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Improving the Understanding of Late Effects of Testicular Cancer in Adolescent and Young Adult Survivors: TRANSCEND-XR

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ABSTRACT

Background: Testicular cancer (TC) is the most common malignancy amongst adolescents and young adults (AYAs) aged 15–39 years assigned male at birth. Survivors often experience late effects of treatment and report unmet supportive care needs.

Objectives: To present the protocol for the TRANSCEND-XR project (TesticulaR cANcer late effects and unmet Supportive CarE NeeDs of AYA survivors using eXtended Reality).

Materials and Methods: TRANSCEND-XR aims to ethically co-create, test, and scale up in a clinical setting an innovative digital intervention to increase AYA TC survivors' knowledge of the late effects of TC treatment and address their unmet supportive care needs using XR. Delivered by a consortium of 15 partners across 12 European countries, guided by the Medical Research Council's framework for complex interventions, and funded by the European Union, TRANSCEND-XR is structured into three phases: co-creation and validation (Phase 1); implementation and evaluation (Phase 2); and impact, guideline development, policy, dissemination, and exploitation (Phase 3).

Results: Phase 1 involves a cross-sectional survey of 500 AYA TC survivors to assess late effects and care needs as well as participatory World Café sessions with healthcare professionals, survivors, and care partners (n = 200) to co-design the TRANSCEND-XR intervention. Phase 2 includes a multicentre, single-arm phase 2 pilot trial (n = 15) across three clinical sites in three countries evaluating intervention feasibility, and a multicentre pragmatic randomised controlled phase 3 trial (n = 230) across eight clinical sites in seven countries, evaluating improvements in knowledge of late effects, cost-effectiveness, implementation, and ethical considerations. Phase 3 focuses on guideline development, policy influence, and strategic dissemination to ensure long-term sustainability and integration into European healthcare systems.

Discussion: TRANSCEND-XR aims to transform survivorship care for AYA TC survivors through a co-created, scalable XR intervention. Its interdisciplinary approach promotes scientific rigour, stakeholder engagement, and policy relevance to improve long-term outcomes and quality of life.

Conclusion: TRANSCEND-XR has the potential to advance survivorship care standards for AYAs with TC whilst providing a model for future digital health interventions in oncology.

1 | Introduction

Testicular cancer (TC) is the most common cancer amongst adolescents and young adults (AYAs) assigned male at birth, aged 15–39 years. Incidence has doubled over the past four decades, with the highest rates in individuals of European ancestry [1]. Around 25,000 new TC cases are diagnosed annually in Europe [2]. Help-seeking delays related to embarrassment, masculinity concerns, and limited healthcare engagement often result in late diagnoses, aggressive treatments, and treatment-related late effects [3–5]. Still, cure rates exceed 90% [6]. Many survivors, particularly those treated with orchiectomy alone, achieve health-related quality of life (HRQoL) and life expectancy that are broadly comparable to age-matched men in the general population [7].

Post-treatment challenges persist, with follow-up adherence remaining poor. In a single-centre study of TC survivors, 20.6% of patients missed at least one follow-up appointment and only 50.6% fully adhered to post-treatment follow-up guidelines [8]. Non-guideline-directed care, including deviations from recommended imaging and surveillance protocols, occurs in approximately 30% of patient with TC and has been associated with both, higher relapse risk and poorer quality of care [9]. Although non-compliance with follow-up has been proposed as a potential predictor of relapse, established prognostic factors remain tumour stage, histology, and baseline tumour marker levels [10].

Advances in treatment, alongside the rising incidence of TC, have contributed to lower mortality rates and a sustained increase in survivor numbers [11]. Orchiectomy alone is curative for most patients with Stage I disease, although a minority will relapse and require additional treatment, whereas advanced cases typically need the multimodal therapy [12, 13]. High survival rates are associated with substantial late effects for a subset of TC survivors, particularly those exposed to multi-cycle bleomycin–etoposide–cisplatin (BEP) or other cisplatin-based regimens [14]. Late effects include secondary cancers; cardiovascular disease; pulmonary, renal and neurological toxicity; infertility; hypogonadism; and psychosocial issues [11, 15, 16]. Risks vary by treatment, patient profile, and modifiable risk factors [17, 18]. Many survivors remain unaware of their late-effect risks, limiting self-management and preventive behaviours [19].

Although late effects such as cardiovascular disease and second malignant neoplasms cannot be considered fully preventable, risk may be partially modifiable and outcomes may improve through risk-reduction strategies and early detection [17]. For instance, modifiable lifestyle factors, including smoking, physical inactivity, and obesity, contribute to cardiovascular risk, particularly amongst survivors treated with platinum-based chemotherapy [15]. Therefore, increasing survivors' awareness of these risks and of warning signs of late effects may promote healthier behaviours, timely help-seeking, higher engagement with recommended follow-up care, and better QoL [17].

Although overall HRQoL amongst TC survivors is often favourable [20], many report persistent psychological, physical, and informational needs, particularly in the first years after treatment and amongst those experiencing late effects [11, 21]. A review of 36 studies identified persistent psychological, physical, interpersonal, and informational needs [11], most acute in the first post-treatment year [22]. These challenges negatively affect QoL, including mental health [22, 23]. Interventions to educate and support AYA TC survivors are urgently needed [4].

Extended reality (XR)—including virtual, augmented, and mixed reality—offers a promising solution. XR engages users through interactive, immersive environments that promote active experiential learning, empathy, and behavioural change [24]. Recent market analyses project substantial economic growth for XR over the next decade, with the combined immersive technology and augmented reality/virtual reality (VR) market estimated at around US$ 40–63 billion in 2023–2024 and forecast to exceed US$ 160–180 billion by 2030 [25], driven partly by healthcare and education use cases [26]. Within this, the standalone VR segment was valued at approximately US$ 12–16 billion in 2024 [27], and is expected to grow more than five-fold by the early 2030s [28]. User data indicate that VR remains most commonly used by younger and middle-aged adults, and a slightly higher proportion of males [29].

The decision to use XR in the current project is grounded in strong empirical evidence and user preference data [30–33]. XR enables complex survivorship information, including mechanisms of late effects, symptom appraisal, and risk-reducing behaviours, to

be communicated through immersive, experiential formats that enhance attention, understanding, and long-term retention [32]. The immersive format is central, not incidental, to the intended behaviour change since XR makes invisible late effects visible, allows simulated experiential learning, provides a safe space for rehearsal, and supports emotional engagement [34]. These characteristics cannot be replicated using traditional formats such as leaflets, videos, or websites. By engaging multiple memory pathways, including episodic, procedural, and semantic learning, XR is particularly well suited for educational interventions [32].

XR is not cumbersome for AYAs, as it aligns with their media habits and allows brief, modular engagement (e.g., 5–10 min late-effect modules). Our previous work co-developing and testing the usability, feasibility, acceptability, and effectiveness of the Enhancing Men's Awareness of Testicular Diseases VR intervention (E-MAT$_{VR}$) with 142 young adults demonstrated that immersive XR approaches are feasible, engaging, and effective in improving knowledge and behaviours, achieving an 89.2% retention rate [31, 33, 35]. Furthermore, given that Europe's Beating Cancer Plan prioritises digitally enabled survivorship care, XR represents a future-proof, policy-relevant educational approach [36].

In our search of nine trial registries and multiple patent databases, we found no active XR interventions for TC survivorship. In a scoping review of 30 supportive care interventions for men with urological cancers, we found only one study—published in 1998—which includes TC survivors, whilst the remainder focused exclusively on prostate cancer [37, 38]. As no XR-based survivorship tools currently exist for TC, TRANSCEND-XR (TesticulaR cANcer late effects and unmet Supportive CarENeeDs of AYA survivors using eXtended Reality) addresses a critical gap. This paper presents the protocol for the TRANSCEND-XR project.

2 | Project Overview

TRANSCEND-XR aims to ethically co-create, test, and scale-up in a clinical setting an innovative digital intervention aiming to increase AYA TC survivors' knowledge of the late effects of treatment and help address their unmet supportive care needs using XR. This project offers an evidence-informed, co-created, interactive, and scalable tool with the potential to communicate complex concepts more effectively than traditional educational formats and to complement follow-up care for AYA TC survivors.

The TRANSCEND-XR intervention will be co-designed as an educational and supportive self-management tool. Its primary mechanism is to improve AYA TC survivors' knowledge of late effects. We hypothesise that increased knowledge will enhance confidence in symptom appraisal, promote timely help-seeking, and strengthen engagement in survivorship self-care behaviours. Together, these changes are expected to support earlier identification and better self-management of late effects, contributing indirectly over time to improved health outcomes and QoL, and ultimately advancing survivorship care for AYAs with TC across Europe and beyond.

Although TC survivors older than 39 years also experience late effects and would benefit from targeted education, TRANSCEND-XR focuses on AYAs aged 15–39 years because this age range reflects both the epidemiology of TC—with a median age at diagnosis of 33 years [39]—and the specific eligibility requirements of the Horizon Europe grant call under which this project is funded. Moreover, AYAs are the most active XR users globally [29], and immersive technologies align with their preferences for brief, visually engaging, and technology-enabled educational experiences [30]. TRANSCEND-XR's objectives are presented in Table 1.

TRANSCEND-XR is a 66-month project funded by the European Union (EU) under Horizon Europe. Its consortium comprises a strategic alliance of 15 partners across 12 European countries (Figure 1). Our team is balanced in terms of expertise, interdisciplinarity, intersectorality, and diversity. It includes eight teaching hospitals and comprehensive cancer centres across seven European countries (Ireland, the United Kingdom [UK], France, Italy, the Netherlands, Croatia, and Slovakia) that have significant expertise in AYA TC patient management (adult and paediatric oncologists) and a strong track record in TC research. It also brings together a group of AYA TC survivors, a large AYA cancer patient organisation, a healthcare professional organisation for AYA cancers, and a pan-European organisation of national and regional cancer societies. Our consortium also includes experts in bioethics, sociology, epidemiology, biostatistics, trial methodology, health economics, implementation science, research communication, XR design, and computer science.

TRANSCEND-XR is governed by a comprehensive management structure to ensure coordination, oversight, and delivery. Governance bodies include the Consortium Executive Committee, Project Management Committee, Project Advisory Committee, Patient Advisory Board, Trial Management Committee, and Trial Steering Committee.

TRANSCEND-XR is guided by the Medical Research Council's (MRC) framework for complex intervention development and evaluation [40]. To minimise the risk of inducing unnecessary fear or healthcare use, the TRANSCEND-XR intervention will use balanced, supportive, and positively framed messaging, informed by clinical follow-up guidelines and underpinned by the Preconscious Awareness to Action Framework—a seven-step framework that guides health-promoting behaviour change from initial awareness to action—which we previously developed and applied in the E-MAT$_{VR}$ trial (Figure 2) [32, 33, 35]. Rather than promoting hypervigilance, the intervention focuses on improving symptom appraisal, confidence, and appropriate help-seeking. Within TRANSCEND-XR, this framework will underpin the development of a novel intervention that seeks to: (i) increase AYA TC survivors' knowledge of late effects of TC treatment; (ii) promote accurate appraisal of symptoms; and (iii) encourage timely help-seeking for symptoms or late effects of concern. Importantly, the predecessor intervention, E-MAT$_{VR}$, which was guided by the same theoretical framework, did not lead to unnecessary healthcare utilisation [41].

3 | Project Methodology

TRANSCEND-XR is organised into three phases aligned with its eight objectives as follows: co-creation and validation (Phase 1);

TABLE 1 | The TRANSCEND-XR project's objectives.

Objective 1	Understand the incidence, severity, and impact of the late effects of testicular cancer (TC) inclusive of unmet supportive care needs amongst adolescent and young adult (AYA) TC survivors, their care partners (also known as caregivers, are unpaid, nonprofessional care assistants such as a family members, partners, or friends who assume primary responsibility for assisting an individual with a serious/chronic illness or disability), and healthcare professionals.
Objective 2	Explore similarities and disparities in experiences of late effects of TC across different treatments and survivor demographics within Europe.
Objective 3	Co-create, refine, and validate the theory-informed TRANSCEND-XR educational intervention with AYA TC survivors, their care partners, and healthcare professionals in an ethically sound fashion using the World Café participatory methodology.
Objective 4	Critically evaluate the feasibility of the intervention amongst AYA TC survivors, their care partners, and healthcare professionals.
Objective 5	Determine the effectiveness and cost-effectiveness of TRANSCEND-XR via a multi-country pragmatic randomised controlled trial (pRCT).
Objective 6	Identify the contextual factors and processes that influence engagement with and implementation of TRANSCEND-XR.
Objective 7	Evaluate the ethico-clinical challenges and implications of TRANSCEND-XR and provide an evidence-base for guideline development and European Union (EU) policy on clinically and ethically appropriate and sustainable digital solutions for educating AYA TC survivors and addressing their unmet supportive care need.
Objective 8	Maximise the uptake, impact, and long-term sustainability of TRANSCEND-XR by (i) driving engagement with key stakeholders across the entire value chain, and (ii) developing an interdisciplinary community that will strategically link with other AYA and cancer-focused projects to accelerate research impact across multiple sectors and disciplines in Europe.

FIGURE 1 | Map of Europe showing the geographical distribution of the 15 project partners across 12 European countries. The seven countries marked with green pins indicate partners that include patients.

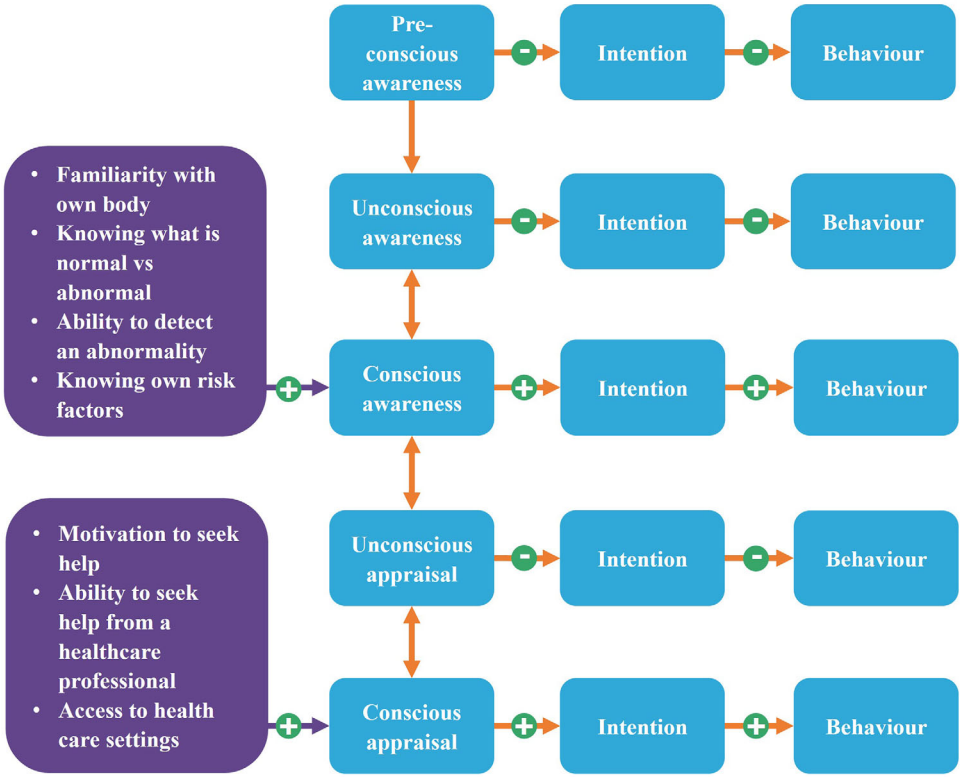

FIGURE 2 | Simplified statements illustrating the relationship between the key concepts of the Preconscious Awareness to Action Framework. The "−" and "+" signs depict a negative and a positive relationship respectively.

implementation and evaluation (Phase 2); and impact, guideline development, policy, dissemination, and exploitation (Phase 3).

3.1 | Phase 1: Co-Creation and Validation

Phase 1 addresses Objectives 1–3 and incorporates two elements of the MRC framework, namely context, and developing a new intervention [40]. This phase is sub-divided into two studies; the first aimed at understanding the late effects of TC treatment, and the second focused on co-creating and validating the TRANSCEND-XR intervention.

3.1.1 | Understanding the Late Effects of Testicular Cancer Treatment

The primary objective of the first study is to determine the incidence, severity, and impact of late effects, and the degree to which TC survivors' supportive care needs are met. The secondary objective is to explore disparities in experiences based on demographic variables (i.e., age, gender identity, sexual orientation, country of birth and residence, highest level of education, relationship status, current living situation, and employment status) and self-reported disease-related variables (i.e., year of diagnosis, stage of TC at diagnosis, treatments received, year of treatment completion, and whether TC has ever recurred).

Eligible participants are individuals diagnosed with TC at any age up until the age of 39 years, aged at least 18 years at the time of the study, who completed curative treatment for TC (any type, Stages I–III) between 1 and 10 years prior. Participants will be recruited amongst individuals who have been followed up at one of the eight partner clinical sites. These sites are medium- to high-volume TC centres and collectively manage approximately 1,500 TC patients per year. Based on an estimated 35% response rate, the target sample size is 500 participants. The target sample size provides approximately ±4%–5% precision for prevalence estimates around 50%, which is adequate for descriptive assessment of late effects and unmet supportive care needs. Accordingly, Phase 1 is exploratory rather than powered for definitive subgroup analyses; such analyses will be interpreted cautiously and considered hypothesis-generating, providing a basis for future hypothesis-driven research by treatment type and country. Participants will be recruited through their follow-up clinics, direct communication (e.g., email and mail), and additionally through the project's website and social media platforms, and outreach via patient organisations.

The survey will be administered online and will be available in the six languages spoken across the seven participating countries. It will be based on established theoretical frameworks, including Fitch's Supportive Care Framework [42], and will incorporate questions assessing participants' familiarity with XR technologies, overall health status, experiences of late effects of TC treatment, and supportive care needs. The survey will be co-designed with 10–15 healthcare professionals from participating clinical sites through two focus groups. It will then be reviewed by the project's Patient Advisory Board. Following translation and ethical approval, it will be pilot tested with a sample of five AYA TC survivors to ensure clarity, cultural relevance, and accessibility.

Ethical approval will be secured in each country as country-specific requirements dictate. A Data Management Plan will guide data handling, cleaning, and analysis. Quantitative data will be analysed, focusing on descriptive statistics and subgroup comparisons. Focus groups with healthcare professionals will be analysed qualitatively [43]. All procedures will adhere to ethical and methodological best practices, including the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) [44]. Survey findings will help shape the implementation and evaluation (Phase 2) of TRANSCEND-XR.

3.1.2 | Intervention Co-Creation, Refinement, and Technical Validation

Concurrently with the survey, we will use the serial World Café (WC) methodology to co-create and refine the TRANSCEND-XR intervention. WC is an iterative participatory approach that fosters group conversations to generate collective insights and cross-pollinate ideas [45]. The TRANSCEND-XR Project Coordinator and the Lead for the WC study have recently used this method to co-create and launch "On the Ball," an inclusive community-based TC awareness campaign [46, 47].

In-person and online WCs will include AYA TC survivors recruited through clinical sites and advertisements, along with their care partners. WCs will be hosted in seven countries, guided by a standardised manual, and conducted in local languages. Data will be translated, coded, and analysed in English, with country-specific consent or assent procedures followed for minors.

Co-creation will begin with consultations with healthcare professionals to explore XR applications in TC survivorship, informing pre-production ideation. WC1 will then be conducted virtually with survivors and care partners to explore needs and preferences, guiding concept development. WC2 will be conducted in person, engaging participants with prototypes refined from WC1 feedback. WC3, also conducted in person, will bring participants together to experience the full TRANSCEND-XR intervention, exploring usability, content, and user scenarios. WC3 will inform the discrete choice experiment, which will assess survivor preferences, trade-offs, and willingness to pay or accept the intervention versus standard care. Participants will evaluate hypothetical options defined by key service attributes.

In each WC, small groups will rotate through three 20-min discussion rounds. Data will be captured using artefact cards, drawing sheets, sticky notes, and voice recordings, and analysed and harvested in real time by each table facilitator. Online WCs will follow the same structure using breakout rooms in 2-h sessions.

A rapid review of international guidelines will be conducted concurrently to ensure evidence-based content. An XR production studio [48] (Khora) will collaborate throughout, defining objectives, gathering requirements, creating storyboards and design documents, and developing prototypes. The TRANSCEND-XR intervention software will be developed by Khora using Unity-based XR development frameworks and custom VR production pipelines that pre-exist within Khora. These tools function only as development infrastructure and do not impose any proprietary software or hardware requirements on the intervention. The final intervention, including software code, 3D assets, scripts, and implementation manuals, will constitute foreground intellectual property owned by the TRANSCEND-XR consortium and produced in accordance with FAIR principles. At this early phase, the equipment description is intentionally broad to reflect the range of standard XR delivery options (e.g., head-mounted displays and mobile devices such as smartphones or tablets). However, the project does not assume parallel multi-platform development. The final TRANSCEND-XR intervention will be optimised for and deployed on a single target medium, using either VR, augmented reality, or mixed reality, which will be selected based on AYA TC survivors' preferences.

The intervention will be finalised based on feedback from WC3 participants. Technical validation will then be conducted to ensure intervention usability, immersion, and acceptability. The discrete choice experiment attributes developed in WC3 will be tested during the technical validation. This study will follow the PRoblem, Objective, Design, (end-) Users, Co-creators, Evaluation, Scalability (PRODUCES) [49], and Planning, Conducting, Evaluating, Reporting [50] frameworks. It will produce an evidence-based, co-created, refined, and validated educational intervention ready for Phase 2, with materials and manuals covering software, hardware, and procedures. Details of this study are provided in Table 2.

Of note, although the survey and WC co-design activities within Phase 1 run concurrently, the co-design process extends several months beyond the survey. Early survey data and WC1 and WC2 findings inform initial ideation and prototype development, whilst the full survey results will inform intervention refinement within WC3 and the technical validation. This staggered, iterative structure ensures that the final intervention remains grounded in the priorities, preferences, and needs identified directly by AYA TC survivors, whilst also supporting a feasible project timeline.

3.2 | Phase 2: Implementation and Evaluation

Phase 2 addresses Objectives 4–7 by incorporating the feasibility, evaluation, and implementation elements of the MRC framework [40]. A pragmatic randomised controlled trial (pRCT) will be conducted and will include a pilot study, health economic evaluation, process evaluation, and ethics study.

A non-randomised, single arm phase 2 pilot study will be initially conducted with 15 participants in three countries (Ireland, France, and Slovakia) to demonstrate the feasibility of implementing the XR educational intervention and analysing associated outcome measures. Conducted alongside the technical validation (Phase 1), findings from this pilot study may inform protocol amendment for the subsequent pRCT. The pilot study will be followed by a pragmatic, multicentre, open-label, controlled randomised phase 3 clinical trial conducted at all eight clinical sites, evaluating standard of care in combination with the TRANSCEND-XR intervention versus standard of care alone. The trial will follow Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines [51].

Eligibility criteria for the pilot study and pRCT include: participants aged 15–39 years at diagnosis, assigned male at birth,

TABLE 2 | Co-creation, refinement, and technical validation of TRANSCEND-XR.

Activity	Sample	Country	Format	Purpose	Instrument	Output
Deep dive	10–20 healthcare professionals and project team members	Ireland, United Kingdom (UK), Slovakia, The Netherlands, France, Italy, Croatia	In-person	Explore use of extended reality (XR) in the context of testicular cancer (TC) survivorship and clinical applications of the intervention	Purposely developed guide	Pre-production ideation
World Café (WC)1	70–84 adolescent and young adult (AYA) TC survivors ages 18–39 years and care partners (10–12 per country)	Ireland, UK, Slovakia, The Netherlands, France, Italy, Croatia and other European countries	Online	Pre-production/ Ideation. Sharing of needs and preferences of end-users.	Purposely developed WC guide	Concept development, technical planning, and design prototyping
WC2	50–60 AYA TC survivors aged 15–39 years and care partners (10–12 per country)	Ireland, UK, Slovakia, The Netherlands, France	In-person	Facilitating interaction with the intervention prototype of one late effect/ module. Allowing co-creators to visualise their ideas and suggest changes.	Purposely developed WC guide	Feedback on journey maps, storyboards, sketches and/or other low-fi prototypes produced based on WC1 findings
WC3	30–36 AYA TC survivors aged 15–39 years and care partners (10–12 per country)	Ireland, Italy, Croatia	In-person	Facilitating interaction with full TRANSCEND-XR experience and design of a discrete choice experiment	Purposely developed WC guide	Brainstorming, scenarios, personas and data on the perceived usability of experience as well as a discrete choice experiment
Technical validation	40–50 participants comprising males aged 18–39 years	Ireland	In-person	Usability	System Usability Scale; NASA Task Load Index	Validated final intervention and findings from the discrete choice experiment
				User experience	Usability Metric for User Experience	
				Immersion	User eXperience in Immersive Virtual Environment Model	
				Presence	iGroup Presence Questionnaire	
				User acceptance	Technology Acceptance Model	
				Discrete choice experiment	Attributes developed in WC3	

diagnosed with germ cell tumours of testicular origin (Stages I–III), have completed curative treatment within 9 months, have received at least one standard TC treatment (surgery, chemotherapy, or radiotherapy), have an Eastern Cooperative Oncology Group performance status of 0–2, and provide written informed consent/assent. XR can cause cybersickness. Therefore, participants with a history of severe motion sickness/cybersickness and/or seizures will be excluded. Prior studies testing E-MAT$_{VR}$ with over 100 participants reported only one mild adverse event [31, 33, 35].

Details of TRANSCEND-XR will be reported using the Template for Intervention Description and Replication (TIDieR) checklist [52]. Intervention components and implementation will be refined based on co-creation (Phase 1). The duration of XR interventions in previous trials has varied from 30 min to 16 weeks [53, 54]. The TRANSCEND-XR intervention will be delivered during routine hospital visits as part of standard care, and participants may also continue to use it at home. It will incorporate modules on late effects recognition, testicular self-examination for contralateral testis (E-MAT$_{VR}$), peer support, high immersion, and gamified interaction. Measures to promote adherence will be considered from the outset within Phase 1. These will include clear information, patient and public involvement, gamification, session reminders, and technical support from the XR production studio.

Usual follow-up care at each of the seven countries/eight sites, in line with European and international guidelines, will remain unmodified. Environmental scans at baseline and during the trial will identify overlapping initiatives to account for potential confounders. Safety monitoring will follow ICH E2A/E2B guidance.

The primary endpoint of the pRCT is knowledge of late effects at 12 months, measured using the Survivor Knowledge Questionnaire (SKQ) [55]. Correct responses regarding 11 late effects are scored against the actual risk determined by clinicians using Children's Oncology Group guidelines [56]. Correlations between knowledge, disease stage, and treatment will be analysed. Participants will be enrolled over 18 months and followed for at least 12 months for the assessment of primary endpoint. Secondary outcomes include unmet supportive care needs measured using the Cancer Survivors' Unmet Needs (CaSUN) questionnaire [57], help-seeking intentions/behaviours for symptoms of late effects measured using the General Help-Seeking Questionnaire (GHSQ) [33, 35, 58], testicular self-examination practices for contralateral testis assessed using the Testicular Self-Examination Questionnaire [33, 35], and HRQoL using QLQ-TC26 [59] and EQ-5D-5L [60]. Clinical outcome data will include adherence to the recommended clinical follow-up schedule and the frequency of unscheduled healthcare visits.

A total of 230 participants is required to detect a 20% improvement in SKQ scores (baseline mean 54.29, SD 21.64) [55], with 80% power and 5% significance, accounting for 30% dropout and 80% adherence. Participants will be randomised 1:1 to TRANSCEND-XR plus standard of care versus standard of care alone. Participants and clinicians will be aware of the allocated arm, but analysts of outcomes assessment will be blinded until database lock.

Data will be collected at baseline, 3, 6, 9, and 12 months, and every 6 months thereafter. Most data will be self-reported. Scheduled and unscheduled follow-up visits will be recorded by the investigators. A trial-specific Data Management and Statistical Analysis Plan will guide analyses, updated based on Phase 1 and pilot study findings. Analyses will be intention-to-treat, with safety analyses reflecting the intervention received. Baseline differences will be adjusted statistically.

3.2.1 | Health Economic Evaluation

Following Consolidated Health Economic Evaluation Reporting Standards (CHEERS) [61], professional society for Health Economics and Outcomes Research (HEOR) recommendations [62], and Enhancing the QUAlity and Transparency of Health Research (EQUATOR) standards, a decision analytic model will synthesise costs and outcomes of TRANSCEND-XR versus standard of care [63]. Participants' willingness to pay and accept the intervention will also be assessed. Costs, QoL (EQ-5D-5L [60]), and trial-based outcomes will be combined iteratively to calculate incremental cost-effectiveness ratios. Sensitivity analyses and Markov models will estimate long-term health and economic impact, informing adoption, pricing, and sustainability strategies.

3.2.2 | Process Evaluation

Using MRC process evaluation guidance [64], we will examine participant experiences and engagement, staff support, contextual factors, and mechanisms of impact. Intervention fidelity will be assessed according to National Institutes of Health Behavioral Change Consortium domains [65]. Quantitative data include recruitment logs, XR usage logs, and engagement metrics. Semi-structured qualitative interviews with 35–56 pRCT participants across participating countries will explore survivors' experiences of the intervention, including any anxiety, concerns, or perceived negative effects. This ensures that any unintended psychological or behavioural impacts, including excessive healthcare use driven by fear, can be identified and interpreted alongside the quantitative outcomes. Moreover, qualitative interviews with 7–10 staff across sites will explore experiences, barriers, and facilitators to implementation. Integration of qualitative and quantitative findings will clarify how TRANSCEND-XR operates across settings and countries.

3.2.3 | Embedded Ethics Study

Empirical bioethics research embedded within TRANSCEND-XR will evaluate equity, digital health ethics, and care ethics throughout intervention development and implementation. A mixed-methods approach will include: (i) online surveys of all pRCT participants (n = 230) on fairness, autonomy, access, and digital engagement; (ii) individual or dyadic interviews with 35–56 AYA TC survivors and care partners, recruited via purposive, maximum-variation sampling; and (iii) focus groups with healthcare professionals. Additional surveys and focus groups will assess shared decision-making (intervention vs. control) using a validated measure. Qualitative data will be analysed using

thematic and framework analyses, integrated with quantitative findings to identify ethical implications such as privacy, consent, digital inclusion, and acceptability. Findings will inform an ethics-by-design approach, supporting iterative intervention adaptation and recommendations for ethically responsible digital survivorship care.

3.3 | Phase 3: Impact, Guideline Development, Policy, Dissemination, and Exploitation

Phase 3 addresses Objectives 7 and 8 and focuses on the implementation element of the MRC framework [40]. This phase focuses on translating the project's evidence into real-world impact through guideline development, policy influence, dissemination, and strategic exploitation. Building on insights from co-creation, implementation, and evaluation, Phase 3 embeds TRANSCEND-XR findings into European healthcare systems and policy frameworks to enhance survivorship care for AYA TC survivors and support equitable access across diverse AYA populations.

A key component is the development of 'ethics-by-design' recommendations, shaped by empirical bioethics research, and refined through international workshops with policymakers, healthcare professionals, patient representatives (e.g., Patient Advisory Board), with the intention of informing clinical practice tools and future policy contributions in Europe. This ensures alignment with EU legislation, including the Artificial Intelligence Act and EU Taxonomy Regulation, whilst promoting sustainability, safety, and digital health equity, and is consistent with broader European initiatives such as the EU Mission on Cancer and Europe's Beating Cancer Plan.

Dissemination and exploitation activities will maximise reach and impact. Data, tools, and results will follow FAIR principles and be shared in platforms like the European Federated Cancer Research Data Hub (UNCAN.eu). Strategic clustering and collaboration across Europe will build "QoL AYA" ecosystems, supporting innovation, knowledge exchange, citizen engagement, addressing inequalities, and efficient implementation.

Ultimately, Phase 3 ensures TRANSCEND-XR becomes a sustainable, scalable solution, informing clinical guidelines, shaping EU survivorship policy, and creating a European framework for immersive, ethically grounded digital interventions that improve long-term outcomes for AYA cancer survivors.

4 | Conclusion

TRANSCEND-XR is a novel project capable of transforming survivorship care for AYAs with TC. By co-creating and evaluating an XR-based educational intervention, the project addresses critical gaps in knowledge, self-management, and supportive care whilst taking advantage of the sophisticated interactive and immersive features offered by XR. Its multi-phase design ensures that the intervention is evidence-based, user-centred, and scalable, whilst embedded bioethics, health economics, and implementation science maximise its real-world relevance and sustainability. Through guideline development, policy influence, and wide dissemination, TRANSCEND-XR aims to advance survivorship care standards, improve QoL, and establish a blueprint for future digital health innovations in oncology.

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Ethics Approval and Consent to Participate

As the TRANSCEND-XR project includes multiple studies, ethical approval will be sought separately for each study, as appropriate, from the relevant institutional ethics committees. Written informed consent will be obtained from all participants prior to participation.

Conflicts of Interest

The authors have no conflict of interest to disclose.

Trial Registration

The protocol for the trials included in the TRANSCEND-XR project was registered on ClinicalTrials.gov (NCT07571499).

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