effects (e.g., cardiovascular disease or second malignancies), infertility or psychosocial effects (e.g., difficulty in romantic relationships, financial toxicity due to unemployment without a prior career job), and have an increased risk of late mortality [5, 6].**

AYAs with cancer are distinct from the paediatric (<15 years) and the older adult (>40 years) cancer populations[2, 7] in their unique spectrum of cancer types with both paediatric-type and adult-type tumours [8]. The AYA group faces an overlap with paediatric tumours (brain tumours, sarcoma, leukaemia and lymphoma), but also with tumours common at older age (breast and increasingly colorectal cancer), and diagnoses which typically peak at AYA age (testicular cancer, thyroid cancer and melanoma). There are also differences in tumour genomic, biology and clinical behaviour in AYA tumours compared to children and older adults [8, 9]. Age-specific molecular features are increasingly seen as therapeutically relevant. There is often a lack of awareness that cancer may occur in this age group (among general population and healthcare professionals (HCPs)),with often results in diagnostic delays and/or difficult access to specialised care, potentially resulting in poor survival outcomes [10]. Crucially, there is also a lack of AYA cancer patients' participation in clinical protocols (reported rate of entering clinical trials ranged from 5% to 34% in published series), limiting the evidence base for treatments [11]. Finally, adolescence and young adulthood are complex phases of life due to the many physical, emotional, cognitive, and social transitions [12]. Important developmental tasks need to be achieved, such as forming one's own identity and a healthy body image, establishing autonomy, responsibility and independence, finishing education and starting a career, starting a romantic relationship and having and raising young children [12]. A cancer diagnosis challenges AYAs' abilities to achieve these developmental milestones [13]. The way in which AYA with cancer adjust to their cancer experience might have life-long implications for the quality of their survival [14].

The AYA Working Group (WG) of the European Society for Medical Oncology (ESMO) and the European Society for Paediatric Oncology (SIOP Europe) concluded in 2021 that finding rapid solutions to 'speak the same language' among healthcare professionals (HCPs) is essential to further improve health outcomes for AYAs [11]. The WG reported that standard clinical trial endpoints, such as five-year overall survival, progression-free survival, and cancer-specific survival, often do not address the specific needs of the AYA population. The WG found a widespread geographic variation, nationally and internationally, in AYA care programs with an unstructured, often merely philanthropic, funding [11]. When ESMO and SIOPE members were asked if their patients had access to specialized services for AYA with cancer, or if

such services were in development, only 33% confirmed that they had, namely: 13% in Eastern and South-Eastern Europe, 45% in Western Europe and 60% in Northern Europe [20]. In addition, substantial inequalities in support by specialised HCPs, such as psychologists, social workers, physiotherapists, dieticians and AYA-dedicated nurses were found between AYA care programs [20]. The WG also reported an absence of outcome measures for monitoring and evaluating AYA cancer care programs and control [11]. In 2016, the NCI updated the AYA cancer progress review group report and examined scientific gaps and opportunities for future AYA oncology [22]. It was concluded that one of the most important contributions to AYA research would be to pool data (e.g. patient-reported outcomes, clinical and treatment data) across institutions and countries and create large cohorts for researchers to address the burden of cancer in AYA [22].

STRONG-AYA seeks to take up this call from the ESMO-SIOPE WG and NCI. STRONG-AYA is an interdisciplinary, multi-stakeholder European network to improve healthcare services, research and outcomes for Adolescents and Young Adults (AYA) with cancer, defined as individuals aged 15-39 years at primary cancer diagnosis. AYA-care and research will benefit from the collection, secure access, and integrative analysis of a large volume and highly inclusive pool of patient-centred data and collaboration among all stakeholders: patients, healthcare professionals, scientists, and policymakers.

Overall project objectives

The overall project objectives for STRONG-AYA are:

(1) The development of an age-specific Core Outcome Set (COS) for AYAs with cancer;

(2) The Implementation of the COS in 5 national healthcare systems (France, Italy, Netherlands, United Kingdom, Poland) and establishment of federated data infrastructure ecosystems for the collection and management of outcome data (both prospective and retrospective);

(3) 3) The enactment of a pan-European STRONG-AYA ecosystem, including a privacy-preserving federated learning infrastructure;

(4) 4) The dissemination of the COS and its insights gleaned from the development of bespoke analytical tools to a wide range of local and pan-European stakeholders to use real world insight to develop data driven, value-based care and research across the continent

Within STRONG-AYA we will make use of federated learning to implement the COS and create the national and pan-European ecosystem. Conventional data analysis requires sharing and centralization of data. But, combining data originating from multiple sources is difficult because of ethical, administrative, legal, and political barriers associated with data sharing [23]. In order to avoid these issues, we will use federated analysis or learning techniques (See below). Centralised approaches will mainly be applied in the local ecosystems, while federated approaches are specifically relevant for learning between ecosystems at a pan-European and the national level. Federated analysis/learning is an Artificial Intelligence technique – i.e. machine learning – that reformulates conventional data analysis algorithms so that data centralization becomes unnecessary and consequently data transfer and associated agreements are not needed [24]. Federated analysis/learning is defined as analysing or learning from data without data leaving the source: algorithms iteratively analyse separate data sources (sites) and only aggregated statistics are produced as outputs with the outside world [24]. In other words: research questions and answers are shared between the databases instead of the data. Federated

analysis/learning is a sustainable approach for AYA data as it offers a privacy-preserving solution to combine dispersed data to yield orders of magnitude more data than traditional approaches [24]. The federated analysis/learning methodology requires and forced the development of data with semantic interoperability: FAIR data [25]. An advantage of federated analysis/learning is that it makes implementation of models in daily clinical practice possible (e.g. clinical decision support systems for diagnostic decision-making), thereby facilitating a rapid learning healthcare practice [26].

This protocol primarily concerns actions related to objectives 2-4 above.

Primary Objective

The objectives of this particular study, in order to meet the overall project objectives 2-4 are as follows:

1) To build a pan-European dataset of outcomes relevant to AYAs with cancer through the creation of local/national and pan-European federated learning data infrastructure ecosystems; and
2) Garner insights from this data, which includes, but is not limited to, the development of outcome prediction models (prevalence/incidence of, risk factors for and mechanisms of poor outcomes) for AYAs with cancer, which will be analyzed through the use of the pan-European federated learning data ecosystems using privacy preserving federated analysis.

To prepare to meet these primary objectives, the following steps have been undertaken:

1. Development of the core outcome set

The development of the COS was divided into three areas of work: 1) a literature review; 2) qualitative interviews with AYA patients and survivors, their caregivers and supporters, and healthcare professionals (HCPs); and 3) a Delphi consensus process consisting of three rounds with three different stakeholder groups (AYAs and caregivers, HCPs, and researchers and policymakers) to draft a core outcome set for the next phase of the project which is data collection and implementation of the COS. The overall protocol for developing the COS in line with the Core Outcome Measures in Effectiveness Trials (COMET) and the International Consortium for Health Outcomes Measurement (ICHOM) was published in O.Husson et al (2024) [27]. Qualitative interviews and the Delphi consensus process were led by researchers at the University of Southampton (approved by Southampton Ethics Committee/IRB 78653). The COS domains were identified in March 2024, and the measurements were finalised with input from the STRONG AYA consortium in October 2024 (see 'Study' section, below).

The COS consists of clinical and patient reported outcomes that will define what data this study will collect.

2. Establish federated data ecosystems

The data collected in this study will share **anonymized or pseudonymized aggregated data insights** using federated learning, a machine learning privacy-preserving technique that allows for multi-centre studies without the transfer or exchange of data outside of each individual centre. This following a similar rationale to the atomCAT2 study where sharing data insight and cooperation in multi-centre studies is invaluable for the development and validation of prognostic models in rare cancers. By definition, rare cancer also encompasses all AYA cancers. Federated learning infrastructures and the data flow principles behind it ensure data insights can be shared whilst preserving patient privacy and local autonomy over

data. Furthermore, the agile nature of federated learning allow insights to be drawn whilst working with, not against, the diverse local contexts and situations around data collection at each participating centre. The following activities have been necessary to establish the data ecosystems at each centre (7) located in the five participating countries (Netherlands, United Kingdom, France, Italy, and Poland), has consisted of:

a) A technical infrastructure and tools for data management that use federated learning in line with FAIR (Findable, Accessible, Interoperable, Reusable) data principles. These are outlined in the attached project deliverables, namely the Data Management Plan (D3.1), the technical blueprint (D3.2), and are also captured in operational plans for the various ecosystems. It is envisioned that this technical infrastructure will include integrated web-portals with various and appropriate levels of access and permissions for use by various stakeholders including HCPs, patients, and policymakers. The software underpinning the STRONG AYA federated infrastructure, vantage6, underwent a penetration test, or "ethical hack" to test for vulnerabilities in December 2023; no major vulnerabilities were identified in the test, and the report (redacted to protect internal IP addresses, etc) has been shared with all consortium members and can be viewed in the attached supplementary materials.

b) A governance model and legal and framework to ensure compliance with European and each country's legal and policy stipulations regarding the collection, use and sharing of health outcomes data (e.g. robust data protection and General Data Protection Regulation (GDPR) compliance. . All members are bound by the STRONG AYA consortium agreement as well as the ethical guidelines laid out by the EORTC (D2.2). A Data Protection Impact Assessment, developed for the project by the EORTC for the *pan-European ecosystem,* has been endorsed by all members of the STRONG AYA consortium. All data-contributing members have signed a service user agreement with Medical Data Works, which provides a central server to act as a "postman" between centres. A Data Access Agreement, similar to a Data Processing Agreement, or Data Transfer Agreement, has been circulated in draft form to all data contributing partners, and final signature is anticipated in December 2024. No federated analysis can, or will, take place on real data without signature of the Data Access Agreement.

c) Secure and locally controlled data warehouses of local data resources that individual partners are able to access solely by themselves as independent institutions, such as:

- research databases,
- clinical trials case reports,
- cancer registries,
- hospital-based electronic health records,
- repositories of patient (or self) reported outcomes, and
- other such databases that the Partner deems relevant for the STRONG-AYA

These specifications are centre-dependent and should conform to local processes and regulations.

Once these ecosystems are in place and connected, approved, certified algorithms developed by the consortium and governed by the Data Access Agreement, will be used to conduct statistical analyses on the data to investigate prevalence/incidence rates, risk factors and mechanisms of poor outcomes as defined in the COS.

The ecosystems consist of local and international data processes that articulate how we store, process and analyse the COS data in a compliant way.

Secondary Objectives

- To refine the COS based on the views of AYAs with cancer
- To investigate the value of COS data collection
- To explore the views of AYAs with cancer and health professionals about the COS data collection process

HypothesIs

We hypothesize that robust and generalizable federated models can be developed across countries, and that these models will demonstrate clinically useful prevalence/incidence rates, risk factors and mechanisms of poor outcomes as defined in the COS, which consists of a series of domains identified and confirmed as most relevant to AYA cancer care and research. By linking multiple international centres, the federated models can be developed using the largest available cohort of AYA cancer patients.

Methodology

Scientific/data collection methodology

This will be a mixed method observational cohort study with a retrospective and prospective part of COS data collection to investigate outcomes of AYA with cancer.

Data collection will take place at three levels:

1. *Retrospectively by use of available national and regional registry data or previously conducted population-based studies*
2. *Retrospectively in clinical practice in STRONG-AYA participating centres among patients in follow-up (survivors);*
3. *Prospectively in clinical practice in STRONG-AYA participating centres among newly diagnosed AYA with cancer;*

This protocol concerns point 3. Retrospective data collection has been approved by [IRB Number]. Patient recruitment is detailed below under “STUDY”.

Technological methodology

Following a similar rationale to the atomCAT2 study, sharing data insight and cooperation in multi-centre studies is invaluable for the development and validation of prognostic models in rare cancers, which by definition encompass all AYA cancers. Federated learning infrastructures and the data flow principles behind it ensure data insights can be shared whilst preserving patient privacy and local autonomy over data. Furthermore, the agile nature of federated learning allow insights to be drawn whilst working with, not against, the diverse local contexts and situations around data collection at each participating centre.

Data flows:

Data flows within the STRONG-AYA consortium will follow the following principles:

Each Partner controls and operates its own local ecosystem. This is expected to consist of, but is not exclusively limited to, local data resources that the Partner is able to access solely by themselves as independent institutions, such as:

- research databases,
- clinical trials case reports,
- cancer registries,
- hospital-based electronic health records,
- repositories of patient (or self) reported outcomes, and
- other such databases that the Partner deems relevant for the STRONG-AYA as per the COS

These "grassroots" data sources are allowed to be either retrospective, or prospective, or a mixture of both. Since each Partner owns, controls and operates in their own space, they will autonomously decide when and which Data to make accessible for Federated Learning through the STRONG-AYA consortium. There is no intellectual, technical or consortium-derived mandatory requirement on every Partner to make all data completely accessible at exactly the same time; noting, as mentioned above, that the data collection paradigm must allow for dynamism, adaptability and step-by-step accumulation (and maturation) of the data over time.

Each Partner will be responsible for requesting individual-level subject data from primary data sources within their own area of control (as above, the electronic health records, cancer registries, etc. etc.) using local governance mechanisms and technical instruments that are feasible for the Partner. These mechanisms and instruments may, for illustration purposes only, include Data Transfer Agreements between themselves and national cancer registries, and customized data extraction tools from electronic health records hosted in their local hospital (see, for a purely illustrative example, Figure 1 below). Existing governance and instruments should be re-used wherever possible, with a view to grow and sustainably reach a better quality of data collection over time.

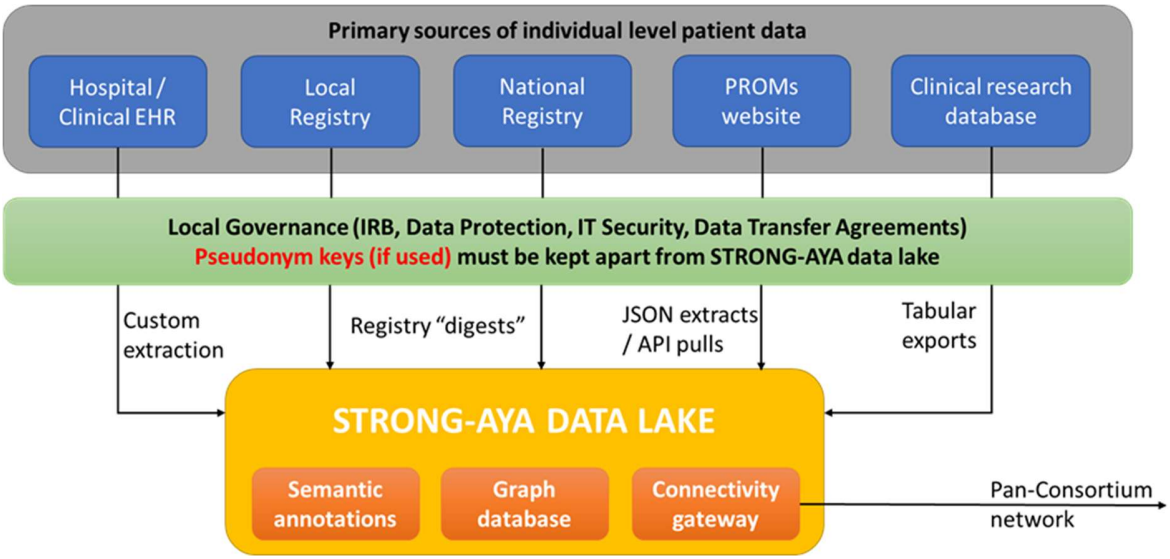


Figure 1: data flows for STRONG AYA

Each Partner stores pseudonymized data they have extracted from their local sources into a secured computation device which is within their institutional data security firewall. This device resides on a sub-network that can be insulated from other mission-critical and operational systems used by the institution. The Partner needs to ensure sufficient security for the private data in their own collection, using the advice of their local data protection officers and information security teams. If a Partner uses pseudonym keys to link information of the same human subject from multiple data sources, such key files must be stored on a separate device from the data itself.

Traditionally, machine learning models are trained on data that are collected centrally from multiple sources. However, the ethical, legal and societal implications regarding sharing of data outside the source organization has led to a paradigm shift in how machine learning models are trained. Instead of sharing data, algorithms are sent to each of the data sources, where they are trained locally. The locally trained algorithms are aggregated to develop a global model in a manner as if the algorithm is trained by traditional approaches. The privacy and confidentiality of data is protected at the source and only necessary analysis is shared.

STRONG-AYA will use the Personal Health Train (PHT) paradigm to create its federated learning infrastructure. The Personal Health Train (PHT) is a privacy-by-design infrastructure for performing federated/distributed machine learning. The data providers (hospitals) can participate in multicentre data analysis without exposing sensitive data outside the organization. The principle of PHT can co-exist with other privacy enhancing measures such as encrypted and perturbed data, but the crucial point here is that the PHT paradigm never relies solely on the unbreakability of encryption nor the irreversibility of perturbation to safeguard patient privacy. PHT ensures that the machine learning process is completed in a data agnostic manner. The data station provides an execution platform for the algorithm and provides secure access to the data repository. In the PHT infrastructure, the metaphor 'train' refers to the Docker containers containing the data query and the algorithm. These containers provide an isolated and secure environment for the query and algorithm. 'Tracks' are the secured communication channels

connecting the central message broker, the researcher and the data stations. Trains are sent to the data station through the tracks and only authenticated users are allowed to trigger a federated learning. The open source implementation of PHT, Vantage (https://vantage6.ai/) will be used as the software solution for performing privacy preserving federated machine learning on the datasets.

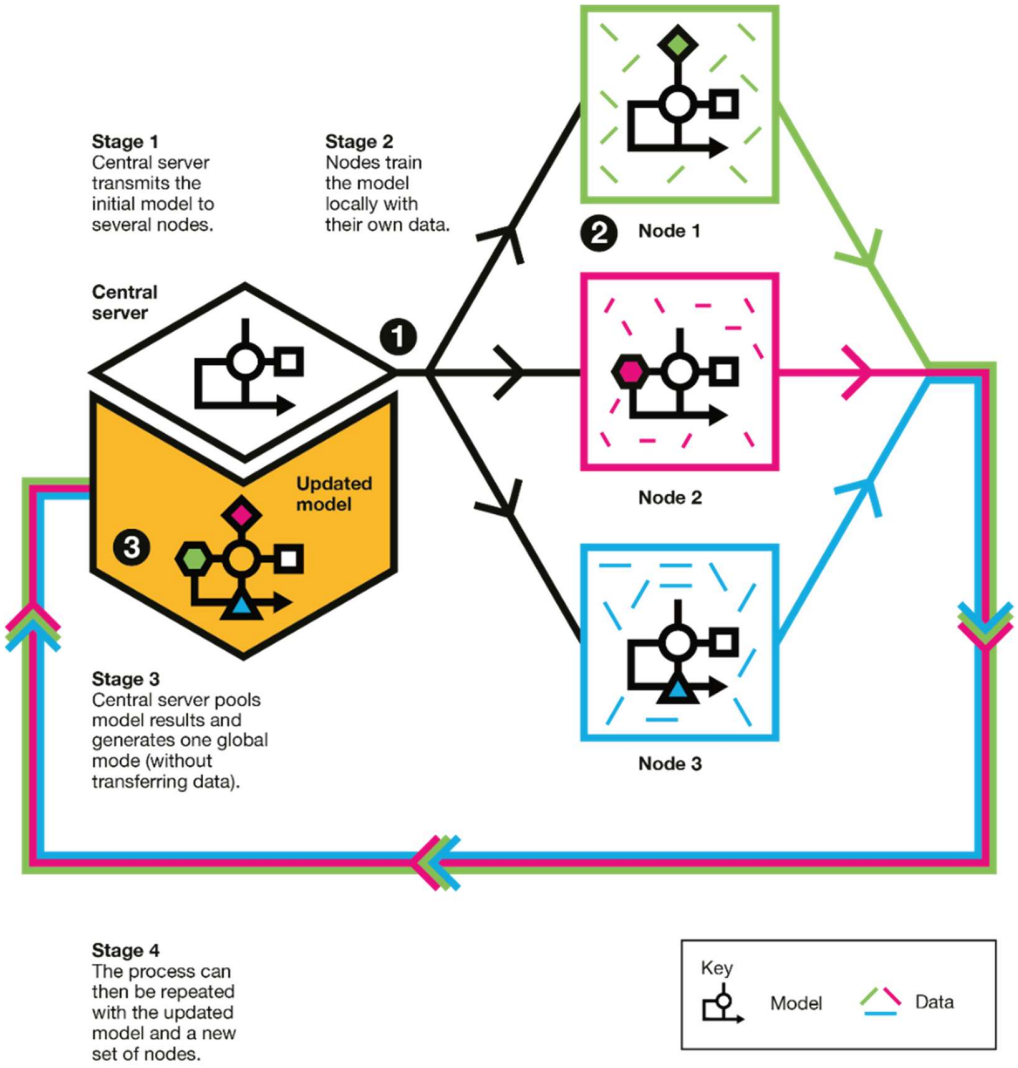


Figure 2: PHT query journey

The PHT was developed by experts at the Netherlands Comprehensive Cancer Organization (IKNL), home of the Dutch National Cancer Registry, and the University of Maastricht and has been applied in numerous oncological use-cases in the Netherlands and internationally. Selected projects include PROSPECT, a prostate cancer study, of which NKI-AvL is a collaborator; rare cancer registry developments such as RARECANnet Asia and BLUEBERRY (IKNL), the atomCAT anal cancer study (NKI-AVL). The specific computing resources required for STRONG-AYA are outlined in the technical blueprint attached which is the evolving standard operating procedure defining the integrity and safety of the system alongside the Data Management Plan.

In the proposed federated structure, the exchange of statistical summaries and model coefficients (e.g., odds ratio) are as close as possible to anonymization without becoming unfit for the purpose of actionable insights and testable hypotheses to improve the care of AYAs with cancer. In so far as the same such statistics and results are printed in public report and articles, then the information exchanged in federated learning is NOT any more identifiable than articles and reports. Safety and integrity of the local data spaces is the responsibility of the local PI and his/her IT team. Safety and integrity of the federation cross-institutional communications networks will be the responsibility of Medical Data Works, who have been subcontracted to host the STRONG-AYA central server. The design of the software safeguards and the algorithmic integrity is a joint undertaking of the University of Maastricht and IKNL.

Inclusion/Exclusion criteria

Inclusion criteria	**Exclusion criteria**
Aged between 15-39 at diagnosis	Low to no ability to provide informed written consent, even when supported
(on treatment) any patients with a diagnosis code C00-D44.5 at any time after diagnosis, on the basis of clinical judgment.	Patients with a cancer diagnosis outside ICD-10 codes C00-D44.5
Cancer survivors, treated with curative intent, who have stopped active treatment (with the exception of maintenance treatment), and are believed to be disease-free (i.e. have no evidence of active disease), based upon clinical judgment	Life expectancy less than 6 months based on the opinion of treating physician
Any type of malignant or benign central nervous system (CNS) tumour	
Able and willing to give informed consent (for themselves, or, if aged 15 or lacking capacity, for their parent/guardian to provide consent)	
Able to read and understand patient-facing materials	

Study

Data to be collected and measurements

For prospective data collection AYAs with cancer will be identified by XXXX and/or may be invited to participate in the study by their treating healthcare professional or via a national patient organisation.

Patients will be invited to participate after diagnosis (ad 3) or around a follow-up consult (ad 1) in the respective centres to enable the evaluation of the impact of cancer diagnosis, treatment and care on short- and long-term outcomes.

From all AYA with cancer diagnosed in the STRONG-AYA centres, we expect that the prospective part (ad 3) of STRONG-AYA will be available to around 4000 patients each year (please see the Table below under sample size) that will be followed longitudinally over time (each year). This number will only grow when STRONG-AYA will open in other countries. When patient inclusion for the prospective part of the data collection is not possible directly after diagnosis, it is also possible to include patients or survivors later in their patient journey (ad 1 – retrospective clinical practice).

Once participants have been invited to the study, they will be asked to provide informed consent (or assent / parental consent for patients aged 15 years old).

The full list of core outcome domains identified in the Delphi study and to be collected in this part of the study are:

Outcome	**Clinical (EHR) or PRO?**	**Measurement**	**Comments**
Overall survival	EHR	From date of diagnosis (date of biopsy/pathology confirmation) Length of time interval in months	Minimum requirements for date interval will be in month/years; overall survival calculate to the exact date is preferable, however, if this is unavailable, then mean days (15 days) should be used. Date of diagnosis refers to date of biopsy / pathology confirmation. If this is not available, then date of first reliable evidence of cancer e.g., appointment / surgery date etc. If date of diagnosis is unavailable (due to patient not being diagnosed at hospital etc), then get date from patient if possible. If not possible, then use date of first contact with AYA (specifically for cancer / cancer treatment). Cause of death to be extracted – is death cancer related; toxicity related; other (please explain).

Cancer progression	EHR	Date interval format (time since diagnosis – date of cancer worsening). Average number of follow-up appointments per cancer type (in months).	Date of diagnosis refers to date of biopsy / pathology confirmation. If this is not available, then date of first reliable evidence of cancer e.g., appointment / surgery date etc. If date of diagnosis is unavailable (due to patient not being diagnosed at hospital etc), then get date from patient if possible. If not possible, then use date of first contact with AYA (specifically for cancer / cancer treatment). Refer to clinician's decision for date of cancer worsening (reason for date chosen to be recorded e.g., new secondary cancers, tumour size increase).
Fertility / infertility	PROMs	2 standalone questions: 1) Has your treatment affected your fertility 2) Were you offered and did you use fertility preservation	Bespoke standalone questions
Damage to the brain caused by cancer / treatment	EHR/Clinician reported, PRO	Mention of cognitive decline / problems mentioned in EHR – "Yes" or "No".	If cognitive decline / other cognitive issues have been mentioned in EHR, record date (MM/YYYY) of when this is reported; if no cognitive issues have been mentioned in EHR, indicate this. If data is available, it is to be extracted, however, this is **not mandatory** – domain to be primarily measured by PROMS.
Organ function	EHR/clinician reported	Evidence of whether organs are functioning abnormally	Information on organ function to be extracted after cancer diagnosis only.

		– "Yes", "No", and "Unknown / not recorded".	If evidence of organs functioning abnormally is found, select from list of organ dysfunction / abnormal functions (including information on grade; refer to CTCAE terminology definitions document for more information) and provide data on how this was diagnosed / investigated (e.g., physical examination, imaging, pathology etc) and date of tests (if date of tests is unavailable, use date of referral).
Quality of life	PRO	EORTC QLQ-AYA (29 items) and C30 (30 items)	
Pain	PRO	QLQ-C30	
Fatigue	PRO	QLQ-C30 and QLQ-AYA	
Psychological distress (inc. anxiety, depression and PTSD)	PRO	HADS	
Access to mental health support	EHR/PROs	Evidence of whether professional mental health support (psychological / psychiatry) has been offered / patient has had a referral – "Yes", "No", and "Unknown / not recorded".	If professional mental health support has been offered / a referral has been made, record date (MM/YYYY) of referral (as well as referral code if available) and type of support offered – we are specifically interested psychological / psychiatric mental health support; other types of mental health support will be measured through PROMS. If data is available, it is to be extracted, however, this is **not mandatory** – domain to be primarily measured by PROMS.in PROs

Social activity / interaction	PRO	QLQ-AYA	
Functional ability	PRO	QLQ-AYA	
Ability to do work /schoolwork	PRO	QLQ-C30	
Financial toxicity	PRO	QLQ-C30	
Receipt of age-appropriate care	PRO	Bespoke questions	1. Did you receive support tailored to what you perceive as important / specific to your age, e.g., education / work, social relationships, caring for family members etc)? 2. Do you feel that your healthcare professionals understood your concerns regarding the impact of cancer and / or treatment?
Life-threatening infection resulting in hospitalisation	EHR/PRO	Evidence of hospital admission due to infection – "Yes", "No", and "Unknown / not recorded".	Information on hospitalisation due to infection to be extracted after cancer diagnosis only. If evidence of hospitalisation due to infection is found, provide data on duration of stay in hospital and outcome of hospitalization e.g., moved to different unit, discharged, change to cancer treatment, death etc.
Participation in clinical trials	EHR/PRO	Question asking whether a patient has taken part in a clinical trial	
Change to life goals	PRO	QLQ-AYA	

Fear of cancer recurrence	PRO	FCRI-SF: Fear of Cancer Recurrence Inventory – Short Form	
Receipt of survivorship support	PRO	Three bespoke standalone questions	Questions asking patients to rate agreement with statements about the provision of information, knowing how to access information and being offered formal survivorship support

Note: green denotes the three additional ON-treatment COS domains; blue denotes the three addition OFF-treatment COS domains.

The types of organ dysfunction to be included are:

List of organ dysfunction / abnormal function:

- Left ventricular systolic dysfunction
- Cardiac disorders - Other, specify
- Hearing impaired
- Diarrhea
- Hepatic failure
- Creatinine increased
- Chronic kidney disease
- Hepatobiliary disorders - Other, specify
- Ejection fraction decreased
- Lymphocyte count decreased
- Platelet count decreased
- Proteinuria
- Amenorrhea
- Azoospermia
- Dyspnea
- Hypertension
- Thromboembolic event
- Cholesterol high
- Cognitive disturbance
- Obesity
- Anorexia
- Peripheral sensory neuropathy
- Other (please describe)

As this study focuses on outcomes related to a cancer diagnosis, specific and relevant clinical information about patients is important. This will primarily be automatically extracted from electronic patient records. Clinical information to be extracted include patients clinical diagnosis and its features (e.g., tumour stage), date of diagnosis, type of treatment, time since diagnosis / treatment, potential cancer progression, cognitive issues caused by cancer / treatment, organ function, referrals to support services, participation in clinical trials, events of hospitalization due to infections, and potential co-morbidities. This information will be updated, as needed for each participant, across the several iterations of the COS.

To accompany the extraction of data from the electronic health record, patients will be asked to complete a number of questionnaires encapsulated in the Core Measurement Set (CMS). The CMS will then be made available to the patient to view and complete either at home or in the hospital. The CMS can be delivered a) electronically; b) paper format (either in clinic or returned via post); or c) verbally (face-to-face in clinic or via telephone / video chat). Once the patient has been provided with the PROMS list, they will have one month to complete and return this.

PROMS data collecting will use an electronic / online or hardcopy version of the questionnaire, adapted to either on treatment or off treatment patients. It consists of specific patient-reported outcomes, that were classified by patients, researchers, and healthcare professional as important to the provision of appropriate support for AYAs with cancer. Outcomes relate to treatment and toxicities (functional ability, pain, fertility, quality of life), psychological distress (emotional distress, fear of cancer recurrence), adverse social late affects (ability to engage with work or school financial burden, cognitive after-effects of cancer / treatment), receipt of support services (e.g., age appropriate care or other relevant referrals such as survivorship support), as well as demographic questions.

The PROMS list is comprised from a variety of validated measurement instruments (including the EORTC C30, EORTC QLQ-AYA, and the HADS), 17 bespoke standalone questions, and 7 bespoke demographic questions (generated from existing literature and validated measurement instruments).

Methodology

In the case of incomplete / not returned CMS, reminder emails will be sent 2 and 4 weeks after the one-month deadline. Both reminders will include the link to the CMS, additionally, if communication with patient takes place via post, the 4-week reminder will include a copy of the CMS in paper format. Subsequent iterations of the CMS will be administrated in the same ways as the initial survey. Administrating the COS takes no longer than 30 minutes.

Each participant will be issued a unique identification code. As well as this, any participants accessing the CMS electronically will be provided with a unique username and password. A recruitment monitoring form will be kept at each recruitment centre to monitor the recruitment progress, record specific procedures used to administrator the survey (including accessibility requests, mode of competition e.g., online, paper, verbal etc; location of completion e.g., clinic or remote, etc), and log of communication with the patients (e.g., when CMS was sent, when CMS was received by the centre, dates of any reminder emails sent etc).

Additionally, a subsample of 5-10 participants who have completed the CMS and provided consent to be re-contacted will be invited to a semi-structed evaluation interview, taking no more than 30 minutes. Patients will be asked to review the current COS and evaluate whether any domains are

missing / domains that should be removed, and if so, why patients feel these missing domains should be included. These interviews will be conducted in each centre's native language, audio recorded, and summaries of the interviews will then be sent to the University of Southampton for analysis. Additional evaluation work will be undertaken throughout the study where patients and HCPs / researchers will be asked to reflect on their experience with the process of completing / distributing the CMS.

Data management

[local data management and storage practices and laws apply, articulate as necessary]

Sample size and number of patients

[Complete as appropriate for study; aim for response rate of 25%]

Statistical Analysis

A full data analysis plan will be developed prior to data analysis initiation and will be pre-registered in a relevant public repository (e.g. Open Science Foundation, https://osf.io). As the research questions applied to STRONG-AYA will be highly variable, this document will be dynamic and ever-evolving.

Data analysis will use a specialised methodology called federated learning, whereby each centre will analyse data locally for their own patients. This analysis will be carried out using the distributed learning specialised software package Vantage6 (https://vantage6.ai and https://github.com/IKNL/vantage6). The summary statistics resulting from this local analysis will be shared between the project teams based at [YOUR CENTRE/S] researchers in University of Maastricht through a central server that will be provided and maintained by Medical Data Works BV (MDW). The analysis will be carried out in an iterative process, with summary statistics being sent back and forth from the central server to all centres over multiple rounds. The summary statistics will be analysed on local devices and then this summary statistic shared externally.

Put another way, the dashboard for the STRONG AYA project will contain a series of (certified) algorithm packages of specific types of statistical analyses designed by IKNL that researchers at all connected centres may use to conduct analyses of aggregated insights.

Anticipated statistical analyses are as follows:

Descriptive data analysis: prevalence/incidence poor outcomes

Summary statistics will be exchanged between centres at the European level in order to calculate prevalence/incidence rates of poor outcomes and explore cohort differences prior to modelling. Categorical variables will be compared using chi-square test, and numerical variables will be compared using a one-way ANOVA test. All tests will be carried out using summary statistics (number of patients, mean and standard deviation values) rather than individual patient data. Estimated survival / recurrence rates and potential follow-up times will be calculated by each centre individually, using the Kaplan-Meier estimator. The median follow-up time will be calculated based on the inverse Kaplan-Meier estimator. A detailed approach to handling missing values, on a within- and between-centre basis, will be specified in the data analysis plan.

Risk factors and mechanisms

Already-established predictive and prognostic factors for the outcomes in question will be identified through a systematic review of the literature. This approach identified the initial list of relevant data to be collected; this was subsequently prioritized in a Delphi study, and additional factors were

added. A final plan for factor selection and model refinement will be available in the data analysis plan.

(Multivariate) linear and logistic regression analyses for continuous and dichotomous outcomes respectively, and Cox regression for time-dependent outcomes will be used. Moderation and mediation effects will be explored, depending on research question. Multivariate analyses will be adjusted for identified case-mix factors.

References

1. Porter, M.E., *A strategy for health care reform--toward a value-based system.* N Engl J Med, 2009. **361**(2): p. 109-12.

2. Group, A.a.Y.A.O.P.R., *Closing the gap: Research and Care Imperaives for Adolescents and Young Adults with Cancer*, in *No. 06-6067*, NIH, Editor. 2006, National Institute of Health, National Cancer Institute, and Livestrong Young Ault Alliance: Bethesda, MD.

3. Trama, A., L. Botta, and E. Steliarova-Foucher, *Cancer Burden in Adolescents and Young Adults: A Review of Epidemiological Evidence.* Cancer J, 2018. **24**(6): p. 256-266.

4. Trama, A., et al., *Survival of European adolescents and young adults diagnosed with cancer in 2000-07: population-based data from EUROCARE-5.* Lancet Oncol, 2016. **17**(7): p. 896-906.

5. Keegan, T.H.M., et al., *Second Primary Malignant Neoplasms and Survival in Adolescent and Young Adult Cancer Survivors.* JAMA Oncol, 2017. **3**(11): p. 1554-1557.

6. Hayashi, R.J., *Adolescent and young adult cancer survivorship: The new frontier for investigation.* Cancer, 2019. **125**(12): p. 1976-1978.

7. Close, A.G., et al., *Adolescent and young adult oncology-past, present, and future.* CA Cancer J Clin, 2019. **69**(6): p. 485-496.

8. Bleyer, A., et al., *The distinctive biology of cancer in adolescents and young adults.* Nat Rev Cancer, 2008. **8**(4): p. 288-98.

9. Tricoli, J.V., et al., *Biologic and clinical characteristics of adolescent and young adult cancers: Acute lymphoblastic leukemia, colorectal cancer, breast cancer, melanoma, and sarcoma.* Cancer, 2016. **122**(7): p. 1017-28.

10. Dommett, R.M., et al., *Features of cancer in teenagers and young adults in primary care: a population-based nested case-control study.* Br J Cancer, 2013. **108**(11): p. 2329-33.

11. Ferrari, A., et al., *Adolescents and young adults (AYA) with cancer: a position paper from the AYA Working Group of the European Society for Medical Oncology (ESMO) and the European Society for Paediatric Oncology (SIOPE).* ESMO Open, 2021. **6**(2): p. 100096.

12. Zebrack, B.J., *Psychological, social, and behavioral issues for young adults with cancer.* Cancer, 2011. **117**(10 Suppl): p. 2289-94.

13. Sodergren, S.C., et al., *A Life Put on Pause: An Exploration of the Health-Related Quality of Life Issues Relevant to Adolescents and Young Adults with Cancer.* J Adolesc Young Adult Oncol, 2018. **7**(4): p. 453-464.

14. Husson, O., et al., *Health-Related Quality of Life in Adolescent and Young Adult Patients With Cancer: A Longitudinal Study.* J Clin Oncol, 2017. **35**(6): p. 652-659.

15. Keegan, T.H., et al., *Comparison of cancer survival trends in the United States of adolescents and young adults with those in children and older adults.* Cancer, 2016. **122**(7): p. 1009-16.

16. Osborn, M., et al., *Models of care for adolescent and young adult cancer programs.* Pediatr Blood Cancer, 2019. **66**(12): p. e27991.

17. Fardell, J.E., et al., *A Narrative Review of Models of Care for Adolescents and Young Adults with Cancer: Barriers and Recommendations.* J Adolesc Young Adult Oncol, 2018. **7**(2): p. 148-152.

18. Keegan, T.H., et al., *Unmet adolescent and young adult cancer survivors information and service needs: a population-based cancer registry study.* J Cancer Surviv, 2012. **6**(3): p. 239-50.

19. Stoneham, S.J., *AYA survivorship: The next challenge.* Cancer, 2020. **126**(10): p. 2116-2119.

20. Saloustros, E., et al., *The care of adolescents and young adults with cancer: results of the ESMO/SIOPE survey.* ESMO Open, 2017. **2**(4): p. e000252.

21. Barr, R.D., et al., *Cancer in Adolescents and Young Adults: A Narrative Review of the Current Status and a View of the Future.* JAMA Pediatr, 2016. **170**(5): p. 495-501.

22. Smith, A.W., et al., *Next steps for adolescent and young adult oncology workshop: An update on progress and recommendations for the future.* Cancer, 2016. **122**(7): p. 988-99.

23. Sullivan, R., et al., *Delivering affordable cancer care in high-income countries.* Lancet Oncol, 2011. **12**(10): p. 933-80.

24. Deist, T.M., et al., *Distributed learning on 20 000+ lung cancer patients - The Personal Health Train.* Radiother Oncol, 2020. **144**: p. 189-200.

25. Wilkinson MD, D.M., Aalbersberg IjJ, Appleton G, Axton M, Baak A, Blomberg N, Boiten J-W, da Silva Santos LB, Bourne PE, Bouwman J, Brookes AJ, Clark T, Crosas M, Dillo I, Dumon O, Edmunds S, Evelo CT, Finkers R, Gonzalez-Beltran A, Gray AJG, Groth P, Goble C, Grethe JS, Heringa J, 't Hoen PAC, Hooft R, Kuhn T, Kok R, Kok J, Lusher SJ, Martone ME, Mons A, Packer AL, Persson B, Rocca-Serra P, Roos M, van Schaik R, Sansone S-A, Schultes E, Sengstag T, Slater T, Strawn G, Swertz MA, Thompson M, van der Lei J, van Mulligen E, Velterop J, Waagmeester A, Wittenburg P, Wolstencroft K, Zhao J, Mons B, *The FAIR Guiding Principles for scientific data management and stewardship. .* Scientific Data 2016. **3**(160018).

26. Jochems, A., et al., *Distributed learning: Developing a predictive model based on data from multiple hospitals without data leaving the hospital - A real life proof of concept.* Radiother. Oncol, 2016. **121**(3): p. 459-467.

27. Husson, O., Janssen, S.H.M., Reeve, B.B. et al. *Protocol for the development of a Core Outcome Set (COS) for Adolescents and Young Adults (AYAs) with cancer*. BMC Cancer 24, 126 (2024). https://doi.org/10.1186/s12885-023-11716-2

The questionnaires

On treatment



Implementing a Core Outcome Set for Adolescents and Young Adults with Cancer

Core Outcome Set Survey for Young People On-Treatment

About You

First, we would like to know a little about you. This information helps us build a picture of your background.

1. What is your annual income before tax?

Note: this section should be edited to reflect local currency. Note that in some contexts, starting with a financial question might be jarring. Please feel free to move the placement of this question within your questionnaire to where you feel it is most appropriate to ask.

- ☐ <10,000
- ☐ 10,000 – 19,999
- ☐ 20,000 – 29,999
- ☐ 30,000 – 39,999
- ☐ 40,000 – 49,999
- ☐ 50,000 – 59,999
- ☐ 60,000 – 69,999
- ☐ 70,000 – 79,999
- ☐ 80,000 – 89,999
- ☐ 90,000 – 99,999
- ☐ 100,000+
- ☐ Prefer not to say

2. What is your gender?

- ☐ Male
- ☐ Female
- ☐ Transgender
- ☐ Non-binary
- ☐ Other (please specify) _____
- ☐ Prefer not to say

3. To which of these ethnic groups do you belong?

- ☐ White (European or any other)
- ☐ Any Mixed or Multiple ethnic group
- ☐ Asian (including Pakistani, Indian, Bangladeshi, Chinese, or any other Asian group)
- ☐ African or any other African group
- ☐ Caribbean
- ☐ Black
- ☐ Any other Caribbean or Black group
- ☐ Arab

☐ Roma communities (including travellers, Sinti, Ashkali, Manusch, Jenische, Kaldaresh, or Kale)
☐ Any other Ethnic Group (please specify) _____
☐ Prefer not to say

4. Can you tell us what you're doing at the moment? (please select all that apply)

☐ In education/training
☐ Taking a break from education/training (agreed leave for at least a half term or longer)

☐ Working full time (≥30hr/week)
☐ Working part time (<30hr/week)
☐ Self-employed
☐ Working on a zero-hours contract
☐ Working on a fixed-term contract
☐ Working full time, but currently on parental leave
☐ Working part time, but currently on parental leave
☐ Currently not employed

☐ Apprenticeship/Internship involving paid work
☐ Apprenticeship/Internship not involving paid work

☐ Registered unemployed/signed onto any type of employment-seeking governmental support
☐ Not registered unemployed but seeking work
☐ Long-term sick or disabled
☐ At home/not seeking paid work (including caring for home or family)
☐ Unpaid/voluntary work

☐ Doing something else (please specify) _____

☐ Prefer not to say

5. What is the highest level of education you have obtained?

Note: This section should be edited to fit local context based on the ISCED (International Standard Classification of Education).

☐ Primary education (e.g. primary school)
☐ Lower secondary school (e.g. GCSEs)

- ☐ Higher secondary school (e.g. A-levels, BTECs, International Baccalaureate diploma)
- ☐ Post-secondary non-tertiary (e.g. HE Access)
- ☐ Short-cycle tertiary education (e.g. NVQ level 4 or equivalent, HE diplomas, Foundation years)
- ☐ Bachelor degree or equivalent
- ☐ Master degree or equivalent
- ☐ Doctorate of equivalent

6. What is your current relationship status?

- ☐ Single/never married or in civil partnership
- ☐ In a relationship
- ☐ Married
- ☐ Civil partner (legal)
- ☐ Divorced
- ☐ Widowed
- ☐ Other (please specify) _____
- ☐ Prefer not to say

7. Do you identify as 'disabled' or 'person with disabilities'?

- ☐ Yes
- ☐ No
- ☐ Prefer not to say

8. Are you registered as disabled?

- ☐ Yes
- ☐ No
- ☐ Don’t know
- ☐ Prefer not to say

About your Health

9. What type of cancer diagnosis do you have/did you have?

_____

10. Has your cancer spread (now or in the past)?

- ☐ Yes
- ☐ No
- ☐ Unable to answer

11. What type of cancer prognosis do/did you have?

(i.e. Good = cancer is likely to be cured/has been cured; Poor = cancer is not likely to be cured)

- ☐ Good
- ☐ Poor
- ☐ Unable to answer

12. Has your cancer ever returned (cancer recurrence)?

- ☐ Yes
- ☐ No
- ☐ Unable to answer

13. Has your medical treatment for cancer affected your fertility?

- ☐ Yes
- ☐ No
- ☐ Unable to answer

14. Were you offered the opportunity for fertility preservation?

- ☐ Yes
- ☐ No
- ☐ I don’t remember
- ☐ Not required

15. Since your cancer diagnosis, have you ever been told by a doctor or other healthcare professional that have, or have had, a problem with your:

15A. Brain

- ☐ Yes
- ☐ No
- ☐ Unable to answer

15B. Heart

- ☐ Yes
- ☐ No
- ☐ Unable to answer

15C. Breathing

- ☐ Yes
- ☐ No
- ☐ Unable to answer

15D. Kidneys

- ☐ Yes
- ☐ No
- ☐ Unable to answer

16. As a result of your cancer and/or treatment have you had any problems with, or are you now receiving any hormone treatment for:

16A. Periods or early menopause (oestrogen/progesterone)

- ☐ Yes
- ☐ No
- ☐ Unable to answer

16B. Testosterone

- ☐ Yes
- ☐ No
- ☐ Unable to answer

16C. Thyroid gland

- ☐ Yes
- ☐ No
- ☐ Unable to answer

16D. Growth hormone

- ☐ Yes
- ☐ No
- ☐ Unable to answer

16E. Low cortisol levels

- ☐ Yes
- ☐ No
- ☐ Unable to answer

16F. Other (describe):

- ☐ Yes (please describe) _____
- ☐ No
- ☐ Unable to answer

EORTC QLQ-C30

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EORTC QLQ-AYA

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Hospital Anxiety and Depression Scale

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Further Bespoke Questions

91. Since your cancer diagnosis were you offered any cancer-specific mental health support (e.g. support groups, self-help guides, complementary therapy, support for family/carers, etc.)**?**

- ☐ Yes
- ☐ No
- ☐ Unable to answer

92. Have you had any life threatening (potentially fatal) infections since receiving treatment?

- ☐ Yes
- ☐ No
- ☐ Unable to answer

93. Have you been offered an opportunity to take part in a clinical trial (a type of research that studies new tests and treatments and evaluates their effects on health outcomes)**?**

- ☐ Yes
- ☐ No
- ☐ Unable to answer

94. If yes, did you take part in a clinical trial?

- ☐ Yes
- ☐ No
- ☐ Unable to answer

Off treatment



Implementing a Core Outcome Set for Adolescents and Young Adults with Cancer

Core Outcome Set Survey for Young People Off-Treatment

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- ☐ Prefer not to say

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- ☐ Widowed
- ☐ Other (please specify) _____
- ☐ Prefer not to say

7. Do you identify as 'disabled' or 'person with disabilities'?

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- ☐ No
- ☐ Prefer not to say

8. Are you registered as disabled?

- ☐ Yes
- ☐ No
- ☐ Don’t know
- ☐ Prefer not to say

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- ☐ Yes
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- ☐ Unable to answer

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- ☐ Unable to answer

15B. Heart

- ☐ Yes
- ☐ No
- ☐ Unable to answer

15C. Breathing

- ☐ Yes
- ☐ No
- ☐ Unable to answer

15C. Kidneys

- ☐ Yes
- ☐ No
- ☐ Unable to answer

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- ☐ Unable to answer

16B. Testosterone

- ☐ Yes
- ☐ No
- ☐ Unable to answer

16C. Thyroid gland

- ☐ Yes
- ☐ No
- ☐ Unable to answer

16D. Growth hormone

- ☐ Yes
- ☐ No
- ☐ Unable to answer

16E. Low cortisol levels

- ☐ Yes
- ☐ No
- ☐ Unable to answer

16F. Other (describe):

- ☐ Yes (please describe) _____
- ☐ No
- ☐ Unable to answer

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EORTC QLQ-AYA

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Hospital Anxiety and Depression Scale

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Please rate how much you agree with the following statements:

	Not at all (0)	A little bit (1)	Somewhat (2)	Quite a bit (3)	Very Much (4)
92. *Note this question replicates Q53 in the EORTC QLQ-SURV100 – not reproduced to respect copyright*	0	1	2	3	4
93. I have all the information I need about my cancer, its treatment, and possible long-term effects (side effects of cancer and / or treatment that occurs over a long period of time)	0	1	2	3	4
94. When I need information about cancer (for example, treatment effects, chronic / long-term effects, possibility of cancer recurrence etc.), I know where to find it	0	1	2	3	4
95. Following completion of your treatment, how would you rate the information you received about survivorship support (help for living with and beyond cancer)?	Poor	Fair	Good	Very Good	Excellent