

Figure S1

User-centered “Positive / Partner p.Phe508del” report.

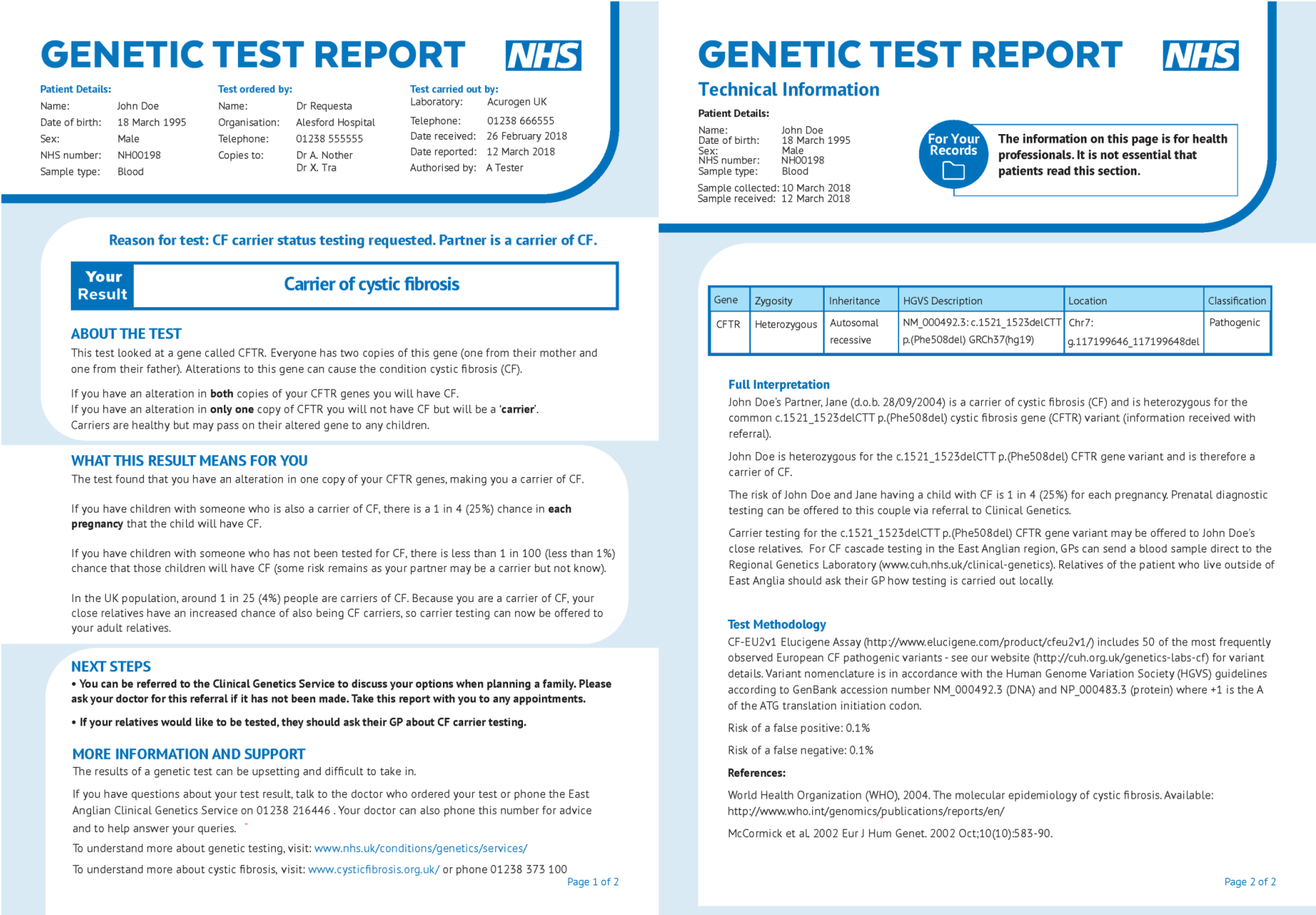


Figure S2

User-centered “Negative / Partner p.Phe508del” report.

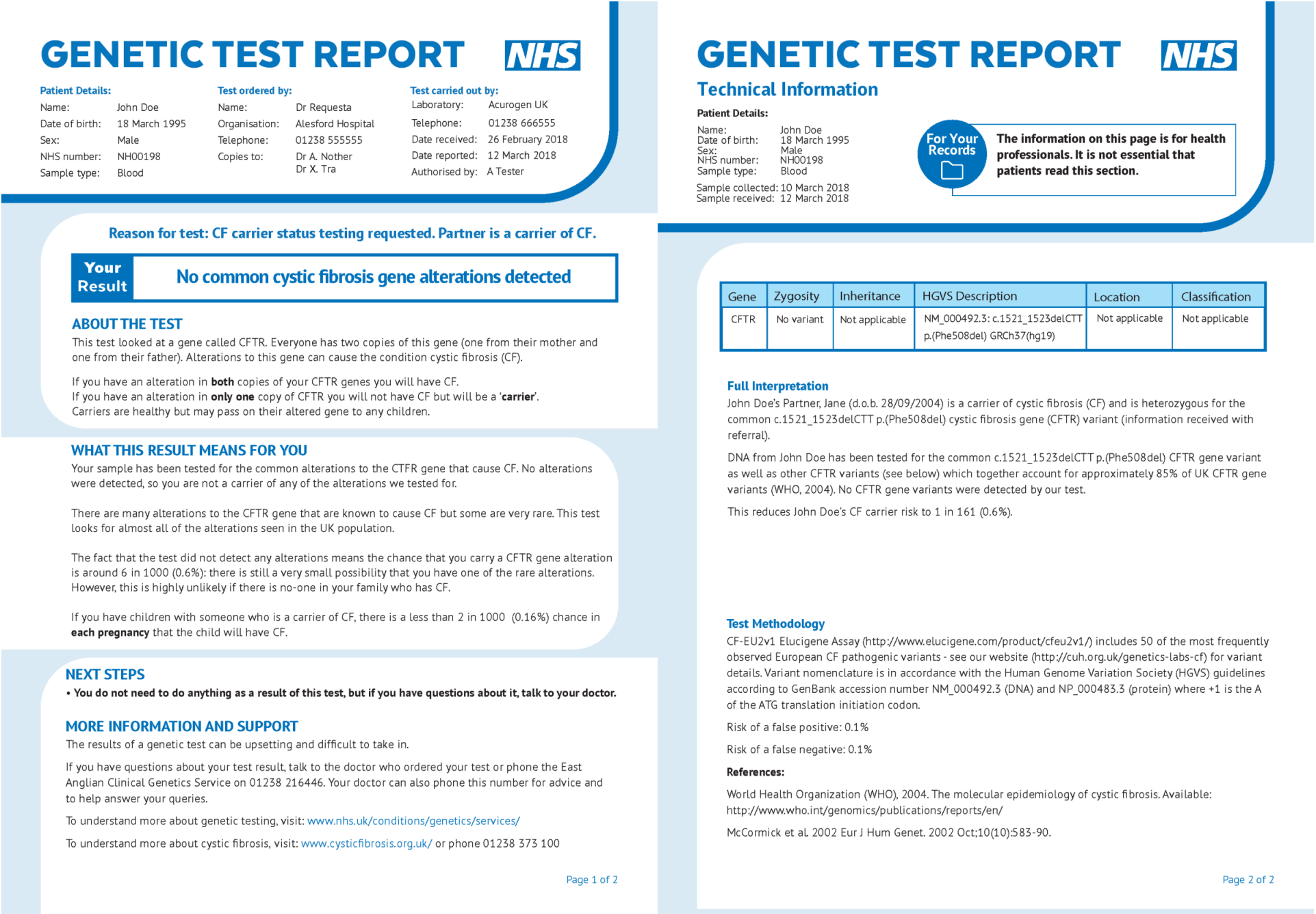


Figure S3

Standard "Positive / Partner p.Phe508del" report.

Acurogen Genetics Laboratory
101 Long Street, Alesford, Devon, AS1 1AB, UK

Website: www.acurogen.co.uk
 Email: info@acurogen.co.uk

Clinical Service Lead:
 Dr H Ead PhD FRCPATH

Tel: 01238 555666
 Fax: 01238 666555

Report of Molecular Genetic Analysis for Cystic Fibrosis

Patient name:	DOE John	Referred by:	Dr Requesta
DOB:	18 Mar 1995	Unit:	
Sex:	Male	Date requested:	26 Feb 2018
NHS No.:	NH00198	Acurogen Pedigree:	
Unit no.:	Not provided	Acurogen Lab no:	
Sample type:	Blood		
Test reason:	Partner is a CF carrier (information provided with referral; no further information available). This patient is assumed to be at ~1 in 25 prior risk of being a CF carrier (population carrier risk). The prior risk to any future child of this patient and their partner of being affected with CF is ~1 in 100. Carrier test.		

Results and Interpretation:

Test	Result	Lab Ref
CF-EU2v1	c.1521_1523del heterozygote	ACU55-5555

CF-EU2v1 analysis indicates that this patient is heterozygous for the pathogenic CFTR mutation c.1521_1523del p.(Phe508del). The remaining CFTR mutations tested for by the CF-EU2v1 kit are absent. This patient is therefore a CF carrier. The risk to any future child of this patient and their partner of being affected with CF is increased to 1 in 4. Assuming that this patient's partner has an identified CFTR mutation, prenatal CF testing is available if appropriate. We strongly recommend that this patient and their partner are referred to their local Clinical Genetics department.

This result also has important implications for relatives of this patient, and testing is available if appropriate. We recommend that these individuals are referred to their local Clinical Genetics department.

Summary:

This patient is heterozygous for the pathogenic CFTR mutation c.1521_1523del, and is therefore a CF carrier. The risk to any future child of this patient and their partner of being affected with CF is increased to 1 in 4.

Reported: Dr A Filer

Authorised: Dr A Tester

Date: 12 Mar 2018

Clinical Scientist

Principal Clinical Scientist

All reports depend upon the diagnosis of affected individuals, identification of samples and biological relationships of the individuals being correct.

Notes: Germline mutations within the CFTR gene cause cystic fibrosis (CF) or a CFTR-related disorder (CFTR-RD), which have autosomal recessive inheritance. The CF-EU2v1 (Elucigene) kit uses fluorescent ARMS (Amplification Refractory Mutation System) allele-specific amplification technology to identify 50 CFTR point mutations, insertions, or deletions. Please see the laboratory website (<http://www.acurogen.co.uk>) for a list of these 50 mutations, including previous nomenclature. In the local Caucasian population these mutations account for approximately 88% of all CF alleles. CFTR mutations are named according to HGVS (www.hgvs.org) guidelines using the reference sequence NM_000492.3. Very rare variants within the CFTR gene may interfere with the CF-EU2v1 assay, causing false positive or false negative results. Please see the laboratory website (<http://www.acurogen.co.uk>) for further information regarding CFTR analysis.

References:

Schwarz et al. Cystic fibrosis mutation analysis: Report from 22 UK regional genetics laboratories. Hum Mutat. 1995;6(4):326-33
 McCormick et al. Demographics of the UK cystic fibrosis population: Implications for neonatal screening. Eur J Hum Genet. 2002 Oct;10(10):583-90

Figure S4
Standard “Negative / Partner p.Phe508del” report.

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Report of Molecular Genetic Analysis for Cystic Fibrosis

Patient name:	DOE John	Referred by:	Dr Requesta
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Unit no.:	Not provided	Acurogen Lab no:	
Sample type:	Blood		
Test reason:	Partner is a CF carrier (information provided with referral; no further information available). This patient is assumed to be at ~1 in 25 prior risk of being a CF carrier (population carrier risk). The prior risk to any future child of this patient and their partner of being affected with CF is ~1 in 100. Carrier test.		

Results and Interpretation:

Test	Result	Lab Ref
CF-EU2v1	c.1521_1523del heterozygote	ACU55-5555

Analysis indicates that the 50 CFTR mutations tested for by the CF-EU2v1 kit are absent in this patient. This result reduces this patient's CF carrier risk to ~1 in 200. The risk to the first child of this patient and their partner, Jane Doe, of being affected with CF is therefore reduced to ~1 in 800. Prenatal testing is not indicated.

Summary:

This patient's CF carrier risk is reduced to ~1 in 200. The risk to the first child of this couple of being affected with CF is reduced to ~1 in 800.

Reported: Dr A Filer

Authorised: Dr A Tester

Date: 12 Mar 2018

Clinical Scientist

Principal Clinical Scientist

All reports depend upon the diagnosis of affected individuals, identification of samples and biological relationships of the individuals being correct.

Notes: Germline mutations within the CFTR gene cause cystic fibrosis (CF) or a CFTR-related disorder (CFTR-RD), which have autosomal recessive inheritance. The CF-EU2v1 (Elucigene) kit uses fluorescent ARMS (Amplification Refractory Mutation System) allele-specific amplification technology to identify 50 CFTR point mutations, insertions, or deletions. Please see the laboratory website (<http://www.acurogen.co.uk>) for a list of these 50 mutations, including previous nomenclature. In the local Caucasian population these mutations account for approximately 88% of all CF alleles. CFTR mutations are named according to HGVS (www.hgvs.org) guidelines using the reference sequence NM_000492.3. Very rare variants within the CFTR gene may interfere with the CF-EU2v1 assay, causing false positive or false negative results. Please see the laboratory website (<http://www.acurogen.co.uk>) for further information regarding CFTR analysis.

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Schwarz et al. Cystic fibrosis mutation analysis: Report from 22 UK regional genetics laboratories. Hum Mutat. 1995;6(4):326-33
McCormick et al. Demographics of the UK cystic fibrosis population: Implications for neonatal screening. Eur J Hum Genet. 2002 Oct;10(10):583-90

Figure S5

Participant answers to the question “Is the patient given enough guidance about the implications of the result and what actions they could now take?” were coded by 3 independent raters (Fleiss’ kappa 0.6) into the categories indicated in the legend. Visualisation on left panel includes all participants, while right panel excludes healthcare providers.

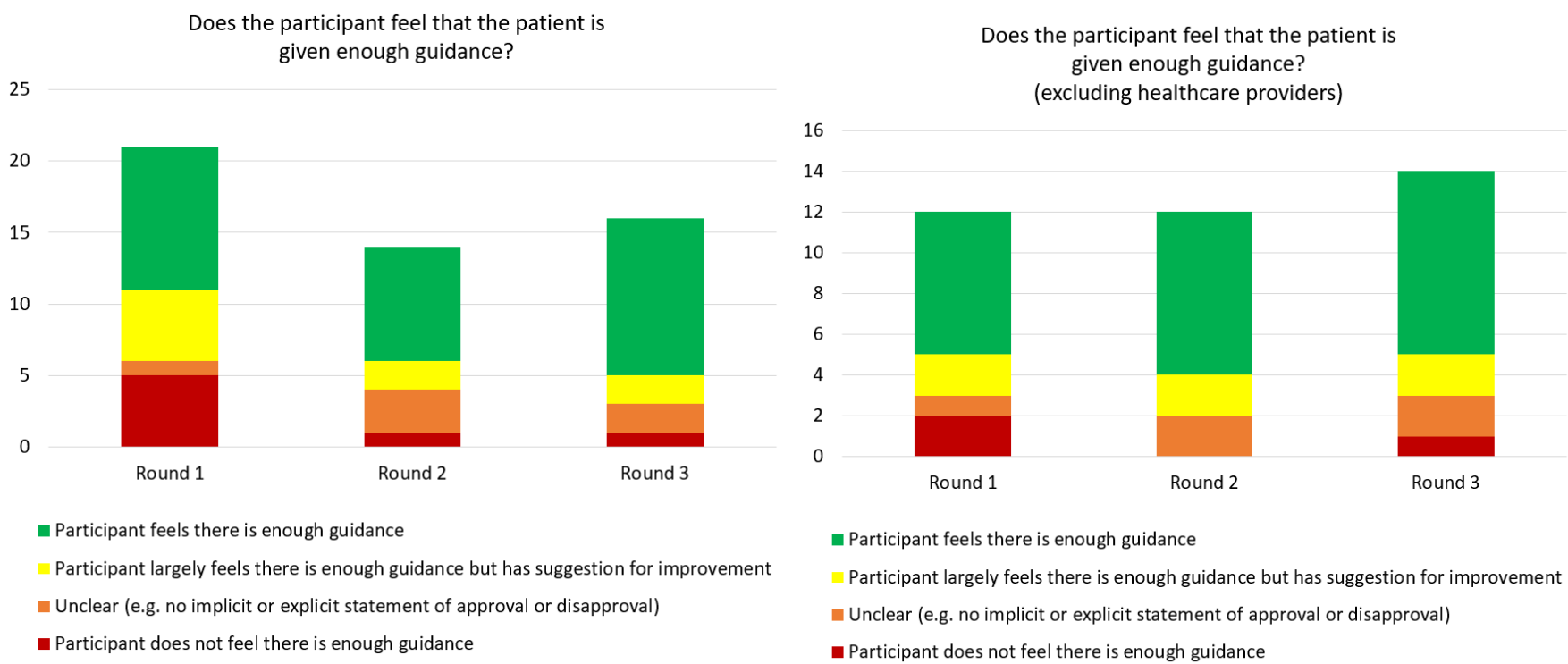


Figure S6

Participant answers to the question “What are your thoughts on the wording of the report and the level of the language used on page 1?” were coded for *participant approval* by 3 independent raters (Fleiss’ kappa 0.7) into the categories indicated in the legend. Visualisation on left panel includes all participants, while right panel excludes healthcare providers.

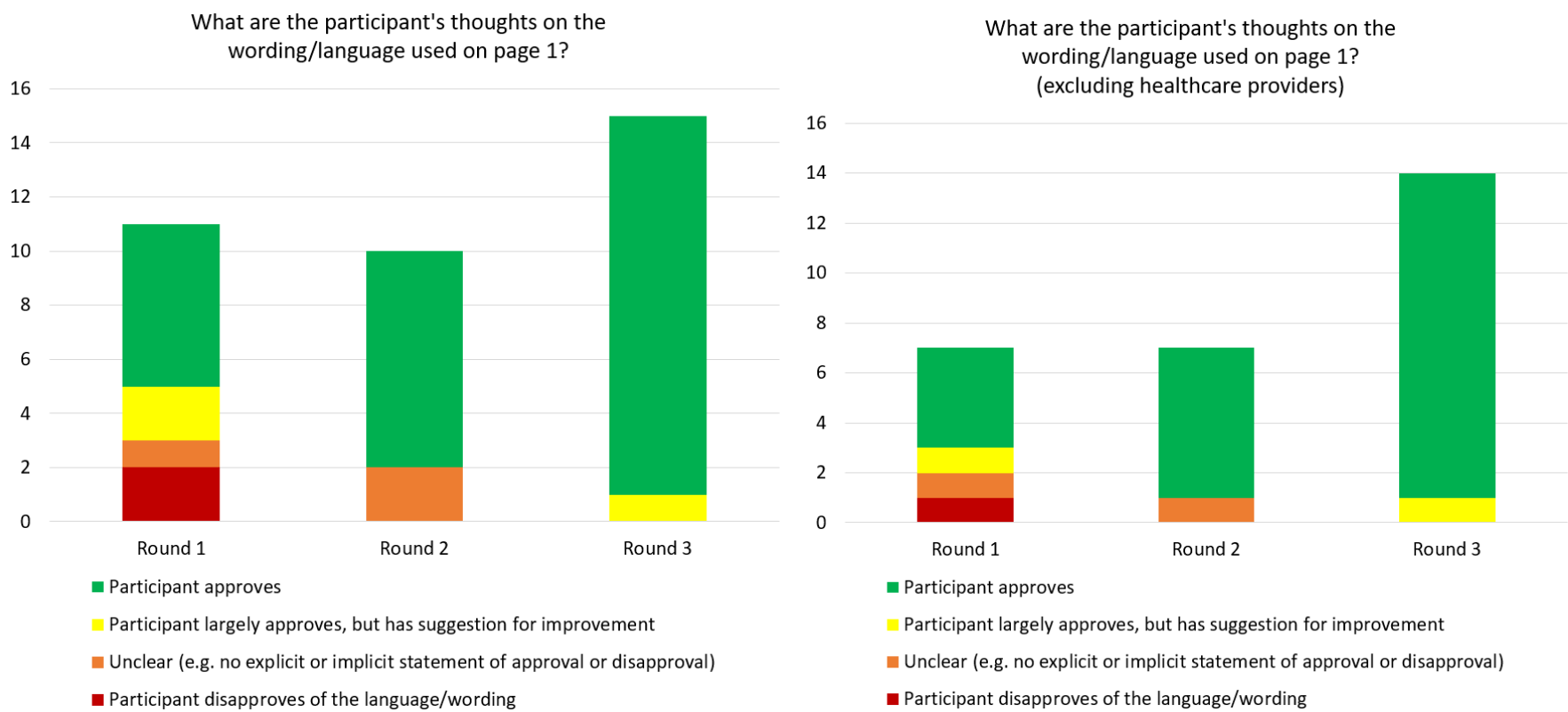


Figure S7

Participant answers to the question “What are your thoughts on the wording of the report and the level of the language used on page 1?” were coded for *confusion* by 3 independent raters (Fleiss’ kappa 0.6) into the categories indicated in the legend. Visualisation on left panel includes all participants, while right panel excludes healthcare providers.

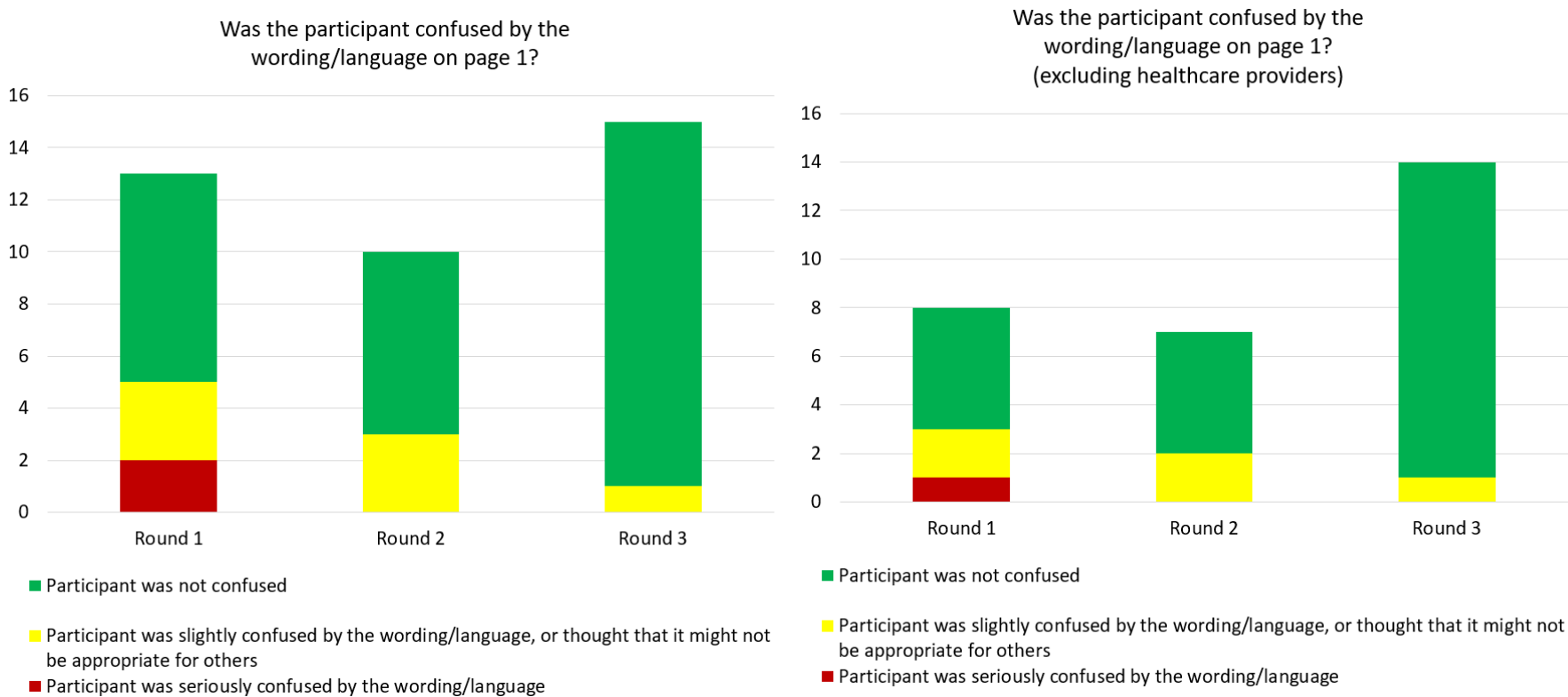


Figure S8

Participant answers to the question “Are there any particular words or phrases that are confusing?” were coded by 3 independent raters (Fleiss’ kappa 0.8) into the categories indicated in the legend. Visualisation on left panel includes all participants, while right panel excludes healthcare providers.

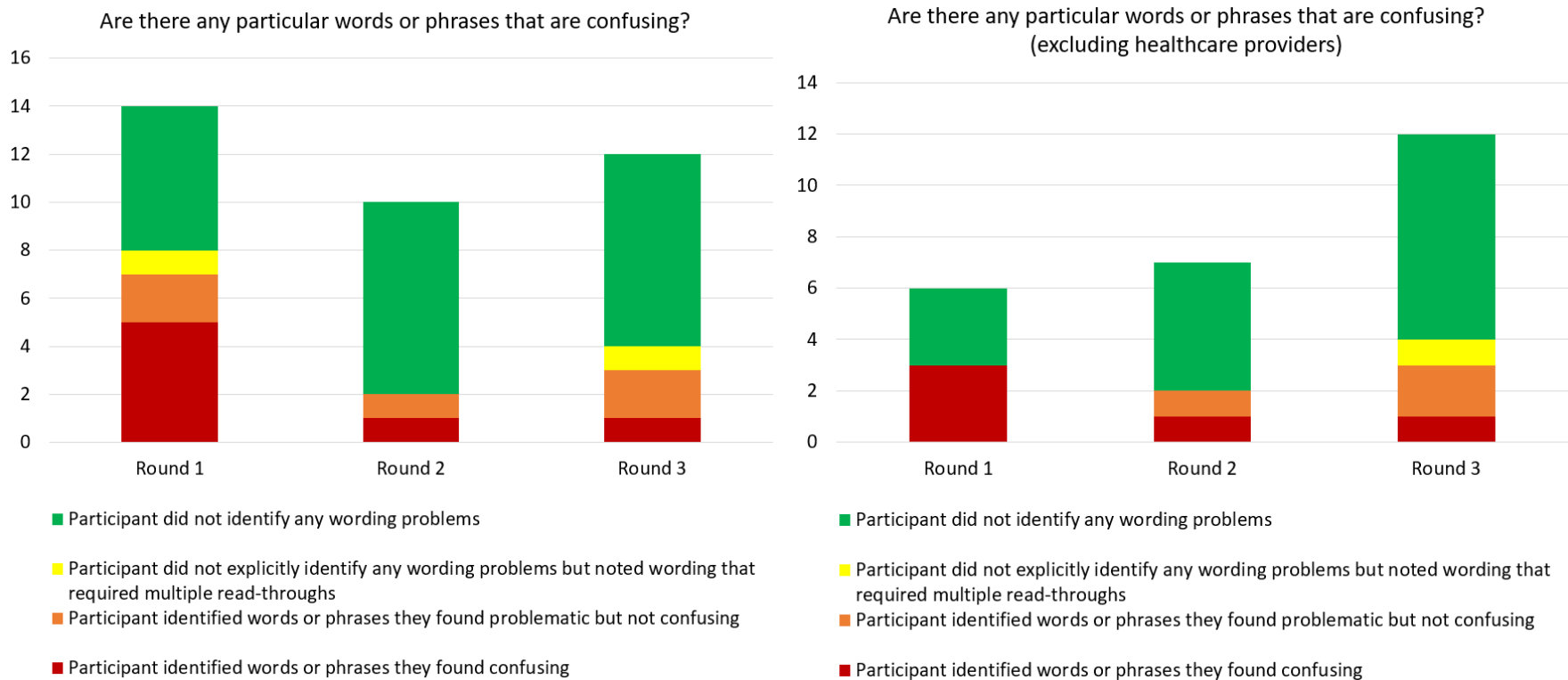


Figure S9

Participant answers to the question “Is there any information that you’d be left wanting to know after reading this report?” were coded by 3 independent raters (Fleiss’ kappa 0.9) into the categories indicated in the legend. Visualisation on left panel includes all participants, while right panel excludes healthcare providers.

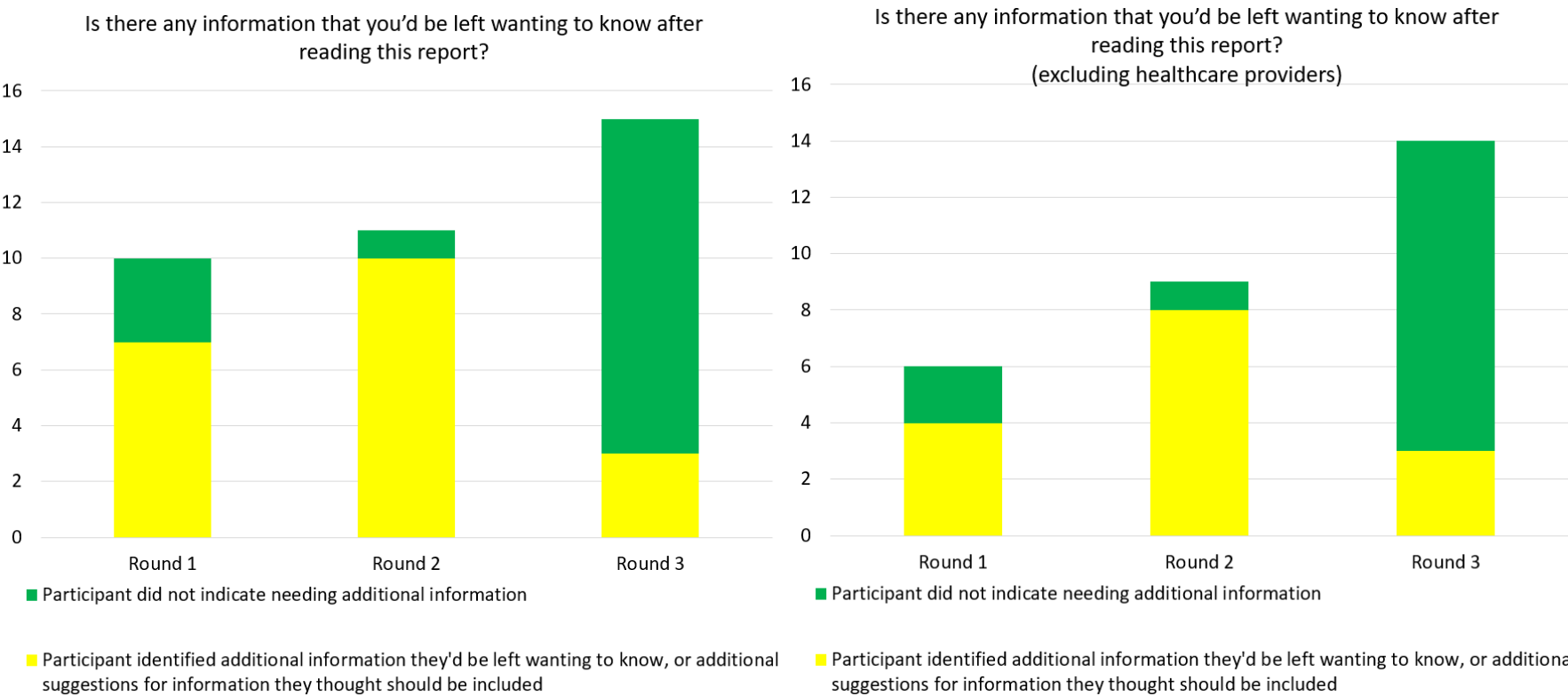


Figure S10

Density plot of communication efficacy.

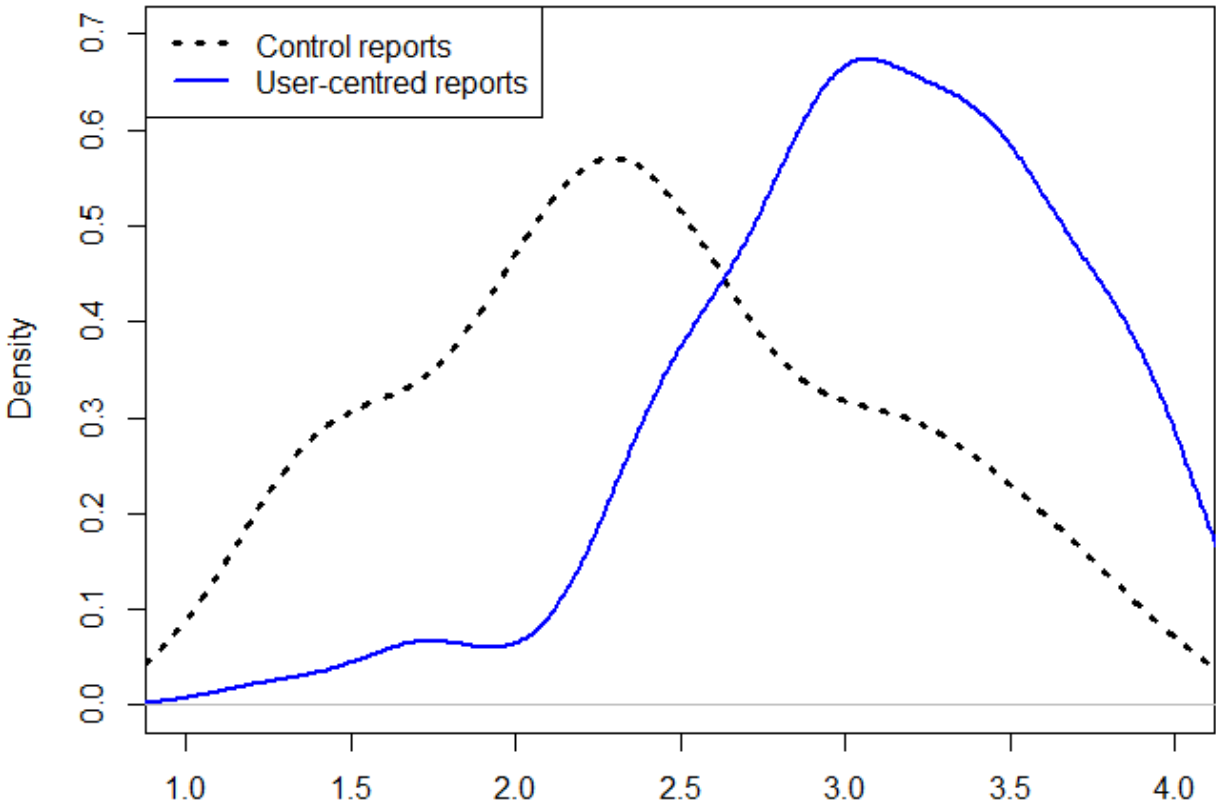


Figure S11

Density plot of subjective comprehension.

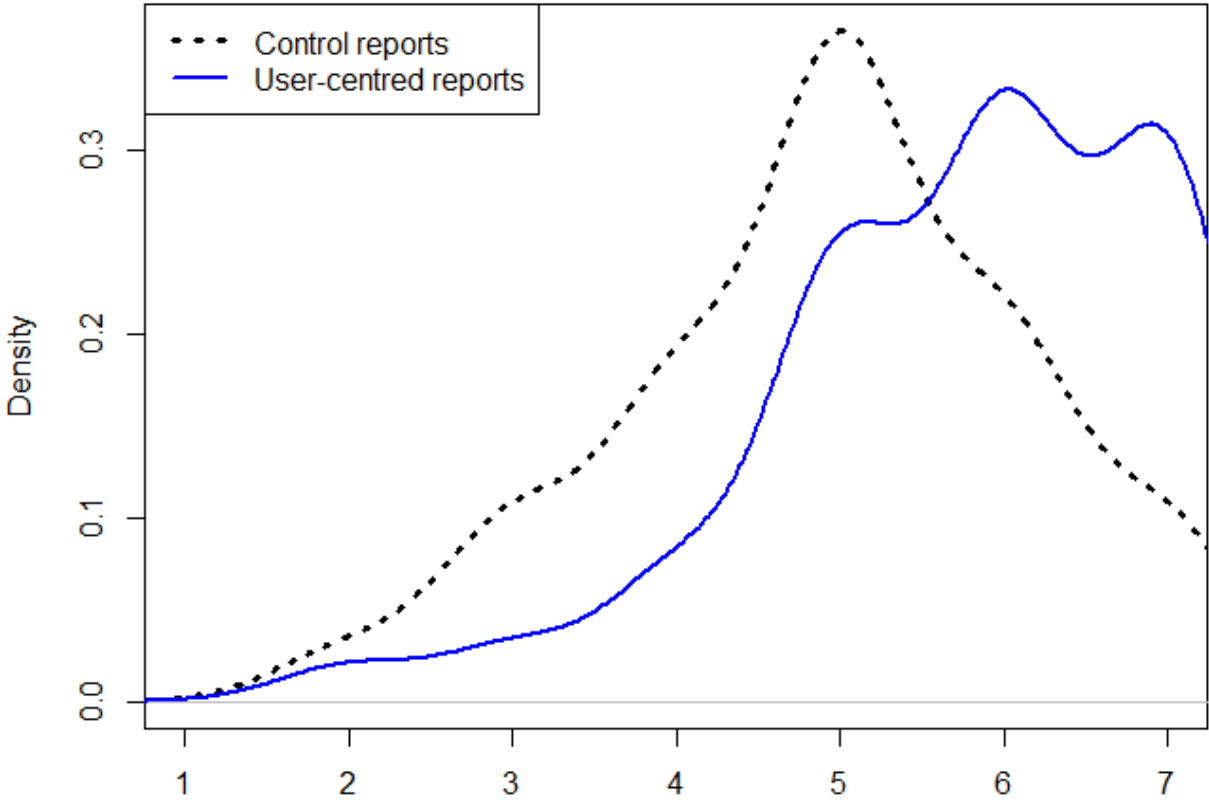


Figure S12

Density plot of objective comprehension.

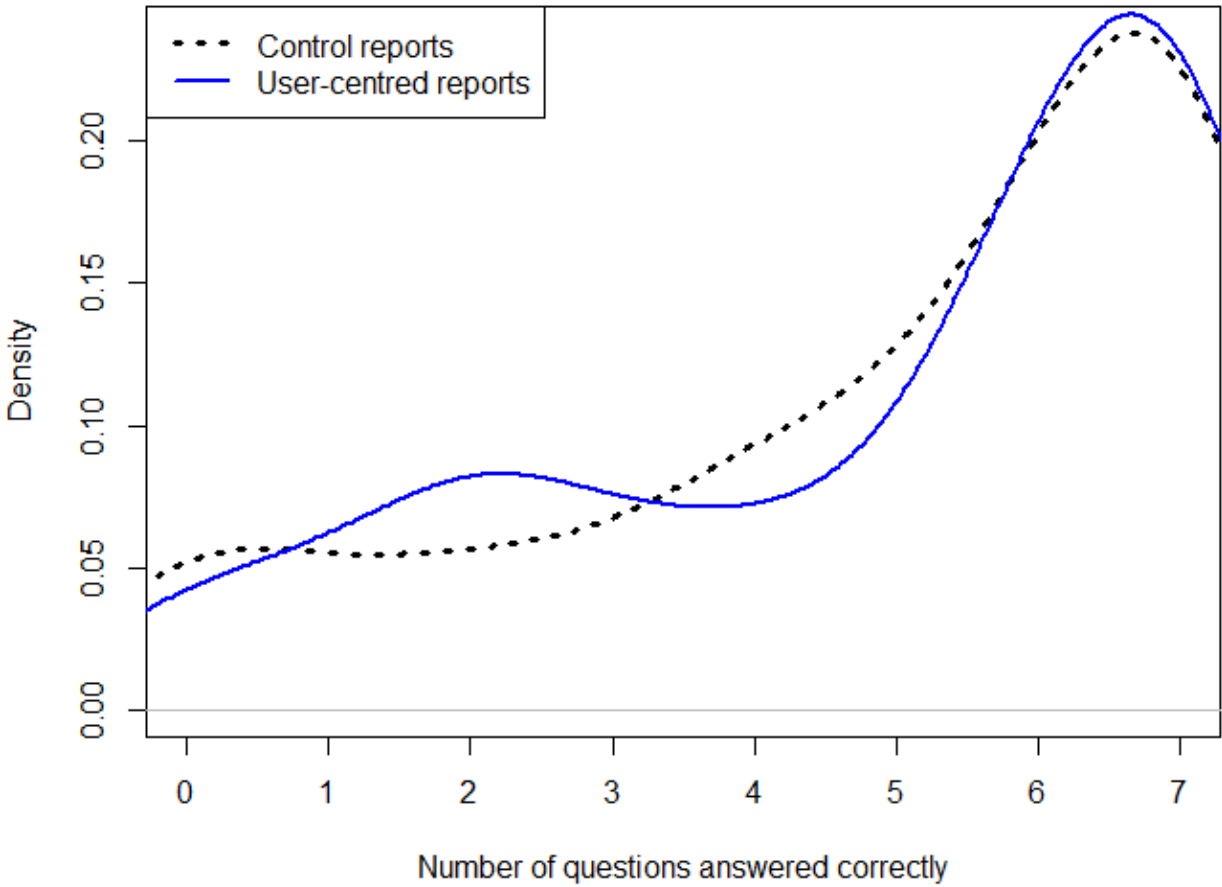


Figure S13

Density plot of subjective clarity.

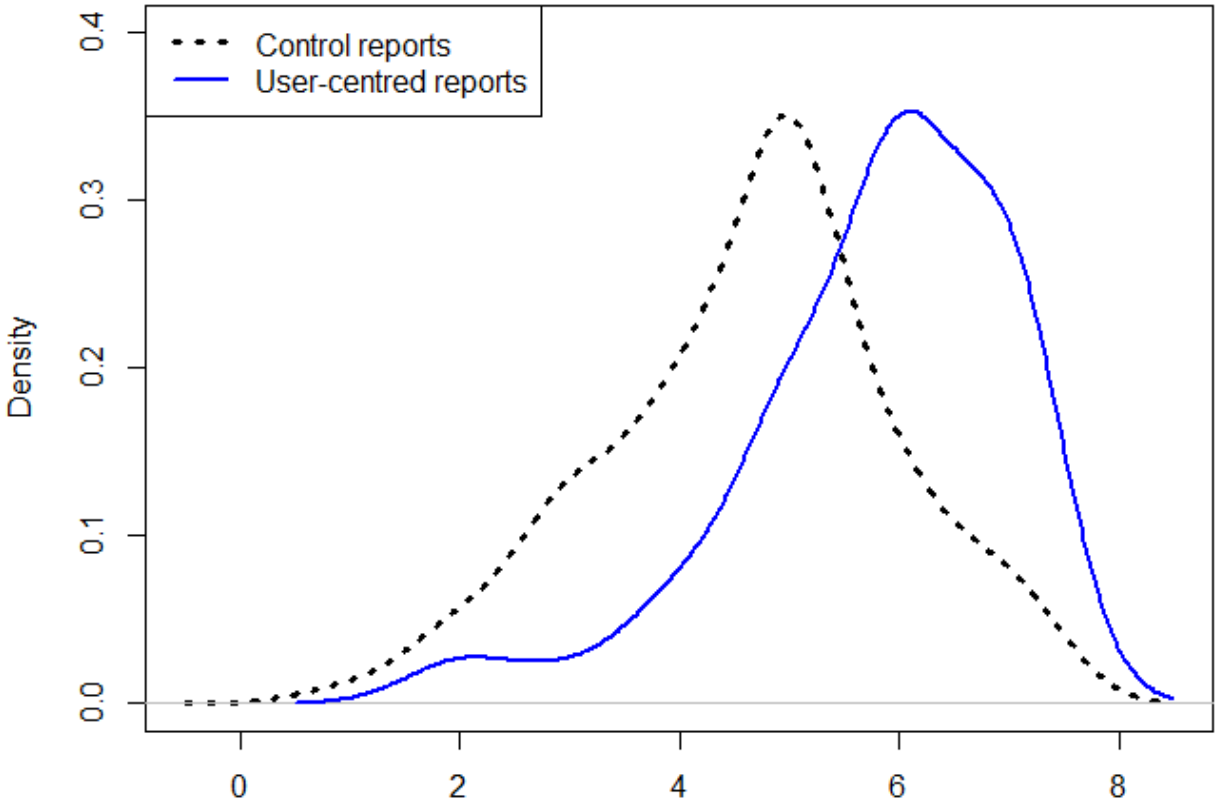


Figure S14

Density plot of subjective trust.

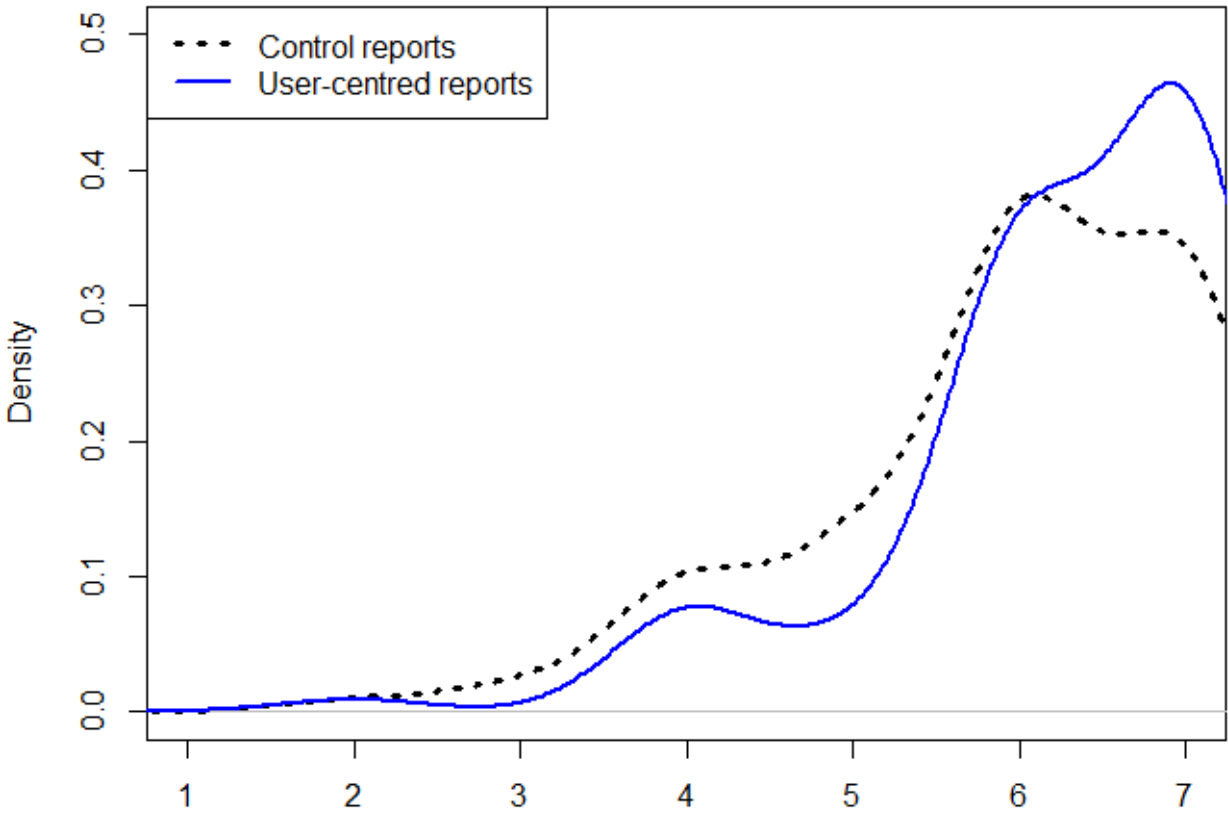


Figure S15

Density plot of actionability.

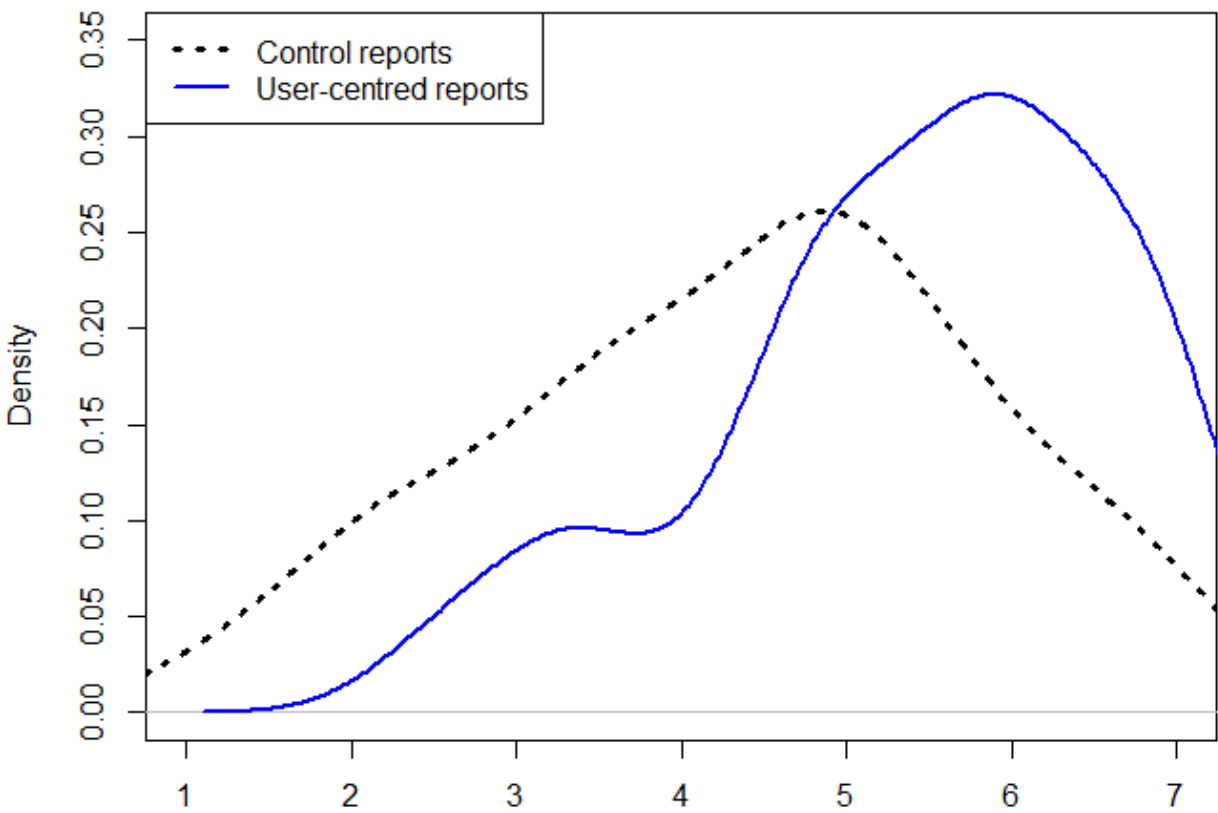


Figure S16

Density plot of ease of understanding of the result summary.

