Interventions facilitating family communication of genetic testing results and cascade screening: A systematic review and meta-analysis

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Introduction

1 in 8 individuals with cancer carry a germline pathogenic variant associated most with Hereditary Breast and Ovarian Cancer (HBOC) or Lynch Syndrome (LS)

Identification of germline pathogenic variants has implications for the patient and her/his blood relatives. Disclosure of genetic test results to untested blood relatives is the sole responsibility of the index patient. However, less than 50% of blood relatives of individuals with HBOC or LS get cancer predisposition cascade genetic testing

Interventions that support mutation carriers disclose genetic test results can facilitate family communication about hereditary cancer risk and provide relatives with accurate and credible information about cascade genetic testing

Aim

This study aimed to identify and synthesize outcomes of interventions designed to facilitate family communication of genetic testing results and/or cancer predisposition cascade genetic testing, with a focus on HBOC and LS

Methods

Inclusion criteria

1. Experimental studies that describe testing of intervention effects and provide quantitative outcomes
2. Published in peer-reviewed journals to enhance methodological rigor
3. The intervention had to:
   ✓ target mutation carriers and/or at-risk individuals belonging to mutation harboring families
   ✓ psychosocially, behaviorally, or cognitively oriented
   ✓ address family communication and/or cascade genetic testing for HBOC or LS either as primary or secondary outcome

Exclusion criteria

1. Studies that were:
   ✓ descriptive, providing qualitative outcomes (e.g., focus group data)
   ✓ protocols of randomized trials, reviews, commentaries, etc.
   ✓ conference abstracts without a subsequent peer-reviewed publication
   ✓ non-English
2. The intervention targeted:
   ✓ disease other than HBOC or LS (e.g., lung cancer)
   ✓ healthcare providers involved in genetic consultation
   ✓ individuals considering genetic testing, but not coming from mutation harboring families (i.e., cascade genetic testing is not applicable)
   ✓ non-adults

Sample: N=14 studies, published between 2002 and 2020

Design: RCT w/ parallel control group (n=12) and cluster RCT (n=2)

Settings: Cancer research institutes and teaching hospitals

- USA (n=7), Australia (n=4), Netherlands (n=2), Sweden (n=1)

Outcomes: Family communication (e.g. frequency, proportion of relatives)

Uptake of cascade genetic testing (e.g. proportion of relatives)

Knowledge of cancer genetics (e.g. number of correct items)

Anxiety

Depression

Risk perception

Figure 1. PRISMA flow diagram for study selection

Table 1. Pooled Effect Sizes of Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of trials</th>
<th>Pooled Effect Size (Hedges’ g, 95% CI)</th>
<th>Q for Heterogeneity</th>
<th>Egger’s I-test for Publication Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family communication</td>
<td>8</td>
<td>0.085 (-0.091 - 0.261)</td>
<td>15.50*</td>
<td>0.53</td>
</tr>
<tr>
<td>Cascade genetic testing</td>
<td>4</td>
<td>0.169 (0.034 - 0.305)</td>
<td>0.925</td>
<td>-0.06</td>
</tr>
<tr>
<td>Knowledge</td>
<td>7</td>
<td>0.244 (0.109 - 0.379)*</td>
<td>15.10*</td>
<td>0.50</td>
</tr>
<tr>
<td>Anxiety</td>
<td>4</td>
<td>0.033 (-0.132 - 0.198)</td>
<td>6.14</td>
<td>-1.47*</td>
</tr>
<tr>
<td>Depression</td>
<td>4</td>
<td>0.183 (0.033 - 0.334)*</td>
<td>2.39</td>
<td>2.89</td>
</tr>
<tr>
<td>Risk perception</td>
<td>3</td>
<td>0.007 (-0.223 - 0.25)</td>
<td>1.89</td>
<td>0.97</td>
</tr>
</tbody>
</table>

*p value ≤ 0.05

Conclusions

✓ Interest about family communication and cascade genetic testing for HBOC and LS worldwide, but there are few rigorously tested interventions

✓ Quality appraisal varies between the studies

✓ Interventions show promise for improving cancer predisposition cascade genetic testing for HBOC and LS