

PERNICIOUS ANAEMIA PRIORITY SETTING PARTNERSHIP

2020/2021

*Identifying the most important questions
for Pernicious Anaemia Research*

FOREWORD

Soon after the Pernicious Anaemia Society's first online forum went live it became clear that there were serious issues with how long it takes for patients to get an accurate diagnosis, and getting treatment tailored to the patient's individual needs.

18 months ago I hadn't heard of the James Lind Alliance (JLA) but I'm glad I was directed to this amazing organisation.

The JLA is an initiative that brings together patients, carers and clinicians to identify questions relating to various diseases – questions that are important to researchers, clinicians and patients.

And that's what this report is all about – it is the culmination of over a year's worth of collaboration between members of the PAS and clinicians in a Priority Setting Partnership (PSP) which has identified the Top Ten possible research questions that are important to clinicians and patients along with their families and friends.



We are now able to publish these Top Ten questions and I am confident that these questions will raise awareness of Pernicious Anaemia and will be a 'call to action' to improve the way the disease is diagnosed and treated.

I have to thank all those who took part in the process as well as all those who applied to take part but were not chosen. It's been a real pleasure to work with so many enthusiastic people who are determined to improve the lives of those who have this forgotten disease – Pernicious Anaemia.

This report will attract the attention of researchers who will pick up the challenges posed by the questions. An online Seminar has already been arranged whereby around 40 researchers will come together to discuss just how these questions will be answered, and the first step in this direction is to take these 'uncertainties' and turn them into research projects.

Then, eventually, these research projects will not only improve patients' experiences but will also help doctors do their job better, not only in the UK but throughout the world.

And that can only be a good thing.

Martyn Hooper MBE

CHIEF EXECUTIVE,
PERNICIOUS ANAEMIA SOCIETY

"The work of the Pernicious Anaemia PSP is ground-breaking: this is the first JLA PSP on PA anywhere in the world, and everyone who has taken part in it is a pioneer."

Katherine Cowan, Senior Adviser to the James Lind Alliance

BACKGROUND

The Pernicious Anaemia Society is an International Charity based in Bridgend, South Wales. The society was founded in 2006 by the current Executive Chair, Martyn Hooper. The original aim of the society was simply to provide an easy-to-understand explanation of Pernicious Anaemia to newly diagnosed patients – at the time there was no such information available. It quickly became obvious that there were serious issues with the way in which B12 deficiency in general, and Pernicious Anaemia in particular, is diagnosed and treated.

There are many uncertainties surrounding the diagnosis and treatment, e.g. some people manage perfectly well on 3 monthly injections, whilst others feel the return of their symptoms shortly after having their injection. Why is this? The truth is we don't know. Some patients report managing very well on tablets but for others, tablets don't work and again, we don't know why. There is no reliable test for vitamin B12 deficiency available and the test to ascertain whether a patient has Pernicious Anaemia is also flawed, thus making it very difficult to get a timely and accurate diagnosis and the necessary treatment.

There have been several Nobel Prizes awarded for PA but amazingly, the treatment has not changed since the 1960's. Pernicious Anaemia has been a medical blind-spot for more than 50 years and it still remains so, which is why this PSP is of the utmost importance to the PA Society and its members.

Headed by the Executive Chair the society campaigns to raise awareness of the problems with the diagnosis and treatment of Pernicious Anaemia. It has been successful in getting health decision makers to appreciate the problems faced by patients but the Covid-19 pandemic brought with it serious problems for patients. Some patients had their treatment stopped altogether, or were told to buy vitamin B12 tablets from internet stores, while others were simply told that they no longer had PA. Our Healthcare Affiliates were horrified by what they were witnessing and made enquiries about funding streams to finance a thorough review of the issues surrounding the diagnosis and treatment of PA. They reported back to the PAS that the James Lind Alliance (JLA) had been suggested as being an ideal way to get patients and clinicians to identify the issues that need to be addressed. In August 2020 the Executive Chairman made a preliminary telephone call to the JLA who then explained the due processes involved. The Pernicious Anaemia Priority Setting Partnership was set up to identify future research priorities relating to the cause, diagnosis, treatment and care of Pernicious Anaemia. This project was a collaboration between the Pernicious Anaemia Society and the James Lind Alliance.

THE AIM

The aim of the Pernicious Anaemia PSP is to identify the unanswered questions about Pernicious Anaemia from patient, carer and clinical perspectives and then prioritise those that patients, carers and clinicians agree are the most important for research to address.

THE SCOPE

The scope of the Pernicious Anaemia PSP is defined as: Uncertainties about the Cause, Diagnosis, Treatment and Care of Pernicious Anaemia, including:

- Identifying the uncertainties with the clinical definition of Pernicious Anaemia
- Identifying the uncertainties with the tests to Diagnose Vitamin B12 Deficiency
- Identifying the uncertainties with the tests to Diagnose Pernicious Anaemia
- Identifying the uncertainties with the current management replacement therapy regimen
- Identifying the uncertainties with other replacement therapy delivery methods

ABOUT THE PAS

The Pernicious Anaemia Society started out as an online forum where newly diagnosed patients could receive a plain English explanation of their disease. However, it soon became obvious from postings by members across the globe, that patients struggled for many years before receiving an accurate diagnosis and subsequent treatment for their Pernicious Anaemia. A survey of members of the Pernicious Anaemia Society showed that 23% of patients waited between one and two years for a diagnosis, 20% waited between two and five years while over 15% waited over ten years. That same survey also found that there were serious problems with the way in which the disease is treated, with 64% of respondents stating they were unhappy with their treatment.

The Pernicious Anaemia Society saw its remit change from being a provider of information to newly diagnosed patients, to being a campaigning group to get the way in which the disease is diagnosed and treated thoroughly reviewed. We have had some success; in 2014 the British Committee for Standards in Haematology published their ‘Guideline on Cobalamin and Folate Disorders’ that acknowledged that the assays (tests) to determine the B12 status of patients, and whether any deficiency was due to Pernicious Anaemia, were seriously flawed. And, after a lengthy consultation, the National Institute for Health and Care Excellence (NICE) has started the process whereby they will produce a Guideline on Vitamin B12 Deficiency including Pernicious Anaemia. NICE guidelines are evidence-based recommendations for health and care in England and we hope that the work carried out by PAS and the JLA will form part of the decision making process. It is anticipated that the guideline will be published in November 2023.

ABOUT THE JLA

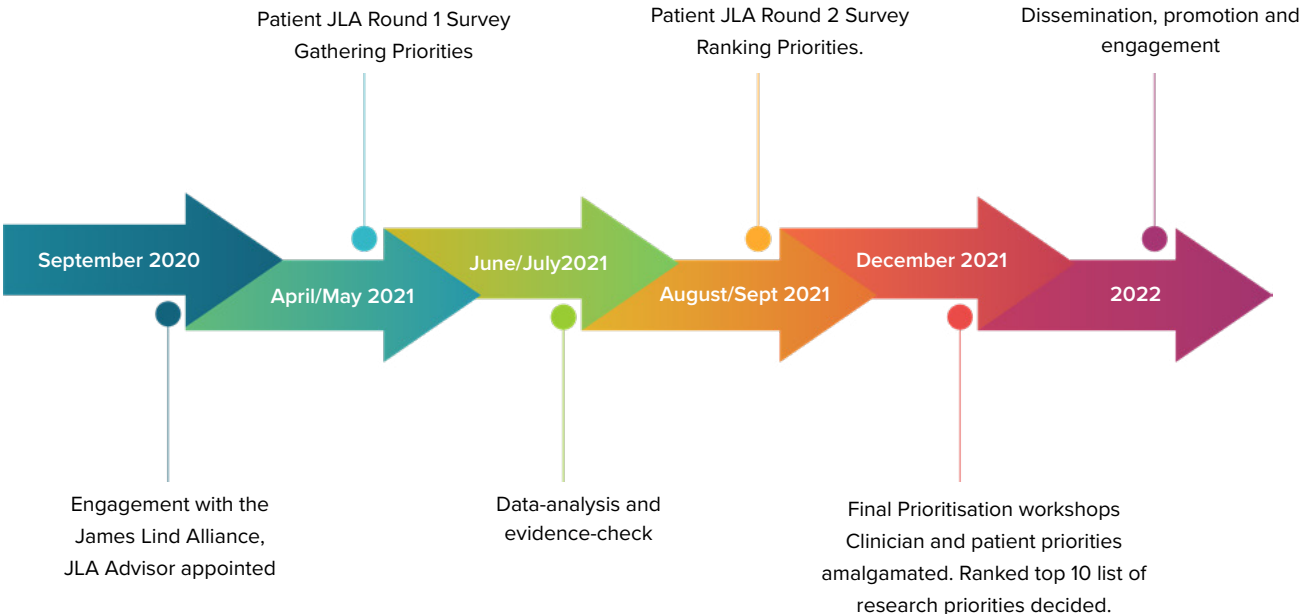
The James Lind Alliance (JLA) was established in the UK in 2004 and is funded by the National Institute for Health Research (NIHR). It is an independent, internationally recognised non-profit organisation with an established transparent process of bringing together people with health conditions and healthcare professionals to identify and prioritise areas for research, taking into account existing evidence.



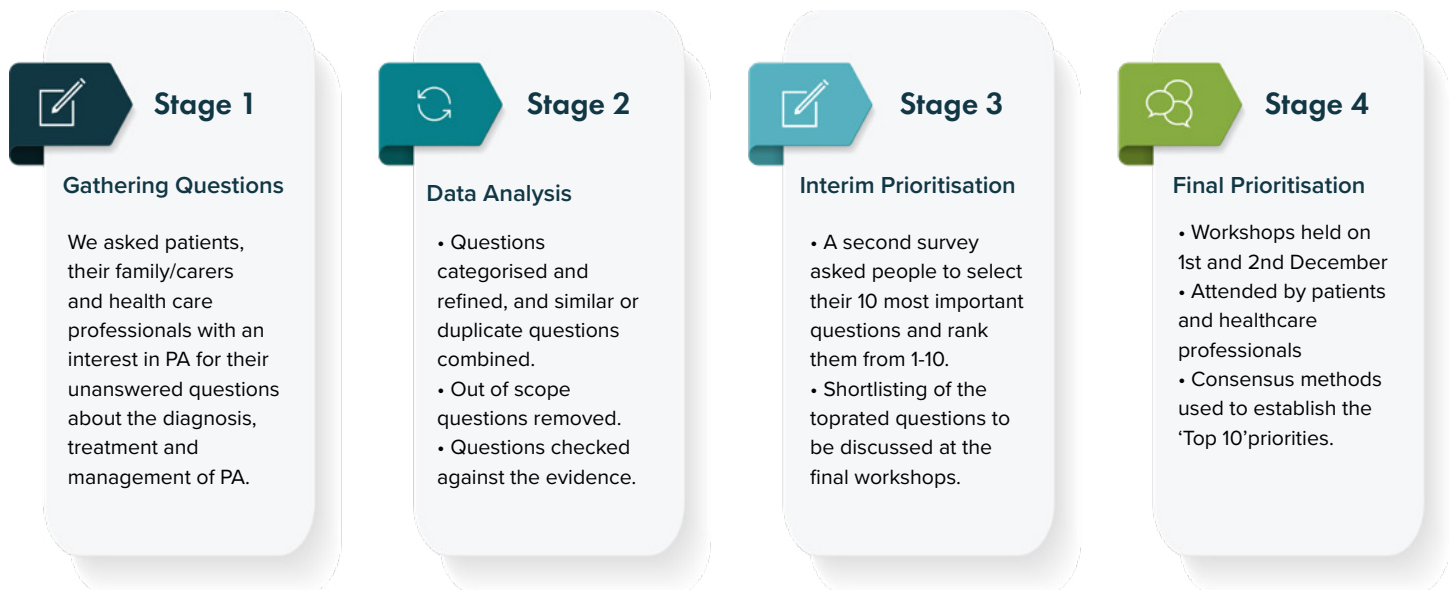
The JLA encourages patients, carers and clinicians to work together in Priority Setting Partnerships to identify and prioritise shared uncertainties. It provides a transparent and structured framework that emphasises patient participation in PSPs, whereby patients have an equal voice to clinicians in influencing the research agenda.

For further information visit www.jla.nihr.ac.uk

PA PRIORITY SETTING PARTNERSHIP TIMELINE



THE PROCESS



STAGE 1: INITIAL SURVEY

We gathered questions from people with Pernicious Anaemia, their families and healthcare professionals via an online public survey. The survey was available from 7th April to 31st May 2021.

The Steering Group developed a single questionnaire for all survey participants via SurveyMonkey™ and piloted with Steering Group members and a small selection of patients. The survey-link was disseminated via email to all PAS members, PAS healthcare affiliates, relevant organisations and via Steering Group members' personal networks. The survey was promoted via PAS social media channels and the PAS website.

Survey respondents were asked the following:

- What question(s) or concern(s) about the diagnosis of Pernicious Anaemia would you like to see answered by research?
- What question(s) or concern(s) about the treatment of Pernicious Anaemia 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 Pernicious Anaemia 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).

Interim analysis of results performed whilst the survey was live revealed under-representation of young patients, healthcare professionals and ethnic communities. To enhance responses from these groups, relevant professional groups targeted specifically and social media messages adapted.

Respondents were invited to leave their name and email address should they wish to be involved in the next stages of the process.



STAGE 2: DATA CHECKING AND ANALYSIS

A professional data-analyst with the help of a core working sub-group of the Steering Group collated and reviewed the suggestions from the first round of survey. Questions that were out-of-scope were excluded (e.g. questions better addressed through an audit, questions that are broad, off-topic or hard to understand, questions asking for information and advice, questions that are about policy and practice and better addressed through campaigning/ lobbying)

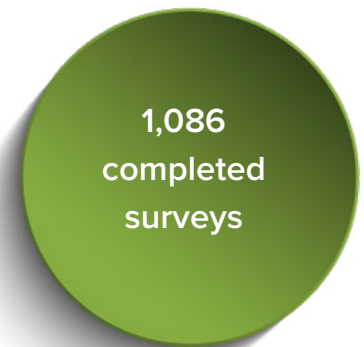
2400 in-scope questions remained which were categorised and refined, and similar or duplicate questions combined. After extraction of multiple questions and following further grouping, 40 questions remained.

Those 40 questions were checked against existing literature to ensure that they were true ‘uncertainties’ i.e. that they had not already been answered by existing research. All 40 indicative questions were submitted for ranking in a second survey.

STAGE 3: INTERIM PRIORITISATION

A further survey was performed to shortlist the long list of questions identified during Stage 2. The survey was available between 16th August and 4th October 2021. The survey was again publicised via social media and email campaigns to relevant individuals, groups and organisations and Steering Group members’ personal networks.

We asked patients, their family/carers and healthcare professionals with an interest in Pernicious Anaemia to choose their top ten questions and rank them from 1-10 from the short-list of 40 questions. The top ranked questions from both clinician and patients/family/carer groups were selected and the Top 16 questions were taken to the next stage.

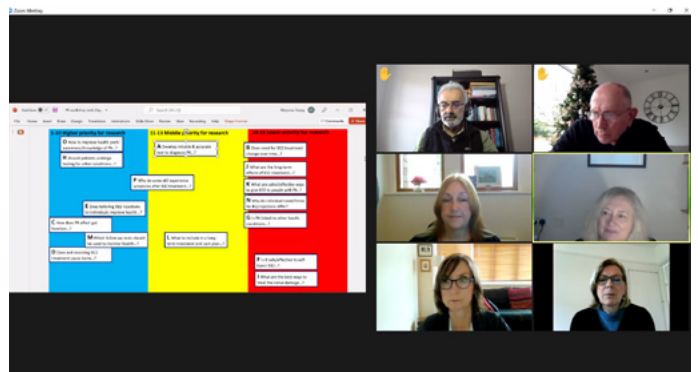


STAGE 4: FINAL PRIORITISATION

Final prioritisation workshops took place on the 1st and 2nd December. Due to the ongoing risk of COVID-19, face-to-face workshops were not possible, however the JLA adapted their process to deliver the workshops online via Zoom. 24 participants, 12 patients and 12 healthcare professionals attended these virtual workshops. The workshops followed the JLA methodology, using a Nominal Group Technique to generate discussion, ranking, consensus and agreement.

Participants were sent an information and guidance pack in advance, which contained the priorities in a random order. They were asked to identify their 3 most and 3 least important priorities and bring this to the workshops to aid and initiate discussions.

Participants were divided into four pre-arranged groups ensuring a balance between patients and professionals. Each group was facilitated by an independent JLA facilitator. For the first step, each person was asked to tell their group the three questions they had ranked highest and lowest in their individual ranking. Discussion followed and 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.



After the first session, the ranking of the 16 questions from the four groups were combined. The next day, in the second session, in new group compositions, the consensus ranking was the starting point for discussion. Following this second round of discussion, the group rankings were again collated and the participants came together as one group to agree the Top 10, debate their order and a final consensus was reached.

The Result: A ranked list of the top 10 most important research priorities for Pernicious Anaemia



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I feel progress has been made and can't wait for the evidence to support patients and improve health and well-being for those who have pernicious anaemia.

“

Thank you for the opportunity to take part in the workshop, I feel I gained a lot from this experience. Hopefully the priorities will progress into funded research to the benefit of all PA sufferers.

“

The decision making process was very robust and good discussions were had, I felt the decisions made on the second day in particular were made as a consensus of all participants.

THE TOP 10 RESEARCH PRIORITIES

01

Can a more reliable and accurate test be developed to diagnose Pernicious Anaemia?

06

Why do people with Pernicious Anaemia need B12 injections at different time intervals?

02

Does an individual's need for B12 treatment change over time or with life circumstances? What factors might affect this day to day (e.g. stress and exercise) and over a lifespan (e.g. aging, menopause)?

07

Why do some people with Pernicious Anaemia still experience symptoms after treatment with B12?

03

What are the safest and most effective ways to give B12 to people with Pernicious Anaemia, tablets, sprays or injections, or a combination? Can better ways be developed?

08

If people with Pernicious Anaemia do not receive B12 treatment according to their needs, does this cause harm or irreversible damage?

04

Why do some health professionals fail to take Pernicious Anaemia seriously? How can this be addressed beyond improving awareness and knowledge of Pernicious Anaemia?

09

What should be included in a long-term, comprehensive treatment and care plan for people with Pernicious Anaemia?

05

If the frequency, dose and timing of B12 injections were tailored to the individual and their symptoms, would this improve the health of people with Pernicious Anaemia?

10

Is Pernicious Anaemia linked to other health conditions, in particular autoimmune conditions or digestive problems? Is there a common cause?

NEXT STEPS

By identifying these priority questions for research the Pernicious Anaemia PSP seeks to ensure that future research is focused on the issues that matter most to people with Pernicious Anaemia and the health care professionals who treat and support them. The priorities are freely available to be researched and we hope they will provide useful guidance to those who are considering funding applications, research strategies or campaign work. Members of the Steering Group will disseminate the questions through their patient and professional networks, by presentation at a PAS hosted webinar for researchers, publication in a peer-reviewed journal, and by liaising directly with research funders and policy makers. We encourage all people with an interest in Pernicious Anaemia to do the same.

We know that the JLA process has a proven track record of increasing investment from research funders, so we will:

- Work with partner organisations and funders over the coming months to get these questions addressed
- Put out a call for research proposals, which will fund a study on the topic of one of the Top Ten questions
- Lobby for increased investment to research Pernicious Anaemia

HOW YOU CAN HELP

Although the consultation has finished, we still have a lot of work to do in deciding how to go about answering these questions. We would very much like to work with you, to keep you updated and to hear from you.

To help us, you can:

- Share your experiences of the issues discussed in this report with us
- Put us in touch with anyone you think might be interested in supporting our work
- Become a member/healthcare affiliated member of the Pernicious Anaemia Society
- Visit our website and follow us on social media for the latest research news and developments on this project

If you are a researcher or funder working on/with Pernicious Anaemia, refer to these questions as it will help guide your strategy, giving your work the greatest impact for those affected by Pernicious Anaemia.

Help us fund the research

Now we have the top ten, we need to fund work in these areas. Support the Pernicious Anaemia Society to address these questions, so that we can maximise the scale and quality of the work we can do together.

Collaborate

The key to future success will be working together and forming partnerships. If we work together, the UK can lead the world in having a strategy for Pernicious Anaemia.

WHAT HAPPENS TO THE REST OF THE PERNICIOUS ANAEMIA RESEARCH PRIORITIES?

Although not all of the priorities made it into the top 10, we won't be ignoring the remaining 30 from our longlist. They will be published on the PAS website and on the JLA website jla.nihr.ac.uk so they can easily be seen by researchers and research funders.

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As treatment and care plans are so different, it is important to consider the needs of the many. It is a disease which affects people differently at different points in life.

ACKNOWLEDGEMENTS

We would like to thank all the people with Pernicious Anaemia, their families and the healthcare professionals who participated in the surveys and attended the workshops. We are grateful to the Steering Group for their oversight and commitment and to everyone who helped promote the survey or participated in the process.

We would also like to thank those that spread the word throughout the Pernicious Anaemia community in the UK. A special thanks to Kristina Staley for her professional data-analysis and to Katherine Cowan, the independent PSP Chair from the James Lind Alliance for her support and guidance throughout.

STEERING GROUP

The project was managed by a steering group, led by an independent chair from the JLA. The role of the Steering Group is to manage the Priority Setting Partnership (PSP), ensuring that it is delivered in a timely way and adheres to the JLA's key principles of transparency, inclusion/exclusion, equality of voice and use of the existing evidence base.

The Steering Group ensured that the process from the initial survey to the identification of the Top Ten Priorities was documented, open and transparent and entirely determined by the responses received from patients, carers and professionals and the review of the existing evidence base.

The Steering Group included people with Pernicious Anaemia and healthcare professionals who together approved the aims and objectives of the process, approved all decisions relating to the project, tested and ensured the surveys were accessible to a wide range of people and provided expert opinions on the evidence checking.

The work of the Pernicious Anaemia PSP was funded by the Pernicious Anaemia Society.

This report was written on behalf of the Pernicious Anaemia PSP Steering Group by Martyn Hooper (PSP Lead), Karyl Carter (PSP Coordinator) and Petra Visser (PSP Informations Coordinator)

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JLA Senior Adviser and Chair of the Steering Group – Katherine Cowan



#PApriorities #HaveYourSayonPA

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pernicious-anaemia-society.org.uk

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