Check for updates

STUDY PROTOCOL

REVISED Behavioural analysis of referral and uptake of care pathways for rare tumour risk syndromes: A cross-cultural mixed-methods study protocol within the PREVENTABLE project

[version 2; peer review: 2 approved, 1 approved with reservations]

Ana Machado[1,2*], Maiara Moreto[1,2*], Isabel Fernandes[1-3], Ana Maria Rodrigues[1,2,4,5], Bárbara Peleteiro[6-9], Joan Brunet[10-12], Judith Balmaña[12-14], Claude Houdayer[12,15], Jean-Christophe Thery[16], Janneke H.M. Schuurs-Hoeijmakers[12,17], Stefan Aretz[12,18,19], Cathrine Bjorvatn[20], Liliana Sousa[12,21], Sara Pereira[21], Carla Oliveira[7,12,21,22], PREVENTABLE Clinical Research Team, Marta M. Marques[23]

[1]Comprehensive Health Research Centre (CHRC), NOVA Medical School, NOVA University of Lisbon, Lisbon, Portugal
[2]EpiDoc Unit, NOVA Medical School, NOVA University of Lisbon, Lisbon, Portugal
[3]Oncology Department, Hospital CUF Descobertas, Lisbon, Portugal
[4]Rheumatology Department, Hospital Egas Moniz, Centro Hospitalar Lisboa Ocidental, Lisbon, Portugal
[5]Rheumatology Department, Hospital dos Lusíadas, Lisbon, Portugal
[6]Hospital Epidemiology Center, Unidade Local de Saúde São João, Porto, Portugal
[7]Faculty of Medicine, University of Porto, Porto, Portugal
[8]EPI Unit, Institute of Public Health, University of Porto, Porto, Portugal
[9]Associate Laboratory for Integrative and Translational Research in Population Health (ITR), University of Porto, Porto, Portugal
[10]Catalan Institute of Oncology, Barcelona-Girona, Spain
[11]Girona Biomedical Research Institute-IDIBGI, Girona, Spain
[12]ERN GENTURIS - European Reference Network on Genetic Tumour Risk Syndromes, Nijmegen, The Netherlands
[13]Medical Oncology Department, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain
[14]Hereditary Cancer Genetics Group, VHIO - Vall d'Hebron Institute of Oncology, Barcelona, Spain
[15]Department of Genetics, Univ Rouen Normandie, INSERM U1245, FHU-G4 Génomique and CHU Rouen, Rouen, France
[16]Department of Medical Oncology, Center Henri Becquerel, University of Medicine of Rouen, Rouen, France
[17]Department of Human Genetics, Expert Center for PHTS, Radboud University Medical Center, Nijmegen, The Netherlands
[18]Institute of Human Genetics, Medical Faculty, University of Bonn, Bonn, Germany
[19]National Centre for Hereditary Tumour Syndromes, University Hospital Bonn, Bonn, Germany
[20]Department of Medical Genetics, Haukeland University Hospital, Bergen, Norway
[21]Universidade do Porto Instituto de Investigacao e Inovacao em Saude, Porto, Portugal
[22]University of Porto Institute of Molecular Pathology and Immunology, Porto, Portugal
[23]New University of Lisbon Comprehensive Health Research Centre National School of Public Health, Lisbon, Portugal

* Equal contributors

v2 **First published:** 15 Apr 2025, **5**:108
https://doi.org/10.12688/openreseurope.19954.1
Latest published: 06 Jul 2026, **5**:108
https://doi.org/10.12688/openreseurope.19954.2

Open Peer Review

Approval Status ? ✓ ✓

Abstract

Background

Individuals with rare tumour risk syndromes (RTRS) navigate complex care pathways, including early diagnosis, monitoring, and tailored treatments, all requiring shared decision-making with their clinical team. Nevertheless, behavioural factors influencing this decision-making process and the best communication practices are unknown.

Objective

This study aims to identify the behavioural factors (i.e., barriers and facilitators) influencing i. the recommendation of RTRS-care pathways by members of clinical teams, ii. the uptake of the care pathways by patients with RTRS, and iii. The factors experienced by patients' social networks. This study is part of PREVENTABLE, an EU-Horizon funded project, aiming to assess the clinical, social and economic impact of RTRS-care pathways.

Methods

A cross-cultural mixed-methods study with a sequential explanatory design will be conducted, consisting of i. a web-based survey study (quantitative phase), and ii. a qualitative study conducted through focus groups (qualitative phase). First, two international web-based surveys, following the COM-B model of behavioural change, will be developed aiming to investigate the barriers and facilitators to i) the recommendations of RTRS-care pathways by 100 members of clinical teams managing these syndromes, and ii) the uptake of the recommended care pathways by 290 patients with RTRS. The results will inform the focus groups phase aiming to provide an in-depth exploration of the main factors affecting the recommendation and adoption of RTRS-care pathways. The study will involve six countries, i.e., France, Germany, Netherlands, Norway, Spain, and Portugal. Both qualitative and quantitative data will first be analyzed separately, and then merged through data triangulation for final interpretation of the results.

Conclusion

This will be the first study exploring the behavioural factors influencing the recommendation and uptake of RTRS-care pathways. This study will guide the development of guidelines for the communication and recommendation of optimized care pathways for RTRS, which might enhance the referral and uptake of RTRS preventive strategies and inform the best care for RTRS.

	1	2	3
version 2 (revision) 06 Jul 2026		✓ view	✓ view
version 1 15 Apr 2025	? view	? view	

1. **Nickola Pallin**, Trinity College Dublin, Dublin, Ireland
2. **Saskia F A Duijts**, Amsterdam University Medical Center, Amsterdam, The Netherlands
3. **Stuthi Perimbeti**, Penn State Cancer Institute, Hershey, USA

Any reports and responses or comments on the article can be found at the end of the article.

Plan language summary
People with rare tumour risk syndromes (RTRS) are confronted with a lot of new information and complex personal decisions about their care. To improve the care these individuals receive, it is essential to improve communication and understand which factors are making it easier and/or more difficult for them to decide on the different care options. This study will explore the behavioural factors that have been influencing the recommendation and uptake of care options for RTRS by clinical teams, patients with RTRS and their social networks. To do this, we will conduct online surveys and group discussions with clinical teams, patients with RTRS and their social networks. This study is part of a larger EU-funded project, the PREVENTABLE project (https://preventable.eu/), and is being conducted in six countries – Portugal, Spain, France, Germany, Netherlands and Norway. Understanding these behavioural factors will help us developing strategies to improve the communication and recommendation of care to these patients, possibly leading to a better care for them.

Keywords
barriers; facilitators; communication; behaviour change; decision-making; hereditary cancer; rare diseases



This article is included in the Horizon Europe gateway.



This article is included in the Cancer collection.

Corresponding author: Marta M. Marques (mmarques@ensp.unl.pt)

Author roles: Machado A: Methodology, Project Administration, Writing – Original Draft Preparation, Writing – Review & Editing; **Moreto M**: Methodology, Project Administration, Writing – Original Draft Preparation, Writing – Review & Editing; **Fernandes I**: Methodology, Supervision, Writing – Review & Editing; **Rodrigues AM**: Methodology, Supervision, Writing – Review & Editing; **Peleteiro B** : Funding Acquisition, Writing – Review & Editing; **Brunet J**: Funding Acquisition, Writing – Review & Editing; **Balmaña J**: Funding Acquisition, Writing – Review & Editing; **Houdayer C**: Funding Acquisition, Writing – Review & Editing; **Thery JC**: Funding Acquisition, Writing – Review & Editing; **H.M. Schuurs-Hoeijmakers J**: Funding Acquisition, Writing – Review & Editing; **Aretz S**: Funding Acquisition, Writing – Review & Editing; **Bjorvatn C**: Funding Acquisition, Writing – Review & Editing; **Sousa L**: Conceptualization, Funding Acquisition, Project Administration, Writing – Review & Editing; **Pereira S**: Conceptualization, Funding Acquisition, Project Administration, Writing – Review & Editing; **Oliveira C**: Conceptualization, Funding Acquisition, Project Administration, Writing – Review & Editing; **Marques MM**: Conceptualization, Funding Acquisition, Methodology, Project Administration, Supervision, Writing – Review & Editing

Competing interests: Machado, Moreto, Marques, Peleteiro, Sousa, Pereira, Oliveira, Brunet, Balmaña, Houdayer, Thery, Schuurs-Hoeijmakers, Aretz & Bjorvatn have no competing interests to declare. Ana Rodrigues has received research grants from Amgen, Astrazeneca, Novartis, Abbvie, Pfizer, MSD, lilly, and Boehringer Ingelheim. Isabel Fernandes has grants for research from PharmaMar and Roche.

Grant information: This project has received funding from the [Horizon Europe Framework Programme under grant agreement No [101095483][PREVENTABLE (PREVENTABLE CANCER PREVENTION VS CANCER TREATMENT: THE RARE TUMOUR RISK SYNDROMES BATTLE)]. Funded by the European Union. Views and opinions expressed are, however, those of the author(s) only and do not necessarily reflect those of the European Union or the Health and Digital Executive Agency (HaDEA). Neither the European Union nor the granting authority can be held responsible for them.
The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Copyright: © 2026 Machado A *et al*. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Machado A, Moreto M, Fernandes I *et al.* **Behavioural analysis of referral and uptake of care pathways for rare tumour risk syndromes: A cross-cultural mixed-methods study protocol within the PREVENTABLE project [version 2; peer review: 2 approved, 1 approved with reservations]** Open Research Europe 2026, **5**:108
https://doi.org/10.12688/openreseurope.19954.2

First published: 15 Apr 2025, **5**:108 https://doi.org/10.12688/openreseurope.19954.1

REVISED **Amendments from Version 1**

The revised manuscript incorporates clarifications made in response to reviewer comments, with no alterations to the study design, objectives, or data collection procedures. In the Background section, the description of care pathways was expanded to provide more explicit examples of primary prevention strategies and surveillance options, and the role of cascade predictive testing and family communication was clarified. In the Methods section of the abstract, the sequential structure of the study was made more explicit. Within the main manuscript, the survey development subsection was updated to clarify that a forward-backward translation was used to ensure linguistic and cultural adequacy of the translated surveys. The description of the sequential explanatory design was also refined to better convey the role of the qualitative phase in broadening the understanding of the quantitative findings. In the data analysis subsection, the process of integrating quantitative and qualitative data was clarified to make explicit that findings will be merged within each stakeholder group, resolving an ambiguity present in the original text. All amendments aimed at improving the clarity and completeness of the manuscript, and no changes were made to the protocol, study registration, or any aspect of data collection.

Any further responses from the reviewers can be found at the end of the article

Background

Rare tumour risk syndromes (RTRS) are a set of genetically determined rare diseases, in which the lifetime risk of developing various types of cancer is up to 100%. Since these syndromes follow an autosomal dominant inheritance, patients have a 50% chance of transmitting the disease to their offspring.[1,2] When undiagnosed or not surveilled, people with RTRS develop particularly aggressive cancers, which result in premature death or severely impact theirs and their family health.[3–5] Nevertheless, cancers in people with RTRS can be prevented and survival rates maximized if: i) asymptomatic carriers are intensively surveilled for RTRS cancer-prone organs, ii) cancer-prone organs are surgically removed prior to disease development, if adequate, and iii) very small cancerous or pre-cancerous lesions are removed or treated.[6–9] RTRS constitute, therefore, an unique context for cancer prevention, early detection and treatment with curative intent.

When diagnosed, individuals with RTRS have not only to understand their diagnosis and its implications, but they are also presented with different care pathways — i.e., sequences of care options that involve multiple decisions, such as primary prevention strategies (e.g., risk-reducing surgeries and lifestyle modifications), surveillance options (e.g., more frequent screenings) and treatment for cancer or premalignant conditions.[2,10] Furthermore, beyond managing their own diagnosis, they are also responsible for communicating the results to their family, and for informing at-risk family members about their genetic risk, leading to a cascade genetic testing.[2,10] These individuals are therefore confronted with complex and personal decisions, which often lead to uncertainty, doubts, distress and feelings of guilt.[11–14] In this context, a clear, empathetic, and evidence-based communication of risks, treatment strategies and surveillance plan is essential for quality decision-making in individuals with RTRS.[10] The vital role of individuals' social support systems in helping managing ongoing medical monitoring and adhering to recommended care must also be acknowledged.[2] Further, any variations in healthcare professionals' guidelines and recommendations for RTRS across countries can influence the decision-making process. Guidelines for RTRS are scarce and rarely address the personal needs or actions of people with RTRS, such as psychosocial support or lifestyle behaviours, posing further challenges to healthcare professionals.[2] Furthermore, gaps still persist in understanding the various factors influencing decision-making in RTRS. These include the preferences of individuals with RTRS, members of clinical teams recommendations, and the best practices for communication and emotional support in RTRS care.[10] In order to improve care in RTRS, it is therefore crucial to overcome the hurdles in communication between these individuals and their clinical teams.[15] Conducting research using behavioural science might help facilitating informed decisions in this context.[2] The behavioural analysis refers to the systematic examination of factors that influence two specific target behaviours: (1) the referral and recommendation of RTRS care pathways by members of clinical teams, and (2) the uptake of recommended care pathways by people with RTRS. Our behavioural analysis explores the psychological, social, and environmental factors that may enable or hinder these behaviours.

In this context, one of the most widely used behaviour science models that was developed to inform and guide practice is the Capability-Opportunity-Motivation-Behaviour (COM-B), which provides comprehensive understanding of the behavioural factors influencing individuals' decision-making process.[16–20] According to this model, for any given behaviour to take place, the individual must have the capability, opportunity and motivation to engage in that behaviour.[21,22] Capability refers to both physical capability, involving skills, strength, and stamina; or psychological capability, involving knowledge and cognitive ability to perform the behaviour.[21,22] Opportunity refers to external factors and includes physical opportunity, which refers to environmental aspects such as resources and time; and social opportunity, which relates to cultural influences, including family and social networks.[21,22] Motivation includes

reflective motivation (e.g., conscious planning) and automatic motivation (e.g., emotions and impulses).[21,22] Furthermore, the COM-B model captures both internal (psychological capability and motivation) and external (physical and social opportunities) determinants of behaviour, enabling to systematically identify barriers and facilitators in health contexts,[20] such as the referral and recommendation of care pathways for RTRS. Its use provides a systematic understanding of the factors influencing behaviour, and offers a structured approach for the development of tailored interventions by mapping the types of strategies likely to influence each construct effectively.[23] For the qualitative component, we will additionally use the Theoretical Domains Framework (TDF) as a complementary framework to support more in-depth exploration of the determinants influencing behaviours.[24]

The PREVENTABLE consortium – an EU-Horizon funded project aiming to assess the clinical, social and economic impact of applying preventive care pathways for families with RTRS. The PREVENTABLE project aims to address the gaps in the risk communication and decision-making process by focusing on two target behaviours: i. referral and recommendation to care pathways by members of clinical teams and ii. uptake of recommended care by patients. The study investigates the behavioural determinants underlying each of these behaviours. These determinants include individual, social, and environmental factors (e.g., knowledge, beliefs, social support, clinical setting) that may act as barriers or facilitators for each distinct behaviour. By examining these determinants, the study aims to clarify how they influence both the members of clinical teams' recommendations and the patients' uptake of care pathways for RTRS.

Objectives

This study protocol describes a mixed-methods study that aims to identify the behavioural factors influencing the recommendation and uptake of care pathways for RTRS across European countries involved in the PREVENTABLE consortium – i.e., Portugal, Spain, France, Germany, the Netherlands, and Norway.

Specifically, we aim to:

1. Identify the barriers and facilitators influencing the recommendation and referral of care pathways for RTRS by members of clinical teams managing these syndromes.

2. Identify the barriers and facilitators influencing the uptake of care pathways for RTRS by individuals with these syndromes.

3. Identify the barriers and facilitators influencing how the social network of individuals with RTRS provide support for, engage in, and influence the uptake of the recommended care pathways.

Protocol

Design

A cross-sectional mixed-methods study with a sequential explanatory design (QUAN → QUAL)[24,25] will be conducted, encompassing two steps: 1) a web-based survey study (quantitative phase), and 2) a qualitative study conducted through focus groups (qualitative phase). In this methodology, qualitative methods are used to provide breath of understanding to the quantitative results by exploring participants' experiencies, perceptions and contextual factors related to barriers and enablers identified in the survey. This approach maximizing the strengths and minimizing the weaknesses of each type of data.[24,25] Study registration is available at Open Science Framework: https://doi.org/10.17605/OSF.IO/KRQFA.

In step 1, two online anonymised surveys – one for members of clinical teams managing RTRS and one for individuals with RTRS are conducted. In step 2, to further elaborate on the findings from the surveys, we will conduct focus groups with: i. members of clinical teams who specialize in RTRS, ii. patients with RTRS and iii. Members of the social network of patients with RTRS. Members of the social network are only included in Step 2 as an additional source to examine how their involvement may affect patients' decisions and support individuals with RTRS in navigating their care pathways.

The study is being conducted in six European countries that are part of the PREVENTABLE consortium, i.e., Portugal, Spain, France, Germany, Netherlands and Norway.

Population

Seven RTRS will be included: Birt-Hogg-Dubé Syndrome (variants in *FLCN* gene), Familial Melanoma (variants in *CDKN2A* or *CDK4* genes), Hereditary Diffuse Gastric Cancer (variants in *CDH1* or *CTNNA1* genes), Li-Fraumeni Syndrome (variants in *TP53* gene), Peutz-Jeghers Syndrome (variants in *STK11* gene), PTEN Hamartoma Tumour Syndrome (variants in *PTEN* gene), Hereditary Leiomyomatosis and Renal Cell Carcinomas (variants in *FH* gene). These seven RTRS are part of the thematic groups 2 and 4 of the ERN Genturis.

The inclusion criteria for the study will be as follows: For members of clinical teams, eligible participants must: 1) be aged ≥18 years old, and 2) be members of clinical teams who have experience in providing recommendations of care to individuals with at least one of the RTRS listed above. For individuals with RTRS, participants must: 1) be aged ≥18 years old, and 2) be diagnosed with one of the RTRS listed above.

For the online surveys, we aim to include 100 healthcare professionals with experience with RTRS and 290 individuals with RTRS. A sample size calculation to obtain a representative sample of individuals with RTRS was performed based on the total number of RTRS cases identified within the PREVENTABLE consortium (n = 1177) and assuming a 95% confidence interval and 5% margin of error. For members of clinical teams, the sample size was determined based on the estimated number of healthcare professionals with expertise in the syndromes included in the PREVENTABLE project and the composition of the participating teams across countries.

For the focus groups, the same inclusion criteria used in the survey will be apply to members of clinical teams and individuals diagnosed with RTRS. In addition, this step will include a third stakeholder: members of the social network of individuals diagnosed with one of the RTRS listed above. All focus groups participants must be aged[3] 18 years old. Following stablished recommendations, approximately six participants per focus group will be included.[26] In each country of the consortium, three focus groups will be conducted (one per target group – i.e., members of clinical teams, individuals with RTRS, social networks). Hence, in total, 18 focus groups will be conducted, corresponding to a total of 108 participants, 36 participants per target group.

All participants in the survey or focus groups must be able to provide informed consent. Potential participants will be excluded if they are not fluent in Portuguese, Spanish, Catalan, French, German, Dutch or Norwegian. Additionally, for the focus groups, individuals with significant hearing or speaking impairments (e.g., deaf, mute) or other conditions that can impair verbal communication will be excluded.

Development of the surveys

The surveys aim to explore the barriers and facilitators to i) the referral of the best care pathways for RTRS by members of clinical teams managing these syndromes, and ii) the uptake of the recommended care pathways by individuals with RTRS. The surveys were developed, in English, based on the COM-B model of behaviour change which attributes behaviour to three factors: physical and psychological capability (e.g., energy, knowledge), physical and social opportunity (e.g., access to care, social support), and reflective and automatic motivation (e.g., beliefs, associative learning).[21]

The process of survey development consisted of 1) drafting the questions by the research team who has expertise in behavioural and social sciences and health sciences, 2) readjusting based on feedback from PREVENTABLE consortium members experts in RTRS, 3) pilot testing, and 4) refinement of surveys and translation to each PREVENTABLE language. The drafting of questions was based on a revision of the literature on RTRS, analysis of previous studies following the COM-B model, and the findings of a preliminary pilot survey conducted with 11 experts of PREVENTABLE, in which six barriers and six facilitators were identified (https://osf.io/j9xmy).[27] The draft surveys were explored in two meetings with experts (one per survey) with the support of the PREVENTABLE consortium members and partners, who are experts in the field. Feedback on the survey for members of clinical teams was obtained in one meeting with the clinical partners of the consortium, which were given time to provide additional feedback by e-mail following the meeting. Feedback on the survey for patients was obtained in one meeting with the patients' association EVITA, which was also given time to provide additional feedback by e-mail following the meeting. Following the adjustments based on experts' feedback, the surveys were pilot tested. The survey for members of clinical teams was tested by two oncologists and one nurse. The survey for patients was pilot tested by four individuals with different rare syndromes. Following the adjustments provided by participants in the pilot testing, the final version of the surveys was reached and translated into Portuguese, Spanish, Catalan, French, German, Dutch and Norwegian, the official languages of the countries integrating the consortium. Translations were performed using the eTranslation service provided by the European Commission.[28] The translations were reviewed and adjusted for cultural adequacy by PREVENTABLE Clinical partners, who are bilingual experts with knowledge of both RTRS and the target healthcare context. This ensures that questions capture the intended concepts while being culturally and linguistically appropriate.

The final surveys are divided into three sections: 1) sociodemographic characteristics, 2) barriers and facilitators, and 3) ranking of barriers and facilitators. In total, the survey for members of clinical teams consists of 30 items and the one for patients includes 36 items. All the items are mandatory response. In the first section, information regarding age, sex (patients) or gender (healthcare professionals), country of residence, experience with RTRS (healthcare professionals), diagnosis (patients), clinical specialty (healthcare professionals), workplace (healthcare professionals) and level of

education (patients) is collected. If a healthcare professional does not have experience with at least one of the RTRS included, or a patient does not have one of these RTRS as diagnosis, the survey will close. In Section 2, participants are asked to rate how much they agree/disagree with the role of different items related with capability, opportunity and motivation in their decisions/choices. Participants rate each item in a 7-points Likert scale ranging from 1-strongly disagree to 7-strongly agree. In the last section, participants are provided with a list of potential barriers and facilitators that could be associated with their referral options or decisions regarding care. Participants are asked to choose the three barriers and three facilitators that influence their decisions the most, and rank them from 1-the one with the most influence to 3-the one with least influence.

In the survey for healthcare professionals, psychological capability is assessed through items regarding knowledge, skills, and access to skills' training. Physical opportunity is explored through items related to environmental context and costs. Social opportunity is explored through items related to social influences, social support and social norms. Reflective motivation is explored through professional role, personal beliefs and beliefs about the patient. Automatic motivation is explored through items related to habits and emotion regulation. The full survey is available at: https://doi.org/10.17605/OSF.IO/KRQFA.

In the survey for patients, physical capability is assessed through physical skills. Psychological capability is explored through items regarding knowledge, and memory, attention and decision processes. Physical opportunity is explored through items related to environmental context and costs. Social opportunity is assessed through social support and social influences. Reflective motivation is explored through beliefs and social influences. Automatic motivation is explored through items related to emotions. The full surveys are available at: https://doi.org/10.17605/OSF.IO/KRQFA.

Development of the topic guides for the focus groups

Focus groups will aim to explore i) the factors that influence healthcare professionals in making referrals and recommendations of care for individuals with RTRS, ii) the factors that influence how individuals with RTRS make decisions about their care options, and iii) the challenges and supportive factors faced by those who provide support to individuals with RTRS.

Semi-structured interview guides, one per target group, will be used to ensure that the topics under investigation are covered in a consistent manner while allowing flexibility for new topics that are important for participants to emerge. The interview guides were developed based on the COM-B model of behaviour change, which categorizes behavioural factors into physical and psychological capability (e.g., energy, knowledge, beliefs), physical and social opportunity (e.g., access to care, social support, social norms) and reflective and automatic motivation (e.g., goals, planning emotions).[21] The process of topic guides development consisted of 1) drafting the discussion topics by the research team who has expertise in behavioural and social sciences and health sciences, 2) readjusting based on feedback from PREVENTABLE consortium members experts in RTRS, and 3) refinement of the topic guides and translation to each PREVENTABLE language. The drafting of the discussion topics was informed by the existing literature,[26,29] the expertise of the members of the consortium, and the results of the surveys. A simulative case study is included to provide a basis for discussion. The interview guides for the focus groups were developed in English and translated into Portuguese, Spanish, Catalan, French, German, Dutch and Norwegian using the eTranslation service provided by the European Commission.[28] Clinical partners will review and adjust the translations for cultural adequacy. The topic guides are available at: https://doi.org/10.17605/OSF.IO/KRQFA.

Recruitment

The survey for members of clinical teams was open for completion from 18th June to 18th October 2024. It was disseminated across Europe by ERN GENTURIS and PREVENTABLE's clinicals partners through their networks. ERN GENTURIS disseminated the survey by e-mail by sending invitations to participate in the survey to their network of healthcare providers. PREVENTABLE's clinical partners shared the survey by word of mouth and by e-mail. Clinical partners invited their colleagues to participate in the survey and to share it through their own networks of RTRS-experts. The survey was also sent by e-mail to nine professional societies linked to RTRS (e.g., Portuguese oncology society, Portuguese society of human genetics) with a request for dissemination through their networks. In addition, the survey was disseminated through PREVENTABLE's social media platforms.

The survey for patients was open for completion from 18th June to 24th November 2024. It was disseminated across Europe by the patients' association EVITA, other patients' associations, ERN GENTURIS and PREVENTABLE's clinical partners. The patients' association EVITA disseminated the survey through their social media platforms, by word of mouth and by e-mail. EVITA contacted their partner patients' associations across Europe and requested their support in sharing the survey with their network of patients. EVITA also engaged with their members to encourage them and their

families to complete the survey. The survey was also sent by e-mail to 17 patients' association related with RTRS with a request for dissemination through their networks. ERN GENTURIS disseminated the survey by inviting their network of patients' associations to share the survey with their network of patients. PREVENTABLE's clinical partners disseminated the survey by word of mouth and by e-mail. Clinical partners invited their patients with RTRS to participate in the survey and encouraged them to also involve their families in the study, both during scheduled appointments and by sending e-mails and invitation letters. In addition, the survey was disseminated through PREVENTABLE's social media platforms.

Focus groups will be conducted between January and May 2025. Recruitment and facilitation of the focus groups will be ensured by each clinical site. A convenience sample will be used. The team at each clinical site will be responsible for identifying the eligible participants and provide them with an explanation about the study. Only the interested individuals will afterwards be contacted by the facilitator of the focus group at each clinical site, who will further explain the study, clarify any doubts and collect the informed consent. No information will be collected before the informed consent is provided. A verbal (recorded) informed consent will also be requested at the beginning of each focus group.

Data collection

The anonymous surveys were made available in an online format using the LimeSurvey platform, which allows the completion of the surveys in any device with internet access (e.g., computer, mobile phone) and includes all the official languages of the countries integrating the consortium. By accessing the link to the online anonymous survey, potential participants were first presented with a welcome message with information about the study, inclusion/exclusion criteria and the informed consent. Participants were then required to provide their digital informed consent prior to any data collection. Only participants that provided the voluntary digital informed consent were able to continue to the survey. Participants were free to save the survey and continue answering later, in a more convenient time, and could also quit at any time by closing the survey. Cookies were used to avoid that the surveys were filled in more than once by the same person, i.e., a participant was not allowed to respond more than once from a single IP address, thus avoiding participants' multiple participation in the LimeSurvey platform. To avoid questionnaire burden, the surveys were designed to take no longer than 10 minutes to be filled in.

Three focus groups will be conducted at each clinical site in Portugal, Spain, France, Germany, Netherlands and Norway, one for each of the target groups. The focus groups will be conducted in a quiet room at each clinical site or online (through the platform Microsoft Teams), depending on what is more convenient for the participants in each group. As recommended, each focus group will have approximately six participants, one facilitator and one assistant.[26] Each focus group is expected to last around 2 hours. All participants will sign an informed consent before participation. Semi-structured interview guides, one per target group, informed by the literature, the results of the surveys on the barriers and facilitators influencing the choice of the care pathways for RTRS, and the expertise of the members of the consortium, will be used to ensure that the topics under investigation are covered in a consistent manner while allowing flexibility for new topics that are important for participants to emerge. All focus groups will be recorded using audio recording devices. A verbal (recorded) informed consent will also be requested at the beginning of each focus group. The recordings will be transcribed verbatim using a dedicated software (i.e., the MAXQDA software) and translated into English language through sub-contracting the services of a translation company. Participants' names will be anonymized. Information about age, sex (patients), gender (clinical teams, social network), diagnosis (patients), relationship (social network) and profession (clinical teams) of the included participants will be collected for sample characterization.

Data analysis

Descriptive statistics will be used to characterize the sample, both in the surveys and in the focus groups.

The surveys will be analysed in an aggregated manner. Data analysis will include descriptive and inferential statistics. Descriptive statistics will be used to analyse each individual item. In addition, survey items will be grouped and analysed by the corresponding COM-B model domains, i.e., physical capability, psychological capability, physical opportunity, social opportunity, reflective motivation and automatic motivation. Within each COM-B domain, items will also be grouped by more granular categories of constructs. Inferential statistics will be used to allow comparisons between different COM-B domains and categories. Specifically, we will explore: (i) comparisons between the different care pathways, (ii) within-domain comparisons of more granular constructs, and (iii) comparisons of total scores across COM-B domains. In addition, we will examine whether the COM-B domain differ among syndromes, clinical specialties and countries.

The data from the focus groups will be analysed through thematic analysis.[30] The procedures proposed by Braun and Clarke will be followed.[30] Two researchers will be responsible for reading all the transcriptions and code them. Then, the research team will review the data coded under each theme/subtheme, contribute to the appropriate naming and definition

of the themes, and produce the report. The criteria of credibility, transferability, dependability, and confirmability will be used to ensure rigor and trustworthiness.[31] The anonymous transcriptions will be analysed in an aggregated manner, per target group. Analysis of the transcripts will be conducted using the MAXQDA software. We will compare existing variations in how the COM-B domains are manifested between countries to address cross-country differences.

Quantitative and qualitative data will first be analysed separately, in a sequential process, and afterwards merged for integration of both methods in the final interpretation of the results. Findings from different stakeholder groups will be reported and interpreted independently. Triangulation of data within each stakeholder will be achieved using a narrative integration with a contiguous approach and integration through joint displays, allowing side-by-side presentation of the findings. This approach will facilitate the interpretations of the data by identifying convergences and divergences between the quantitative and qualitative findings.

Privacy and data protection

All surveys are confidential and anonymous. No personal information is collected, hence, every data collected is irreversibly anonymous from the start. The anonymous surveys are built in and distributed through the LimeSurvey platform. This platform was chosen because it fully complies with the European Union's general data protection regulation. To ensure full compliance, the German server location was defined. In addition, each participant's anonymity is ensured by not using URLs, store internet protocol (IP) addresses nor requesting participants to register their identities, contact or email. By accessing the link to the online anonymous survey, potential participants are first presented with a welcome message with information about the study, inclusion/exclusion criteria and the informed consent. Participants are then required to provide their digital informed consent prior to any data collection. Only participants that provide the voluntary digital informed consent are able to continue to the survey. Participants are free to quit at any time by closing the survey.

Regarding focus groups data, personal information will be processed and secured in accordance with ethical principles and applicable international, European union and national legislation. All data subjects will confirm their consent by signing a free and fully informed consent form containing a detailed description in lay terms of the study and how data will be stored. All audio recordings collected within this study will be temporarily stored on a secured, password-protected folder in the central server from NOVA University of Lisbon, and immediately destroyed after the transcription and translation to English language.

Three databases will be generated in this study. Two databases are generated by the LimeSurvey platform, one per survey. In addition, characterization data from the focus groups will be anonymously stored, based on study ID, on a secured, anonymized, password-protected database. All anonymized databases will be stored in the central server from NOVA University of Lisbon. Only the research team involved in the study will have access to the anonymous databases. The anonymous databases will be kept for the duration of the project and 3 years beyond the project ending.

The privacy and confidentiality policies of the NOVA University of Lisbon will be followed. The study will comply with the ethical principles, data privacy protection and applicable Data Protection in all involved Institutions and Bodies, following the Regulation 2018/1725.

Data collection. The protocol for data collection was made available as a pre-registry at Open Science Framework, and no alterations have been made since its initial publication. Data collection is currently underway.

Dissemination

The results from this study will be made available to the scientific community and general population through their dissemination in peer-reviewed scientific publications, presentations in national and international conferences, and PREVENTABLE's social media platforms.

Conclusions

This will be the first study exploring the behavioural factors influencing the recommendation and uptake of care pathways for RTRS. By using a behaviour science model, this study will provide a systematic understanding of the main behavioural factors – i.e., barriers and facilitators – that should be targeted through behaviour change strategies to improve decision-making, referral and uptake of RTRS preventive care, among both patients with RTRS, their social networks, and members of clinical teams. The integration of the results of the focus groups and surveys will inform the development of guidelines on how the care pathways for RTRS should be communicated to patients using a person-centred approach, hence ensuring uptake. The guidelines will include sufficient information to allow improving the communication and understanding of RTRS prevention-related care pathways by the actors involved (members of clinical teams, patients, families), with a focus on risk communication, clinical outcomes and service facilitation.

Ethics and consent

The study will be conducted in full conformance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. It will comply with the ethical principles in all involved Institutions and Bodies, following the European Union Regulation 2018/1725. Written informed consent will be obtained from all participants previously to any data collection. Additionally, oral consent will be obtained at the beginning of the focus groups.

Ethical approval was obtained by the Ethical Committees of all the involved institutions – NOVA Medical School (ref. 73/2024/CEFCM; ref. 175/2024/CEFCM), i3S (ref. N10/CECRI/2024), Unidade Local de Saúde São João (ref. 265–23), University Hospital of Bellvitge (ref. PR075/24), University Hospital of Girona (ref. 2024.137), University Hospital Vall d'Hebron (ref. PR (AG)330/2023), CHU-Rouen (ref. 2025/0043/OB), RADBOUDUMC (ref. 2024–17792), Haukeland University Hospital (ref. 757236; ref. 789646; ref. 850836) and University Hospital Bonn (ref. 281/23-EP).

Data availability statement

Underlying data

No data are associated with this article.

Extended data

OSF: Behavioural analysis of the referral and uptake of care pathways for RTRS, DOI: https://doi.org/10.17605/OSF.IO/KRQFA[32]

The final surveys for patients and healthcare professionals, and the topic guides for patients, social networks and healthcare professionals are available at Open Science Framework (https://doi.org/10.17605/OSF.IO/KRQFA).

This project contains the following extended data:

- Focus groups topic guides.pdf
- Survey clinicians.pdf
- Survey patients.pdf

All data are available on Open Science Framework.

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

The final survey for patients is available at the Open Science Framework repository: https://doi.org/10.17605/OSF.IO/KRQFA

The final survey for healthcare professionals is available at the Open Science Framework repository: https://doi.org/10.17605/OSF.IO/KRQFA

The topic guides for the focus groups with patients, social networks and healthcare professionals are available at the Open Science Framework repository: https://doi.org/10.17605/OSF.IO/KRQFA

Reporting guidelines

This study protocol followed the guidelines for pre-registry at Open Science Framework and publication in Open Research Europe. Resulting studies will be following the Consolidated Criteria for Reporting Qualitative Research (COREQ),[33] the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE),[34] and the Good Reporting of A Mixed Methods Study (GRAMMS)[35] guidelines.

Acknowledgments

The authors would like to acknowledge the support of all the participants in this study. We also want to thank the patients' association EVITA, the ERN GENTURIS (European Reference Network on Genetic Tumour Risk Syndromes) for all patients with one of the rare genetic tumour risk syndromes, every member of the PREVENTABLE consortium, and all the institutions, clinicians and staff involved in the recruitment process.

References

1. Chompret A, Brugières L, Ronsin M, *et al.*: **P53 germline mutations in childhood cancers and cancer risk for carrier individuals.** *Br J Cancer.* 2000; **82**(12): 1932–1937.
PubMed Abstract | Publisher Full Text | Free Full Text

2. de Los D, Rios de la Serna C, Lluch-Canut MT, *et al.*: **Hereditary cancer syndrome carriers: feeling left in the corner.** *Semin Oncol Nurs.* 2024; **40**(3): 151624.
PubMed Abstract | Publisher Full Text

3. van der Post RS, Gullo I, Oliveira C, *et al.*: **Histopathological, molecular, and genetic profile of hereditary diffuse gastric cancer: current knowledge and challenges for the future.** *Adv Exp Med Biol.* 2016; **908**: 371–391.
PubMed Abstract | Publisher Full Text

4. Bougeard G, Renaux-Petel M, Flaman JM, *et al.*: **Revisiting Li-Fraumeni Syndrome from *TP53* mutation carriers.** *J Clin Oncol.* 2015; **33**(21): 2345–2352.
PubMed Abstract | Publisher Full Text

5. Werner-Lin A, Young JL, Wilsnack C, *et al.*: **Waiting and "weighted down": the challenge of anticipatory loss for individuals and families with Li-Fraumeni Syndrome.** *Fam Cancer.* 2020; **19**(3): 259–268.
PubMed Abstract | Publisher Full Text | Free Full Text

6. Vos JR, Giepmans L, Röhl C, *et al.*: **Boosting care and knowledge about hereditary cancer: European Reference Network on Genetic Tumour Risk Syndromes.** *Fam Cancer.* 2019; **18**(2): 281–284.
PubMed Abstract | Publisher Full Text | Free Full Text

7. Geilswijk M, Genuardi M, Woodward ER, *et al.*: **ERN GENTURIS clinical practice guidelines for the diagnosis, surveillance and management of people with Birt-Hogg-Dubé syndrome.** *Eur J Hum Genet.* 2024; **32**(12): 1542–1550.
PubMed Abstract | Publisher Full Text | Free Full Text

8. Wagner A, Aretz S, Auranen A, *et al.*: **The management of Peutz–Jeghers syndrome: European Hereditary Tumour Group (EHTG) guideline.** *J Clin Med.* 2021; **10**(3): 473.
PubMed Abstract | Publisher Full Text | Free Full Text

9. Taja-Chayeb L, Vidal-Millán S, Trejo-Becerril C, *et al.*: **Hereditary Diffuse Gastric Cancer (HDGC). An overview.** *Clin Res Hepatol Gastroenterol.* 2022; **46**(4): 101820.
PubMed Abstract | Publisher Full Text

10. Kohut K, Morton K, Turner L, *et al.*: **Patient decision support resources inform decisions about cancer susceptibility genetic testing and risk management: a systematic review of patient impact and experience.** *Front Health Serv.* 2023; **3**: 1092816.
PubMed Abstract | Publisher Full Text | Free Full Text

11. Bartley N, Napier C, Best M, *et al.*: **Patient experience of uncertainty in cancer genomics: a systematic review.** *Genet Med.* 2020; **22**(9): 1450–1460.
PubMed Abstract | Publisher Full Text | Free Full Text

12. Dean M, Fisher CL: **Uncertainty and previvors' cancer risk management: understanding the decision-making process.** *J Appl Commun Res.* 2019; **47**(4): 460–483.
Publisher Full Text

13. Oliveira FFB, de Barros Silva PG, de Sant'Ana RO, *et al.*: **How does genetic testing influence anxiety, depression, and quality of life? A hereditary breast and ovarian cancer syndrome suspects trial.** *Support Care Cancer.* 2021; **29**(7): 3521–3530.
PubMed Abstract | Publisher Full Text

14. Pollard S, Kalloger S, Weymann D, *et al.*: **Genetic testing for hereditary cancer syndromes: patient recommendations for improved risk communication.** *Health Expect.* 2020; **23**(4): 884–892.
PubMed Abstract | Publisher Full Text | Free Full Text

15. Bolz-Johnson M, Meek J, Hoogerbrugge N: **"Patient Journeys": improving care by patient involvement.** *Eur J Hum Genet.* 2020; **28**(2): 141–143.
PubMed Abstract | Publisher Full Text | Free Full Text

16. Clark EC, Burnett T, Blair R, *et al.*: **Strategies to implement evidence-informed decision making at the organizational level: a rapid systematic review.** *BMC Health Serv Res.* 2024; **24**(1): 405.
PubMed Abstract | Publisher Full Text | Free Full Text

17. Ahmed N, Barlow S, Reynolds L, *et al.*: **Mental health professionals' perceived barriers and enablers to shared decision-making in risk assessment and risk management: a qualitative systematic review.** *BMC Psychiatry.* 2021; **21**(1): 594.
PubMed Abstract | Publisher Full Text | Free Full Text

18. Kwong MH, Ho L, Li ASC, *et al.*: **Integrative Oncology in cancer care–implementation factors: mixed-methods systematic review.** *BMJ Support Palliat Care.* 2023; **14**: e183–e199.
PubMed Abstract | Publisher Full Text

19. Shpendi S, Norman P, Gibson-Miller J, *et al.*: **Utilising the COM-B model to interpret barriers and facilitators to cervical cancer screening in young women.** *J Health Psychol.* 2024; **30**: 2340–2353.
PubMed Abstract | Publisher Full Text | Free Full Text

20. Xiao L, Li T, Lin J, *et al.*: **Determinants of cancer patients' involvement in treatment decision-making based on the COM-B model: a cross-sectional study.** *Patient Educ Couns.* 2023; **114**: 107795.
Publisher Full Text

21. Michie S, van Stralen MM, West R: **The behaviour change wheel: a new method for characterising and designing behaviour change interventions.** *Implement Sci.* 2011; **6**: 42.
PubMed Abstract | Publisher Full Text | Free Full Text

22. Mitchie S, Atkins L, West R: *The behaviour change wheel: a guide to designing interventions.* Silverback Publishing; 2014.
Reference Source

23. Richardson M, Khouja CL, Sutcliffe K, *et al.*: **Using the theoretical domains framework and the behavioural change wheel in an overarching synthesis of systematic reviews.** *BMJ Open.* 2019; **9**(6): e024950.
PubMed Abstract | Publisher Full Text | Free Full Text

24. Palinkas LA, Mendon SJ, Hamilton AB: **Innovations in mixed methods evaluations.** *Annu Rev Public Health.* 2019; **40**(1): 423–442.
PubMed Abstract | Publisher Full Text | Free Full Text

25. Creswell JW, Klassen AC, Plano Clark VL, *et al.*: **Best practices for mixed methods research in the health sciences.** *Office of Behavioral and Social Sciences Research.* 2011.

26. Krueger RA: *Focus groups: a practical guide for applied research.* 5th ed. Sage Publications; 2014.
Reference Source

27. Machado A, Moreto M, Fernandes I, *et al.*: **Barriers and facilitators for uptake of care pathways for rare tumour risk syndromes–PREVENTABLE project.** *In: Health Psychology for a Sustainable Future.* 2024; 226.

28. European Commission: Machine translation for public administrations — eTranslation. Accessed 13/03/2024.
Reference Source

29. Michie S, Atkins L, West R: **The behaviour change wheel**. *A guide to designing interventions.* 1st ed. Great Britain: Silverback Publishing; 2014; **1003**: 1010.
Reference Source

30. Braun V, Clarke V: **Using thematic analysis in psychology.** *Qual Res Psychol.* 2006; **3**(2): 77–101.
Publisher Full Text

31. Lincoln Y, Guba E: **Validity trustworthiness and rigor: quality and the idea of qualitative research.** *Methodological Issues in Nursing Research.* 1985: pp. 304–310.

32. Machado A, Moreto M, Marques MM: **Behavioural analysis of the referral and uptake of care pathways for RTRS.** *Open Science Framework.* 2025.
Publisher Full Text

33. Tong A, Sainsbury P, Craig J: **Consolidated criteria for Reporting Qualitative research (COREQ): a 32-item checklist for interviews and focus groups.** *Int J Qual Health Care.* 2007; **19**(6): 349–357.
PubMed Abstract | Publisher Full Text

34. von Elm E, Altman DG, Egger M, *et al.*: **The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies.** *Lancet.* 2007; **370**(9596): 1453–1457.
PubMed Abstract | Publisher Full Text

35. O'Cathain A, Murphy E, Nicholl J: **The quality of mixed methods studies in health services research.** *J Health Serv Res Policy.* 2008; **13**(2): 92–98.
PubMed Abstract | Publisher Full Text

Open Peer Review

Current Peer Review Status: ? ✓ ✓

Version 2

Reviewer Report 20 August 2026

https://doi.org/10.21956/openreseurope.26468.r77374

© **2026 Perimbeti S.** This is an open access peer review report distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

✓ **Stuthi Perimbeti**
Penn State Cancer Institute, Hershey, USA

The authors have taken on a very rare and challenging research question, and they have addressed the prior reviewer comments thoroughly. There is a notable lack of published data in this area, particularly regarding the behavioral factors influencing healthcare professionals and the barriers affecting referral pathways and access to care. The development of the survey instruments and focus group discussion guides appears to be well thought out and methodologically sound. The findings are highly informative and have the potential to be applied to other clinical areas facing similar challenges. Overall, this work makes a valuable contribution to an underexplored field.

Is the rationale for, and objectives of, the study clearly described?
Yes

Is the study design appropriate for the research question?
Yes

Are sufficient details of the methods provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Genitourinary malignancies

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 10 July 2026

https://doi.org/10.21956/openreseurope.26468.r76965

© **2026 Duijts S.** This is an open access peer review report distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Saskia F A Duijts
Medical Psychology, Amsterdam University Medical Center, Amsterdam, The Netherlands

I would like to thank the authors for responding to my comments and concerns. I have reviewed the responses carefully, and consider them thorough, and well-reasoned. The concerns have been addressed in a satisfactory manner. In my view, the manuscript has been strengthened as a result of the revisions. I have no further comments and support the manuscript in its revised form.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Psychosocial oncology; rare cancers

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 05 June 2025

https://doi.org/10.21956/openreseurope.21585.r54335

© **2025 Duijts S.** This is an open access peer review report distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Saskia F A Duijts
Medical Psychology, Amsterdam University Medical Center, Amsterdam, The Netherlands

ABSTRACT (and plain language summary)
- The authors state as a gap / problem that 'the behavioural factors influencing this decision making process and best communication practices are unknown'. Then: the aim of PREVENTABLE is to assess the clinical, social and economic impact of RTRS-care pathways. Whilke the gap / problem is clear, and the aim is clear: the combination of the two is less clear. However, this becomes clear when looking at the specifc objective for THIS study. To prevent confusion, replace the overall aim of PREVENTABLE to the objective section. First state the aim of the current study there, and then that the study is part of ... and so on.
- Not clear where (n=100) is referring to. Or do the authors actually mean 100 clinical teams? The

same goes for n=290. Since this is places at the end of the sentence, it is not fully clear where it relates to. I suppose patients? Yet, this sentence is about patients' adoption. Or do the authors refer to 290 care pathways? Anyways, it is unclear (when reading the abstract only).
- In the plain language summary, the authors talk about social networks. This has nog been mentioned in the abstract.
BACKGROUND
- It increases readability when sentences are less long. First sentence is 6 lines! Please place a period (.) after / begin new sentence: ... up to 100%. Since these syndromes follow...
- The authors state that... ultimately, they aim to develop person-centred guidelines to improve communication and recommendation of prevention-related care pathways for RTRS. It is unclear / not sufficienlty addressed throughout the paper if this concerns guidelines for individual countries, nor what gathering data in several countries (with - supposingly - different care pathways regarding RTRS) implies and how this will be taken into account addressing this aim.
PROTOCOL
- One of the surveys wll be for clinical teams managing RTRS. Will specific persons in a team be invited to complete the survey? Will teams be invited to complete the survey as a team? Probably, this will be explained, yet, at this point, it raises questions.
- Split the inclusion criteria in three groups (clinical teams, individuals, social network). - Here, it becomes clear that the number of persons to be included is 100 professionals and 290 patients. Not clear in the abstract. Also, what about the number of persons from the social networks of patients? Or wil they only participate in the FG?
- The surveys are developed in English? What about the translation to Portugese, Spanish and so on. And cross-cultural translation and validation of the survey in each country to make sure similar concepts will be measured? Note: later on it becomes clear that translation to each PREVENTABLE language has taken place. Throughout the paper, some issues raise questions yet are answered later on in the paper. While it is good that such issues become clear later on, try to avoid confusion at the first place.
- The authors talk about the survey for clinical teams and for healthcare professionals. Maybe better to explain only once that the survey will be distributed amongst healthcare professionals of clinical teams, and then stick to healthcare professionals.
- Regarding data analysis, the authors state that they focus on behavioural analysis of referral and uptake of care pathways. Both the behavioural analyses and how they define care pathways need more explanation.

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?

Yes

Are the datasets clearly presented in a useable and accessible format?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Psychosocial oncology; rare cancers

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 26 Jun 2026

Maiara Eliza Moreto

We sincerely thank you for your time, thorough reading, and constructive feedback on our manuscript. Your suggestions have greatly improved the structure, clarity, and readability of our work. Please find below our point-by-point responses.

1. The authors state as a gap/problem that 'the behavioural factors influencing this decision-making process and best communication practices are unknown'. The aim of PREVENTABLE is to assess the clinical, social and economic impact of RTRS-care pathways. While the gap and the aim are clear, the combination of the two is less clear. To prevent confusion, replace the overall aim of PREVENTABLE to the objective section. First state the aim of the current study there, and then that the study is part of... and so on.

Response: We agree with this structural suggestion. We have restructured the abstract to separate the specific study aim from the broader project context. The overall aim of PREVENTABLE has been moved to the Objective section. The abstract now first states the aim of the current study, followed by a clarification that it is conducted within the framework of the PREVENTABLE project.

2. Not clear where (n=100) is referring to. Or do the authors actually mean 100 clinical teams? The same goes for n=290. Since this is places at the end of the sentence, it is not fully clear where it relates to. I suppose patients? Yet, this sentence is about patients' adoption. Or do the authors refer to 290 care pathways? Anyways, it is unclear (when reading the abstract only).

Response: Thank you for pointing this out. We agree that the abstract text needed to specify the exact units being sampled. The abstract has been revised to make explicit that *n* =100 refers to members of clinical teams and *n*=290 refers to individual patients with RTRS.

3. In the plain language summary, the authors talk about social networks. This has not been mentioned in the abstract.

Response: We thank the reviewer for this observation. Social networks are mentioned in the abstracs, specifically in the Objectives and Methods sections. The restructuring described in our response to Comment 1 has made the integration of social networks much more explicit and highly visible to the reader in the revised abstract.

4. It increases readability when sentences are less long. First sentence is 6 lines! Please place a period (.) after / begin new sentence: ...up to 100%. Since these syndromes

follow...

Response: We completely agree with this assessment. The opening sentence of the Background section has been divided into two shorter, clearer sentences, exactly as suggested:

5. The authors state that... ultimately, they aim to develop person-centred guidelines to improve communication and recommendation of prevention-related care pathways for RTRS. It is unclear / not sufficienlty addressed throughout the paper if this concerns guidelines for individual countries, nor what gathering data in several countries (with - supposingly - different care pathways regarding RTRS) implies and how this will be taken into account addressing this aim.

Response: This is an important point regarding our methodology, and we thank the reviewer for raising it. We have clarified throughout the manuscript that our mixed-methods design allows for cross-cultural comparison of COM-B domains, and that country-level differences will be explicitly examined during data analysis. The Objectives section now explicitly frames the study as a multi-country investigation. The Data Analysis section states that inferential statistics will be used to examine whether COM-B domains differ by country, and that qualitative analysis will compare variations in how COM-B domains manifest across regions. Finally, the reference to person-centered guidelines has been moved to the Conclusion section where we clarify that these guidelines will draw directly on the integrated cross-cultural findings.

6. One of the surveys will be for clinical teams managing RTRS. Will specific persons in a team be invited to complete the survey? Will teams be invited to complete the survey as a team? Probably, this will be explained, yet, at this point, it raises questions.

Response: The survey was directed to members of clinical teams with expertise in RTRS, rather than at entire clinical teams completing a single survey collectively. Each eligible professional was invited to complete the survey individually and anonymously. To make this clear from the outset, we have revised the Design section to specify that the survey targets individual members of clinical teams rather than teams as a collective unit.

7. Split the inclusion criteria in three groups (clinical teams, individuals, social network). Here, it becomes clear that the number of persons to be included is 100 professionals and 290 patients. Not clear in the abstract. Also, what about the number of persons from the social networks of patients? Or wil they only participate in the FG?

Response: We appreciate this suggestion to improve the structural layout of our participant descriptions. We have reorganized the Population section to present the inclusion criteria separately for each stakeholder group and each study phase (surveys and focus groups). This restructuring clarifies that the social network participants are exclusively included in the focus group phase. We have also detailed their sample size based on qualitative standards (~6 participants per group), yielding 18 focus groups in total across the study (108 participants; 36 per target group).

8. The surveys are developed in English? What about the translation to Portugese, Spanish and so on. And cross-cultural translation and validation of the survey in each country to make sure similar concepts will be measured? Note: later on it becomes clear that translation to each PREVENTABLE language has taken place. Throughout the paper, some issues raise questions yet are answered later on in the paper. While it is good that such issues become clear later on, try to avoid confusion at the first place.

Response: We thank the reviewer for this feedback and for the broader observation regarding text flow. We acknowledge that introducing operational details late in the text can raise questions, and we have adjusted the sequencing to address this. The survey development subsection has been revised to immediately clarify that surveys were developed in English and subsequently translated into all six PREVENTABLE languages using the European Commission's eTranslation service. We now explicitly specify that a forward-backward translation protocol was utilized, and that PREVENTABLE clinical partners (i.e., bilingual experts with deep knowledge of both RTRS and local healthcare contexts) reviewed all translations to ensure cultural and conceptual adequacy.

9. The authors talk about the survey for clinical teams and for healthcare professionals. Maybe better to explain only once that the survey will be distributed amongst healthcare professionals of clinical teams, and then stick to healthcare professionals.

Response: We agree that using multiple terms interchangeably created unnecessary ambiguity. We have standardized our terminology across all sections of the manuscript. The phrase *"members of clinical teams"* is now used consistently.

10. Regarding data analysis, the authors state that they focus on behavioural analysis of referral and uptake of care pathways. Both the behavioural analyses and how they define care pathways need more explanation.

Response: We agree that foundational concepts must be explicitly introduced early on. We have added an explicit definition of "care pathways" in the Background section and incorporated a dedicated paragraph defining behavioural analysis. These modifications ensure both core concepts are explicitly defined and contextualized before they are applied in the Methods and Data Analysis sections.

Competing Interests: No competing interests were disclosed.

Reviewer Report 19 May 2025

https://doi.org/10.21956/openreseurope.21585.r53345

© 2025 Pallin N. This is an open access peer review report distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

?

Nickola Pallin
Trinity College Dublin, Dublin, Ireland

Thank you for the opportunity to review this study protocol. I think an appropriate plan has been developed for the study. I left some comments below which I hope will be helpful to the authors.

The manuscript refers to 'care pathways' as the focus of the study and it would be helpful to clarify what is meant by this term in the research context.

Consider expanding on what the behavioural factors being explored are influencing or what the ‘target behaviour’ is. This would improve clarity as it is not entirely clear whether the focus is on the care pathways themselves, the recommendation of those pathways by HCPs, communication, decision-making by those with RTRS, or the interaction between these elements. At times this distinction is blurred.

It would strengthen the manuscript by explaining the intervention or practice being studied (e.g., the RTS care pathways, communication strategies, or decision-making processes) and the behaviour being investigated (e.g., referral of the pathway or patient uptake).

The sentence “Furthermore, gaps still persist in understanding the various factors influencing decision-making in RTRS, such as, preferences of individuals with RTRS, healthcare professionals recommendations, and the best practices for communication and emotional support in RTRS care” includes several important points, but they are a bit crowded and the authors might consider breaking this up. In addition, the sentence ‘best practices for communication and emotional support in RTRS care’ feels loosely connected to the rest of the list which makes the message hard to follow. The authors might consider clarifying how this sentence relates to decision-making and care pathways.

The manuscript proposes the use of the COM-B model. It would be helpful if the authors explain why COM-B has been selected instead of other determinant frameworks as the focus of the study is on identifying barriers and enables.

The paper seems to equate behavioural factors with barriers and facilitators, but this could be clarified. Not all barriers and facilitators may be behavioural, for example, resources or guidelines and policies may influence opportunity or capability without being behavioural themselves. Clarifying how these factors (barriers and facilitators) are behavioural factors and influence the recommendation and uptake of care pathways would strengthen the paper.

Clarifying what is meant by behavioural analysis would be helpful.

Aim 3 - it is unclear whether recommendation refers to those made by the clinical team or those made by the social network.

I was also unsure if the study is exploring the perception of social network members on the barriers and facilitators that individuals with RTRS experience or if it is the barriers and facilitators that the social network experience. This clarification will help the reader understand aim 3 and objective iii (in the abstract), as well as the purpose of including social networks and family in this study.

The paper mentions sample sizes for healthcare professionals and patients, but I cannot seem to see a sample size provided for the social networks.

Is there a separate survey for social networks? this should be clarified in the methods section.

Was there only a sample size calculation for the RTRS sample? I was wondering why this is.

Will inferential statistics be conducted for all the surveys?

Using inferential statistics what categories will be compared to the COM-B domains?

The authors note that they will use triangulation to integrate survey and focus group data. The surveys are designed to identify barriers and facilitators, and it seems that the focus groups are described more generally in terms of exploring factors and challenges. For greater coherence, the authors could clarify how the focus group findings will directly address the overall study aims.

The authors could expand on how they plan to handle the analysis and integration of data across the three groups (HCPs, patients, and social networks) for each of the surveys and focus groups. The authors could also clarify how all these elements will be integrated within the mixed methods design and joint display and narrative synthesis. A figure illustrating these steps might also be useful here.

The last two sentences of the data analysis where the authors state “This integration of the results of the focus groups and surveys will inform the development of guidelines on how the care pathways for RTRS….” I suggest moving this statement to the discussion, where the implications of the study findings for guideline development could be discussed.

Is the rationale for, and objectives of, the study clearly described?

Partly

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?

Partly

Are the datasets clearly presented in a useable and accessible format?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Implementation Science, Oncology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 26 Jun 2026

Maiara Eliza Moreto

We sincerely thank you for your time and constructive feedback on our manuscript. Your comments have improved the clarity and quality of the paper. Please find below our point-by-point responses.

1. The manuscript refers to 'care pathways' as the focus of the study and it would be helpful to clarify what is meant by this term in the research context.

Response: We thank the reviewer for this observation. We have now added an explicit definition in the second paragraph of the Background section. The revised text clarifies that care pathways refer to sequences of care options involving multiple decisions, including primary prevention (e.g., risk-reducing surgery, chemoprevention, changes in diet), surveillance (e.g., earlier, more frequent mammogram/colonoscopy), and treatment for cancer or premalignant conditions.

2. The sentence "Furthermore, gaps still persist in understanding the various factors influencing decision-making in RTRS, such as, preferences of individuals with RTRS, healthcare professionals recommendations, and the best practices for communication and emotional support in RTRS care" includes several important points, but they are a bit crowded. The sentence 'best practices for communication and emotional support in RTRS care' feels loosely connected to the rest of the list which makes the message hard to follow. The authors might consider clarifying how this sentence relates to decision-making and care pathways.

Response: We agree. The original sentence was dense and the connection between communication/emotional support and decision-making was insufficiently explicit. We have broken up the sentence and now connect communication challenges and the emotionally charged nature of decision-making in RTRS explicitly to the gap in care.

3. The manuscript proposes the use of the COM-B model. It would be helpful if the authors explain why COM-B has been selected instead of other determinant frameworks, as the focus of the study is on identifying barriers and enables.

Response: We thank the reviewer for this important suggestion. A justification for the selection of the COM-B model has been added following the explanation of the model in the third paragraph of the Background section. We highlight the model's capacity to capture both internal (psychological capability and motivation) and external (physical and social opportunities) determinants of behavior, enabling systematic identification of barriers and facilitators. We additionally note the complementary use of the Theoretical Domains Framework (TDF) for the qualitative component.

4. Consider expanding on what the behavioural factors being explored are influencing or what the 'target behaviour' is. This would improve clarity as it is not entirely clear whether the focus is on the care pathways themselves, the recommendation of those pathways by HCPs, communication, decision-making by those with RTRS, or the interaction between these elements. At times this distinction is blurred.

Response: We thank the reviewer for pointing this out. The two distinct target behaviours of the study: (i) referral and recommendation of RTRS care pathways by clinical teams, and (ii) uptake of recommended care by patients, are now clearly stated and distinguished in the Background section. The text also clarifies that the study investigates individual, social, and environmental determinants of each behaviour.

5. It would strengthen the manuscript by explaining the intervention or practice being studied (e.g., the RTS care pathways, communication strategies, or decision-making processes) and the behaviour being investigated (e.g., referral of the pathway or patient uptake).

Response: In line with the previous comment, we have provided a clearer account of both the clinical context (RTRS care pathways) and the specific behaviours under investigation in the final paragraph of the Background section. The two target behaviours are explicitly named and distinguished from the care pathways themselves, which are the object of the behavioural analysis rather than the behaviour per se.

6. The paper seems to equate behavioural factors with barriers and facilitators, but this could be clarified. Not all barriers and facilitators may be behavioural, for example, resources or guidelines and policies may influence opportunity or capability without being behavioural themselves. Clarifying how these factors (barriers and facilitators) are behavioural factors and influence the recommendation and uptake of care pathways would strengthen the paper.

Response: The reviewer raises a valid conceptual point. We have revised the language in the final paragraph of the Background section to refer more precisely to "individual, social, and environmental determinants" rather than using "behavioural factors" as an umbrella term for all barriers and facilitators. This avoids conflating the behavioural analysis framework with the full range of determinants captured under the COM-B model, which includes non-behavioural factors such as environmental resources and social norms.

7. Clarifying what is meant by behavioural analysis would be helpful.

Response: We have added a dedicated paragraph in the Background section defining behavioural analysis in the context of this study.

8. Aim 3 — it is unclear whether recommendation refers to those made by the clinical team or those made by the social network.

Response: We thank the reviewer for this observation. Aim 3 has been rewritten to make

clear that the focus is on the barriers and facilitators experienced by the social network itself — specifically, how they provide support for, engage in, and influence the uptake of care pathways — not on recommendations made by the social network.

9. I was also unsure if the study is exploring the perception of social network members on the barriers and facilitators that individuals with RTRS experience or if it is the barriers and facilitators that the social network experience. This clarification will help the reader understand aim 3 and objective iii (in the abstract), as well as the purpose of including social networks and family in this study.

Response: We clarify that this study explores the barriers and facilitators experienced by the social network when providing support for and engaging in the uptake of the recommended care pathway for RTRS. The third aim has been revised accordingly. This now clearly distinguishes the perspective of the social network from that of the patients themselves.

1**0. The authors note that they will use triangulation to integrate survey and focus group data. The surveys are designed to identify barriers and facilitators, and it seems that the focus groups are described more generally in terms of exploring factors and challenges. For greater coherence, the authors could clarify how the focus group findings will directly address the overall study aims.**

Response: We agree that this needed greater clarity. The Design section now explicitly states that focus groups serve to explore participants' experiences, perceptions, and contextual factors related to the barriers and enablers identified in the survey phase, thereby providing a broader understanding of the quantitative findings.

11. Is there a separate survey for social networks? This should be clarified in the methods section.

Response: The social network was not included in the survey phase. To make this explicit, we have added a clarifying sentence in the Design section stating that members of the social network are only included in Step 2 (focus groups) as an additional source and are not part of the survey phase.

12. The paper mentions sample sizes for healthcare professionals and patients, but I cannot seem to see a sample size provided for the social networks.

Response: As noted above, the social network was not included in the survey phase. Sample size was determined only for the two survey target groups (members of clinical teams: n=100; individuals with RTRS: n=290). Social network members participate only in the focus groups, where sample size follows established focus group recommendations (approximately six participants per group). This is now clearly stated in the Population section.

13. Was there only a sample size calculation for the RTRS sample? I was wondering why this is.

Response: A sample size calculation was conducted for both target groups. For individuals with RTRS, the calculation was based on the total number of cases identified within the PREVENTABLE consortium (n=1177), using a 95% confidence interval and 5% margin of error. For members of clinical teams, the sample size was estimated based on the number of healthcare professionals with expertise in the RTRS included in the project and the composition of the participating teams across countries. This distinction is now explicitly stated in the Population section.

14. Will inferential statistics be conducted for all the surveys?

Response: Yes, inferential statistics will be applied to the survey data for both target groups (members of clinical teams and patients with RTRS). The Data Analysis section outlines this approach. Focus group data, by contrast, will be analysed using thematic analysis. Both phases are structured around the COM-B framework, which allows for coherent integration of findings across methods.

15. Using inferential statistics, what categories will be compared to the COM-B domains?

Response: We have added more detail on this point in the Data Analysis section. Inferential statistics will be used to explore: (i) comparisons between the different care pathways, (ii) within-domain comparisons of more granular constructs, and (iii) comparisons of total scores across COM-B domains. In addition, we will examine whether COM-B domains differ by syndrome, clinical specialty, and country.

16. The authors could expand on how they plan to handle the analysis and integration of data across the three groups (HCPs, patients, and social networks) for each of the surveys and focus groups. The authors could also clarify how all these elements will be integrated within the mixed methods design and joint display and narrative synthesis. A figure illustrating these steps might also be useful here.

Response: We have clarified in the Data Analysis section that data will be integrated within each stakeholder group separately, with findings from different groups reported and interpreted independently. Triangulation within each group will be achieved through narrative integration using a contiguous approach and through joint displays, allowing side-by-side presentation of findings.

17. The last two sentences of the data analysis where the authors state "This integration of the results of the focus groups and surveys will inform the development of guidelines on how the care pathways for RTRS…." I suggest moving this statement to the discussion, where the implications of the study findings for guideline development could be discussed.

Response: We agree with this suggestion. The relevant sentences have been moved to the Conclusion section, where they more appropriately convey the practical implications of the study findings for guideline development.

Competing Interests: No competing interests were disclosed.