

## Objective

People at risk of genetic ALS/FTD (e.g. children of an affected patient) face a variety of challenges; those who learn they carry an ALS-causing gene may experience significant stress, panic, worry about developing ALS, and even suicidal ideation. However, there is surprisingly little formal support available. While experts suggest pre- and post-test genetic counseling are important, in practice this can be applied inconsistently and there are calls for the development of new guidelines to fill the gaps. Globally, there are insufficient genetic counselors to provide timely and adequate support for individuals, necessitating novel approaches.

## Authors

Paul Wicks<sup>1,2\*</sup>, Lindsey Wahlstrom-Edwards<sup>1</sup>, Hayley Holt<sup>1</sup>, Patrick Short<sup>1</sup>  
\*Presenting author email: paul@wicksdigitalhealth.com

## Affiliations

1. Sano Genetics, London, United Kingdom
2. Wicks Digital Health, Lichfield, Staffordshire, United Kingdom

## Methods

With the support of scientific advisors and people at risk of ALS/FTD, we developed an online research platform, "Light The Way", to offer those on this journey the education, counseling, peer support, and connections to research that they need.

For those who want to understand their personal risks of developing ALS/FTD (if presymptomatic) or understand the cause of their condition (if already diagnosed), participants are offered 1:1 pre-test genetic counseling, genetic testing via at-home saliva collection with whole exome sequencing and PCR for repeat expansions covering over 30 genes, with 1:1 post-test genetic counseling for the return of results, all free of charge (Figure 1).

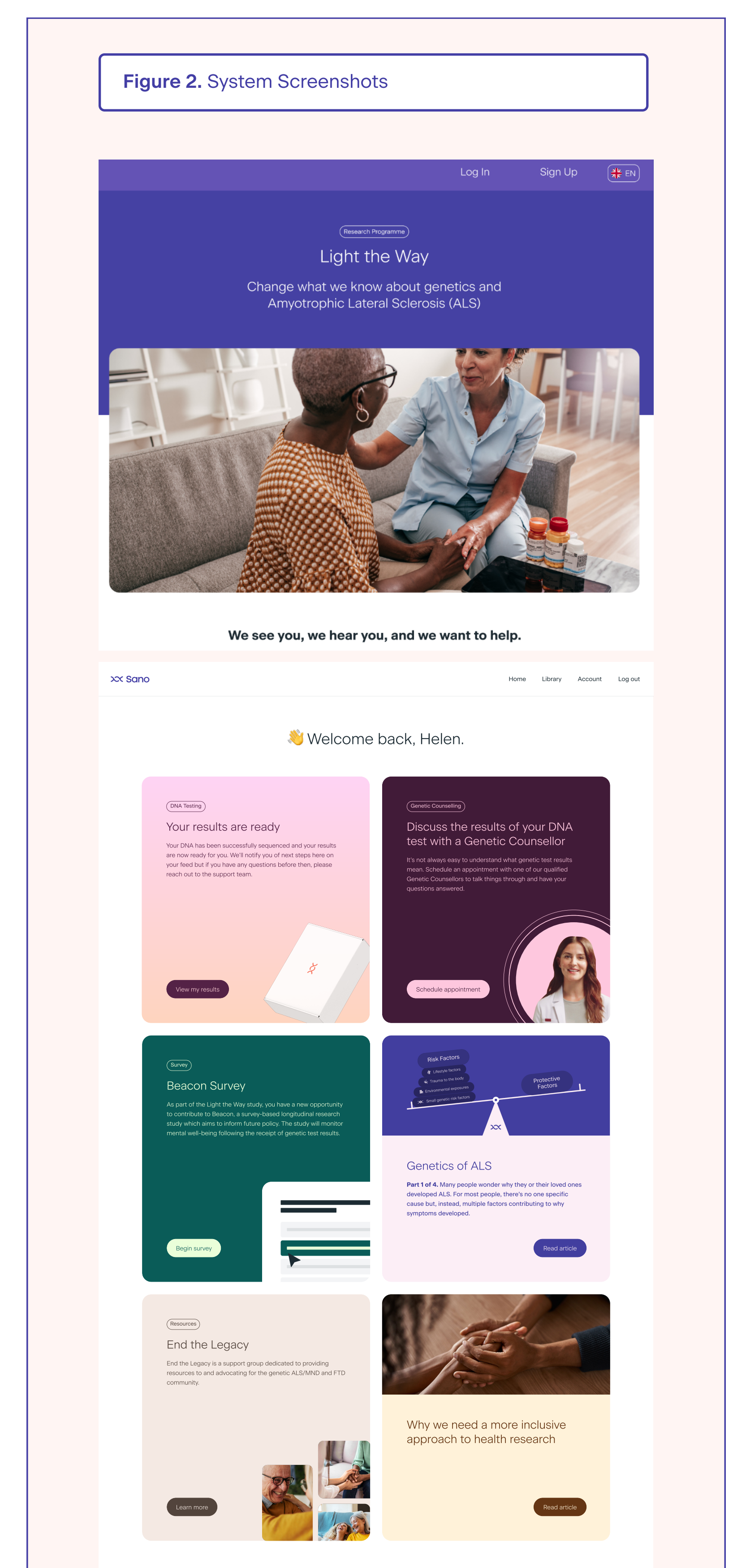
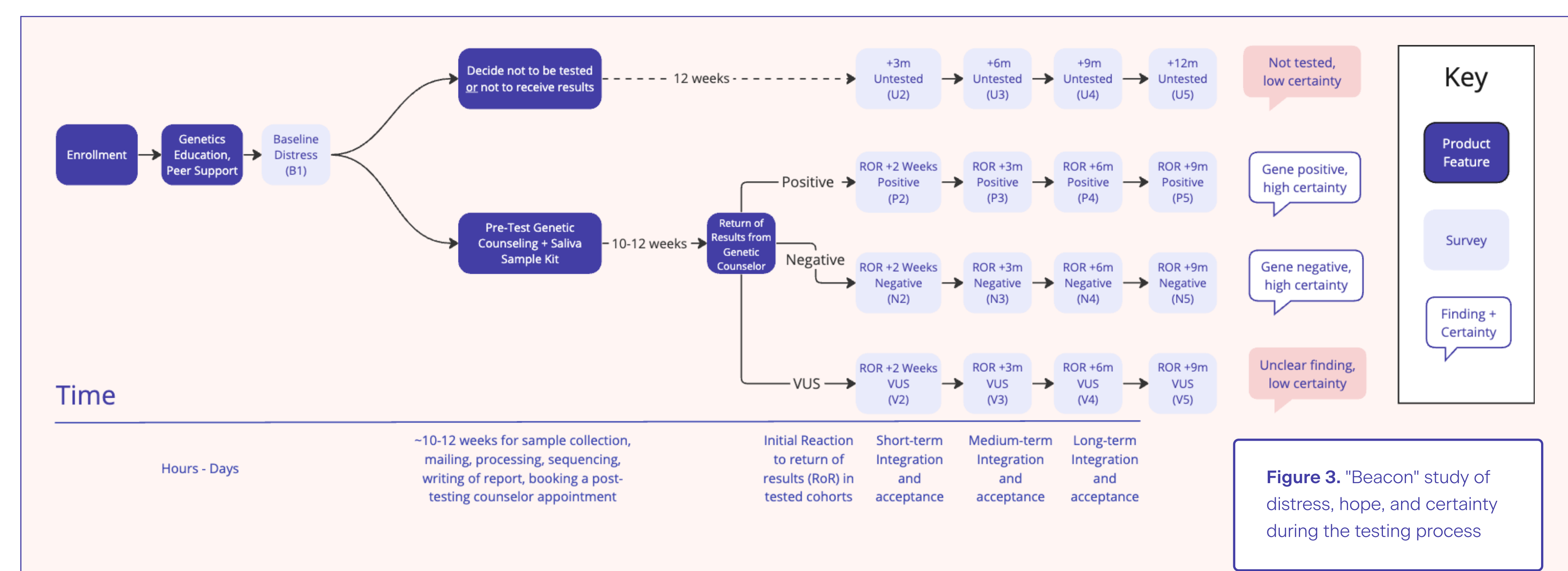
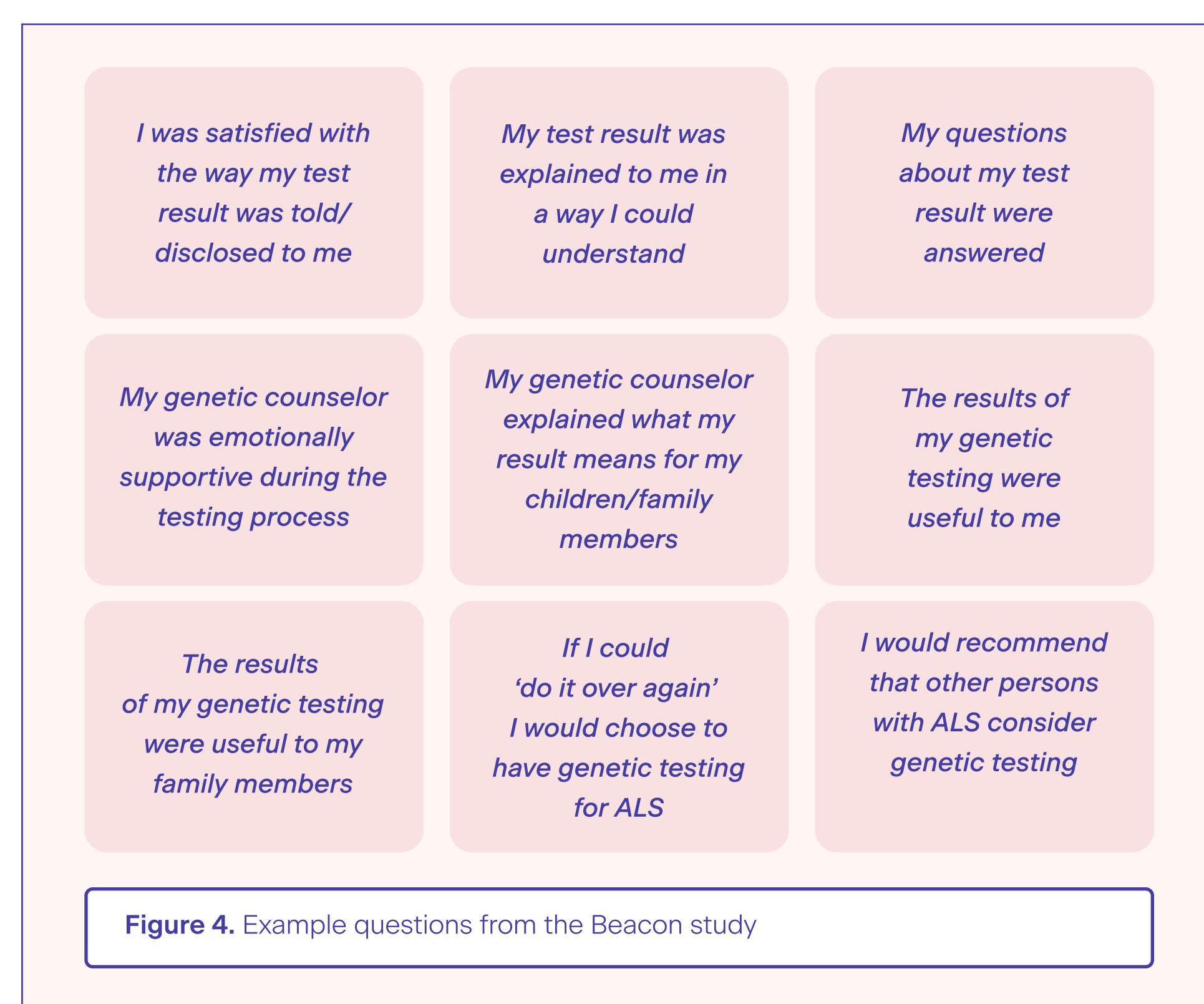
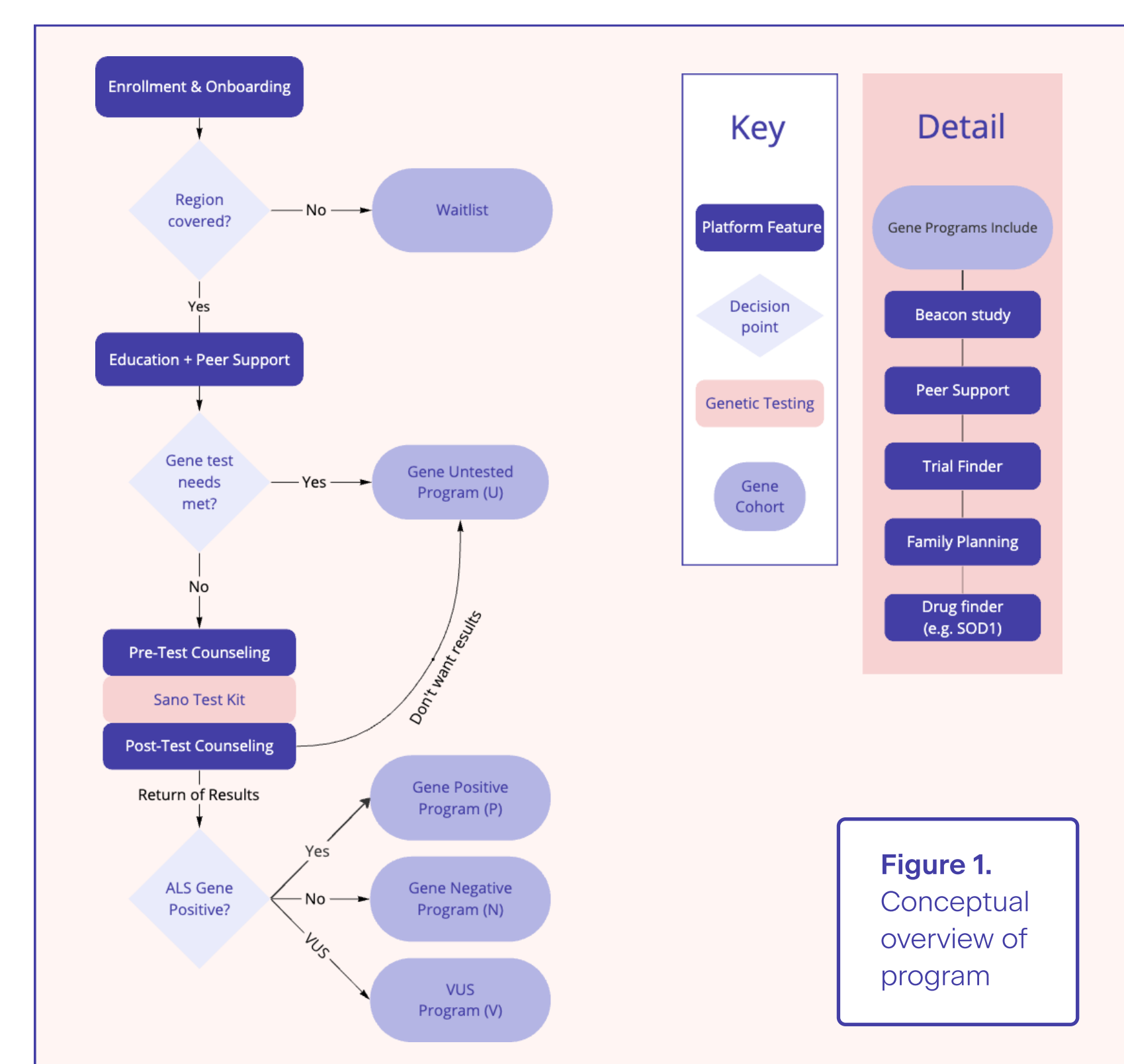
Light The Way has a dynamic flow of content and modules that are responsive to each individual's path and preferences. All participants are offered signposting to peer-led social support groups like "End the Legacy", and a "Genetics 101" education program written by a genetic counselor presented in video and blog formats (Figure 2).

A series of brief psychological distress screeners (PHQ-9, GAD-7, Hopelessness, perceived benefits / regrets) will be fielded longitudinally at baseline and at key milestones to describe the impact of the program in a substudy called "the Beacon project" (Figure 3). In this exploratory substudy, a multivariate analysis of covariance (MANCOVA) will be used to:

- Estimate the frequency of ALS-causing genetic variants among individuals genetically at risk of ALS
- (Within-subjects) Explore whether, compared to their scores at enrolment, users report statistically significant improvements in self-reported measures of psychological distress (PHQ-9 + GAD-7), hopefulness, uncertainty, and genetic concern, as well as satisfaction with participation in the project.
- (Between-subjects) Explore differences in scores between individuals who test positive for ALS-causing genes, negative for ALS-causing genes, have a test showing a variant of uncertain significance, and those who opt not to get tested at multiple timepoints (3 months, 6 months, and 9 months after the return of results, or a time-matched equivalent for those who opt not to be tested).
- Investigate the correlation structure among and between the self-reported measures of psychological distress (PHQ-9 + GAD-7), hopefulness, uncertainty, and genetic concern.

## Results

Light The Way is currently pending ethical review in the UK and US, with a planned launch window of Q3 2023 for the UK and Q4 for the US. Individuals can share their genetic results with their healthcare providers, and initial funding from Innovate UK has been allocated for 1,000 users of which up to 200 are anticipated to receive sequencing for ALS genes.



## Conclusion

Genetic forms of ALS affect families far beyond local boundaries, and with the support of the community we will develop a sustainable platform to offer education, support, and fellowship to those in need.

## Acknowledgements

We are grateful to the members of our Scientific and Patient Advisory Board (SAPAB), our Patient and Public Involvement (PPI) advisors, to our partners at End the Legacy, and to the whole ALS community for their support.

## Funding

Innovate UK SMART Award