

HAEM-PR SPECT

Exploring patient and clinician views of the risk and benefits of emerging gene therapy for the treatment of haemophilia: a qualitative study

John Spors

UKHCDO Training Day

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Acknowledgements and Funding



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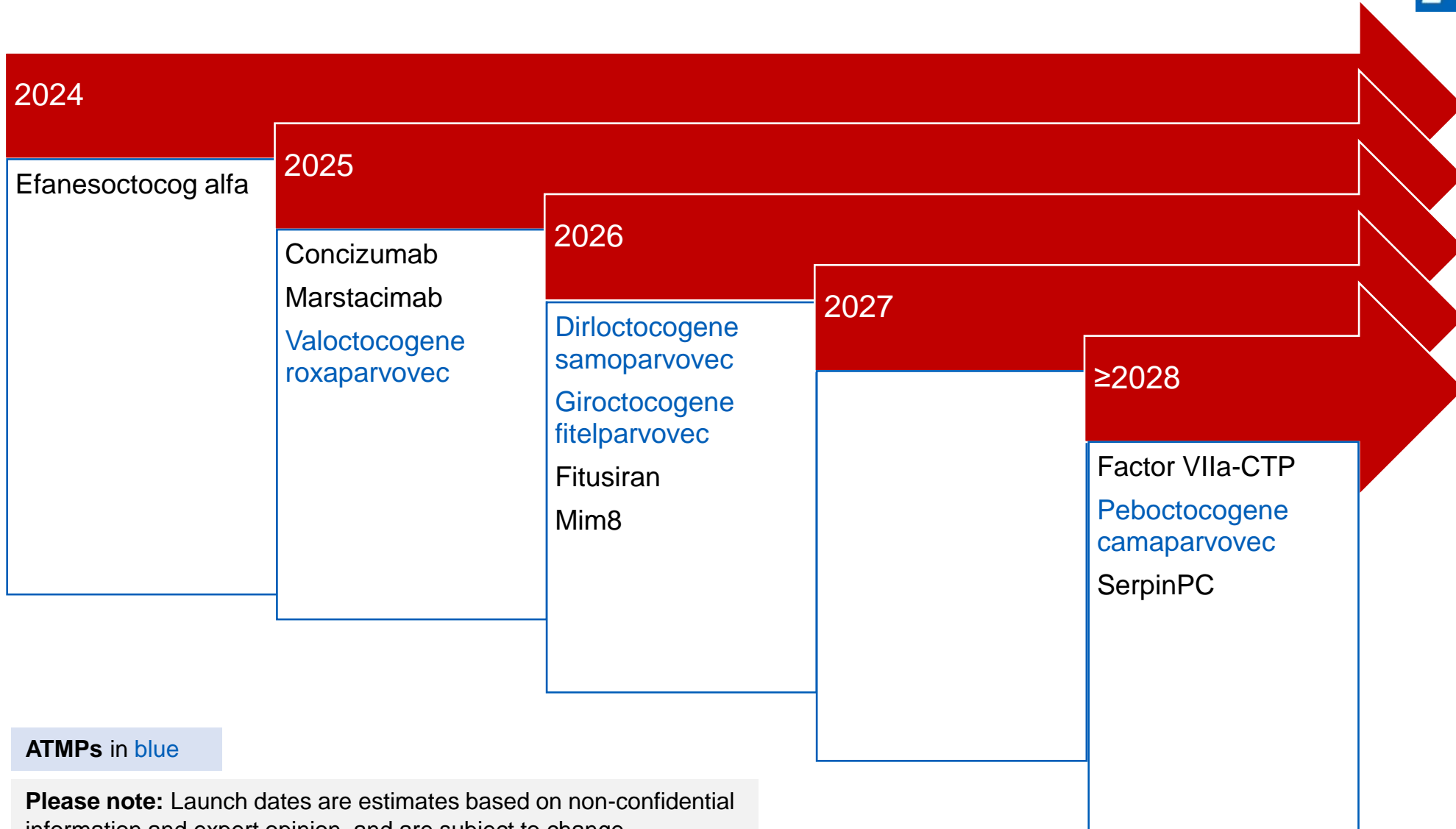
Core Study Team

- John Spors – PhD Candidate – LSHTM
- Professor John Cairns – Main Supervisor – LSHTM
- Professor Katherine Payne – Supervisory Team – University of Manchester
- Dr Stuart Wright – Supervisory Team – University of Manchester

Funding

- John Spors is funded by NHS England to undertake a part-time PhD looking at patient preferences in relation to ATMPs in haemophilia at the LSHTM

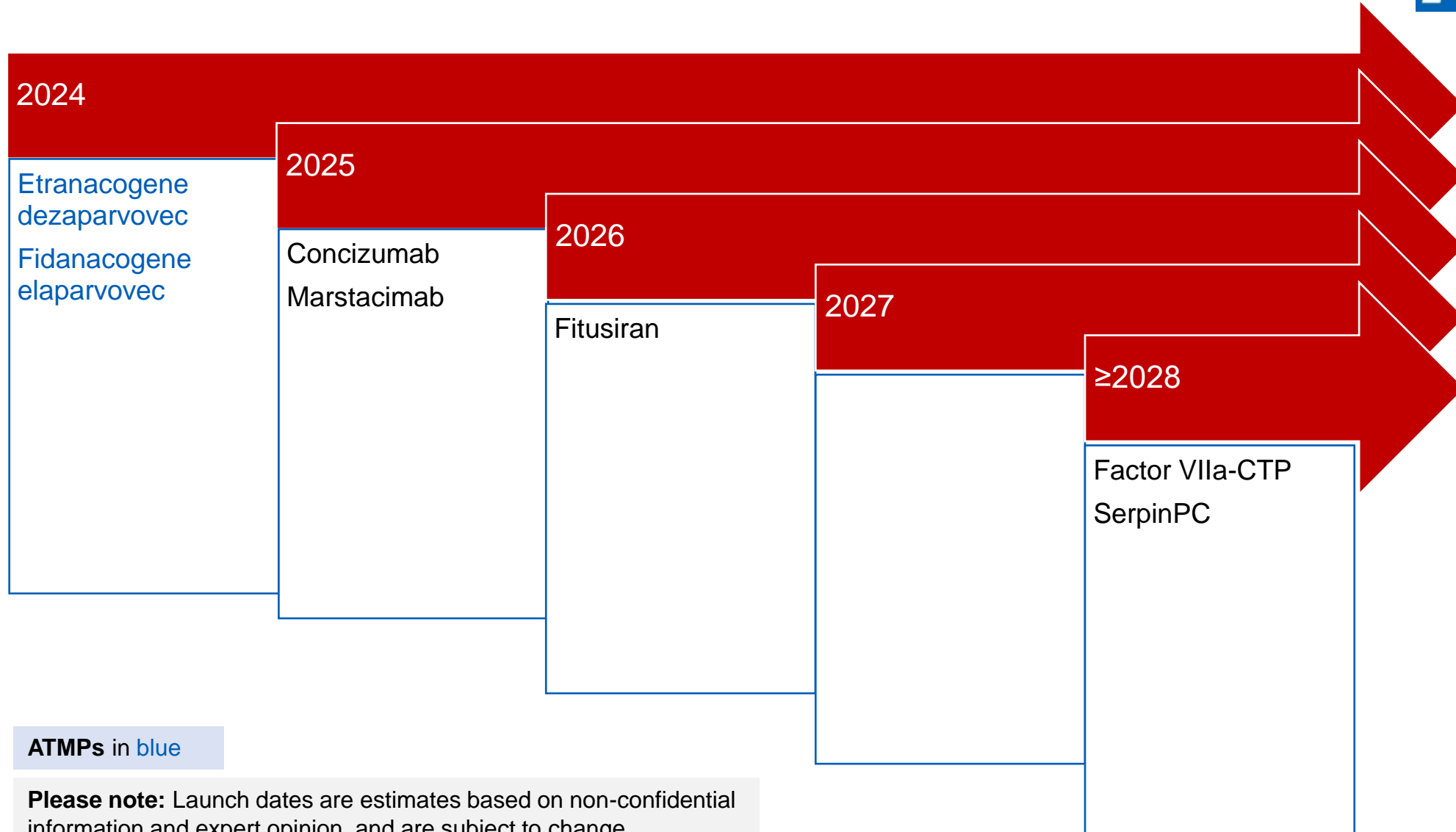
Haemophilia A pipeline 2024 onwards



ATMPs in blue

Please note: Launch dates are estimates based on non-confidential information and expert opinion, and are subject to change

Haemophilia B pipeline 2024 onwards

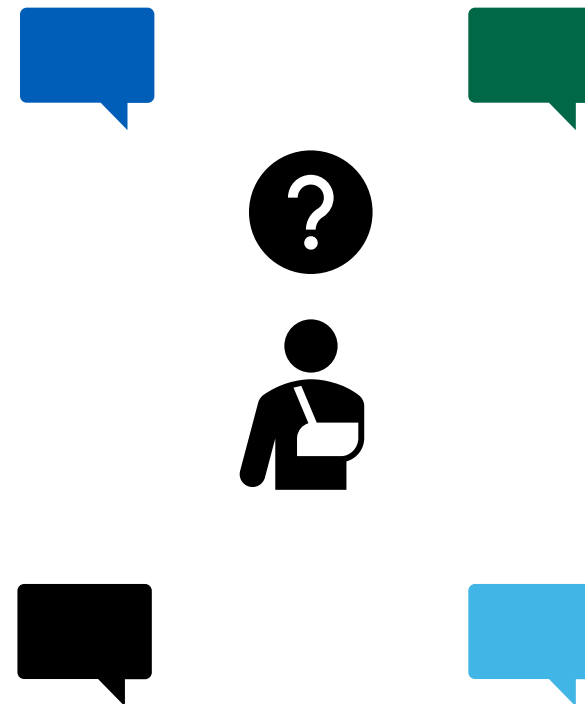


ATMPs in blue

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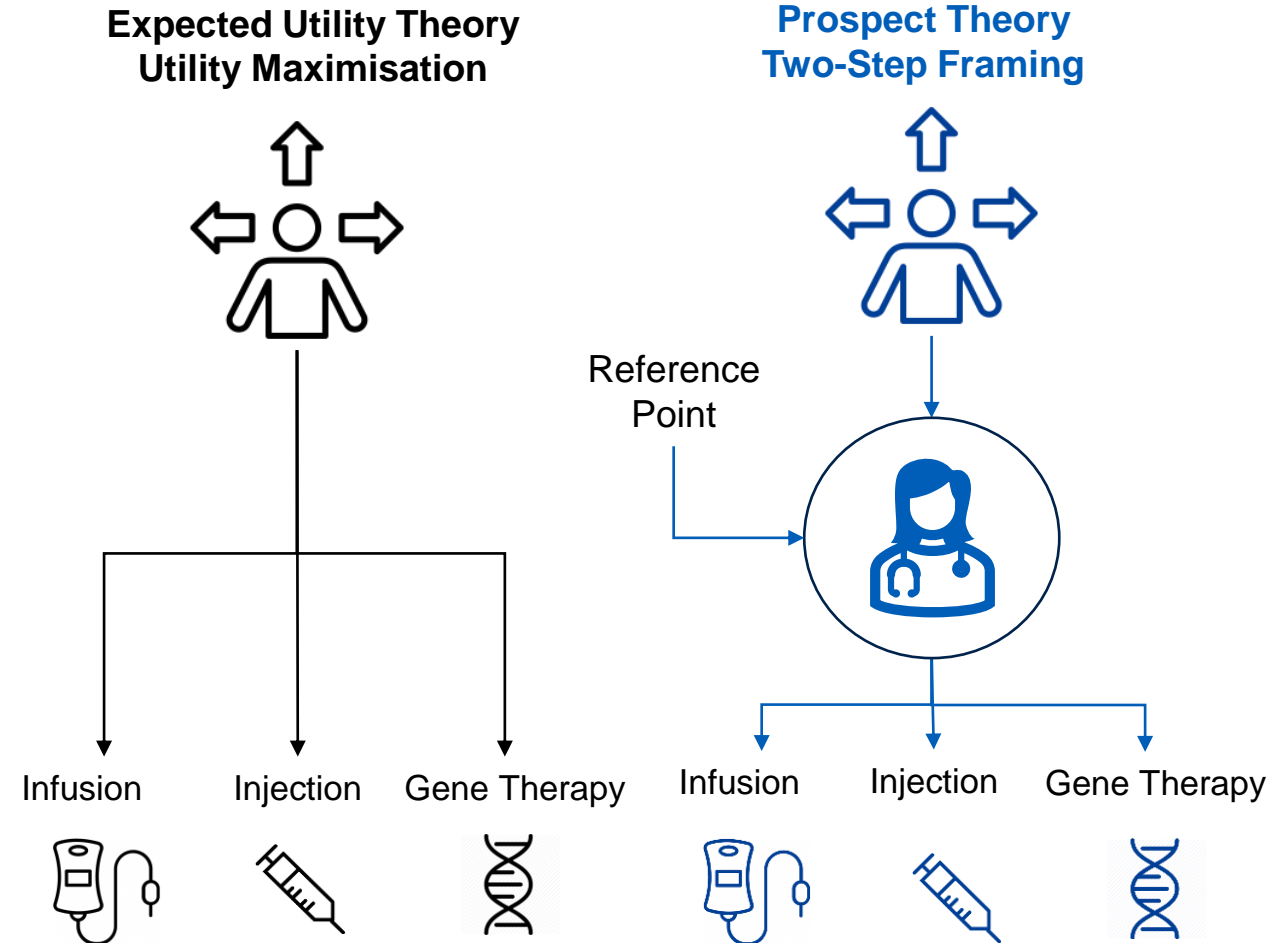
How to capture the patient voice most effectively remains subject to debate

- Patient voice is an important consideration in the availability and choice of pharmaceuticals - how to apply it formally within regulation, health technology assessment and reimbursement remains subject to ongoing debate.
- 21st Century Cure Act in the USA facilitates submission of patient experience data in regulatory submissions.
- Regulators are accelerating pharmaceutical development programs for medicines which address high unmet need - in short, products are coming through faster with less evidence.
- As healthcare systems such as NHS respond to this scenario – important to consider how patient preference data can be utilised to support evaluation and availability of products.



Prospect theory was conceptualised by Kahneman and Tversky as an alternative to expected utility theory

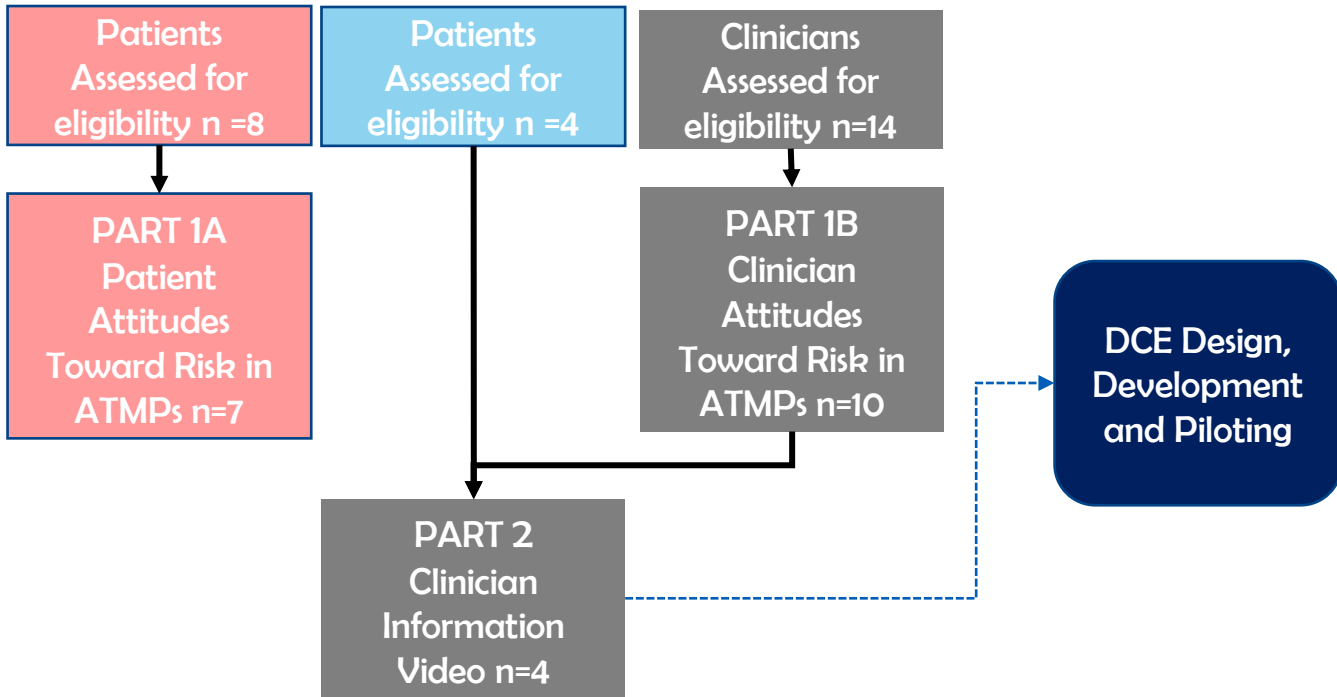
- Patient preference studies and Discrete Choice Experiments (DCEs) have a theoretical foundation in expected utility theory and the assumptions of economic rationality and utility maximisation.
- Under expected utility theory individuals choose outcomes which maximise utility given the probability presented.
- Under prospect theory individuals utilise a **two-step editing and evaluation process** to make decisions based on the expectations of loss or gain from their current relative position.
- Reference point and framing is critically important, particularly when focusing on the impact of clinician-patient relationship in treatment decision-making.



2023

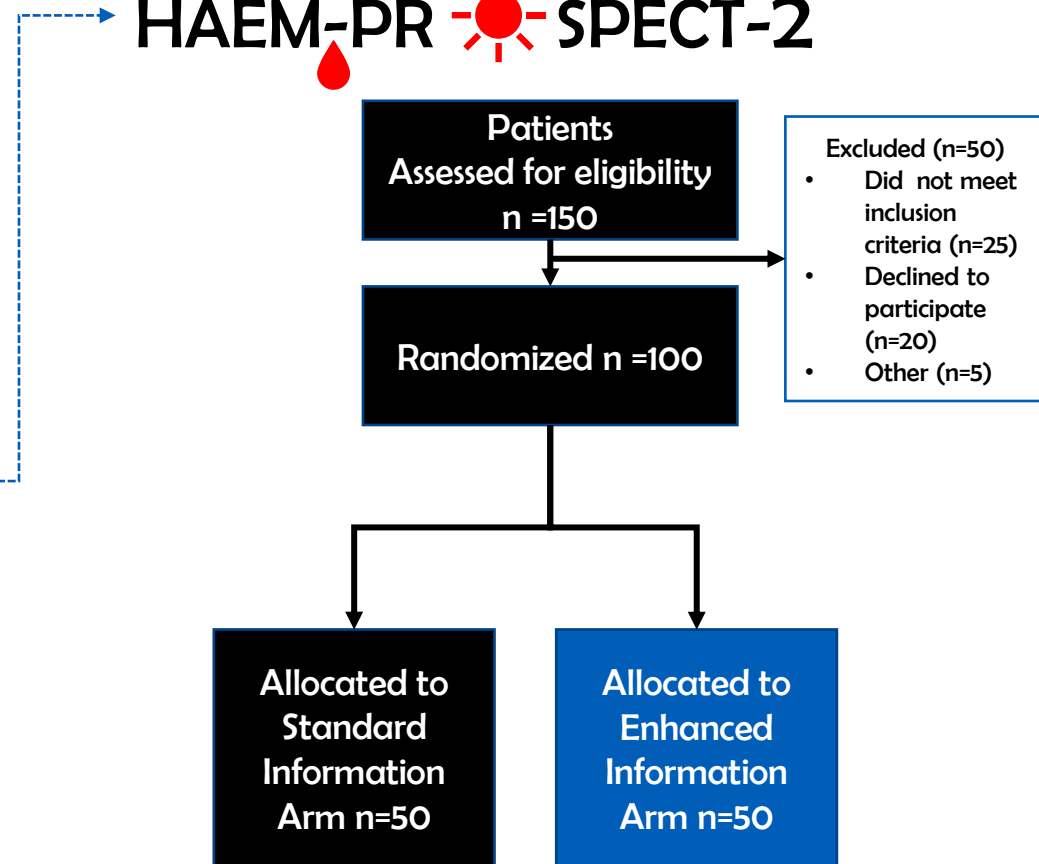
HAEM-PR SPECT-1

Key
 → Participant Flow
 → Outcome Influence



2024

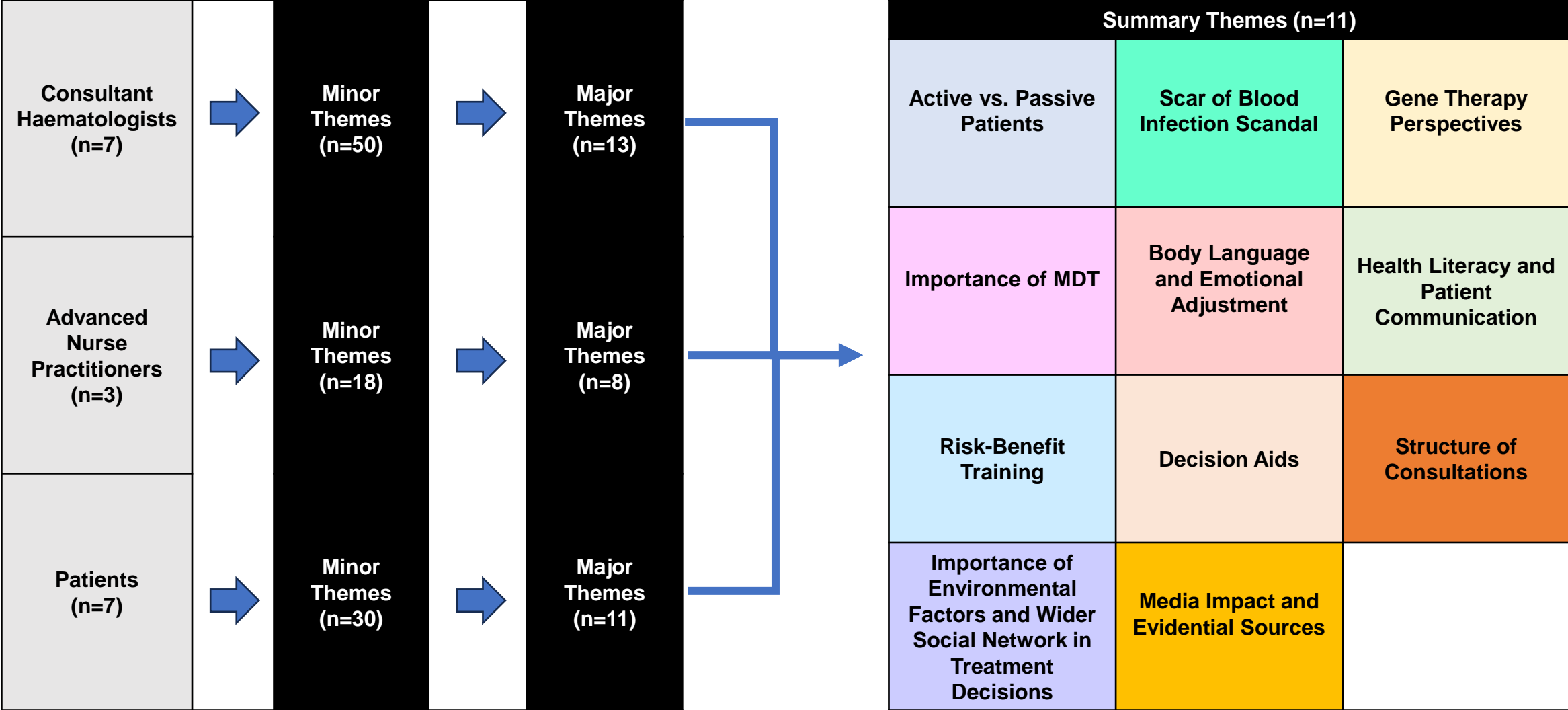
HAEM-PR SPECT-2



HAEM-PROSPECT-1: Methods

- Protocol for HAEM-PROSPECT-1 study was subject to ethical approval from the NHS Health Research Authority (HRA) (IRAS ID 318248) and the London School of Hygiene and Tropical Medicine (LSHTM) Ethics Committee (LEO Ref 28099).
- Non-probability sampling utilised.
- Recruitment undertaken through collaboration with national patient organisations (the National Haemophilia Society) and clinician networks (e.g. UKHCDO, NHS England Clinical Reference Group (CRG) and HAEMNET).
- Study sought feedback from UK-based:-
 - Consultant haematologists (n=7)
 - Advanced nurse practitioners (n=3)
 - Severe adult haemophilia patients (n=7).
- 6/7 (86%) patients in the sample had severe haemophilia A and 1/7 (14%) had severe haemophilia B. All patients were on prophylaxis therapy during the study, and none had been initiated on gene therapy.
- Focus groups or 1:1 interviews were held virtually via Microsoft Teams.
- NVivo 12 software was utilised to facilitate the thematic analysis.
- Theoretic and inductive thematic analysis used based on the guidelines suggested by Braun and Clarke.
- Independent member of the research team assessed the qualitative data for transferability, credibility, reflexivity and transparency and to confirm consensus on the included themes.

Summary of Thematic Codes



5 Key Themes for Discussion Today

5 Themes to Discuss Today				
Active vs. Passive Patients	Scar of Blood Infection Scandal	Gene Therapy Perspectives	Health Literacy and Patient Communication	Risk-Benefit Training

Theme 1: Active vs Passive Patients

- Evidence suggests patients playing an active role is important for improving patient outcomes
- Clinicians acknowledged they brought unconscious bias into the clinic
- Clinicians were aware they had the potential to and did influence patient therapeutic choice
 - ✓ Some bold and utilise their clinical expertise to drive health outcomes
 - ✓ Some more balanced and happy to take a less directive stance
- Clear difference between patients - non-Haemophilia Society affiliated patient respondents were much more 'passive' than their Haemophilia Society affiliated counterparts
- Second opinions were considered rare and some clinicians estimated this occurred in less than 1% of their patients

"I think that clinicians need to accept they influence patients, but it is then as soon as you accept that you influence patients, then comes an additional responsibility of actually moving to how do you then make sure you are able to get your patient around to thinking from a different perspective? How to control the disease?" Consultant Haematologist 2

"Last year, and it sort of was a bit of an eye opener, I kind of learnt what I have access to if I speak loud enough, which wrongly or rightly, it is what it is." Patient 2

"I think you have to put trust in your doctors. You have to, because they're the ones that know and they know their jobs And if you're gonna turn up there because you've read an article somewhere in Google about gene therapy and now you think you know everything, it's not right." Patient 6

Theme 2: Scar of Blood Infection Scandal

- Clinicians were influenced by current blood infection inquiry - expressing caution around risk communication and being more diligent with recording conversations, particularly about unknown risks
- ANPs highlighted the impact of the contaminated blood scandal on patient decision-making - trauma could be deep-rooted within individual patients and families which impacted therapeutic choices
- Three of the participants were old enough to be directly impacted by the infected blood enquiry - gave vivid accounts of the mental and physical devastation of the blood infection scandal
 - survivor's guilt
 - shame of having haemophilia and stigma
 - devastating impact of the medications required to clear hepatitis C
- Patients still live with the effects day after day

"I am scarred, the patient certainly are scarred and I'm having a lot more conversations with my patients about it because they've been retraumatized by the inquiry." Consultant Haematologist 5

"I had quite a bit of survivor guilt frankly, so that when in 1993-94, they said you've got hepatitis, and here's what you've got to do. And I was just thinking I've got something you know, I didn't get off scot-free, that makes me feel a little bit better if anything." Patient 4

"I mean, my cousin, he had his windows smashed at his house and things like that... some people might say, ohh, you know, just try and put it out your mind. You can't put it out your mind..... You can't have a day off, you have it everyday. It's as simple as that." Patient 5

Theme 3: Gene Therapy Perspectives

- Clinicians were clearly very cautious about gene therapy
 - ✓ stressed burden of delivering gene therapy which would impact demand
 - ✓ concerns about the requirements for long-term steroids or other immunosuppressants
 - ✓ concerned about the durability of gene therapy and variability of patient response
 - ✓ unsure about future therapeutic options (including gene therapy) for patients if efficacy with the gene therapy waned or failed
 - ✓ irreversibility of the treatment in comparison to existing therapeutic options
- The non-haemophilia society affiliated patients were more positive towards gene therapy than their haemophilia society affiliated counterparts
- Physical and mental burden is considered to be underrepresented in current narrative

“I think it will be really interesting to see how many people take it up because I think we’re in a really different situation with longer acting therapies and novel therapies now compared to 10 years ago.” Consultant Haematologist 6

“If you mention cancer, that’s the end of the conversation.” Consultant Haematologist 7

“Two weeks ago at a conference, someone presented on stage saying we’re all a bunch of guinea pigs and he wouldn’t trust it with a barge pole and especially haemophilia A And yeah, I don’t wanna be the guinea piggy.” Patient 4

“Ohh yeah, I mean it’s the Holy Grail, isn’t it? It’s just as good as we’re gonna get.” Patient 6

“The kind of heartache of not getting on the previous gene therapy was kind of like. I don’t want anything for a good couple of years. I was like, I don’t want anything to do with haemophilia anymore. It was my life – it broke me.” Patient 07

Theme 4: Health Literacy and Patient Communication

- Universally acknowledged that comprehension is challenging – health literacy varies significantly in the population
- Patients often suffer from poor concentration, struggle to remember key details or had challenges dealing with numerous complex topics
- Clinicians tailored language in consultations - main driver being education and health literacy. Other key factors included age, family history and specific acute concerns.
- Educating patients and their parents over a long time period was stressed - lifelong learning was therefore considered essential
- Important to engage early to avoid misunderstandings taking patients on a trajectory which is difficult to correct
- Patient advantages of being involved with the haemophilia society in terms of access to information and networks

“I mean it's well known that what you tell people and what they perceive and what they take in, it can be very different.” Consultant Haematologist 7

“You know they can often go away and have conversations in their own head and come back with a completely different idea of what has been said. They take a bit of information and then they build their own story, their own narrative around that. And sometimes it's quite hard to rein that back in if they've got it wrong.” Advanced Nurse Practitioner 3

“So the way I speak to someone and kind of what I say, Yes, I do individualise it - but within that, I don't think it's based on age, I think it's based on their level of education and a level of medical understanding.” Consultant Haematologist 6

“I think I have a responsibility now, taking on a role to actually get better informed and speak to those who are actually impacted.” Patient 1

Theme 5 : Risk-Benefit Training

- Ongoing risk-benefit training is not routinely available to the clinical community - trained on elements of patient communication, but not specifically risk-benefit
- Despite lack of formal training on risk communication, clinicians were all comfortable with explaining risk-benefit to patients
- Evidence of using analogies, drawings or simple examples to try and communicate trial data results, risk-benefit and highlight uncertainty – majority of patients thought not to want detailed statistics
- Rapid pace of treatment development in haemophilia and the challenge of staying informed
- Genomics and informed consent training also considered to be useful
- Training needs to be tailored and relevant to clinical practice

“So I thought that was a really interesting question. Not that I can remember. As a medical student, you have communication skills sessions, but a lot of that focus is breaking bad news.” Consultant Haematologist 6

“I do end up drawing quite a lot in clinic - I think that everyone responds really differently. But certainly for something like factor levels and different products, I find like a graph just where I can scribble.” Consultant Haematologist 6

“I think modules around informed consent and making it part of that process.... Training around genomics as you know they [discussions] have become more complex.” Advanced Nurse Practitioner 1

Discussion Points

No.	Discussion Points
1	<ul style="list-style-type: none"> Risk-benefit communication in the clinic remains challenging - the evolution of the care pathway to include ATMPs with highly uncertain risk/benefit profiles only further exacerbates this.
2	<ul style="list-style-type: none"> The study has demonstrated a broad range of influences on patient choice and that clinicians clearly play a key role in framing the discussion. Creates a definitive reference point under prospect theory and has potential implications for patient preference methodologies such as DCE.
3	<ul style="list-style-type: none"> Wide range of health literacy within the population and the need for (1) high-quality gene therapy patient materials and (2) risk-communication training for clinicians.
4	<ul style="list-style-type: none"> Unfeasible to mandate that all patients are active and challenge their clinician with data-based scientific arguments, request second opinions and email in advance of consultations. Patients must have time and space to make decisions, based on tailored information and have a safe decision-making environment which can include family, friends, social networks and the broader haemophilia community.
5	<ul style="list-style-type: none"> Scepticism surrounding gene therapy and the infected blood inquiry in the UK has heightened and strengthened risk-aversity via a mistrust of the healthcare system. Uptake of gene therapy is therefore likely to be slow with an even more challenging scenario for Haemophilia A driven by existing treatment options and observed performance in the trials to date.

Haemophilia is unique in risk-benefit discussions due to being heavily influenced by the infected blood scandal

Humanistic

- Building relationships
- Assessing mood and affect
- Clinician as a gatekeeper for health service

Mechanistic

- Formal checklists
- Decision-Aids
- Read-back
- Pre-consultation engagement

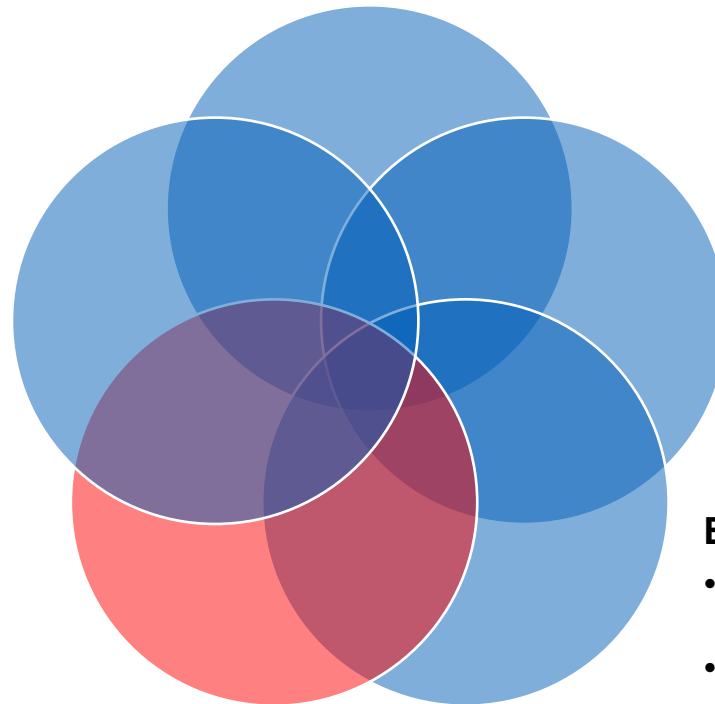
Paternalistic

- Clinical expertise and application
- Influence therapeutic choice
- Tailoring information based on assessment of health literacy

Haemophilia is unique in that the contaminated blood scandal adds an additional layer (5th ring) of complexity to healthcare decision-making

Contaminated Blood Scandal

- Mistrust of healthcare system
- Physical scars (e.g. Hepatitis C)
- Mental scars (e.g. death of family member)



Environmental

- Impact of broader life anxieties
- Age and evolving life circumstance
- Family and friends
- Social and other media
- Broader MDT

HAEM-PROSPECT-1: Study Limitations



Overall sample size (n=17) which was UK-based



Sample did not include caregivers, adolescents, women with haemophilia and mild and moderate patients with haemophilia



Large majority of patients (6/7) in study had severe haemophilia A

A photograph of a person's legs and feet as they ascend a set of blue metal stairs. The person is wearing bright orange high-top sneakers with white soles. The stairs have a blue metal railing and a blue metal mesh side panel. The background is a bright, overcast sky.

Next Steps

- Aim is to publish full HAEM-PROSPECT-1 outcomes in the *Journal of Haemophilia Practice* – article submission in December 2023
- Record clinician information videos – December 2023
- Ethics application for HAEM-PROSPECT-2 – Jan 2024
- HAEM-PROSPECT-2 Discrete Choice Experiment (DCE) – 2024

Conclusions

1

HAEM-PROSPECT-1 has demonstrated that treatment decision-making and risk-benefit discussions is a complex and multi-faceted issue which in haemophilia is heavily influenced by the infected blood scandal

2

Clinicians frame treatment decision-making which necessitates the requirement for risk-benefit training and high-quality tailored patient gene therapy information materials

3

There remains scepticism about gene therapy across all research participant groups which suggests that uptake is likely to be relatively slow with divergence anticipated between haemophilia A and B

Thank
you!

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