BMJ Open

Research priorities in pernicious anaemia: James Lind Alliance Priority Setting Partnership

Kristina Staley ,[1] Kourosh R Ahmadi,[2] Karyl Carter,[3] Katherine Cowan,[4] Heidi Seage ,[5] Petra Visser,[3] Nicola Ward,[6] Martyn Hooper[3]

To cite: Staley K, Ahmadi KR, Carter K, *et al*. Research priorities in pernicious anaemia: James Lind Alliance Priority Setting Partnership. *BMJ Open* 2022;**12**:e065166. doi:10.1136/bmjopen-2022-065166

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-065166).

Received 08 June 2022
Accepted 09 August 2022

[1]TwoCan Associates, Ross-on-Wye, UK
[2]School of Biosciences and Medicine, University of Surrey, Guildford, UK
[3]The Pernicious Anaemia Society, Bridgend, UK
[4]James Lind Alliance, Southampton, UK
[5]School of Sport and Health Sciences, Cardiff Metropolitan University, Cardiff, UK
[6]Leicester School of Pharmacy, De Montfort University, Leicester, UK

Correspondence to
Dr Martyn Hooper;
chair@pasoc.org.uk

ABSTRACT

Objectives To form a James Lind Alliance (JLA) Priority Setting Partnership (PSP) to determine research priorities related to the cause, diagnosis, treatment and management of pernicious anaemia (PA) from the perspectives of patients, carers and clinicians.

Design The PSP conducted two surveys and a workshop to identify the Top 10 questions for research. A first survey identified questions relating to the cause, diagnosis, treatment and management of PA. A literature search checked whether any of these questions had already been answered. A second survey asked respondents to identify and rank their top 10 questions from the list of questions from the first survey. An online workshop used an adapted nominal group technique to agree a final Top 10.

Results In the first survey, 933 people submitted 3480 responses that were categorised and summarised to generate a long list of 40 questions. None had been answered by previous research. The combined rankings from the 1068 patients, carers and clinicians who took part in the second survey identified a short list of 16 questions. These were discussed at the final workshop to agree the final Top 10. The number one question was about an accurate and reliable diagnostic test for PA. The other nine questions were about making treatment safe and effective, understanding why people with PA vary in their need for treatment, links to other conditions, and how to encourage clinicians to take PA seriously and provide long-term care.

Conclusions This JLA PSP enabled patients, carers and clinicians to work together to agree the Top 10 uncertainties relating to the cause, diagnosis, management and treatment of PA. Addressing any of these questions will greatly benefit the end-users of research, the people whose daily lives and decisions will be directly affected by generating high quality research evidence.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The Pernicious Anaemia Society has for the first time established a Priority Setting Partnership to combine the views of patients, carers and clinicians on the most important questions for future pernicious anaemia research.
⇒ The project followed the robust and respected James Lind Alliance approach for identifying priorities for research.
⇒ The numbers of survey respondents among minority groups and younger people were limited.
⇒ The surveys and workshops were mostly online that may have dissuaded or excluded participation from older and more vulnerable patients and carers.

INTRODUCTION

In pernicious anaemia (PA), absorption of vitamin B_{12} is impaired by a lack of intrinsic factor (IF) in the stomach. It is an autoimmune disease that damages the IF-producing parietal cells in the stomach lining.[1] B_{12} is an essential micronutrient for normal functioning of the nervous system and for synthesis of red blood cells, white blood cells and platelets.[2] Around 2% of people aged >60 years have PA and it is commonly associated with other autoimmune disorders (thyroid/adrenal disorders and type-1 diabetes).[3]

PA is a challenging condition to diagnose and treat. The presentation of PA is more diverse than previously recognised.[4] It is estimated that 10%–15% of patients experience anaemia (although this percentage varies depending on the study population[5 6]), while neurological and cognitive symptoms are present in 85%–90% of new cases.[7] This has led some to suggest that the condition should be renamed. Both diagnosis and ongoing monitoring over rely on serum B_{12} measurements, which have low sensitivity and specificity for the disease and limited correlation with its severity.[8 9] Many patients experience fluctuating symptoms, which persist despite correction of their B_{12} deficiency.[10] These challenges result in a very high rate of late or misdiagnoses and undertreatment.[11] An inadequate one-size-fits-all treatment of 3 monthly B_{12} injections, results in unnecessary and preventable consequences, including further illness, increased healthcare costs, loss of productivity and severely reduced quality of life.[11]

The Pernicious Anaemia Society (PAS) was established in 2004 with the remit to provide information for patients. An online forum

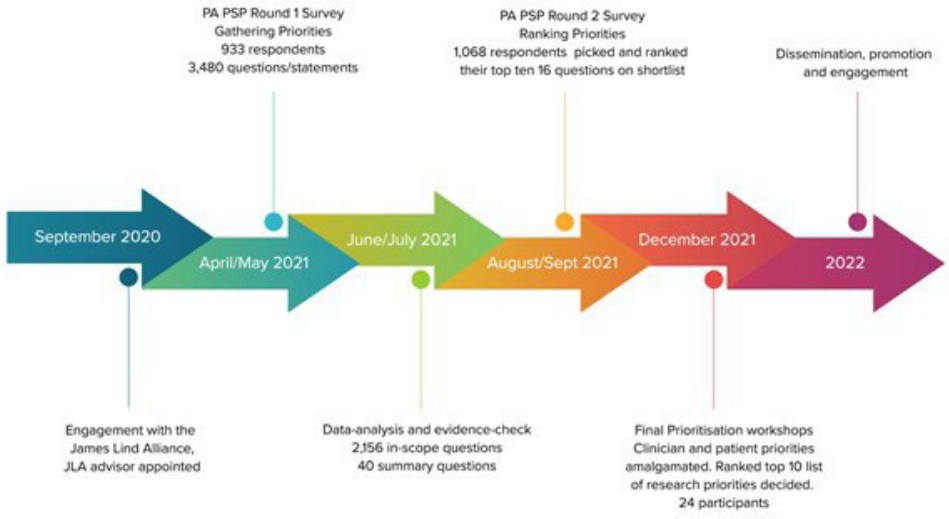

Figure 1 Overview of the PA PSP process. PA, pernicious anaemia; PSP, Priority Setting Partnership.

soon became populated with stories of poor patient experience.[12] PA treatment has not changed since the 60s, has not been comprehensively evaluated and the regimen is based on limited evidence.[4] The PAS, therefore, established new collaborative partnerships between patients, clinicians and researchers, to support campaigns for developing NICE (The National Institute for Health and Care Excellence) guidance and for funding high-quality research on PA to address the known gaps in the evidence base. In 2020, the PAS formed a James Lind Alliance (JLA) Priority Setting Partnership (PSP) to prioritise the Top 10 research questions that patients, carers and clinicians would like investigated relating to the cause, diagnosis, treatment and management of PA.

METHODS

The methods were based on the standard JLA approach[13] and included the stages described in figure 1. This involved establishing the PA PSP, defining its scope and conducting two surveys and a workshop to identify, prioritise and finalise the Top 10 questions.

Establishing the PSP

The PA PSP was overseen by a Steering Group that consisted of patients with PA (n=6) and clinicians (n=5). The patients included PAS staff (n=3), some of whom had affected family members. Four Group members had a dual identity as both patient and clinician. A senior JLA adviser chaired the Group to ensure the process was faithful to JLA principles, the Group's decisions were transparent and views from all perspectives were included in every decision at all stages. The Group agreed the scope of the PSP and published their protocol.[14]

The scope of the PSP

The scope of the PA PSP was to identify uncertainties about the cause, diagnosis, treatment and management (ongoing monitoring and care) of PA, including:

- The clinical definition of PA.
- The tests used to diagnose vitamin B_{12} deficiency.
- The tests or protocol used to diagnose PA.
- The current management and B_{12} replacement therapy regimen.
- Other vitamin B_{12} replacement therapy delivery methods.

First survey: identifying questions to be answered by research

A survey was developed by the Steering Group using SurveyMonkey and piloted with Steering Group members and a small number of diverse patients. The survey link was sent by email to all PAS members, PAS healthcare affiliates, relevant organisations and to Steering Group members' contacts. It was promoted via PAS social media channels, the PAS website and via other organisations' communication channels. PAS members could choose to complete the survey on paper. The survey was available from 7 April 2021 to 31 May 2021.

Survey respondents were asked to respond to the following questions in an open-text format:

- What question(s) or concern(s) about the diagnosis of PA would you like to see answered by research?
- What question(s) or concern(s) about the treatment of PA would you like to see answered by research?
- What question(s) or concern(s) about the ongoing management and impact on day-to-day life with PA would you like to see answered by research?

Other information collected included age, gender, ethnicity, UK area of residence and healthcare profession (for health professionals) and years since diagnosis (for patients). The demographic data were analysed while the survey was live to check for low response rates from any groups. Initially, responses from young patients, clinicians and minority ethnic communities were smaller in number. Therefore, additional communications targeted relevant professional groups and social media messages were adapted to reach desired audiences. All respondents were invited to leave their name and email address should they wish to be involved in subsequent stages.

Categorising the survey responses

The responses to the first survey were categorised to identify questions that needed to be researched and were within the agreed scope of the PSP. Questions about prognosis or symptoms caused by inadequate treatment of PA were considered by the Steering Group to be beyond the scope and were excluded. Other responses were not thought to need research including questions where consensus already exists around explaining PA, its treatment and care. These questions will be used by the PAS to develop new patient information.

Similarly, questions relating to current healthcare practice that may need to be addressed by audit, by revising treatment guidelines, changing NHS (The National Health Service) policy or improving the education and training of clinicians were not included. These will be addressed through future campaigning and strategy development at the PAS. Survey responses that were not about PA, or were very broad (eg, Can treatment for PA be improved?) were also excluded. Responses from people outside of the UK were removed on the basis that respondents from other countries are unlikely to have experiences relevant to UK research and service development.

All of the survey responses that were in-scope and needed researching were then categorised into groups and a summary question drafted to summarise all the questions within each group. Each group included questions about the same topic that had been expressed in slightly different ways[15] (online supplemental table 1).

The initial categorisation of the survey responses was carried out by the information specialist with extensive input from Steering Group members, who volunteered to form a data subgroup, reporting back to the full Steering Group. The subgroup members drew on their experience and in-depth knowledge of PA to inform decisions about whether questions were in or out of scope, whether they needed researching, how to group the questions and whether the summary question was clear and would be easily understood by their peers.

Evidence checking to exclude questions already answered by research

The evidence check in July 2021, searched for systematic reviews published in English during the last ten years in the UK which addressed any of the summary questions. The sources searched for evidence included the Cochrane Database of Systematic Reviews, PubMed, Google Scholar and the British Society for Haematology Guidelines.[4]

Second survey: prioritising questions to be answered by research

The second survey presented the complete list of summary questions and asked respondents to choose their top 10 questions and rank them from 1 to 10. Each question ranked 1 was given 10 points, rank 2 received 9 points, down to rank 10 which was given 1 point. Points for patients/carers and clinicians were calculated separately to ensure equal influence over the combined shortlist.

The survey was again publicised on the PAS website, via social media and by email to all PAS members, relevant groups and organisations and Steering Group members' networks. The people who had expressed an interest in the first survey were also sent the survey link. Steering Group members sent personal emails to clinicians in their network explaining the importance of the PSP and asking them to complete the survey. It was available online between 16 August 2021 and 4 October 2021.

Final workshops to agree the Top 10 questions

Due to the ongoing risk of COVID-19, face-to-face workshops were not possible. However, the JLA have adapted the final workshop to a format suitable for Zoom.[13] Two virtual workshops took place on 1 December 2021 and 2 December 2021. Twenty-four participants, 12 patients and 12 clinicians attended. They were recruited via an email invitation to PAS members and healthcare affiliates. The participants were selected from over 200 applicants using their demographic data to include a diverse range of perspectives and experience. The patients selected had a confirmed diagnosis of PA, and the clinicians selected included a range of professions with clinical experience of PA, avoiding conflicts of interest by excluding those with a particular research interest. Three Steering Group members attended as observers. The workshops used an adapted nominal group technique to generate discussion, ranking, consensus and agreement.[16]

Participants were sent an information and guidance pack in advance which contained the shortlisted questions in a random order. They were asked to prepare by either ranking all the questions, or by identifying their three most and three least important questions and to bring these reflections with them. They were sent a care package in appreciation for their participation, which included refreshments and PAS-branded stationery, a mug and a torch.

Participants were divided into four prearranged groups ensuring a balance between patients and professionals. Each group was facilitated by an independent JLA facilitator to encourage equal and open contributions. Initially, each person was asked to tell their group about their most and least important questions, providing an opportunity for everyone to speak uninterrupted and to learn about each other's perspectives.

In the following discussion, the groups were asked to place the 16 questions in a collective order of importance. Each participant was encouraged to share their views and give consideration to other people's opinions. The ranking of the 16 questions from the 4 groups were then combined. The following day, in new group compositions, the consensus ranking was the starting point for discussion to reflect on the rankings of the 16 questions. Any changes to rankings were collected and collated to identify the final Top 10. This was presented to the whole workshop in a final session.

Patient and public involvement

The PSP was instigated by the PAS who are in a unique position to understand the needs of patients and carers affected by PA. The PAS staff, all patients themselves, ensured that all stages and all decisions were influenced by all perspectives. They were supported by the JLA adviser, whose role is to ensure this happens in the Steering Group meetings and the final workshops.

RESULTS

Outcomes of the first and second surveys

A total of 1599 and 1330 respondents took part in the first and second survey, respectively. Respondents for the first survey included 1467 (92%) patients with PA, 101 (6%) carers and 103 (6%) clinicians. Respondents for the second survey included 1164 (88%) patients with PA, 59 (4%) carers and 107 (8%) clinicians. The expertise of the respondents for surveys 1 and 2 and their demographic details are described in table 1.

Categorising the responses to the first survey

Of the 1599 respondents who took part in the first survey, 644 did not submit any questions and the responses from 22 people from other countries were removed. In total, 933 people submitted 3480 questions/statements. A total of 1324 of the 3480 responses were categorised as being out of scope (38%). The remaining 2156 in-scope questions (62%) were grouped into 40 summary questions (table 2).

The evidence check identified four systematic reviews,[17–20] which did not answer any of the summary questions. Therefore, all 40 questions went through to the next stage.

Analysing the responses to the second survey

A total of 1068 people actually completed the second survey including 982 (92%) patients and carers and 86 (8%) clinicians. The final rankings from patient/carer and clinician perspectives are listed in table 2.

The Steering Group agreed that questions ranked in the top 14 from the two different perspectives should be taken forward to the next stage, to ensure equal influence on the shortlisting. They decided to merge questions 1 and 7 (as listed in table 2) into 1 question, so that a total of 16 questions were shortlisted for discussion at the workshops.

Final workshops

At the final workshops, clinicians and patients/carers came together for the first time to discuss their different views on priority research topics and to reach consensus on the ranking of the 16 questions under review. The workshop enabled an exchange of knowledge and perspectives to support shared decision making, which would not be achieved by a survey.

The Top 10 priorities for research in PA, as identified by the people who most need the research evidence to inform their day-to-day decisions, are listed below.

Table 1 Perspectives and demographic details of the respondents to the first and second surveys

Demographic	First survey	Second survey
Total no respondents	1599	1330
Experience		
Patient	1467 (92%)	1164 (88%)
Family/friend/carer	101 (6%)	59 (4%)
Clinician	103 (6%)	107 (8%)
Where respondent lived		
London	49 (3%)	50 (4%)
South East England	195 (12%)	201 (15%)
South West England	121 (8%)	126 (9%)
East of England	47 (3%)	59 (4%)
West Midlands	57 (4%)	66 (5%)
North West England	112 (7%)	82 (6%)
Yorkshire and Humber	61 (4%)	61 (5%)
East Midlands	51 (3%)	45 (3%)
North East England	45 (3%)	43 (3%)
Scotland	97 (6%)	90 (7%)
Wales	97 (6%)	113 (8%)
Northern Ireland	23 (1%)	24 (2%)
Other	45 (3%)	54 (4%)
Not answered	599 (37%)	316 (24%)
Gender		
Female	869 (54%)	868 (65%)
Male	152 (10%)	171 (13%)
Prefer not to say	4 (<1%)	2 (<1%)
Other	2 (<1%)	1 (<1%)
Not answered	572 (36%)	288 (22%)
Age		
<15	0 (0%)	0 (0%)
15–25	16 (1%)	9 (1%)
26–35	47 (3%)	45 (3%)
36–45	143 (9%)	129 (10%)
46–55	274 (17%)	271 (20%)
56–65	251 (16%)	297 (22%)
>65	298 (19%)	292 (22%)
Not answered	570 (36%)	287 (22%)
Ethnicity		
White	979 (61%)	964 (72%)
Asian or Asian British	8 (<1%)	28 (2%)
Black/African/Caribbean/ Black British	8 (<1%)	12 (1%)
Arabic	0 (0%)	1 (<1%)
Mixed/multiple ethnic background	13 (1%)	10 (1%)
Other (please specify)	15 (1%)	11 (1%)
Not answered	576 (36%)	304 (23%)

Continued

Table 1 Continued

Demographic	First survey	Second survey
Professional background of clinician respondents	**188 people answered this question in survey 1**	**104 people answered this question in survey 2**
General practitioner	51 (27%)	75 (72%)
Haematologist	2 (1%)	0 (0%)
Gastroenterologist	3 (2%)	2 (2%)
Geriatrician	1 (<1%)	1 (1%)
Other consultant physician	3 (2%)	2 (2%)
Psychiatrist	3 (2%)	1 (1%)
Pharmacist	6 (3%)	2 (2%)
Dentist	0 (0%)	0 (0%)
Nurse practitioner/nurse	33 (18%)	9 (9%)
Other	86 (46%)	12 (12%)
Years since diagnosis for people with PA	**1024 people answered this question in survey 1**	**1045 people answered this question in survey 2**
< 1 year ago	55 (5%)	52 (50%)
1–2 years ago	73 (7%)	51 (49%)
2–5 years ago	207 (20%)	193 (18%)
5–10 years ago	224 (22%)	209 (20%)
> 10 years ago	356 (35%)	394 (38%)
Not applicable	109 (11%)	146 (14%)

Some respondents fell into more than one category which is why totals sometimes add up to more than 100%.
PA, pernicious anaemia.

Top 10 questions

1. Can a more reliable and accurate test be developed to diagnose PA?
2. Does an individual's need for B_{12} treatment change over time or with life circumstances? What factors might affect this day to day (eg, stress and exercise) and over a lifespan (eg, ageing, menopause)?
3. What are the safest and most effective ways to give B_{12} to people with PA, tablets, sprays or injections, or a combination? Can better ways be developed?
4. Why do some health professionals fail to take PA seriously? How can this be addressed beyond improving awareness and knowledge of PA?
5. If the frequency, dose and timing of B_{12} injections were tailored to the individual and their symptoms, would this improve the health of people with PA?
6. Why do people with PA need B_{12} injections at different time intervals?
7. Why do some people with PA still experience symptoms after treatment with B_{12}?
8. If people with PA do not receive B_{12} treatment according to their needs, does this cause harm or irreversible damage?
9. What should be included in a long-term, comprehensive treatment and care plan for people with PA?
10. Is PA linked to other health conditions, in particular autoimmune conditions or digestive problems? Is there a common cause?

Dissemination of the Top 10

On 16 December 2021, the PAS hosted a seminar to officially launch the Top 10, which was attended by 25 world-leading researchers from the UK, USA, Denmark, Germany, Spain and Sweden. On the same day, Steering Group members disseminated the Top 10 through their personal and professional networks, social media channels and the PAS website. The PAS produced a plain English report of the PSP process and outcomes. This was sent to all the seminar attendees, PAS members and healthcare affiliates and published on the PAS website.[21] PAS staff continue to liaise directly with research funders and policy-makers to encourage and instigate future research collaborations.

DISCUSSION

The PA PSP successfully used the JLA approach to identify the Top 10 unanswered questions relating to the cause, diagnosis, treatment and management of PA. These uncertainties were prioritised through a consensus process supported by effective partnership working between patients, carers and clinicians.

Not surprisingly, 7 of the Top 10 questions focus on improving the safety and effectiveness of the treatment for PA, reflecting widespread inconsistency and dissatisfaction among PA patients. This reinforces findings from a survey of PAS members in 2014,[11] the recommendations in the British Committee for Standards in Haematology's Guidelines[4] and from qualitative research where patients have likened their experiences of accessing PA treatment to a 'battle'.[22 23]

The other three questions in the Top 10 related to identifying the causes of PA, improving the diagnosis and addressing the lack of empathy towards people with PA among some clinicians. The latter issue was prioritised by patients and carers in the second survey, but not by clinicians themselves. While the JLA process highlighted many areas of common concern between patients/carers and clinicians, this particular difference may underpin the more negative patient perceptions of treatment, and their reports of potentially stigmatising clinician attitudes.[22 24] Overall the Top 10 questions re-emphasise the low level of knowledge of PA among healthcare professionals.

Recent studies have shown that the COVID-19 pandemic has made many of these problems worse for people with PA. Across the UK, many patients have had their treatment stopped, or have been advised to self-manage symptoms by purchasing B_{12} tablets, when there is no robust evidence to suggest that this is safe or effective.[17 25] Such distancing from the medical community is problematic given that PA is a chronic long-term condition, requiring continual care due to increased risk of gastric cancers and neuropathies.[26] The PSP has provided one mechanism to

Table 2 The rankings of all 40 summary questions by patients/carers and clinicians

	Summary question	Ranked priorities by respondent group	
		Patient and carer	Clinician
1	If the frequency and dose of B_{12} injections were tailored to the individual, would this improve the health of people with PA?	1	3
2	Should people with PA undergo regular testing for other conditions, because of an increased risk of stomach cancer or other autoimmune conditions?	2	13
3	Why do some health professionals fail to take PA seriously? How can this be addressed beyond improving awareness and knowledge of PA?	3	37
4	Can a more reliable and accurate test be developed to diagnose PA?	4	1
5	Is it safe and effective for people with PA to self-inject B_{12}? What are the potential benefits for the individual and the NHS?	5	6
6	If people with PA do not receive B12 treatment according to their needs, does this cause harm or irreversible damage?	6	10
7	If the timing of B_{12} injections was determined by the experience of symptoms would this improve the health of people with PA?	7	7
8	Does an individual's need for B_{12} treatment change over time or with life circumstances? What factors might affect this day to day (eg, stress and exercise) and over a lifespan (eg, ageing, menopause)?	8	9
9	Why do some people with PA still experience symptoms after treatment with B_{12}?	9	5
10	What are the long-term effects of B_{12} treatment for people with PA?	10	21
11	Which follow-up tests should be used routinely for people with PA to monitor their health?	12	8
12	Why do people with PA need B_{12} injections at different time intervals?	18	4
13	What are the safest and most effective ways to give B_{12} to people with PA, tablets, sprays or injections, or a combination? Can better ways be developed?	22	2
14	Is PA linked to other health conditions, in particular autoimmune conditions or digestive problems? Is there a common cause?	11	14
15	How does PA affect gut function? Do people with PA have difficulty absorbing nutrients in addition to B_{12}?	13	11
16	What should be included in a long-term, comprehensive treatment and care plan for people with PA?	19	12
17	Are there cofactors or supplements that are needed in addition to B_{12} to successfully treat people with PA?	15	15
18	Does a delayed diagnosis of PA cause harm or irreversible damage?	16	17
19	Should there be widespread testing for PA for example, as part of a screening programme or routine blood tests?	17	18
20	What are the best ways to treat the nerve damage caused by PA?	14	23
21	Is there a genetic link to PA? If yes, how does it affect the risk of PA in families?	20	29
22	How does PA affect the nervous system?	50	27
23	What are the best ways to manage the digestive problems caused by PA?	23	28
24	Why do people with PA have different responses to different forms of B_{12} and what does this mean for treatment?	34	16
25	Can a scale be developed to measure the seriousness of the symptoms of PA and their impact on quality of life?	28	24
26	Does PA affect fertility and pregnancy and does PA treatment need to change during pregnancy and breast feeding?	35	19
27	Would a specific diet help people with PA?	33	22
28	Why do the symptoms of PA vary from person to person and from day to day?	30	26
29	How is B_{12} used and stored in the body in people with PA? What does this mean for treatment?	27	31

Continued

Table 2 Continued

	Summary question	Ranked priorities by respondent group	
		Patient and carer	Clinician
30	What psychological harm do people with PA experience as a result of health professionals not taking them seriously?	24	35
31	How does PA affect muscle function?	25	34
32	Can the parietal cells in the stomach be repaired in people with PA?	26	33
33	Is a lowered immune response a symptom of PA?	31	30
34	Can PA be prevented?	39	25
35	Would people with PA benefit from specialist care?	29	39
36	Can the autoimmune response that causes PA be stopped with treatment?	36	32
37	What psychological impacts does PA have on people? How can these be managed?	32	38
38	Would lifestyle changes (eg, exercise, changing work) help people with PA? What are the best ways for people with PA to stay fit?	38	20
39	What are the impacts of PA on people's work, social life and finances?	37	36
40	Would complementary therapies benefit people with PA?	40	Not ranked

Questions 1 and 7 were combined so that 16 questions were shortlisted for discussion at the final workshop.
NHS, National Health Service; PA, pernicious anaemia.

encourage clinicians and patients to work more closely together and develop a clearer understanding of patient concerns. A unique aspect of this PSP was that many of the clinicians involved were also patients themselves. Having this dual perspective enabled them to promote effective collaboration by bridging the gaps in knowledge in both patient and professional communities.

The Top 10 research priorities represent a call to action to improve the way PA is currently diagnosed, managed and treated via the generation of high-quality research evidence that will fill the gaps in the evidence base. It is expected that the priorities will provide useful guidance to researchers developing projects for funding applications and for funders developing research strategies and portfolios, while recognising that making this shift to addressing patient, carer and clincian's priorities for research requires largescale and systematic culture change across the research community.[27] In common with all JLA PSPs, the PA PSP will continue its efforts in years to come, to raise awareness of its Top 10 and to persuade and influence funders and researchers. It hopes that all future endeavours to develop responsive research projects will continue to involve patients, carers and clinicians to ensure the research stays relevant and genuinely useful to those it intends to help.

Strengths and limitations

The PSP was instigated by the PAS. Although a small charity, they are the only charity dedicated to PA, representing a global community. This puts them in a uniquely strong position to understand the needs of people affected by PA and to promote their interests and concerns. The main strength of this work was the formation of a PSP that for the first time combined the views of patients, carers and clinicians to establish the most important questions for future PA research. The robustness of JLA approach was guaranteed by its previous application to over 100 different medical conditions by other research and patient organisations.

Steering Group members had a major influence on outreach. Among clinicians, this PSP had one of the highest rates of GP engagement, due to efforts made by PAS staff and a GP Steering Group member. Other efforts ensured that small numbers of people from BAME groups and young people with PA did complete both surveys. Finally, the PAS went to great efforts to widely disseminate the Top 10, in parallel to a productive round table discussion with leading scientists which is currently being written up for publication.

In terms of limitations, it could be surmised that, as a patient support group the PAS will be a focal point for those who have had difficult diagnostic and treatment journeys.[28] As such, the views and experiences of PAS members might not be considered representative of the wider patient base with PA. However, Wolffenbuttel *et al* report these challenges as a common experience worldwide.[8] This is further backed up by the plethora of social media groups whose message boards are heavily laden with stories of patients' negative experiences.

Other limitations included the small number of survey respondents among minority groups and younger people. The pandemic and use of online surveys may have also dissuaded or excluded participation from older and more vulnerable patients, carers and healthcare professionals.

Acknowledgements We would like to thank all the patients, carers and clinicians who contributed as members of the Steering Group, survey respondents and workshop participants.

Contributors MH (guarantor) led the development of this project and KCo provided the lead on methodology. KS, KCa, HS, PV and NW categorised the responses to the initial survey. KCa and KCo, HS, KS, PV, NW and MH contributed to finalising the protocol, designing the two surveys and sharing these with stakeholders and patient and professional networks. KRA, PV, KCa and MH organised and participated in the seminar for researchers. KS, KRA, HS, PV and NW drafted the manuscript. All authors reviewed and approved the final manuscript before submission.

Funding The Pernicious Anaemia Society funded this project.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants but an Ethics Committee(s) or Institutional Board(s) exempted this study under the guidance of the Health Research Authority (HRA) in the UK, all James Lind Alliance Priority Setting Partnerships do not come under their remit. The HRA is the oversight body for all ethics committees in the UK.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as online supplemental information. Survey responses supporting the development of all 40 summary questions are available at:https://www.jla.nihr.ac.uk/priority-setting-partnerships/pernicious-anaemia/.

ORCID iDs
Kristina Staley http://orcid.org/0000-0001-7747-1634
Heidi Seage http://orcid.org/0000-0002-8590-867X

REFERENCES

1 Green R, Allen LH, Bjørke-Monsen A-L, *et al*. Vitamin B12 deficiency. *Nat Rev Dis Primers* 2017;3:17040.
2 Green R, Miller JW. *Handbook of vitamins*. 5th edition. Abingdon-on-Thames, UK: Taylor & Francis, 2013: 447–89.
3 Lenti MV, Rugge M, Lahner E, *et al*. Autoimmune gastritis. *Nat Rev Dis Primers* 2020;6:56.
4 Devalia V, Hamilton MS, Molloy AM, *et al*. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. *Br J Haematol* 2014;166:496–513.
5 Rustgi SD, Bijlani P, Shah SC. Autoimmune gastritis, with or without pernicious anemia: epidemiology, risk factors, and clinical management. *Therap Adv Gastroenterol* 2021;14:17562848211038771.
6 Song I-C, Lee HJ, Kim H-J, *et al*. A multicenter retrospective analysis of the clinical features of pernicious anemia in a Korean population. *J Korean Med Sci* 2013;28:200–4.
7 Lindenbaum J, Healton EB, Savage DG, *et al*. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. *N Engl J Med* 1988;318:1720–8.
8 Wolffenbuttel BHR WH, Heiner-Fokkema M, van der Klauw MM. The many faces of cobalamin (vitamin B12) deficiency. *MCP:IQ&O* 2019;3:200–14.
9 Harrington DJ. Laboratory assessment of vitamin B12 status. *J Clin Pathol* 2017;70:168–73.
10 Carmel R. How I treat cobalamin (vitamin B12) deficiency. *Blood* 2008;112:2214–21.
11 Hooper M, Hudson P, Porter F, *et al*. Patient journeys: diagnosis and treatment of pernicious anaemia. *Br J Nurs* 2014;23:376–81.
12 Pernicious Anaemia Society. What we do, 2022. Available: https://pernicious-anaemia-society.org/what-we-do/
13 Alliance JL. *JLA Guidebook*. Version 10. Southampton, UK: James Lind Alliance, 2021. https://www.jla.nihr.ac.uk/jla-guidebook/
14 JLA. Pernicious anaemia PSP protocol, 2021. Available: https://www.jla.nihr.ac.uk/documents/pernicious-anaemia-psp-protocol/26652
15 JLA. Pernicious anaemia PSP, final datasheet, 2022. Available: https://www.jla.nihr.ac.uk/priority-setting-partnerships/pernicious-anaemia/
16 Gallagher M, Hares T, Spencer J, *et al*. The nominal group technique: a research tool for general practice? *Fam Pract* 1993;10:76–81.
17 Chan CQH, Low LL, Lee KH. Oral vitamin B12 replacement for the treatment of pernicious anemia. *Front Med* 2016;3:38.
18 Vannella L, Lahner E, Osborn J, *et al*. Systematic review: gastric cancer incidence in pernicious anaemia. *Aliment Pharmacol Ther* 2013;37:375–82.
19 Lahner E, Capasso M, Carabotti M, *et al*. Incidence of cancer (other than gastric cancer) in pernicious anaemia: a systematic review with meta-analysis. *Dig Liver Dis* 2018;50:780–6.
20 Song M, Latorre G, Ivanovic-Zuvic D, *et al*. Autoimmune diseases and gastric cancer risk: a systematic review and meta-analysis. *Cancer Res Treat* 2019;51:841–50.
21 Pernicious anaemia priority setting partnership final report. Available: https://pernicious-anaemia-society.org/articles/pernicious-anaemia-priority-setting-partnership-final-report/ [Accessed Apr 2022].
22 Seage CH, Glover E, Mercer J. Receiving a diagnosis of pernicious anemia: exploring experiences of relationships with health professionals. *J Patient Exp* 2020;7:766–70.
23 Tyler N, Giles S, Daker-White G, *et al*. A patient and public involvement workshop using visual art and priority setting to provide patients with a voice to describe quality and safety concerns: vitamin B12 deficiency and pernicious anaemia. *Health Expect* 2021;24:87–94.
24 Seage CH. Living with pernicious anaemia: exploring the link between anticipated stigma and wellbeing. *J Psychosom Res* 2018;113:72–3.
25 Seage CH, Semedo L. How do patients receiving prescribed B_{12} injections for the treatment of PA perceive changes in treatment during the COVID-19 pandemic? A UK-based survey study. *J Patient Exp* 2021;8:237437352199884.
26 Murphy G, Dawsey SM, Engels EA, *et al*. Cancer risk after pernicious anemia in the US elderly population. *Clin Gastroenterol Hepatol* 2015;13:2282–9.
27 Staley K, Crowe S, Crocker JC, *et al*. What happens after James Lind alliance priority setting partnerships? A qualitative study of contexts, processes and impacts. *Res Involv Engagem* 2020;6:41.
28 Van Uden-Kraan CF, Drossaert CHC, Taal E, *et al*. Determinants of engagement in face-to-face and online patient support groups. *J Med Internet Res* 2011;13:e106.