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1 **Choosing not to know: accounts of non-engagement with pre-symptomatic testing**
2 **for Machado-Joseph disease**

3

4 **ABSTRACT**

5 This paper reports accounts from people at-risk for, or affected by, Machado-Joseph
6 disease, and their family members, about their decisions not to seek pre-symptomatic
7 testing, therefore remaining (for the time) uninformed about their genetic status. We
8 draw on individual and family semi-structured interviews with participants recruited
9 through a national patient's association (n=25). Qualitative thematic analysis revealed
10 three main categories of accounts: (1) justifying the decision "not to know", because
11 either no clinical benefit was expected or predictive knowledge was anticipated as
12 psychologically burdensome; (2) prioritizing everyday life, maintaining hope and the
13 goal of living a valid life; and (3) the wish to know: ambivalence and conflict within the
14 family. Findings suggest the value of genetic information is often questioned when no
15 effective treatment or cure is available; and that people have different tolerance
16 thresholds for predictive information, and this impacts individuals within the family
17 differently. We discuss this in the context of the making of "responsible" decisions, and
18 of the tensions that may arise within families between the best interests or wishes of a
19 person and those of other family members. We hope this will clarify the reasoning of
20 those who opt for non-engagement with medical genetic services and, more specifically,
21 pre-symptomatic testing. Further, we hope it will be relevant for the provision of genetic
22 counselling and psychosocial support to such families.

23

24 **Keywords:** predictive testing, genetic risk, Portugal, Machado-Joseph disease,
25 spinocerebellar ataxia type 3, late-onset neurological diseases.

26

27 INTRODUCTION

28 Decisions to undergo pre-symptomatic testing (PST) for highly-penetrant, late-onset
29 neurological diseases (LONDs) are commonly permeated by great psychosocial
30 complexity¹. Genetic counselling and PST are standard procedures offered to
31 individuals at-risk for LONDs, in accordance with guidelines that might be applied in
32 different contexts and for a range of diseases². For some, PST can provide helpful
33 information, namely clinical surveillance for early signs of the disease and early
34 treatment of complications; however, for severely incapacitating LONDs, such as
35 Machado-Joseph disease (MJD) and when no medical intervention is currently
36 available, PST provides information without leading to any direct clinical benefit.
37 MJD (also known as spinocerebellar ataxia type 3, SCA3) is a dominantly inherited,
38 multisystem degenerative disorder (average age-of-onset: 40.5 years); symptoms
39 generally include progressive motor difficulties, incoordination of gait, speech and fine
40 movements of the hands, involuntary eye movements, and, later on, complete loss of
41 autonomy in daily living³. MJD is the most common SCA worldwide; its highest
42 frequency is described in Brazil, Portugal and China⁴. In Portugal, MJD has an overall
43 prevalence of 3.1:100,000, but some clusters have higher rates (835.2 in Flores and 27.1
44 in São Miguel, Azorean islands; and 14.4:100,000 in central areas of the mainland,
45 especially along the Tagus valley)⁵.
46 Research indicates that relatively few individuals at-risk for LONDs request PST. For
47 example, in Brazil, only 9% of the estimated population at 50% risk for MJD completed
48 PST⁶; uptake of PST for Huntington disease (HD) in the UK was estimated as 17.4%⁷,
49 while in Cuba the uptake of PST for SCA2 was estimated to be 24.9%⁸. While the
50 psychological and social understanding of the experiences and consequences of PST for

51 MJD, is well documented⁹⁻¹⁴, far less is known about those who decide not to undertake
52 PST. Most psychosocial studies have been conducted in the context of PST, and thus
53 recruit self-selected individuals already attending genetics clinics; it is far more difficult
54 to access a representative, unselected population. One factor that may make those at risk
55 reluctant to take part in research and to contact clinical genetics services is their wish
56 (and right) not to know their genetic status or not to be reminded of their risks too often.
57 Much previous research has focused on at-risk subjects who request PST but then
58 decide not to proceed^{15,16}; or on what is reported second-hand by those who proceed
59 with testing, about their relatives who chose not to know.

60 To our knowledge, only one study has addressed those who chose not to undertake PST
61 for MJD: an ethnographic study reported concerns among Brazilian MJD families with
62 the emotional impact of a positive test result, including that it could hasten evolution of
63 symptoms, and prevent attaining normative life goals¹⁷. Other research reported how
64 individuals who made no attempts to seek PST for HD may be judged negatively by
65 relatives and are often asked to justify their decision¹⁸; this creates tension in family
66 relationships, as others regard it as a moral imperative to do so. Comparable findings
67 have been reported in a family with limb-girdle muscular dystrophy¹⁹ and a kinship with
68 Lynch syndrome (LS)²⁰. A recent study described *decliners* of predictive testing for LS
69 (which has the possibility of medical follow-up and preventive measures) as ranging
70 from being uninformed to declining testing at all, not perceiving benefits and fearing
71 negative consequences²¹. Taken together, these findings suggest that ‘decliners’ or
72 ‘non-requesters’ have different positionings towards genetic information and make their
73 decisions within a different logic and morality, when compared with each other or with
74 those who have engaged with genetic testing. Thus, circumstances around non-
75 engagement with PST for MJD may not have been adequately reported so far. This

76 paper aims to contribute to this knowledge, by reporting accounts from persons at-risk
77 of, or affected by, MJD and their family members, about their (current or past) decisions
78 of not seeking PST, or their opinions concerning relatives who decided not to undertake
79 PST.

80

81 **METHODS**

82 This exploratory, qualitative study was drawn from a larger empirical study examining
83 processes of communication of information about genetic risks in families affected by
84 LONDS, including familial amyloid polyneuropathy TTR Val30Met, HD and MJD²²⁻²⁴.
85 We present here the sub-corpus of data focusing on decisions of non-engagement with
86 PST, a relevant theme that emerged during that analysis, drawing on data from families
87 with MJD (the majority in that study).

88

89 **Recruitment**

90 Following approval by the IBMC Human Ethics Committee, participants were recruited
91 through the national patients' association for hereditary ataxias. Inclusion criteria
92 involved persons potentially competent to give consent, either affected or at-risk for
93 MJD, or their family members. A leaflet with information about the study and its aims,
94 inviting people for an interview, was circulated in newsletters and website of the
95 association and in social media, asking those potentially willing to participate to contact
96 the researcher. The patients' association also made the study known at members'
97 meetings; those agreeing to participate authorized their contact information to be sent to
98 the main researcher, who then contacted them. Snowball sampling²⁵ was also adopted
99 by asking participants whether they knew other persons or families that might be
100 interested to participate.

101

102 **Participants**

103 Data pertaining to non-engagement with PST involved a sub-corpus of 12 interviews,
104 out of 32; of those, 8 interviews involved participants from MJD families, 6 of which
105 included multiple family members (i.e., a joint interview with relatives and non-
106 biological family members). Overall, this study comprised 25 participants (subsequent
107 contact with two potential participants failed), all of white-European ethnic background
108 (*cf.* Table 1 for socio-demographic and disease-related information).

109 [INSERT TABLE 1 ABOUT HERE]

110

111 **Data collection**

112 Interviews were conducted between April 2014 and June 2017, at the participant's home
113 (5), in a primary health centre (2), or in a public space (1), as chosen by them. All were
114 conducted by ÁM, after written consent had been obtained. Interviews were audiotaped
115 with the participants' consent, transcribed and translated into English. Each lasted
116 approximately one hour. Social, demographic and disease-related data were collected,
117 followed by an open question about experiences of living with, or at risk of, the disease.
118 Interviews centred on the value of genetic information, motivations and engagement
119 with PST, and experiences of talking to relatives about test results or genetic risks more
120 broadly. The focus was on what issues they found important and how they expressed
121 and elaborated their arguments. Case summaries were created, highlighting the most
122 relevant aspects, contextual observations and emerging ideas about topics to discuss in
123 future interviews²⁶.

124

125 **Data analysis**

126 The transcribed interviews were analysed thematically using coding and the method of
127 constant comparison²⁶. Each transcript and the corresponding interview notes were read
128 repeatedly and the key topics addressed were mapped out. These were then coded, by
129 breaking them down into small sections to identify the most significant items. Next,
130 coded data were constantly compared within and among transcripts, to identify any
131 likely connections. Recognized themes relating to non-engagement with PST were then
132 grouped together in an iterative process, according to their main features and meaning.
133 Findings were then interpreted with reference to a broad psychosocial framework aimed
134 at understanding the interpersonal context that surrounds individuals and families, as
135 they live with, or at risk for, an inherited disease²⁷⁻²⁹.

136

137 **RESULTS**

138 Each theme is presented (with data extracts) to illustrate key points. Quotations are
139 accompanied by a code for the participants (consecutive lettering, to protect
140 confidentiality), age and sex (F, female; M, male), as well as disease-related features.
141 Content in square brackets is used to add intelligibility to the participant's quote;
142 ellipsis with a single/double dot means a brief/extended pause; underscored text
143 indicates louder, more emphatic speech; "... " indicates some words or sentences were
144 omitted; and "~" indicates overlapping speech.

145

146 **(1) Justifying the decision “not-to-know”, because either no clinical benefit was** 147 **expected or predictive knowledge was anticipated as psychologically burdensome**

148 This theme was expressed in seven interviews and focuses on the reasons given by
149 participants for remaining uninformed about their genetic status. In general, participants

150 framed access to presymptomatic genetic information as being pointless, because no
151 effective or acceptable treatment or palliation of symptoms was yet available for their
152 family's disease:

153 *"I preferred to wait and see, because there is nothing one could do about it. If there were a treatment,*
154 *a drug, something (.) I only did the analysis last year, because I started to feel my legs sort of tight (.)*
155 *to lose balance and falling (.) I wanted to postpone it until I could not stand on my own any more". [A,*
156 *49y, M, clinically affected (mild symptoms); two children]*

157 Several participants framed engagement with genetic knowledge, although removing
158 uncertainty, as having the potential to become seriously burdensome. Therefore, they
159 preferred to live free from the psychological concerns posed by a pre-symptomatic
160 diagnosis of an impending severe disease:

161 *"I rather not think about it, I really prefer not to know. I don't want to have that constantly popping*
162 *up in my head (..) I prefer to deal with one thing at a time". [B, 30y, M, at 50% risk; 56y father*
163 *severely affected]*

164 *Next, C* describes how her decision not to undertake PST was also based on family
165 members' experiences and reactions after knowing their results; by avoiding genetic
166 testing and its potentially destabilizing knowledge, not only does she seek to preserve
167 her own psychological wellbeing, but also that of her daughter:

168 *"My sister decided to do the test and everything started to change: she sold her house and moved to a*
169 *ground floor apartment, taking all decisions thinking that the future would come up badly and quick.*
170 *It's just too frightening (.) I prefer to live the here and now (..) And I think: if I do it I'll start to over-*
171 *think it all the time, like 'I'll get it, I'll get it!' It happened to one of my cousins; she started to feel*
172 *psychologically affected, you know (.) really down [...]* *And my daughter, she'd probably start to*
173 *think she would have it as well and would miss the best years of her youth with this worry." [C, 52y,*
174 *F, 50% risk; one daughter]*

175

176 **(2) Prioritizing everyday life, maintaining hope and the goal of living a normal life**

177 This theme was widely shared among participants and shows how they articulated
178 lifeworld considerations while discussing their options. Some participants anticipated
179 that the potential worry regarding future health risks, following a “positive” test result,
180 would impair their capacity to focus on their everyday life. Other participants claim the
181 need to be psychologically “available” (i.e., free from the emotional unrest caused by a
182 potentially adverse pre-symptomatic result) to assure caregiving for those affected, as
183 well as parenting their children:

184 *“I don’t think much about the disease (..) I really make an effort to avoid thinking about it. Now, I am*
185 *very keen to be a father, you know (.) I just want to be a good father, it’s my first [baby], I’m focused*
186 *on that.” [B, 30y, M, at 50% risk; 56y father severely affected]*

187 When asked if he would undertake PST if his (at-risk) mother had tested “positive”, D
188 described his reasoning:

189 *“I guess I wouldn’t, no. I’d see how it’d go (..) We just can’t give up our lives! E [referring to his 59y*
190 *uncle, severely affected, present at this family interview] is staying at a day-care facility (.) we need*
191 *to stay united, and keep our jobs, so we can give him the best care we can; his brother, my other*
192 *uncle, is staying at home because they can’t afford the day-care centre, so they need to stay with him,*
193 *to take care for him. It’s like one step at a time.” [D, 41y, M, non-carrier; 2 children]*

194 F describes the case of his wife, who had not requested PST and has preferred to face
195 the consequences of the disease only as they have arisen. In doing so, they framed this
196 decision as an attempt to live in hope while they were a young couple:

197 *“She [G, wife] hasn’t had the test as she rather wanted to live day by day ... and I think it was right, I*
198 *agreed all along (.) One can’t always be thinking about the worst, can we? When we got married ...*
199 *people used to say ‘watch it, her mother has it and she [G] might have it too!’; but at that time you*
200 *just want to move ahead, instead of not having a life, right?” [F, 54y, M, husband of G, 48y, F,*

201 severely affected; no children]

202

203 **(3) The wish to know: ambivalence and conflict within the family**

204 Lastly, this theme describes considerations against deciding “not-to-know” and how it
205 involved ambivalence and conflicting views within the family; it was addressed in about
206 half of the interviews. Some participants described situations that would make them
207 consider undertaking PST. These exceptions to their decision not-to-know were often
208 framed for the sake of their children, as it could inform their reproductive decisions:

209 *C: “When she [H, daughter] wants to have children, then I’ll be happy to do the test, that’s different.*
210 *When another life is at stake you need to be sure. At that time, I didn’t know anything about this, if I*
211 *knew I would have done it”. ~*

212 *~ H: “Honestly, I don’t think much about it. Of course, it’s important to know what you can count on*
213 *in the future, but I guess that’s not a priority at this point in my life (.) Maybe when I decide I want to*
214 *have a baby (..) It makes sense to be cautious: first to ask my mother to do the test, then to do it myself*
215 *if needed, and then have the in vitro test [PGD]. [C, 52y, F, at 50% risk; one daughter, H, 20y, F, at*
216 *25% risk]*

217 There were instances, however, where some ambivalence and tension were noticeable in
218 managing the way non-engagement with PST was perceived within the family,
219 especially in relation to decisions about reproduction. The next excerpts are from a
220 family interview:

221 *I: “My nephews (.) they’re young, [they] are having children, they don’t want to know... of course it’s*
222 *their life but that’s (..) I don’t think it’s right (.) one thing is when you have children before you know*
223 *it; but when you know and you run the risk of having a child with the disease, that’s different.”~*

224 *~ D: “This isn’t like that, no, they deserve to be a whole family, to have a normal life! We can even be*

225 *looked as being selfish, but they have the right to be parents, to give grandchildren to their parents,*
226 *and so on, no matter what it may come to in the future. They deserve to have a family!”*

227 *E: “They’re doing right, they have time to know (..) what’s the point of knowing when you’re young*
228 *anyway? (..) I’ve worked all my life (.) until I couldn’t do it anymore (..) they shouldn’t get stuck by*
229 *that.” [I, 63y, F, non-carrier; three sons; D, 41y, M, son of I, non-carrier; 2 children; E, 59y, M,*
230 *severely affected, brother of I; two sons]*

231 There were also accounts that more explicitly showed criticism towards relatives’
232 decisions not to undertake PST. These emphasize mainly the potential benefits of
233 genetic knowledge to the planning of offspring’s lives:

234 *“He [ex-partner, at 50% risk for MJD] never wanted to know. I have been telling him he should do the*
235 *test ever since, but he always preferred to avoid facing it (..) Now we’re divorced, and I’d like to know*
236 *whether my children might have it or not, it’s a matter of organizing our life. He [looking at the older*
237 *son, aged 11] already asks about it. I don’t want to live hiding this from them. He understands what*
238 *this is all about. You can only be prepared for something if you have the chance to know it in advance,*
239 *right?” [J, 35y, F; two children at 25% risk]*

240

241 **DISCUSSION**

242 This is one of few studies exploring non-engagement with PST outside the usual
243 cohorts seen in genetic counselling research. We report on individuals at-risk or affected
244 by MJD about their decisions not to seek PST, therefore having remained uninformed
245 about their genetic status. Accounts were made by participants about themselves or
246 about family members, or made about them by other relatives. Decisions of non-
247 engagement with PST were either reported as being the participant’s current option or
248 preferred option prior to becoming clinically affected. The main findings suggest that
249 the value of genetic information is in the beholder and that (i) knowledge of genetic

250 information is questioned when no effective treatment or cure is available; (ii) people
251 have different tolerance thresholds for predictive information (and this impacts
252 individuals within the family differently); (iii) the making of “responsible” decisions
253 involves trading potential health risks, against a corresponding burden to present life,
254 including its anticipated psychosocial impact; and (iv) tensions may arise between the
255 best interest or wishes of a patient and those of other family members.

256 Participants were aware that PST could remove uncertainty as to whether they would be
257 affected or not in the future; however, the incurable nature of MJD and lack of effective
258 treatment, prompted most of these participants to perceive PST as being of little use.

259 Under those circumstances, they also anticipated genetic knowledge as potentially
260 burdensome. This is in line with research suggesting that participants tend to remain
261 unengaged with predictive testing if it is perceived as too distressing³⁰. Therefore, most
262 participants acknowledged the possibility of undertaking a genetic (diagnostic) test in
263 the future, only if or when they come to experience incipient symptoms. That was a
264 preferred account for non-engagement with PST.

265 Decisions to remain uninformed about one’s genetic status were also made to protect
266 others in the family from this potentially destabilizing knowledge. As found in other
267 studies, the assumption “to care not-to-know” was a compelling justification to avoid
268 PST³¹. By deciding to avoid formal knowledge of their genetic status, these at-risk
269 individuals seem not so much to *actively reject* PST, but rather choose to *defer*
270 *knowledge* of their genetic status. This may represent an attempt to regain some sense of
271 control over the impact that foreknowledge about their family’s disease may have on
272 their lives. In doing so, they seem to prioritize the focus of their lives on everyday
273 pressing concerns (such as parenting their children or caregiving for affected relatives),
274 without the destabilizing knowledge of an impending disease. Others prioritized

275 keeping open the prospect of living a “valid”, worthwhile life, as that allowed them to
276 preserve hope towards the future. These reflections ultimately evidence the participants’
277 personal and familial values, as to management of genetic risks^{17,21,28,29,31-33}.

278 Furthermore, our data provide accounts about other relatives’ non-engagement with
279 PST. While the accounts we elicited were generally supportive of those who chose not
280 to know, differences were noticeable among family members regarding the value of
281 information and implications towards others, especially pointing out reproductive
282 decisions. Some participants described possible future events that might lead them to
283 change their mind, as when their adult offspring would like to know their genetic status
284 or are considering having children, so that the disease would not be passed down to the
285 next generation. As such, those participants recognized some utility of their predictive
286 genetic information, presenting themselves as responsible parents³¹⁻³³; however, there
287 was also criticism and blame, particularly directed towards at-risk relatives who had
288 opted to pursue reproduction irrespective of the risk of transmitting the disease to
289 offspring. This allocation of blame may represent a dominant moral consensus that sees
290 engagement with genetic services as the morally sound way to conduct life in the
291 presence of genetic risks³¹⁻³⁴.

292 The great majority of participants – at least overtly, on the surface – did not seem to
293 regard non-engagement in genetics as something detrimental, irresponsible or immoral.
294 This is in contrast to previous studies focusing on other untreatable conditions^{17,18,31-33}.

295 In fact, some accounts framed the wish to protect family members from being actors of
296 potentially blameworthy actions. While this may be explained by the unsettling
297 emotional effects that may be promoted by divergent test results, this exonerates them
298 from any charge of irresponsibility in the management of their lives and their genetic
299 risks³⁴. This suggests that the notion of genetic responsibility goes beyond the rational

300 calculation of the use of genetic information and engagement with formal genetics
301 knowledge and healthcare, extending to lifeworld goals and personal and family values.

302

303 **Implications for practice and future research perspectives**

304 Although the numbers are small, this study may contribute to highlight some aspects of
305 the thinking of at-risk individuals and their family members, particularly how they
306 negotiate decisions regarding PST and access to genetic knowledge. This may be
307 relevant to the practice of genetic counselling and the provision of psychosocial support
308 to families, by bringing further insights into the decision-making process of at-risk
309 family members. Future research would benefit from collecting data from larger
310 samples, including persons in a wide range of social and demographic circumstances
311 and from diverse geographies, which may generate additional understanding of this
312 topic. Styles of dealing with health risks vary with social and cultural values, and so
313 does the influence played by genetic technology in shaping morality and decisions in
314 regard to genetic disease^{13,14,21,22} and testing³⁵, and this certainly differs between regions
315 and countries.

316 People's decisions and accounts may change once effective and acceptable therapies are
317 available (or people think they are imminent). To what extent do the dynamics of hope
318 for those at risk and their family members prompt changes in their mode of reasoning
319 and decision-making in relation to genetic testing? How may a sense of empowerment
320 and engagement with genetic healthcare best be promoted among at-risk individuals,
321 while acknowledging their personal and collective experiences and decisions managing
322 genetic risks and family relationships?

323

324 **Limitations of the study**

325 This study had a small data corpus and focused on Portuguese families with MJD,
326 mostly living in the rural region of the Tagus valley (a high prevalence region) and its
327 findings cannot be generalized. Therefore, conclusions may not apply to other
328 populations or to other similar diseases. Also, we must consider that about one third of
329 our participants did not complete high-school education, which may have impacted the
330 findings. Finally, as participants were involved in snowball recruiting to the research,
331 they may have invited to participate with them in an interview those family members
332 with whom they anticipated less disagreement. They may also have felt somewhat
333 inhibited in their statements due to the presence of other family members.

334

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345

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