RUNNING HEAD: Efficacy of genetic counseling for psychiatric disorders

The efficacy of genetic counseling for psychiatric disorders: a meta-analysis

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Abstract:

Psychiatric illnesses are complex, highly heritable disorders that have substantial implications for both affected individuals and their families. Though genetic testing is currently limited in its clinical usefulness in this area, interest in genetic counseling for psychiatric disorders has a relatively long history and many positive outcomes have been posited. Yet, empirical studies of genetic counseling outcomes have been emerging only more recently. The aim of the current meta-analysis was to analyze the efficacy of genetic counseling and explore potential moderators of its effect. An extensive electronic search was conducted investigating the literature published until July 2016. The initial search resulted in 2367 articles, four of which met the inclusion criteria and were included in the quantitative meta-analysis. Effect size parameters and sample sizes for all variables in each study were included. The efficacy has ben demonstrated both at post-intervention and at follow up, with an overall statistically significant effect size of moderate intensity. Implications of this study are discussed in detail.

Key words: genetic counseling, psychiatric disorders, meta-analysis

Introduction

Psychiatric illnesses are complex disorders involving multiple genetic variants (Insel & Collins, 2003; Merikangas & Risch, 2003) that interact with each other and with environmental exposures to place an individual at a greater risk (Pestka, 2003). Relative to many other complex disorders, psychiatric disorders are highly heritable (Kendler, Gallagher, Abelson, & Kessler, 1996), with schizophrenia and bipolar disorder having estimated heritabilities of 60–85% (Parnas et al., 1993; Sham et al., 1994), and 70–85% respectively (Papadimitriou et al., 2003; Prescott & Gottesman, 1993). Though at present, genetic testing is limited in its clinical usefulness in the context of psychiatric illness, genetic counseling (which is neither synonymous with nor dependent on genetic testing) has been shown to be of interest to individuals with psychiatric illness and their families (DeLisi, & Bertisch, 2006; Lyus, 2007). Though "genetic counseling" is often understood as a term used to describe an activity concerned with discussing recurrence risks (Gershon & Alliey-Rodriguez, 2013), it is more accurately defined as "a process of helping people to understand and adapt to the medical, psychological and familial implications of genetic contributions to disease" (Resta et al., 2006), and is therefore highly relevant to the context of psychiatric illness.

Interest in genetic counselling for psychiatric disorders has a relatively long history (Finn & Smoller, 2006; Hippman et al., 2013; Hodgkinson, Murphy, O'Neill, Brzustowicz, & Bassett, 2001; Papadimitriou & Dikeos, 2003; Reveley, 1985; Tsuang, Stone, & Faraone, 2001), and many positive outcomes have been posited (including decreases in internalized stigma and guilt, etc.), empirical studies of genetic counseling outcomes have been emerging only more recently.

The aim of the current meta-analysis was to analyze the efficacy of genetic counseling and explore potential moderators of its effect.

Methods

Literature review

An extensive electronic search was conducted investigating the literature published until July 2016, without a specific starting point. Studies included in the sample were identified through a computer search of the MEDLINE database. The following keywords were used to conduct the literature search: a) genetic counseling and mental health; b) genetic counseling and mental/psychiatric illness/disorders; c) genetic counseling and schizophrenia; d) genetic counseling and schizoaffective disorder; e) genetic counseling and bipolar disorder; f) genetic counseling and autism spectrum disorders; g) genetic counseling and depression; h) genetic counseling and attention deficit and hyperactivity disorder.

Inclusion / Exclusion Criteria for Study Selection

The initial search resulted in 2367 articles. Initial inclusion criteria were quantitative studies, published in English that: (1) investigated the efficacy/effects/impact/outcomes of genetic counseling for psychiatric disorders; (2) clearly defined the genetic counseling session/intervention; (3) clearly defined the psychiatric disorder(s); (4) provided sufficient data reported to allow calculation of effect sizes.

Based on the criteria mentioned above, four studies were identified for inclusion. Figure 1 shows the flowchart of the study selection for the meta-analysis.

Figure 1: Flow diagram showing the review process

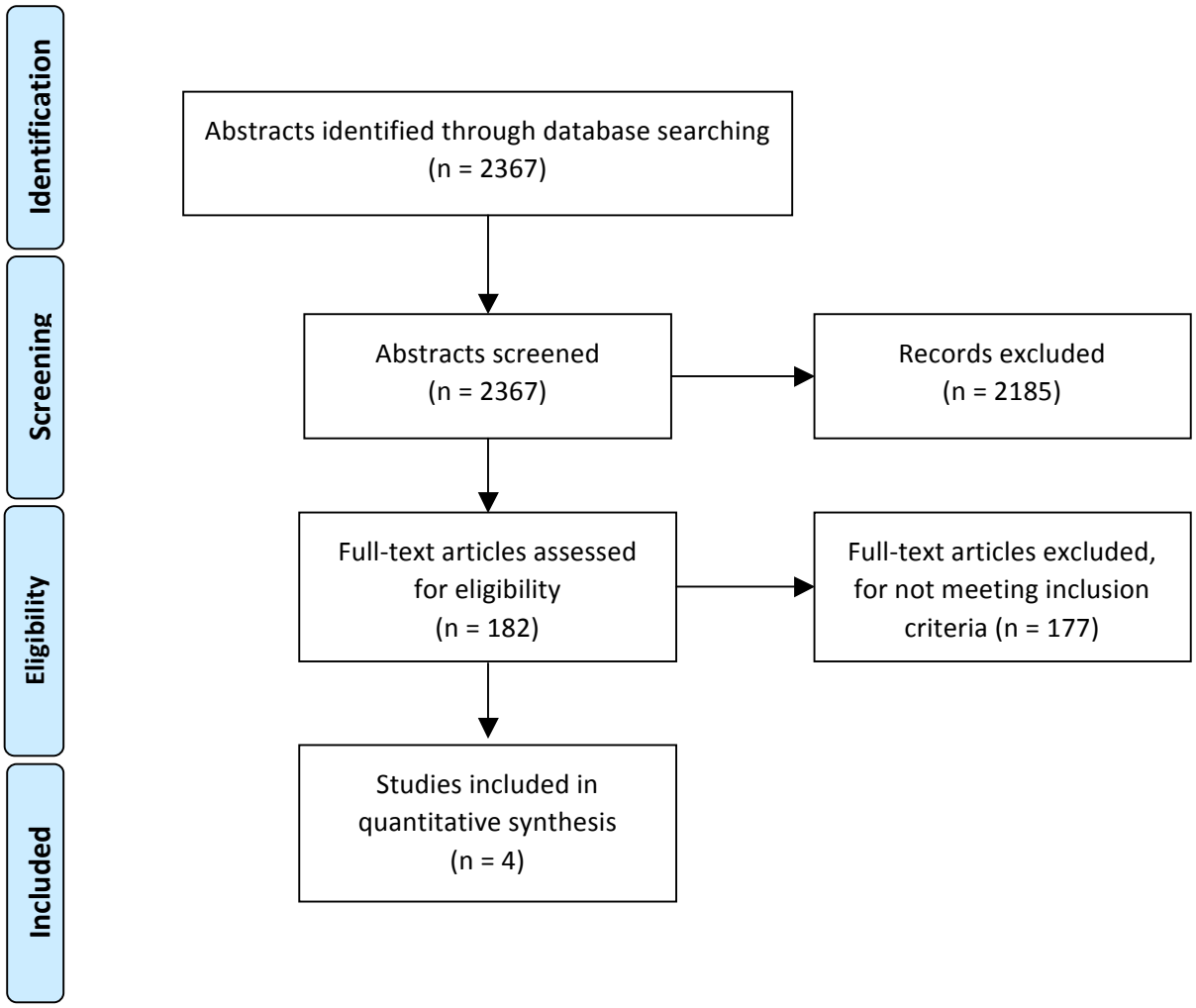


Table 1 presents a summary of these studies and their characteristics, including sample size, type of disorder, outcome measures and assessment procedure.

Table 1. Summary of studies included in the review

Study	Participants (N, Age)	Disorder	Status	Measures	Assessment	Session	Outcome
Costain et al., 2014 (a)	N=25 (M=46.8, SD=12.6)	Schizophrenia Schizoaffective disorder	Patients	Purpose-designed questionnaires Internalized stigma of mental illness	Prior GC 1wk after GC 7wk FU GC	1 (1h)	Recurrence risk perception Concern about risk Knowledge of etiology Satisfaction
Costain et al., 2014 (b)	N=52 (M=60.2, SD=10.3)	Schizophrenia Schizoaffective disorder	Family members	Purpose-designed questionnaires Internalized stigma of mental illness	Prior GC 1wk after GC 7wk FU GC	(1h)	Recurrence risk perception Concern about risk Knowledge on etiology Satisfaction
Inglis et al., 2014	N=75 (M=45.9)	Depression Bipolar Disorder Anxiety Schizophrenia	Patients	Genetic counseling outcome scale Illness Management Self Efficacy Scale	Prior GC 4 wk FU GC	1	Empowerment Self-efficacy
Hipmann et al., 2016	N=120 (M=41.6)	Bipolar Disorder Schizoaffective Disorder Schizophrenia Major Depression	Patients	Knowledge and Risk Perception Questionnaire Internalized Stigma of Mental Health Scale Illness Perception Questionnaire Brief Symptom Inventory	Prior GC After GC 4 wk FU GC	1 (1h)	Knowledge Risk perception Internalized stigma Perceived control Current symptoms

Study coding procedures

Studies were coded to identify: sample size, diagnosis, status of participants, a minimum control group, number of sessions and outcomes.

Statistical analysis

Effect size (ES) parameters as well as pre- and post- means, pre- and post- standard deviations, and sample sizes for all variables in each study were included. Cohen's d (Cohen, 1988) was used as a measure of ES. When data were not presented in this format, we transformed them into Cohen's d to compute the ES. To interpret ES, we used Cohen's (1992) definitions according to which an ES of 0.20 indicates a small effect, 0.50 a medium effect, and 0.80 a large effect. In computing the ES, the intent to treat principle was applied for determining sample size.

Results

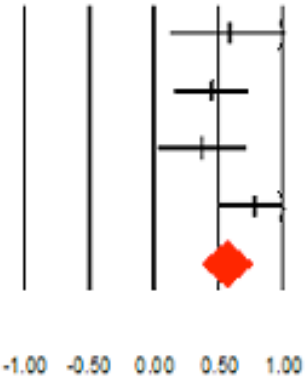
Ideally, when evaluating the efficacy of an intervention data are extracted from particularly rigorous studies such as randomized clinical trials (RCTs). As empirical studies of genetic counseling outcomes have been emerging only more recently, there is only one RCT currently available. As such, 3 of the 4 studies included in the analysis had no control group.

The results of the meta-analysis include pre-intervention vs. post-intervention vs. follow-up comparisons. Details regarding the effect size computed for each subgroup within studies - type of participants: patients vs. family members, type of professionals: GC vs. Non GC and type of outcome: knowledge (understanding of causes, knowledge on etiology) vs. psychological (anxiety, stigma, empowerment, self-efficacy) - are also presented.

Although the heterogeneity of the effects at post-intervention and at follow-up was not significant [Q(3)=3.989, p= .263 and Q(3)=.001, p= .999], due to the fact that studies use different measures and analyze different populations, we decided to perform all analysis with a random effects model. In the moderator analysis, in order to determine the significance of moderators, we used the heterogeneity-based Q.

Table 2. Forest plot and overall effect size of genetic counseling at post-intervention (random effects)

Studyname	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
	Statistics for each study						
Costain et al., 2014 (a)	0.585	0.233	0.054	0.129	1.041	2.516	0.012
Costain et al., 2014 (b)	0.449	0.151	0.023	0.152	0.745	2.966	0.003
Hippman et al., 2016	0.373	0.179	0.032	0.024	0.723	2.092	0.036
Inglis et al., 2014	0.782	0.145	0.021	0.498	1.066	5.393	0.000
Overall effect	0.557	0.099	0.010	0.364	0.750	5.656	0.000

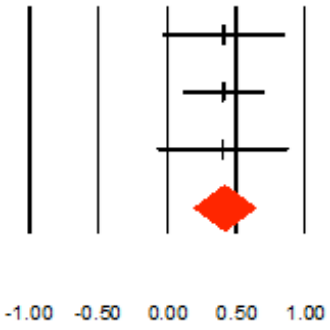


The results show that, from pre-intervention to post-intervention, genetic counseling has an overall statistically significant effect size, d=0.557 (95% CI [.364, .750]), of medium intensity.

The same approach was used to detect the overall effect size at follow-up. Table 3 presents the results for this set of data.

Table 3. Forest plot and overall effect size of genetic counseling at follow-up (random effects)

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Costain et al., 2014 (a)	0.412	0.230	0.053	-0.038	0.862	1.795	0.073
Costain et al., 2014 (b)	0.409	0.155	0.024	0.106	0.712	2.649	0.008
Hippman et al., 2016	0.405	0.244	0.060	-0.074	0.884	1.657	0.098
Overall effect	0.409	0.114	0.013	0.187	0.632	3.603	0.000



As table 3 shows, the overall effect size of genetic counseling at follow-up is statistically significant, d=0.409 (95% CI [.187, .632]), of small to moderate intensity.

In order to test if there is a significant difference between the effect at post-treatment and the effect at follow-up, we performed a Z-test on the difference of effect sizes for all outcomes (from post-treatment to follow-up). The results showed no significant differences of effect sizes between post-treatment and follow-up, Z=0.407, p= .684.

For each time point of the measurement we took into account three major potential moderators of the effect sizes: type of participants (patients vs. family members), type of professional (genetic counselor - GC vs. other specialists – Non GC) and type of outcome (knowledge vs. psychological variables). Table 4 shows the analysis of the three moderators for the effect sizes obtained in the pre-intervention vs. post-intervention comparison.

Table 4. Moderator analysis for the effect size at post-intervention

Moderators	No. of studies	Random effects model		
		Cohen's d	95%CI	Q_b
Type of participants				
family	2	.616	.273-.960	.076 (p= .783)
patients	3	.554	.342-.768	
Type of professional				
GC	2	.601	.298-.903	0.197 (p= .657)
Non GC	2	.499	.170-.828	
Type of outcome				
knowledge	3	.853	.633-1.073	7.614** (p= .006)
psychological	4	.455	.277-.633	

95% Cl: 95% Confidence Interval; **difference significant at p <.01

As table 4 shows, a medium effect size at post-intervention was recorded for both family members (d=.616) and patients (d=.554), with no significant differences between the two Qb(1)=.076, p=.783). Also, the two categories of professionals involved in genetic counseling sessions generated similar effect sizes for GC (d=.601) and Non GC (d=.499), with no significant differences, Qb(1)=.197, p=.657). As far as the type of outcome is concerned, the results showed a large and significantly higher effect size for knowledge (d=.853) than for the psychological outcomes (d=.455), Qb(1)= 7.614, p= .006.

The same type of analysis was performed for the effect size at follow-up. The results are presented in table 5.

Table 5. Moderator analysis for the effect size at follow-up

Moderators	No. of studies	Random effects model		
		Cohen's d	95%CI	Q_b
Type of participants				
family	1	.409	.107- .712	0.000 (p= .997)
patients	2	.409	.082- .735	
Type of professional				
GC	1	.405	-.074 -.884	.001 (p= .984)
Non GC	2	.410	.159- .662	
Type of outcome				
knowledge	3	.881	.641- 1.121	12.132** (p= .001)
psychological	3	.306	.088- .523	

95% Cl: 95% Confidence Interval; **difference significant at p <.01.

As table 5 shows, a small to medium effect size at follow-up was recorded for both family members and patients (d=.409), with no significant differences between the two type of participants, Qb(1)= 0.000, p=.997. The analysis performed for the type of professionals showed that both categories had small to moderate effect sizes [GC (d=.405), non-GC (d=.410)], with no significant differences, Qb(1)= 0.001, p=.984. In terms of outcome, the effect of GC at follow up is similar with the effect at post-intervention: knowledge has a large effect size and significantly higher (d=.881) than psychological outcomes (d=.306), Qb(1)=12.132, p=.001.

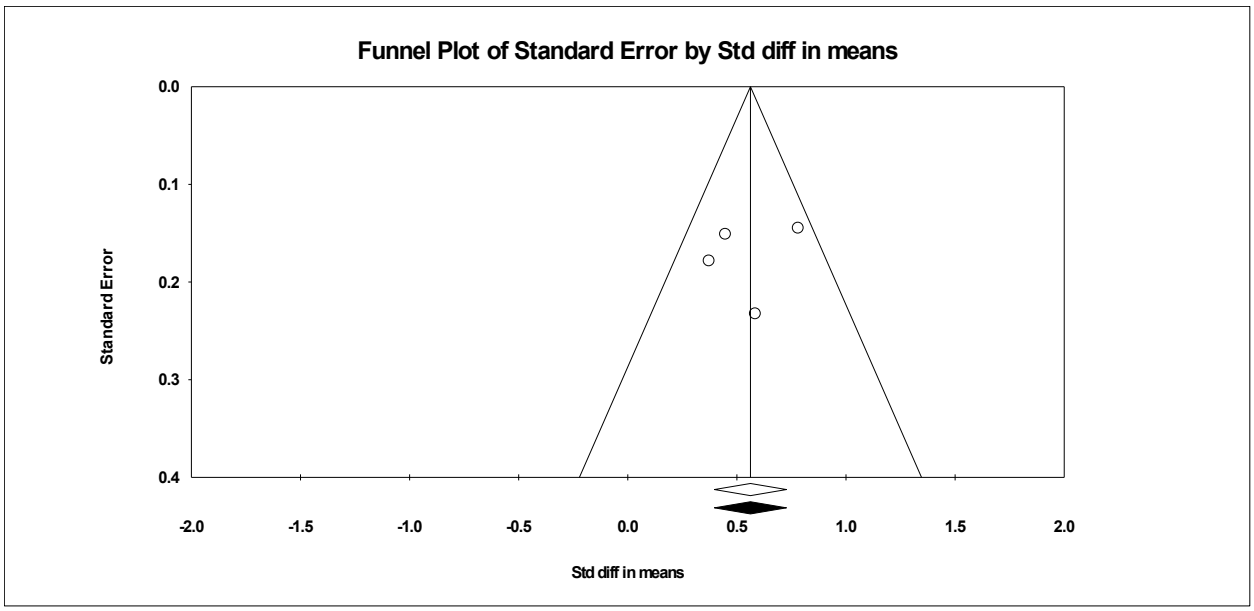


Figure 2. Funnel plot for post-treatment results

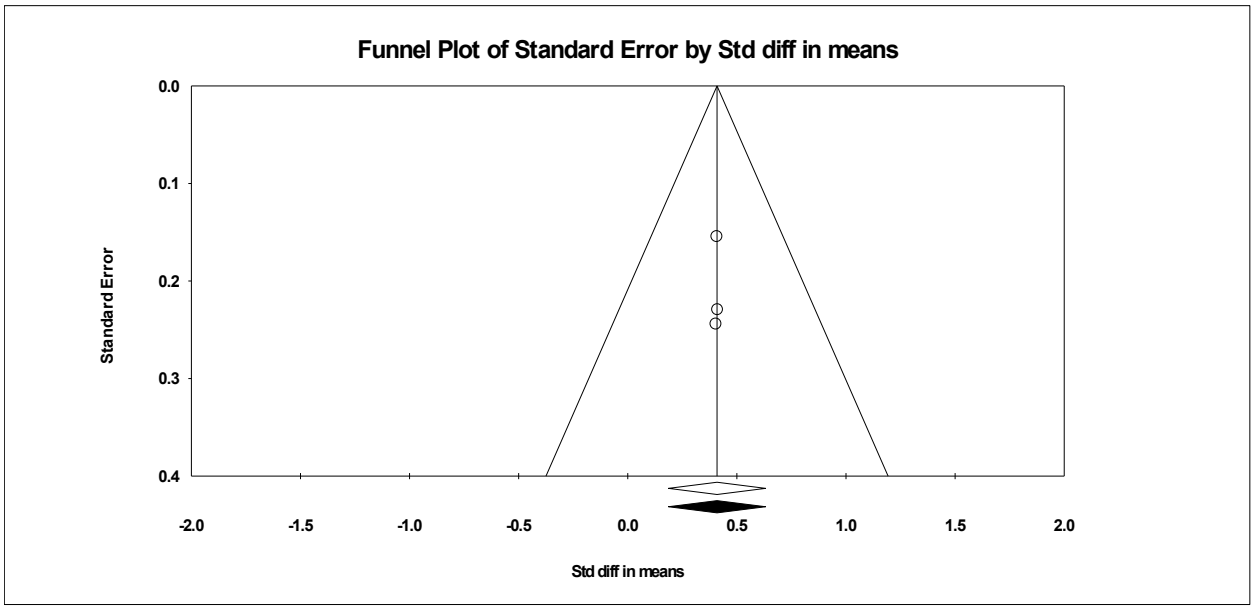


Figure 3. Funnel plot for follow-up results

In order to assess the risk of publication bias for the results of the meta-analysis we performed for both post-intervention and follow-up results an analysis of the funnel plots using

the trim-and-fill method. For the funnel plot, in the absence of publication bias we would expect the studies to be distributed symmetrically about the combined effect size. The trim-and-fill method offers a nuanced perspective, and asks how the effect size would shift if the apparent bias (asymmetrical distribution of studies) was to be removed. Our analysis revealed that for both post-treatment and follow-up effects, there is a symmetrical distribution of the studies around the combined effect (figure 2 and figure 3), and the trim-and-fill method showed that the combined effects and their confidence intervals previously presented were completely unchanged.

Discussion

We found that genetic counseling is beneficial at both post-intervention and follow-up. The genetic counseling efficacy has an overall statistically significant effect size of moderate intensity. The efficacy has been demonstrated at both at post-intervention and at follow up, which indicates that the benefits gained during the genetic counseling session are maintained over time. Clearly, genetic counseling has a measurable effect, but further testing is needed to establish the relative effect compared to other interventions or no-intervention controls.

Results indicate that genetic counseling for psychiatric disorders is effective for both psychological (i.e. anxiety, guilt, empowerment, self-efficacy) and knowledge variables (i.e. understanding of causes, knowledge on etiology), for both family members and patients, when delivered by both genetic counselors and other specialists (effect sizes did appear to be higher for genetic counselors but the differences identified did not reach statistical significance). This suggests that genetic counseling for psychiatric disorders could be effectively delivered by professionals if based on an evidence-based protocol, with supervision provided by experienced

genetic counselors. These results are particularly encouraging given that psychiatric genetic counseling is relatively new and access to specialized clinics for patients and families is not yet widespread and suggest that adequate training and supervision for other specialists, could in fact be particularly timely and appropriate. As far as the type of outcome is concerned, data show clearly that genetic counseling is more effective in terms of improving knowledge rather than other psychological outcomes; this result is not entirely unexpected since the effect on knowledge may be easier to achieve during a one session intervention and less vulnerable to change after the session. Additionally, when discussing these results one should bear in mind that the description of the interventions for the studies included in the analysis was rather variable and may not have been informative enough in order to provide a more comprehensive view of the aspects addressed during the genetic counseling session.

Our data is in line with previous studies (Austin & Honer, 2004; Austin & Honer, 2008; Hunter et al., 2010; Peay et al., 2009) that have discussed or anticipated the potential impact of genetic counseling for psychiatric disorders. The aims of genetic counseling, which include facilitating a clearer understanding of the illness, accurate risk perception and successful adaptation, are directly applicable to psychiatric disorders and existing data shows that psychiatric genetic counseling can in fact have this effect.

The present study is not without its limitations. Although the inclusion criteria were broad, the small number of studies currently available in the literature is rather small. Another limitation that needs to be taken into consideration is the fact that 3 of the 4 studies included in the analysis had no control group; with only one study able to rigorously attribute changes in scores to genetic counseling, results should be viewed with caution.

In spite of these constraints, we did find clear indications that genetic counseling is

effective for psychiatric disorders. In fact, to our knowledge, this is the first metaanalysis investigating the efficacy of genetic counseling for psychiatric disorders. Our data may be particularly important given the early phase of the research in this area. The implications of this study are particularly relevant when considering the process of genetic counseling: specifically, it is the psychological outcomes of genetic counseling that are (arguably) the most impactful and important – at least from the patient perspective (Edwards et al., 2008) - yet, these are the most challenging measures in which to achieve lasting effects. This suggests that a model of genetic counseling that emphasizes the psychological aspects of the intervention may be most useful, and that perhaps there may be a rationale for trialing a model that involves follow-up sessions. The data showing the efficacy of genetic counseling provided in this metaanalysis should encourage theoretical analyses and empirical studies exploring the process and rationale of genetic counseling from a more programmatic perspective.

In conclusion, our analysis showed that genetic counseling is effective for psychiatric disorders. Clearly, future studies need to replicate the present results and refine our conclusions as empirical data on the efficacy and effectiveness of genetic counseling are still pioneering but undoubtedly have enormous implications for research and practice.

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