BRIEF COMMUNICATION

Intentions to share exome sequencing results with family members: exploring spousal beliefs and attitudes

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Abstract

Given familial implications of genetic information, it is important to understand intentions to share carrier results with family members. To our knowledge, no studies among individuals undergoing exome sequencing have used dyadic data analysis to examine the effect of spousal perceptions and beliefs. Survey responses from 136 individuals (68 couples) undergoing exome sequencing in a research study were analyzed using dyadic analysis (the actor-partner interdependence model). Intention to share carrier results with family members was correlated between spouses ($ICC = 0.43$; 95% CI: 0.21–0.61; $p = 0.004$), as was worry about risk of a genetic condition in the family ($ICC = 0.45$; 95% CI: 0.24–0.62; $p < 0.001$). Perceived value of result and worry about risk of a genetic condition in the family were associated with one's own intentions to share carrier results. However, spousal status on these variables did not explain additional variance in an individual's intentions. Although we found no partner effects on intentions, spouses have comparable intentions to share carrier results, suggesting it may be important to account for non-independence in other research studies.

Introduction

With increasing use of exome sequencing, detection of carrier status for autosomal recessive conditions will also increase. The typical individual carries ~3–5 recessive, lethal variants [1]. It is important to understand intentions to communicate with family members about receiving and responding to these types of sequencing results.

Dyadic analyses describe studies of interpersonal phenomena at the level of the dyad or pair [2]. The application of dyadic methods in healthcare research is increasing (e.g.,

spousal, physician-patient, parent-child, and physician-nurse relationships) [2–4]. Among spouses, there is evidence that couples' health behaviors (i.e., diet, exercise, smoking, and preventative screening) are often concordant [5, 6]. Furthermore, theory suggests that couples have significant influence on each other's health decision making [7]. However, to our knowledge, no previous research has examined how spousal perceptions and attitudes affect decisions to share genomic test results with family members.

Perceived value, worry, and attitudes all appear to influence how individuals interact with genomic results [4–7]. For example, individuals are more likely to want their genome sequenced (clinically or for research), and receive sequencing information when it is perceived as providing value to other family members [8]. Women with higher levels of worry about cancer communicate less openly about genetic test results with relatives [9]. Attitudes predict intentions to engage in family communication about risk information in a range of monogenic conditions [10]. In addition to this empirical evidence, the Health Belief Model relates these constructs to predict individuals' prevention efforts [11]. However, it is unclear how spousal standing on these cognitions might be related to one's intentions to share sequencing results with family.

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The high proportion of spouses enrolled in the ClinSeq[®] exome sequencing study affords an opportunity to study dyadic effects in the sequencing context. Our study had two objectives; first, to assess whether beliefs about perceived value of sequencing results, worry about genetic conditions in the family, and attitudes toward carrier results are correlated between the two spouses. Secondly, we explored how one's own and one's spouse's responses are related to intentions to share results with other family members.

Given the aforementioned evidence in other health related areas [5–7] and the interpersonal implications for exome sequencing, we hypothesized that spouses' intentions to share their results with family members would be correlated. Further, we hypothesized that spousal beliefs (perceived value of results, worry and attitudes) would explain unique variance in intentions to share carrier results with family members (above the role of one's own beliefs).

Methods

Participants and recruitment

Individuals aged 45–65 in the greater Bethesda area, USA were recruited to participate in a clinical exome sequencing study [12] using word of mouth and advertisements in local newspapers and at health-care facilities. Participants were informed that they may have the opportunity to receive medically relevant sequencing results, when available. Prior to any opportunity to receive sequencing results, participants completed a baseline survey either online or on a paper copy which was mailed to them. The cross-sectional survey included a range of measures assessing attitudes, intentions, and behaviors related to exome sequencing.

Although participants were not intentionally recruited in couples, a substantial number of spousal pairs were identified in the final sample. Spouses were identified in one of three ways; (1) if they checked an item on the baseline survey stating that their spouse was a ClinSeq[®] participant (verified by street address), (2) if participants had the same street address and last name as another participant (other relations, like siblings, were excluded from the sequencing study), or it was indicated on their pedigree that their spouse was enrolled in the study, or (3) if they self-disclosed to a staff member that their spouse/partner was also in the study.

Outcome variables

Intentions to share carrier results with “family members” were assessed as the sum of two items: intentions to share carrier results with family members (1 = definitely no to 5 = definitely yes) and likelihood of sharing carrier results

with family members (1 = extremely unlikely to 7 = extremely likely). “Carrier result” was defined as “a gene variant that does not affect your health, but may be important to the health of other relatives, such as your children”. The correlation between the two items was $r = 0.75$, $p < 0.001$.

Predictor variables

Perceived value of results was assessed using a mean score of three items about the value of sequencing results (in maintaining own and family's future health) and the usefulness of results to a physician. Possible scores ranged from 1 (disagree; of low value) to 6 (agree; of high value). Cronbach's alpha was 0.87.

Worry about risk of a genetic condition in the family was assessed using one item: “On a scale of 1 (low)—7 (high) how worried are you that your relatives could be affected with a genetic condition that you have passed on?”.

Attitudes toward carrier results were assessed using a previously published six-item scale [13]. Participants indicated their response on a 7-point scale, in reference to carrier results to: “for me, learning such a result would be” followed by the semantic differentials: “bad to not bad”, “not beneficial to beneficial”, “harmful to not harmful”, “not a good thing to good thing”, “not worthwhile to worthwhile” and “unimportant to important”. Cronbach's alpha was 0.94.

Covariates

Demographic characteristics were collected: age, gender, race, ethnicity, education, household income, have children with spouse in study and whether they had a previous genetic test.

Analysis

As the spousal pairs included heterosexual and a homosexual couple, data were treated as indistinguishable, meaning we did not use any systematic method to order the scores from the two dyad members (e.g., gender). Non-independence was measured using the intraclass correlation coefficient (ICC) [14]. Dyadic effects were examined using the actor-partner interdependence model (APIM) [2]. Using a multilevel modeling technique, the APIM tested interactions between predictor variables and the outcome variable (intentions to share carrier results). The APIM allows identification of interactions of one's own variables (actor effects) and interactions of partner's variables with own variables (partner effects). To account for potential order effects whereby the first spouse could influence responses from the second spouse, the APIM was repeated with order

of survey completion included as a covariate. We additionally treated the spouses as distinguishable based on order of survey completion. Data were analyzed using SPSS (Released 2011. IBM SPSS Statistics for Macintosh, Version 20.0. Armonk, NY: IBM Corp).

Power calculation

Based on the number of dyads (68) with complete data available for analysis we calculated that we could detect correlations of 0.35 and above with 80% power and alpha 0.05 [2].

Results

Descriptive statistics

From a total dataset of 725, 136 individuals (68 dyads) were identified to be in a spousal pair with survey data available for both individuals. The sample consisted of 52% males (one spousal pair included two males). Most were white (97%), educated at the college graduate level or higher (97%), had children with their spouse in the study (71%) and had not previously undergone genetic testing (78%). (Table 1).

Mean worry about risk of a genetic condition in the family was 4.0 out of 7 ($SD = 1.9$). Attitudes were high overall with a mean of 6.5 out of 7 ($SD = 1.0$) as was the perceived value of results ($M = 4.0$ out of 6, $SD = 0.8$). Overall, individuals had high intentions to share carrier results with their family members ($M = 9.9$ out of 12, $SD = 2.3$).

Non-independence

The outcome measure, intentions to share carrier results with family, was correlated between spouses. Of the three predictor variables tested, only worry about risk of a genetic condition in the family was correlated between spouses (Table 2).

Covariates

None of the covariates included in bivariate analyses were associated with intentions to share carrier results (all $p > 0.05$).

Dyadic analysis: actor effects

Two actor effects (of the three predictor variables tested) were associated with intentions to share carrier results with family: an individual's own perceived value of results and

Table 1 Participant characteristics ($N = 136$)

Demographic characteristic	Frequency n (%)
Gender	
Male	70 (51)
Female	66 (49)
Race	
White	132 (97)
Other	4 (3)
Ethnicity	
Hispanic/Latino	3 (2)
Non-Hispanic/Latino	133 (98)
Age (mean, SD)	62 (5.3)
Education ($N = 129$)	
Less than college grad	11(9)
College grad/beyond	118 (91)
Household income ($N = 125$)	
≤\$100,000	17 (14)
>\$100,000	108 (86)
Have children together: yes	48 couples (71)
Ever had a genetic test: yes	30 (22)

worry were associated with intentions to share carrier results (Table 3).

Dyadic analysis: partner effects

There was a partner effect estimate of 0.47 for perceived value of results, but this effect was non-significant ($p = 0.07$). Partners' worry and attitudes were not associated with intentions to share carrier results. (Table 3)

Actor and partner effects did not change significantly when accounting for order of survey completion among spouses.

Discussion

We found that intentions to share carrier results with family were correlated among spouses, as were levels of worry about risk of a genetic condition in the family. Nevertheless, we did not detect significant partner effects, that is, we saw no associations between partners' beliefs or attitudes and individuals' intentions to share carrier results with family.

Participants with higher worry had lower intentions to share carrier results. Prior research examining worry and behavior (e.g., cancer screening) has found mixed results, with both positive and negative associations reported [15, 16]. Despite worry being correlated among spouses in our study, spousal worry was not associated with one's own intentions to share carrier results. Attitudes were not associated with intentions to share carrier results, perhaps

Table 2 Non-independence between couples

Variable	Intraclass correlation coefficient (<i>ICC</i>)	95% confidence interval	<i>P</i> value
Intentions to share carrier results with family	0.43	0.21–0.61	0.004
Perceived value of results	0.155	–0.087–0.381	0.104
Worry about risk of a genetic condition in the family	0.45	0.24–0.62	<0.001
Attitudes toward carrier results	–0.076	0.162–0.307	0.265

Table 3 Results of the APIM analyses

APIM parameters	β estimate	95% CI	<i>P</i> value
Actor effects			
Perceived value of results	0.55	0.043, 1.05	0.03
Worry about risk of a genetic condition in the family	–0.27	–0.52, –0.03	0.03
Attitudes	0.078	–0.41, 0.56	0.8
Partner effects			
Perceived value of results	0.47	–0.03, 0.98	0.07
Worry about risk of a genetic condition in the family	0.082	–0.17, 0.33	0.5
Attitudes	0.20	–0.27, 0.67	0.4

because (1) participants overall had highly positive attitudes (a ceiling effect), or (2) we did not specifically explore participants' attitudes about sharing carrier results with family members, only about intentions to receive carrier results for themselves.

The Family Systems Theory has been applied previously to research about family communication of genetic information [17]. This theory assumes individuals do not operate and make decisions in a vacuum; rather, they are part of a wide network of social systems. Despite this recognition, there is a paucity of research employing dyadic analysis in this area. One qualitative study that used social network analysis found family communication about genetic information is more likely to occur in the presence of cohesion, leadership, and lack of conflict [18]. Our analyses did not specifically explore these family functioning concepts.

Dyadic analysis methods such as the APIM described here are important to consider among genome sequencing cohorts potentially containing dyads such as partners or offspring. Close to 20% (136/725) of participants in our cohort enrolled with their spouse; this observation may be useful to predict likelihood of enrollment of dyads in future sequencing studies. Key examples include: (1) the “All of Us Research Program”, which aims to enroll over one million individuals and will include analysis of genetic information (<https://www.nih.gov/research-training/allofus-research-program>)—often among multiple family members, and (2) pediatric sequencing studies where trio analyses (sequencing of affected child and parents) are the most

common approach [19]. In studies like these, statistical approaches like the APIM should be used to account for non-independence. It is important to control for non-independence, as non-independent data can bias *p* values in significance testing [20]. Furthermore, analyzing data through the APIM could lead to novel insights about consequential decision making and behavior in dyads. Although we did not detect any partner effects in our study, the correlations between variables support the notion that family communication studies should incorporate dyadic models.

The strengths of our study include the uniqueness of the sample and analytical methods; however, there are several limitations. The parent study was not designed to explore partner relationships or communication; variables like relationship dynamics and satisfaction were not collected. Further, our small sample size did not allow us to detect small individual or dyadic effect sizes that may be present. Despite these limitations, our results provide a preliminary exploration of dyadic relationships among spouses enrolling in an exome sequencing study. Future studies should examine additional factors such as communication and relationship dynamics to better understand family communication intentions with spouses or other dyads.

Conclusion

Although we found spouses' intentions to share carrier results with family members to be non-independent, spousal perceptions, attitudes, and worry did not explain additional variance in intentions. To our knowledge, this study is the first to assess the impact of spousal effects among individuals undergoing exome sequencing. Although we found no partner effects, we did find correlations among predictors and outcomes. As such, it may be important to consider accounting for non-independence in other research studies.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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