PROTOCOL FOR A PROSPECTIVE EXPERIMENT

Digital Innovation for Personalised Nutrition in Adolescent Oncology

MybYte

Version number: v2 **– Date** 16/07/2026

UZ/KU Leuven ref. number: S72397

Sponsor:

UZ Leuven (University Hospital Leuven)

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Sponsor-Investigators:

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Confidentiality Statement

The information in this document is strictly confidential and is available for review to Investigators, potential Investigators and appropriate Ethics Committees, Institutional Review Boards or Competent Authorities. No disclosure should take place without written authorization from the Sponsor.

LIST OF PARTICIPATING SITES

(as applicable)

List of participating sites	**Principal Investigator** *(must be a 'WUG' profession)*
UZ Leuven, Kinderhemato-oncologie	Dr. Anne Uyttebroeck (co-PI) Dr Julie Messiaen (co-PI)

SIGNATURES

Title: Digital Innovation for Personalised Nutrition in Adolescent Oncology

Protocol: MybYte

The undersigned confirm that the above referenced protocol has been acknowledged and accepted, and agree to conduct the study in compliance with the approved protocol, and will adhere to: the ICH guidelines, the most recent version of the Declaration of Helsinki, the Belgian law of May 7th 2004 regarding experiments on the human person, the EU General Data Protection Regulation 2016/679 (GDPR), the Belgian law of July 30th 2018 on the protection of natural persons with regard to the processing of personal data, the Belgian Law of August 22nd 2002 on participant rights, and any other regulatory requirements and Standard Operating Procedures (SOPs), as applicable.

The undersigned agree not to disclose the confidential information contained in this document for any purpose other than the evaluation or conduct of the study, without prior written consent of the Sponsor.

The undersigned Sponsor-Investigator also commit to making the findings of the study publicly available through publication and/or other dissemination tools, in accordance with this protocol and applicable regulations, without any unnecessary delay and to provide an honest, accurate and transparent account of the study; and to explain any discrepancies or deviations from the approved study protocol.

Sponsor-Investigator:

.....	.....	.....
Name & Title	Signature	Date

Principal Investigator of participating site:

ANNE UYTTEBROECK MD PHD		30/06/26
Name & Title	Signature	Date

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LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse Event
AESI	Adverse Event of Special Interest
APR	Annual Progress Report
ASAP	As soon as possible
ASR	Annual Safety Report
AR	Adverse Reaction
CA	Competent Authorities
CSR	Clinical Study Report
CTC	Clinical Trial Center
CME	Centrum Menselijke Erfelijkheid
DMP	Data Management Plan
DTA	Data Transfer Agreement
DPA	Data Processing Annex
EC	Ehics Committee
eCRF	electronic Case Report Form
ECG	Electrocardiogram
EU	European Union
EoS	End of Study
FPFV	First Participant First Visit
GCP	Good Clinical Practice (latest version of ICH E6)
GDPR	EU General Data Protection Regulation 2016/679
HBM	Human Body Material
IC(F)	Informed Consent Form
ICH	International Council on Harmonisation
IMD	Investigational Medical Device
IMP	Investigational Medicinal Product
ISF	Investigator Site File
IUD	Intra-uterine device
IVRS/IWRS	Interactive Voice/Web Reporting System
LAG	Laboratoriumgeneeskunde
LPLV	Last Participant Last Visit
MRI	Magnetic Resonance Imaging
PI	Principal Investigator (of participating research site)
PRO	Participant Reported Outcome
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
TMF	Study Master File
VIB	Vlaams Instituut voor Biotechnologie
WUG	Wet uitoefening gezondheidszorgberoepen

Extra abbreviations	Definition
BMR	Basal metabolic rate
BIA	Bioelectrical impedence analysis
BIS	Bioelectrical impedence spectroscopy
ESM	Experience sampling methodology
FM	Fat mass
FFM	Fat free mass
HRQL	Health-related quality of life
IC	Indirect calorimetry
REE	Resting energy expenditure
SMM	Skeletal muscle mass

FUNDING & SUPPORT

Funder or service provider	Type of Support (financial or non-financial)
Fonds Wetenschappelijk Onderzoek Vlaanderen (FWO), Kom op Tegen Kanker	Full financial support for this project: *(G054226N) Digital innovation for personalised nutrition in paediatric and adolescent oncology* has been awarded. .
Service providers m-Path	m-Path is an electronic research platform specialised in Experience Sampling Methodology (ESM). M-Path is a spin-off company of KU Leuven. In this study, m-Path will serve the following supporting roles: (1) hosting the digital tool, (2) developing the technical components of the dashboard, and (3) delivering ESM prompts and questionnaires to participants via smartphone. These services will be provided to the research team at market-related rates and will be invoiced to KU Leuven. UZ Leuven will not be invoiced for any service related to this study.
Participant reimbursement	During Phase 1 of the study, participants will receive a gift bag containing a selection of nutritious and appealing snacks to try. Travel costs to and from the study visits will also be reimbursed to parents or legal guardians according to the Belgian Association of Research Ethics Committees guidance on fixed amounts for travel expenses. In Phase 2, participants will receive a €20 Standaard Boekhandel digital gift voucher as a token of appreciation for their time and contribution to the study. The voucher will be provided upon completion of the study, including if a participant withdraws before completing all study procedures. Digital gift vouchers will be sent electronically to the participant's parent or legal guardian. No travel reimbursement will be provided as all study procedures will take place as part of routine hospital admissions or outpatient visits.

ROLES & RESPONSIBILITIES

The Principal Investigator (PI) is responsible for the conduct of the study at his/her participating research site, and for protecting the rights, safety and well-being of the study participants. As such the PI must ensure adequate supervision of the study conduct at the participating site. If any tasks are delegated, the PI will maintain a log of appropriately qualified persons to whom he/she has delegated specified study-related duties. The PI will ensure that adequate training is provided and documented for all study staff, prior to conducting assigned study-related activities.

It is the Sponsor-Investigator's responsibility to supervise the general conduct of the study (e.g. study progress, communication, protocol training and support of the participating research sites, annual reporting to the Ethics Committee (EC), end of study notification(s) and results reporting, etc.). The UZ/KU Leuven Sponsor-Investigator fulfills mostly both Investigator **and** Sponsor responsibilities, as outlined in latest version of the International Council on Harmonisation – Good Clinical Practice (ICH-GCP) E6 and applicable regulations.

PI and Sponsor-Investigator shall each be referred to as «Investigator(s)».

STUDY SYNOPSIS

Title of clinical study («study»)	Digital Innovation for Personalised Nutrition in Adolescent Oncology
Protocol number / acronym	MybYte
Sponsor name	UZ Leuven (University Hospital Leuven)
Sponsor-Investigator	Prof. dr. Anne Uyttebroeck, Dr. Julie Messiaen
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Study nbr in public database	TBC
Medical condition or disease under investigation	Adolescent oncology
Study rationale	Malnutrition (under- and overnutrition) is common during adolescent cancer treatment and is linked to morbidity, mortality, and health-related quality of life (HRQL). As such, nutritional status is considered a modifiable prognostic factor across the cancer continuum. To mitigate malnutrition during treatment, a personalised approach to nutritional care has been suggested. Such an approach must be low burden, innovative, interactive, disease- and individual specific, and use available technology to meet the needs of this unique population.
Primary objective	This study will take part in two phases. Phase 1: Co-create a personalised digital nutrition tool (MybYte) for adolescents aged 12- 18 years undergoing cancer treatment. Phase 2: Investigate the feasibility and acceptability of the MybYte tool.
Secondary objective(s)	Phase 1: 1. Qualitatively assess adolescent perspectives on nutrition during cancer treatment 2. Qualitative and quantitative assessment of the MybYte tool Phase 2: Longitudinal monitoring of: 1. Dietary intake measured by MybYte tool 2. Nutritional status measured by bioelectrical spectroscopy 3. Resting energy expenditure (REE) measured by indirect calorimetry 4. Health Related Quality of Life (HRQL) measured by Pediatric Quality of Life Inventory™ (PedsQL™) and PedsQL™ Cancer Module
Endpoints	Phase 1: 1. Final version of the MybYte tool 2. Thematic analysis of adolescents' perspectives on nutrition during cancer treatment Phase 2: 1. Feasibility of MybYte tool as determined by recruitment feasibility (%) and engagement (response) feasibility (%) and retention(%) 2. Acceptability of MybYte tool as determined by the following categories: engagement, functionality, aesthetics, content, relevance, interference, quality, and perceived impact (%). 3. Longitudinal trends in dietary intake (macronutrients g/day, food groups units/day) body composition (fat mass, fat free mass, skeletal muscle mass, phase angle), REE (kcal/day), and HRQL.

Sample Size	Phase 1: 15 participants (Sample 1) Phase 2: 15 participants (Sample 2)
Date of anticipated First Participant First Visit (FPFV)	01-10-2026
Date of anticipated Last Participant Last Visit (LPLV)	01-03-2029
Expected study duration for a single participant	Phase 1, Sample 1: 8 months Phase 2, Sample 2: 6 months

STUDY FLOWCHART

Table 1: MybYte study schedule of events – Study specific procedures & assessments

Measure	**Phase 1: Sample 1**					**Phase 2: Sample 2**						
Visits*/ contacts	**Visit 1*: Screening**	**Visit 2/ Remote contact: Interview**	**Remote contact**	**Remote contact**	**Visit 3: Focus grp**	**Visit 1**: Screening**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**
Timing (months)	**1**	**1**	**2**	**5**	**7**	**1**	**1**	**2**	**3**	**4**	**5**	**6**
Informed consent	x					x						
Inclusion/ Exclusion criteria	x					x						
Demographics												
Age	x					x						
Sex	x					x						
Ethnicity	x					x						
Clinical data												
Age at first cancer diagnosis	x					x						
Cancer diagnosis	x					x						
Cancer staging I-V or risk group	x					x						
Metastatic disease (Y/N)	x					x						
Treatment modality	x					x						
Interview		x										
Digital tool use												
YONAS tool use (3 days)			x									
MybYte tool use (7 days)				x			x	x	x	x	x	x
Digital tool assessment questionnaire			x	x								
Focus group					x							
Acceptability questionnaire									x			x
Body composition measurement												
Weight (kg)							x	x	x	x	x	x

Height (cm)							x	x	x	x	x	x
Fat mass (kg)							x	x	x	x	x	x
Fat free mass(kg)							x	x	x	x	x	x
Skeletal muscle mass (kg)							x	x	x	x	x	x
Phase angle (°)							x	x	x	x	x	x
Nutritional intervention data												
Type received (ONS/EN/PN)							x	x	x	x	x	x
Start, end date							x	x	x	x	x	x
Volume							x	x	x	x	x	x
Energy expenditure measurement												
REE via BIS (kcal/day)							x	x	x	x	x	x
REE vis IC (Kcal/day)							x		x			x
Taste profile												
Taste strips							x	x		x		x
Health-Related Quality of Life												
PedsQL™ 4.0							x		x			x
PedsQL™ 3.0 Cancer Module							x		x			x

ONS: Oral nutritional supplementation; EN: Enteral nutrition; PN: Parenteral nutrition; BIS: Bioelectrical spectroscopy; IC: Indirect calorimetry

*Visit 1 (screening) in Phase 1 will occur during routine admission or outpatient appointments

** All data in Phase 2 will be collected during routine patient admissions or outpatient appointments

All assessments highlighted in blue indicate study- specific activities above the scope of standard care

1 Background, rationale & risk assessment

Children and adolescents with cancer face a heightened risk of both under- and overnutrition throughout the cancer continuum.[1]The aetiology of undernutrition is multifactorial, involving underlying disease, inflammatory responses, increased metabolic demands, and treatment side effects.[2,3] Undernutrition is associated with treatment delays, infections, impaired healing, reduced treatment response, and decreased survival.[2,4,5] Conversely, a higher BMI at diagnosis or during treatment correlates with increased mortality, poorer event-free survival, and greater treatment toxicities.[3] Survivors are further at risk for overnutrition, metabolic disease, endocrinopathies, and hypertension.[6] Consequently, nutritional status is recognised as a modifiable prognostic factor across the continuum of paediatric oncology.[7] Malnutrition also negatively impacts health-related quality of life (HRQL), demonstrating its influence on both prognosis and patient experience.[8,9]

Personalised nutrition in paediatric oncology- where are we and what needs to be done?

Given the complex aetiology of malnutrition during cancer treatment, a personalised approach to nutrition therapy is advocated.[1] Pedretti *et al.* conclude that tailored nutrition, considering individual variability, could transform patient management.[10] Despite such calls, the concept remains underdefined and underexplored, representing a promising research frontier for improving outcomes.

Key components crucial to the delivery of personalised nutrition include routine assessments of nutritional status, energy requirements, and dietary intake.[11] In addition, low-burden digital approaches, which incorporate patient voices, have been identified as crucial when implanting personalised health interventions among adolescents in particular.[12] These recommendations underpin our framework for developing a personalised nutrition strategy for adolescents undergoing cancer treatment, as discussed below:

1.Body composition to assess nutritional status

Improving the nutritional status of children with cancer starts with accurate assessment.[3,11] There is growing consensus to include body composition measurements in routine practice, which provides critical insights into fat and lean tissue distribution.[1,5,10] Most Paediatric Oncology Units still rely on anthropometric measures—weight, height, BMI—which are influenced by hydration status and tumour mass and fail to reflect body compartment distribution.[2,9] As an accessible alternative to costly gold-standard methods, bioelectrical impedance analysis (BIA) or spectroscopy (BIS) offer a portable, cost-effective, minimally invasive approach to assess body composition and have proven feasible in paediatric settings.[4]

2.Assessment of nutritional requirements

Whether basal metabolic rate (BMR) in children with cancer is elevated compared to healthy peers remains debated, with early studies yielding conflicting results.[10,11] Gold-standard methods to assess resting energy expenditure (REE)—a clinical proxy for BMR—are costly and impractical in routine care.[13,14] Consequently, most units rely on predictive equations to predict energy expenditure. These, however, are derived from healthy children, and have shown poor accuracy in clinical populations.[13,14] To enable personalised nutrition, experts recommend novel approaches over traditional equations, and emphasise the importance of including body composition when determining energy needs.[1,10,15,16] BIA/BIS devices offer a practical alternative, by estimating REE from fat-free mass (FFM)—the primary contributor to BMR. Our proposed study will utilise BIS to routinely assess REE in addition to intermittent gold standard measurement using indirect calorimetry.

3.Low- burden dietary intake assessment – the use of Experience Sampling Methodology

Supportive care strategies must work to relieve, rather than add to, the burden of oncological treatment.[12] Traditional dietary assessment methods are, however, burdensome and prone to bias, participant fatigue, and misreporting, which lead to measurement errors.[17,18] To address these limitations, our broader research team recently developed **YONAS (YOur Nutrition ASsistant)**, a novel dietary assessment tool using experience sampling methodology (ESM) to assess dietary intake.[18] ESM collects real-time, context-specific data by sending short, random prompts to individuals' smartphones two to three times a day, aiming to reduce participant burden and bias.[17,19] Consequently, the use of ESM as a dietary assessment tool represents an emerging field in nutrition research.[17]

4.ESM for low burden, digital, personalised nutrition interventions

Advances in technology have expanded the use of ESM in paediatrics to chronic conditions such as asthma, diabetes, and arthritis for symptom tracking, treatment adherence, and self-monitoring.[19] ESM has several key strengths within paediatrics: it collects data in real-life contexts, linking symptoms and well-being to children's daily environments; it is especially suitable for adolescents, who spend an average of 3 h 45 min daily on smartphones; and it enables clinicians to deliver personalised, timely feedback. While still in its infancy in paediatrics, ESM is thought to have the potential to inspire innovative, patient-centred care.[19]

5.Shared decision making and adolescent perspectives in digital health interventions

ESM aligns with the growing emphasis on shared decision-making in paediatric oncology, recognising that valuing the perspectives of the child can positively influence outcomes.[19,20] Older children and adolescents who are actively involved in their own care often experience greater autonomy, reduced fear, and prefer collaborative decision-making.[21] Digital health interventions, including digital nutritional counselling, have been shown to improve access to care, self-management, quality of life, physical outcomes, and support behaviour change in cancer survivors.[22,23] In fact, early involvement of adolescents and young adults (AYAs) in the development and usability testing of such digital health interventions is now recommended to ensure feasibility and acceptability.[24] AYAs have also identified a need for age-appropriate nutrition and health information in accessible formats, underscoring the importance of incorporating patient perspectives when developing personalised nutrition strategies.[25,26]

Summary

In summary, the following key points should be considered within the context of paediatric and adolescent oncology:

1. Nutritional status is linked to both clinical outcomes and health-related quality of life.
2. Nutritional strategies aimed at optimising nutritional status have the potential to enhance quality of life.
3. A personalised nutrition approach is recommended, necessitating routine assessments of body composition, energy requirements, and dietary intake.
4. Supportive care strategies, including nutrition, should be innovative, low-burden, and leverage available technology.
5. Experience sampling methodology, employed within a digital nutrition intervention, presents a promising strategy for achieving personalised nutrition, particularly in older children and adolescents.

Development of a personalised nutrition strategy:

Within the above framework this research group plans to design a digital, disease-specific, personalised nutrition tool using experience sampling methodology. Such a tool is novel to paediatric and adolescent oncology, as is the use of ESM as a dietary assessment method within this group.

Risk vs benefit:

Participation in this study involves minimal risk and consists exclusively of non-invasive assessments and the use of digital research tools (Table 1). Participant burden is a key consideration in paediatric oncology; therefore, the study design includes safeguards to mitigate this as described in 5.3.2: Study safety risks and mitigation measures. Involvement may be beneficial to the participant as evidence suggests that meaningful engagement in care can support autonomy and reduce anxiety, with children and adolescents often expressing a preference for collaborative involvement in decision-making.[21,27] For participants enrolled in

phase 2 of the study, assessments of nutritional status, energy requirements, and HRQL will be shared with both participants and their medical team, extending beyond the current standard of care.

2 Study objectives & design

2.1 Study objectives

Research Question: What is the feasibility and acceptability of a digital personalised nutrition tool, using experience sampling methodology, in adolescents with cancer undergoing treatment? We **hypothesise** that such a tool can be successfully developed and that feasibility and acceptability can be established within this specific population.

Our **research aim** is to develop and thereafter to assess the feasibility and acceptability of a digital personalised nutrition tool for use within this group. The study will occur over two phases:

Primary objectives:

- Phase 1:
  Co-creation of MybYte- a digital, disease-specific, personalised nutrition tool using experience sampling methodology.

- Phase 2:
  To investigate the feasibility (recruitment, engagement, retention) and acceptability of the MybYte tool among adolescents with cancer.

Secondary objectives:

- Phase 1:
  1. Qualitative assessment of adolescent perspectives of nutrition during cancer treatment
  2. Qualitative and quantitative assessment of the MybYte tool in terms of engagement, functionality, aesthetics, content, relevance, interference, and quality.
- Phase 2:
  Longitudinal monitoring of:
  1. Dietary intake measured by MybYte tool
  2. Nutritional status measured by bioelectrical spectroscopy
  3. Resting energy expenditure (REE) estimated by bioelectrical spectroscopy and by indirect calorimetry
  4. Health Related Quality of Life (HRQL) measured by PedsQL 4.0 and Peds QL 3.0 Cancer Module

2.2 Primary endpoints

- Phase 1:
  1. Final version of MybYte tool, hosted by the digital platform m-Path

- Phase 2:
  1. Feasibility of MybYte tool as determined by recruitment, engagement (response), and retention (%)
  2. Acceptability of MybYte tool as assessed by the following categories: engagement, functionality, aesthetics, content, relevance, interference, quality, and perceived impact (%).

2.3 Secondary endpoints

- Phase 1:
  1. Thematic analysis of adolescent perspectives of nutrition during cancer treatment

- Phase 2:
  Longitudinal trends in:

1. Dietary intake (macronutrients g/day, food groups units and g/day)
2. Body composition (fat mass, fat free mass, lean skeletal muscle mass, phase angle)
3. REE (kcal/day)
4. HRQL as determined by PedsQL 4.0 and Peds QL 3.0 Cancer Module

2.4 Study design

This prospective mixed-methods study is guided by the updated Medical Research Council (MRC) framework for developing and evaluating complex interventions, specifically focusing on intervention development and feasibility/acceptability assessment.[28] Methodology was additionally informed by the CONSORT extension for pilot and feasibility studies, as well as the Guidelines for reporting of health interventions using mobile phones: mERA checklist.[29,30] The study consists of two phases as shown in Figure 1.

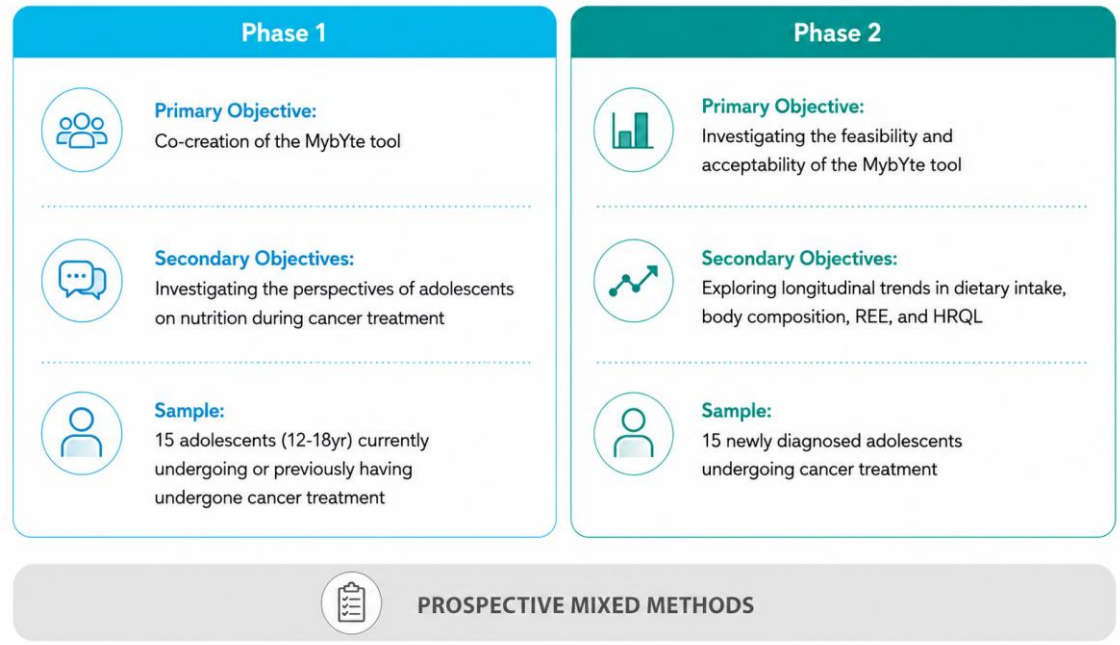


Figure 1: MybYte study design

2.5 Expected duration of the study

Phase 1 (Sample 1):

The total duration of Phase 1 for each participant is estimated at approximately 8 months. At the study site level, Phase 1 is expected to span around 12 months to allow sufficient time for recruitment, tool development, and completion of all participant activities.

Phase 2 (Sample 2):

During Phase 2 of the study, participants will be recruited within six weeks of diagnosis. Following enrolment, data will be collected on a monthly basis over a 6-month period. Accordingly, the total duration of participation for each individual is estimated at 6months.

Based on current admission rates of adolescents to the UZ Leuven Kinderhematologie en Oncologie unit, the overall duration of Phase 1 at the site is expected to be approximately 18 months to ensure completion of recruitment and follow-up of all participants.

The total duration of the study (Phase 1 and 2) at the site is therefore anticipated to be approximately 2 years and 6 months.

The End of Study (EoS) is defined as Last Participant Last Visit (LPLV). The Sponsor-Investigator shall notify the EC of the end of the study. The Sponsor-Investigator will submit a final report with the results of the study, including any publications/abstracts, to the Competent Authorities (CA)/Ethics Committee (EC) within 1 year of study termination or within 6 months for paediatric studies.

The Sponsor or EC can decide to halt or prematurely terminate the study when new information becomes available whereby the rights, safety and well-being of study participants can no longer be assured, when the integrity of the study has been compromised, or when the scientific value of the study becomes obsolete and/or unjustifiable.

Circumstances requiring premature treatment interruption or discontinuation of the study, include but are not limited to:

- Safety concerns or unacceptable intolerability

Should the study be temporarily suspended or, ended prematurely, the Sponsor-Investigator will notify the EC and include the reasons for suspension/premature termination within 15 days of the decision.

3 Study population / Eligibility criteria

3.1 Inclusion criteria

Participants eligible for inclusion in this study must meet **all** of the following criteria:

Phase 1: Sample 1

1. Written informed consent has been obtained from a parent/legal guardian.
2. Written assent has been obtained from participants.
3. Aged between 12 and 18 years at the time of enrolment.
4. Currently receiving, or having previously received cancer treatment (including chemotherapy) at UZ Leuven within the specified age range.
5. Ability to use a smartphone independently.
6. Adequate cognitive capacity to participate in study procedures, as determined by the research team.
7. Proficiency in Dutch

Phase 2: Sample 2

1. Written informed consent has been obtained from a parent/legal guardian.
2. Written assent has been obtained from participants
3. Aged between 12 and 18 years at the time of enrolment .
4. New histological diagnosis of cancer.
5. Enrolled into the study within 6 weeks of diagnosis.
6. Currently receiving cancer treatment (including chemotherapy) at UZ Leuven.
7. Ability to use a smartphone independently.
8. Adequate cognitive capacity to participate in study procedures, as determined by the research team.
9. Proficiency in Dutch.

All participants that are considered for study participation, per the above criteria will be documented via applicable log forms in the Investigator Site File (ISF) (including screen failures).

3.2 Exclusion criteria

Phase 1 and Phase 2:

Participants eligible for this study must **not** meet any of the following criteria:

1. Presence of cognitive, developmental, or neurological impairments that compromise the ability to provide informed consent or assent, or that impair independent use of a digital tool.
2. Medical instability or clinical condition deemed too unwell for participation, as determined by the treating clinician.
3. Admitted to the intensive care unit during the enrollment period.
4. Currently on a palliative care trajectory.

Participants who meet one or more of the above exclusion criteria **must not proceed** to be enrolled/randomized in the study and will be documented as a screen failure via applicable log forms in the Investigator Site File.

4 Study period and procedures

4.1 Selection of participants / Recruitment

4.1.1 Recruitment and screening

Phase 1

Eligible participants will be identified by a paediatric oncologist at UZ Leuven or by the researcher through screening of medical records. Participants will be recruited using convenience sampling, whereby adolescents aged 12–18 years who are currently receiving or have previously received cancer treatment and meet the inclusion criteria will be invited to participate via telephone or email (correspondence will be directed to a parent or legal guardian). Additional recruitment will take place through a poster on UZ Leuven Paediatric Oncology, Adolescent and Young Adult (AYA) social media platforms (e.g. Instagram and Facebook), as well as via a physical poster displayed in the paediatric haematology and oncology ward and outpatient day unit, allowing current and former patients to self-refer. Note that links such as likes or comments will be blocked on social media platforms to avoid the sharing of personal data.

Phase 2

Screening and recruitment will take place on the UZ Leuven Paediatric Haematology and Oncology ward. Eligible participants will be identified by a paediatric oncologist or by the researcher through screening of hospital admission records. Newly diagnosed participants will be recruited using consecutive sampling, whereby all newly diagnosed adolescents aged 12–18 years who meet the inclusion criteria will be approached whilst admitted on the ward to participate in the study. No posters or social media platforms will be used for this phase.

4.1.2 Informed consent and assent

Phase 1 and 2

All individuals who express interest in participating will be invited to attend a screening visit. Whenever feasible, this visit will be scheduled to coincide with a routine outpatient appointment. For individuals approached by a researcher during an outpatient appointment or inpatient admission, screening procedures and informed consent will be completed during that same visit. At least one parent or legal guardian will be required to attend. Detailed verbal and written information will be provided by the researcher with opportunity given for questions. For those who choose to take part, written informed consent will be obtained from a parent or legal guardian, alongside assent from the adolescent.

4.2 Study assessments & procedures

4.2.1 Phase 1: Co-creation of the MybYte tool

Phase 1 will be achieved in several steps as illustrated in Figure 2.

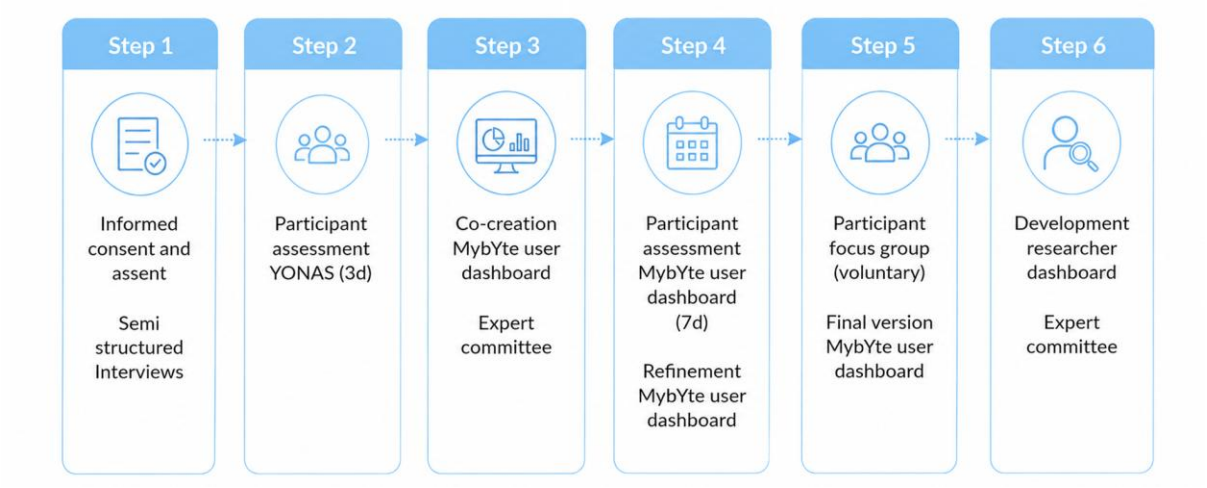


Figure 2: Phase 1 methodology

Step 1: Semi-structured interviews

Semi-structured interviews will be conducted in Dutch and will last approximately 60–90 minutes. Where necessary, interviews can be conducted across two sessions to minimise participant burden. Using a standardized interview guide (Appendix 3) adapted from previous studies, interviews will explore adolescents' experiences of nutrition during cancer treatment, including barriers and facilitators to adequate intake, access to nutrition support, autonomy in decision-making, preferences for nutrition information delivery, and engagement with digital nutritional support.[25,31] Interviews will be audio-recorded, transcribed verbatim, and participants may be contacted for clarification during qualitative analysis.

Step 2: Three day assessment of the YONAS tool

Participants will use the existing digital dietary assessment tool YONAS for three consecutive days on their smartphone via the m-Path application. YONAS, designed for use in adults, estimates food portions and macro- and micronutrient intake using the Belgian Food Composition Table and will serve as the foundation for the development of a more age-appropriate, disease-specific tool.[32] Participants will receive three daily prompts asking about food and beverage intake during the preceding two hours. Responses are recorded using multiple-choice questions. Following the assessment period, participants will complete a brief (approximately 5-10 minutes) questionnaire, adapted from the Mobile App Rating Scale User Version (uMARS) and a previous feasibility study of ecological momentary assessment (EMA) in adolescent and young adult cancer survivors.[33,34] The questionnaire will be sent via smartphone and will evaluate the tool based on the categories: engagement, functionality, aesthetics, content, quality, relevance, and interference (Appendix 4).

Step 3: Co-creation of the MybYte tool user dashboard

In this step, results from the semi-structured interviews (step 1) and the assessment of the YONAS tool (step 2) will be used to expand and adapt the YONAS tool to: 1) assess the dietary intake of adolescents with cancer using relevant, age-appropriate content 2) incorporate disease- specific information about nutrition-related symptoms and treatment side effects, appetite, taste changes, and preferences and 3) deliver targeted information for participants based on their own responses. This will result in version 1 of the MybYte tool user dashboard. The user dashboard is the part of the tool that is visible to the user on their smartphone.

During daily use of the tool, and based on their own responses, adolescents will receive immediate self-management tips for common nutrition-related symptoms (e.g. nausea, reduced appetite) which are specific

to taste preference and location. This information is widely available and does not constitute clinical advice. It will, however, be targeted to ensure relevance to the user.

Version 1 of the dashboard will subsequently be evaluated by an expert committee comprising a paediatric oncologist, two paediatric oncology dietitians, and a paediatric oncology nutrition researcher. Feedback from this stakeholder review will inform further refinement of the tool in line with updated MRC guidance for complex interventions.[28]

Step 4: Seven day assessment of the MybYte tool user dashboard

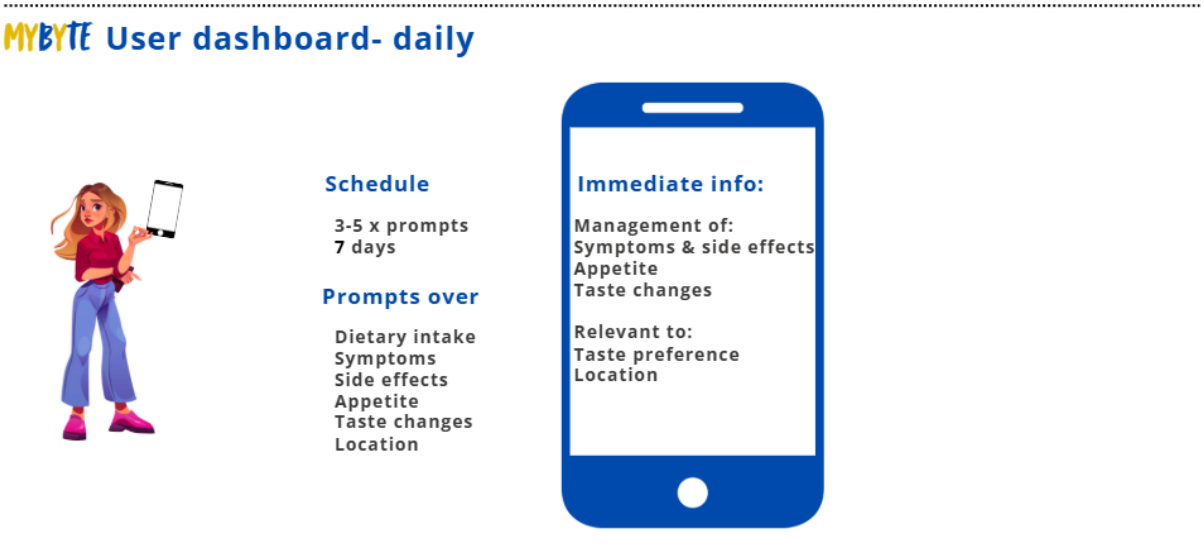
Each participant will subsequently be asked to use the first version of the MybYte user dashboard for a period of seven days, during which they will receive 3-5 prompts per day. Prompts will take approximately 5 minutes to complete. Following this, they will evaluate the tool by completing a second semi-structured questionnaire via their smartphone, again adapted from the Mobile App Rating Scale User Version and the acceptability questionnaire of Heathcote et al (completion time approximately 10-15 minutes, Appendix 4).[33,34] Based on participant evaluations obtained in Step 4, the MybYte user dashboard will be further refined by the research team, resulting in a second version of the tool.

Step 5: Focus group and final refinement of the MybYte user dashboard

Participants will then be invited to take part in a voluntary focus group, during which they will be given the opportunity to use the second version of the MybYte. This semi-structured focus group will primarily aim to inform the final iteration of the user dashboard and will last approximately 90 minutes.

Step 6: development of the researcher dashboard

The researcher dashboard will be accessible only to the research team. The researcher dashboard will enable researchers to view dietary intake data as well as input the following parameters on a monthly basis: weight, body composition, and resting energy expenditure. The dashboard will display longitudinal trends for each of these parameters. Based on these trends, the researcher (who is also a recognised dietitian) will be able to send personalised nutritional information directly to an individual's user dashboard each month. This advice will target energy and protein intake, food group distribution, and meal frequency, incorporating examples tailored to the individual's taste preferences, and will be given in collaboration with the dietitian team on the unit. All advice will be manually generated, meaning that **no autonomous digital decision-making will occur within the tool. The tool will be used for the communication of nutritional information.** The researcher dashboard will not be used or evaluated by participants during Phase 1 but will instead undergo review by the expert committee prior to proceeding to Phase 2.



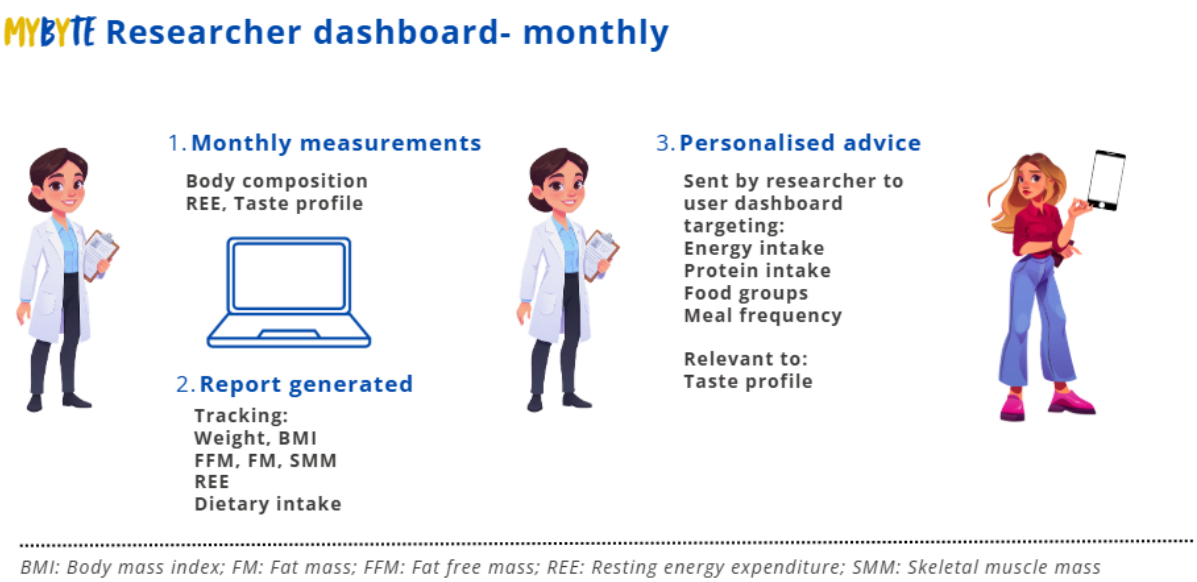


Figure 3: Proposed MybYte tool

4.2.2 Phase 2: Feasibility and acceptability of MybYte tool

Participants will be recruited into phase 2 of the study for six months. Data collection will take place every month during routine admissions or outpatient appointments as indicated in Table 1. Relevant data collection procedures are described in more detail below.

MybYte tool use

Participants will use the MybYte tool for seven consecutive days each month over a six-month period via the m-Path smartphone application. During each assessment period, participants will receive 3-5 semi-random prompts per day between 08:00 and 22:00. Based on their responses, participants will receive immediate (daily) non-clinical dietary tips as well as monthly nutritional advice generated by the researcher (dietitian) via the researcher dashboard (Figure 3).

Prompt timing will not be disclosed to participants. Unanswered prompts will trigger a reminder notification after 30 minutes and will remain accessible for two hours following initial delivery. In line with experience sampling methodology, surveys are designed to require approximately five minutes to complete, thereby minimizing participant burden.

Body composition

Body composition will be measured monthly using bioelectrical impedance spectroscopy (BIS) with the BodyStat Multiscan 5000 (CE mark 1639), a device validated for use in children from the age of 6 years. BIS allows for reliable measurements across varying states of hydration and in non-fasted conditions; both of which are particularly advantageous in adolescents undergoing cancer treatment. Participants will be measured in a supine position after voiding the bladder.

Anthropometry

Weight and height will also be measured each month. Measurements will be taken using calibrated, standardized equipment. Participants will be weighed in light clothing without shoes. Height will also be measured without shoes with participants standing with their heels and scapula against the stadiometer with their heads in the position of the Frankfurt plane. Body mass index will be calculated from weight and height measurements (kg/m^2).

Resting energy expenditure
Resting energy expenditure (REE) will be estimated monthly using the BodyStat 5000, which derives REE from muscle mass in combination with variables such as age, sex, height, and weight. In addition REE will be measured at diagnosis, months 3 and 6 using the gold standard methodology open-circuit indirect calorimetry (Quark RMR, Cosmed); a procedure which takes approximately 20 minutes.

Taste testing
Previous research suggests that self-reported taste changes do not correlate well with validated taste recognition testing in paediatric and adolescent oncology.[35,36] Therefore, in addition to self-reported taste preferences collected via the MybYte dashboard, objective taste recognition will be assessed using Taste Strips (Burghard, Wedel, Germany). These filter paper strips are impregnated with sweet, sour, salty, bitter, and umami tastes at four concentrations each. Taste Strips are feasible in both paediatric and adolescent populations and can be easily administered at the bedside.[35] Strips will be placed on the mid-tongue, after which participants will identify the taste from five response options. Scores for each taste modality range from 0–4, with higher scores indicating greater taste recognition. Total scores will be compared with established paediatric (6–15 years) and adult (>15 years) normative values.[36] Testing takes approximately 10 minutes.

Health- Related Quality of Life
Health-related quality of life (HRQoL) will be assessed using the Pediatric Quality of Life Inventory (PedsQL™ 4.0 Generic Core Scales) and the PedsQL™ 3.0 Cancer Module. These validated self-report questionnaires will be administered to participants at diagnosis, and at 3 and 6 months.[37,38] The PedsQL 4.0 assesses physical, emotional, social, and school functioning, while the Cancer Module evaluates cancer-specific symptoms and treatment-related concerns. Items are rated on a 5-point Likert scale (0 = never to 4 = almost always), and scores are linearly transformed to a 0–100 scale, with higher scores indicating better HRQoL. Completion time is approximately 5–10 minutes per questionnaire.[37–39] Questionnaires will be administered in paper format and completed independently by the adolescent.

Acceptability
Acceptability of the MybYte tool will be evaluated at months 3 and 6 using a semi-structured questionnaire adapted from Stoyanov et al's Mobile App Rating Scale User Version and a previous feasibility study of ecological momentary assessment (EMA) in adolescent and young adult cancer survivors.[33,34] The questionnaire aligns with the mERA guidelines for mHealth reporting (Appendix 5).[30] The questionnaires will be administered via smartphone and will include 30 closed-ended Likert-scale items assessing engagement, functionality, aesthetics, content, quality, relevance, interference, and perceived impact, as well as 7 open-ended questions exploring participant experiences, challenges, and suggestions for improvement. Completion time is estimated at 10-15 minutes.

4.2.3 Participant consent & withdrawl of consent

The study will be conducted only on the basis of prior informed consent by the Study participants and/or their legally authorized representative(s). As such, no study-related procedures will be conducted prior to obtaining written informed consent from potential study participants.

The process for obtaining and documenting initial and continued informed consent from potential study participants will be conducted in accordance with Good Clinical Practice (GCP), applicable regulatory requirements and internal Standard Operating Procedures (SOPs).

All originally signed obtained Informed Consent Forms (ICFs) must be retained/archived in the Investigator Site File (ISF) at the participating site and must not be destroyed (even when a scanned copy is available) before expiration of the legal archiving term as defined in the protocol section entitled "Archiving".

Participants may voluntarily withdraw consent to participate in the study for any reason at any time. The participant's request to withdraw from the study must always be respected without prejudice or consequence to further treatment. Consent withdrawal will be documented in the participant's medical record.

Study data and samples collected before withdrawal can be used in the study. No new study data or samples will be collected after withdrawal of the participant.

4.2.4 Other study assessments and procedures

4.2.4.1.Study specific and other procedures/investigations:

Study procedures and their timing are summarized in the Study flowchart and in the text above. Table 2 provides further clarification.

Table 2: Study Investigations

	Investigations	Total	Completion time (min)	Location
Phase 1	Interview	x 1	60-90	UZ Leuven/Remote
	YONAS tool use (3 days)	3 prompts/day	15/ day	Remote
	MybYte tool use (7 days)	3-5 prompts/day	15/ day	Remote
	Focus group	x 1	60-90	UZ Leuven
Phase 2	MybYte tool use (7 days)	3-5 prompts/day	15/ day	Remote
	Body composition	x 6	5	UZ Leuven
	Energy expenditure	x 3	20	UZ Leuven
	Taste profile	x 4	10	UZ Leuven

4.2.4.2 Questionnaires & participant reported outcomes (PROs):

Study questionnaires are summarised in the Study flowchart and in the text above. Table 3 provides further clarification.

Table 3: Study questionnaires

	Questionnaires	Total	Completion time (min)	Format
Phase 1	Digital YONAS tool assessment	x 1	5-10	
	Digital MybYte tool assessment	x 1	10-15	Digital
Phase 2	PedsQL™ 4.0		5-10	
	PedsQL™ 3.0 Cancer Module	x 3	5-10	Paper
	Acceptability	x 2	10-15	Digital

4.2.4.3 Location of the study:

Phase 1 and Phase 2 of the study will take place at UZ Leuven, Kinderhemato-oncologie unit.

4.3 Premature discontinuation of study

Participants may voluntarily discontinue from study treatment and/or prematurely end their participation in the study for any reason at any time. In such case the Investigator must make a reasonable effort to contact the participant (e.g. via telephone and/or e-mail) in order to document the primary reason for this decision.

The Investigator may also decide at any time during the course of the study, to temporarily interrupt or permanently discontinue the study treatment if it is deemed that continuation would be detrimental to, or not in the best interest of the participant.

Circumstances requiring premature treatment interruption or discontinuation of the study, include but are not limited to:

- Study participation while in violation of the inclusion and/or exclusion criteria

In any such case of early study termination and/or treatment interruption/discontinuation, the treating physician will continue to closely monitor the participant's condition and ensure adequate medical care and follow-up. It is recommended that follow-up information will be collected as follows: Not applicable

For participants whose status is unclear because they fail to appear for study visits without stating an intention to discontinue or withdraw, the Investigator must make every effort to demonstrate "due diligence" by documenting in the source documents which steps have been taken to contact the participant to clarify their willingness and ability to continue their participation in the study (e.g. dates of telephone calls).

A participant should not be considered lost to follow-up until due diligence has been completed.

5. Safety reporting

5.1 Definitions

5.1.2 Adverse Event (AE)

An AE is any untoward medical occurrence in a patient or participant during an experiment, and which does not necessarily have a causal relationship with the treatment or intervention.

An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a product or intervention, whether or not considered related. Any worsening (i.e., any clinically significant adverse change in the frequency or intensity of a pre-existing condition) should be considered an AE.

5.1.3 Adverse Reaction (AR)

An AR is any untoward and unintended response in a participant during an experiment in which a causal relationship between the study intervention and an adverse event is a reasonable possibility.

5.1.3 Serious Adverse Event (SAE)

An SAE is any unfavourable medical occurrence that results in any of the following:

- Inpatient hospitalisation or prolongation of existing hospitalization
- A persistent or significant disability or incapacity
- A congenital anomaly or birth defect
- A life-threatening[a] experience
- Death
- Important medical events that may be considered an SAE when - based on appropriate medical judgement - they may jeopardise the participant and may require medical or surgical intervention to prevent one of the above outcomes

[a] The term "life threatening" in the definition of SAE refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it was more severe.

5.1.4 Serious Adverse Reaction (SAR)

A SAR is an adverse reaction that meets the criteria for a serious adverse event (see definition SAE).

5.2 Recording & reporting of Adverse Events

5.2.1 AE recording

Investigators will seek information on AEs during each participant contact. All events, whether reported by the participant or noted by study staff, will be recorded in the participant's medical record and in the eCRF within a reasonable time after becoming aware. The diagnosis rather than the individual signs or symptoms should be reported, if available. If no diagnosis is available, the Investigator should record each sign and symptom as individual AEs.

The following minimum information should be recorded for each (S)AR:

- AE description
- Start and stop date of the AE
- Severity
- Seriousness
- Causality assessment to the study interventions

- Outcome

5.2.2 Study safety risks & mitigation measures

The risks associated with the study are:

- Fatigue in Phase 1: The interview and focus group procedures may result in fatigue in this population. To minimise this risk, sessions may be paused to allow for breaks, or, if needed, conducted across two separate sessions.
- Participant burden in Phase 2: Safeguards are embedded into the study to mitigate participant burden. At the three-month timepoint, participants will complete an acceptability survey and will be explicitly asked whether they wish to continue or withdraw from the study. In addition, PedsQL and PedsQL Cancer Module scores will be reviewed, and any clinically meaningful decline in health-related quality of life (HRQL) will prompt referral to the UZ Leuven Paediatric Oncology Psychological Service, with the option to discontinue participation.

5.2.3 Assessment

All AEs must be evaluated by an Investigator as to:

- **Seriousness:** whether the AE is an SAE. See above for the seriousness criteria.
- **Severity:**

  Severity must be evaluated by an Investigator according to the following definitions:

  - *Mild* – no or transient symptoms, no interference with the participant's daily activities
  - *Moderate* – marked symptoms, moderate interference with the participant's daily activities
  - *Severe* – considerable interference with the participant's daily activities, unacceptable
- **Causality:**
  - *None* – An AE which is not related to the study related interventions.
  - *Unlikely* – An AE for which an alternative explanation is more likely (e.g. concomitant medication(s), concomitant disease(s)), and/or the relationship in time suggests that a causal relationship is unlikely.
  - *Possible* – An AE which might be due to the study related interventions. An alternative explanation is inconclusive. The relationship in time is reasonable; therefore the causal relationship cannot be ruled out.
  - *Probable* - An AE which might be due to study related interventions. The relationship in time is suggestive (e.g. confirmed by dechallenge). An alternative explanation is less likely.
  - *Definitely* – An AE which is listed as a possible adverse reaction and cannot be reasonably explained by an alternative explanation. The relationship in time is very suggestive (e.g. it is confirmed by dechallenge and rechallenge).

5.2.4 Timelines for reporting

After informed consent has been obtained and after initiation of study related interventions:

All AEs and SAEs causally related to a study-related intervention and AESIs will be reported until 30 days after the last study-related intervention or until last follow-up visit (whichever occurs first).

5.2.5 Death

Deaths of subjects who were participating in the study at the time of their death will be reported to the Sponsor without delay (irrespective of whether the death is related to disease progression, study procedure or is an unrelated event). The Sponsor will notify all deaths, as soon as possible after becoming aware, to the Central EC. Additionally, deaths occurring at a specific site will be reported to the EC of the concerned site, if requested by the respective EC.

5.3 Reporting requirements to Ethics Committee's (EC's)

The Investigator is responsible for ensuring that all safety events are recorded in the eCRF and reported to the Sponsor in accordance with instructions provided below.

The Sponsor will promptly evaluate all SARs and AESIs against medical experience to identify and expeditiously communicate possible new safety findings to the Investigators and to the EC(s) based on applicable legislation.

5.3.1 Annual reporting

The Sponsor has the obligation to, once a year throughout the study (or on request), submit a progress report to the ECs containing an overview of all SARs that occurred during the reporting period and taking into account all new available safety information received during the reporting period.

5.3.2 Overview reporting requirements

	WHAT	HOW	TO	TIMELINES
Investigator	AR	AE form in eCRF	Sponsor	In a timely manner
	SAR	SAE form in eCRF	Sponsor	Immediately (within 24 hours of becoming aware of the event) Exceptions: as defined in protocol
	death	SAE form in eCRF	Sponsor	asap
Sponsor	death	SAE form + narrative	ECs	asap
	Annual Progress Report	APR template	ECs	annually

6 Statistics and data analysis

A study-specific Statistical Analysis Plan (SAP) will be developed by the Sponsor, to supplement the information below with further details.

6.1 Sample size determination

Phase 1 Sample 1:

For the qualitative analysis of semi-structured interviews, data collection must continue until thematic saturation is reached. As prospective estimation of sample size is challenging in qualitative research, a sample of 15 adolescents was selected based on recommendations that approximately 12 participants are generally sufficient to achieve data saturation while capturing diverse experiences and perspectives, with additional participants included to account for potential dropout.[40]

Phase 2 Sample 2:

Fifteen participants will be recruited for Phase 2 of the study. As this is a feasibility study, no formal sample size calculation is required, which is consistent with recommendations outlined in the CONSORT 2010 extension for pilot and feasibility studies.[29] Instead, the sample size is determined based on practical considerations, including the admission rate of new diagnoses, the duration of data collection, and the overall

study timeline. This sample size is considered sufficient to inform the research team about the practicalities of implementing the tool, recruitment, engagement, and attrition.

6.2 Statistical analysis

Qualitative data will be managed and analysed using NVivo 15 (QSR International, Melbourne, Australia). Quantitative data will be analysed using R, version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria, 2022). Descriptive statistics, including counts, percentages, means (±SD), and medians (IQR), will be used to summarise demographic and clinical characteristics across both study phases. Missing data will not be imputed due to the exploratory nature and small sample size of this feasibility study. Table 4 provides a summary of the statistical approach.

Semi-structured interviews
Interview transcripts will be imported into NVivo (QSR International, Melbourne, Australia) and analysed using inductive thematic analysis within a generic qualitative framework, guided by Braun and Clarke's six-phase approach.[41] Initial coding will be conducted by the doctoral researcher, with a subset of transcripts independently coded by a second researcher. Regular team meetings will be held to review coding decisions and refine theme development. Dependability will be enhanced through comprehensive documentation of methodological and analytical decisions throughout the study. Reporting of findings will follow the Consolidated Criteria for Reporting Qualitative Research (COREQ) to ensure transparency and methodological rigour.[42]

Semi-structured questionnaires (Phase 1 and 2)
Descriptive statistics will summarise quantitative data from the structured components of the Phase 1 YONAS and MyByte questionnaires and the Phase 2 acceptability questionnaires. Qualitative data from unstructured questionnaire components will be analysed using inductive thematic analysis (described above).

Feasibility (Phase 2):
Feasibility will be assessed through recruitment, engagement, and retention, with predefined benchmarks of 55%, 65%, and 65%, respectively. These thresholds were informed by prior feasibility studies using Experience Sampling Methodology in adolescent and young adult cancer survivors and digital health interventions in adolescents, and are intended to guide progression to a future definitive trial.[34,43]

Exploratory analysis (Phase 2)
Dietary intake, REE, body composition, and HRQL data, will be analysed descriptively. Given the feasibility design and limited sample size, inferential statistical testing will not be used to draw definitive conclusions. Instead, exploratory analyses will focus on estimating effect sizes which will be reported with 95% confidence intervals, without p-values, as feasibility studies are not designed or powered for formal hypothesis testing.[29]

Associations between continuous variables will be assessed using Pearson's or Spearman's correlation coefficients. Predefined, exploratory subgroup analyses will be conducted despite limited power, to support hypothesis generation, identify potential signals of effect, and inform future meta-analyses.[28] Where applicable, subgroup comparisons of continuous outcomes will be summarised using standardised mean differences (Cohen's d).

Table 4: Statistical approach

Endpoint	Statistical analysis methods
Primary:	Phase 1 (Co-creation of digital tool): Descriptive statistics, inductive thematic analysis Phase 2 (Feasibility, acceptability): Descriptive statistics
Secondary	Phase 1 (Adolesecent perspectives): Inductive thematic analysis Phase 2 (Exploratory analysis): Descriptive statistics, correlation co-efficients, Cohen's d

7 Data handling

A study-specific Data Management Plan (DMP) will be developed by the Sponsor providing a.o. further details on data flows, data handling, processing and discrepancy management.

7.1 Data collection tools and source document identification

7.1.1 Operational aspects

Data collection, handling, processing and transfer for the purpose of this study will be performed in compliance with applicable regulations, guidelines for clinical studies and internal procedures, as follows:

7.1.1.1 Data collection:

Source data will be collected and recorded in the study participant's files/medical records.

If applicable, worksheets may be used for capturing some specific data in order to facilitate completion of the eCRF. Any such worksheets will become part of the study participant's source documentation and will be filed together with or as part of the medical records (during, and at the latest following completion of the study).

It remains the responsibility of the Investigator to check that all data relating to the study, as specified in the study protocol, are entered into the eCRF in accordance with the instructions provided and that the forms are filled out accurately, completely and in a timely manner.

eCRFs are provided by the Sponsor for each participant. The study data will be transcribed from the source records (i.e. participant's medical file or study-specific source data worksheets) into an eCRF by site study staff. Transcription to the eCRF will be done as soon as possible (preferably within 2 weeks of the participant's study visit, in order to allow for timely safety reviews by the Sponsor) and in a pseudonymized manner using a unique study-specific code assigned by the Sponsor.

Each participating research site shall maintain a log of the type of source documents and their location during and after completion of the study.

eCRF system:	REDCap
Questionnaire system:	The following assessments and questionnaires will be sent electronically to participants via m-Path, after which the data will be uploaded into REDCap: - YONAS tool prompts using ESM - MybYte tool prompts using ESM - Phase 1 digital tool assessment questionnaires - Phase 2 acceptability questionnaires Health-related quality of life questionnaires will be issued in paper form and entered into REDCap manually by the researcher.
The following data will be collected:	Quantitative data: 1. Demographical information 2. Relevant clinical history 3. Dietary intake data 4. Energy expenditure 5. Body composition 6. Taste profile 7. Health-related Quality of Life score 8. Structured components of the Phase 1 digital tool assessment questionnaires 9. Structured components of the Phase 2 acceptability questionnaires Qualitative data: 1. Interview and focus group transcripts 2. Interview and focus group audio recordings 3. Coding and thematic summaries 4. Observation notes 5. Unstructured components of Phase 1 and Phase 2 questionnaires

7.1.1.2 Data validation:

All data relating to the study must be prepared and validated by the Investigator. Any eCRF entries, corrections and alterations must be made by the Investigator or other authorized study staff.

Proper audit trails must be available to demonstrate the validity of the study data collected. This includes historical records of original data entries, by whom and when the data was entered, as well as detailed records of any corrections or additions made to the original data entry (i.e. who made the correction/addition, when and why), without obliterating the original data entry information.

7.1.1.3 Data management:

The Study Data Manager will perform extensive logic and consistency checks on the received data. Queries will be issued in case of discrepancies in accordance with internal procedures.

7.1.1.4 Data transfer:

Any participant records or datasets that are transferred to the Sponsor or any partners of the Sponsor will contain the study-specific participant pseudonym only; participant names or any information which would make the participant identifiable will not be transferred. All pseudonymized data relating to the study must be transmitted in a secure manner to the Sponsor or any partners of the Sponsor (see 7.1.2. legal requirements).

7.1.2 Legal requirements

All source data will be kept at a secured location with restricted access at all times. These data must be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data protection laws and regulations and more in particular the GDPR and relevant national laws implementing the GDPR. Appropriate technical and organizational measures to protect the data against unauthorized disclosure or access, accidental or unlawful destruction, or accidental loss or alteration must be established. Study staff whose responsibilities require access to personal data agree to keep the data confidential.

The Investigator and the participating site(s) (as applicable) shall treat all information and data relating to the study disclosed to them as confidential and shall not disclose such information to any third parties or use such information for any purpose other than the objectives of the study as described in this protocol. The collection, processing and disclosure of personal data, such as participant health and medical information is subject to compliance with applicable laws and regulations regarding personal data protection and the processing of personal data.

The Investigator will maintain all source documents and completed eCRFs that support the data collected from each study participant, and will maintain a Study Master File (TMF)/Investigator Site File (ISF) containing all study documents as specified in GCP and as specified by applicable regulatory requirement(s).
The Investigator will take appropriate measures to prevent accidental or premature destruction of these documents.

Transfer of the pseudonymized data will be performed via a secured method of transfer taking into account all applicable security arrangements and regulations (such as the GDPR). The receiving party will be bound by contractual agreement to keep the transferred data confidential at all times and to only process the data for the purpose of the study. To this end, additional appropriate Data Transfer Agreements (DTAs)may be established.

7.2 Audits and inspections

The Investigator will permit direct access to study data and documents for the purpose of monitoring, audits and/or inspections by authorized entities such as but not limited to: the Sponsor or its designees and competent regulatory or health authorities. As such eCRFs, source records and other study related documentation (e.g. Investigator Site File, the Study Master File, etc.) must be kept current, complete and accurate at all times.

7.3 Monitoring

In accordance with GCP the Sponsor is responsible for monitoring the study to ensure compliance with GCP and current legislation, and to verify, among other requirements, that proper written informed consent has

been obtained and documented, that the study procedures have been followed in accordance with the approved protocol, and that relevant study data have been collected and reported in a manner that assures data integrity.

According to UZ/KU Leuven policy, monitoring by the UZ/KU Leuven Clinical Trial Center (CTC) is not applicable for this study without IMP/IMD. Hence, based on this policy and as permitted by GCP, the Sponsor of the study accepts the minimal risks associated with this study and determines that monitoring activities (as defined by GCP) by a qualified individual, independent of the study team, is not necessary as it will provide little or no added value in protecting the safety of study participants and assuring the integrity of collected study data. Nonetheless, the Sponsor-Investigator study team will take all possible measures to assure the quality and integrity of study data and to safeguard the safety and wellbeing of study participants, in accordance with the requirements set out in GCP.

7.4 Archiving

As specified in GCP, the Sponsor and Investigator/participating site(s) will maintain a record of the location(s) of all respective essential study documents (including but not limited to source documents, completed and final eCRF and ISF/TMF). The Sponsor should ensure that the Investigator has control of and continuous access to the eCRF data reported to the sponsor during the study.

The Investigator/participating site should have control of all essential study documents and records generated by the Investigator/participating site before, during and following termination of the study.

Study-specific documentation (such as but not limited to the study protocol, any modifications thereto, the final Clinical Study Report (CSR) and the study database), as well as source data and site-specific study documents (such as but not limited to the original signed ICFs) will be archived by the participating site(s) according to local practice, and for at least 25 years following termination of the study. Archived data may be held on electronic record, provided that media back-up exists, hard copies can be obtained if required, and measures are taken to prevent accidental or premature loss or destruction of data. Destruction of essential study documents prior to, during or upon completion of the required archival period, will require written authorisation from the Sponsor.

8 Ethical & regulatory considerations

8.1 EC review and reports

Before the start of the study, this protocol and other related documents (e.g. ICF, advertisement and/or recruitment materials, Investigator Brochure (IB), etc.) will be submitted for review to the EC for approval. The study shall not commence until such approvals have been obtained and, until other relevant essential study documents, such as duly signed contract agreements, evidence of adequate study financing etc. are in place. In accordance with Sponsor policies, UZ/KU Leuven's Clinical Trial Center (CTC) will authorize study start-up (by means of "activating" the study) when all the above are available.

It is the responsibility of the Sponsor-Investigator to produce the Annual Progress Report (APR) and submit it to the EC within 30 days of the annual anniversary date on which favourable opinion to conduct the study was given, until the study is declared to have ended.

The Sponsor-Investigator shall notify the EC of the end of the study. Should the study be temporarily suspended or, ended prematurely, the Sponsor-Investigator will notify the EC and include the reason(s) for suspension/premature termination within 75 days of the decision. The Sponsor-Investigator will submit a final report with the results of the study, including any publications/abstracts, to the EC within 1 year of study termination.

8.2 Regulatory compliance

The study will be conducted in compliance with ICH-GCP E6(R3) guidelines, other GxP guidelines, the most recent version of the Declaration of Helsinki, the Belgian law of May 7th 2004 regarding experiments on the human person (as amended) and with the EU General Data Protection Regulation 2016/679 (GDPR), the relevant Belgian laws implementing the GDPR, the Belgian Law of August 22nd 2002 on patient rights and all other applicable legal and regulatory requirements.

8.3 Protocol / GCP and regulatory compliance

The study will be performed in accordance with the protocol, current ICH and GCP guidelines, and applicable regulatory and country-specific requirements. ICH guidelines are an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human participants. Compliance with this standard provides public assurance that the rights, safety, and well-being of study participants are protected, consistent with the principles that originated in the most recent version of the Declaration of Helsinki, and that the study data are credible, reliable and reproducible.

The Investigator and study team acknowledge and agree that prospective, planned deviations or waivers to the protocol are not permitted under applicable regulations on clinical studies. However, should there be an accidental protocol deviation, such deviation shall be adequately documented in the source documents and on the relevant forms and promptly reported to the Sponsor/Sponsor-Investigator. Deviations should also be reported to the EC as part of the EC's continued review of the study (e.g. through the annual safety report (ASR), annual progress report (APR), etc.). Protocol deviations which are found to frequently recur, will require (immediate) action. The Investigator acknowledges that such recurring protocol deviations could potentially be classified as a major deviation of ICH and/or the protocol.

It is understood that "a major deviation" is likely to affect to a significant degree:

- the safety or physical or mental integrity of the study participant(s); or
- the scientific validity of the study

The Investigator is expected to take any immediate action required to protect the safety of any participant included in the study, even if this action represents a deviation from the protocol. In such cases, the Sponsor should be notified of this action and the EC at the study site should be informed according to local procedures and regulations.

8.4 Data protection and participant confidentiality

The study will be conducted in compliance with the requirements of the GDPR, the relevant Belgian laws implementing the GDPR including the Belgian Law of July 30th 2018 on the protection of natural persons with regard to the processing of personal data. Any collection, processing and disclosure of personal data, such as participant health and medical information is subject to compliance with the aforementioned personal data protection laws (cfr. Data Processing Annex (DPA) in Appendix). In case personal data is transferred outside the European Economic Area, safeguards will be taken to ensure that appropriate protection travels with the data in accordance with the GDPR.

Any personal data shall be treated as confidential at all times including during collection, handling and use or processing, and the personal data (including in any electronic format) shall be stored securely at all times and with all technical and organizational security measures that would be necessary for compliance with EU and national data protection legislation (whichever is more stringent). The Sponsor shall take appropriate measures to ensure the security of all personal data and guard against unauthorized access thereto or disclosure thereof or loss or destruction while in its custody.

8.5 Insurance

The participating site, the Investigator and Sponsor shall have and maintain in full force and effect during the term of this study, and for a reasonable period following termination of the study, adequate insurance coverage for: (a) medical professional and/or medical malpractice liability, and (b) general liability.

(i) ***For Belgian participating sites***

Art 29 of the Belgian Law relating to experiments on human persons dated May 7th, 2004 applies.

Prior to the start of the study, the Sponsor shall enter into an insurance contract in order to adequately cover study participants from Belgian sites in accordance with art. 29 of the said law.

(ii) ***For non-Belgian participating sites (if applicable)***

The participating site shall have and maintain in full force and effect during the term of this study (and for a reasonable period following termination of the study, adequate insurance coverage for other possible damages resulting from the study at the participating site, as required by local law. Each such insurance coverage shall be in amounts appropriate to the conduct of the services of the participating site under this study.

The participating site and Sponsor shall be solely responsible for any deductible or self-insured retention under any such policies.

8.6 Modifications

During the study the Sponsor may modify the study. It is the Sponsor's responsibility to assess whether a modification is substantial or non-substantial.

A "substantial modification" is defined as any change of the study which is made after a decision is issued on a previously submitted application and that is likely to 'substantially impact the participants' safety or rights or the reliability and robustness of the data generated in the study. A substantial modification may only be implemented if it has been approved by the EC with no prejudice to the right of Sponsor and the investigator to take urgent safety measures without awaiting prior authorisation. In that case, the event and the measures taken should be reported to the EC as soon as possible. The EC will provide a response in accordance with timelines defined by applicable regulations.

A "non-substantial modification" is any change outside the scope of a substantial modification and irrelevant to the supervision of the study. A non-substantial modification should not be notified as such. These changes should be implemented during the next substantial modification. Non-substantial modifications need to be listed and identified as such in the cover letter of the next substantial modification application to EC.

9 Research registration, dissemination of results & publication

The Declaration of Helsinki (latest version) and European and Belgian regulations require that every study involving human participants be registered in a publicly accessible database before recruitment of the first participant. The Sponsor-Investigator is responsible for registering the study.

In addition, the Sponsor-Investigator will fulfil its ethical obligation to disseminate and make the research results publicly available. As such the Sponsor-Investigator is accountable for the timeliness, completeness and accuracy of the reports. Researchers, authors, sponsors, editors and publishers must adhere to accepted guidelines for ethical reporting. Negative and inconclusive, as well as positive results must be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in publication.

Publications will be coordinated by the Sponsor-Investigator. Authorship to publications will be determined in accordance with the requirements published by and in accordance with the requirements of the International Committee of Medical Journal Editors in accordance with the requirements of the respective medical journal and the KU Leuven policy on authorship.

10 Intellectual property

Any know how, inventions, methods, developments, innovations, discoveries and therapies, whether patentable or not, arising from the study or made in the performance of the study protocol ("Inventions") shall vest in the Sponsor. The participating site, its employees and Investigator(s) shall promptly disclose to the Sponsor any such inventions. Parties have expressly agreed that any and all study data as collected and prepared in the performance of the study protocol shall be the sole property of Sponsor unless otherwise agreed in a clinical study agreement.

11 Quality

In order to ensure the same quality and safety standards in participant care for clinical research as commonly applied by the Sponsor in its regular activities, the Sponsor shall comply with the following obligations: (a) the Sponsor will use trained and qualified employees or contractors to manage and coordinate the study; (b) the Sponsor will ensure that (multi-center) study reporting is reliable and valid, statistically accurate, ethical, and unbiased. (c) the Sponsor will not grant incentives, other than standard compensations and reimbursement of costs, to study participants or to participating site's staff that would compromise the integrity of the research; (d) the Sponsor is responsible for monitoring and evaluating the quality, safety, and ethics of the study and will respect the participating site's policies and processes when performing such monitoring and evaluation activities; (e) the Sponsor will protect the privacy and confidentiality of the study participants in accordance with all applicable laws.

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APPENDICES

APPENDIX 1: Research protocol history

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Complete the table below for each protocol amendment, provide a summary of the modifications made to the protocol while referencing the relevant protocol sections that were altered. Copy, insert and complete the table for each subsequent protocol amendment, while maintaining the completed table for previous protocol amendments. If no protocol amendments have been issued: keep the amendment table, but do not complete.

Original protocol version:	1.0 dated 16/07/2026

Amendment #1:	<protocol version nbr> dated 16/07/2026
	Modifications made / Reason for amendment:
<protocol section reference>	<describe modifications made>
<protocol section reference>	<describe modifications made>
<protocol section reference>	<describe modifications made>
<protocol section reference>	<describe modifications made>

Amendment #2:	<protocol version nbr> dated 16/07/2026
	Modifications made / Reason for amendment:
<protocol section reference>	<describe modifications made>
<protocol section reference>	<describe modifications made>
<protocol section reference>	<describe modifications made>
<protocol section reference>	<describe modifications made>