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Identifying Research Priorities in Primary Sclerosing Cholangitis: Driving Clinically Meaningful Change from the Patients' Perspective

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Introduction

Primary sclerosing cholangitis [PSC] is a chronic fibro-inflammatory disorder characterised by multifocal stricturing throughout the biliary tree, most often coexisting with inflammatory bowel disease [IBD]

Patients experience a complex burden of symptoms relating to fatigue, abdominal pain and pruritus, and the advancing nature of PSC results in ~50% of individuals needing a liver transplant or succumbing to their illness.

Living with an incurable and progressive disease, together with a complex symptom profile, is likely to have devastating psychological, social and economic effects.

As such, patients and their families are highly motivated to help progress our knowledge of PSC and actively participate in research. It is a core democratic principle that people who are affected have a right to say "what and how" research is undertaken, with patient involvement being considered an intrinsic part of public accountability, transparency and citizenship.

Aim

Prospectively inform basic and targeted outcomes' research in PSC, by examining the opinions, attitudes and experiences of those living with the disease.

Methods

This was a cross-sectional study led by the UK charity 'PSC Support' in partnership with '**albi**' France. Participants were invited to detail the most difficult aspects of living with PSC, and identify key research priorities based on present unmet need.

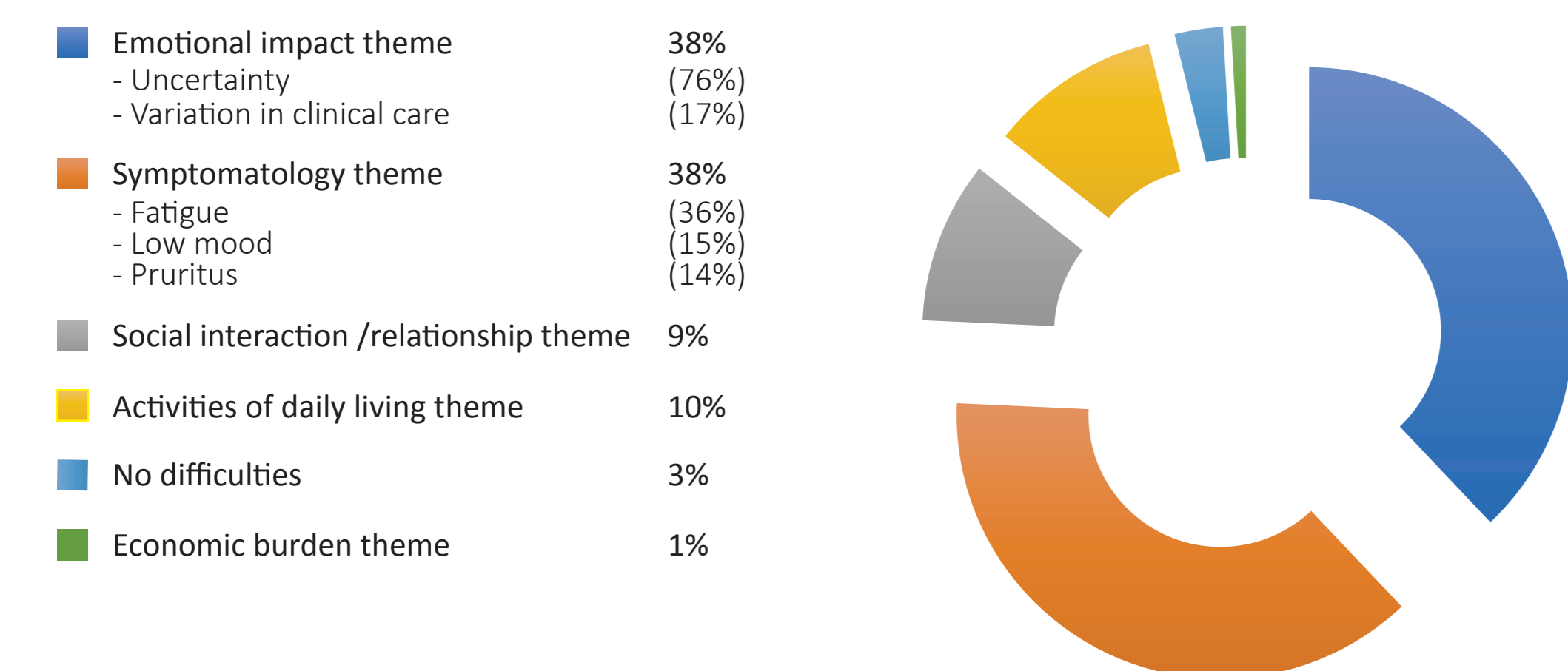
Concurrently, we gauged patient willingness to undergo specific interventions as part of PSC research and attribute confidence levels to currently proposed therapeutic endpoints.

The study was conducted between October 2014 and March 2017, accruing the viewpoints of 511 individuals (including 38 patients who were post-transplant and 93 caregivers of PSC patients).

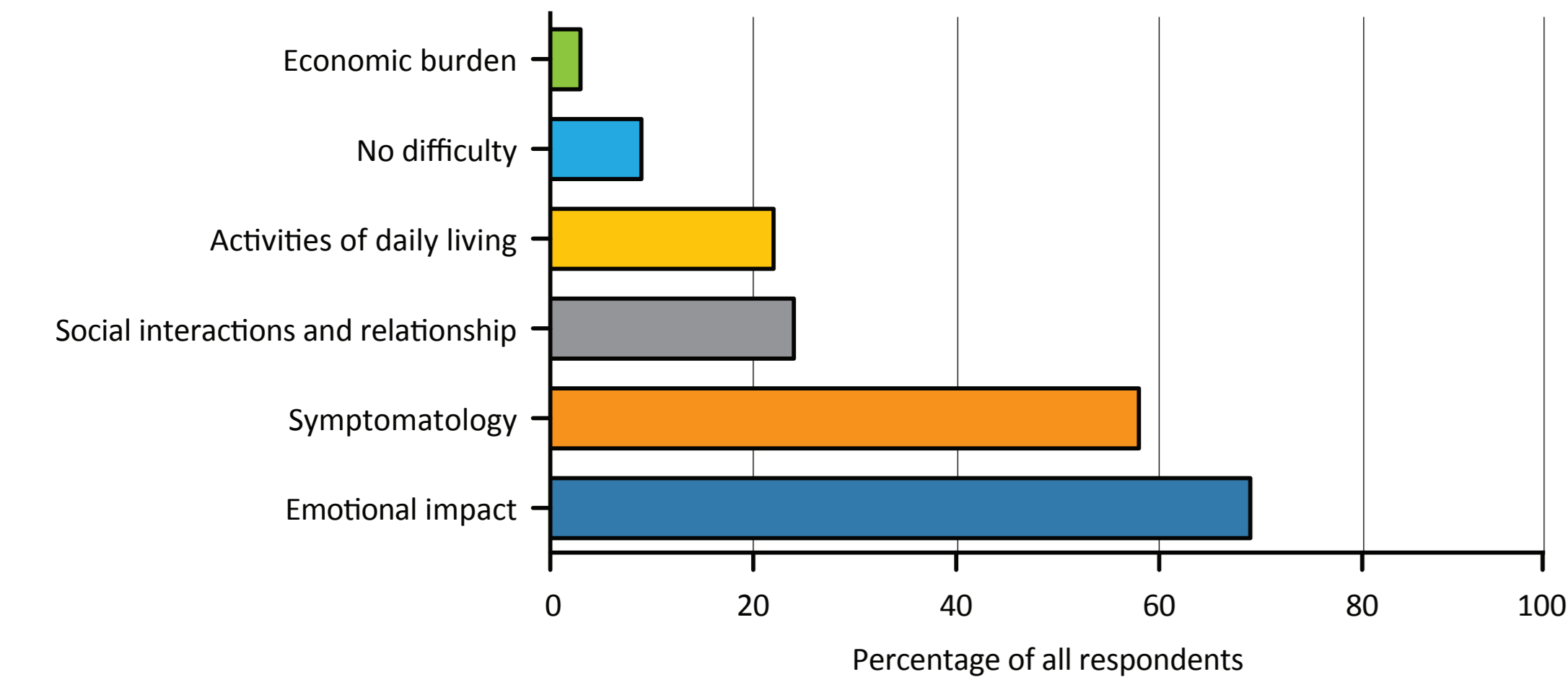
Results

Figure 1: The most difficult part of living with PSC

A) Proportional representation of all concerns reported (n=1,318)



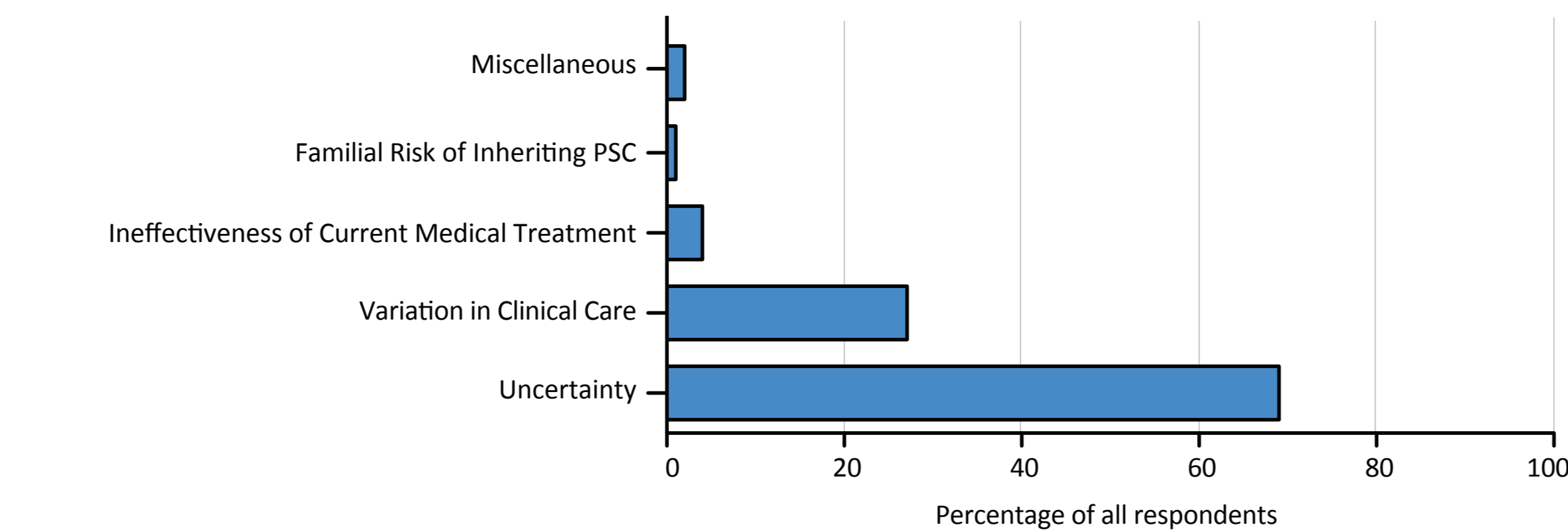
B) Proportional representation of concerns reported; per-respondent analysis (n=394)



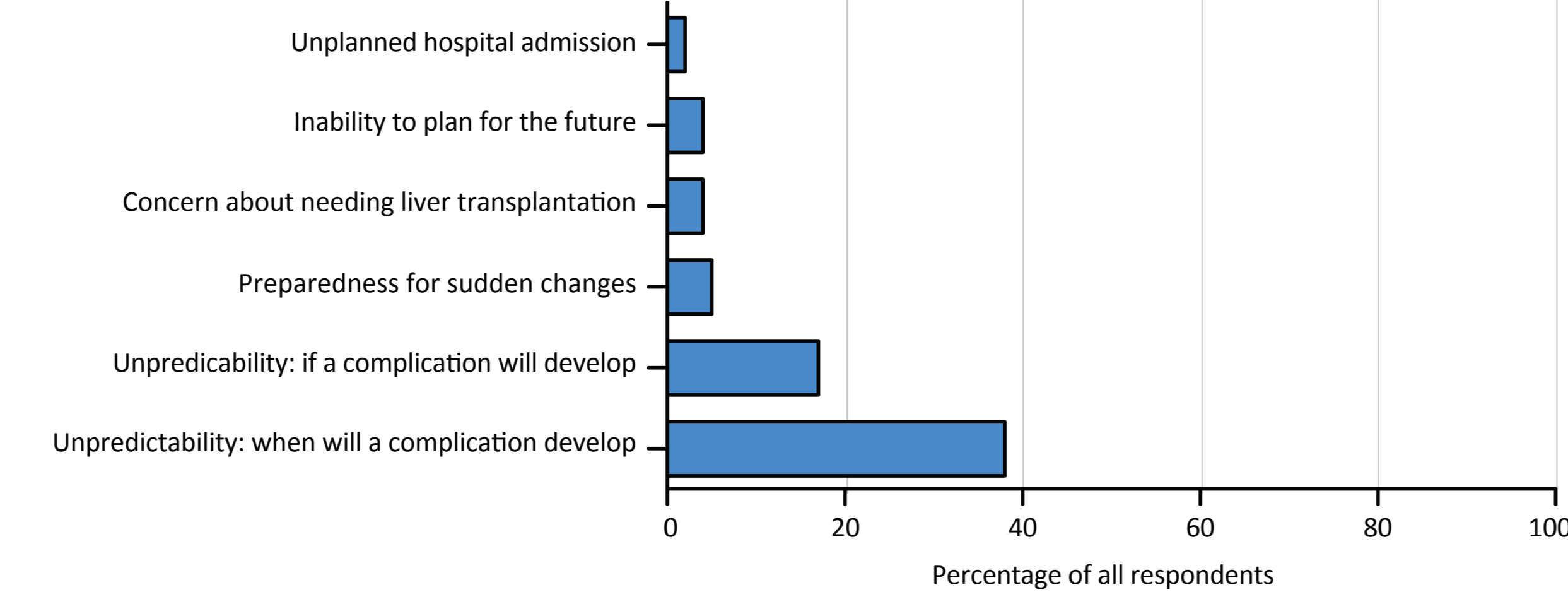
Overall, 394 participants detailed 1,318 concerns (mode 2 per patient; range 0-19), which they felt to be the most difficult aspect of living with PSC. Responses capturing the emotional impact were most prevalent (Fig. 1).

Figure 2: The emotional impact of living with PSC

A) Proportional representation of concerns within the emotional impact theme; per-respondent analysis



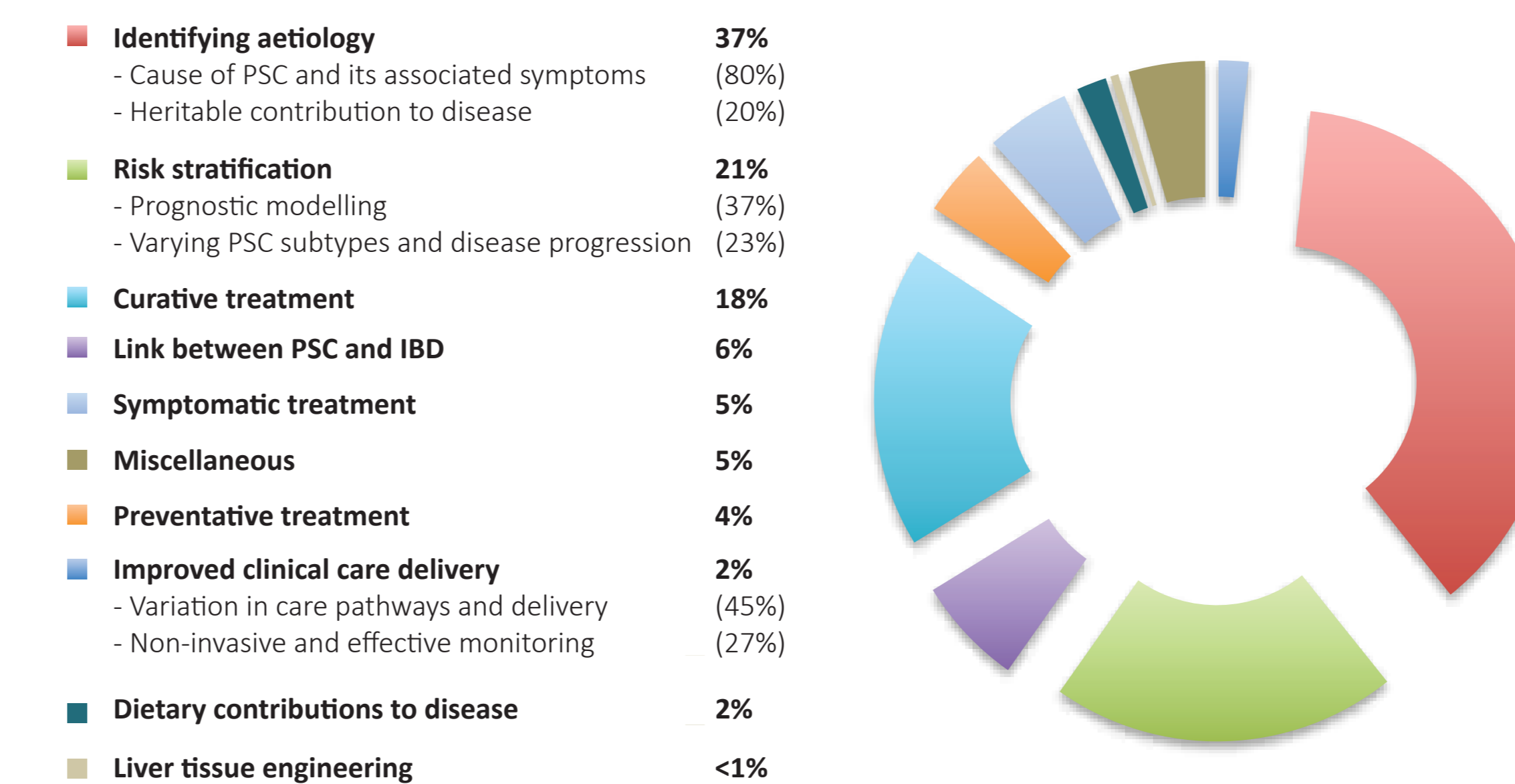
B) Proportional representation of concerns within the uncertainty domain; per-respondent analysis



Within the emotional impact theme, concerns relating to disease uncertainty were most prevalent (Fig. 2). An additional 25% of emotional impact responses highlight variation in care delivery as a lead cause of apprehension.

Figure 3: Priority areas for future research activity

A) Proportional representation of all nominated areas of research priority (n=619)



B) Proportion of respondents nominating specific areas of research priority

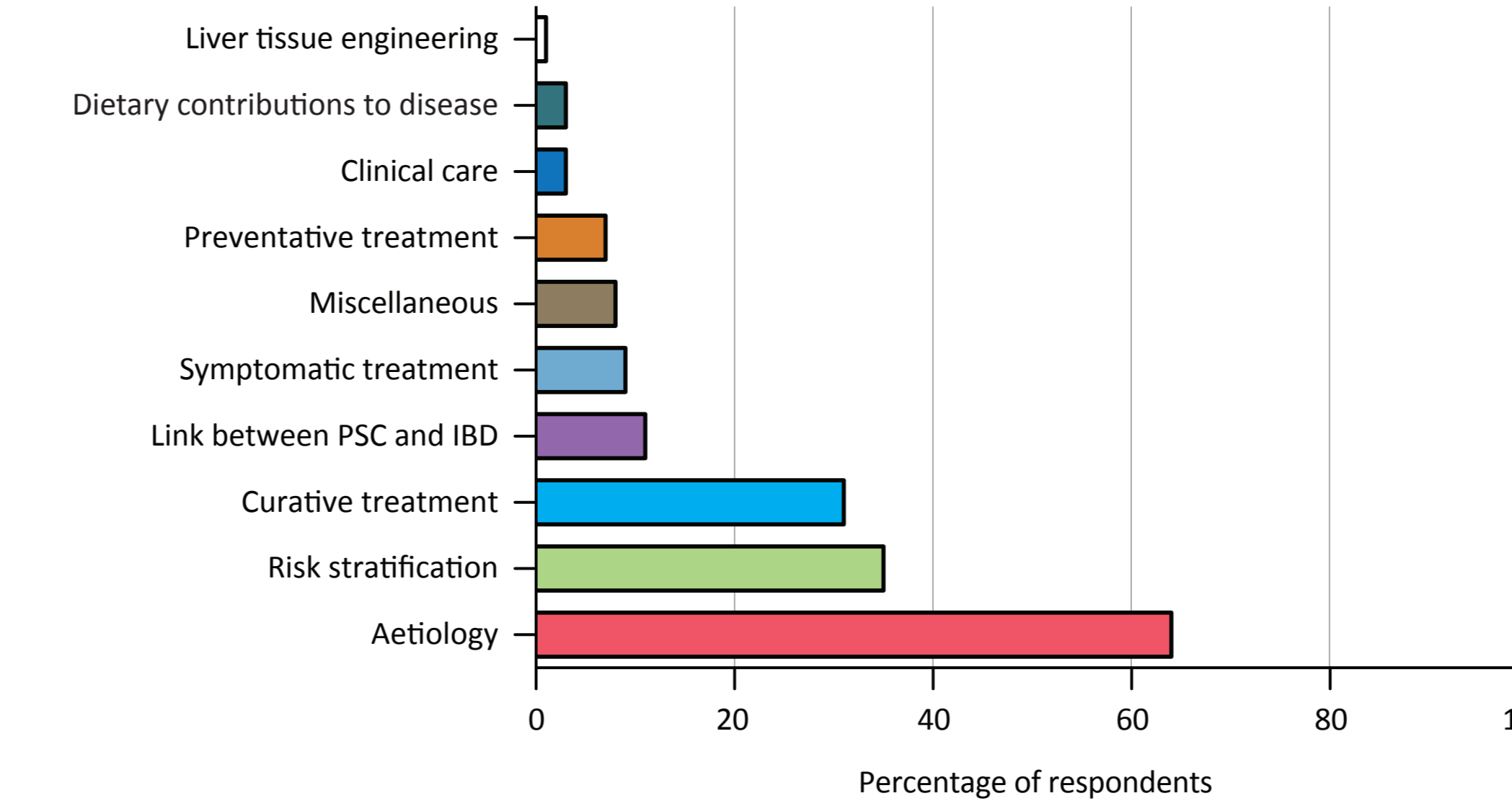


Figure 4: Patient readiness to undergo procedures as part of clinical trials

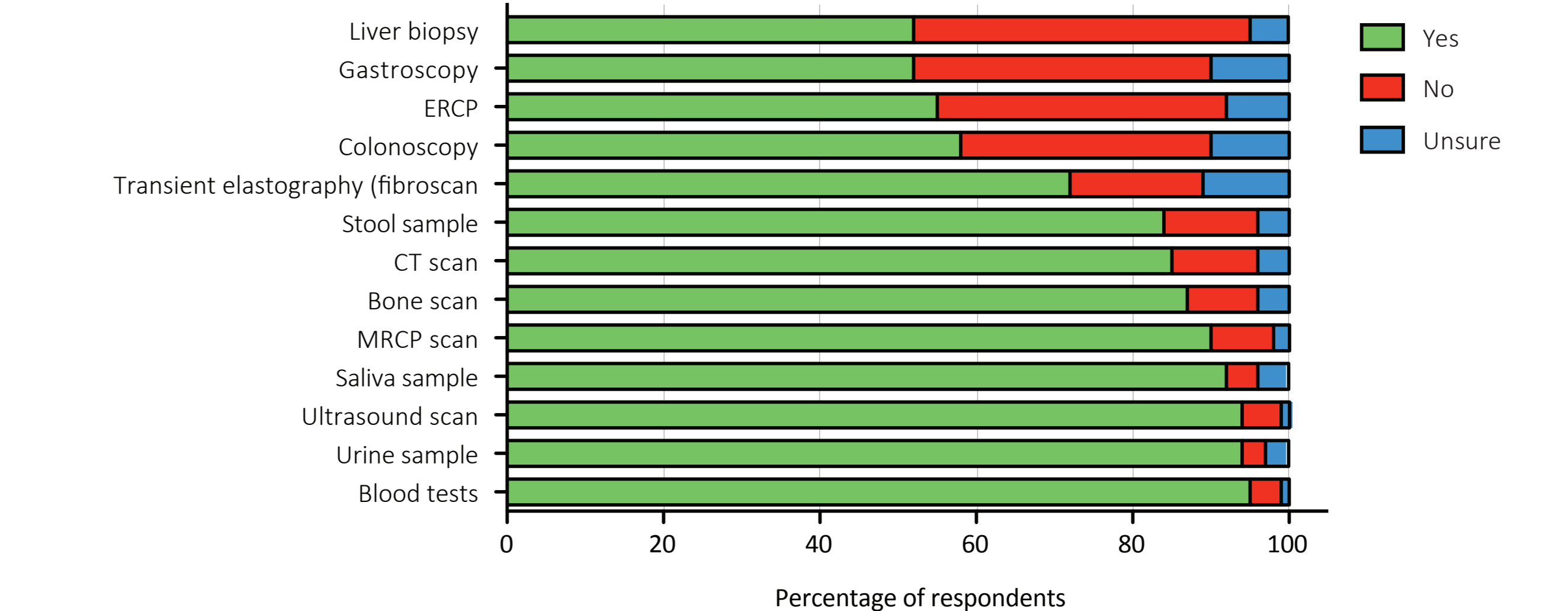
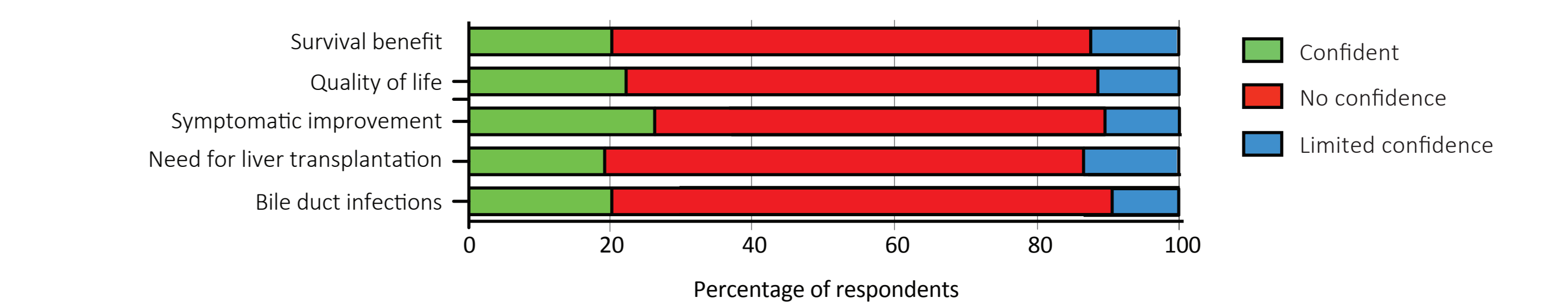


Figure 5: Patient confidence levels in serum ALP as a surrogate of clinical outcome



When asked to develop a hierarchy of research priority by nominating the most important "unanswered questions" relating to PSC (Fig. 3); finding the cause of disease was of greatest concern, in addition to improved methods for prognostication, and identification of curative treatment.

317 patients detailed their readiness to undergo specific procedures as part of research (Fig. 4); 52% were willing to undergo liver biopsy. <25% of patients were confident that reduction in ALP correlates with clinical outcome (Fig. 5).

Conclusion

For patients, the unpredictable nature of PSC results in far-reaching feelings of uncertainty, including toward the inconsistencies and variation in healthcare.

Determining the cause of PSC and associated symptoms is a key priority area for patients, in addition to developing more accurate risk stratification systems.

The low confidence in currently proposed surrogate endpoints (ALP), suggest need to develop novel non-invasive endpoints for clinical trials.

Disclosures

This paper presents independent research supported by the NIHR Birmingham Biomedical Research Centre at the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham.

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.