A Pilot Randomized Clinical Trial Evaluating the Impact of Genetic Counseling for Serious Mental Illnesses

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ABSTRACT

Objective: The serious mental illnesses schizophrenia, schizoaffective disorder, and bipolar disorder are complex conditions affecting 1% to 4% of the population. Individuals with serious mental illnesses express interest in genetic counseling, an intervention showing promise for increasing patient knowledge and adaptation. This trial aimed to evaluate the effects of genetic counseling for people with serious mental illnesses as compared to an educational intervention or wait list.

Method: A pilot 3-arm (each n = 40; genetic counseling, a control intervention involving an educational booklet, or wait list), parallel-group, randomized clinical trial was conducted from September 2008 through November 2011 in Vancouver, Canada. Participants with schizophrenia, bipolar disorder, or schizoaffective disorder (*DSM-IV*) completed outcome measures assessing knowledge, risk perception, internalized stigma, and perceived control over illness at baseline and 1-month follow-up. The Brief Symptom Inventory was administered to control for current symptoms. Analyses included linear mixed-effects models and χ^2 tests.

Results: Knowledge increased for genetic counseling/educational booklet compared to wait list at follow-up ($LRT_1 = 19.33$, Holm-adjusted $P = .0003$, $R^2_{LMM(m)} = 0.17$). Risk perception accuracy increased at follow-up for genetic counseling compared to wait list (Yates continuity corrected $\chi^2_1 = 9.1$, Bonferroni $P = .003$) and educational booklet (Yates continuity corrected $\chi^2_1 = 8.2$, Bonferroni $P = .004$). There were no significant differences between groups for stigma or perceived control scores.

Conclusions: Genetic counseling and the educational booklet improved knowledge, and genetic counseling, but not the educational booklet, improved risk perception accuracy for this population. The impact of genetic counseling on internalized stigma and perceived control is worth further investigation. Genetic counseling should be considered for patients with serious mental illnesses.

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The serious mental illnesses (SMIs) schizophrenia, schizoaffective disorder, and bipolar disorder cumulatively affect approximately 1% to 4% of the population worldwide[1,2] and, like other common conditions (eg, diabetes, cardiovascular disease), have a heterogeneous etiology typically involving both genetic variants and environmental factors.[3,4] Currently, no genetic tests are clinically useful in establishing, refining, or excluding a psychiatric diagnosis.

Genetic counseling (GC) is "the process† of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease."[5(p79)] Individuals and families affected by SMIs express interest in receiving GC,[6,7] which has potential benefits, even without genetic testing.[8–10] Although GC for SMI is suggested in clinical practice guidelines of the American[11] and Canadian[12] Psychiatric Associations, there is little empirical evidence regarding outcomes of GC in this context.

Two nonrandomized pilot studies[13,14] of GC for family members of individuals with psychotic disorders revealed positive effects, as did a similarly designed study in a group of people with schizophrenia or schizoaffective disorder.[15] In the latter, GC increased knowledge of causes of schizophrenia, and decreased recurrence risk (RR) estimates, concern regarding recurrence, stigma, and self-blame (albeit temporarily).

We conducted the first pilot randomized clinical trial of the impact of GC for SMI, and also the first empirical investigation into the effect of GC for bipolar disorder.

Hypotheses

We hypothesized that (1) mean scores for knowledge, risk perception accuracy, and perceived control over illness would be higher and scores for internalized stigma would be lower for the GC group compared to an intervention group provided with an educational booklet (EB) and (2) mean differences in scale scores between outcome (T3) and baseline (T1) for the 2 intervention groups (GC, EB) would be significantly different from those for wait list (WL), with GC and EB mean scores being higher for knowledge, risk

†The genetic counseling process integrates the following: interpretation of family and medical histories to assess the chance of disease occurrence or recurrence; education about inheritance, testing, management, prevention, resources, and research; and counseling to promote informed choices and adaptation to the risk or condition. Genetic and environmental contributors to illness are discussed in a holistic fashion.

Clinical Points

- Patients with serious mental illnesses are interested in genetic counseling when it is made available to them, and genetic counseling is recommended by clinical practice guidelines, but systematic evaluation of its outcomes for these populations has been limited or unavailable in the case of bipolar disorder.
- Physicians seeing patients with serious mental illnesses should consider referring these patients to a specialist psychiatric genetic counselor (who can be found using the "Find a counselor" tool at www.findageneticcounselor.com), particularly when patients have sufficient insight into their illness and would benefit from a greater understanding of risk and protective factors in managing their illness.

perception accuracy, and perceived control over illness and lower for internalized stigma.

METHOD

Participants and Ethics Statement

The Institutional Review Boards at the University of British Columbia and BC Children's and Women's Hospital approved this study (H07-02427), and it was registered on ClinicalTrials.gov (NCT00713804). Participants were recruited from the community in Vancouver, Canada (September 2008 through November 2011) via referrals from psychiatrists and self-referrals from study advertisements. Study appointments occurred in inpatient or outpatient settings. Each potential participant received a consent form and, if interested, an in-person baseline appointment (T1) to provide written consent and confirm eligibility. After an informed consent process, written consent was obtained. Individuals were enrolled if they reported a diagnosis of schizophrenia, bipolar disorder, or schizoaffective disorder; were fluent in English; and had the capacity to provide informed and autonomous consent (eg, were ≥ 19 years of age). Individuals were ineligible if their SMI diagnosis was substance-induced or their ability to provide autonomous informed consent was compromised (eg, intellectual disability [IQ < 70] or currently floridly psychotic or intoxicated).

Study Design and Treatments

This study was a pilot, prospective, 3-arm, parallel-group randomized controlled trial (N = 120). Randomization was equal (1:1:1) and stratified (43% male, 57% female—a ratio balancing desire to have male representation against feasibility concerns regarding male recruitment). In the absence of more relevant data, we used information on the effect of GC on knowledge/anxiety in the context of cancer[16] to set our sample size assuming an attrition rate of 25%, equal loss to follow-up between groups, and a power of > 80% to detect a medium effect size ($d = 0.5$) at $P \leq .01$ for each outcome variable (see footnote "a" in Figure 1).

The 3 arms were (1) receiving GC from a board certified/eligible genetic counselor (BC/EGC), (2) meeting with a research coordinator to read an EB, and (3) WL. The EB intervention was designed as a rigorous control intervention; it was face-to-face and provided the same general information as GC, but without the "active ingredient" of personalization of information/counseling by a BC/EGC. All participants who were not randomized to GC were offered GC after study completion. Questionnaires were administered at baseline (T1), immediately post-intervention (T2, GC and EB groups only), and at 1-month follow-up (T3).

While the nature of the study and interventions precluded blinding for participants or providers, an independent party blind to group status conducted data analyses.

Baseline

All participants completed the Structured Clinical Interview for *DSM-IV-TR* disorders[17] and signed a release of information for their psychiatric history records. A psychiatrist (J.C.) reviewed these data to confirm diagnoses. To confirm IQ ≥ 70, the Kaufman Brief Intelligence Test, Second Edition (KBIT-2)[18] was administered. Participants completed a demographic questionnaire and then were randomly assigned. For the randomization procedure, equally sized laminated cards were sorted into 2 opaque envelopes (1 for males, containing 18 GC, and 17 of each EB and WL; and 1 for females, containing 22 GC, and 23 of each EB and WL). Participants were asked to choose a card from the appropriate (male/female) envelope without looking (under the supervision of A.R. or A.I.). Baseline appointments lasted approximately 1–3 hours, depending on informational detail shared by the participant. Questionnaires assessing outcome measures (Figure 1) were administered at T1 (~ 1 hour).

Interventions

For participants in EB/GC, outcome measures were assessed immediately pre-intervention and post-intervention.

GC sessions (~ 1 hour) were provided by a psychiatric-specialist BC/EGC (J.C.A., C.H., A.I.). The GC session followed standard procedures.[19–21] Specifically, family histories and existing explanations for illness were elicited, and then participants were provided with evidence-based information about illness etiology in the context of a psychotherapeutically oriented interaction designed to support and address emotional sequelae, as described elsewhere.[21] Participants received written information to take home(booklet described later in this section) and information on RR, personalized to family history, if requested. No genetic testing was provided. A.I. and C.H. were trained by J.C.A. to ensure competency/consistency. Adherence to GC protocol was ensured by GC checklist completion, peer session observation and feedback, and regular peer-supervision meetings.

EB sessions (~ 30 minutes) were provided by the research coordinator (A.R.), who answered questions regarding literal interpretations of text, but responded to participants' queries that aimed to make personal meaning of the material with responses such as "I'm sorry, but I'm afraid I'm unable to answer that. If you'd like to meet with someone who can help you with questions like that, we can set up a genetic

counseling appointment after you finish the study." Thus, EB sessions did not evolve into GC, yet were a stringent control intervention. Through observation, the research coordinator confirmed participant adherence to the intervention.

The booklet (16 color pages, reading grade level 8) was designed in collaboration with individuals with SMI and included a graphical depiction of the concepts of vulnerability (genetic and environmental) and resilience (the "mental illness jar"[13]), with specific examples and a table of general RRs for relatives of people with SMI.

Outcome Measures

The choice of outcome measures—knowledge, risk perception, internalized stigma, and perceived control over illness—was informed by the definition and goals of GC as well as psychiatric GC literature[5,7,8,10,13–15,22–25] (eAppendix 1). One month post-intervention, outcome assessments were sent to participants, usually by mail, including a postage-paid return envelope. For GC only, participants completed the Genetic Counseling Satisfaction Scale[26] (GCSS) immediately post-intervention.

Knowledge and risk perception. The 9-item Knowledge and Risk Perception (KRP) questionnaire was designed for this study (see eAppendix 1). The risk perception item was previously piloted extensively with the target population (N > 400).[24] Six knowledge items were adapted from ones used previously in studies of GC.[23] One item asked whether participants found the GC/EB useful (Likert-type item [0 = not at all useful, 4 = very useful]) and another whether they had shared information from the GC/EB.

Internalized stigma. The Internalized Stigma of Mental Illness scale (ISMI)[27] is a 29-item self-report scale designed to measure subjective experiences of stigma among people with SMI, with subscales measuring alienation, stereotype endorsement, perceived discrimination, social withdrawal, and stigma resistance. Each item is rated on a Likert scale (1 = strongly disagree, 4 = strongly agree). The ISMI has strong internal consistency (α = .90), good test-retest reliability (r = 0.92), and robust construct validity.

Perceived control. We used a version of the Illness Perception Questionnaire that was revised and validated for individuals with SMI (IPQ-S).[28] The 5 subscales used in this study consist of 34 items, rated on a Likert scale (1 = strongly disagree, 5 = strongly agree). All of these subscales have shown good internal consistency (α ~ .75) and test-retest reliability (r = 0.57–0.95). There is no total score for the IPQ-S.

Current symptoms. We administered the Brief Symptom Inventory (BSI, a 53-item self-report measure that assesses psychological symptoms over the previous week[29]) to control for the potential confound of current mood. It has good internal consistency (α = .71–.85), test-retest reliability, and construct validity. It yields 3 global domains (a global severity index [GSI], a positive symptom distress index, and a total positive symptom score). Items are rated on a Likert scale (0 = not at all, 4 = extremely); higher scores indicate greater symptom severity. For all analyses, we used the GSI.

Statistical analysis. The primary analysis included all participants with complete demographic and baseline data. Two analyses were carried out in R[30] to (1) examine differences over the 3 time points for GC and EB groups (longitudinal; n = 69), and (2) assess effects of treatment (GC/EB) relative to WL between T3 and T1 (n = 112). Analyses 1 and 2 both used linear mixed effects models with subject ID as the random nesting effect and ln(GSI) at T1 and diagnosis type (bipolar disorder, schizophrenia, or schizoaffective disorder) as moderating covariates. The main effects were time (1, 2 and 3 for analysis 1; 1 and 3 for analysis 2) and group membership. Tests for group × time interaction terms were conducted. P values for all tests of interactions and main effects were corrected using the Holm correction.[31] Uncorrected P values are also reported for comparison when relevant. $R^2_{LMM(m)}$ (marginal R^2 for linear mixed effects models = variance explained by the fixed effects) was calculated for all significant models using the method of Nakagawa and Schielzeth.[32]

Perceived RR estimates were transformed into dichotomous responses, accurate versus not accurate (see Table 2 footnote "b" for definition of "accurate"), and compared among groups using χ^2 tests at each time point. P values for these tests were included in the Holm adjustment for KRP, ISMI, and IPQ-s analyses. Post hoc pairwise χ^2 comparisons were conducted and Bonferonni-corrected when required. We also calculated effect sizes (d) for ISMI, KRP, and IPQ-s scores and effect sizes (ϕ or Cramer V) for the RR comparisons. Data analysis was conducted using SPSS 17.0 (IBM) and R.

RESULTS

Patient Characteristics

Characteristics of participants are summarized in Table 1. Flow of participants through the trial is depicted in Figure 1.

Outcomes

Mean scores and effect sizes for outcome measures are listed in Table 2 and Table 3, respectively.

Knowledge. For analysis 1, there was no significant interaction between time and group with the likelihood ratio test statistic (LRT_2 = 3.13, P = .21) and no significant difference between GC and EB for knowledge score (LRT_1 = 0.14, P = .71); however, there was a significant difference across time points (LRT_2 = 60.4, Holm-adjusted P < .0001, $R^2_{LMM(m)}$ = 0.25) with T1 significantly lower than T2 (Tukey-adjusted P < .001) and T3 (Tukey-adjusted P < .001), but no significant difference between T2 and T3 (Tukey-adjusted P > .05) (Figure 2A). For analysis 2, there was a significant group (GC/EB vs WL) by time (T1 vs T3) interaction term for knowledge scores (LRT_1 = 19.33, Holm-adjusted P = .0003, $R^2_{LMM(m)}$ = 0.17), with treatment groups having knowledge scores that were a mean of 1.59 (95% CI, 0.91–2.26) points higher than WL at T3.

Risk perception. There was a significant difference among groups in the proportion of accurate responses at T1, but not after P value adjustment (unadjusted P = .005, χ^2_2 = 10.8,

Table 1. Sociodemographic Characteristics of Participants (N = 120)[a]

Variable	All Groups	GC Group	EB Group	WL Group
Demographics				
Sex				
Female	68 (56.7)	22 (55)	23 (57.5)	23 (57.5)
Male	52 (43.3)	18 (45)	17 (42.5)	17 (42.5)
Age, mean (range), y[b]	41.6 (17–73)	40.1 (21–62)	40.5 (17–68)	44.1 (23–73)
Diagnosis and Illness Severity				
Diagnosis				
Bipolar disorder	83 (69.2)	29 (72.5)	28 (70)	26 (65)
Schizoaffective disorder	13 (10.8)	4 (10)	6 (15)	3 (7.5)
Schizophrenia	20 (16.7)	7 (17.5)	3 (7.5)	10 (25)
Other[c]	4 (3.3)	0 (0)	3 (7.5)	1 (2.5)
Global Severity Index score at T1, mean (SD)	1.0 (0.8)	1.0 (0.8)	1.0 (0.8)	1.1 (0.8)
Marital Status				
Single (including divorced, separated)	79 (65.8)	22 (55)	25 (62.5)	32 (80)
Partnered (including married, common law)	41 (34.2)	18 (45)	15 (37.5)	8 (20)
Socioeconomic Status (annual household income in Can$)				
< 20,000	61 (51.3)	18 (45)	18 (46.2)	25 (62.5)
20,000–40,000	17 (14.3)	6 (15)	6 (15.4)	5 (12.5)
41,000–60,000	13 (10.9)	2 (5)	4 (10.3)	7 (17.5)
61,000–80,000	11 (9.2)	5 (12.5)	6 (15.4)	0 (0)
81,000–100,000	10 (8.4)	5 (12.5)	3 (7.7)	2 (5)
> 100,000	7 (5.9)	4 (10)	2 (5.1)	1 (2.5)
Highest Level of Education				
Some high school	19 (16.0)	5 (12.5)	8 (20.5)	6 (15)
Completed high school	9 (7.6)	1 (2.5)	3 (7.7)	5 (12.5)
Attended college or university	91 (76.5)	34 (85)	28 (71.8)	29 (72.5)

[a]Values shown as n (%) unless otherwise noted. Percentages are based on non-missing data. The mean number of years since diagnosis was 11.5 years (range, 0–42 years).
[b]After consulting with the Institutional Review Board, we allowed one 17-year-old to participate due to the individual's desire to do so and capability to provide fully informed consent.
[c]Examples of other diagnoses included major depressive disorder and major depressive disorder with psychosis.
Abbreviations: EB = educational booklet, GC = genetic counseling, WL = wait list.

Holm-adjusted $P = .11$), with EB having significantly fewer accurate responses than GC (Yates continuity corrected $\chi^2_1 = 8.6$, Bonferroni $P = .003$). There were no significant differences between GC and WL or between EB and WL at T1. At T2, GC had a significantly greater proportion of accurate responses compared to EB, but not after P value adjustment (unadjusted $P = .02$, Yates continuity corrected $\chi^2_1 = 5.9$, Holm-adjusted $P = .32$). There was a significant difference among groups at T3 (unadjusted $P = .001$, $\chi^2_2 = 13.8$, Holm-adjusted $P = .03$), with GC having more accurate responses than both EB (Yates continuity corrected $\chi^2_1 = 8.2$, Bonferroni $P = .004$) and WL (Yates continuity corrected $\chi^2_1 = 9.1$, Bonferroni $P = .003$).

Internalized stigma. For analysis 1, there were no significant interaction terms and no significant differences between GC and EB or over time for any ISMI subscale or total ISMI score (all unadjusted $P > .05$), except alienation, which showed a marginally nonsignificant difference across time points after P value adjustment (unadjusted $P = .003$, $LRT_2 = 11.74$, Holm-adjusted $P = .07$). Specifically, scores at T1 were significantly higher than at T2 (Tukey-adjusted $P = .002$), but there was no difference between T1 and T3 or between T2 and T3 (all $P > .05$) (Figure 2B). For analysis 2, there were no significant interaction terms and no differences between groups (GC/EB vs WL) for any ISMI subscale or ISMI total score (all unadjusted $P > .05$).

Perceived control. For analysis 1, there were no significant interaction terms and no significant differences between GC and EB or time for all 5 IPQ-S subscales (all Holm-adjusted $P > .1$). For analysis 2, there were no significant interaction terms and no differences between groups (GC/EB vs WL) or time for any IPQ-S subscale (all Holm-adjusted $P > .1$).

Impact of GC/EB. Mean scores for "usefulness" of GC were 3.31 (T2) and 2.93 (T3); for EB, scores were 3.03 (T2) and 2.68 (T3).

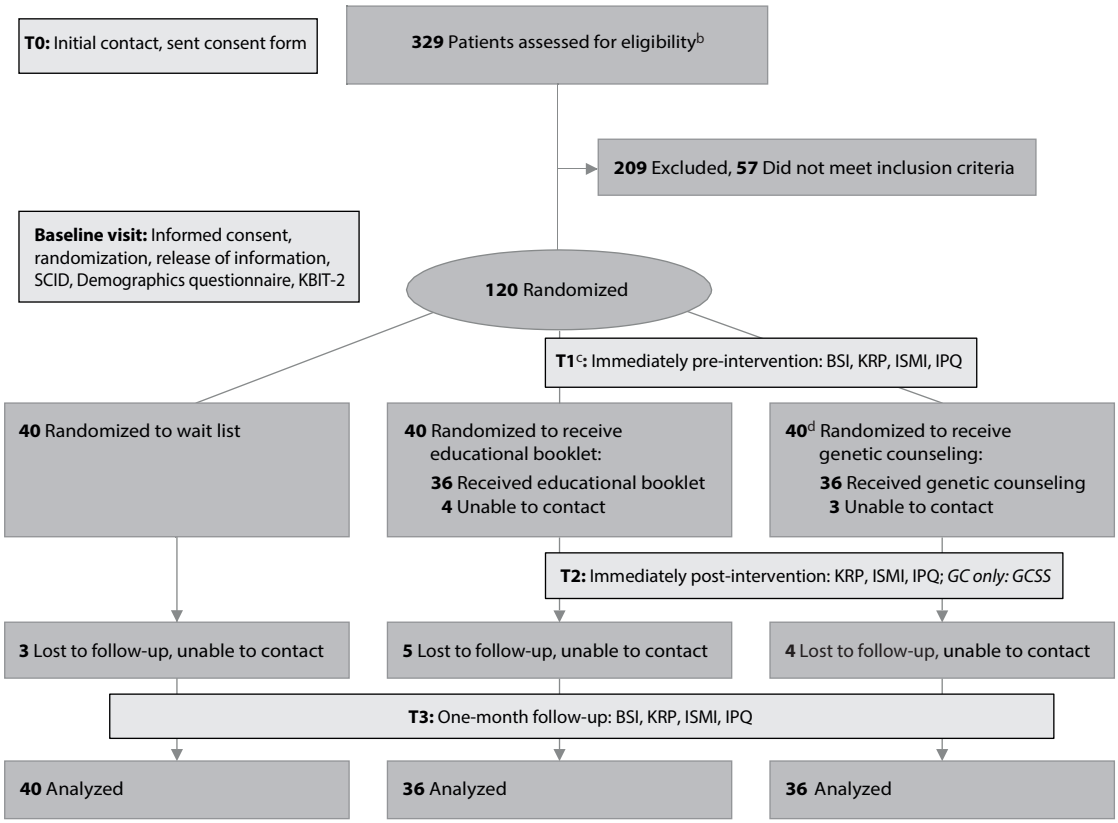
In GC, 23 participants reported sharing information from GC with family, friends, health care professionals, and teachers (mean = 2.52; range, 1–6). In EB, 15 participants reported sharing information from EB with family, friends, health care professionals, and fellow participants in a self-help group (mean = 2.13; range, 1–6).

GCSS data are reported elsewhere.[33]

DISCUSSION

This study represents the first pilot randomized controlled trial of GC for individuals with SMI. Consistent with studies of GC in other areas,[34–37] we observed significant increases in knowledge scores post-intervention (GC/EB) as compared to WL and increases in risk perception accuracy for GC as compared to EB and WL. This is subtly,

Figure 1. Flow of Participants Through the Trial[a]



[a]At the time of study initiation, there were no existing data about the impact of genetic counseling for individuals with serious mental illness, and the effect sizes for our outcome variables were unknown. Therefore, we based our a priori power calculation on the effect of genetic counseling for hereditary cancer on increasing knowledge and diminishing anxiety.[16]

[b]We used diverse recruitment strategies to reach potential participants, including posters in psychiatrists' offices/waiting areas/inpatient units, online advertisements, direct approach at community mental health organizations' meetings/events, direct approach at low-income housing units catering to those with mental illness, email messages to mental health professionals and clients' LISTSERVs, and mental health practitioners who provided information about the study (recruitment brochure) to their patients.

[c]For the wait-list group, baseline and T1 occurred on the same day. Participants had the option of bringing a support person with them to appointments if they wished. In-person visits were arranged for some participants to complete the outcome measures at 1-month follow-up at their request. One of the participants in the wait list group had received genetic counseling for serious mental illness prior to the study. The trial was stopped once the predetermined number of participants had been recruited and those who were not lost to follow-up had completed the study. The full protocol can be obtained from the corresponding author.

[d]One patient discontinued participation because of rapid exacerbation of illness.

Abbreviations: BSI = Brief Symptom Inventory (current symptoms), GCSS = Genetic Counseling Satisfaction Scale, IPQ = Illness Perception Questionnaire (perceived control), ISMI = Internalized Stigma of Mental Illness scale, KBIT-2 = Kaufman Brief Intelligence Test version 2, KRP = Knowledge and Risk Perception Questionnaire, SCID = Structured Clinical Interview for *DSM-IV-TR* disorders.

yet importantly, different from previous findings,[14,15] in which mean risk perception estimates decreased from a baseline of overestimation, but remained overestimated. Increasing knowledge and risk perception accuracy may play a necessary, though insufficient, role in empowering patients to make informed decisions about managing their mental health and, for some, whether to have children.[38]

Participants felt that EB and GC were useful, with GC having qualitatively higher mean scores on usefulness than EB (statistical testing was not conducted). Proportionally more participants who had GC, as compared to EB, reported knowledge sharing, and the mean score for the number of people with whom knowledge was shared was also higher for the GC group (although, again, no statistical testing was conducted). It is possible that participants who received GC had greater confidence in sharing their new knowledge, as compared to those who received EB. These promising results are worthy of further investigation.

While the effect of GC on ISMI scores was largely not significant, mean scores did decrease following GC, while for the EB group an initial drop in ISMI scores was followed by an increase 1 month later. Given the clinical importance of decreasing internalized stigma for those with SMI, and that our sample was underpowered, future studies with larger group sizes may be worthwhile, especially given other recent (uncontrolled) work that showed an effect of GC on ISMI scores.[15]

There was a decrease in mean IPQ-S consequences subscale scores post-intervention that persisted at 1-month follow-up. Changes in scores on this subscale seem to indicate feelings of greater optimism for the future and that SMI is perceived to be more manageable. Although this

difference was not significant, we attribute the lack of statistical significance to small sample size. This is the first study to evaluate the impact of any intervention on perceived control in SMI. Previous studies evaluating GC in other contexts have shown increases in perceived control.[39,40]

It is possible that overall effects of the intervention on the outcomes of interest were influenced by difference in response between diagnostic groups (see Table 3). However, as the sample sizes for groups of individuals with schizophrenia and schizoaffective disorder were small, further study is required.

Strengths and Weaknesses

Strengths of this study include a rigorous control group and recruitment of individuals from the general population rather than using individuals recruited for studies of the genetics of SMI (avoiding potential bias toward individuals with more strongly genetic causal attributions at baseline). Additionally, this study avoids a common confound of other GC studies: the impact of receiving genetic test results at the same time as GC. However, importantly, our sample size was underpowered to detect the observed effect sizes for internalized stigma and perceived control. It is possible that differing responses to GC between individuals with bipolar disorder and schizophrenia diluted our ability to detect differences. Additionally, blinding was not possible; due to the nature of the study, participants were aware of the group to which they had been randomized. Furthermore, the risk range used in the educational booklet was narrower than that typically provided on the basis of a family history evaluation, thus biasing toward less accurate results for the EB group. However, the ranges for the GC and WL groups were comparable. We excluded individuals not fluent in English; our findings, therefore, may not be generalizable to other cultural contexts.

Future Research

There are many avenues ripe for future psychiatric GC research: studies of GC efficacy for other psychiatric illnesses, the timing of GC in relation to time of diagnosis, and optimal number of GC sessions. Adequately powered RCTs of GC for individuals and family members of individuals with psychiatric illnesses, including recordings and manualization of the intervention(s), are an important next step. We would recommend that future RCTs focus on GC for only 1 psychiatric illness (rather than 3, as in this pilot), especially given the potential difference in size of the effect of the intervention between diagnostic groups. Last, in future studies, the use of outcome measures related to those used here, but purpose-designed for exploring the outcomes of GC,[41] could be considered. Conducting research into

Table 2. Raw Data for Knowledge, Internalized Stigma, and Perceived Control and Participants Reporting "Accurate," Overestimated, and Underestimated Recurrence Risks by Group (GC, EB, WL) at Each Time Point (T1, T2, T3)

Variable	T1	T2	T3
Knowledge[a]	Score, Mean (SD)	Score, Mean (SD)	Score, Mean (SD)
GC	2.8 (1.9)	4.6 (2.1)	4.8 (1.2)
EB	3.2 (1.9)	4.1 (2.0)	4.4 (1.8)
WL	3.3 (1.6)	NA	3.4 (1.8)
Risk Perception[b]	n (%)	n (%)	n (%)
"Accurate"			
GC	12 (50.0)	20 (80.0)	17 (85.0)
EB	3 (8.6)[b]	17 (48.6)	8 (29.6)
WL	5 (21.7)	n/a	7 (31.8)
Overestimate			
GC	11 (45.8)	3 (12.0)	1 (5.0)
EB	30 (85.7)	14 (40.0)	14 (51.9)
WL	16 (69.6)	n/a	14 (63.6)
Underestimate			
GC	1 (4.2)	2 (8.0)	2 (10.0)
EB	2 (5.7)	4 (11.4)	5 (18.5)
WL	2 (8.7)	NA	1 (4.5)
Internalized Stigma[c]	Score, Mean (SD)	Score, Mean (SD)	Score, Mean (SD)
GC	59.2 (14.8)	57.6 (15.4)	56.8 (14.3)
EB	60.3 (15.2)	58.7 (14.8)	61.4 (15.9)
WL	61.2 (17.5)	NA	62.7 (17.8)
Perceived Control	Score, Mean (SD)	Score, Mean (SD)	Score, Mean (SD)
Consequences subscale[d]			
GC	37.5 (6.9)	34.6 (7.8)	34.6 (7.8)
EB	39.8 (7.9)	39.7 (10.2)	40.4 (5.9)
WL	39.4 (7.9)	NA	39.1 (8.6)
Personal control subscale[e]			
GC	16.9 (3.4)	16.3 (3.2)	17.3 (2.9)
EB	16.4 (2.5)	17.1 (2.9)	16.6 (3.3)
WL	16.5 (2.9)	NA	17.2 (2.0)
Treatment control subscale[e]			
GC	19.0 (3.5)	19.9 (3.5)	19.6 (3.1)
EB	18.6 (3.5)	19.9 (3.5)	18.2 (4.2)
WL	19.0 (3.4)	NA	19.2 (3.5)
Illness coherence subscale[e]			
GC	10.3 (3.2)	9.4 (3.0)	9.3 (3.1)
EB	10.1 (3.1)	9.6 (3.2)	9.5 (3.5)
WL	11.3 (4.0)	NA	10.3 (3.9)
Emotional representation subscale[d]			
GC	29.1 (7.8)	28.3 (8.2)	27.5 (8.0)
EB	29.2 (8.1)	28.1 (8.0)	31.4 (6.1)
WL	29.0 (7.6)	NA	28.8 (8.4)

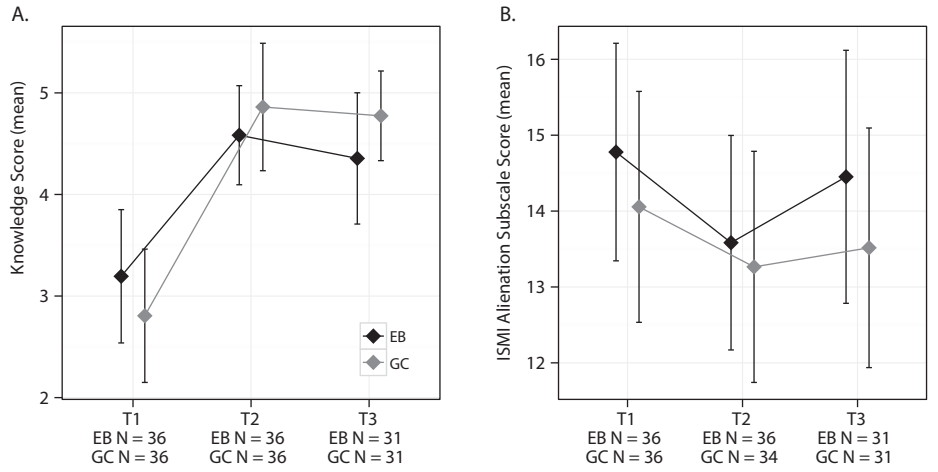
[a]High knowledge scores reflect a greater number of questions answered correctly.
[b]"Accurate" responses for each group were as follows: for the GC group, if they fell within the range provided in the GC session; for the EB group, if they fell within the range quoted in the booklet; for the WL group, if they fell within the range determined by consensus of the 3 board certified/eligible genetic counselors (C.H., A.I., J.C.A.) based on family history analysis. It was more difficult to achieve an "accurate" rating at baseline for the EB group because the risk range (10%–15%) was typically narrower than for those that were personalized to the family history (for the GC and WL groups).
[c]High scores reflect high levels of internalized stigma.
[d]High scores on the consequences and emotional representation subscales represent strongly held beliefs about the negative consequences of the illness and a strong negative emotional response to the illness, respectively.
[e]High scores on the personal control, treatment control, and illness coherence subscales represent positive beliefs about the controllability of the illness and a personal understanding of the condition.
Abbreviations: EB = educational booklet, GC = genetic counseling, NA = not applicable, WL = wait list.

Table 3. Effect Sizes for Risk Perception Comparisons at all 3 Time Points and for Treatment vs Wait List (Analysis 2; T3 Minus T1) for Knowledge, Internalized Stigma, and Perceived Control[a]

Variable	Overall	Schizophrenia	Schizoaffective	Bipolar Disorder
Knowledge	0.87 (0.46 to 1.28)	1.11 (−0.67 to 2.89)	0.67 (−0.96 to 2.3)	0.41 (−0.15 to 0.98)
Risk perception				
T1	Cramer $V = 0.37$	NA	NA	NA
T2	$\phi = 0.35$	NA	NA	NA
T3	Cramer $V = 0.44$	NA	NA	NA
Internalized stigma	−0.12 (−0.52 to 0.27)	−1.13 (−2.92 to 0.65)	−0.41 (−2.01 to 1.2)	−0.44 (−1.01 to 0.13)
Perceived control				
Consequences	−0.26 (−0.66 to 0.13)	−1.35 (−3.19 to 0.48)	−1.47 (−3.25 to 0.32)	−0.45 (−1.02 to 0.12)
Personal control	−0.16 (−0.56 to 0.23)	−1.35 (−3.19 to 0.48)	0.24 (−1.35 to 1.83)	0.37 (−1.32 to 2.05)
Treatment control	−0.05 (−0.44 to 0.34)	1.13 (−0.66 to 2.91)	−1.16 (−2.88 to 0.55)	0.28 (−0.29 to 0.84)
Illness coherence	0.10 (−0.29 to 0.49)	−1.93 (−3.92 to 0.06)	0.12 (−1.47 to 1.71)	0.30 (−0.27 to 0.87)
Emotional representation	−0.02 (−0.41 to 0.37)	−0.81 (−2.54 to 0.92)	−1.46 (−3.25 to 0.32)	−0.41 (−0.97 to 0.16)

[a]Values shown as effect size (95% CI) unless otherwise noted. The effect sizes for schizophrenia, schizoaffective disorder, and bipolar disorder were calculated from the difference in scores (T3 minus T1) between groups (GC minus EB) for each diagnostic group separately.
Abbreviations: EB = educational booklet, GC = genetic counseling, NA = not applicable.

Figure 2. (A) Knowledge Scores by Group and Time and (B) ISMI Alienation Subscale Scores by Group and Time[a]



[a]All error bars represent 95% CI.
Abbreviations: EB = educational booklet, GC = genetic counseling, ISMI = Internalized Stigma of Mental Illness scale.

psychiatric GC efficacy for populations with a variety of cultural backgrounds would be valuable.

CONCLUSIONS

These data support the value in referral to GC for individuals with SMI, the creation of psychiatric GC clinical practice guidelines, and the establishment of specialist psychiatric GC services. The potential for psychiatric GC to empower individuals with psychiatric illness makes it a very exciting addition to the range of services that are available to this disadvantaged population. Physicians seeing patients with serious mental illness and who wish to refer them can find a genetic counselor at www.findageneticcounselor.com.

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Coastal Health Authorities, and the Canadian Psychiatric Association; and received grants from the Canadian Institutes of Health Research (CIHR). **Ms Hippman** reported serving on the Canadian Association of Genetic Counselors Board of Directors from 2013 to 2016. **Dr Austin** reported serving on the National Society of Genetic Counselors Board of Directors from 2011 to 2013 and has received grants from CIHR, the Michael Smith Foundation for Health Research, and Pfizer (investigator-initiated grant).

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Supplementary material: See accompanying pages.

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Supplementary material follows this article.

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Supplementary Material

Article Title: A Pilot Randomized Clinical Trial Evaluating the Impact of Genetic Counseling for Serious Mental Illnesses

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List of Supplementary Material for the article

1. **eAppendix 1** Supplementary Method, including Knowledge and Risk Perception Questionnaire

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

eAppendix 1.

Methods

Design

Choice of Outcome Measures

Knowledge has been used frequently as an outcome measure for GC, and relates to the aspect of GC that involves "education about inheritance, testing, management, prevention, resources and research". Risk perception is particularly important in the context of psychiatric GC because previous studies have shown that families consistently overestimate RRs and, moreover, choose not to have children on the basis of these erroneous risk estimates[13-15,24]. Perceived control over illness is an outcome measure that has been postulated as useful for studies of the impact of GC as it relates to the goal of promoting adaptation to a condition[22]. Last, internalized stigma has been described as the facet of stigma that is the most damaging but is also posited to be potentially modifiable[25]. Decreased internalized stigma has been proposed as an outcome of GC for families affected by SMI[7,8,10] and recent work supports this, as described in the introduction[14,15].

Knowledge and Risk Perception Questionnaire

Risk Perception Question

If you had to guess what the chance would be for a child of yours to become affected with the same mental illness that you have, what would that chance be? (Please write your guess whichever way you like – for example, you might write your guess as: X in 100 or X%)

_____

Usefulness Questions

Was the genetic counseling appointment/educational brochure useful to you?

☐ Very useful
☐ Quite useful
☐ Somewhat useful
☐ Not very useful
☐ Not at all useful

(T2) What did you like most about the appointment?

(T3) Has what you liked most about genetic counseling changed since your appointment? If so, please write what you like most now about it below:

Have you shared some of what you learned in genetic counseling/the educational brochure with others?

☐ Yes ☐ No

If yes, who did you share information with?

☐ My partner
☐ A relative of mine who has a mental illness
☐ A relative of mine who does not have a mental illness
☐ A friend of mine who has a mental illness
☐ A friend of mine who has a relative with a mental illness
☐ A friend of mine who does not have any relatives with a mental illness
☐ Other (please specify)_____

Knowledge Questions

The questions on this page ask about what you know about genes and mental illness. Please answer each question by ticking only one box (Star* denotes the correct answer).

1) The genetic make-up that a person is born with is entirely responsible for deciding whether or not a person develops an illness like schizophrenia or bipolar disorder.

☐ True
☐ False*
☐ Don't know

2) Aspects of a person's environment (e.g. stressful life events, diet, drug use) influence whether or not a person develops an illness like schizophrenia or bipolar disorder.

☐ True*
☐ False
☐ Don't know

3) If a person is genetically vulnerable to developing schizophrenia or bipolar disorder, then they will certainly develop the illness.

☐ True
☐ False*
☐ Don't know

4) It is likely that everyone has some amount of genetic vulnerability to illnesses like schizophrenia and bipolar disorder.

☐ True*
☐ False
☐ Don't know

5) The way a person's genes work in their body might cause the chemicals in their brain to become imbalanced.

☐ True*
☐ False
☐ Don't know

6) Genetic tests can/will be able to predict exactly who will, and who will not, develop a mental illness.

☐ True
☐ False*
☐ Don't know

For Knowledge and Risk Perception Questionnaire: