J Genet Counsel (2018) 27:426–438
DOI 10.1007/s10897-017-0133-4

ORIGINAL RESEARCH

Online Module for Carrier Screening in Ashkenazi Jewish Individuals Compared with In-Person Genetics Education: A Randomized Controlled Trial

Chia Wei Fan[1] · Lysanne Castonguay[1] · Sonja Rummell[1] · Sébastien Lévesque[2] · John J. Mitchell[1,3,4] · Guillaume Sillon[1,3]

Received: 4 December 2015 / Accepted: 18 July 2017 / Published online: 9 August 2017

Abstract To increase accessibility to genetics services for low-urgency patients seeking Ashkenazi Jewish (AJ) carrier screening, we designed an interactive computer (IC) module that provides pre-test genetics education and allows genetics professionals to order the test without meeting the patients beforehand. We compared this module with in-person genetic counseling (GC) using a randomized trial. AJ individuals were randomized to undergo genetics education via the IC module (n = 26) or GC (n = 28). We compared post-interventional genetics knowledge, perceived genetic risk, and anxiety between the two groups, after accounting for pre-interventional scores, using ANCOVA. Wilcoxon Rank-Sum test was used to compare post-interventional satisfaction. Post-interventional genetics knowledge, risk perception, or anxiety were not significantly different between the two groups after accounting for baseline scores (p = 0.50–0.54), although the data are inconclusive regarding the module's non-inferiority at a 5% margin. Post-intervention satisfaction scores were generally higher in the GC group than the IC module group. Our IC module has the potential to improve access to clinical genetics services for patients and staff, but it is not suitable for all AJ patients and cannot completely replace the benefits of in-person consultations.

Keywords Carrier detection · Online education · Interactive computer program · Genetic counseling · Genetic services · Randomized controlled clinical trial · Ashkenazi Jewish screening

Chia Wei Fan, Lysanne Castonguay and Sonja Rummell have contributed equally to this work.

Electronic supplementary material The online version of this article (doi:10.1007/s10897-017-0133-4) contains supplementary material, which is available to authorized users.

✉ Guillaume Sillon
guillaume.sillon@muhc.mcgill.ca

[1] Department of Human Genetics, Faculty of Medicine, McGill University, Montreal, Quebec, Canada

[2] Department of Pediatrics, Division of Medical Genetics, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Sherbrooke, Quebec, Canada

[3] Department of Medical Genetics, McGill University Health Center, 1001 boul. Décarie, Room A04.3140, Montreal, Quebec H4A 3J1, Canada

[4] Department of Endocrinology and Metabolism, McGill University Health Center, Montreal, Quebec, Canada

Introduction

Because certain genetic conditions are more prevalent in the Ashkenazi Jewish (AJ) population than in the non-AJ Caucasian population (Klugman and Gross 2010), several clinical practice guidelines have been published regarding carrier screening in this population (ACOG Committee on Genetics 2009; Gross et al. 2008; Wilson et al. 2016). In Canada, the Canadian College of Medical Geneticists and the Society of Obstetricians and Gynaecologists of Canada recommend offering carrier screening for Tay-Sachs disease (TSD [OMIM 272800]), Canavan disease (CD [OMIM 271900]), and familial dysautonomia (FD [OMIM 223900]) to all couples of AJ ancestry (Wilson et al. 2016). The Canadian healthcare system is publicly funded, but the medical services that are covered by public resources vary from province to province. In Quebec, carrier screening for these three conditions is publicly available to individuals over 14 years of age with at least one grandparent of AJ descent.

The AJ community is a significant ethnic minority in Montreal, Quebec (Statistics Canada 2013a, b), and the

McGill University Health Centre (MUHC) has been intimately involved in providing genetic screening to this group since 1972 (Clow and Scriver 1977; Mitchell et al. 1996). Currently, the MUHC hosts the only publicly-funded laboratory that offers AJ screening in Quebec, and most of the samples that this lab receives for AJ screening also come from within the MUHC (A. Ruchon, personal communication, April 7, 2015). In the MUHC Department of Medical Genetics, all individuals seeking AJ carrier screening are offered a pre-test genetics education and counseling session by a genetic counselor. New referrals for this service are triaged according to urgency. While pregnant couples are typically seen within a week, other patients may experience longer wait times. Anecdotally, low-urgency patients seeking only AJ carrier screening are often satisfied with genetics education and require only minimal psychosocial counseling. We thus considered alternate means of delivering pre-test genetics education to this patient group.

Interactive computer (IC) programs are used for patient education in many healthcare settings. They encourage patient self-care and self-efficacy (Kukafka et al. 2002; Neafsey et al. 2002; Wang and Chiou 2011), and provide alternate means of educating people with low literacy or socioeconomic statuses (Joseph et al. 2010; Kinzie et al. 1993). On the other hand, patients may prefer in-person sessions over IC modules for psychosocial and decision-making support (Green et al. 2001b; 2004). In medical genetics, IC modules have been used to complement pre-test counseling for hereditary breast and ovarian cancer (Albada et al. 2012; 2015; Green et al. 2001a, b; 2005; 2004; Joseph et al. 2010), cystic fibrosis carrier screening (Castellani et al. 2010), and prenatal and ethnicity-based screening (Griffith et al. 2005a, b; Kuppermann et al. 2009; Yee et al. 2014). They have also been used in high school screening programs for TSD among AJ teenagers (Gason et al. 2004; 2005). Individuals use these modules before meeting with a genetics professional in order to facilitate the meeting and to allow for greater focus on their decisional, psychosocial and personal needs.

JScreen is a national, at-home web-based program that provides expanded AJ screening without any in-person pre-test counseling (Grinzaid et al. 2015). The authors report that the users of that program are generally pleased with their experience, though they have not yet reported a quantitative study to compare *JScreen* with traditional genetic counseling (GC).

We developed a web-based IC module to provide pre-test genetics education to low-urgency patients seeking AJ screening through our clinic. We conducted a randomized controlled trial (RCT) to evaluate this module. The primary objective of our trial was to assess whether using the web-module is non-inferior to in-person GC with respect to knowledge acquisition. Our secondary objectives were to assess the difference between the web-module and traditional GC with respect to patient perceived risk, anxiety, or satisfaction. We also solicited feedback about our module from study participants. To our knowledge, this is the first pre-test medical genetics IC module in a public health care system that is not complemented by any further GC. Our goal is to launch a program that meets the needs of all stakeholders including patients, staff, and public health authorities.

Methods

Web-Based Module Design

We based the content of our online tool on the IC module by Castellani et al. (2010) and on personal experience, while following recommendations from the MUHC Education Portfolio (a hospital-based department specialized in producing effective patient education materials; Olivier et al. 2008; Thomas 2010). Texts and images for the IC tool were created using plain, value-neutral and person-first language. Our team, the MUHC Education Portfolio, and the Montreal Jewish Hereditary Disease Fund (MJHDF, a Montreal-based non-profit organization whose aim is to raise awareness about AJ screening) reviewed the content of the module continuously during its development until a consensus was reached. Both French and English versions of the text were produced, as required of any MUHC-produced information material developed for the general public. The English version of our online genetics education module was written at the eighth to twelfth grade level, depending on the section, as evaluated by the Flesch-Kincaid Grade Level Index tool in Microsoft Office Word (Kincaid et al. 1975).

The module contains three parts. The first part is called the "Screening Program," described below in (A). The second part is called "Post Test," described below in (B). The third part is called "Health Care Professionals," described in (C). Figure 1 contains a schematic diagram representing the tool's sections. The module can be found online at http://muhc.ca/med-genetics-ajprogram

(A) The "Screening Program" part of the module starts with a series of questions to screen for individuals who meet the criteria to use the module. In addition to the criteria set in our healthcare system to access AJ screening, the module targets patients who do not require personalized risk assessments (i.e. no family history of a Jewish genetic disorder [JGD]). This is to exclude patients who may require more psychosocial support, although the module does not use a psychosocial screening tool to capture all of these individuals. The module also excludes individuals between ages 14 and 17, as it is our clinic's policy to evaluate the maturity and motivations of all teenaged patients, which cannot be done using the IC module. Finally, the module excludes individuals who are requesting GC for any purpose other than genetics

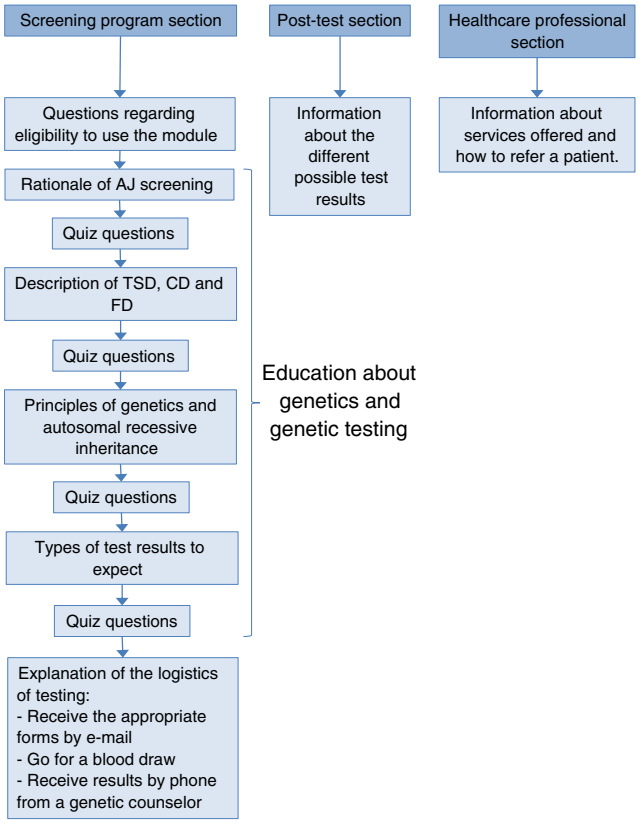


Fig. 1 Sections of the web-based IC module. IC = Interactive computer; AJ = Ashkenazi Jewish; TSD = Tay-Sachs disease; CD = Canavan disease; FD = Familial dysautonomia

Table 1 Eligibility criteria for provincially-funded AJ genetic screening, use of the IC module, and participation in the study

Criteria	Publicly-funded coverage for AJ screening (Quebec)	Use of the IC module and participation in the study
Covered by Quebec Medicare [a]	X	
≥ 1 grandparent who is AJ	X	X
≥ 14 years of age	X	
≥ 18 years of age	X	X
No ongoing pregnancy [b]		X
No family history of a JGD		X
No other medical genetics-related concerns		X
Easy access to a computer with Internet		X

[a] Health coverage by Quebec Medicare is needed if patients wanted access to publicly-funded genetic testing. However, coverage was not necessary for individuals who wanted to participate strictly in the study without having access to subsequent genetic testing

[b] The individual must not be pregnant, or the individual's partner must not be pregnant

AJ = Ashkenazi Jewish; IC = interactive computer; JGD = Jewish genetic disorder

education about JGDs (Table 1). Individuals who select responses that exclude them from using the web-module are presented with an explanation and, if applicable, follow-up instructions to contact the Department of Medical Genetics for an in-person GC session.

Once the participants complete the eligibility questions, they move on to the educational portion of the module. Participants read through web-pages that address four different topics: "Introduction to the Screening Program" reviews the rationale for population-based screening for JGDs; "Genetic Conditions More Common in the AJ Community" describes TSD, CD, and FD; "Principles of Genetics" explains autosomal recessive inheritance and population genetics; and "Details of Testing and Possible Results" outlines the interpretation of different test results and the genetic testing process. Although the information is presented at a basic level, users can expand the text in some sections to see more advanced content on specific topics (such as information on founder effects or specific symptoms of the screened conditions). We did not design the website with the capacity to record and differentiate between those who chose to expand the text and those who did not. To ensure that users are well-informed before consenting to genetic testing, each topic ends with a series of quiz questions that must be answered correctly before continuing. Like the rest of the module, quiz questions were inspired by Castellani et al. (2010) and personal experience. They were reviewed by members of our team and by a representative of the MJHDF. If users do not respond to a question correctly, they are invited to re-read the corresponding section and take the quiz again in order to proceed to the next topic. After reading the four topics, the user is informed that he/she can email his/her personal information to a genetic counselor. He/she is then sent a blood draw requisition for AJ carrier screening endorsed by a medical geneticist and specific to the Montreal General Hospital test centre. Test results are returned via telephone by a genetic counselor as per standard of care, and further follow-up via an in-person session is available if desired.

(B) The "Post Test" section of the module provides supplementary information to people who have already received their genetic results. It complements the discussion they had with the genetic counselor when they received their results by explaining the personal and reproductive implications of a positive or a negative test result. It also outlines the reproductive options for each possible result combination that a couple might receive. Participants are invited throughout the "Screening Program" and the "Post Test" sections of the module to contact our clinic if they have questions or prefer to meet a genetic counselor in person.

(C) Lastly, the "Health Care Professionals" section of the module informs healthcare providers about AJ carrier screening in Montreal. It provides a brief explanation of the

screening protocol, the prevalence of TSD, CD, and FD, and the procedure for making a medical genetics referral.

Participants

We evaluated the efficacy of the English version of the "Screening Program" section of the IC module through an RCT. This trial took place at the MUHC Adult Genetics Department in Montreal, Canada. The study protocol was approved by the MUHC Genetics and Population Research Ethics Board. We were also approved by the Jewish General Hospital (JGH) Research Ethics Office to recruit participants from that site. Informed consent was obtained from all study participants.

Study participants were recruited from within the Greater Montreal Area during a ten-month period from May 2014 to March 2015. We targeted patients from the Greater Montreal Area as those who decided to pursue testing after reviewing the IC module had to travel to and from the Montreal General Hospital to provide a blood sample, which is the method of choice for genetic testing at the MUHC. Some participants were patients referred to our clinic for AJ carrier screening. Others contacted our team directly after hearing about our study through social media, paper advertisements and flyers, online advertisements, press releases, our www.ClinicalTrials.gov posting (ID number: NTC01999257), and word-of-mouth.

All potential participants were contacted by phone by either administrative staff or a study coordinator who asked questions regarding inclusion and exclusion criteria and their will to participate in the study. Eligibility criteria for the study are the same as those listed above for using the IC module, with two exceptions. First, we targeted patients who were low urgency (i.e. no ongoing pregnancy), to exclude another category of patients who may require more psychosocial support. Second, all participants needed to have access to the internet, even if they were assigned to have in-person GC and did not review the IC module at all (Table 1).

After initial screening, recruited participants were randomized by the same study coordinator using Microsoft Excel's random number generator into one of two educational interventions: a participant who was attributed an odd number was assigned to using our web-based IC module ("web-based"), and a participant who was attributed an even number was assigned to meeting with a genetic counselor as per current clinic protocol ("in-person").

The study coordinator would then explain to the participants their involvement in the study. If a participant from either group had not yet spoken with the study coordinator, they would be later contacted by phone in order to discuss this point and also to verify the initial screening of eligibility criteria.

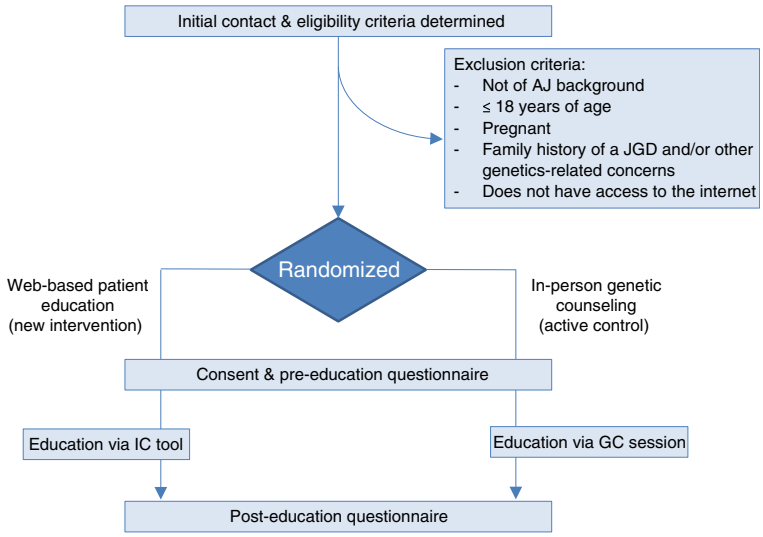
As discussed earlier, the study and the IC module are aimed for people who may not require specific psychosocial support. Even though no specific tool was used to assess a participant's psychosocial needs, if the study coordinators determined during these phone conversations that a participant (from either group) needed more psychosocial support, then that participant had the choice to exit the study. These participants would be returned to the clinic's queue to attend a regular GC session. Both web-based and in-person participants could exit the study at this point. There was no explicit attempt to actively seek out inappropriate study participants from either treatment group.

Participants who were randomized to the "in-person" group attended a standard GC session at the Montreal General Hospital. GC sessions were provided by one of two genetic counselors, who are certified by the Canadian Association of Genetic Counsellors. These sessions usually lasted between 30 and 60 min and included information gathering (medical and family history), genetics education about the conditions that are more frequent in the AJ population (specifically TSD, CD and FD), autosomal recessive inheritance, and the types of genetic test results to expect. The information about genetics that was provided during the in-person sessions was similar to the information in the web-based IC module.

If couples entered the study together, we randomized them only once so that they were part of the same intervention group. In-person participants usually attended their counseling sessions together as is typical for AJ couples.

In both interventions, participants completed an informed consent form, a pre-education questionnaire, their designated educational intervention, and a post-education questionnaire. The pre-education and post-education questionnaires could only be attempted once per participant regardless of intervention group. In-person participants completed the questionnaires on the same day as their in-person GC session. The time that in-person participants spent on filling the questionnaires was not recorded. Web-based participants were emailed all necessary instructions and links, and completed the online questionnaires at their own convenience. Dates and times when web-based participants started and exited their pre-education and post-education questionnaires were recorded by the online questionnaire platform. Questionnaire responses were automatically saved so that an individual's responses would be saved even if they have not formally "exited" the link. Study participation ended once patients completed all the questions from the post-education questionnaire. At that point, all participants were treated with the standard of care for our clinic and had the option of pursuing genetic testing through our center. Figure 2 is a graphical summary of the study methodology.

The pre-education questionnaire assessed basic demographic information using four multiple choice questions; knowledge of JGDs using ten multiple choice questions;



Legend: AJ: Ashkenazi Jewish; JGD: Jewish genetic disorder; IC: interactive computer; GC: genetic counseling

Fig. 2 Algorithm for the randomized controlled trial to evaluate the non-inferiority of a web-based education module compared to in-person genetic counseling. AJ = Ashkenazi Jewish; JGD = Jewish genetic disorder; IC = interactive computer; GC = genetic counseling

perceived reproductive risk using one four-point Likert scale question; state anxiety using the shortened form of the Spielberger State-Trait Anxiety Inventory (Marteau and Bekker 1992); and the ability to seek reliable health information on the Internet (e-health literacy) using the eHEALS tool (Norman and Skinner 2006). Eight of the ten knowledge questions were identical to the quiz questions that are found in the "Screening Program" part of the online module. Two questions were added based on the content of the module; these questions were also reviewed by our team. The pre-education questionnaire was identical for in-person and web-based participants. The post-education questionnaire re-administered all questions regarding the participants' knowledge, perceived risk, and anxiety. It also asked questions derived from Shiloh et al. (1990) and Yip et al. (2003) regarding participants' satisfaction with their experience. Web-based participants provided constructive feedback about our module through questions derived from Shiloh et al. (1990) and Yip et al. (2003) and through questions specific to our current study. Participants had the option to write comments in response to satisfaction or feedback questions. Participants were not provided the correct answers for the knowledge questions during the course of their study participation, nor were they provided their "scores" for the questionnaires. The pre-education and post-education questionnaires are available in Online resource 1.

Outcome Measures and Data Analysis

Descriptive statistics were computed for all data provided in the questionnaires.

Fisher's Exact Test (FET) and the Wilcoxon Rank Sum Test were used to compare the differences in demographics and e-health literacy between the two groups, respectively.

Our primary goal was to evaluate the non-inferiority (NI) of our IC tool to in-person GC with respect to knowledge acquisition. Most RCTs aim to demonstrate the superiority of an intervention over a placebo control: A superior intervention would have a 95% confidence interval (CI) of the effect size that is wholly greater than zero (Fig. 3A) and the p value would be low (generally, less than 0.05). In our RCT, on the other hand, a "placebo" control (i.e. offering genetic testing without pre-test counseling) would not be ethical. Our RCT was comparing a new intervention with a standard-of-care. A successful intervention would *not* be expected to have significantly different outcomes from the standard-of-care control. The traditional statistical interpretations of p values would be useful but insufficient for this purpose. In an NI trial, statistical interpretation is based on measuring the effect size of the intervention compared with the gold-standard control, and on the "NI margin." The NI margin is the boundary that separates whether an intervention is unacceptably inferior to the gold standard. To interpret an intervention as non-inferior, the 95% CI of the effect size of that intervention must be fully above the NI margin. CIs that are wholly below the NI margin demonstrate that the intervention is inferior and is unethical for clinical use if the standard-of-care is available. If the CI straddles the NI margin, then the data are inconclusive. Figure 3 graphically represents how to use CIs of effect sizes in RCTs to interpret superiority or NI. For an in-depth review of NI trials, please refer to Schumi and Wittes (2011).

To analyze the NI of the IC tool with respect to knowledge acquisition, we used one-way ANCOVA to compare the post-education knowledge scores between the two groups while controlling for the pre-education scores. An NI margin of 5% was based on clinical judgment. There is a paucity of RCTs with a pre-post design evaluating IC modules (Castellani et al. 2010; Gason et al. 2005; Green et al. 2001a

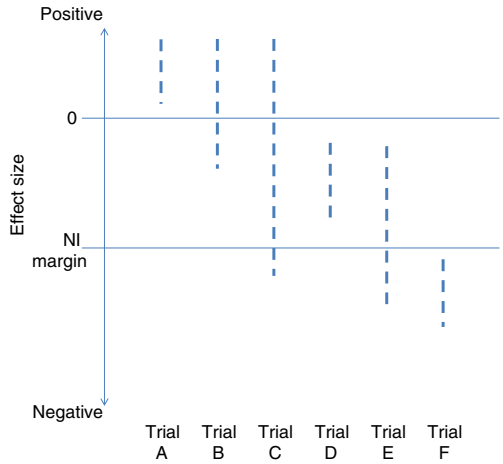


Fig. 3 Effect size in randomized controlled trials in interpreting superiority and non-inferiority when comparing a new intervention to a control. NI = non-inferiority. Dashed lines = 95% confidence interval of the effect size of the new intervention. Trial A = The new intervention is both superior and non-inferior to the control. Trial B = The new intervention is non-inferior to the control, but its superiority has not been demonstrated. Trial C = The data are inconclusive with respect to the new intervention's non-inferiority; the new intervention's superiority has not been demonstrated. Trial D = The control intervention is superior to the new intervention, but the new intervention is also non-inferior to the control. Trial E = The control intervention is superior to the new intervention, and the data are inconclusive regarding the new intervention's non-inferiority. Trial F = the new intervention is not non-inferior to the control, and the control is superior to the new intervention

[which actually did not use a pre-post design but had a third arm where baseline knowledge was assessed and used as a substitute for pre-education measurements]; Green et al. 2004), none of which were NI trials. We determined that the existing studies were insufficient to guide a mathematical NI margin, but we reviewed these papers to help guide a clinical NI margin. In these studies, the mean post-education scores between those who used an IC module compared to those who received genetics education through the standard of care were either not statistically-significant or favored the IC module. We therefore decided to set our clinical NI margin with a high degree of stringency. According to preliminary data from 24 individuals, a 5% NI margin represented a difference in mean post-educational knowledge scores of only 0.45/10 points between the two groups. We felt that this difference in knowledge would be clinically acceptable. We also expected that a sample size of 30 individuals per group was needed for 80% power to detect NI at this margin.

Our secondary goals were to assess psychosocial outcomes and satisfaction. In order to assess differences in post-education risk perception and anxiety scores, we once again used ANCOVA with the pre-education scores as covariates. We compared participant satisfaction between the two groups using the Wilcoxon Rank Sum Test, analyzing each question independently.

Web-based participants could complete the questionnaires at their own convenience, while in-person participants needed to complete both questionnaires immediately before and after their GC session. To determine whether the difference in time is a confounding factor in the web-based participants' post-educational knowledge scores, we used the Wilcoxon Rank Sum Test to determine whether post-educational knowledge scores were significantly different between web-based participants who started and completed the study in the same calendar day ("same-day"), and those who started and completed the study on different calendar days ("different-day"). We also calculated the Spearman's rank correlation coefficient (rho) between total time elapsed during the study (the time between the moment that participants opened the pre-education questionnaire and the moment they closed the post-education questionnaire, measured in minutes for same-day participants, or in days for different-day participants) and post-educational knowledge scores. Finally, a *post-hoc* sensitivity power analysis was done by calculating Cohen's *d* (Ellis 2009).

Descriptive statistics, FET and Wilcoxon Rank Sum Tests were performed using the Real Statistics Resource Pack for Microsoft Excel (Zaiontz 2014). Confidence intervals (CI) and the calculation of Spearman's Rank correlation coefficients were calculated using the Microsoft Excel Data Analysis ToolPak. ANCOVA was performed using the linear model (lm) function in R (R Development Core Team 2008). Cohen's *d* was calculated from an online effect size calculator (Ellis 2009). All reported *p* values were from two-tailed tests of significance.

Two authors (CWF and GS) reviewed the written comments submitted by participants. The comments were pooled across different questions for each intervention group. Duplicate comments from the same individual and comments that were non-contributory or did not pertain to genetics education in some way were not considered. The remaining comments were categorized as either suggestions for changing the module or remarks about the participants' experiences with their services. In this paper, we describe only the comments regarding the participants' experiences.

Results

Randomized Controlled Trial

Ninety-six individuals were initially contacted. Sixty-eight were recruited and randomized to one of the two educational interventions. Fourteen participants withdrew from the study (i.e. were not interested anymore or could not participate for logistical reasons), were no longer eligible (i.e. became pregnant, or were never eligible but were not screened appropriately), or did not complete the study. There is no evidence that the people who were recruited but did not complete the study had different demographic characteristics from the people who remained in the study. None of these people, however,

completed their pre-education questionnaire so we do not have a thorough assessment of their characteristics. We collected data from 54 individuals (Fig. 4). Ten participants entered and completed the study as couples in the in-person group (37% of the participants in this group) and six in the web-based group (23%). The two groups were not significantly different in terms of demographic make-up (Table 2) or e-health literacy (score from 8 to 40 with higher scores indicating increased e-health literacy; mean values ± SD [95% CI] = 31 ± 6 [28–33] for in-person and 31 ± 5 [29–33] for web-based participants; $p = 0.88$).

Knowledge scores for both groups improved after genetics education, but risk perception and anxiety remained relatively constant (Table 3). Post-education scores for all three measures were associated with each individual's pre-education scores ($p < 0.0001$; Table 4).

The majority of web-based participants (15 out of 26) answered both of their questionnaires on the same day; one participant answered the post-education questionnaire one day after the pre-education questionnaire; one participant opened the post-education questionnaire the same day as the pre-education questionnaire but did not formally exit the questionnaire until one day later; and the rest of the participants (9) answered the post-education questionnaire between 6 and 85 days after the pre-education questionnaire. One of these nine formally exited their pre-education questionnaire six days after opening it, then opened and finished the post-educational questionnaire after another two days. Same-day participants spent a mean of 89 min on the study (SD = 1.9×10^2; 95% CI = 0–196). Their mean pre-educational knowledge and post-educational knowledge scores were 6.7 (SD = 2.7; 95% CI = 5.2–8.2) and 9.7 (SD = 0.58; 95% CI = 9.4–10), respectively. Different-day participants spent a mean of 23 days on the study (SD = 25; 95% CI = 6–40). Their mean pre-educational knowledge and post-educational knowledge scores were 5.7 (SD = 2.6; 95% CI = 4.0–7.4) and 8.5 (SD = 2.0; 95% CI = 7.2–9.8), respectively. Post-educational knowledge scores were significantly higher for same-day participants than for different-day participants ($p = 0.048$). There was no strong correlation between the amount of time that same-day participants spent on the study and their post-educational knowledge scores (rho = −0.12). There was no positive correlation between the time different-day participants spent on the study and their post-educational knowledge scores (rho = −0.59).

Post-education scores for all outcome measures were not associated with the type of educational intervention that the individual received ($p = 0.50$–0.54; Table 4; full ANCOVA results are available in Online resource 2). We were thus

Table 2 Demographic Information of Study Participants

	In-Person (n [%])	Web-Based (n [%])	*p* value
Total:	28 (100)	26 (100)	
Gender:[a]			0.40
Male	9 (32)	12 (46)	
Female	19 (68)	14 (54)	
Age (years):[a]			1.0
18–25	6 (21)	3 (12)[b]	
26–35	15 (54)	15 (58)[b]	
36–45	4 (14)	5 (19)[b]	
46+	3 (11)	3 (12)[b]	
Education:[ac]			0.67
Some college	4 (14)	2 (8)	
Bachelor's degree	14 (50)	10 (38)	
Master's/Doctoral	10 (36)	14 (54)	
I have had a medical genetics consultation in the past:			0.13[d]
Yes	2 (7)	6 (23)	
No	26 (93)	19 (73)	
Not sure	0 (0)	1 (4)[d]	

[a] No participants selected "Prefer not to disclose" for these questions

[b] Due to rounding error, these percentages do not add up to 100%

[c] We offered "Max high school" as an option, but no participants from either group selected this response

[d] We did not include the single "not sure" response in the FET analysis

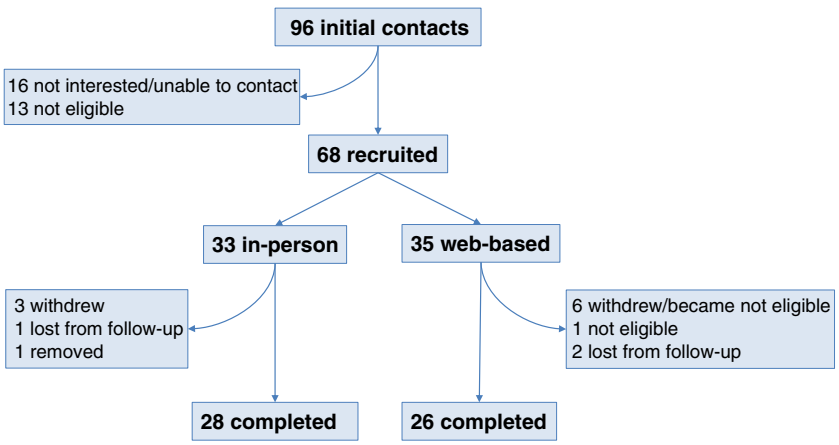


Fig. 4 Participant recruitment breakdown

Table 3 Knowledge, Risk Perception, and Anxiety Scores Before and After Genetics Education

	Knowledge (number of correct questions out of 10) (Mean ± SD [95% CI])		Risk Perception (score from 1 to 4)[a] (Mean ± SD [95% CI])		Anxiety (score from 6 to 24)[a] (Mean ± SD [95% CI])	
	Pre-Education	Post-Education	Pre-Education	Post-Education	Pre-Education	Post-Education
In-Person	6.5 ± 2.6 (5.5–7.6)	9.4 ± 0.9 (9.1–9.8)	1.8 ± 0.5 (1.6–2.0)	1.8 ± 0.6 (1.6–2.1)	9.0 ± 3.4 (7.7–10)	8.6 ± 3.0 (7.4–9.8)
Web-Based	6.3 ± 2.7 (5.2–7.4)	9.2 ± 1.5 (8.6–9.8)	1.7 ± 0.7 (1.5–2.0)	1.8 ± 0.6 (1.6–2.1)	9.0 ± 3.1 (7.8–10)	9.0 ± 3.1 (7.7–10)

[a] The higher the score, the greater the risk perception/anxiety

unable to find a statistically significant difference between the two groups. The 95% CI of the effect size that web-based intervention has on post-educational knowledge scores compared to in-person intervention was −0.74 – 0.38 (Table 4). This straddles our NI margin of 5% (−0.45). Therefore, this 95% CI was too wide to make any conclusions about the NI of our IC module with respect to knowledge acquisition (Fig. 5). The calculated Cohen's *d* is 0.16, which is the difference between the two intervention scores divided by the typical standard deviation (pooled).

Most participants in both groups were satisfied with their services (Table 5). Satisfaction scores were not significantly different between the groups, with one exception: Web-based participants were statistically less likely to consider their educational intervention as an acceptable way to receive services than in-person participants ($p = 0.0062$; Table 5).

Participant Feedback

We reviewed 25 written comments from 13 individuals in the in-person group. Most people reported satisfaction; only two reported negative experiences. Two people appreciated the use of supplementary educational materials and teaching aids to facilitate comprehension during the GC session (one individual also suggested that a pamphlet be made available to patients). One participant also acknowledged how different learning styles influence the way individuals internalize information. We also reviewed 16 comments from six web-based participants. Over half of the comments, mostly from two participants, were positive. Two people expressed reservations with the module's generalizability to other health care services. Negative comments were related to preferences for an in-person session and difficulties with the quiz questions. Online resource 3 contains all the comments that were submitted.

We asked web-based participants questions regarding their experience in using the IC module. Most people reported positive experiences (Table 6). Eighteen people (69%) needed one attempt on average to pass the quiz questions; six (23%) individuals needed two attempts; and two (8%) needed at least three attempts. We also asked them to identify the sections of our IC module that were difficult. One person responded that the language in the sections "Genetic Conditions More Common in the AJ community" and "Principles of

Table 4 Summary of ANCOVA Regression Coefficients[a]: Estimated Effect of Pre-Education Scores and Web-Based Intervention on Post-Education Scores Compared to In-Person Intervention

	Estimated coefficient (SE)	*t* value	*p* value	95% CI
Effect of pre-ed scores on post-ed scores[b]				
Knowledge questions	0.24 (0.053)	4.5	<0.0001	0.13–0.35
Risk perception	0.63 (0.11)	5.7	<0.0001	0.40–0.85
Anxiety	0.64 (0.096)	6.6	<0.0001	0.45–0.83
Effect of web-based intervention on post-ed scores[c]				
Knowledge questions	−0.18 (0.28)	−0.65	0.52	−0.74–0.38
Risk perception	0.081 (0.13)	0.62	0.54	−0.18–0.35
Anxiety	0.42 (0.61)	0.68	0.50	−0.82–1.6

Pre-ed = pre-education; post-ed = post-education

[a] ANCOVA regression for each outcome measure: A positive coefficient represents a positive correlation, and a negative coefficient represents a negative correlation

[b] Effect size of pre-ed scores on post-ed scores: The effect size that an individual's pre-education score has on their post-education score. The coefficient here represents how a pre-education score is modified to produce a post-educational score

[c] Effect size of web-based intervention on post-ed scores: The effect size that being included in the web-based group has on post-educational scores compared to the in-person group as the baseline. The coefficient here represents whether a web-based participant's post-educational score is expected to be higher (positive coefficient) or lower (negative coefficient) than an in-person participant, and by how much

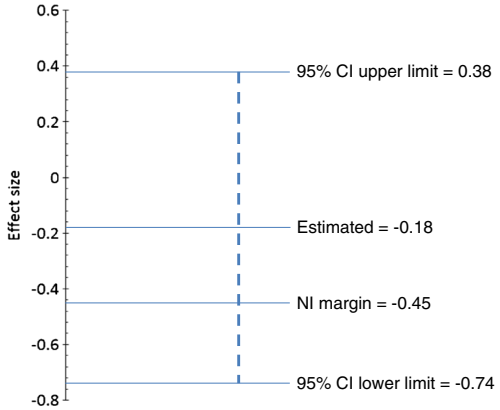


Fig. 5 Effect size that the web-based intervention has on knowledge acquisition compared to the in-person intervention. CI = confidence interval; dashed lines = 95% CI of the effect size

Genetics" was not clear. Another said that the time required to go through the section "Introduction to the Screening Program" was too long. One participant felt that the quizzes in the section "Genetic Conditions More Common in the AJ community" were difficult, and three others felt the same about the section "Principles of Genetics."

Discussion

Online Module Content and Development

We developed a web-based tool to provide pre-test education for AJ individuals seeking genetic screening. To our knowledge, this is the first tool that allows genetics professionals in a public health care system to order tests without a complementary in-person session.

Even though patient materials are ideally written at a grade 6–8 level of literacy, our module was at a grade 8–12 reading level, depending on the section, due to terms such as "recessive," "mutation," or "carrier." While removing these words would reduce the literacy rating, we chose instead to account for the increased difficulty by explaining all genetics jargon thoroughly. Only one participant identified difficulties with the language in our module, suggesting that the terminology was not a concern for most study participants.

Online Module has the Potential to Provide Genetics Education for Many Patients

Like many other randomized controlled trials that evaluated medical genetics IC modules, the post-education knowledge scores between our two intervention groups were not significantly different (Castellani et al. 2010; Gason et al. 2004; 2005; Green et al. 2001a), even if NI could not be established conclusively. There was, however, variability in how efficacious the module was at educating each individual participant: Most participants passed the quizzes in our module with ease, but a minority needed at least three attempts on average to progress through the module.

While knowledge scores in both groups improved dramatically after genetics education, risk perception and state anxiety remained constant even in the in-person group. This is in contrast to Green et al. (2004) who found that state anxiety remained constant after using only an IC module but decreased after in-person counseling for *BRCA1/2* testing, and to Gason et al. (2005) who found that students' predicted anxiety in the event of being a carrier for TSD decreased after genetics education. One possible explanation for our findings is that we designed the study to select against individuals likely to have psychosocial concerns relating to their genetic health. For these people, genetics education may have little influence on their pre-existing anxiety. We find from clinical experience that patients fitting our target demographic are generally not as anxious as some other patients, so improving psychosocial measures was not a priority in our study. Indeed, average risk perception and anxiety scores were relatively low amongst the participants.

We did not study risk perception, anxiety, or satisfaction as primary outcomes: While patients prefer in-person sessions

Table 5 Participant Satisfaction with Genetics Education

	I found in-person/web-based patient education to be an acceptable way to receive healthcare services[a] (Mean ± SD [95% CI])	I am satisfied with the amount of information I received[a] (Mean ± SD [95% CI])	I am satisfied with the way information was transmitted to me[a] (Mean ± SD [95% CI])	Overall, I am satisfied with the service provided[a] (Mean ± SD [95% CI])
In-Person	4.0 ± 0.2	3.9 ± 0.3	3.9 ± 0.3	3.9 ± 0.3
	(3.9–4.0)	(3.8–4.0)	(3.8–4.0)	(3.8–4.0)
Web-Based	3.2 ± 1.0	3.7 ± 0.6	3.7 ± 0.5	3.7 ± 0.5
	(2.8–3.6)	(3.4–3.9)	(3.5–3.9)	(3.5–3.9)
p value	0.0062	0.20	0.21	0.31

[a] Each of these questions are on a scale from 1 to 4, with 4 being most satisfied

Table 6 Web-Based Participants' Quantitative Feedback Regarding the Interactive Computer Module

Total $n = 26$	Not at all (n [%])	Somewhat (n [%])	Moderately (n [%])	Very much (n [%])
I saved time as a result of using the online module:				
	1 (4)[a]	2 (8)[a]	3 (12)[a]	20 (77)[a]
I would consider recommending the online module to a friend or family member:				
	1 (4)	1 (4)	4 (15)	20 (77)
I found that the navigation between the different pages of the website was easy:				
	1 (4)	4 (15)	6 (23)	15 (58)
I found that the language used on the website was clear:				
	0 (0)	1 (4)	1 (4)	24 (92)
I felt that the amount of time required was too long:				
	24 (92)	1 (4)	1 (4)	0 (0)
I felt that the quiz questions were difficult:				
	20 (77)	6 (23)	0 (0)	0 (0)

[a] Due to rounding errors, these percentages do not add up to 100%

for non-educational needs (Green et al. 2001b; 2005), our module was intended strictly as a learning tool. In our study, web-based participants were generally satisfied with the amount of information received, the way the information was transmitted, and with the services they received. Fewer web-based participants than in-person participants, however, agreed that they found their intervention to be an appropriate way to deliver healthcare services (Table 5). We do not have a way to explore the reasons for this difference. One possible explanation is that the question asked was referring to "healthcare services" without specifying a specific discipline or context. In fact, some participants expressed in their written comments that web-based patient education may not be appropriate for all types of clinical situations.

Based on these preliminary data, we propose that the IC module has the potential to be a convenient alternative to in-person GC to all individuals who fit the selection criteria. Patients should also be aware before starting the module that they can decline the IC module and opt for traditional GC based on their preference. They should be explicitly given that choice at the same time that the IC module is presented as an option. Those who opt to use the IC module should also be encouraged to contact a genetic counselor if further assistance is needed at any point, including if the content of the module is difficult to understand (e.g. patient has trouble progressing through the skill-testing questions) or if the patient finds the IC module to be unacceptable (e.g. patient has questions that were not answered by the module, or would prefer an in-person meeting for any other reason).

Study Strengths and Limitations

Our study was an RCT, which allowed for quantitative comparisons between a web-based intervention and standard of care while removing selection and subversion biases in intervention assignment. Our pre-post study design also accounted for confounding factors such as baseline knowledge.

In addition to computing p values in comparing knowledge acquisition between our two interventions, we also used an NI design. NI trials are used to demonstrate that an experimental intervention is not unacceptably worse than the standard intervention or active control, and when it is unethical to use a "placebo" control (Schumi and Wittes 2011). As we intended for our IC module to be a stand-alone tool with no expectation for it to excel over the standard intervention, this study design was the most appropriate. Statistical inferences regarding an NI hypothesis derive from the CI of the difference in scores between the two interventions rather than the p values. While some studies from other centers showed the superiority of their IC modules over in-person counseling for knowledge acquisition (Green et al. 2004), others showed the absence of a statistically-significant difference between educational interventions without attempting to demonstrate NI (Castellani et al. 2010; Gason et al. 2004; 2005; Green et al. 2001a). Our ability to infer NI was limited. We designed our study using an NI margin of 5%, but our results were inconclusive at this level: The 95% CI of the effect size that web-based intervention has on knowledge acquisition compared to in-person intervention (−0.74–0.38) straddles the NI margin of −0.45 (Fig. 5). This is a situation equivalent to "Trial C" in Fig. 3. There are two possible explanations to consider. The first is that the IC tool is truly non-inferior at this margin but our study is underpowered. The estimated intergroup score difference (−0.18) is above the NI margin (−0.45), which is consistent with this possibility. Alternatively, our module may not be non-inferior at the 5% margin. We believe that a 5% NI margin is very strict, as it would represent an average difference in score of half of one question between the two groups. We chose a narrow margin in order to increase the stringency of our study, but it may have been an unreasonable

expectation. Regardless, our sample size was insufficient to exclude either possibility. A sensitivity power analysis was also conducted to demonstrate the minimally detectable effect size with our current data. The calculated Cohen's *d* is 0.16 (Ellis 2009), which is the difference between the two intervention scores divided by the typical standard deviation (pooled). This result reflects the degree of the mean difference between the patient scores in the two intervention groups when the responses have normal distributions with equal variances. Larger samples would narrow the CI of the mean difference in post-intervention scores and provide more definitive interpretations.

There were several factors that could have skewed our participants' post-educational knowledge scores and confounded the intergroup comparison. First, while in-person participants completed their post-education surveys immediately after their genetics education, web-based participants completed the surveys on their own time. Consequently, web-based participants may have reported lower knowledge scores if they completed their surveys long after reviewing the module. Also, for individuals who took multiple days to complete the study, there tends to be a negative correlation (Spearman's rank correlation coefficient = −0.58) between the number of days and their score, possibly suggesting that the retention of information was limited over a long period of time. Although it would have been ideal to correlate post-educational knowledge scores with the time between completing the pre-education questionnaire and completing the post-education questionnaire, we are unable to accurately calculate this variable. This is because some individuals completed all the questions in the pre-education questionnaire and saved their responses, but forgot to "exit" the survey prior to opening the post-education questionnaire. Therefore, we used total time elapsed during the study (from starting the pre-education questionnaire to exiting the post-education questionnaire). Second, the genetic counselors in our team were not blinded and knew the questions in the surveys. This may have influenced the information emphasized in the education sessions and positively biased the in-person participants' scores. Third, the questions in the pre- and post-education questionnaires were identical and may have primed participants to pay attention to key points, causing the scores from both groups to be higher. Fourth, we cannot control whether web-based participants looked up the correct answer to the questionnaires online. There is no positive correlation, however, between the time spent during the study and the scores of the participants. This finding makes it less likely that web-based participants looked for answers online or from other sources. Fifth, web-based participants had to answer correctly quiz questions as part of the online module, which provides an active knowledge check to the participants. Since eight of the ten knowledge questions in the post-education questionnaire were identical to the quiz questions, the score of web-based participants may have been inflated due to the fact that they knew the correct answers to the quiz questions. We could not find, however, any statistically significant influence that the intervention type had on the post-education scores (Table 4). Sixth, couples who did web-based education together may have consulted each other for help. Seventh, study participants from either group who had prior medical genetics encounters would be expected to score higher both pre- and post-educationally, although the ANCOVA would already account for pre-educational differences. Finally, the post-educational mean knowledge scores for both groups were very high, and in fact many individuals from both groups scored 10/10 on their post-educational questionnaire (raw data not presented). This makes it difficult for us to differentiate variation in knowledge acquisition among top-scoring individuals (ceiling effect). All of these factors made it difficult to evaluate the NI of the IC tool.

Other limitations to our study included the inherent shortcomings of self-reported questionnaires, the fact that we excluded potential participants who may need more psychosocial support with criteria based on our own clinical experience (ongoing pregnancy, family history of a JGD, subjective evaluation during a phone conversation), and the fact that one participant was uncertain if he should have reported state or trait anxiety. These shortcomings, however, did not affect the primary outcome measure of knowledge acquisition.

Finally, the results of our study may not be generalizable to all patient populations as our participants were mostly university-educated with high levels of e-health literacy.

Practice Implications and Future Directions

While our data regarding the IC module's NI are inconclusive at this time, we believe it shows great promise. Implementing an IC module in routine clinic may save time and resources for the medical genetics team, as genetic counselors and geneticists can order AJ screening tests without meeting the patient. The tool may also increase accessibility to genetic testing for individuals who are content to use the web-module and for all non-urgent patients who would benefit from a shorter waitlist. We also believe that our IC module may be adaptable to many clinical situations, such as other ethnicity-specific carrier screening programs, even for pregnant couples. Genetics clinics worldwide can also use our module as a template for their own needs. As the attitudes in modern medicine continue to promote patient autonomy, health care providers need to support patients in accessing services at their own request. Providing user-friendly IC modules, with the support of a clinical genetics department, is one way to promote these values.

JScreen is an American web-based program that also delivers genetic screening to individuals of AJ descent without in-person pre-test counseling (Grinzaid et al. 2015). Like our

module, genetics professionals review the appropriateness of each request for testing. This distinguishes both our programs from direct-to-consumer tests that also bypass in-person pre-test education. Unlike our module, *JScreen* allows patients to submit samples from home. These differences can be explained by different health care infrastructures. Although *JScreen*'s at-home spit kit system removes many barriers for individuals to access genetic testing, sending sample collection kits to each requesting individual is financially risky for a taxpayer-funded, public healthcare system. For these reasons, recreating an identical program in Quebec may not be realistic. In contrast, we designed and piloted our IC module specifically for the genetic testing infrastructure in Quebec, working closely with the MUHC Molecular Genetics Laboratory to ensure a smooth implementation.

We did not specifically measure long-term knowledge retention. Long-term recall for GC patients is highly variable and depends on factors such as level of education, prior knowledge, or the type of information (Michie et al. 1997; Rowley et al. 1984; Somer et al. 1988). Long-term recall for patients who used genetics IC modules also varies between studies (Albada et al. 2015; Kuppermann et al. 2009; Yee et al. 2014). Gason et al. (2004), whose study design is similar to ours, found that Jewish teenagers who learned about TSD through an IC program or an oral presentation maintained high knowledge scores ten days and three months post-education. Future directions for our study may include assessing long-term recall by re-administering knowledge questionnaires.

In the present study, we developed and evaluated an online module for providing pre-test genetics education to individuals seeking AJ carrier screening. With respect to knowledge acquisition, there was no statistically significant difference between the in-person group and the web-based group in terms of post-education scores compared to pre-education scores. We were not able to prove non-inferiority of the module at a margin of 5%. Further research is needed to demonstrate the non-inferiority of the module at this margin, or at a less strict margin. A few participants did not report equal satisfaction with the online tool, underscoring the irreplaceable value of in-person meetings for certain patients. IC modules such as ours may have a growing role in medical genetics and in other health professions by possibly increasing patient accessibility to services while reducing strains on human resources.

Acknowledgements We thank Julie Kristof (MJHDF; testjgd.com) for helping to develop educational resources; Lyndsay Hodgson (MUHC Education Portfolio; muhcpatienteducation.ca) for her health literacy review of our IC module; Cindie Bilodeau (MUHC Information Services) for translating the module to an online interface; Andrea Ruchon, Ron Agatep and Laura Russell for accommodating new test protocols; Nora Wong and William Foulkes (Cancer Genetics, JGH) for representing our study before the JGH REB; Rimi Joshi, Karen El-Akouri, and Mara Caplum for assisting with participant recruitment; Natalie Palfreeman for assisting with counseling in-person participants; and Xianming Tan and Raman Agnihotram (Centre for Innovative Medicine Biostatistics Services, MUHC Research Institute) for assisting with our statistical analysis. Funding was provided by the McGill University Department of Human Genetics, the Quebec Association of Genetic Counsellors Student/New Graduate Research Project Bursary, and the British Columbia Children's Hospital Foundation/Rare Disease Foundation Microgrant.

Compliance with Ethical Standards

Conflict of Interest All of the authors, Chia Wei Fan, Lysanne Castonguay, Sonja Rummell, Sébastien Lévesque, John J. Mitchell, and Guillaume Sillon, declare that they have no conflict of interest.

Human Studies and Informed Consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all patients for being included in the study.

Animal Studies No animal studies were carried out by the authors for this article.

References

ACOG Committee on Genetics. (2009). ACOG committee opinion no. 442: Preconception and prenatal carrier screening for genetic diseases in individuals of eastern European Jewish descent. *Obstetrics and Gynecology, 114*, 950–953.

Albada, A., van Dulmen, S., Lindhout, D., Bensing, J. M., & Ausems, M. G. E. M. (2012). A pre-visit tailored website enhances counselees' realistic expectations and knowledge and fulfils information needs for breast cancer genetic counselling. *Familial Cancer, 11*, 85–95.

Albada, A., van Dulmen, S., Spreeuwenberg, P., & Ausems, M. G. E. M. (2015). Follow-up effects of a tailored pre-counseling website with question prompt in breast cancer genetic counseling. *Patient Education and Counseling, 98*, 69–76.

Castellani, C., Perobelli, S., Bianchi, V., Seia, M., Melotti, P., Zanolla, L., et al. (2010). An interactive computer program can effectively educate potential users of cystic fibrosis carrier tests. *American Journal of Medical Genetics. Part A, 155*, 778–785.

Clow, C. L., & Scriver, C. R. (1977). Knowledge about and attitudes toward genetic screening among high-school students: The Tay-Sachs experience. *Pediatrics, 59*, 86–91.

Development Core Team, R. (2008). *R (Version 3.1.2)*. Vienna: R Foundation for Statistical Computing Retrieved from http://www.R-project.org.

Ellis, P. D. (2009). Effect size calculators. Retrieved July 16, 2016, from http://www.polyuedu.hk/mm/effectsizefaqs/calculator/calculator.html

Gason, A. A., Aitken, M., Delatycki, M. B., Sheffield, E., & Metcalfe, S. A. (2004). Multimedia messages in genetics: Design, development, and evaluation of a computer-based instructional resource for secondary school students in a Tay-Sachs disease carrier screening program. *Genetics in Medicine, 6*, 226–231.

Gason, A. A., Metcalfe, S. A., Delatycki, M. B., Petrou, V., Sheffield, E., Bankier, A., & Aitken, M. (2005). Tay Sachs disease carrier screening in schools: Educational alternatives and cheekbrush sampling. *Genetics in Medicine, 7*, 626–632.

Green, M. J., Biesecker, B. B., McInerney, A. M., Mauger, D., & Fost, N. (2001a). An interactive computer program can effectively educate patients about genetic testing for breast cancer susceptibility. *American Journal of Medical Genetics, 103*, 16–23.

Green, M. J., McInerney, A. M., Biesecker, B. B., & Fost, N. (2001b). Education about genetic testing for breast cancer susceptibility: Patient preferences for a computer program or genetic counselor. *American Journal of Medical Genetics, 103*, 24–31.

Green, M. J., Peterson, S. K., Wagner Baker, M., Harper, G. R., Friedman, L. C., Rubinstein, W. S., & Mauger, D. T. (2004). Effect of a computer-based decision aid on knowledge, perceptions, and intentions about genetic testing for breast cancer susceptibility: A randomized controlled trial. *JAMA, 292*, 442–452.

Green, M. J., Peterson, S. K., Wagner Baker, M., Friedman, L. C., Harper, G. R., Rubinstein, W. S., et al. (2005). Use of an educational computer program before genetic counseling for breast cancer susceptibility: Effects on duration and content of counseling sessions. *Genetics in Medicine, 7*, 221–229.

Griffith, J. M., Sorenson, J. R., Bowling, J. M., & Jennings-Grant, T. (2005a). Assessment of an interactive computer-based patient prenatal genetic screening and testing education tool. *Health Education & Behavior, 32*, 613–626.

Griffith, J. M., Sorenson, J. R., Jennings-Grant, T., & Fowler, B. (2005b). Development of an interactive computer-assisted instruction (ICAI) program for patient prenatal genetic screening and carrier testing for use in clinical settings. *Patient Education and Counseling, 59*, 199–204.

Grinzaid, K. A., Zartman Page, P., Johnson Denton, J., & Ginsberg, J. (2015). Creation of a national, at-home model for Ashkenazi Jewish carrier screening. *Journal of Genetic Counseling, 24*, 381–387.

Gross, S. J., Pletcher, B. A., Monaghan, K. G., Practice, P., & Committee, G. (2008). Carrier screening in individuals of Ashkenazi Jewish descent. *Genetics in Medicine, 10*, 54–56.

Joseph, G., Beattie, M. S., Lee, R., Braithwaite, D., Wilcox, C., Metrikin, M., et al. (2010). Pre-counseling education for low literacy women at risk of hereditary breast and ovarian cancer (HBOC): Patient experiences using the cancer risk education intervention tool (CREdIT). *Journal of Genetic Counseling, 19*, 447–462.

Kincaid, J. P., Fishburne, R. P., Rogers, R. L., & Chissom, B. S. (1975). *Derivation of new readability formulas (automated readability index, fog count, and flesch reading ease formula) for navy enlisted personnel Research Branch Report*. Naval Air Station Memphis: Chief of Naval Technical Training.

Kinzie, M. B., Schorling, J. B., & Siegel, M. (1993). Prenatal alcohol education for low-income women with interactive multimedia. *Patient Education and Counseling, 21*, 51–60.

Klugman, S., & Gross, S. J. (2010). Ashkenazi Jewish screening in the twenty-first century. *Obstetrics and Gynecology Clinics of North America, 37*, 37–46.

Kukafka, R., Lussier, Y. A., Eng, P., Patel, V. L., & Cimino, J. J. (2002). Web-based tailoring and its effect on self-efficacy: Results from the MI-HEART randomized controlled trial. *Proc AMIA Symp, 2002*, 410–414.

Kuppermann, M., Norton, M. E., Gates, E., Gregorich, S. E., Learman, L. A., Nakagawa, S., et al. (2009). Computerized prenatal genetic testing decision-assisting tool: A randomized controlled trial. *Obstetrics and Gynecology, 113*, 53–63.

Marteau, T. M., & Bekker, H. (1992). The development of a six-item short-form of the state scale of the Spielberger state-trait anxiety inventory (STAI). *The British Journal of Clinical Psychology, 31*, 301–306.

Michie, S., McDonald, V., & Marteau, T. M. (1997). Genetic counselling: Information given, recall and satisfaction. *Patient Education and Counseling, 32*, 101–106.

Mitchell, J. J., Capua, A., Clow, C., & Scriver, C. R. (1996). Twenty-year outcome analysis of genetic screening programs for Tay-Sachs and β-thalassemia disease carriers in high schools. *American Journal of Medical Genetics, 59*, 793–798.

Neafsey, P. J., Strickler, Z., Shellman, J., & Chartier, V. (2002). An interactive technology approach to educate older adults about drug interactions arising from over-the-counter self-medication practices. *Public Health Nursing, 19*, 255–262.

Norman, C. D., & Skinner, H. A. (2006). eHEALS: The ehealth literacy scale. *Journal of Medical Internet Research, 8*, e27.

Olivier, C., Asselstine, J., Peterson, E. B., Rosati-White, L., & Stephenson, L. (2008). MUHC standards for developing effective written patient learning materials. Retrieved June 7, 2015, from http://muhcpatienteducation.mcgill.ca/muhc_patient_education_standards.pdf.

Rowley, P. T., Lipkin Jr., M., & Fisher, L. (1984). Screening and genetic counseling for beta-thalassemia trait in a population unselected for interest: Comparison of three counseling methods. *American Journal of Human Genetics, 36*, 677–689.

Schumi, J., & Wittes, J. T. (2011). Through the looking glass: Understanding non-inferiority. *Trials, 12*, 106.

Shiloh, S., Avdor, O., & Goodman, R. M. (1990). Satisfaction with genetic counseling: Dimensions and measurement. *American Journal of Medical Genetics, 37*, 522–529.

Somer, M., Mustonen, H., & Norio, R. (1988). Evaluation of genetic counselling: Recall of information, post-counselling reproduction, and attitude of the counsellees. *Clinical Genetics, 34*, 352–365.

Statistics Canada. (2013a). Ethnic Origin (264), Single and Multiple Ethnic Origin Responses (3), Generation Status (4), Age Groups (10) and Sex (3) for the Population in Private Households of Canada, Provinces, Territories, Census Metropolitan Areas and Census Agglomerations (table). Ottawa, ON: Retrieved from http://www12.statcan.gc.ca/nhs-enm/2011/dp-pd/dt-td/Rp-eng.cfm?LANG=E&APATH=3&DETAIL=0&DIM=0&FL=A&FREE=0&GC=0&GID=0&GK=0&GRP=0&PID=105396&PRID=0&PTYPE=105277&S=0&SHOWALL=0&SUB=0&Temporal=2013&THEME=95&VID=0&VNAMEE=&VNAMEF=.

Statistics Canada. (2013b). Religion (108), Immigrant Status and Period of Immigration (11), Age Groups (10) and Sex (3) for the Population in Private Households of Canada, Provinces, Territories, Census Metropolitan Areas and Census Agglomerations (table). Ottawa, ON: Retrieved from http://www12.statcan.gc.ca/nhs-enm/2011/dp-pd/dt-td/Rp-eng.cfm?LANG=E&APATH=3&DETAIL=0&DIM=0&FL=A&FREE=0&GC=0&GID=0&GK=0&GRP=0&PID=105399&PRID=0&PTYPE=105277&S=0&SHOWALL=0&SUB=0&Temporal=2013&THEME=95&VID=0&VNAMEE=&VNAMEF=.

Thomas, J. (2010). *Creating effective patient education material: Workshop manual*. QC: Montreal.

Wang, L.-M., & Chiou, C.-P. (2011). Effectiveness of interactive multimedia CD on self-care and powerlessness in hemodalysis patients. *The Journal of Nursing Research, 19*, 102–111.

Wilson, R. D., De Bie, I., Amour, C. M., Brown, R. N., Campagnolo, C., Carroll, J. C., Okun, N., Nelson, T., & Zwingerman, R. (2016). Joint SOGC-CCMG opinion for reproductive genetic carrier screening: An update for all Canadian providers of maternity and reproductive healthcare in the era of direct-to-consumer testing. *JOGC, 38*, 742–762.

Yee, L. M., Wolf, M., Mullen, R., Bergeron, A. R., Bailey, S. C., Levine, R., & Grobman, W. A. (2014). A randomized trial of a prenatal genetic testing interactive computerized information aid. *Prenatal Diagnosis, 34*, 1–6.

Yip, M. P., Chang, A. M., Chan, J., & MacKenzie, A. E. (2003). Development of the telemedicine satisfaction questionnaire to evaluate patient satisfaction with telemedicine: A preliminary study. *Journal of Telemedicine and Telecare, 9*, 46–50.

Zaiontz, C. (2014). *Real statistics (version 3.6.2)*. Milan: Zaiontz, Charles Retrieved from www.real-statistics.com.