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Top ten research priorities for Idiopathic Intracranial Hypertension (IIH)

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Complete List of Authors:	Mollan, Susan; Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham; Birmingham Neuro-Ophthalmology Unit, Ophthalmology Department, University Hospitals Birmingham NHS Trust, Queen Elizabeth Hospital Birmingham Hemmings, Krystal; IIH UK Herd, Clare; University of Birmingham, Institute of Applied Health Research Denton, Amanda; IIH UK Williamson, Shelley; Idiopathic Intracranial Hypertension UK, Sinclair, AJ; University of Birmingham, Metabolic Neurology; University Hospitals Birmingham
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Running title: PSP IIH top ten

Top ten research priorities for Idiopathic Intracranial Hypertension (IIH)

Mollan SP* (<http://orcid.org/0000-0002-6314-4437>),
Hemmings K*,
Herd C,
Denton A,
Williamson M,
Sinclair AJ (orcid.org/0000-0003-2777-5132)

- 1 Metabolic Neurology, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom (UK)
- 2 Birmingham Neuro-Ophthalmology, Queen Elizabeth Hospital, Birmingham, UK
- 3 IIH UK, Washington, Tyne and Wear, UK
- 4 Institute of Applied Health Research, University of Birmingham, Edgbaston, UK
- 5 Department of Neurology, University Hospitals Birmingham, Queen Elizabeth Hospital, Birmingham, UK
- 6 Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, UK

* Both authors should be considered joint first author, as they contributed equally to the paper.

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Corresponding Author: Dr Alexandra J Sinclair, Metabolic Neurology, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham B15 2TT, UK; a.b.sinclair@bham.ac.uk

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Running title: PSP IIH top ten

Abstract

Objective

Idiopathic Intracranial Hypertension (IIH) is under-researched and the aim was to determine the top 10 research priorities for this disease.

Design

A modified nominal group technique was used to engage participants who had experience of IIH.

Setting

This James Lind Alliance Priority Setting Partnership was commissioned by IIH UK, a charity.

Participants

People with IIH, carers, family and friends, and healthcare professionals participated in two rounds of surveys to identify unique research questions unanswered by current evidence. The most popular 26 uncertainties were presented to stakeholders who then agreed the top 10 topics.

Results

The top 10 research priorities for IIH included aetiology of IIH; the pathological mechanisms of headache in IIH; new treatments in IIH; the difference between acute and gradual visual loss; the best ways to monitor visual function; biomarkers of the disease; hormonal causes of IIH; drug therapies for treatment of headache; weight loss and its role in IIH; and finally, the best intervention to treat IIH and when should surgery be performed.

Conclusions

This priority setting encouraged people with direct experience of IIH to collectively identify critical gaps in the existing evidence. The overarching research aspiration was to understand the aetiology and management of IIH.

Running title: PSP IIH top ten

Strengths and limitations

- This is the first collaboration of patients, carers and clinicians with experience of Idiopathic Intracranial Hypertension (IIH) to achieve consensus on the priorities for future research.
- The James Lind Alliance (JLA) methods are patient centred and give funding bodies an unbiased agenda for research in IIH.
- Using online surveys as the main method for gathering questions for this Priority Setting Partnership (PSP) may mean that not all those with experience of IIH were aware or able to participate in the process.
- While the JLA process and IIH PSP study recommend those research priorities that are important, there is no guarantee of research funding.

Running title: PSP IIH top ten

Introduction

Clinical uncertainty in Idiopathic Intracranial Hypertension (IIH) is evident, with the first consensus guidelines for investigation and management stating uncertainties in every aspect of the disease .[1] The 2015 Cochrane review concluded that there is a lack of evidence to guide pharmacological treatment.[2] There are few published randomised clinical trials (RCTs)[3,4] and a small number of ongoing trials.[5,6] Research is infrequent due to the rarity of the IIH [7,8] and the lack of understanding of the underlying pathology.[9]

IIH predominantly affects overweight women of childbearing age with the incidence of the disease predicted to rise with the increasing global prevalence of obesity.[7,8] In those with severely affected vision, surgery may be indicated.[1] For the majority, it can be a chronic condition, with headaches impacting on the quality of life of patients, [10] and an economic burden [11].

Understanding where research should be directed was a priority for IIH UK, the leading charity for IIH in the United Kingdom (UK). The James Lind Alliance (JLA), a UK National Institute for Health Research-supported initiative, aims to provide a transparent process that enables patients and healthcare professionals (HCP) to work together to agree on the most important uncertainties to inform the research agenda. The aim of this IIH priority setting partnership (PSP), was to identify gaps in knowledge that matter most to key stakeholders (patients, carers and clinicians), and to indicate where future funding should be placed.

Running title: PSP IHH top ten

Methods

Patient and public involvement

This research priority partnership was established by IHH UK, a charity that is run by carers and people with IHH. At each stage of the JLA process, patients and carers were equal collaborators in the design and decisions including the survey design and piloting, survey participation and the final workshop. They disseminated the surveys on the charity website and via social media. All participants were able to indicate a desire for further involvement and for information about the results.

IHH PSP process

The University of Birmingham, UK, acted as academic partner to the IHH PSP and the process was led by the IHH UK research representative, in collaboration with the James Lind Alliance (JLA, www.jla.nihr.ac.uk). A steering group with representation from IHH UK, patients and all the major specialities associated with IHH plus an independent information specialist oversaw the process (supplemental table 1). In February 2017, key organisations accepted the invitation to become partners. They included the Association of British Neurologists; the British Association for the Study of Headache; the British and Irish Orthoptic Society; Fight for Sight; The Royal College of Ophthalmologists; The Society of British Neurological Surgeons CSF group; Shine; Neurological Alliance and the United Kingdom Neuro-Ophthalmology Special Interest Group (supplemental table 2). The PSP stages were broadly based on the four step process developed by the JLA (figure 1).[12]

This PSP was concerned with adult IHH only and any responses relating to children were excluded. Responses concerning the classification of the disease, healthcare funding/entitlements, or statements without a discernible question were excluded.

Running title: PSP IIH top ten

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5 The IIH UK internal review board formally reviewed the project and further ethical approval
6 was not required. All data was anonymised and sent to the information specialist at the
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8 University of Birmingham for processing.
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14 The prioritisation survey questions were constructed (supplemental table 3) and the survey
15 was advertised by partners (supplemental table 2), IIH UK and steering group members. All
16 responses were refined to understandable 'uncertainties' with the exception of those
17 considered to be 'out of scope'. These were categorised using the UK Clinical Research
18 Collaboration Health Research Classification System, sorted into themes and then
19 formulated into indicative questions by steering group members. A literature search was
20 conducted with the electronic databases CENTRAL, Embase and Medline searched from
21 inception to March 2018 for systematic reviews using strategies based on those used by
22 Piper *at al.* [2]. The "known knowns" with reference to the appropriate literature and
23 duplicate questions were removed. Questions were amalgamated when practical to do so.
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25 The long list was then verified by the PSP lead and discussions were held with the wider
26 steering group if disagreements occurred.
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44 The known unknowns were then used for the interim survey. Respondents ranked the
45 questions, returning their top ten. The rankings were reverse scored and the total scores for
46 the two groups: individuals with IIH, friends, or carers; and HCP, were calculated separately
47 to ensure an equal weighting. The most popular 26 questions were then taken forward,
48 which included the top 10 for both groups, to the final workshop, with the aim of consensus
49 on the top 10 priorities.[12]
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Running title: PSP IHH top ten

Results

The prioritisation survey generated 356 responses (figure 1). Demographic data for those with IHH is provided in supplemental table 5 and details of HCP specialisms in supplemental table 6. Of the 2,405 generated uncertainties, 140 were out of scope. The resulting 2,265 were grouped into 64 indicative questions. Sixteen were deemed to be already known or unanswerable by research, leaving 48 questions for presentation in the interim survey. Responses from 512 people were collected in a ratio of 4:1 people with IHH, friends and carers to HCP.

A final list of 26 prioritised questions was generated from the analysis of the interim survey, which included the top 10 for both groups (supplemental table 4). The commonest themes from non-HCP was why the disease develops and progresses; hormonal causes and female predominance; and the conditions associated with IHH. For HCP education; the utility of biomarkers; and biological mechanisms of headache were the commonest. At the consensus workshop the top 10 priorities were agreed (figure 2; supplemental table 7).

Running title: PSP IIH top ten

Discussion

Understanding the most relevant research projects to fund can be challenging. It is imperative that the topics identified in a disease area have the utmost relevance to patients affected by the disease and recognised by clinicians that have clear understanding of the clinical entity. We have undertaken a JLA PSP to establish the top 10 research areas for IIH.

The IIH JLA PSP was funded by IIH UK and set up those who have an active collaboration to improve care for people with IIH.[13] The principles and structured process outlined by the JLA was adhered to steadfastly throughout.[12] All data was maintained in a manner that could be tracked back at any point to the original questions and demographic source; this provided transparency.

Within the feedback people with IIH voiced that they felt their opinions were often not heard. There was a good response rate from all groups when considering how rare IIH is. Submissions with low duplication rates were not removed, a process which can introduce bias. All submitted uncertainties were considered in the long list if they were determined to be known unknowns, including those asked by a single respondent. The data analysis followed standard protocols, though it was complicated by the use of multiple questions in the initial survey (supplemental table 3) as each respondent could appear in up to seven separate initial categories.

Running title: PSP IIH top ten

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3 Despite the use of identification codes, the multi-level process meant that the number of
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5 individuals contributing to the final data set could not be reasonably calculated. The project
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7 took 18 months and surveys were closed on schedule, leaving the possibility that this
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9 happened before the maximum number of respondents could contribute.
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15 A major challenge for the IIH PSP steering group was to engage all the relevant HCP (namely
16
17 neurologists, ophthalmologists, neurosurgeons, radiologists, orthoptists). The speciality
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19 diversity brought strength to the process and allowed for a broad inclusion, however during
20
21 the final selection for the top ten, clinicians were clearly polarised by their individual
22
23 specialism. For example, surgeons were keen for novel interventions, whereas physicians
24
25 were promoting better medical therapies.
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33 At the interim survey it was clear there was a discrepancy between the non-HCP and HCP in
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35 their most popular themes, with patients keen for research into the aetiology, and HCP
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37 more commonly ranked education, biomarkers and the pathological mechanisms driving
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39 headache. The top priority of the patients' group at the interim survey, was the same as the
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41 final result of the consensus workshop.
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48 Some differing opinions between non-HCP and HCP were expressed at the workshop. One
49
50 issue was surrounding weight loss, seen by physicians as the only disease modifiable
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52 therapy and so a high priority for further understanding. This was a highly sensitive issue
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54 among the patients and carers present who voiced that it was not considered so important
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Running title: PSP IIH top ten

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3 by patients. During the workshop a collective decision was made to have a wide scope
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5 within the top 10 areas. If a topic was already featured high within the list, questions that
6
7 contained a similar theme were purposely voted lower. For example, weight loss, the
8
9 longer more detailed question was ranked higher than the question regarding bariatric
10
11 surgery, with the reasoning that it could be answered not only by the weight loss question
12
13 but also by number 10: the intervention question. For this reason, no further ranking below
14
15 the top 10 should be published. Of note two areas that did not feature in the top 10, namely
16
17 multidisciplinary clinics and an education program. They were scored as important during
18
19 the interim survey, particularly by HPC. The consensus workshop delegates agreed that
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21 although these are highly important, the PSP is intended to inform grant bodies who fund
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23 research and these areas were universally accepted to require improvement.
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31 The IIH PSP has been an opportunity to understand the areas that are important to all. It
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33 has the potential to influence the research agenda and consequently treatment and
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35 management of this idiopathic disease.
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Running title: PSP IIH top ten

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Declarations or Conflicts of Interest

No authors contributing have a conflict of interest in the subject matter.

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Contributor Statement

Mollan SP: interpretation of the survey results; drafting and review of the manuscript.
Hemmings K: PSP patient lead; administration of both surveys; drafting and review of the manuscript.
Herd C: literature review; independent information specialist; drafting and review of the manuscript.
Denton A: critical review of the manuscript.
Williamson M: organisation of the consensus final workshop; and critical review of the manuscript.
Sinclair AJ: PSP clinical lead; interpretation of the survey results and critical review of the manuscript.

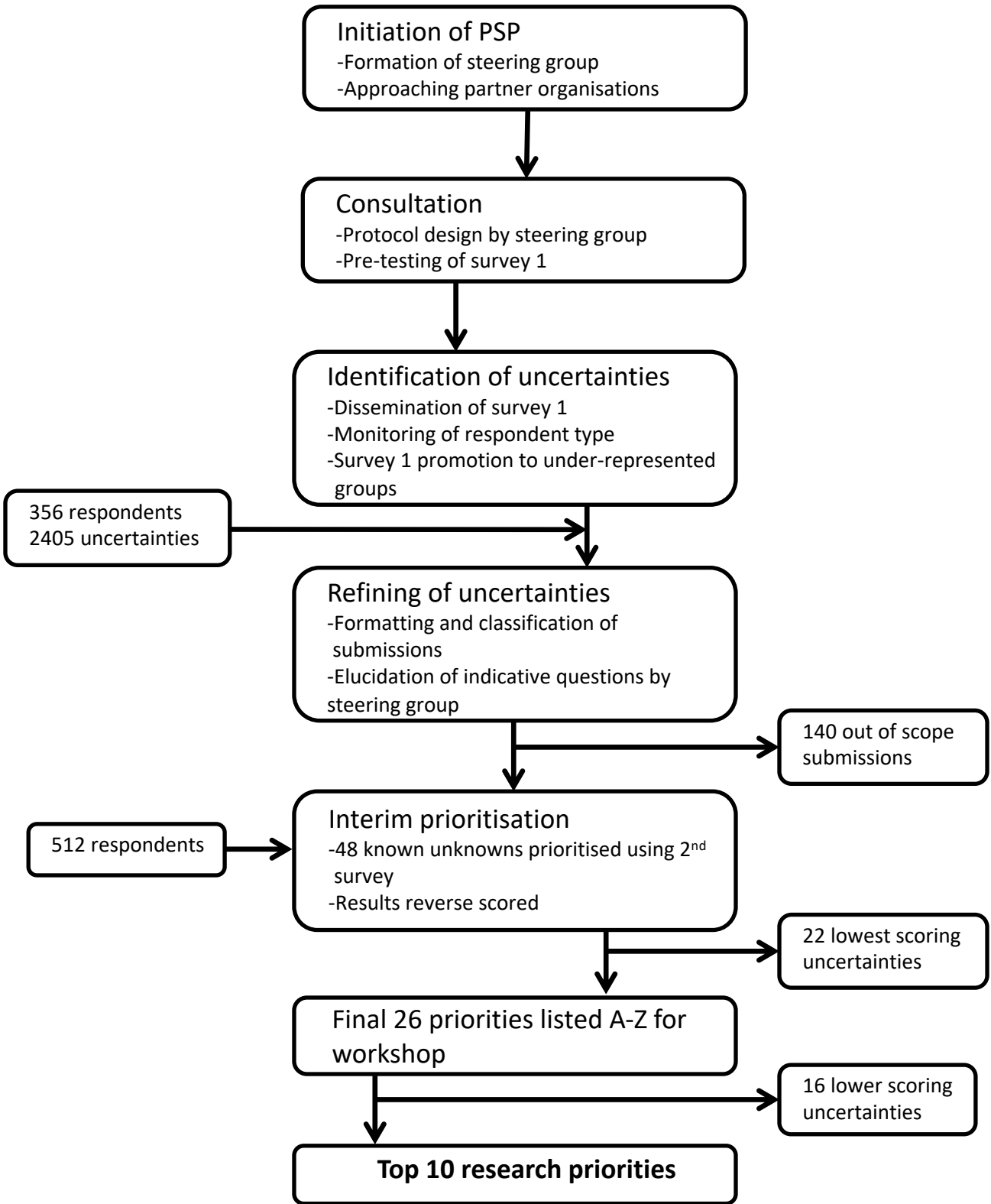
All authors were steering group members and have read and approved the final manuscript.

Legend to figures:

Figure 1: Consort diagram and details of the JLA IHH PSP

Figure 2: Final Top 10 ranked uncertainties for the concerning the treatment and management of people with Idiopathic Intracranial Hypertension

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IDIOPATHIC INTRACRANIAL HYPERTENSION

PRIORITY SETTING PARTNERSHIP

Top 10 Priorities for IIH Research

1 CAUSES OF IIH

In the individual with IIH; what causes the disease, the symptoms and the progression of the disease?

2 MECHANISMS OF HEADACHE

What are the biological mechanisms of headache in IIH and why in some do headaches continue even after papilloedema has resolved?

3 NEW THERAPIES FOR IIH

Can new medical therapies for IIH be developed which are effective, safe, and tolerable and potentially help with weight loss as well as reducing brain

4 PREDICTING VISUAL LOSS

What is the biological explanation for the differences between rapid visual loss compared with gradual visual loss in IIH and how can this be predicted?

5 MONITORING VISUAL FUNCTION

What are the best ways to monitor visual function?

6 IIH BIOMARKERS

Can IIH biomarkers (tests in body fluids for example urine, saliva, blood, or brain scans) help diagnosis, predict the risk and guide therapy decisions in IIH?

7 HORMONES

What are the hormonal causes for IIH and why is IIH primarily associated with female sex?

8 MEDICATION TO TREAT HEADACHE

What medications are effective and safe to treat IIH headaches?

9 WEIGHT LOSS

With regard to weight loss in IIH: how much is needed to treat IIH and how quickly does it work? What is the best, safest and most acceptable method to achieve this in the short and long term? Additionally, does the initial Body Mass Index (BMI) of the patient have an effect?

10 BEST TYPE OF INTERVENTION

Which is the best type of intervention to treat IIH and when should surgery be performed?

Supplemental table 1: The steering group members and their role

Person	Role
Krystal Hemmings	IIH UK Research representative and PSP patient led
Alex Sinclair	Clinical lead and neurologist
Michelle Williamson	IIH UK Chair trustee, project coordinator and carer
Clare Herd	Information specialist
Martin Plowright	IIH patient
Norma-Ann Dan	IIH UK patient representative
Amanda Denton	IIH UK patient representative
Rachel Bennett	IIH patient
Jayne Best	Neuro-Ophthalmologist
Arun Chandran	Neuro-radiologist
Julie Edwards	Headache nurse specialist
Anita Krishnan	Neurologist
Kamal Mahawar	Bariatric surgeon
Susan Mollan	Neuro-Ophthalmologist
Caroline Rick	Trial methodologist
Ahmed Toma	Neurosurgeon

Supplemental table 2: Partner organisations in alphabetical order

ABN - Association of British Neurologists
BASH - British Association for the Study of Headache
BIOS - British and Irish Orthoptic Society
Fight for Sight – The Eye Research Charity
RCOphth – The Royal College of Ophthalmologists
SBNS CSF subgroup - The Society of British Neurological Surgeons
Shine – Spina bifida, Hydrocephalus, Information, Networking, Equality
The Neurological Alliance
UKNOSIG - The United Kingdom Neuro-Ophthalmology Special Interest Group

Supplemental table 3: The prioritisation survey was designed using Qualtrics software (www.qualtrics.com) and responses were requested to the following seven questions:

1. What questions do you have about how the diagnosis of IIH is made?
2. What questions do you have about why people get IIH?
3. What questions do you have about the management of vision in IIH?
4. What questions do you have about the management of headache in IIH?
5. What questions do you have about weight management in IIH?
6. What questions do you have about care provision for patients with IIH? (e.g. General Practice, inpatient, outpatient care)
7. Do you have any other questions about IIH that you feel are important but do not fall into the categories above?

Supplemental table 4: 26 Questions for IIH PSP final workshop in alphabetical order

1	Are multidisciplinary clinics (joint clinics of neurology, ophthalmology, neurosurgery, dietetics and specialist nurses etc.) clinically and cost effective for the management of IIH and would they improve patient experience?
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5	Are multidisciplinary clinics (joint clinics of neurology, ophthalmology, neurosurgery, dietetics and specialist nurses etc.) clinically and cost effective for the management of IIH and would they improve patient experience?
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8	Are non-invasive intracranial pressure (ICP) measurements accurate and clinically useful?
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11	Can IIH biomarkers (tests in body fluids for example urine, saliva, blood, or brain scans) help diagnosis, predict the risk and guide therapy decisions in IIH?
12	
13	Can novel therapies for IIH be developed which are effective, safe, and tolerable and potentially help with weight loss as well as reducing brain pressure?
14	
15	Do lumbar punctures (LPs) have long-term safety complications?
16	
17	Do the benefits of the drug treatments for IIH outweigh the side effects?
18	How big is the impact of headache in IIH (how severe are headaches, how often do they
19	occur, how many years do they continue for and how do they impact patients quality of life)?
20	
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23	Is bariatric surgery effective in IIH and at what point in the disease should it be performed?
24	
25	Is cerebral venous stenosis the cause or consequence of IIH?
26	Is IIH a lifelong condition?
27	Is IIH caused by increased production or lack of cerebral spinal fluid (CSF) absorption?
28	Is there a genetic cause of IIH?
29	Is there a single or are there multiple causes for IIH?
30	What are the best ways to monitor visual function?
31	What are the biological mechanisms of headache in IIH and why in some do headaches
32	continue even after papilloedema has resolved?
33	
34	What are the hormonal causes for IIH and why is IIH primarily associated with female gender?
35	
36	What are the triggers for periods of high intracranial pressure (ICP) in people with IIH?
37	What is happening in the body of a person with IIH which causes the development of the disease, the symptoms and the progression of the disease?
38	
39	What is the biological explanation for the differences between rapid visual loss compared with gradual visual loss in IIH and how can this be predicted?
40	
41	What medications are effective and safe to treat IIH headaches?
42	What other conditions / features are associated with IIH (e.g. depression, sleep apnoea, endocrine disorders, cognition, nerve pain)?
43	
44	Which is the best type of surgery to treat IIH and when should surgery be performed?
45	Why do people get IIH without papilloedema (IIHWOP) and how should this be treated?
46	
47	Why is obesity a risk factor for IIH in women and why is this not the case in men?
48	With regard to weight loss in IIH: how much is needed to treat IIH and how quickly does it work? What is the best, safest and most acceptable method to achieve this in the short and long term? Additionally, does the initial Body Mass Index (BMI) of the patient have an effect?
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Would an education program for health care professionals and patients with IHH improve care and disease experience for IHH patients?

For peer review only

Supplementary Table 5: Characteristics of participants with IIH of first survey

Number	180
Female (%)	96
Median age (years)	35
Ethnicity (%)	
White	92
Black or Asian	3
Multiple ethnic backgrounds	4
Not stated	1

Supplementary Table 6: Declared specialism of the healthcare professionals in first survey

Declared specialism of the healthcare professional	% of respondents
Neurologist	45
Ophthalmologist	11
Neurosurgeon	10
Neuro-Ophthalmologist	9
Other	8
Trainee	6
Bariatric Surgeon	3
General Practitioner	3
Nurse	2
Neuroradiologist	1
Orthoptist	1
Not declared	1

Supplemental Table 7: Final Top 10 ranked uncertainties for the concerning the treatment and management of people with Idiopathic Intracranial Hypertension

Ranking	Research priority
1	In the individual with IIH; what causes the disease, the symptoms and the progression of the disease?
2	What are the biological mechanisms of headache in IIH and why in some do headaches continue even after papilloedema has resolved?
3	Can new medical therapies for IIH be developed which are effective, safe, and tolerable and potentially help with weight loss as well as reducing brain pressure?
4	What is the biological explanation for the differences between rapid visual loss compared with gradual visual loss in IIH and how can this be predicted?
5	What are the best ways to monitor visual function?
6	Can IIH biomarkers (tests in body fluids for example urine, saliva, blood, or brain scans) help diagnosis, predict the risk and guide therapy decisions in IIH?
7	What are the hormonal causes for IIH and why is IIH primarily associated with female sex?
8	What medications are effective and safe to treat IIH headaches?
9	With regard to weight loss in IIH: how much is needed to treat IIH and how quickly does it work? What is the best, safest and most acceptable method to achieve this in the short and long term? Additionally, does the initial Body Mass Index (BMI) of the patient have an effect?
10	Which is the best type of intervention to treat IIH and when should surgery be performed?

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Research priorities for idiopathic intracranial hypertension

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Research priorities for idiopathic intracranial hypertension

Mollan SP* (<http://orcid.org/0000-0002-6314-4437>) [1]

Hemmings K* [2]

Herd C [3]

Denton A [2]

Williamson S [2]

Sinclair AJ (orcid.org/0000-0003-2777-5132)[4,5,6]

- 1 Birmingham Neuro-Ophthalmology, Queen Elizabeth Hospital, Birmingham, UK
- 2 IHH UK, Washington, Tyne and Wear, UK
- 3 Institute of Applied Health Research, University of Birmingham, Edgbaston, UK
- 4 Metabolic Neurology, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom (UK)
- 5 Department of Neurology, University Hospitals Birmingham, Queen Elizabeth Hospital, Birmingham, UK
- 6 Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, UK

* Both authors should be considered joint first author, as they contributed equally to the paper.

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Corresponding Author: Dr Alexandra J Sinclair, Metabolic Neurology, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham B15 2TT, UK; a.b.sinclair@bham.ac.uk

Key Words: Idiopathic Intracranial Hypertension; Priority setting; Research priorities; Patient involvement; Patient and carer involvement; PPI; Service-user involvement; Impact; Research agenda

Running title: PSP IIH top ten

Abstract

Objective

Idiopathic Intracranial Hypertension (IIH) is under-researched and the aim was to determine the top 10 research priorities for this disease.

Design

A modified nominal group technique was used to engage participants who had experience of IIH.

Setting

This James Lind Alliance Priority Setting Partnership was commissioned by IIH UK, a charity.

Participants

People with IIH, carers, family and friends, and healthcare professionals participated in two rounds of surveys to identify unique research questions unanswered by current evidence. The most popular 26 uncertainties were presented to stakeholders who then agreed the top 10 topics.

Results

The top 10 research priorities for IIH included aetiology of IIH; the pathological mechanisms of headache in IIH; new treatments in IIH; the difference between acute and gradual visual loss; the best ways to monitor visual function; biomarkers of the disease; hormonal causes of IIH; drug therapies for treatment of headache; weight loss and its role in IIH; and finally, the best intervention to treat IIH and when should surgery be performed.

Conclusions

This priority setting encouraged people with direct experience of IIH to collectively identify critical gaps in the existing evidence. The overarching research aspiration was to understand the aetiology and management of IIH.

Running title: PSP IIH top ten

Strengths and limitations

- This is the first collaboration of patients, carers and clinicians with experience of Idiopathic Intracranial Hypertension (IIH) to achieve consensus on the priorities for future research.
- The James Lind Alliance (JLA) methods are patient centred and give funding bodies an unbiased agenda for research in IIH.
- Using online surveys as the main method for gathering questions for this Priority Setting Partnership (PSP) may mean that not all those with experience of IIH were aware or able to participate in the process.
- It is conceivable that possibly all the research questions gathered are not exhaustive.
- While the JLA process and IIH PSP study recommend those research priorities that are important, there is no guarantee of research funding.

Running title: PSP IIH top ten

Introduction

Clinical uncertainty in Idiopathic Intracranial Hypertension (IIH) is evident, with the first consensus guidelines for investigation and management stating uncertainties in every aspect of the disease .[1] The 2015 Cochrane review concluded that there is a lack of evidence to guide pharmacological treatment.[2] There are few published randomised clinical trials (RCTs)[3,4] and a small number of ongoing trials.[5,6] Research is infrequent due to the rarity of the IIH [7,8] and the lack of understanding of the underlying pathology.[9]

IIH predominantly affects overweight women of childbearing age with the incidence of the disease documented to be rising [10] with the increasing prevalence of obesity.[7,8] In those with severely affected vision, surgery may be indicated.[1] For the majority, it can be a chronic condition, with headaches impacting on the quality of life of patients, [11] and an economic burden [10,12].

Understanding where research should be directed was a priority for IIH UK, the leading charity for IIH in the United Kingdom (UK). The James Lind Alliance (JLA), a UK National Institute for Health Research-supported initiative, aims to provide a transparent process that enables patients and healthcare professionals (HCP) to work together to agree on the most important uncertainties to inform the research agenda. The aim of this IIH priority setting partnership (PSP), was to identify gaps in knowledge that matter most to key stakeholders (patients, carers and clinicians), and to indicate where future funding should be placed.

Running title: PSP IIH top ten

Methods

Patient and public involvement

This research priority partnership was established by IIH UK, a charity that is run by carers and people with IIH. At each stage of the JLA process, patients and carers were equal collaborators in the design and decisions including the survey design and piloting, survey participation and the final workshop. They disseminated the surveys on the charity website and via social media. All participants were able to indicate a desire for further involvement and for information about the results.

IIH PSP process

The University of Birmingham, UK, acted as academic partner to the IIH PSP and the process was led by the IIH UK research representative, in collaboration with the James Lind Alliance (JLA, www.jla.nihr.ac.uk). A steering group with representation from IIH UK, patients and all the major specialities associated with IIH plus an independent information specialist oversaw the process (supplemental table 1). In February 2017, key organisations accepted the invitation to become partners. They included the Association of British Neurologists; the British Association for the Study of Headache; the British and Irish Orthoptic Society; Fight for Sight; The Royal College of Ophthalmologists; The Society of British Neurological Surgeons CSF group; Shine; Neurological Alliance and the United Kingdom Neuro-Ophthalmology Special Interest Group (supplemental table 2). The PSP stages were broadly based on the four step process developed by the JLA (figure 1).[13]

This PSP was concerned with adult IIH only and any responses exclusively relating to children were excluded. There was limited funding for the project, and including the paediatric population would have required funding for two different work streams. It is well

Running title: PSP IIH top ten

1
2
3 documented the expectantly different phenotype between adult and those prepubescent
4 children with IIH.[14] However responses were not limited by those who submitted, and
5
6 hence those with children with IIH are likely to be included. Indeed, at the final stakeholder
7
8 meeting there was representation from carers of children with IIH. Responses concerning the
9
10 classification of the disease, healthcare funding/entitlements, or statements without a
11
12 discernible question were excluded.
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20 The IIH UK internal review board formally reviewed the project and further ethical approval
21 was not required. All data was anonymised and sent to the information specialist at the
22
23 University of Birmingham for processing.
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30 The prioritisation survey questions were constructed (supplemental table 2) by the steering
31 group, aided by the first guidelines in IIH where uncertainties exist around the diagnosis,
32 investigation and management.[1] This first survey was advertised by partners (supplemental
33 table 3), IIH UK and steering group members. All responses were refined to understandable
34
35 'uncertainties' with the exception of those considered to be 'out of scope'. These were
36
37 categorised using the UK Clinical Research Collaboration Health Research Classification
38
39 System, sorted into themes and then formulated into indicative questions by steering group
40
41 members, working in groups with at least one HCP and one patient representative. A
42
43 literature search was conducted with the electronic databases CENTRAL, Embase and Medline
44
45 searched from inception to March 2018 for systematic reviews using strategies based on
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47 those used by Piper *at al.* [2]. The "known knowns" with reference to the appropriate
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49 literature and duplicate questions were removed. Questions were amalgamated when
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Running title: PSP IiH top ten

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3 practical to do so. The long list was then verified by the PSP lead and discussions were held
4
5 with the wider steering group if disagreements occurred.
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10 The known unknowns were then used for the interim survey. Respondents ranked the
11
12 questions, returning their top ten. The rankings were reverse scored and the total scores for
13
14 the two groups: individuals with IiH, friends, or carers; and HCP, were calculated separately
15
16 to ensure an equal weighting. The most popular 26 questions were then taken forward, which
17
18 included the top 10 for both groups, to the final workshop, with the aim of consensus on the
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20 top 10 priorities.[13] Data relating to the PSP are available upon reasonable request to IiH UK
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25 (www.iih.org.uk).
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30 **Results**

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32 The prioritisation survey generated 356 responses (figure 1). Demographic data for those with
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34 IiH is provided in supplemental table 4 and details of HCP specialisms in supplemental table
35
36 5. Of the 2,405 generated uncertainties, 140 were out of scope. The resulting 2,265 were
37
38 grouped into 64 indicative questions. Sixteen were deemed to be already known or
39
40 unanswerable by research, leaving 48 questions for presentation in the interim survey.
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42 Responses from 512 people were collected in a ratio of 4:1 people with IiH, friends and carers
43
44 to HCP.
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51 A final list of 26 prioritised questions was generated from the analysis of the interim survey,
52
53 which included the top 10 for both groups (supplemental table 6). The commonest themes
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55 from non-HCP was why the disease develops and progresses; hormonal causes and female
56
57 predominance; and the conditions associated with IiH. For HCP education; the utility of
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Running title: PSP IHH top ten

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3 biomarkers; and biological mechanisms of headache were the commonest. At the consensus
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5 workshop the top 10 priorities were agreed (figure 2; supplemental table 7).
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8 9 **Discussion**

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11 Understanding the most relevant research projects to fund can be challenging. It is
12
13 imperative that the topics identified in a disease area have the utmost relevance to patients
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15 affected by the disease and recognised by clinicians that have clear understanding of the
16
17 clinical entity. We have undertaken a JLA PSP to establish the top 10 research areas for IHH.
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25 The IHH JLA PSP was funded by IHH UK and set up those who have an active collaboration to
26
27 improve care for people with IHH.[15] The principles and structured process outlined by the
28
29 JLA was adhered to steadfastly throughout.[13] All data was maintained in a manner that
30
31 could be tracked back at any point to the original questions and demographic source; this
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33 provided transparency.
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41 Within the feedback people with IHH voiced that they felt their opinions were often not
42
43 heard. There was a good response rate from all groups when considering how rare IHH is.
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45 Submissions with low duplication rates were not removed, a process which can introduce
46
47 bias. All submitted uncertainties were considered in the long list if they were determined to
48
49 be known unknowns, including those asked by a single respondent. The data analysis
50
51 followed standard protocols, though it was complicated by the use of multiple questions in
52
53 the initial survey (supplemental table 3) as each respondent could appear in up to seven
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55 separate initial categories.
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Running title: PSP IHH top ten

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Despite the use of identification codes, the multi-level process meant that the number of individuals contributing to the final data set could not be reasonably calculated. The project took 18 months and surveys were closed on schedule, leaving the possibility that this happened before the maximum number of respondents could contribute.

A major challenge for the IHH PSP steering group was to engage all the relevant HCP (namely neurologists, ophthalmologists, neurosurgeons, radiologists, orthoptists). The speciality diversity brought strength to the process and allowed for a broad inclusion, however during the final selection for the top ten, clinicians were clearly polarised by their individual specialism. There are a number of surgical treatments for fulminant visual loss in the form of CSF diversion, as directed by neurosurgeons, and optic nerve sheath fenestration, as performed by ophthalmic surgeons. [16] More recently interventional radiologists have performed venous sinus stenting for IHH. [17] Physicians (both neurologists and ophthalmologists) use weight loss and medical therapies such as acetazolamide and topiramate. [1,18] This mix of specialism and approach in certain patient groups, i.e. those at threat of visual loss or those with chronic headache, led to expectantly different opinions: for example, surgeons were keen for novel interventions, whereas physicians were promoting better medical therapies.

At the interim survey it was clear there was a discrepancy between the non-HCP and HCP in their most popular themes, with patients keen for research into the aetiology, and HCP

Running title: PSP IHH top ten

1
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3 more commonly ranked education, biomarkers and the pathological mechanisms driving
4
5 headache. The top priority of the patients' group at the interim survey, was the same as the
6
7 final result of the consensus workshop.
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14 Some differing opinions between non-HCP and HCP were expressed at the workshop. One
15
16 issue was surrounding weight loss, seen by physicians as the only disease modifiable
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18 therapy and so a high priority for further understanding. This was a highly sensitive issue
19
20 among the patients and carers present who voiced that it was not considered so important
21
22 by patients. During the workshop a collective decision was made to have a wide scope
23
24 within the top 10 areas. If a topic was already featured high within the list, questions that
25
26 contained a similar theme were purposely voted lower. For example, weight loss, the
27
28 longer more detailed question was ranked higher than the question regarding bariatric
29
30 surgery, with the reasoning that it could be answered not only by the weight loss question
31
32 but also by number 10: the intervention question. For this reason, no further ranking below
33
34 the top 10 should be published. Of note two areas that did not feature in the top 10, namely
35
36 multidisciplinary clinics and an education program. They were scored as important during
37
38 the interim survey, particularly by HPC. The consensus workshop delegates agreed that
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40 although these are highly important, the PSP is intended to inform grant bodies who fund
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42 research and these areas were universally accepted to require improvement.
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54 The IHH PSP has been an opportunity to understand the areas that are important to all. The
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56 primary topic of underlying aetiology requires work both clinically and within the basic
57
58 laboratory research. Another key area highlighted by this PSP is that of mechanisms of
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Running title: PSP IHH top ten

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2
3 headache in IHH. There is increasing evidence regarding the phenotype of the IHH headache,
4
5 which is challenging tradition regarding the raised ICP headache. [19,20] Future work should
6
7 explore novel therapies for headache in IHH, which is the key driver in lowering quality of life
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9 in this patient cohort. [11] The PSP has the potential to influence the research agenda and
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11 consequently in time all area of management, from medical to surgical interventions for this
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13 currently idiopathic disease.
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For peer review only

Running title: PSP IIH top ten

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- 4 the Treatment of Idiopathic Intracranial Hypertension Failing Maximum Medical
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Running title: PSP IHH top ten

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Conflicts of Interest

No authors contributing have a conflict of interest in the subject matter.

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Data Sharing statement

No additional data is available.

Contributor Statement

Mollan SP: interpretation of the survey results; drafting and review of the manuscript.
Hemmings K: PSP patient lead; administration of both surveys; drafting and review of the manuscript.
Herd C: literature review; independent information specialist; drafting and review of the manuscript.
Denton A: critical review of the manuscript.
Williamson M: organisation of the consensus final workshop; and critical review of the manuscript.
Sinclair AJ: PSP clinical lead; interpretation of the survey results and critical review of the manuscript.

All authors were steering group members and have read and approved the final manuscript.

Legend to figures:

Figure 1: Consort diagram and details of the JLA IHH PSP

Figure 2: Final Top 10 ranked uncertainties for the concerning the treatment and management of people with Idiopathic Intracranial Hypertension

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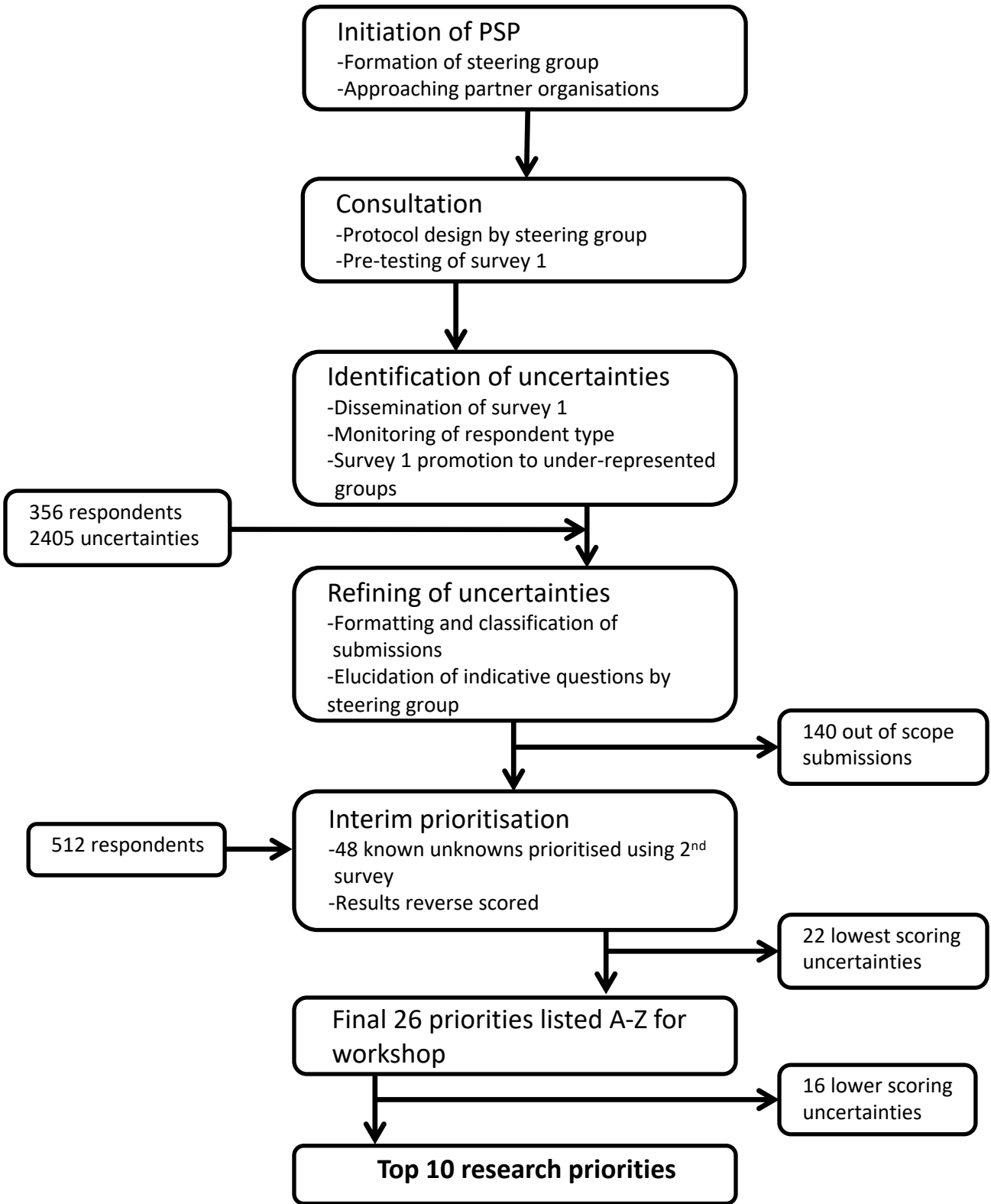




Figure 2: The top ten research priorities in IIH

192x267mm (150 x 150 DPI)

Supplemental table 1: The steering group members and their role

Person	Role
Krystal Hemmings	IIH UK Research representative and PSP patient led
Alex Sinclair	Clinical lead and neurologist
Michelle Williamson	IIH UK Chair trustee, project coordinator and carer
Clare Herd	Information specialist
Martin Plowright	IIH patient
Norma-Ann Dan	IIH UK patient representative
Amanda Denton	IIH UK patient representative
Rachel Bennett	IIH patient
Jayne Best	Neuro-Ophthalmologist
Arun Chandran	Neuro-radiologist
Julie Edwards	Headache nurse specialist
Anita Krishnan	Neurologist
Kamal Mahawar	Bariatric surgeon
Susan Mollan	Neuro-Ophthalmologist
Caroline Rick	Trial methodologist
Ahmed Toma	Neurosurgeon

Supplemental table 2: The prioritisation survey was designed using Qualtrics software (www.qualtrics.com) and responses were requested to the following seven questions:

1.	What questions do you have about how the diagnosis of IIH is made?
2.	What questions do you have about why people get IIH?
3.	What questions do you have about the management of vision in IIH?
4.	What questions do you have about the management of headache in IIH?
5.	What questions do you have about weight management in IIH?
6.	What questions do you have about care provision for patients with IIH? (e.g. General Practice, inpatient, outpatient care)
7.	Do you have any other questions about IIH that you feel are important but do not fall into the categories above?

Supplemental table 3: Partner organisations in alphabetical order

ABN - Association of British Neurologists
BASH - British Association for the Study of Headache
BIOS - British and Irish Orthoptic Society
Fight for Sight – The Eye Research Charity
RCOphth – The Royal College of Ophthalmologists
SBNS CSF subgroup - The Society of British Neurological Surgeons
Shine – Spina bifida, Hydrocephalus, Information, Networking, Equality
The Neurological Alliance
UKNOSIG - The United Kingdom Neuro-Ophthalmology Special Interest Group

Supplementary Table 4: Characteristics of participants with IIH of first survey

Number	180
Female (%)	96
Median age (years)	35
Ethnicity (%)	
White	92
Black or Asian	3
Multiple ethnic backgrounds	4
Not stated	1

Supplementary Table 5: Declared specialism of the healthcare professionals in first survey

Declared specialism of the healthcare professional	% of respondents
Neurologist	45
Ophthalmologist	11
Neurosurgeon	10
Neuro-Ophthalmologist	9
Other	8
Trainee	6
Bariatric Surgeon	3
General Practitioner	3
Nurse	2
Neuroradiologist	1
Orthoptist	1
Not declared	1

Supplemental table 6: 26 Questions for IIH PSP final workshop in alphabetical order

1	Are multidisciplinary clinics (joint clinics of neurology, ophthalmology, neurosurgery, dietetics and specialist nurses etc.) clinically and cost effective for the management of IIH and would they improve patient experience?
2	
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6	Are non-invasive intracranial pressure (ICP) measurements accurate and clinically useful?
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12	Can IIH biomarkers (tests in body fluids for example urine, saliva, blood, or brain scans) help diagnosis, predict the risk and guide therapy decisions in IIH?
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15	Can novel therapies for IIH be developed which are effective, safe, and tolerable and potentially help with weight loss as well as reducing brain pressure?
16	
17	Do lumbar punctures (LPs) have long-term safety complications?
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19	Do the benefits of the drug treatments for IIH outweigh the side effects?
20	
21	How big is the impact of headache in IIH (how severe are headaches, how often do they occur, how many years do they continue for and how do they impact patients quality of life)?
22	
23	Is bariatric surgery effective in IIH and at what point in the disease should it be performed?
24	
25	
26	Is cerebral venous stenosis the cause or consequence of IIH?
27	Is IIH a lifelong condition?
28	Is IIH caused by increased production or lack of cerebral spinal fluid (CSF) absorption?
29	Is there a genetic cause of IIH?
30	Is there a single or are there multiple causes for IIH?
31	What are the best ways to monitor visual function?
32	What are the biological mechanisms of headache in IIH and why in some do headaches continue even after papilloedema has resolved?
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35	What are the hormonal causes for IIH and why is IIH primarily associated with female gender?
36	
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38	What are the triggers for periods of high intracranial pressure (ICP) in people with IIH?
39	What is happening in the body of a person with IIH which causes the development of the disease, the symptoms and the progression of the disease?
40	
41	
42	What is the biological explanation for the differences between rapid visual loss compared with gradual visual loss in IIH and how can this be predicted?
43	
44	What medications are effective and safe to treat IIH headaches?
45	
46	What other conditions / features are associated with IIH (e.g. depression, sleep apnoea, endocrine disorders, cognition, nerve pain)?
47	
48	Which is the best type of surgery to treat IIH and when should surgery be performed?
49	Why do people get IIH without papilloedema (IIHWOP) and how should this be treated?
50	
51	Why is obesity a risk factor for IIH in women and why is this not the case in men?
52	With regard to weight loss in IIH: how much is needed to treat IIH and how quickly does it work? What is the best, safest and most acceptable method to achieve this in the short and long term? Additionally, does the initial Body Mass Index (BMI) of the patient have an effect?
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57	Would an education program for health care professionals and patients with IIH improve care and disease experience for IIH patients?
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For peer review only

Supplemental Table 7: Final Top 10 ranked uncertainties for the concerning the treatment and management of people with Idiopathic Intracranial Hypertension

Ranking	Research priority
1	In the individual with IIH; what causes the disease, the symptoms and the progression of the disease?
2	What are the biological mechanisms of headache in IIH and why in some do headaches continue even after papilloedema has resolved?
3	Can new medical therapies for IIH be developed which are effective, safe, and tolerable and potentially help with weight loss as well as reducing brain pressure?
4	What is the biological explanation for the differences between rapid visual loss compared with gradual visual loss in IIH and how can this be predicted?
5	What are the best ways to monitor visual function?
6	Can IIH biomarkers (tests in body fluids for example urine, saliva, blood, or brain scans) help diagnosis, predict the risk and guide therapy decisions in IIH?
7	What are the hormonal causes for IIH and why is IIH primarily associated with female sex?
8	What medications are effective and safe to treat IIH headaches?
9	With regard to weight loss in IIH: how much is needed to treat IIH and how quickly does it work? What is the best, safest and most acceptable method to achieve this in the short and long term? Additionally, does the initial Body Mass Index (BMI) of the patient have an effect?
10	Which is the best type of intervention to treat IIH and when should surgery be performed?

BMJ Open

What are the research priorities for idiopathic intracranial hypertension? A priority setting partnership between patients and health care professionals.

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Article Type:	Research
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Manuscripts

Running title: PSP IIH top ten

What are the research priorities for idiopathic intracranial hypertension? A priority setting partnership between patients and health care professionals.

Mollan SP* (<http://orcid.org/0000-0002-6314-4437>) [1]

Hemmings K* [2]

Herd C [3]

Denton A [2]

Williamson S [2]

Sinclair AJ (orcid.org/0000-0003-2777-5132)[4,5,6]

- 1 Birmingham Neuro-Ophthalmology, Queen Elizabeth Hospital, Birmingham, UK
- 2 IIH UK, Washington, Tyne and Wear, UK
- 3 Institute of Applied Health Research, University of Birmingham, Edgbaston, UK
- 4 Metabolic Neurology, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom (UK)
- 5 Department of Neurology, University Hospitals Birmingham, Queen Elizabeth Hospital, Birmingham, UK
- 6 Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, UK

* Both authors should be considered joint first author, as they contributed equally to the paper.

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Corresponding Author: Dr Alexandra J Sinclair, Metabolic Neurology, Institute of Metabolism and Systems Research, University of Birmingham, Birmingham B15 2TT, UK; a.b.sinclair@bham.ac.uk

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Running title: PSP IIH top ten

Abstract

Objective

Idiopathic Intracranial Hypertension (IIH) is under-researched and the aim was to determine the top 10 research priorities for this disease.

Design

A modified nominal group technique was used to engage participants who had experience of IIH.

Setting

This James Lind Alliance Priority Setting Partnership was commissioned by IIH UK, a charity.

Participants

People with IIH, carers, family and friends, and healthcare professionals participated in two rounds of surveys to identify unique research questions unanswered by current evidence. The most popular 26 uncertainties were presented to stakeholders who then agreed the top 10 topics.

Results

The top 10 research priorities for IIH included aetiology of IIH; the pathological mechanisms of headache in IIH; new treatments in IIH; the difference between acute and gradual visual loss; the best ways to monitor visual function; biomarkers of the disease; hormonal causes of IIH; drug therapies for treatment of headache; weight loss and its role in IIH; and finally, the best intervention to treat IIH and when should surgery be performed.

Conclusions

This priority setting encouraged people with direct experience of IIH to collectively identify critical gaps in the existing evidence. The overarching research aspiration was to understand the aetiology and management of IIH.

Running title: PSP IIH top ten

Strengths and limitations

- This is the first collaboration of patients, carers and clinicians with experience of Idiopathic Intracranial Hypertension (IIH) to achieve consensus on the priorities for future research.
- The James Lind Alliance (JLA) methods are patient centred and give funding bodies an unbiased agenda for research in IIH.
- Using online surveys as the main method for gathering questions for this Priority Setting Partnership (PSP) may mean that not all those with experience of IIH were aware or able to participate in the process.
- It is conceivable that possibly all the research questions gathered are not exhaustive.
- While the JLA process and IIH PSP study recommend those research priorities that are important, there is no guarantee of research funding.

Running title: PSP IIH top ten

Introduction

Clinical uncertainty in Idiopathic Intracranial Hypertension (IIH) is evident, with the first consensus guidelines for investigation and management stating uncertainties in every aspect of the disease .[1] The 2015 Cochrane review concluded that there is a lack of evidence to guide pharmacological treatment.[2] There are few published randomised clinical trials (RCTs)[3,4] and a small number of ongoing trials.[5,6] Research is infrequent due to the rarity of the IIH [7,8] and the lack of understanding of the underlying pathology.[9]

IIH predominantly affects overweight women of childbearing age with the incidence of the disease documented to be rising [10] with the increasing prevalence of obesity.[7,8] In those with severely affected vision, surgery may be indicated.[1] For the majority, it can be a chronic condition, with headaches impacting on the quality of life of patients, [11] and an economic burden [10,12].

Understanding where research should be directed was a priority for IIH UK, the leading charity for IIH in the United Kingdom (UK). The James Lind Alliance (JLA), a UK National Institute for Health Research-supported initiative, aims to provide a transparent process that enables patients and healthcare professionals (HCP) to work together to agree on the most important uncertainties to inform the research agenda. The aim of this IIH priority setting partnership (PSP), was to identify gaps in knowledge that matter most to key stakeholders (patients, carers and clinicians), and to indicate where future funding should be placed.

Running title: PSP IIH top ten

Methods

IIH PSP process

The University of Birmingham, UK, acted as academic partner to the IIH PSP and the process was led by the IIH UK research representative, in collaboration with the James Lind Alliance (JLA, www.jla.nihr.ac.uk). A steering group with representation from IIH UK, patients and all the major specialities associated with IIH plus an independent information specialist oversaw the process (supplemental table 1). In February 2017, key organisations accepted the invitation to become partners. They included the Association of British Neurologists; the British Association for the Study of Headache; the British and Irish Orthoptic Society; Fight for Sight; The Royal College of Ophthalmologists; The Society of British Neurological Surgeons CSF group; Shine; Neurological Alliance and the United Kingdom Neuro-Ophthalmology Special Interest Group (supplemental table 2). The PSP stages were broadly based on the four step process developed by the JLA (figure 1).[13]

This PSP was concerned with adult IIH only and any responses exclusively relating to children were excluded. There was limited funding for the project, and including the paediatric population would have required funding for two different work streams. It is well documented the expectantly different phenotype between adult and those prepubescent children with IIH.[14] However responses were not limited by those who submitted, and hence those with children with IIH are likely to be included. Indeed, at the final stakeholder meeting there was representation from carers of children with IIH. Responses concerning the classification of the disease, healthcare funding/entitlements, or statements without a discernible question were excluded.

Running title: PSP IiH top ten

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6 The prioritisation survey questions were constructed (supplemental table 2) by the steering
7
8 group, aided by the first guidelines in IiH where uncertainties exist around the diagnosis,
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10 investigation and management.[1] This first survey was advertised by partners (supplemental
11
12 table 3), IiH UK and steering group members. All responses were refined to understandable
13
14 'uncertainties' with the exception of those considered to be 'out of scope'. These were
15
16 categorised using the UK Clinical Research Collaboration Health Research Classification
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18 System, sorted into themes and then formulated into indicative questions by steering group
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20 members, working in groups with at least one HCP and one patient representative. A
21
22 literature search was conducted with the electronic databases CENTRAL, Embase and Medline
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24 searched from inception to March 2018 for systematic reviews using strategies based on
25
26 those used by Piper *at al.* [2]. The "known knowns" with reference to the appropriate
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28 literature and duplicate questions were removed. Questions were amalgamated when
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30 practical to do so. The long list was then verified by the PSP lead and discussions were held
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32 with the wider steering group if disagreements occurred.
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42 The known unknowns were then used for the interim survey. Respondents ranked the
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44 questions, returning their top ten. The rankings were reverse scored and the total scores for
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46 the two groups: individuals with IiH, friends, or carers; and HCP, were calculated separately
47
48 to ensure an equal weighting. The most popular 26 questions were then taken forward, which
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50 included the top 10 for both groups, to the final workshop, with the aim of consensus on the
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52 top 10 priorities.[13] Data relating to the PSP are available upon reasonable request to IiH UK
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57 (www.iih.org.uk).
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Running title: PSP IiH top ten

Ethics

The IiH UK internal review board formally reviewed the project and further ethical approval was not required. All data was anonymised and sent to the information specialist at the University of Birmingham for processing. Each participant gave their consent for the anonymised data to be used when entering their opinions through the online surveys.

Patient and public involvement

This research priority partnership was established by IiH UK, a charity that is run by carers and people with IiH. At each stage of the JLA process, patients and carers were equal collaborators in the design and decisions including the survey design and piloting, survey participation and the final workshop. They disseminated the surveys on the charity website and via social media. All participants were able to indicate a desire for further involvement and for information about the results.

Results

The prioritisation survey generated 356 responses (figure 1). Demographic data for those with IiH is provided in supplemental table 4 and details of HCP specialisms in supplemental table 5. Of the 2,405 generated uncertainties, 140 were out of scope. The resulting 2,265 were grouped into 64 indicative questions. Sixteen were deemed to be already known or unanswerable by research, leaving 48 questions for presentation in the interim survey. Responses from 512 people were collected in a ratio of 4:1 people with IiH, friends and carers to HCP.

Running title: PSP IHH top ten

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3 A final list of 26 prioritised questions was generated from the analysis of the interim survey,
4
5 which included the top 10 for both groups (supplemental table 6). The commonest themes
6
7 from non-HPC was why the disease develops and progresses; hormonal causes and female
8
9 predominance; and the conditions associated with IHH. For HCP education; the utility of
10
11 biomarkers; and biological mechanisms of headache were the commonest. At the consensus
12
13 workshop the top 10 priorities were agreed (figure 2; supplemental table 7).
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24 Discussion

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26 Understanding the most relevant research projects to fund can be challenging. It is
27
28 imperative that the topics identified in a disease area have the utmost relevance to patients
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30 affected by the disease and recognised by clinicians that have clear understanding of the
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32 clinical entity. We have undertaken a JLA PSP to establish the top 10 research areas for IHH.
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40 The IHH JLA PSP was funded by IHH UK and set up those who have an active collaboration to
41
42 improve care for people with IHH.[15] The principles and structured process outlined by the
43
44 JLA was adhered to steadfastly throughout.[13] All data was maintained in a manner that
45
46 could be tracked back at any point to the original questions and demographic source; this
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48 provided transparency.
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55 A major challenge for the IHH PSP steering group was to engage all the relevant HCP (namely
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57 neurologists, ophthalmologists, neurosurgeons, radiologists, orthoptists). The speciality
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Running title: PSP IHH top ten

1
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3 diversity brought strength to the process and allowed for a broad inclusion, however during
4
5 the final selection for the top ten, clinicians were clearly polarised by their individual
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7 specialism. There are a number of surgical treatments for fulminant visual loss in the form
8
9 of CSF diversion, as directed by neurosurgeons, and optic nerve sheath fenestration, as
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11 performed by ophthalmic surgeons. [16] More recently interventional radiologists have
12
13 performed venous sinus stenting for IHH. [17] Physicians (both neurologists and
14
15 ophthalmologists) use weight loss and medical therapies such as acetazolamide and
16
17 topiramate. [1,18] This mix of specialism and approach in certain patient groups, i.e. those
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19 at threat of visual loss or those with chronic headache, led to expectantly different opinions:
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21 for example, surgeons were keen for novel interventions, whereas physicians were
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23 promoting better medical therapies.
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34 At the interim survey it was clear there was a discrepancy between the non-HCP and HCP in
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36 their most popular themes, with patients keen for research into the aetiology, and HCP
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38 more commonly ranked education, biomarkers and the pathological mechanisms driving
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40 headache. The top priority of the patients' group at the interim survey, was the same as the
41
42 final result of the consensus workshop.
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50 Some differing opinions between non-HCP and HCP were expressed at the workshop. One
51
52 issue was surrounding weight loss, seen by physicians as the only disease modifiable
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54 therapy and so a high priority for further understanding. This was a highly sensitive issue
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56 among the patients and carers present who voiced that it was not considered so important
57
58 by patients. During the workshop a collective decision was made to have a wide scope
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Running title: PSP IIH top ten

1
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3 within the top 10 areas. If a topic was already featured high within the list, questions that
4
5 contained a similar theme were purposely voted lower. For example, weight loss, the
6
7 longer more detailed question was ranked higher than the question regarding bariatric
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9 surgery, with the reasoning that it could be answered not only by the weight loss question
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11 but also by number 10: the intervention question. For this reason, no further ranking below
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13 the top 10 should be published. Of note two areas that did not feature in the top 10, namely
14
15 multidisciplinary clinics and an education program. They were scored as important during
16
17 the interim survey, particularly by HPC. The consensus workshop delegates agreed that
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19 although these are highly important, the PSP is intended to inform grant bodies who fund
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21 research and these areas were universally accepted to require improvement.
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28 **Strengths**

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31 Within the feedback people with IIH voiced that they felt their opinions were often not
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33 heard, therefore the IIH PSP has allowed them a voice. There was a good response rate from
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35 all groups when considering how rare IIH is. Submissions with low duplication rates were
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37 not removed, a process which can introduce bias. All submitted uncertainties were
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39 considered in the long list if they were determined to be known unknowns, including those
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41 asked by a single respondent. The data analysis followed standard protocols, though it was
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43 complicated by the use of multiple questions in the initial survey (supplemental table 3) as
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45 each respondent could appear in up to seven separate initial categories.
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55 **Limitations**

Running title: PSP IIH top ten

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3 Despite the use of identification codes, the multi-level process meant that the number of
4
5 individuals contributing to the final data set could not be reasonably calculated. The project
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7 took 18 months and surveys were closed on schedule, leaving the possibility that this
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9 happened before the maximum number of respondents could contribute. Using online
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11 surveys as the main method for gathering questions for this Priority Setting Partnership
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13 (PSP) may mean that not all those with experience of IIH were aware or able to participate
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15 in the process. It is conceivable that possibly all the research questions gathered are not
16
17 exhaustive. While the JLA process and IIH PSP study recommend those research priorities
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19 that are important, there is no guarantee of research funding.
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29 **Conclusions**

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31 The IIH PSP has been an opportunity to understand the areas that are important to all. The
32
33 primary topic of underlying aetiology requires work both clinically and within the basic
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35 laboratory research. Another key area highlighted by this PSP is that of mechanisms of
36
37 headache in IIH. There is increasing evidence regarding the phenotype of the IIH headache,
38
39 which is challenging tradition regarding the raised ICP headache. [19,20] Future work should
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41 explore novel therapies for headache in IIH, which is the key driver in lowering quality of life
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43 in this patient cohort. [11] The PSP has the potential to influence the research agenda and
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45 consequently in time all area of management, from medical to surgical interventions for this
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47 currently idiopathic disease.
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Running title: PSP IIH top ten

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Running title: PSP IHH top ten

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- 4 the Treatment of Idiopathic Intracranial Hypertension Failing Maximum Medical
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Running title: PSP IHH top ten

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Conflicts of Interest

No authors contributing have a conflict of interest in the subject matter.

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Data Sharing statement

No additional data is available.

Contributor Statement

Mollan SP: interpretation of the survey results; drafting and review of the manuscript.
Hemmings K: PSP patient lead; administration of both surveys; drafting and review of the manuscript.
Herd C: literature review; independent information specialist; drafting and review of the manuscript.
Denton A: critical review of the manuscript.
Williamson M: organisation of the consensus final workshop; and critical review of the manuscript.
Sinclair AJ: PSP clinical lead; interpretation of the survey results and critical review of the manuscript.

All authors were steering group members and have read and approved the final manuscript.

Legend to figures:

Figure 1: Consort diagram and details of the JLA IHH PSP

Figure 2: Final Top 10 ranked uncertainties for the concerning the treatment and management of people with Idiopathic Intracranial Hypertension

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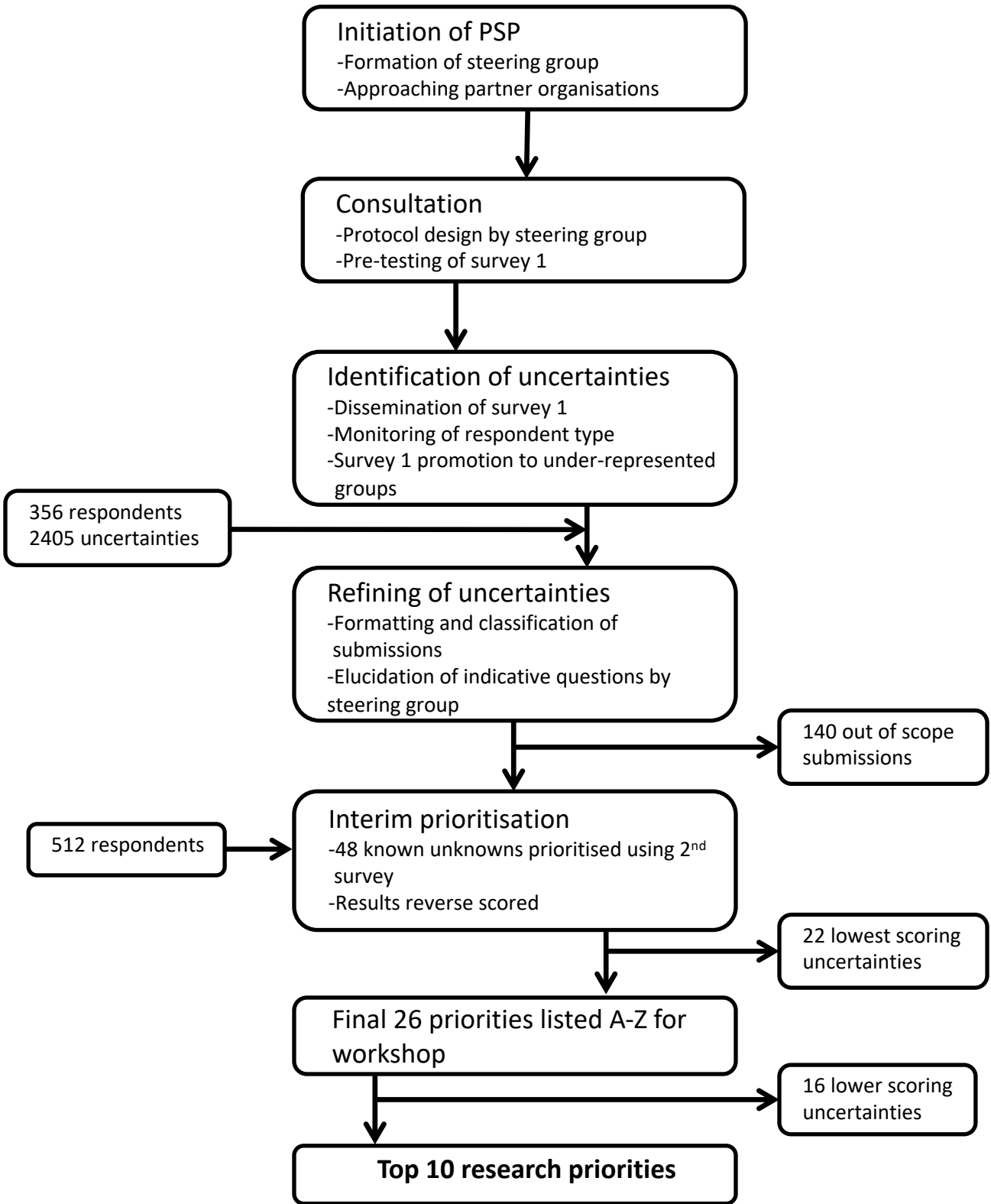




Figure 2: The top ten research priorities in IIH

192x267mm (150 x 150 DPI)

Supplemental table 1: The steering group members and their role

Person	Role
Krystal Hemmings	IIH UK Research representative and PSP patient led
Alex Sinclair	Clinical lead and neurologist
Michelle Williamson	IIH UK Chair trustee, project coordinator and carer
Clare Herd	Information specialist
Martin Plowright	IIH patient
Norma-Ann Dan	IIH UK patient representative
Amanda Denton	IIH UK patient representative
Rachel Bennett	IIH patient
Jayne Best	Neuro-Ophthalmologist
Arun Chandran	Neuro-radiologist
Julie Edwards	Headache nurse specialist
Anita Krishnan	Neurologist
Kamal Mahawar	Bariatric surgeon
Susan Mollan	Neuro-Ophthalmologist
Caroline Rick	Trial methodologist
Ahmed Toma	Neurosurgeon

Supplemental table 2: The prioritisation survey was designed using Qualtrics software (www.qualtrics.com) and responses were requested to the following seven questions:

1.	What questions do you have about how the diagnosis of IIH is made?
2.	What questions do you have about why people get IIH?
3.	What questions do you have about the management of vision in IIH?
4.	What questions do you have about the management of headache in IIH?
5.	What questions do you have about weight management in IIH?
6.	What questions do you have about care provision for patients with IIH? (e.g. General Practice, inpatient, outpatient care)
7.	Do you have any other questions about IIH that you feel are important but do not fall into the categories above?

Supplemental table 3: Partner organisations in alphabetical order

ABN - Association of British Neurologists
BASH - British Association for the Study of Headache
BIOS - British and Irish Orthoptic Society
Fight for Sight – The Eye Research Charity
RCOphth – The Royal College of Ophthalmologists
SBNS CSF subgroup - The Society of British Neurological Surgeons
Shine – Spina bifida, Hydrocephalus, Information, Networking, Equality
The Neurological Alliance
UKNOSIG - The United Kingdom Neuro-Ophthalmology Special Interest Group

Supplementary Table 4: Characteristics of participants with IIH of first survey

Number	180
Female (%)	96
Median age (years)	35
Ethnicity (%)	
White	92
Black or Asian	3
Multiple ethnic backgrounds	4
Not stated	1

Supplementary Table 5: Declared specialism of the healthcare professionals in first survey

Declared specialism of the healthcare professional	% of respondents
Neurologist	45
Ophthalmologist	11
Neurosurgeon	10
Neuro-Ophthalmologist	9
Other	8
Trainee	6
Bariatric Surgeon	3
General Practitioner	3
Nurse	2
Neuroradiologist	1
Orthoptist	1
Not declared	1

Supplemental table 6: 26 Questions for IIH PSP final workshop in alphabetical order

1	Are multidisciplinary clinics (joint clinics of neurology, ophthalmology, neurosurgery, dietetics and specialist nurses etc.) clinically and cost effective for the management of IIH and would they improve patient experience?
2	
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6	Are non-invasive intracranial pressure (ICP) measurements accurate and clinically useful?
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12	Can IIH biomarkers (tests in body fluids for example urine, saliva, blood, or brain scans) help diagnosis, predict the risk and guide therapy decisions in IIH?
13	
14	
15	Can novel therapies for IIH be developed which are effective, safe, and tolerable and potentially help with weight loss as well as reducing brain pressure?
16	
17	Do lumbar punctures (LPs) have long-term safety complications?
18	
19	Do the benefits of the drug treatments for IIH outweigh the side effects?
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21	How big is the impact of headache in IIH (how severe are headaches, how often do they occur, how many years do they continue for and how do they impact patients quality of life)?
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23	Is bariatric surgery effective in IIH and at what point in the disease should it be performed?
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26	Is cerebral venous stenosis the cause or consequence of IIH?
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28	Is IIH a lifelong condition?
29	
30	Is IIH caused by increased production or lack of cerebral spinal fluid (CSF) absorption?
31	Is there a genetic cause of IIH?
32	Is there a single or are there multiple causes for IIH?
33	What are the best ways to monitor visual function?
34	What are the biological mechanisms of headache in IIH and why in some do headaches continue even after papilloedema has resolved?
35	
36	What are the hormonal causes for IIH and why is IIH primarily associated with female gender?
37	
38	What are the triggers for periods of high intracranial pressure (ICP) in people with IIH?
39	What is happening in the body of a person with IIH which causes the development of the disease, the symptoms and the progression of the disease?
40	
41	What is the biological explanation for the differences between rapid visual loss compared with gradual visual loss in IIH and how can this be predicted?
42	
43	What medications are effective and safe to treat IIH headaches?
44	
45	What other conditions / features are associated with IIH (e.g. depression, sleep apnoea, endocrine disorders, cognition, nerve pain)?
46	
47	Which is the best type of surgery to treat IIH and when should surgery be performed?
48	
49	Why do people get IIH without papilloedema (IIHWOP) and how should this be treated?
50	
51	Why is obesity a risk factor for IIH in women and why is this not the case in men?
52	With regard to weight loss in IIH: how much is needed to treat IIH and how quickly does it work? What is the best, safest and most acceptable method to achieve this in the short and long term? Additionally, does the initial Body Mass Index (BMI) of the patient have an effect?
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57	Would an education program for health care professionals and patients with IIH improve care and disease experience for IIH patients?
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Supplemental Table 7: Final Top 10 ranked uncertainties for the concerning the treatment and management of people with Idiopathic Intracranial Hypertension

Ranking	Research priority
1	In the individual with IIH; what causes the disease, the symptoms and the progression of the disease?
2	What are the biological mechanisms of headache in IIH and why in some do headaches continue even after papilloedema has resolved?
3	Can new medical therapies for IIH be developed which are effective, safe, and tolerable and potentially help with weight loss as well as reducing brain pressure?
4	What is the biological explanation for the differences between rapid visual loss compared with gradual visual loss in IIH and how can this be predicted?
5	What are the best ways to monitor visual function?
6	Can IIH biomarkers (tests in body fluids for example urine, saliva, blood, or brain scans) help diagnosis, predict the risk and guide therapy decisions in IIH?
7	What are the hormonal causes for IIH and why is IIH primarily associated with female sex?
8	What medications are effective and safe to treat IIH headaches?
9	With regard to weight loss in IIH: how much is needed to treat IIH and how quickly does it work? What is the best, safest and most acceptable method to achieve this in the short and long term? Additionally, does the initial Body Mass Index (BMI) of the patient have an effect?
10	Which is the best type of intervention to treat IIH and when should surgery be performed?

Standards for Reporting Qualitative Research (SRQR)*

<http://www.equator-network.org/reporting-guidelines/srqr/>

Page/line no(s).

Title and abstract

<p>Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended</p>	1
<p>Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions</p>	2

Introduction

<p>Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement</p>	4
<p>Purpose or research question - Purpose of the study and specific objectives or questions</p>	4/last paragraph

Methods

<p>Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**</p>	5 and 6
<p>Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability</p>	5 and 7
<p>Context - Setting/site and salient contextual factors; rationale**</p>	5
<p>Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**</p>	5,6,7
<p>Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues</p>	7 top paragraph
<p>Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**</p>	5,6,7

1 2 3 4 5	Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	N/A
6 7 8	Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	7; table 4
9 10 11 12	Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	5,6,7
13 14 15 16	Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	5,6
17 18 19 20	Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	6 first paragraph

Results/findings

23 24 25 26	Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	7,8 figure 2
27 28 29	Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	Table 4,5,6,7

Discussion

32 33 34 35 36 37	Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	8-11
38 39	Limitations - Trustworthiness and limitations of findings	3

Other

42 43 44	Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	14
45 46	Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	14

*The authors created the SRQR by searching the literature to identify guidelines, reporting standards, and critical appraisal criteria for qualitative research; reviewing the reference lists of retrieved sources; and contacting experts to gain feedback. The SRQR aims to improve the transparency of all aspects of qualitative research by providing clear standards for reporting qualitative research.

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**The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options available, the assumptions and limitations implicit in those choices, and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.

Reference:

O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. **Standards for reporting qualitative research: a synthesis of recommendations.** *Academic Medicine*, Vol. 89, No. 9 / Sept 2014
DOI: 10.1097/ACM.0000000000000388

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