J Clin Psychiatry. Author manuscript; available in PMC 2016 August 01.

Published in final edited form as:
J Clin Psychiatry. 2016 February ; 77(2): e190–e198. doi:10.4088/JCP.14m09710.

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 1–4% 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 waitlist.

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Conflict of Interest Disclosures:
AR, AA, AI, JC, and RR report no competing interests. WGH has received consulting fees or sat on paid advisory boards for: MDH Consulting, In Silico, Lundbeck, Lilly and Roche; received honoraria from Rush University and the University of Ottawa, the Interior and Vancouver Coastal Health Authorities, the Canadian Psychiatric Association; and received grants from the Canadian Institutes of Health Research (CIHR). CH reported serving on the Canadian Association of Genetic Counselors Board of Directors from 2013–2016. JCA reported serving on the National Society of Genetic Counselors Board of Directors from 2011–2013 and has received grants from CIHR, the Michael Smith Foundation for Health Research, and Pfizer (investigator initiated grant).

Role of the sponsor:
Not applicable.

Disclaimer:
The content is solely the responsibility of the authors and does not necessarily represent the official views of the BC Medical Services Foundation, the Canadian Association of Genetic Counsellors, the Mood Disorders Association of BC, the National Society of Genetic Counselors, the University of British Columbia, or the Women's Health Research Institute.

Previous Presentations:
The 5th International Stigma Conference, Ottawa, Canada. June 4 – 6, 2012.
National Society of Genetic Counselors Annual Education Conference, Boston, U.S.A, Oct. 24 – 27, 2012
World Congress of Psychiatric Genetics, Boston, U.S.A., Oct 17 – 21, 2013.
Canadian Association of Genetic Counsellors Annual Education Conference, Toronto, Canada, Nov. 6 – 9, 2013

Additional Contributions:
We thank all those who participated in this study. We thank Dr. Allen Thornton, PhD, Simon Fraser University Department of Psychology, for his assistance in supervising and interpreting the KBIT-2. Dr. Thornton did not receive compensation for this contribution. We would like to thank Claudia Li for her graphic design work; the educational booklet wouldn't have been the same without her. Claudia received compensation for this contribution (Mood Disorders Association of BC funding). We would like to thank Nick Alexander for his technical assistance. Finally, we thank all members of the Translational Psychiatric Genetics Group for their manifold support, insight, guidance, and commitment. None of these individuals have any conflicts of interest with this work.

Methods—A pilot three-arm (each n=40; genetic counseling, a control intervention involving an educational booklet, or waitlist), parallel group, randomized clinical trial was conducted from September 2008–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 one-month follow-up. The Brief Symptom Inventory was administered to control for current symptoms. Analyses included linear mixed effects models and chi-squared tests.

Results—Knowledge increased for genetic counseling/educational booklet compared to waitlist at follow-up (LRT=19.33, df=1, Holm-adjusted p=0.0003, $R^2_{LMM(m)}$=0.17). Risk perception accuracy increased at follow-up for genetic counseling compared to waitlist (Yates' continuity corrected χ^2=9.1, df=1, Bonferroni p=0.003) and educational booklet (Yates' continuity corrected χ^2=8.2, df=1, Bonferroni p=0.004). 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.

Trial registration—clinicaltrials.gov identifier: NCT00713804; http://clinicaltrials.gov/ct2/show/NCT00713804?term=genetic+counseling&rank=4

Keywords

mental illness; genetic counseling; psychiatric disorders; bipolar disorder; schizophrenia; schizoaffective disorder; internalized stigma; perceived control; knowledge; risk perception; randomized clinical trial

INTRODUCTION

The serious mental illnesses (SMIs) schizophrenia, schizoaffective disorder, and bipolar disorder cumulatively affect ~1–4% of the population worldwide[1,2] and, like other common conditions (e.g. 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]. 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 and Canadian Psychiatric Associations[11,12], there is little empirical evidence regarding outcomes of GC in this context.

*This 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.

Two non-randomized 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 (RCT) 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 two intervention groups (GC, EB) would be significantly different than waitlist, with GC/EB mean scores being higher for knowledge, risk perception accuracy, and perceived control over illness, and lower for internalized stigma.

METHODS

Participants & 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–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 (e.g. ≥19 years of age). Individuals were ineligible if their SMI diagnosis was substance-induced, or their ability to provide autonomous informed consent was compromised (e.g. intellectual disability (IQ<70), or currently floridly psychotic and/or intoxicated).

Study Design and Treatments—This was a pilot, prospective, three-arm, parallel RCT (N=120). Randomization was equal (1:1:1) and stratified (44% males, 56% females – 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≤0.01 for each outcome variable (See Figure 1 *Note*). The three arms were: 1. receiving GC from a board certified/eligible genetic counselor (BC/EGC), 2. meeting with a research coordinator to read an educational booklet (EB), and 3. waitlist (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 following study completion. Questionnaires were administered at baseline (T1), immediately post-intervention (T2, GC/EB groups only), and at one-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 a Structured Clinical Interview for DSM disorders[17] and signed a release of information for their psychiatric history records. A psychiatrist (JC) 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 were randomized. For the randomization procedure, equally-sized laminated cards were sorted into two opaque envelopes (one for males, containing 18 GC, and 17 of each EB and WL, and one 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 AR or AI). Baseline appointments lasted ~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- and post-intervention.

GC sessions (~1 hour) were provided by a psychiatric-specialist BC/EGC (JA, CH, AI). The GC session followed standard procedures[19–21]. Specifically, family histories and existing explanations for illness were elicited, 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 below) and information on RR, personalized to family history, if requested. No genetic testing was provided. AI and CH were trained by JA 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 (AR), 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 GC 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] (Supplemental Material). 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 Questionnaire (KRP) was designed for this study (Supplemental Material). 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'd shared information from the GC/EB.

Internalized stigma—The Internalized Stigma of Mental Illness scale (ISMI) 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[27]. 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=.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=.57–.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 three time points for GC and EB groups (longitudinal; n=69), and 2) to 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 (BD, SZ, or SZA) 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 x time interaction terms were conducted. *P*-values for all tests of interactions and main effects were corrected using Holm's correction[31]. Uncorrected *p*-values are also reported for comparison where 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 vs. not accurate (see Table 2 *Note* for definition of 'accurate'), and compared among groups using chi-square tests at each time-point. *P*-values for these tests were included in the Holm adjustment for Knowledge, ISMI and IPQ analyses. Post-hoc pairwise chi-square comparisons were conducted and Bonferonni-corrected where required. We also calculated effect sizes (d) for ISMI, KRP, and IPQ scores and effect sizes (phi or Cramer's *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 in Table 2 and Table 3, respectively.

Knowledge—For analysis 1, there was no significant interaction between time and group (Likelihood ratio test statistic (LRT)=3.13, df=2, p=0.21), and no significant difference between GC and EB for knowledge score (LRT=0.14, df=1, p=0.71); however, there was a significant difference across time points (LRT=60.4, df=2, Holm-adjusted p<0.0001, $R^2_{LMM(m)}$=0.25) with T1 significantly lower than T2 (Tukey-adjusted p<0.001) and T3 (Tukey-adjusted p<0.001), but no significant difference between T2 and T3 (Tukey-adjusted p>0.05) (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=19.33, df=1, Holm-adjusted p=0.0003, $R^2_{LMM(m)}$=0.17) with treatment groups having knowledge scores on average 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=0.005, χ^2=10.8, df=2, Holm-adjusted p=0.11), with EB having significantly fewer accurate responses than GC (Yates' continuity corrected χ^2=8.6, df=1, Bonferroni p=0.003). There were no significant differences between GC and WL, or 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=0.02, Yates' continuity corrected χ^2=5.9, df=1, Holm-adjusted p=0.32). There was a significant difference among groups at T3 (unadjusted p=0.001,

χ^2=13.8, df=2, Holm-adjusted p=0.03), with GC having more accurate responses than both EB (Yates' continuity corrected χ^2=8.2, df=1, Bonferroni p=0.004) and WL (Yates' continuity corrected χ^2=9.1, df=1, Bonferroni p=0.003).

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>0.05), except Alienation, which showed a marginally non-significant difference across time points after p-value adjustment (unadjusted p=0.003, LRT=11.74, df=2, Holm-adjusted p=0.07). Specifically, scores at T1 were significantly higher than at T2 (Tukey-adjusted p=0.002), but there was no difference between T1 and T3, or T2 and T3 (all p>0.05) (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>0.05).

Perceived Control—For analysis 1, there were no significant interaction terms, and no significant differences between GC and EB or time for all five IPQ subscales (all Holm-adjusted p>0.1). For analysis 2, there were no significant interaction terms, and no differences between groups (GC/EB vs. WL) or time for any IPQ subscale (all Holm-adjusted p>0.1).

Impact of GC/EB—Average 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 RCT 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 accuracy for GC as compared to EB and WL. This is subtly, yet importantly, different from previous findings[14,15], where mean risk estimates decreased from a baseline of overestimation, but remained overestimated. Increasing knowledge and risk perception accuracy may play a necessary, though not sufficient, 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 one 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 which showed an effect of GC on ISMI scores[15].

There was a decrease in IPQ consequences subscale mean scores post-intervention that persisted at one-month follow up. Changes in this subscale seem to indicate feelings of greater optimism for the future, and that SMI is perceived to be more manageable. Though 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, this requires further study.

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 towards 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 towards 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 one psychiatric illness (rather than three, 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 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding/Support:

We would like to acknowledge the BC Medical Services Foundation (grant number: BCM07-0155), the Women's Health Research Institute, and the Mood Disorders Association of BC, all of whom contributed financial assistance but had no role in the design or conduct of the study, data collection/interpretation, or manuscript development or approval. CH and AA are supported by the Women's Health Research Institute. JCA was supported by the Canada Research Chairs program, the Canadian Institutes for Health Research, the Michael Smith Foundation for Health Research, and the BC Mental Health and Addictions Research Institute.

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Clinical Points

1. 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 have been limited or unavailable, in the case of bipolar disorder.
2. Physicians seeing patients with serious mental illnesses could consider referring to a specialist psychiatric genetic counselor (who can be found using the “Find a counselor” tool at www.nsgc.org), 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.

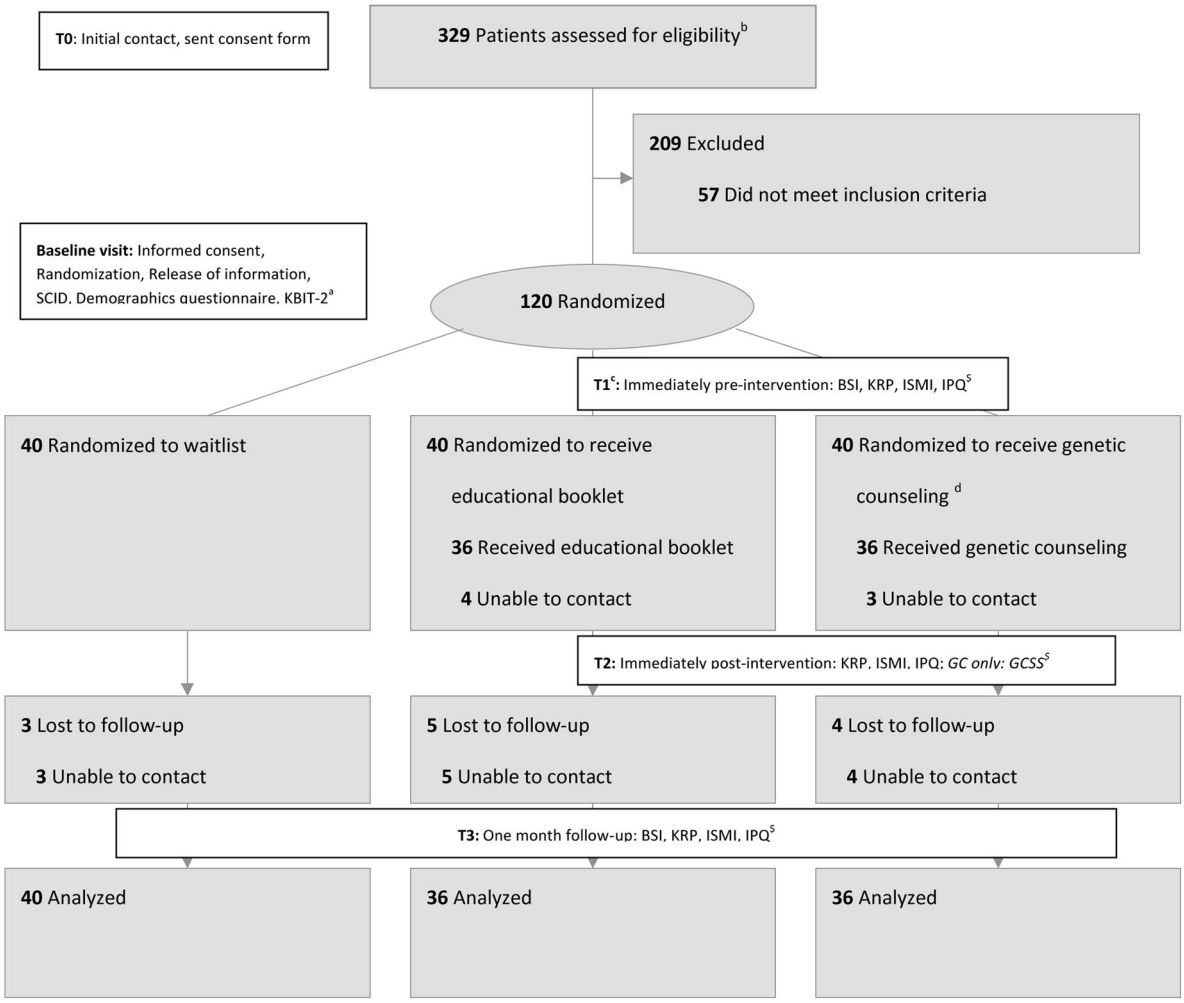

Figure 1.

Flow of participants through the trial

[a] Abbreviations: SCID = Structured Clinical Interview for Diagnosis; KBIT-2 = Kaufman Brief Intelligence Test version 2; BSI = Brief Symptom Inventory (current symptoms); KRP = Knowledge and Risk Perception Questionnaire; ISMI = Internalized Stigma of Mental Illness Scale; IPQ = Illness Perception Questionnaire (perceived control); GCSS = Genetic Counseling Satisfaction Scale. At the time of study initiation, there were no existing data about the impact of GC for individuals with SMI, and the effect sizes for our outcome variables were unknown. Therefore, we based our *a priori* power calculation on the effect of GC 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, emails to mental health professionals and clients' listservs, and mental health practitioners providing information about the study (recruitment brochure) to their patients.

[C]For the waitlist 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 one month follow-up at their request. One of the participants in the waitlist group had received GC for SMI prior to the study. The trial was stopped once the pre-determined 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.

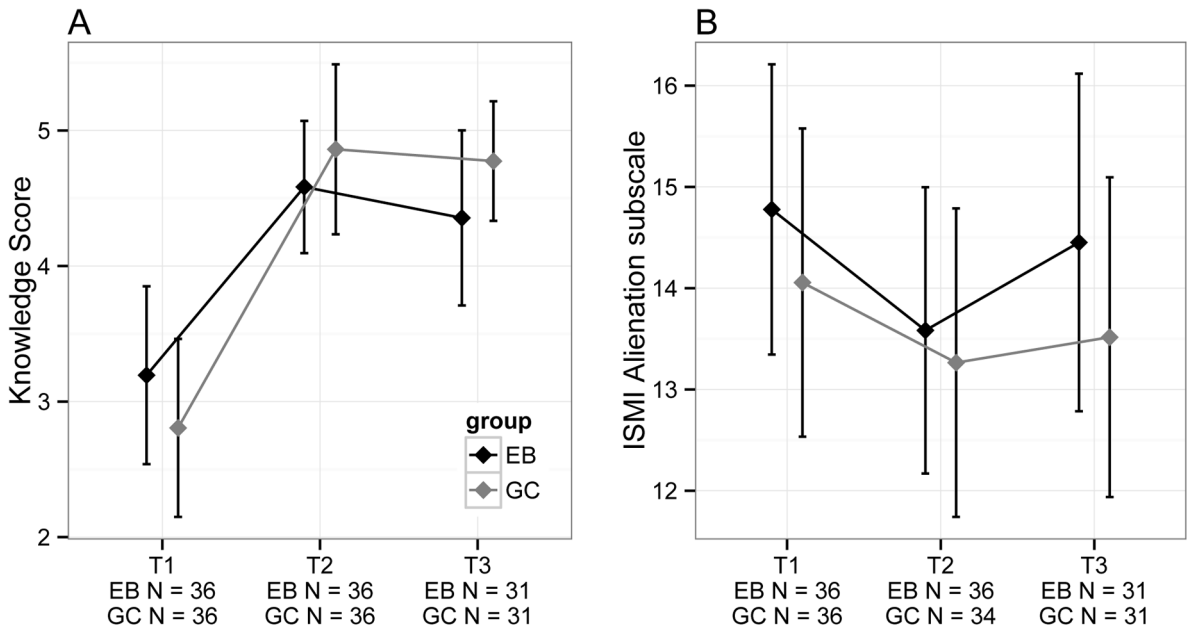

Figure 2.

a) Mean knowledge scores by group and time, b) Mean ISMI alienation subscale scores by group and time. All error-bars represent 95% CI.

Table 1

Sociodemographic Characteristics of Participants (*N*=120)

	n **(%) for all groups**	***n*** **(%) for GC group**	***n*** **(%) for EB group**	***n*** **(%) for WL group**
Sex				
Female	68 (56.3)	22 (55)	23 (57.5)	23 (57.5)
Male	52 (43.7)	18 (45)	17 (42.5)	17 (42.5)
Age (mean, range[a])	41.6 (17 – 73)	40.1 (21 – 62)	40.5 (17 – 68)	44.1 (23 – 73)
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[b]	4 (3.3)	0 (0)	3 (7.5)	1 (2.5)
Global Severity Index (GSI) 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 - CAD)				
<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)

Note. Percentages are based on non-missing data. The average number of years since diagnosis was 11.5 years (range: 0–42).

[a]After consulting with the IRB we allowed one 17 year old to participate, due to their desire to do so, and their capability to provide fully informed consent.

[b]Examples of other diagnoses included Major Depressive Disorder and Major Depressive Disorder with Psychosis.

Table 2

Mean scores (+SD) of the raw data for knowledge, internalized stigma, and perceived control, as well as numbers and percentages of participants reporting 'accurate' RRs, overestimated RRs, and underestimated RRs by group (GC, EB, WL) at each time point (T1, T2, T3).

	T1	T2	T3
Knowledge[a]	Mean Scores (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)	n/a	3.4 (1.8)
Risk Perception	Number (Percentage)		
GC – Accurate	12 (50.0)	20 (80.0)	17 (85.0)
EB – Accurate	3 (8.6)[b]	17 (48.6)	8 (29.6)
WL – Accurate	5 (21.7)	n/a	7 (31.8)
GC – Overestimate	11 (45.8)	3 (12.0)	1 (5.0)
EB – Overestimate	30 (85.7)	14 (40.0)	14 (51.9)
WL – Overestimate	16 (69.6)	n/a	14 (63.6)
GC – Underestimate	1 (4.2)	2 (8.0)	2 (10.0)
EB – Underestimate	2 (5.7)	4 (11.4)	5 (18.5)
WL – Underestimate	2 (8.7)	n/a	1 (4.5)
Internalized Stigma[c]	Mean Scores (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)	n/a	62.7 (17.8)
Perceived Control	Mean Scores (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)	n/a	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)	n/a	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)	n/a	19.2 (3.5)
Illness coherence subscale[e]			

	T1	T2	T3
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)	n/a	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)	n/a	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 three BC/EGCs (CH, AI, JA) 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.

Table 3

Effect sizes for risk perception comparisons at all three time points and for treatment vs. WL (analysis 2; T3 minus T1) for knowledge, internalized stigma, and perceived control.

	Overall effect size [95%CI]	Effect size [95%CI] – Schizophrenia	Effect size [95%CI] – Schizoaffective disorder	Effect size [95%CI] – 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's $V = 0.37$	-	-	-
Risk Perception: T2	phi = 0.35	-	-	-
Risk Perception: T3	Cramer's $V = 0.44$	-	-	-
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]
Perceived Control: 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]
Perceived Control: 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]
Perceived Control: 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]
Perceived Control: 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]

Note. 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.