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Genetics Navigator: protocol for a mixed methods randomized controlled trial evaluating a digital platform to deliver genomic services in Canadian pediatric and adult populations

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ABSTRACT

Introduction Genetic testing is used across medical disciplines leading to unprecedented demand for genetic services. This has resulted in excessive waitlists and unsustainable pressure on the standard model of genetic healthcare. Alternative models are needed; e-health tools represent scalable and evidence-based solution. We aim to evaluate the effectiveness of the Genetics Navigator, an interactive patient-centred digital platform that supports the collection of medical and family history, provision of pregenetic and postgenetic counselling and return of genetic testing results across paediatric and adult settings.

Methods and analysis We will evaluate the effectiveness of the Genetics Navigator combined with usual care by a genetics clinician (physician or counsellor) to usual care alone in a randomised controlled trial. One hundred and thirty participants (adults patients or parents of paediatric patients) eligible for genetic testing through standard of care will be recruited across Ontario genetics clinics. Participants randomised into the intervention arm will use the Genetics Navigator for pretest and post-test genetic counselling and results disclosure in conjunction with their clinician. Participants randomised into the control arm will receive usual care, that is, clinician-delivered pretest and post-test genetic counselling, and results disclosure. The primary outcome is participant distress 2 weeks after test results disclosure. Secondary outcomes include knowledge, decisional conflict, anxiety, empowerment, quality of life, satisfaction, acceptability, digital health literacy and health resource use. Quantitative data will be analysed using statistical hypothesis tests and regression models. A subset of participants will be interviewed to explore user experience; data will be analysed using interpretive description. A cost-effectiveness analysis will examine the incremental cost of the Navigator compared with usual care per unit reduction in distress or unit improvement in quality of life from public payer and societal perspectives.

Ethics and dissemination This study was approved by Clinical Trials Ontario. Results will be shared through stakeholder workshops, national and international conferences and peer-reviewed journals.

Trial registration number NCT06455384.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Our study uses a randomised controlled trial design and includes a comprehensive range of outcome measures, which will provide a rigorous and thorough assessment of an e-health platform that integrates all the components of genetics services delivery.
⇒ This study will include a cost-effectiveness analysis, which will provide quantitative evidence about the economic impact from the perspective of the healthcare system and society.
⇒ The qualitative component in our study will generate evidence to foster deeper understanding of the needs and experiences of patients requiring genetics services.
⇒ All participants in our study are English speaking and need to have access to a computer and the internet, which could limit the generalisability of our results.

INTRODUCTION

Genetic testing, including targeted panels, exome and genome sequencing (GS), is increasingly being used in mainstream care across medical disciplines as it improves diagnosis and patient management. With substantial improvements in diagnostic performance, there has been unprecedented demand for genetic testing for a broad range of clinical indications.[1–3] The volume of testing and complexity of genomic analysis places unsustainable pressure on the standard model of care for delivering genetics services, which is heavily dependent on multiple interconnected specialists including medical geneticists, genetic counsellors, clinical laboratory directors, bioinformaticians and genome analysts based in tertiary care centres.[2 4] This pressure is intensified by already critical workforce shortages in genetics, shortages that will become more severe in coming years as genetic knowledge and clinical applications continue to expand.[2 3] These shortages have resulted in excessive waitlists, prompting the use of alternative models of care including remote genetic counselling (telephone, e-mail and videoconferencing),[5–8] electronic consultations between specialists and patients or primary care,[9–11] and the integration of genetics education strategies into primary care.[12–15] While these approaches have contributed to mitigating current service delivery challenges, comprehensive adaptive patient-facing e-health tools can provide more scalable and patient-centred solutions.

The patient preference literature supports the use of e-health tools in a range of clinical settings.[16–19] A systematic review of patient portals found that they can improve psychological outcomes such as decision-making and self-efficacy.[20] In interviews, patients with cancer report that waiting for a verbal confirmation of results from a provider was more distressing than accessing the results online through a portal as it enabled a sense of control.[21–23] Portals also provide patients with timely access to their health information, increasing efficiency of service delivery.[24 25] Patients have also found e-health tools to be acceptable, easy to use, trustworthy and facilitative of personalised care in various clinical settings.[26–33] Many e-health tools exist in clinical genetics, and these have also been well-received by patients, particularly with respect to enabling self-paced, private and informative counselling.[16–18] However, the e-health tools developed to date, including chatbots,[34] support single components of genetic service delivery, such as pretest or risk education,[16 17 24 25 35–37] decision-making to pursue testing and receive various result types,[18 22 23 38–40] or results disclosure.[41–44] These innovations are limited in scope and scale, as none of them integrates all of the components of the service delivery pathway for both paediatric and adult populations.

We developed the Genetics Navigator, a patient-centred e-health navigation platform for genetic service delivery in paediatric and adult populations. This platform extends the Genetics Adviser[45] to include collection of medical and family history, and a chatbot to provide responses to frequently asked questions and store additional patient questions (the chatbot's development and evaluation will be described in a separate manuscript).[46]

AIMS AND HYPOTHESES

Aims

We aim to evaluate the effectiveness, cost-effectiveness and user experience of the Genetics Navigator compared with usual care (clinician-delivered care) with patients undergoing genetic testing.

Theoretical framework and hypotheses

Consistent with the Theory of Planned Behavior (TPB),[47] we hypothesise that using the Genetics Navigator will improve emotional functioning (decrease distress, anxiety/depression and decisional conflict), knowledge and satisfaction with decision-making compared with usual care. In addition, we hypothesise that the Genetics Navigator will be cost effective compared with usual care and associated with less health resource use.

METHODS

Study design

This is a mixed-method, non-blinded randomised controlled superiority trial where we will evaluate the effectiveness and the cost-effectiveness of the Genetics Navigator and usual care (intervention) in reducing patient distress compared with usual care alone (control). Within this trial, patients will receive genetic test results related to a range of clinical indications as part of their standard of care testing. All participants will complete baseline measures and randomisation, after which they will either use the Genetics Navigator platform prior to or after their medical geneticist/genetic counsellor appointment (intervention) or receive usual care and meet with their medical geneticist/genetic counsellor as is standard clinic practice (control). Outcomes will be measured at baseline (T0), pretest (T1–T2) and posttest (T3–T4) (figure 1). Consistent with the TPB,[47] the primary outcome is patient distress after receiving genetic test results, and secondary outcomes include knowledge, decisional conflict, anxiety/depression, empowerment, quality of life, satisfaction, acceptability, digital health literacy and health resource use (table 1). We will also conduct a qualitative study with a subgroup of participants, who will be interviewed about their experience using the Genetics Navigator. The study was approved by Clinical Trials Ontario and this manuscript follows the 2013 and 2022 Standard Protocol Items: Recommendations for Interventional Trials guidance for protocols on clinical trials (see online supplemental file 1).[48 49]

Population

We will recruit adult genetics patients at Sinai Health, and parents/legal guardians of paediatric patients at the Hospital for Sick Children (SickKids) who have

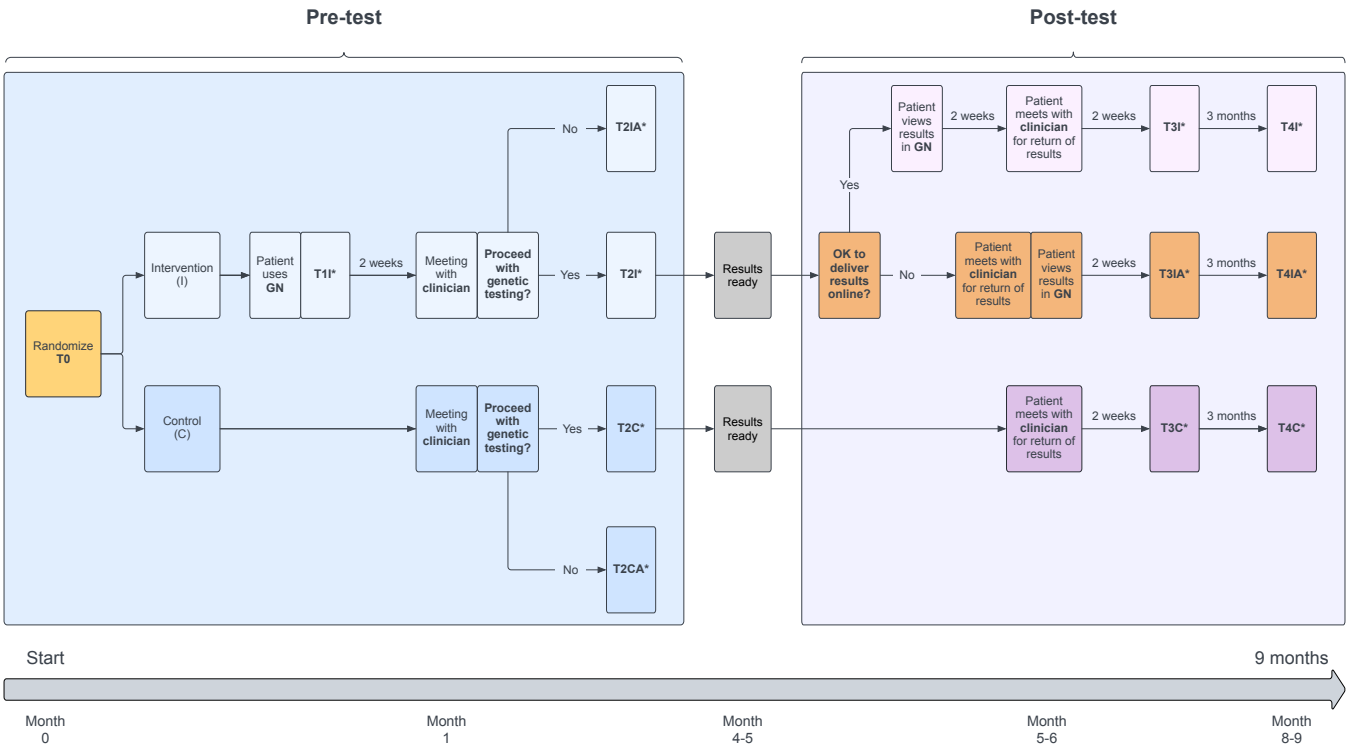

Figure 1 Study flow: timing of follow-up measures for each participant group. Follow-up measures will be collected from participants at baseline (T0, yellow) and four subsequent timepoints (T1, T2, T3 and T4) in the intervention arm (I, light blue, pink and orange) and three subsequent timepoints (T2, T3 and T4) in the control arm (C, dark blue and purple). Participants who do not proceed with genetic testing will complete a subset of measures (T2IA and T2CA). All participants in the intervention arm will complete the same measures. Primary outcome will be collected 2 weeks after meeting with the clinician for post-test counselling (T3) in both arms (T3I, T3IA and T3C). *A: alternative pathway; C: control arm; I: intervention arm; T0: baseline; T1: 2 weeks before first appointment with clinician; T2: immediately after pretest meeting with clinician; T3: 2 weeks after post-test meeting with clinician; T4: 3 months after T3 measures.

been referred to clinical genetics and for whom genetic testing may be offered as part of their standard care. These specialised clinics (area of specialisation listed in the inclusion criteria below) were selected for feasibility purposes, since they evaluate patients with a more predictable clinical pathway who have a high likelihood of being eligible for genetic testing.

Eligibility criteria

Inclusion

- Adult patients (18 years of age or older) who are referred to the clinical genetics service at Sinai Health for the following primary indication: at risk for a cancer predisposition syndrome.
- Parents/legal guardians (18 years of age or older) of paediatric patients who are referred to the clinical genetics service at SickKids for one or more of the following primary indications: epilepsy, neurodevelopmental or cardiac conditions.

Exclusion

- Known not to be eligible for clinical genetic testing coverage in Ontario.
- Requires urgent clinical genetic testing or prenatal genetic testing.
- Not fluent in English (speaking and reading).

Intervention

Participants in the intervention arm will use the Genetics Navigator to support the delivery of genetic services, including intake, education, pretest and post-test counselling, and results delivery with physician-generated management recommendations. All participants will use the Genetics Navigator prior to their pretest visit with their genetics clinician. They will also use the Genetics Navigator as part of results delivery by their genetics clinician, either before, or after their post-test genetic counselling visit. The Navigator will be supported by a mix of in-person/phone/video-conferencing consults with genetics professionals. The timing of use of the Genetics Navigator will be determined by the participant's clinician. This is further described under data collection.

Control

Control arm participants will complete their scheduled appointments (pre-test and post-test) with their genetics clinician. During these appointments, the clinician will follow standard of care procedures, as further described under data collection.

Table 1 Summary of study measures across time points* for each participant arm†

	Pre-test				Post-test			
	Baseline	+~2 weeks	+ 1 month		+ 6 months		+ 9 months	
Measure	T0	T1I	T2I/T2C	T2IA/T2CA	T3I/T3IA	T3C	T4I/T4IA	T4C
Demographics	•							
Brief Health Literacy Screening Tool (BRIEF)	•							
Digital Literacy Scale (DHLS)	•							
University of North Carolina Genomic Knowledge Scale (UNC-GKS)	•	•	•		•	•	•	•
Hospital Anxiety and Depression Scale (HADS)	•	•	•	•	•	•	•	•
SF-36: Quality of life	•	•	•		•	•	•	•
Decisional Conflict (SURE)			•	•				
Genomics Outcome Scale (GOS)		•	•		•	•	•	•
Preparation for Decision Making Scale			•					
Satisfaction with Decision Making			•					
Acceptability eScale		•	•		•		•	
Duration of platform use (minutes)		•			•		•	
Frequency of platform access		•			•		•	
Health resource use (RUQ)			•‡				•§	•§
Multidimensional Impact of Cancer Risk Assessment (MICRA–Adapted)					•¶	•¶	•	•

*Time points abbreviations. T0: baseline; T1: 2 weeks before first appointment with clinician; T2: immediately after pretest meeting with clinician; T3: 2 weeks after post-test meeting with clinician; T4: 3 months after T3 measures.
†Participant arm abbreviations. A: alternative pathway; C: control group; I: intervention group (see online supplemental table 1 for specific measures in each arm).
‡In the past 3 months.
§Since receiving results.
¶Primary outcome (test-specific distress subscale).

Outcomes

Primary outcomes

The primary outcome is Test-Specific Distress 2 weeks after receiving results (post-test genetic counselling visit), as measured by an adapted version of the Multidimensional Impact of Cancer Risk Assessment (MICRA).[50] The MICRA is a validated 25-item questionnaire with excellent psychometric properties that measures distress, uncertainty and positive experiences following genetic testing.[50] Questions will be adapted for non-cancer-based genetic test results. There are 6 items measuring distress, scored from 0 to 5, and total score for this domain ranges from 0 (no distress) to 30 (very high distress).

Secondary outcomes

The following secondary outcomes will be measured for patient and parent participants: Test-Specific Uncertainty and Positive Experiences (measured by the MICRA),[50] Knowledge (measured by the University of North Carolina Genomic Knowledge Scale),[51] Decisional Conflict (measured by the SURE),[52] Anxiety and Depression (measured by the Hospital Anxiety and Depression Scale,[53] Empowerment (measured by the Genomics Outcome Scale),[54] Health Literacy (measured by the Brief Health Literacy Screening Tool),[55] Quality of Life (measured by the 36-item Short Form Survey (SF-36)),[56] Satisfaction (measured by the Satisfaction with Decision Making Scale and the Preparation for Decision Making Scale),[57 58] Acceptability (measured by the acceptability eScale),[59] mental health resources utilisation (measured by the Resource Use Questionnaire developed by Ungar *et al*) and Digital Health Literacy (measured by the Digital Health Literacy Scale).[60] Duration of visits with the genetics clinician (physician and/or genetic counsellor) and time spent on clinical tasks by genetics assistants (if applicable) will be tracked in 15-min increments by the participating clinician for a representative subset of participants in the intervention and the control groups. Medical information will be collected via chart review. Frequency of platform use, duration of platform session and readiness (for genetic testing and for results disclosure) will be gathered from the platform.

Demographics variables to be collected include age, sex, gender,[61 62] education, self-reported ethnicity, employment status, marital status, number of children, geographical location of residence (via first segment of the postal code to identify Forward Sortation Area) and reason for referral to genetics.

Sample size

The primary outcome is patient/parent distress; Cella *et al* reported a SD ranging 2–7 on the MICRA distress subscale.[50] Using a minimally clinically important difference (MCID) of 0.5 SDs results in absolute differences

ranging between 1 and 3.5 depending on SD.[50] Assuming this, we estimate that 65 participants/arm will be required to have 80% power at a two-sided significance level of 0.05 to detect the MCID using a standard two-sample t-test. The MICRA distress subscale has a range of 0–30; based on Cella *et al*,[50] we expect the control group to have means between 1 and 6, which leaves sufficient room for improvement on the scale. Based on previous studies attrition rates, we anticipate having to possibly oversample to account for attrition and to account for participants who are not offered or opt not to receive genetic testing, up to a total sample size of 170 participants (85 per group).[63]

Recruitment

Adult patients or parents/legal guardians of paediatric patients will be recruited from participating genetics clinics at Sinai Health and the SickKids, starting July 2024. Prospectively, adult patients or parents/legal guardians of paediatric patients referred to clinical genetics for testing will be identified by the medical geneticist to whom they have been referred. Eligible participants will be briefly informed about the study by the respective clinic's coordinator or genetics assistant during their phone consult to book their standard-of-care genetics appointment. Names and contact information of prospective participants who agree to be contacted by the study team for more information will be provided by the genetic clinic to the study team via secure file transfer or over the phone. Potential participants will also have the option of contacting the study coordinator directly and the genetics clinic will offer to provide the study invitation package, as well as the study coordinator's phone and email contact information. The study team will then contact interested participants via phone and explain the study further and explore potential participants' level of interest.

Any patients who are not interested in participating in the study will be asked by the genetics clinic or the study team if they are willing to provide a reason for declining. This information will be recorded on the recruitment log. After the study is completed, data on individuals who declined to participate in the study will be aggregated so that this subpopulation can be accurately described. Recruitment will last for up to 1 year, and data collection is expected to end in July 2026.

Randomisation

Participants will be consecutively randomised and allocated using a computer-generated randomisation scheme in a 1:1 ratio with random permuted blocks of varying sizes, stratified by adult patients versus parents of paediatric patients. A list of allocations will be generated using the randomisation function within REDCap.

Data collection

Once the participant has consented to the study, they will be assigned a study ID. The study coordinator will administer the baseline survey (T0) and then obtain allocation from REDCap. The distribution of study measures is schematised in figure 1, and specific measures collected at each timepoint are summarised in table 1. Outcomes will be measured at baseline (T0), in the pretest period (T1–T2), and in the post-test period (T3–T4). There will be four outcome measure timepoints after baseline: 2 weeks before (T1I) and immediately after the pretest visit with the genetics clinician (T2I/T2C), 2 weeks after (T3I/T3IA/T3C) and 3 months after (T4I/T4IA/T4C) the post-test visit with the genetics clinician.

Health resource use will be assessed immediately after the pretest visit with the genetics clinician (T2I/T2C) and 3 months after the post-test visit (T4I/T4IA/T4C). The health resource use questionnaire focuses on the use of mental health and support services during and immediately following the study period. Finally, the duration of visits with the genetics clinician and the time spent on clinical tasks by genetics assistants (if applicable) will be tracked by the participating clinician for a subset of participants selected across all clinicians by the research team in both groups. For the intervention group, the duration of participants' platform use and frequency of platform access will be assessed immediately after using the Genetics Navigator (T1I), and 2 weeks after the post-test visit with the clinician (T3I/T3IA), as well as 3 months after the post-test visit (T4I/T4IA) via platform data collection and google analytics.

Intervention

At the end of the baseline session (T0), intervention arm participants will be given the link to the online Genetics Navigator with instructions to log into the Genetics Navigator within 2 weeks before their scheduled pretest appointment with their genetics clinician. Two weeks prior to the participant's appointment with their clinician, the study coordinator will send a reminder email with the link and instructions. The use of the Genetics Navigator will take approximately 30 min. After completing this pretest portion, the Genetics Navigator will prompt the participant to complete the follow-up measures (T1I).

The Genetics Navigator platform will notify the study coordinator that the participant has completed the pretest portion of the Genetics Navigator via an automated email. Prior to the clinician and participant appointment, the clinician will review the participant's medical and family history, and readiness for genetic testing, which will be discussed with the participant during the appointment. The clinician will also address other clarifications or questions they may have. After the appointment, the clinician will order the genetic testing, if indicated and desired by the participant.

If the participant does not wish to pursue testing or the clinician determines that testing is not appropriate for the participant, they will be asked to complete a subset of follow-up measures (T2IA). After the participant has completed the clinician visit, the clinician will notify the study coordinator, who will email the participant a REDCap link instructing them to complete a set of follow-up measures (T2I/T2IA).

Once the participant's genetic test results are ready, they will be contacted by the clinician to schedule an appointment to discuss their results following their standard clinical practice. The clinical team will upload the results and care plan to the platform and determine if they can be delivered to the patient before the appointment based on provider's criteria. The recruiting clinic will also notify the study team of the participant's appointment and the nature of their results.

Intervention participants—results returned online before the appointment with clinician

- Participants will be able to view their results prior to meeting with the clinician. Participants will be notified 2weeks prior to their scheduled clinician appointment to log in to the Genetics Navigator to review their results and care plan.
- The participant will then meet with their clinician to review their results and complete a final set of post-test follow-up measures (T3I and T4I).

Intervention participants—results returned during appointment with clinician

- During the results appointment, the clinician will explain the participant's results and any recommended referrals or management plans.
- After the appointment, participants will use the Genetics Navigator platform to review their results and care plan.
- The participant will complete a final set of post-test follow-up measures (T3IA and T4IA).

All participant accounts in the Genetics Navigator will remain functional until the end of the study and will automatically be disabled once their participation is over.

Control

Control arm participants will complete their scheduled pretest appointment with their genetics clinician, during which standard of care procedures will be followed. If genetic testing is indicated and the participant chooses to proceed with testing, the clinician will order testing after their meeting. If the participant does not choose to go through with genetic testing or if their clinician determines that testing is not appropriate for the participant, they will be asked to complete a subset of follow-up measures (T2CA).

Following the clinician visit, the clinician will notify the study coordinator that the participant has completed their meeting. The study coordinator will then send the participant a link to REDCap survey via email with instructions to complete the pretest follow-up measures (T2C/T2CA).

If testing is performed, once the participant's results are ready, they will be contacted by the clinician to schedule an appointment to receive and discuss their results following their standard clinical practice.

Control participants

- During the results appointment, the clinician will explain the participant's results and any recommended referrals or management plans (standard of care).
- The clinician will then notify the study coordinator that the participant has completed their clinician meeting.
- After the appointment, the study coordinator will send the participant a link (via email) to REDCap with instructions to complete the post-test follow-up measures (T3C and T4C).

Medical chart data

For both intervention and control participants, medical information will be obtained from the medical chart notes from pretest and post-test visits. The study team will access medical chart information for all participants (with their consent), or child of the participants, from the recruiting clinic. The following information will be extracted: clinical indication for testing, medical history, genetic testing history and dates of clinical visits, genetic testing, test result and result disclosure. Wait times for clinic appointments will not be captured and are not expected to differ between randomised groups as patients will have their appointments scheduled the same way for both arms (scheduled according to standard clinical procedures at their clinic). The interval between testing and results disclosure will be calculated for each participant and mean intervals are expected to be similar between the control and intervention arms. If they differ, this variable will be included as a potential confounder for the analysis of the primary outcome.

Data analysis

Primary and secondary outcomes

Adult patient and parent/legal guardian data will be analysed together as the primary analysis, and separately as a subanalysis. Each analysis will follow the intention-to-treat approach. As this trial is positioned as a superiority trial, the null and alternative hypotheses are posited for the primary outcome: the Genetics Navigator is not better than or the same as the standard of care (H_0), or the Genetics Navigator is better than the standard of care (H_1). The mean scores for test-specific distress (distress subscale on the MICRA) will be compared using a t-test and the mean difference with 95% CI will be reported. The t-test is robust to non-normality; however, if diagnostics reveal significant concerns with respect to the distribution, a non-parametric test will be used to compare the locations of the distributions and bootstrapping will be used to derive 95% CIs on the mean difference. MICRA subscales (uncertainty and positive experience) and secondary outcomes of knowledge, decisional conflict, anxiety/depression, empowerment, quality of life, satisfaction, acceptability, digital health literacy and consult time will also be analysed using a t-test or regression model adjusting for baseline where appropriate with treatment

effects expressed a mean (adjusted) differences with 95% CIs. These additional analyses are for hypothesis-generating purposes; therefore, no multiplicity corrections will be applied.

The primary time point of comparison will be T3I/T3IA (pooled) for the intervention group (Genetics Navigator+clinician) versus T3C for the control group (clinician only) (figure 1).

Exploratory outcomes

Secondary exploratory analyses will examine the impact of the platform at baseline and follow-up timepoints (ie, T1, T2 and T4) on all outcomes using mixed-effects regression models. Mean total consult times and frequency of genetics encounters between those assigned to the platform and those assigned to usual care will be analysed descriptively and compared using a t-test if appropriate. Proportion of cases from specific geographical regions assigned to the platform and usual care will be compared using a χ^2 test.

Cost-effectiveness analysis

An incremental cost-effectiveness analysis (CEA) that compares the GN platform costs to usual care per unit improvement in MICRA score from the perspectives of the healthcare system and society will be undertaken alongside the randomised controlled trial (RCT). Adult patients and parents will be analysed separately. The CEA will be undertaken using data from cases who have completed the resource-use questionnaire and the MICRA. No imputation will be undertaken. The economic evaluation will use recommended methods.[64]

Costing

Direct healthcare resource use for diagnosis, genetic counselling and education pre-GS and post-GS will be measured over the study period for both study groups in adults and in parents. Use of the platform (navigation time and costs), mental health services, genetic testing, genetic counselling, genetics education, laboratory tests and any other services related to diagnosis and mental health will be collected prospectively using a customised team-developed resource use questionnaire. Data collection will occur in tandem with other RCT assessments. Prices for interventions, services and other direct costs will be obtained from study partners, provincial programme administrators, agencies, provincial fee schedules and published sources. Total costs per patient and per parent will be determined by multiplying the volume of resource use for each item over the study period by a corresponding unit price. For indirect costs, time losses from paid and unpaid labour of patients and parents will be collected in the resource questionnaire and multiplied by a standard wage. The mean cost per patient and parent will then be calculated for each group and aggregated to major cost categories. In the case of skewed total costs, non-parametric bootstrapping or log transformation will be applied.

Outcomes

The primary measure of effectiveness used in the CEA will be distress as measured with the MICRA. A secondary analysis will examine the incremental cost per unit improvement in SF-36 total score and mental health score.

Analysis

Person-level regressions will be conducted to determine mean costs and mean effectiveness per person for each group and results will be represented in an incremental cost-effectiveness ratio—the ratio of the difference between groups in mean cost per person to the difference in mean effectiveness. Subgroups based on age group, clinical diagnosis, GS result type, sex or other important clinical or demographic factors may be analysed. Sensitivity analysis will be undertaken to test the robustness of the results to variations in underlying assumptions regarding costly resources, such as the cost of the platform and costs of genetic testing. Results will be presented from the perspectives of the healthcare system and society.

Qualitative study

The qualitative study will explore participants' experience using semistructured interviews. We will use an interpretive description approach[65] to analyse the data. This methodology is particularly appropriate to examine and understand clinical phenomena with the goal to inform practical applications in clinical settings.[66 67]

Sampling

All individuals participating in the study will be asked to take part in the qualitative component of the study during the consent process. After the study is completed, a subset of participants in the intervention group will be selected to participate in the qualitative portion of the study (up to 20 adult patients and 20 parents/legal guardians in each arm). Participants will be selected by purposeful sampling, in order to attain a maximally varied sample of participants across a range of clinical indications, test results and demographic characteristics (age, sex, gender and ethnicity). Participation in the qualitative component is optional: participants will be able to decline to take part in the qualitative component and still participate the main trial.

Data collection

The study coordinator will schedule an interview with selected participants who agreed to participate in the qualitative component of the study. This interview will take place by videoconferencing or over the phone after the participant has completed all the other study activities. These interviews will take approximately 1 hour to complete and will be audio recorded and transcribed. The interview guide, developed based on a literature review and expert input, will explore participants' perceived value and usefulness of the Navigator (see online supplemental file 2).

Data analysis

The qualitative analyses will draw on interpretive description. We will use coding and constant comparison to identify common and divergent themes to characterise the entire dataset. Two researchers will code transcripts independently; consensus on codes will be reached through discussion. Data analysis will consider participants' sociodemographic factors that may influence perceptions of the Navigator. In keeping with qualitative methodology, data analysis will occur in conjunction with data collection. Ongoing analysis will inform the development of progressive iterations of the interview guides. Validation methods may include triangulation and member checking.[68] We will use a mixed-method matrix to integrate quantitative and qualitative data to better understand participants' experience.

Data management

All data collection activities will be coordinated from St. Michaels Hospital (SMH). Only participant recruitment and usual care clinical visits (see below) will take place at the participating hospitals (Sinai and SickKids). Contact forms from all recruiting sites will be emailed to the study team at SMH via secure file transfer. Data from medical charts will be abstracted on site and entered by the study team into a REDCap database, located at Applied Health Research Centre at SMH. Answers to follow-up questions for both groups will also be entered into REDCap. Patient name, date of birth (to confirm identity), contact information (email), personal and family health history, and results will be stored on the Genetics Navigator platform. Participants will also be able to upload photos of themselves to the platform that can be helpful for their genetics clinician to make clinical decisions, such as which genetic test to order; this will be optional and it will be made clear to participants that they are not required to upload photos to the platform. The Genetics Navigator will be stored on a server hosted by MedStack, a secure PHIPA-compliant platform for digital healthcare. A service provider agreement will be set up in order to ensure data on the server are adequately protected. Participants will be able to set up their own password when they log into the Genetics Navigator for the first time. Only study staff will have access to the secure REDCap database and the study data on the MedStack server within Canada, in compliance with privacy reviews at the institutions involved in the study. Once the study is over, the data will be removed from the REDCap and MedStack servers and stored on a secure restricted access server at SMH.

Patient and public involvement

The intervention was codeveloped with end-users and patient partners (*manuscript in preparation*). Patient partners were also involved in the development of the study design and will be involved throughout its conduct. In collaboration with our patient partners, we will disseminate study progress and updates through our study website and emails to participants and hold workshop with stakeholders at the end of our study to disseminate and exchange knowledge gained as described in our dissemination strategy below.

ETHICS AND DISSEMINATION

Ethical approval

This study has been approved by Clinical Trials Ontario (REB#4033).

Ethics

Informed consent will take place over the phone or Zoom Healthcare and will be conducted by the study coordinator. All participants will receive a copy of the consent for their own records (see online supplemental file 3). The study coordinator will review the information contained in the consent form and answer any questions regarding the study. The consent will ask for permission for access to medical records at recruiting clinics and to recontact participants for future studies. If applicable, consent or assent to access medical records will be solicited from the paediatric patients (children of participants), depending on their age and capacity. All information collected during this study, including personal or genetic information, will be kept confidential. Major protocol modifications will be communicated to institutional boards and the trial registry without delay.

Dissemination

This trial will evaluate the effectiveness of a comprehensive patient platform—the Genetics Navigator—to improve genetic service delivery and patient experience across paediatric and adult populations. We will convene a stakeholder workshop with key opinion leaders, champions of societies, laboratories and broader groups of end-users to discuss optimal approaches to integrating the platform into clinic and laboratory workflows. We will provide platform training, deliberate opportunities and strategies for its implementation in a range of clinical settings and develop a strategy to integrate and evaluate the platform within clinical and laboratory systems. We will disseminate our results to academic, patient, provider and technology development audiences, through peer-reviewed journal articles, and presentations at national and international academic meetings.

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REFERENCES

1 GeneDx. 2000. Available: https://www.genedx.com [Accessed 1 Mar 2019].
2 Hoskovec JM, Bennett RL, Carey ME, *et al*. Projecting the supply and demand for certified genetic counselors: a workforce study. *J Genet Couns* 2018;27:16–20.
3 Cooksey JA, Forte G, Benkendorf J, *et al*. The state of the medical geneticist workforce: findings of the 2003 survey of American Board of Medical Genetics certified geneticists. *Genet Med* 2005;7:439–43.
4 Concert Genetics. Landscape of genetic testing market growth, reimbursement trends, challenges and opportunities. *Am J Hum Genet* 2018.
5 Otten E, Birnie E, Ranchor AV, *et al*. Online genetic counseling from the providers' perspective: counselors' evaluations and a time and cost analysis. *Eur J Hum Genet* 2016;24:1255–61.
6 Zierhut HA, MacFarlane IM, Ahmed Z, *et al*. Genetic counselors' experiences and interest in telegenetics and remote counseling. *J Genet Couns* 2018;27:329–38.
7 Rayes N, Bowen DJ, Coffin T, *et al*. MAGENTA (Making Genetic testing accessible): a prospective randomized controlled trial comparing online genetic education and telephone genetic counseling for hereditary cancer genetic testing. *BMC Cancer* 2019;19:648.
8 Elliott AM, Mhanni AA, Marles SL, *et al*. Trends in telehealth versus on-site clinical genetics appointments in Manitoba: a comparative study. *J Genet Couns* 2012;21:337–44.
9 Kibar Y, Frimberger D, Kropp BP, *et al*. Accuracy of perinatal diagnosis of 45,X/46,XY mosaicism and electronic consultation of affected parents. *J Pediatr Urol* 2009;5:274–8.
10 Bhola PT, Liddy C, Afkham A, *et al*. A pilot eConsultation service in Eastern Ontario: bridging clinical genetics and primary care. *Eur J Hum Genet* 2019;27:1026–32.
11 Carroll JC, Liddy C, Afkham A, *et al*. Use of eConsult to enhance genetics service delivery in primary care: A multimethod study. *Genet Med* 2022;24:2034–41.
12 Carroll JC, Makuwaza T, Manca DP, *et al*. Primary care providers' experiences with and perceptions of personalized genomic medicine. *Can Fam Physician* 2016;62:e626–35.
13 Harding B, Webber C, Ruhland L, *et al*. Primary care providers' lived experiences of genetics in practice. *J Community Genet* 2019;10:85–93.
14 Harding B, Webber C, Rühland L, *et al*. Bridging the gap in genetics: a progressive model for primary to specialist care. *BMC Med Educ* 2019;19:195.
15 Carroll JC, Grad R, Allanson JE, *et al*. The gene messenger impact project: An innovative genetics continuing education strategy for primary care providers. *J Contin Educ Health Prof* 2016;36:178–85.
16 Green MJ, Biesecker BB, McInerney AM, *et al*. An interactive computer program can effectively educate patients about genetic testing for breast cancer susceptibility. *Am J Med Genet* 2001;103:16–23.
17 Green MJ, McInerney AM, Biesecker BB, *et al*. Education about genetic testing for breast cancer susceptibility: Patient preferences for a computer program or genetic counselor. *Am J Med Genet* 2001;103:24–31.
18 Green MJ, Peterson SK, Baker MW, *et al*. Effect of a computer-based decision aid on knowledge, perceptions, and intentions about genetic testing for breast cancer susceptibility: a randomized controlled trial. *JAMA* 2004;292:442–52.
19 Biesecker BB, Lewis KL, Umstead KL, *et al*. Web platform vs in-person genetic counselor for return of carrier results from

exome sequencing: A randomized clinical trial. *JAMA Intern Med* 2018;178:338–46.
20 Stinson J, Wilson R, Gill N, *et al*. A systematic review of internet-based self-management interventions for youth with health conditions. *J Pediatr Psychol* 2009;34:495–510.
21 Royal College of Physicians. Consultant physicians working with patients. 2013.
22 Schwartz MD, Valdimarsdottir HB, DeMarco TA, *et al*. Randomized trial of a decision aid for BRCA1/BRCA2 mutation carriers: impact on measures of decision making and satisfaction. *Health Psychol* 2009;28:11–9.
23 Bombard Y, Clausen M, Shickh S, *et al*. Effectiveness of the genomics ADvISER decision aid for the selection of secondary findings from genomic sequencing: a randomized clinical trial. *Genet Med* 2020;22:727–35.
24 Hanprasertpong T, Rattanaprueksachart R, Janwadee S, *et al*. Comparison of the effectiveness of different counseling methods before second trimester genetic amniocentesis in Thailand. *Prenat Diagn* 2013;33:1189–93.
25 Sanderson SC, Suckiel SA, Zweig M, *et al*. Development and preliminary evaluation of an online educational video about whole-genome sequencing for research participants, patients, and the general public. *Genet Med* 2016;18:501–12.
26 Birnie KA, Kulandaivelu Y, Jibb L, *et al*. Usability testing of an interactive virtual reality distraction intervention to reduce procedural pain in children and adolescents with cancer. *J Pediatr Oncol Nurs* 2018;35:406–16.
27 Jibb LA, Cafazzo JA, Nathan PC, *et al*. Development of a mHealth real-time pain self-management app for adolescents with cancer: An iterative usability testing study. *J Pediatr Oncol Nurs* 2017;34:283–94.
28 Stiles-Shields C, Garcia B, Villota K, *et al*. Exploring an existing weight management app for use with adolescents and young adults with spina bifida: usability study. *JMIR Pediatr Parent* 2019;2:e15153.
29 Sandhu H, Wilson K, Reed N, *et al*. A mobile phone app for the self-management of pediatric concussion: Development and usability testing. *JMIR Hum Factors* 2019;6:e12135.
30 Hanghøj S, Boisen KA, Hjerming M, *et al*. Usability of a mobile phone app aimed at adolescents and young adults during and after cancer treatment: qualitative study (preprint). *JMIR Cancer* [Preprint].
31 Korus M, Cruchley E, Stinson JN, *et al*. Usability testing of the internet program:"teens taking charge: managing my transplant online. *Am J Hum Genet* 2015;19:107–17.
32 Breakey VR, Warias AV, Ignas DM, *et al*. The value of usability testing for Internet-based adolescent self-management interventions: "Managing Hemophilia Online." *BMC Med Inform Decis Mak* 2013;13.
33 Stinson J, McGrath P, Hodnett E, *et al*. Usability testing of an online self-management program for adolescents with juvenile idiopathic arthritis. *J Med Internet Res* 2010;12:e30.
34 Schmidlen T, Schwartz M, DiLoreto K, *et al*. Patient assessment of chatbots for the scalable delivery of genetic counseling. *J Genet Couns* 2019;28:1166–77.
35 Wang C, Gonzalez R, Milliron KJ, *et al*. Genetic counseling for *BRCA1 / 2* : A randomized controlled trial of two strategies to facilitate the education and counseling process . *Am J Med Genet* 2005;134A:66–73.
36 Yee LM, Wolf M, Mullen R, *et al*. A randomized trial of a prenatal genetic testing interactive computerized information aid. *Prenat Diagn* 2014;34:552–7.
37 Castellani C, Perobelli S, Bianchi V, *et al*. An interactive computer program can effectively educate potential users of cystic fibrosis carrier tests. *Am J Med Genet* 2011;155:778–85.
38 Green MJ, Peterson SK, Baker MW, *et al*. Use of an educational computer program before genetic counseling for breast cancer susceptibility: effects on duration and content of counseling sessions. *Genet Med* 2005;7:221–9.
39 Hooker GW, Leventhal K-G, DeMarco T, *et al*. Longitudinal changes in patient distress following interactive decision aid use among BRCA1/2 carriers: a randomized trial. *Med Decis Making* 2011;31:412–21.
40 Birch P, Adam S, Bansback N, *et al*. DECIDE: a decision support tool to facilitate parents' choices regarding genome-wide sequencing. *J Genet Couns* 2016;25:1298–308.
41 Biesecker BB, Lewis KL, Biesecker LG. Web-based platform vs genetic counselors in educating patients about carrier results from exome sequencing-reply. *JAMA Intern Med* 2018;178:999.
42 Haga SB, Barry WT, Mills R, *et al*. Impact of delivery models on understanding genomic risk for type 2 diabetes. *Public Health Genomics* 2014;17:95–104.
43 Williams JL, Rahm AK, Zallen DT, *et al*. Impact of a patient-facing enhanced genomic results report to improve understanding, engagement, and communication. *J Genet Couns* 2018;27:358–69.
44 Tabor HK, Jamal SM, Yu J-H, *et al*. My46: a Web-based tool for self-guided management of genomic test results in research and clinical settings. *Genet Med* 2017;19:467–75.
45 Shickh S, Hirjikaka D, Clausen M, *et al*. Genetics Adviser: a protocol for a mixed-methods randomised controlled trial evaluating a digital platform for genetics service delivery. *BMJ Open* 2022;12:e060899.
46 Luca S, Clausen M, Shaw A, *et al*. Finding the sweet spot: a qualitative study exploring patients' acceptability of chatbots in genetic service delivery. *Hum Genet* 2023;142:321–30.
47 Ajzen I. The theory of planned behavior. *Organ Behav Hum Decis Process* 1991;50:179–211.
48 Chan A-W, Tetzlaff JM, Altman DG, *et al*. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158:200–7.
49 Butcher NJ, Monsour A, Mew EJ, *et al*. Guidelines for reporting outcomes in trial protocols: The SPIRIT-outcomes 2022 extension. *JAMA* 2022;328:2345–56.
50 Cella D, Hughes C, Peterman A, *et al*. A brief assessment of concerns associated with genetic testing for cancer: the Multidimensional Impact of Cancer Risk Assessment (MICRA) questionnaire. *Health Psychol* 2002;21:564–72.
51 Langer MM, Roche MI, Brewer NT, *et al*. Development and validation of a genomic knowledge scale to advance informed decision making research in genomic sequencing. *MDM Policy Pract* 2017;2:2381468317692582.
52 Légaré F, Kearing S, Clay K, *et al*. Are you SURE?: Assessing patient decisional conflict with a 4-item screening test. *Can Fam Physician* 2010;56:e308–14.
53 Snaith RP. The hospital anxiety and depression scale. *Health Qual Life Outcomes* 2003;1:29.
54 Grant PE, Pampaka M, Payne K, *et al*. Developing a short-form of the genetic counselling outcome scale: The genomics outcome scale. *Eur J Med Genet* 2019;62:324–34.
55 Haun J, Luther S, Dodd V, *et al*. Measurement variation across health literacy assessments: implications for assessment selection in research and practice. *J Health Commun* 2012;17 Suppl 3:141–59.
56 McHorney CA, Ware JE, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care* 1993;31:247–63.
57 Holmes-Rovner M, Kroll J, Schmitt N, *et al*. Patient satisfaction with health care decisions: the satisfaction with decision scale. *Med Decis Making* 1996;16:58–64.
58 Bennett C, Graham ID, Kristjansson E, *et al*. Validation of a preparation for decision making scale. *Patient Educ Couns* 2010;78:130–3.
59 Tariman JD, Berry DL, Halpenny B, *et al*. Validation and testing of the acceptability E-scale for Web-based patient-reported outcomes in cancer care. *Appl Nurs Res* 2011;24:53–8.
60 Nelson LA, Pennings JS, Sommer EC, *et al*. A 3-litem measure of digital health care literacy: Development and validation study. *JMIR Form Res* 2022;6:e36043.
61 Pelletier R, Ditto B, Pilote L. A composite measure of gender and its association with risk factors in patients with premature acute coronary syndrome. *Psychosom Med* 2015;77:517–26.
62 Oswald PA. An examination of the current usefulness of the bem sex-role inventory. *Psychol Rep* 2004;94:1331–6.
63 Shickh S, Clausen M, Mighton C, *et al*. Health outcomes, utility and costs of returning incidental results from genomic sequencing in a Canadian cancer population: protocol for a mixed-methods randomised controlled trial. *BMJ Open* 2019;9:e031092.
64 CADTH. Guidelines for the economic evaluation of health technologies: Canada. 2017.
65 Thorne S, Kirkham SR, MacDonald-Emes J. Interpretive description: A noncategorical qualitative alternative for developing nursing knowledge. *Res Nurs Health* 1997;20:169–77.
66 Thorne S, Kirkham SR, O'Flynn-Magee K. The analytic challenge in interpretive description. *Int J Qual Methods* 2004;3:1–11.
67 Hunt MR. Strengths and challenges in the use of interpretive description: reflections arising from a study of the moral experience of health professionals in humanitarian work. *Qual Health Res* 2009;19:1284–92.
68 Charmaz KC. *Qualitative interviewing and grounded theory analysis. Inside interviewing: New lenses, new concerns*. Thousand Oaks, CA: Sage Publications Inc, 2003:311–30.