

Depression and anxiety in the 'at-risk' phase of frontotemporal dementia

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Background

Frontotemporal dementia (FTD) is a highly heritable neurodegenerative disorder. Approximately 30% cases are caused by an autosomal dominant mutation in 3 main genes: microtubule associated protein tau (MAPT), progranulin (GRN) or an expansion in chromosome 9 open reading frame 72 (C9orf72). Some individuals from families with a known genetic mutation undergo predictive genetic testing to find out if they carry the mutation. However, many individuals choose to live with the knowledge that they are at-risk of FTD for much of their lives. In this study we aimed to assess the psychological impact of living at-risk of FTD compared with knowledge of genetic status, and the decision making around predictive genetic testing.

Methods

38 participants were recruited from the GENetic Frontotemporal dementia Initiative (GENFI) and were all at-risk of genetic FTD. 53% of participants had completed predictive testing. 17 were known mutation carriers (MC), 3 were known non-carriers (NC) and the remaining 18 participants' genetic status were unknown (UN).

Participants completed a questionnaire exploring their experiences during the 'at-risk' period. The General Anxiety Disorder scale (GAD7) and the Patient Health Questionnaire depression module (PHQ-9) were used to assess symptoms of anxiety and depression. Participants also rated the importance of a number of statements regarding their reasoning on whether to have predictive testing (five-point Likert scale from one, not important, to five, extremely important). An ANOVA compared the effect of knowing genetic status on psychological symptoms.

Results

Mental health problems

18% participants had a diagnosis of an ongoing mental health problem and 21% had a previous diagnosis of a mental health problem. 35% mutation carriers (MC), 39% of those with unknown status (UN) and 66% NC had a mental health diagnosis. All diagnoses were either depression (24%), anxiety (5%) or both (11%). There was a significant effect of knowing genetic status on having a diagnosis of any mental health problem when adjusting for gender ($F(2) = 4.104, p = 0.03$).

However, when looking at individual symptoms there was a difference between the groups. There was a trend towards significance for anxiety symptoms (GAD7) ($F(2) = 2.537, p = 0.094$) with those with the UN group scoring higher than NC and MCs. The UN group also scored significantly higher on a question about general nervousness and anxiety in the past month ($F(2) = 3.294, p < 0.05$) adjusting for gender in both cases. Those who knew their status (MC & NC) scored higher for depressive symptoms (PHQ9) than the UN group [mean (standard deviation)]: MC & NC 3.42 (4.32), UN 3.24 (3.67) however this was not statistically significant (see figure 1).

Reasons for having predictive testing

MC and NC groups rated 'relieving uncertainty' highest as the reason for testing: MC 4.75 (0.58), NC 5.00 (0.00), whilst the UN group rated this as less important: 3.44 (1.24) (see figure 2).

Similarly, 'relieving anxiety' was also rated highly by MC and NC groups compared with the UN group: MC 3.69 (1.25), NC 4.00, (1.00), UN 3.22 (1.39). The UN group rated 'worrying about children's risks' highest as the reason: 3.18 (1.70) followed by being 'preoccupied with onset': 3.06 (1.20) and 'wouldn't alter medical care: 3.06 (1.34) (see figure 3).

Support

34% participants had accessed support. In addition to this 13% people saw a psychologist, 5% a psychiatrist and 42% had seen either GP, counsellor or genetic counsellor. However 53% would like more support. Qualitatively, participants suggested that they would benefit from:

- Talking to someone who understands about FTD and their genetic risk and the problems associated with it
- More access to support groups
- Specific counselling for the genetic diagnosis in particular
- Advice on positive planning for the future and making the most of life

Mean depression and anxiety rating by genetic status

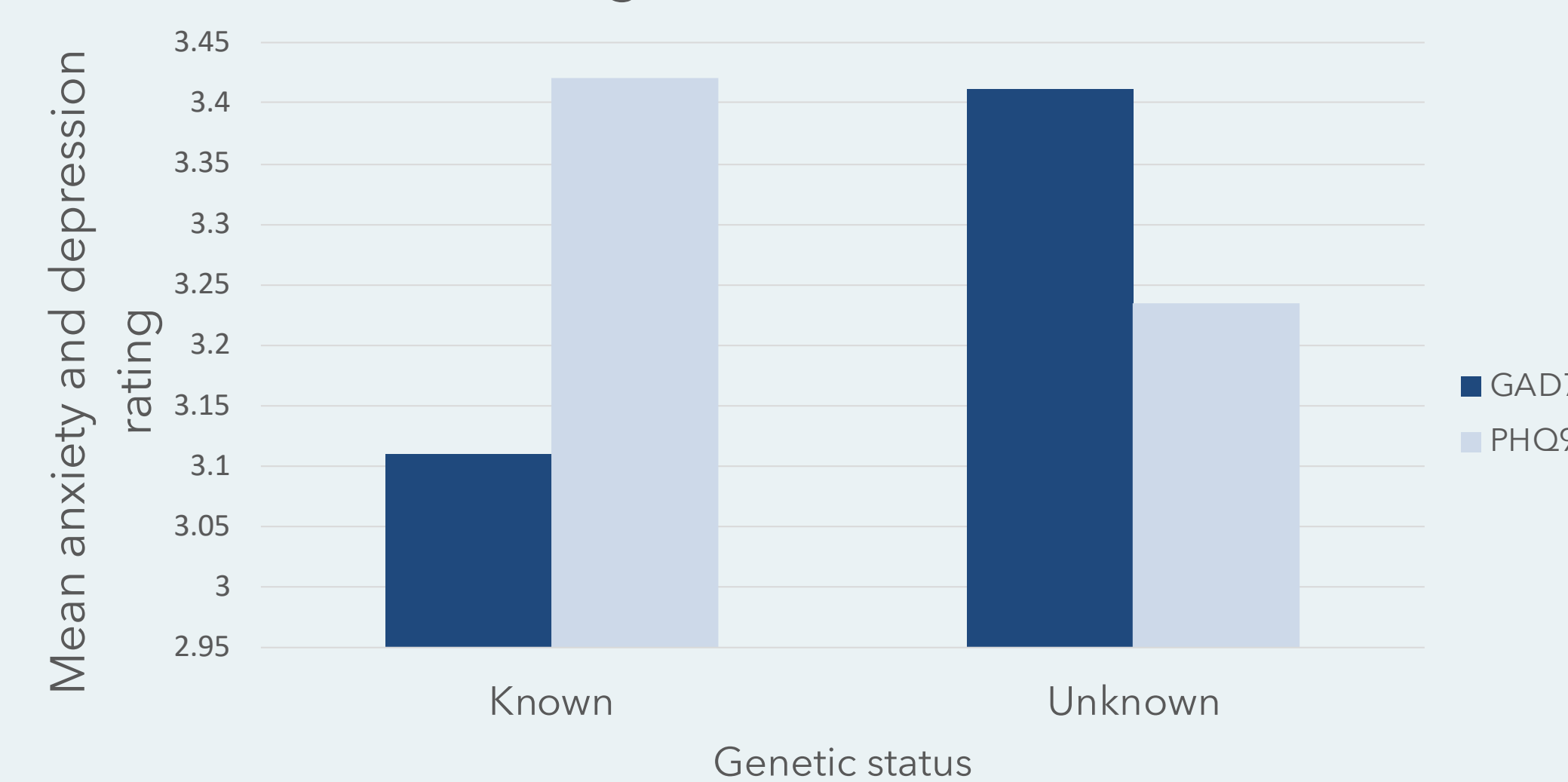


Figure 1: Mean GAD7 and PHQ9 ratings by genetic status

Reasons for undertaking predictive testing

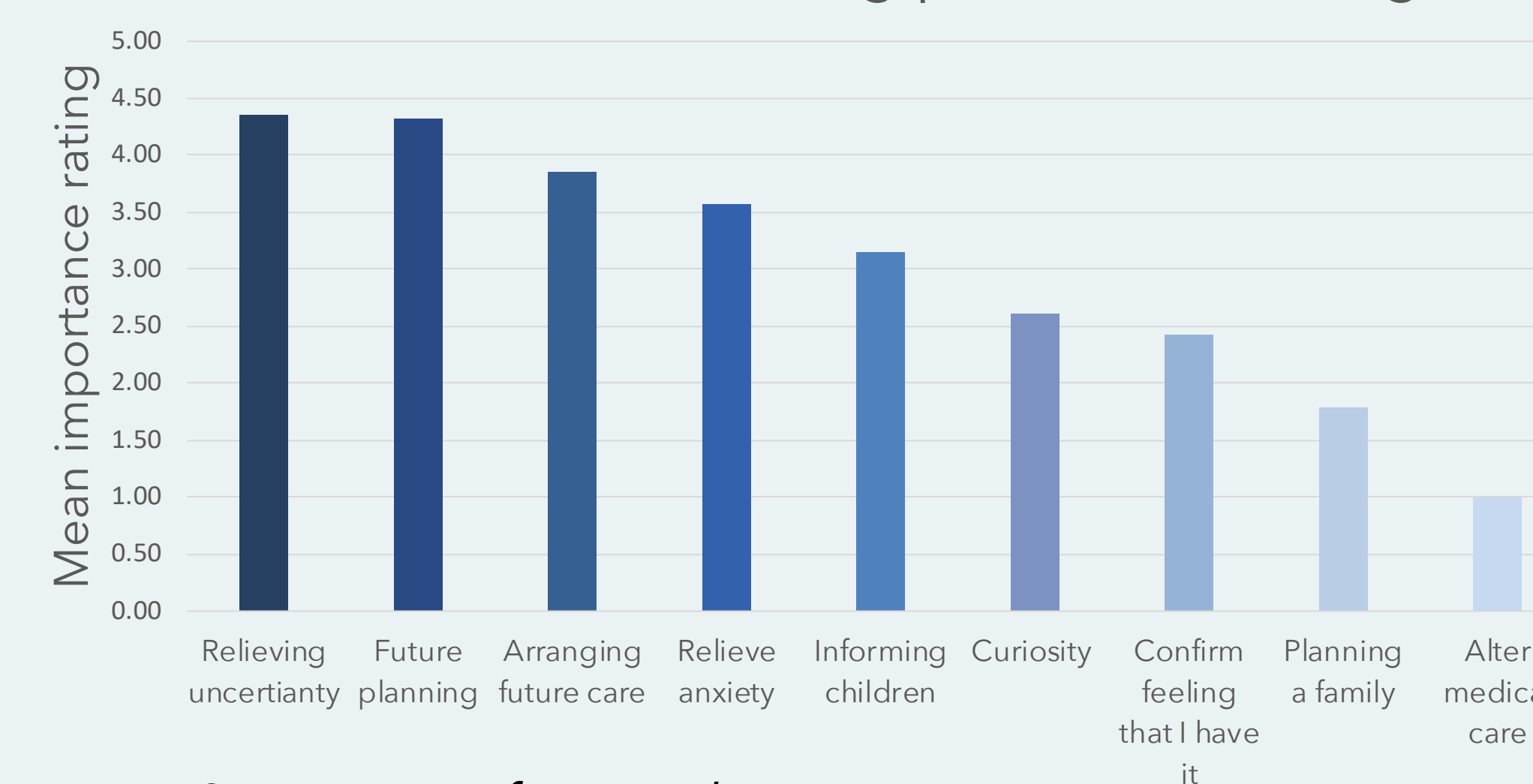


Figure 2: Reasons for predictive testing

Reasons for not undertaking predictive testing

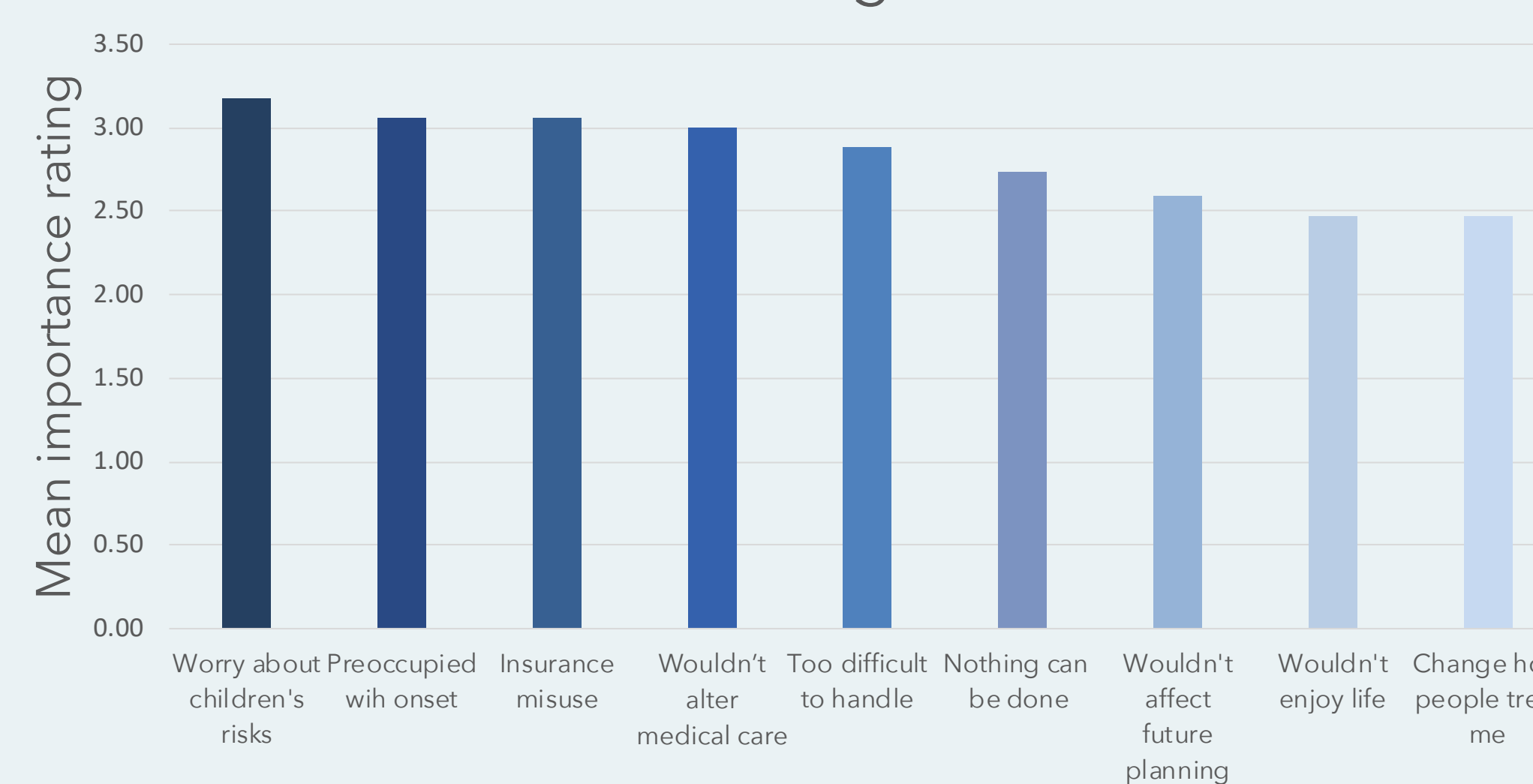


Figure 3: Reasons for not undertaking predictive testing

Discussion

There was a significant effect of knowing genetic status on diagnosis of a mental health problem when adjusting for gender differences with known carriers and non-carriers having higher rates of mental health diagnosis than those with unknown status. Levels of depression were higher in those with known genetic status compared to those who didn't know. While this was not statistically significant, it suggests that the relief from uncertainty from finding out one's genetic status may reduce anxiety, however there may be increased depressive symptoms. There was a trend towards significance on the GAD7, suggesting higher levels of anxiety in those who don't know their status. Therefore, learning one's genetic status may be associated with higher risk of a mental health diagnosis and more depressive symptoms, however lower anxiety levels may be a result of the 'relief in uncertainty' gained from predictive testing.

Conversely, the unknown status group scored significantly higher on nervousness and anxiety within the past month. Suggesting that in the short term, the unknown status group were experiencing more frequent symptoms of general anxiety.

'Relieving uncertainty' was the highest rated overall reason for undertaking predictive testing with those who knew their status also rating 'relieving anxiety' highly in terms of their reasoning for pursuing predictive testing. This could provide a potential explanation for the lower levels of anxiety observed in the known status group.

Overall, results suggest that those living 'at-risk' demonstrate higher short term levels of sadness and anxiety than those who are aware of their status, whereas those who knew their status had higher levels of depression on the PHQ9 and higher rates of mental health diagnosis. Those who knew their status also had lower levels of anxiety, suggesting predictive testing may be associated with reduced uncertainty and anxiety, as rated high in importance by participants.

Few people had accessed support, with most relying on family, friends and the research team and over half said that they would like to have more support. This suggests a need for a targeted psychosocial intervention within this unique population.

