

Anencephaly: Insights for Genetic Counseling

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Abstract: Genetic counselors may meet with expectant parents to facilitate decision making following prenatal diagnosis of anencephaly. Factors that contribute to pregnancy management decisions and the perceived helpfulness of genetic counseling in this patient population are not fully understood. Women and their male partners who previously received a prenatal diagnosis of anencephaly completed mixed-methods questionnaires to assess decision-making factors and the impact of genetic counseling. Lethality of the anomaly and religious and ethical views factored most into pregnancy management decisions. Over half of participants met with a genetic counselor; however nearly one-third did not find the meeting helpful. Genetic counselors may need to prioritize psychosocial support and provision of resources to meet the needs of expectant couples receiving a prenatal diagnosis of anencephaly.

Keywords: anencephaly, pregnancy, abortion, genetics

Anencephaly, a neural tube defect not compatible with long-term survival, is caused by failure of the rostral end of the neural tube to close by roughly day 26 post ovulation (Detrait et al., 2005). The etiology of anencephaly is largely unknown but thought to be primarily multifactorial in nature, inclusive of genetic risk factors. However, chromosome anomalies account

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30 for only approximately 1% of cases and specific genetic variants that
31 appear to be causal have only rarely been identified (Chen et al., 2017;
32 Goetzinger, Stamilio, Dicke, Macones, & Odibo, 2008). Referral for genetic
33 counseling may not be intuitive following diagnosis of anencephaly, a
34 condition for which the likelihood of identifying a genetic etiology is
35 presently low. However, when lethal fetal anomalies are identified, the
36 foremost decision faced by women and their partners is whether or not to
37 continue the pregnancy.

38 Even in the absence of an identifiable genetic etiology, genetic
39 counseling may be beneficial, as genetic counselors couple information
40 giving with psychosocial counseling, enabling patients to make informed
41 decisions. Unfortunately, investigations into the perceived helpfulness of
42 genetic counseling following diagnosis of multifactorial conditions are
43 scarce. One survey of parents of children with psychotic disorders reported
44 that all participants (9/9) found genetic counseling helpful (Austin & Honer,
45 2008). Another study assessing perceptions of genetic counseling for alcohol
46 addiction reported that 62% of participants felt that genetic counseling
47 could potentially be beneficial (Kalb, Vincent, Herzog, & Austin, 2017).
48 However, the perceived helpfulness of genetic counseling for multifactorial
49 conditions in a prenatal setting has yet to be investigated.

50 While genetic counselors often facilitate decision making following
51 detection of fetal anomalies, the factors that ultimately contribute to the
52 decision to continue or terminate a pregnancy are not fully understood.
53 Intrinsic factors reported to influence the decision include maternal age,
54 ethnicity, education, religious and moral views, severity of the anomaly,
55 and gestational age at diagnosis (Chaplin, Schweitzer, & Perkoulidis,
56 2005; Hawkins, Stenzel, Taylor, Chock, & Hudgins, 2013; Nell et al., 2013;
57 Pryde et al., 1992; Redlinger-Grosse, Bernhardt, Berg, Muenke, &
58 Biesecker, 2002a; Schechtman, Gray, Baty, & Rothman, 2002; Shaffer,
59 Caughey, & Norton, 2006). The most consistently reported variable in
60 electing termination has been the severity of the fetal anomaly. Prior
61 studies have shown that women are more likely to continue pregnancies
62 in the presence of minor fetal anomalies that have a more favorable
63 outcome (Chaplin et al., 2005; Hawkins et al., 2013; Nell et al., 2013;
64 Pryde et al., 1992; Schechtman et al., 2002; Shaffer et al., 2006). Therefore,
65 it could be assumed that lethal fetal diagnoses, such as anencephaly would
66 be terminated at rates greater than fetal diagnoses compatible with
67 survival. However, a recent review found that in North America one in
68 four (26%) pregnancies prenatally diagnosed with anencephaly were
69 continued (Johnson et al., 2012). This is a greater percentage continuing
70 than what has been reported for Trisomy 21 (13% continued), a condition
71 compatible with survival (Shaffer et al., 2006). This suggests that decision
72 making following diagnosis of anencephaly may differ from fetal diagnoses
73 compatible with survival and warrants further attention.

74 The purpose of this project was to explore factors that influenced
75 pregnancy management decisions subsequent to receiving a prenatal
76 diagnosis of anencephaly and to investigate the perceived helpfulness of
77 genetic counseling in this patient population.

78 **Materials and Methods**

81 **Participants**

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83 Participants were recruited from the Hereditary Basis of Neural Tube
84 Defects study conducted at Duke University Medical Center and through
85 several anencephaly Facebook support groups. Eligible participants were
86 women and men who previously lost a pregnancy to anencephaly.
87 Participants were included so long as the pregnancy had already ended,
88 irrespective of how long ago the pregnancy occurred. Questionnaires were
89 mailed to 215 women and 177 men who responded to study
90 advertisements between March and October, 2013. Approval to conduct
91 this study was obtained from the Institutional Review Board at Duke
92 University Medical Center (Pro00042930). All participants provided
93 written informed consent.

95 **Measures**

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97 Self-administered questionnaires were utilized due to the sensitive
98 topic under investigation and to allow inclusion of greater numbers of
99 participants. Questionnaires included two items from the Duke
100 University Religion Index (DUREL), which measured organizational
101 religious activity such as attending church or other religious meetings and
102 non-organizational religious activity such as prayer, meditation, or Bible
103 study (Koenig & Bussing, 2010). Participants also completed the
104 Pregnancy History and Choices Questionnaire (PHCQ), a mixed-methods
105 questionnaire containing 32 quantitative multiple-choice questions and
106 seven qualitative, open-ended questions, developed specifically for this
107 project to collect relevant information about demographics, decision
108 making factors and genetic counseling. Responses to the following four
109 qualitative questions from the PHCQ are presented herein;

- 111 1) Please describe the reasons why you decided to continue/not to
112 continue the pregnancy after receiving the diagnosis of anencephaly?
- 113 2) Do you regret any of the choices you made during or after your
114 pregnancy? If yes, please explain what you regret doing or not doing
115 and why you regret that choice.
- 116 3) If you met with a genetic counselor, what were the most helpful things
117 she/he said or did?

118 4) What advice would you give to health care providers working with
119 women/couples who learn during pregnancy that their baby has
120 anencephaly?
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122 Qualitative responses were coded into themes by the first author.
123 Responses to question three and four were compared to a genetic
124 counseling practice analysis performed by the American Board of Genetic
125 Counseling (ABGC) (Hampel et al., 2009). Representative comments were
126 selected for inclusion in the manuscript that exemplified frequently
127 reported participant viewpoints.

128 Participants also completed three standardized instruments
129 commonly used in pregnancy loss research; the Perinatal Grief Scale
130 (PGS), Impact of Event Scale – Revised (IES-R) and Beck Depression
131 Inventory-II (BDI-II), which measure symptoms of grief, post-traumatic
132 stress and depression, respectively (Creamer, Bell, & Failla, 2003; Steer,
133 Clark, Beck, & Ranieri, 1999; Toedter, Lasker, & Janssen, 2001).
134 Quantitative analyses of psychosocial outcome were reported previously
135 (Cope, Garrett, Gregory, & Ashley-Koch, 2015).
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137 **Statistical Methods**
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139 Participant demographics were tested for association with pregnancy
140 outcome (terminate or continue), including organizational religious activity
141 and non-organizational religious activity as covariates. Pregnancy outcome
142 and seeing a genetic counselor were also tested for association with
143 endorsement of regrets. Analyses including both partners were performed
144 using generalized estimating equations (GEE) to control for correlation
145 between the mother and father for a particular pregnancy. Gender-
146 stratified analyses were performed using logistic regression. All analyses
147 were conducted using SAS version 9.4 (SAS Systems, Cary, NC). A *p*
148 value<0.05 was considered statistically significant for all data analyzed.
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150 **Results**
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152 A total of 160 women (74%) and 110 of their male partners (62%)
153 completed the study questionnaires. Enrolled participants were primarily
154 from throughout the United States, with 15 participants from the United
155 Kingdom, Canada or Australia. The median time between the end of the
156 pregnancy and participation in the current study was 3.2 years, ranging from
157 0.1 to 32.9 years. Demographics of the study group are presented in Table I.
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162 **Table I** Study participant demographics (N=270; 160 women, 110 men)

	Women (n)	Women (%)	Men (n)	Men (%)
Ethnicity/Race				
Non-Hispanic Caucasian	152	95	99	90
Hispanic	2	1	5	5
Asian	2	1	3	2.5
Mixed race	4	3	3	2.5
Age at Pregnancy				
Teen (17-19)	3	2	0	0
Young adult (20-25)	31	19	13	12
Adult (26-34)	106	66	72	65
Older adult (35-44)	20	13	25	23
Time Since Pregnancy Ended				
< 1 year	24	15	22	20
1-2 years	45	28	29	26
3-5 years	44	28	38	35
6-9 years	24	15	11	10
10+ years	23	14	10	9
Organizational Religious Activity				
Never	39	24	34	31
Once a year or less	5	3	7	6
A few times a year	23	14	12	11
A few times a month	20	13	12	11
Once a week	41	26	32	29
More than once/week	32	20	13	12
Non-organizational Religious Activity				
Rarely or never	51	32	55	50
A few times a month	1	1	0	0
Once a week	0	0	0	0
Two or more times/week	40	25	16	15
Daily	42	26	24	22
More than once a day	26	16	14	13
Genetic Counseling				
Yes	91	57	60	55
No	63	39	42	38
Unsure	6	4	8	7
Pregnancy Decision				
Terminate	67	42	48	43.5
Continue	90	56	59	53.5
No Choice	3	2	3	3

Table II Reported reasons to terminate or continue the pregnancy

Chi-square test was employed to test for differences between women and men. Fisher's exact test was used for comparisons with <5 observations.

Reported Reasons to Terminate					
	Women (N=60)		Men (N=41)		Gender Differences
	N	%	n	%	p-value
No chance the baby would survive	31	52	24	59	0.50
Too emotionally difficult	24	40	10	24	0.10
Doctor advised termination	15	25	2	5	0.01
Didn't want baby to suffer	14	23	4	10	0.11
Best for sibling/other young family members	10	17	1	2	0.03
Didn't want to delay trying to conceive again	9	15	0	0	0.01
Health of the mother	7	12	11	27	0.05
Didn't want to face questions from strangers	6	10	0	0	0.08
Felt it was the best decision for the other parent	3	5	7	17	0.09

Reported Reasons to Continue					
	Women (N=90)		Men (N=57)		Gender Differences
	n	%	n	%	p-value
Religious beliefs	30	33	24	42	0.28
Not their decision to make (let nature take its course)	27	30	9	16	0.05
Wanted to allow the baby to have as much life as possible	26	29	12	21	0.29
Felt that life is valuable in all forms	25	28	16	28	0.97
Wanted to meet/allow others to meet the baby	19	21	9	16	0.42
Do not believe in abortion for any reason	18	20	8	14	0.36
Wanted as much time with the baby as possible	17	19	5	9	0.09
Had already bonded with the baby	16	18	1	2	0.003
Couldn't be the one to end his/her life	14	16	4	7	0.20
Multiple gestation pregnancy	11	12	6	11	0.75

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Factors Influencing Decision Making

Participants who attended church or other religious meetings ($p < 0.0001$) or engaged in private religious activities such as prayer ($p < 0.0001$) were more likely to continue the pregnancy. We observed a trend where participants were more likely to terminate the pregnancy if the baby was a boy ($p = 0.09$). Parental age, education, birth of a prior

178 healthy child, and genetic counseling were not associated with the
179 decision to terminate or continue.

180 Women who terminated the pregnancy reported a total of 26 distinct
181 reasons why they chose to terminate. Men whose partner terminated the
182 pregnancy reported 11 reasons why termination was chosen. Reasons to
183 terminate reported by 10% or more of women or men are listed in Table II.

184 The most commonly reported reason to terminate by both women and
185 men was the fact that there was no chance the baby would survive,
186 "Because my baby had no chance at life, no possibility of living, we decided
187 to say goodbye at 20 weeks [47-year-old woman]." Many participants
188 expressed not being able to continue the pregnancy knowing the baby
189 would die. A 50-year-old man wrote, "We were told the child would die.
190 There was no hope of other outcome, pregnancy in that circumstance
191 seemed cruel." Some participants expressed that terminating the
192 pregnancy was simply speeding up the inevitable, "I equated myself to a
193 life support machine and my baby to a life support patient with a coma
194 [28-year-old woman]."

195 Significant gender differences existed for four reported reasons to
196 terminate the pregnancy. Women were more likely to report that
197 termination was elected because their doctor had advised that option. For
198 example, a 30-year-old woman wrote, "My OB sent us to a maternal fetal
199 medicine doctor and both indicated to us that a D&E would be the best
200 way to go." Women were more likely to report feeling that termination was
201 best for their other child(ren), "I had fears for my older daughter because
202 I was afraid if she saw the baby in that condition she wouldn't know how
203 to handle it [28-year-old woman]." Women were also more likely to report
204 not wanting to delay conceiving again. One 33-year-old woman explained,
205 "We had been dealing with infertility for 2.5 years prior. Due to our ages,
206 it would not be medically wise to be out of commission for another year
207 (birth, recovery, etc.). We wanted a take-home child." In contrast, men
208 were more concerned about the health and wellbeing of the mother,
209 "Because there was some health risks at stake and I wouldn't want my
210 wife to go through any more emotional and physical stress [28-year-old
211 man]." Of note, five participants (5%) reported that they didn't have
212 enough time to consider other options and two participants (2%) reported
213 that they were not presented with any other options.

214 Women who continued the pregnancy reported a total of 24 distinct
215 reasons why they chose to continue. Men whose partner continued the
216 pregnancy reported 19 reasons why continuation was chosen. Reasons to
217 continue reported by 10% or more of women or men are listed in Table II
218 (above). For both women and men, the most commonly reported reason to
219 continue the pregnancy was religious beliefs. A 46-year-old woman
220 explained simply that, "God is the giver and taker of all life. The decision
221 is His." Many participants expressed religious viewpoints that guided

222 their decision, “Being Catholic, my husband and I are believers in God’s
223 plan of natural conception to natural death. We feel blessed to have
224 carried an angel for Him [25-year-old woman].” Similarly, a 33-year-old
225 man wrote, “I believe as a Christian that only God has authority to take
226 life. He decides how long we live and brings good out of suffering. A
227 person’s life is of value to God, from conception – so I trust my child to
228 Him knowing that God is kind and loving – even when I can’t see why
229 something occurs.”

230 Significant gender differences existed for two reported reasons to
231 continue the pregnancy. Women were more likely to report that they had
232 already bonded with the baby. A 32-year-old woman wrote, “I had already
233 felt her moving and had bonded with her. I was told she will die, but I
234 wanted to let nature take its course. I am not a religious person.” Women
235 were also more likely to report that they felt it was not their decision to
236 make. While this was often expressed in conjunction with religious beliefs,
237 other participants, such as this 28-year-old woman made no mention of God
238 or religion, “We believed that it wasn’t our decision to end [the baby’s] life.
239 We felt strongly her days were numbered just as ours.” Of note, five
240 participants (3%) reported that they continued because of state laws (found
241 out too late for termination), four participants (3%) were hopeful the
242 diagnosis was wrong and two participants (1%) could not afford termination.

243 Participants who terminated the pregnancy were significantly more
244 likely to regret pregnancy management decisions than participants who
245 continued ($p < 0.0001$). When asked about regrets, 13 participants who
246 terminated (12%) regretted their decision to terminate, eight (8%)
247 regretted having a surgical termination instead of induction of labor and
248 another eight (8%) regretting not investigating other options. None of the
249 participants who continued regretted their decision to continue. Four
250 participants (3%) who continued regretted not having a C-section.

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252 **Helpfulness of Genetic Counseling**

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254 Over half of participants met with a genetic counselor (Table 1 -
255 above). The majority of participants reported at least one thing their
256 genetic counselor had said or did that they felt was helpful (Table III).
257 When compared to the ABGC genetic counseling practice analysis, the
258 reported tasks primarily fell into three categories; 1) inheritance and risk
259 counseling, 2) diagnosis and natural history discussion, and 3)
260 psychosocial support and counseling.

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Table III: Most helpful things the genetic counselor said or did (N=134)

	n	%
Nothing/not helpful	42	31
Discussed recurrence risks	30	22
Explained causes of anencephaly	22	16
Explained anencephaly diagnosis	16	12
Told me it was not my fault	15	11
Discussed testing options and/or results	15	11
Was compassionate and listened	15	11
Can't remember/it was a blur	13	10
Gave hope for a future healthy baby	12	9
Discussed folic acid/ways to reduce risk of NTDs	10	8
Provided information about research opportunities	9	7
Shared stories of other families	5	4
Never told what to do/not judgmental	4	3

Discussion of recurrence risks was the most commonly reported helpful aspect of genetic counseling. A 41-year-old woman wrote, "She gave us information. Actual numbers about chances of these things happening again. She was honest about what was known and not known and did not try to sooth us or speak to us as if we were injured children." Several participants expressed that the low chance of recurrence was reassuring, "I was just glad to hear that it was not likely a genetic problem, but at the same time sad that it just seemed like a 'fluke.' She was very compassionate and not harsh when discussing with us, which was very much appreciated [32-year-old woman]."

Participants reported that an explanation of the diagnosis and natural history of anencephaly was helpful, "She was great and took her time explaining everything. She even drew pictures for us! [31-year-old woman]." A 33-year-old man stated, "[The genetic counselor] explained how anencephaly occurs/forms and we were very clear about the diagnosis, i.e. he would not survive." Explaining the potential causes of anencephaly and reassuring the parents that it wasn't caused by something they did was also reported as helpful. A 36-year-old woman wrote, "She explained there was no definitive reasons why this occurs and that it was nothing I or my partner did that caused anencephaly." A 38-year-old man explained, "Just understanding that anencephaly was...not due to specific behavior, gave us the hope and confidence to try again afterwards."

Several participants voiced appreciating the genetic counselor's expressed compassion and time spent listening to their questions and concerns. A 34-year old man wrote, "She sat with us for a long time – answered questions about viability, but also just provided a ministry of peace." A 41-year-old woman found it helpful for the genetic counselor to,

293 “Offer her sympathy and kindness, to listen, then to share stories of others
294 so I knew it wasn’t just my bad luck.”

295 While the majority of participants reported at least one thing their
296 genetic counselor had said or did that they felt was helpful, 31% of
297 participants reported that they did not find meeting with a genetic
298 counselor helpful. Many of these participants reported that genetic
299 counseling provided little concrete information, “We didn’t get many
300 answers through that. Just that it may have been a fluke, might not.
301 Exactly what we already knew [28-year-old woman].” Another participant
302 wrote, “She had very little accurate or helpful info, only one small
303 pamphlet [31-year-old woman].” Others participants expressed a
304 perceived lack of connection with their genetic counselor, “Well I wouldn’t
305 say they were helpful. They gave me facts and statistics. They were cold
306 with no empathy. I felt like just a number to them [30-year-old woman].”
307 Some participants who chose to continue the pregnancy reported not
308 finding genetic counseling helpful because they didn’t feel supported in
309 their decision, “Meeting with the genetic counselor was not very helpful.
310 She seemed to believe that we would just terminate the pregnancy and
311 she did not fully seem to understand our choice to carry to term. I called
312 her to ask about organ donation and she was no use in answering my
313 questions and seemed a little annoyed when I continued asking about
314 possibilities [27-year-old woman].”

315 Ten percent of participants reported that they could remember very
316 little about the genetic counseling visit or that “it was a blur.” A 38-year-
317 old woman wrote, “We had a brief meeting with a genetic counselor at
318 [hospital]. I believe she called me back with the results from our amnio
319 test to confirm it was a girl and that there were no other chromosomal
320 abnormalities. It was such a brief meeting at such a hectic time that I
321 honestly can’t say what was helpful.” There was no association between
322 time since the pregnancy ended and reporting that genetic counseling was
323 not helpful or a blur. Participants who met with a genetic counselor were
324 no less likely to report regrets than participants who did not meet with a
325 genetic counselor.

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327 **Patient Recommendations**

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329 Patient recommendations were numerous and varied but primarily
330 involved conveying comprehensive information to facilitate decision-
331 making and provision of psychosocial support and resources. The
332 seventeen recommendations reported by ten or more participants are
333 reported in Table IV. Again using the ABGC genetic counseling practice
334 analysis to categorize participant responses, the majority of patient
335 recommendations fell within; 1) diagnosis and natural history, 2)
336 psychosocial support and counseling, and 3) resources and follow-up.

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Table IV: Patient recommendations (N=253)

	n	%
Be compassionate and kind	86	34
Give information and resources on all pregnancy management options	70	28
Allow women/couples to make their own decisions	69	27
Give lots of information about anencephaly including best and worst case scenarios	51	20
Support whatever decisions women/couples make	39	15
Give as much time as women/couples need, do not rush	39	15
Value the baby as any other, worth your time and attention	37	15
Discuss/offer memory making options	29	12
Provide support group information	26	10
Provide therapist/counselor names	21	8
Make sure the whole health care team knows the situation to avoid insensitive comments	18	7
Tailor care to each individual person, not one size fits all	13	5
Be there with them/for them	12	5
Connect with other women/couples who have experienced the same thing	12	5
Call to check on them	11	4
Help develop a birth plan	10	4
Provide information about studies/donation options and help them to participate	10	4

Participants recommended providing in-depth information about anencephaly, including best and worst-case scenarios, “Educate them on all the possibilities. Some babies with anencephaly live a few months. I didn’t think that was possible with the info I was given [36-year-old woman].” Participants also felt that all pregnancy management options should be discussed, “Give the parents as much information as they need to make decisions they feel not only comfortable with, but confident about [31-year-old woman].” While participants recommended discussing all options, they were adamant that ultimately they want to make their own decisions. A 32-year-old man wrote, “Give information and try to not give direction of what to do or not do. The more women/couples can make

352 decisions themselves, the less regrets there may be.” A 38-year-old man
353 recommended, “Provide the information and give the couple space to make
354 an informed decision. Be compassionate and supportive. Help them feel in
355 control, as much as possible, given the fundamental events over which
356 they have no control.”

357 Most of all participants expressed wanting to be treated with
358 compassion and kindness. A 41-year-old woman wrote, “Compassion and
359 honesty are the most important things I think. To establish trust for all of
360 the decisions that have to be made after the parents are told the news.” A
361 28-year-old man recommended, “First, be sympathetic. There is no way to
362 imagine what these parents are going through, there are only those who
363 have been there and those that have not.” Participants voiced wanting
364 time and not being rushed, “Give them time to absorb the news. Don’t rush
365 them into a decision on what to do about the pregnancy. Listen, answer
366 questions. Be compassionate [36-year-old woman].” A 37-year-old man
367 wrote, “Spend time with the patient. Clear your calendar, cancel your golf
368 game, turn off your cell phone. Basically be there, with your patient.”

369 Participants also wanted health care providers to respect and support
370 their decisions. A 26-year-old man commented that, “They need to be
371 respectful of whatever decision the parents have made.” A 32-year-old
372 woman wrote, “Once the family decides...be respectful to them even if you
373 don’t agree with their choice.” Participants who chose to continue the
374 pregnancy reported wanting health care providers to treat their baby as any
375 other. A 36-year-old man wrote, “I wish they would have talked more about
376 our baby that had anencephaly. Just because she was not going to survive
377 did not mean that I didn’t want to hear or see how she was doing.” A 26-
378 year-old woman wrote, “It’s a baby, it’s wanted and loved and is NOT an ‘it’
379 or ‘a fetus’ to the couple – it’s offensive and down plays his or her importance.”

380 Participants recommended providing many resources including
381 written information about anencephaly and pregnancy management
382 options, support group and therapist referrals, and assistance with
383 memory making, developing a birth plan, and participating in research.
384 As a 39-year-old woman put it, “The more support you can give and
385 resources you can offer, the better the outcome will be. A 33-year-old
386 woman wrote, “Go beyond common knowledge and really dig deep. Help
387 them learn about studies they can participate in, donating organs, support
388 groups.” Along the same lines a 31-year-old woman wrote, “More
389 information is always good. Books, websites, support groups – all of these
390 can help to let them know that they are not alone. Also, they can be more
391 informed about what to expect physically and emotionally.” Another
392 participant recommended, “Resources. I was told to go home and think
393 about our options, but I did not have an understanding of what
394 anencephaly is and when I Googled it on my own I got scared and had
395 nightmares. I wish I was given material on what it was and where I could
396 go for more information [31-year-old woman].”

397 Participants also recommended improved communication within the
398 practice to prevent insensitive comments and facilitate patient coping.
399 Many participants shared hurtful experiences that could have been
400 prevented, including one 32-year-old woman who wrote, “I would encourage
401 healthcare workers to be mindful and attentive to the diagnosis of each
402 pregnancy. I had several encounters ...that were hurtful. For example,
403 during one of my last OB visits prior to delivery, the nurse reminded me to
404 bring a car seat to the hospital. It wasn’t until I said, ‘Our baby is dying’
405 that she realized my diagnosis.” Several participants also recommended a
406 follow-up phone call, “The main thing I have learned from this it meant so
407 much when the doctors and genetic counselor would check in on me. Calling
408 just saying hello or seeing if I was okay [31-year-old woman].”
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410 Discussion

411 While decision-making following an anencephaly diagnosis appears to
412 overlap with other, less severe fetal anomalies, the consequences of the
413 decision differ greatly. Neither decision will result in a lifetime of caring for
414 a disabled child, which may account for the increased continuation rates
415 observed in this population. Consistent with prior research, the severity of
416 the fetal anomaly was the factor most influencing the decision to terminate
417 (Chaplin et al., 2005; Hawkins et al., 2013; Nell et al., 2013; Pryde et al.,
418 1992; Schechtman et al., 2002; Shaffer et al., 2006). The lethal nature of
419 anencephaly was the number one reason reported by both women and their
420 male partners that factored into their decision to end the pregnancy.
421

422 In contrast, religious and ethical beliefs were the primary factors
423 reported by both women and men that contributed to the decision to
424 continue the pregnancy. The influence of religiosity on pregnancy
425 continuation has been reported previously and is recognized in clinical
426 practice (Allen & Mulhauser, 1995; Chaplin et al., 2005; Redlinger-Grosse,
427 Bernhardt, Berg, Muenke, & Biesecker, 2002b). However, assumptions
428 should not be made when presenting pregnancy management options to
429 patients with strong religious convictions, and all options should still be
430 raised. In order to improve cultural competency in a religious capacity, it
431 may be helpful for genetic counselors to receive education on the major
432 religious groups’ positions on pregnancy termination (Warren, 2011). As a
433 group, participants who continued the pregnancy were less likely to regret
434 pregnancy management decisions than those who terminated. In order to
435 prevent decisional regret, which can negatively impact psychological
436 outcome, it is essential to discuss the natural history of anencephaly and
437 all pregnancy management options to empower women and their partners
438 to make self-directed, well-informed decisions (Brondino et al., 2013;
439 Wilson, Sogc Genetics, & Special, 2014).

440 Many participants had the opportunity to meet with a genetic
441 counselor subsequent to receiving the anencephaly diagnosis. This is the
442 first report of perceived helpfulness of genetic counseling in this patient
443 population. A number of tasks central to the practice of genetic counseling,
444 such as discussion of diagnosis and natural history and provision of
445 recurrence risks and psychosocial support, were reported as helpful
446 (Hampel et al., 2009). Unexpectedly, nearly one-third of individuals in this
447 study group did not find genetic counseling helpful. One reason reported
448 for the perceived lack of helpfulness of genetic counseling was that little
449 concrete information was obtained. This is likely attributable to the fact
450 that while empiric recurrence risks for anencephaly can be estimated, a
451 specific genetic etiology is rarely identified (Joo et al., 2007).

452 This etiological ambiguity may be frustrating to prospective parents
453 and negatively impact genetic counseling. To address this ambiguity,
454 genetic counselors should acknowledge the unknowns and spend time
455 exploring psychosocial issues related to decision-making and uncertainty.
456 In addition, some participants reported that they could not remember
457 anything specific about their meeting with the genetic counselor. In
458 clinical practice, it is common for patients to meet with a genetic counselor
459 immediately following or very soon after fetal anomalies are identified.

460 Negative emotions, undoubtedly expected following a diagnosis of
461 anencephaly, both enhance and impair retention of information.
462 Following traumatic events, individuals are typically able to vividly
463 remember the central experience but peripheral details are often forgotten
464 (LaBar & Cabeza, 2006). A follow-up visit or phone call, which also
465 happened to be a patient recommendation, would provide an opportunity
466 to reinforce information and provide additional psychosocial support.
467 Further research into the relationship between genetic counseling
468 following diagnosis of anencephaly and other multifactorial conditions
469 and patient satisfaction is warranted.

470 Patient recommendations primarily involved conveying
471 comprehensive information to facilitate pregnancy management decisions
472 and provision of psychosocial support and resources. Most of these
473 recommendations fall within the scope of practice of genetic counselors
474 (Hampel et al., 2009). Additionally, two of the top recommendations,
475 “allow women/couples to make their own decisions” and “support whatever
476 decisions women/couples make” are consistent with the nondirective
477 approach embraced by genetic counselors (Weil, 2000). However, some of
478 the recommendations, such as discussing memory making options and
479 developing a birth plan, fall outside the typical scope of practice of genetic
480 counselors.

481 That being said, genetic counselors often practice in conjunction with
482 a multidisciplinary team and play an important role in connecting
483 patients with services such as palliative care to ensure that patient needs,
484 such as these, are met (Wool & Dudek, 2013). Based on patient

485 recommendations, genetic counselors may need to prioritize natural
486 history and psychosocial discussions to meet the needs of women and their
487 partners receiving a prenatal diagnosis of anencephaly. In addition, every
488 effort should be made to identify applicable psychosocial support resources
489 and research opportunities.

490
491 **Study Limitations**

492
493 While we took great care to perform the research presented here,
494 limitations to the present study nonetheless do exist. Due to the
495 retrospective nature of this study, qualitative responses relied solely on
496 participant recollection of a prior traumatic event. Negative emotion
497 accompanying events such as these may impact memory and retention of
498 details. Participants were included if they had received a prenatal
499 diagnosis of anencephaly at any point in the past, some of which had
500 occurred many years before. However, there was no association between
501 time since the pregnancy ended and reporting that genetic counseling was
502 a blur. In addition, while self-administered questionnaires allowed
503 enrollment of a large cohort of participants, responses are likely not as in-
504 depth as what could be gleaned from qualitative interviews. Finally, the
505 study group consisted of primarily Caucasian Americans; therefore,
506 findings may not be representative of other ethnic groups or cultures.

507
508 **Conclusions**

509
510 Genetic counselors are in the position to facilitate decision-making
511 and coping following prenatal diagnosis of anencephaly. However, current
512 practices may need to be altered to increase perceived helpfulness. Patient
513 recommendations presented herein can be used as a guide to tailor care
514 for this patient population.

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518 **References**

519 Allen, J.S., & Mulhauser, L.C. (1995). Genetic counseling after abnormal prenatal
520 diagnosis: Facilitating coping in families who continue their pregnancies. *J*
521 *Genet Couns*, 4(4), 251-265.
522 Austin, J.C., & Honer, W.G. (2008). Psychiatric genetic counselling for parents of
523 individuals affected with psychotic disorders: A pilot study. *Early Interv*
524 *Psychiatry*, 2(2), 80-89. doi:10.1111/j.1751-7893.2008.00062.x
525 Brondino, N., Colombini, G., Morandotti, N., Podavini, F., De Vidovich, G.,
526 Formica, M., Caverzasi, E. (2013). Psychological correlates of decision-making
527 during prenatal diagnosis: A prospective study. *J Psychosom Obstet Gynaecol*,
528 34(2), 68-74. doi:10.3109/0167482X.2013.797404

- 529 Chaplin, J., Schweitzer, R., & Perkoulidis, S. (2005). Experiences of prenatal diagnosis
530 of spina bifida or hydrocephalus in parents who decide to continue with their
531 pregnancy. *J Genet Couns*, *14*(2), 151-162. doi:10.1007/s10897-005-0488-9
- 532 Chen, X., An, Y., Gao, Y., Guo, L., Rui, L., Xie, H., . . . Zhang, T. (2017). Rare
533 deleterious PARD3 variants in the aPKC-binding tegion are implicated in the
534 pathogenesis of human cranial neural tube defects via disrupting apical tight
535 junction formation. *Hum Mutat*, *38*(4), 378-389. doi:10.1002/humu.23153
- 536 Cope, H., Garrett, M.E., Gregory, S., & Ashley-Koch, A. (2015). Pregnancy
537 continuation and organizational religious activity following prenatal
538 diagnosis of a lethal fetal defect are associated with improved psychological
539 outcome. *Prenat Diagn*, *35*(8), 761-768. doi:10.1002/pd.4603
- 540 Creamer, M., Bell, R., & Failla, S. (2003). Psychometric properties of the Impact
541 of Event Scale - Revised. *Behav Res Ther*, *41*(12), 1489-1496.
- 542 Detrait, E.R., George, T.M., Etchevers, H.C., Gilbert, J.R., Vekemans, M., & Speer,
543 M.C. (2005). Human neural tube defects: Developmental biology,
544 epidemiology, and genetics. *Neurotoxicol Teratol*, *27*(3), 515-524.
545 doi:10.1016/j.ntt.2004.12.007
- 546 Goetzinger, K.R., Stamilio, D.M., Dicke, J.M., Macones, G.A., & Odibo, A.O.
547 (2008). Evaluating the incidence and likelihood ratios for chromosomal
548 abnormalities in fetuses with common central nervous system malformations.
549 *Am J Obstet Gynecol*, *199*(3), 285 e281-286. doi:10.1016/j.ajog.2008.06.100
- 550 Hampel, H., Grubs, R.E., Walton, C.S., Nguyen, E., Breidenbach, D.H., Nettles,
551 S., . . . Weik, L. (2009). Genetic counseling practice analysis. *J Genet Couns*,
552 *18*(3), 205-216. doi:10.1007/s10897-009-9216-1
- 553 Hawkins, A., Stenzel, A., Taylor, J., Chock, V.Y., & Hudgins, L. (2013). Variables
554 influencing pregnancy termination following prenatal diagnosis of fetal
555 chromosome abnormalities. *J Genet Couns*, *22*(2), 238-248.
556 doi:10.1007/s10897-012-9539-1
- 557 Johnson, C.Y., Honein, M.A., Dana Flanders, W., Howards, P.P., Oakley, G.P., Jr.,
558 & Rasmussen, S.A. (2012). Pregnancy termination following prenatal
559 diagnosis of anencephaly or spina bifida: A systematic review of the literature.
560 *Birth Defects Res A Clin Mol Teratol*, *94*(11), 857-863. doi:10.1002/bdra.23086
- 561 Joo, J.G., Beke, A., Papp, Z., Csaba, A., Rab, A., & Papp, C. (2007). Risk of
562 recurrence in major central nervous system malformations between 1976 and
563 2005. *Prenat Diagn*, *27*(11), 1028-1032. doi:10.1002/pd.1827
- 564 Kalb, F.M., Vincent, V., Herzog, T., & Austin, J. (2017). Genetic counseling for
565 alcohol addiction: Assessing perceptions and potential utility in individuals
566 with lived experience and their family members. *J Genet Couns*, *26*(5), 963-
567 970. doi:10.1007/s10897-017-0075-x
- 568 Koenig, H.G., & Bussing, A. (2010). The Duke University Religion Index (DUREL):
569 A five-item measure for use in epidemiological studies. *Religions*, *1*(1), 78-85.
570 doi:10.3390/rel1010078
- 571 LaBar, K.S., & Cabeza, R. (2006). Cognitive neuroscience of emotional memory.
572 *Nat Rev Neurosci*, *7*(1), 54-64. doi:10.1038/nrn1825
- 573 Nell, S., Wijngaarde, C.A., Pistorius, L.R., Slieker, M., ter Heide, H., Manten, G.T.,
574 & Freund, M.W. (2013). Fetal heart disease: Severity, associated anomalies
575 and parental decision. *Fetal Diagn Ther*, *33*(4), 235-240.
576 doi:10.1159/000346564

- 577 Pryde, P.G., Isada, N.B., Hallak, M., Johnson, M.P., Odgers, A.E., & Evans, M.I.
578 (1992). Determinants of parental decision to abort or continue after non-
579 aneuploid ultrasound-detected fetal abnormalities. *Obstet Gynecol*, *80*(1), 52-56.
580 Redlinger-Grosse, K., Bernhardt, B.A., Berg, K., Muenke, M., & Biesecker, B.B.
581 (2002a). The decision to continue: The experiences and needs of parents who
582 receive a prenatal diagnosis of holoprosencephaly. *Am J Med Genet*, *112*(4),
583 369-378. doi:10.1002/ajmg.10657
- 584 Redlinger-Grosse, K., Bernhardt, B.A., Berg, K., Muenke, M., & Biesecker, B.B.
585 (2002b). The decision to continue: The experiences and needs of parents who
586 receive a prenatal diagnosis of holoprosencephaly. *American Journal of*
587 *Medical Genetics*, *112*(4), 369-378. doi:10.1002/ajmg.10657
- 588 Schechtman, K.B., Gray, D.L., Baty, J.D., & Rothman, S.M. (2002). Decision-
589 making for termination of pregnancies with fetal anomalies: Analysis of
590 53,000 pregnancies. *Obstet Gynecol*, *99*(2), 216-222.
- 591 Shaffer, B.L., Caughey, A.B., & Norton, M.E. (2006). Variation in the decision to
592 terminate pregnancy in the setting of fetal aneuploidy. *Prenat Diagn*, *26*(8),
593 667-671. doi:10.1002/pd.1462
- 594 Steer, R.A., Clark, D.A., Beck, A.T., & Ranieri, W.F. (1999). Common and specific
595 dimensions of self-reported anxiety and depression: The BDI-II versus the
596 BDI-IA. *Behav Res Ther*, *37*(2), 183-190.
- 597 Toedter, L.J., Lasker, J.N., & Janssen, H.J. (2001). International comparison of
598 studies using the perinatal grief scale: A decade of research on pregnancy loss.
599 *Death Stud*, *25*(3), 205-228. doi:10.1080/07481180125971
- 600 Warren, N.S. (2011). Introduction to the special issue: Toward diversity and
601 cultural competence in genetic counseling. *J Genet Couns*, *20*(6), 543-546.
602 doi:10.1007/s10897-011-9408-3
- 603 Weil, J. (2000). *Psychosocial genetic counseling*. New York: Oxford University Press.
- 604 Wilson, R.D., Sogc Genetics, C., & Special, C. (2014). Prenatal screening,
605 diagnosis, and pregnancy management of fetal neural tube defects. *J Obstet*
606 *Gynaecol Can*, *36*(10), 927-939. doi:10.1016/S1701-2163(15)30444-8
- 607 Wool, C., & Dudek, M. (2013). Exploring the perceptions and the role of genetic
608 counselors in the emerging field of perinatal palliative care. *J Genet Couns*,
609 *22*(4), 533-543. doi:10.1007/s10897-013-9581-7
- 610