Navigating family dynamics and ethical considerations in genetic diagnosis of pulmonary arterial hypertension: insights from in-depth semi-structured interviews

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Shareable abstract (@ERSpublications)
Genetic diagnosis and precision medicine impact family dynamics and ethics in PAH. This study shows PAH diagnosis reshapes family roles, introducing challenges. Comprehensive genetic counselling and support are essential for familial wellbeing. https://bit.ly/4864fBJ

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Abstract

Background Genetic diagnosis and precision medicine are rapidly advancing, driven by innovations in next-generation sequencing and omic methods. The UK's collaboration between national research initiatives and the National Health Service facilitates translation of research into clinical practice. This rapid transition impacts family dynamics and family planning, and raises ethical concerns, compounded by limited public and practitioner awareness of the long-term consequences of genetic diagnosis. Our objective is to explore the impact of genetic diagnosis on family dynamics and the ethical considerations of genetic testing at different life stages in patients with pulmonary arterial hypertension (PAH) and their at-risk relatives.

Methods Stakeholders from the National Institute for Health Research BioResource Rare Diseases Study and the National Cohort Study of Idiopathic and Heritable Pulmonary Arterial Hypertension were recruited using purposive sampling. 53 interviews and focus groups with 63 participants were recorded, transcribed and thematically analysed using MAXQDA data analysis software.

Results The study revealed three main themes: the impact of diagnosis on family dynamics, considerations for family planning, and genetic testing of relatives. Two attitudes toward testing offspring emerged: proactive advocates and gatekeepers. The gatekeeper stance was driven by three key factors: shielding children from genetic risk awareness, feelings of guilt or a desire to avoid blame for disease transmission, and limited family connections. Each theme highlighted various moral and ethical dilemmas faced by individuals.

Conclusions A PAH diagnosis reshapes family roles and responsibilities. Genetic risk awareness strengthens bonds but also introduces challenges such as disclosing information and deciding on testing for at-risk relatives. Our research highlights the need for comprehensive genetic counselling and support systems to enhance patient care and familial wellbeing.

Introduction

Genetic diagnosis and precision medicine are advancing rapidly, driven by technological innovations such as next-generation sequencing and omic methods. In the UK, collaborative efforts between national research initiatives and the National Health Service (NHS) ensure the efficient translation of research breakthroughs into clinical practice [1–3]. However, this swift transition brings about broader implications beyond individual patients, impacting family dynamics and family planning, raising questions about the ownership of genetic information, and presenting ethical dilemmas for policy and practice [4]. These issues become even more intricate when testing involves minors for late-onset diseases or carrier status without clear medical interventions [5, 6]. These ethical concerns are compounded when clinical and research settings overlap [7]. Adding to these challenges is the prevailing limited awareness and understanding among both the public and medical practitioners regarding the long-term consequences of genetic diagnosis.

Our objective is to shed light on the impact of genetic diagnosis on family dynamics and ethical considerations surrounding genetic testing at different life stages in patients with pulmonary arterial hypertension (PAH) and their at-risk relatives. This article explores patients', carers' and relatives' perspectives, highlighting where their narratives align or diverge from clinicians' views. Clinical and research voices are discussed separately [2].

Methods

Recruitment

A diverse sample of participants was selected from the National Institute for Health Research BioResource Rare Diseases Study and the National Cohort Study of Idiopathic and Heritable Pulmonary Arterial Hypertension, considering roles, age, gender and mutations in PAH risk genes. All included patients had idiopathic or heritable PAH, with 34% having PAH gene mutations. One caregiver, a mother of a PAH-diagnosed child and sibling who died from PAH, was not tested due to the absence of known mutations. Two relatives were healthy carriers, and a third was undecided about testing; none had PAH (table 1). Confirmatory testing for patients with genetic findings was done in NHS laboratories with genetic counselling and spearheaded the development of new healthcare services and pathways [2, 8].

The RAPID-PAH study recruited from all UK pulmonary hypertension centres using local teams, referrals, online methods and the Pulmonary Hypertension Association webpage, continuing until targets were met (figure 1). Clinical, research and study teams were contacted directly, and the UniPHy UK trial network's Patient and Public Involvement Team reviewed patient documents.

Ethical approval

Ethical approval was obtained from the North of Scotland Research Ethics Service (REC: 22/NS/0127). All participants provided written informed consent prior to enrolment in the study.

Data collection and analysis

Semi-structured interviews and focus groups were conducted with patients, relatives and clinical team members. Using topic guides and led by M. Fay, an experienced qualitative researcher, one-on-one interviews with patients and researchers and focus groups with clinical teams were conducted between January and August 2023. These sessions, held *via* phone or Zoom, lasted 30–60 min. Recordings were transcribed verbatim, ensuring participant anonymity. Using Grounded Theory [9], transcripts were thematically coded by two authors (E.M. Swietlik and M. Fay) with consensus discussions utilising MAXQDA data analysis software (www.maxqda.com). Specifically, MAXQDA was employed to store, categorise, code the data, identify patterns and themes, perform inter-rater agreement analysis, and create summary tables; additionally, word exploration and similarity analysis were performed. The study followed COREQ (COnsolidated criteria for REporting Qualitative research) [10] and SRQR (Standards for Reporting Qualitative Research) standards [11], omitting identifying details for confidentiality (supplementary material).

Results

Summary of key themes

The interviews revealed three main themes: the impact of diagnosis on family dynamics, family planning considerations, and genetic testing of relatives. Two attitudes toward testing offspring emerged: proactive advocates and gatekeepers. Gatekeepers were influenced by a desire to protect children from genetic risk awareness, feelings of guilt or blame for disease transmission and limited family connections. These themes highlighted various moral and ethical dilemmas faced by individuals (table 2, and figures 2 and 3).

Family dynamics

Strengthening family bonds, particularly with children

Several stakeholders observed that, in numerous cases, the experience of illness strengthened familial relationships. This was especially evident during the recruitment process of trios at the paediatric centre. Similarly, the fortification of familial bonds between spouses and the evolution of roles within the family unit in the face of debilitating disease was evident. Notably, some children who spent their entire lives with a parent affected by the disease assumed the roles of caregivers and primary responders.

Among adult patients, a common theme emerged where parents shared the experience of the disease with their adolescent or young adult children, leading to a significant turning point in their relationship. Parents unanimously expressed their willingness to wait for their children to reach emotional maturity before fully handling the burden of the disease. One parent shared:

TABLE 1 Demographic characteristics of participants

Clinical and research teams (n=28)	
Role	
Clinical trial coordinator	3 (11)
Doctor	15 (54)
Research assistant	1 (4)
Research nurse	4 (14)
Researcher	3 (11)
Specialist nurse	2 (7)
Centre	
Great Ormond Street	4 (14)
Imperial and Hammersmith	6 (21)
Newcastle Freeman	2 (7)
NHS Greater Glasgow and Clyde	3 (11)
Royal Brompton	1 (4)
Royal Free	1 (4)
Royal Papworth Hospital	8 (29)
Royal United Hospital Bath	2 (7)
Sheffield, Royal Hallamshire Hospital	1 (4)
Research involvement	
Yes	26 (93)
No	2 (7)
Patients, relatives and carers (n=35)	
Role	
Carer	1 (3)
Patient	31 (89)
Relative	3 (9)
Centre	
Great Ormond Street	1 (3)
Imperial and Hammersmith	10 (29)
Newcastle Freeman	1 (3)
NHS Greater Glasgow and Clyde	7 (20)
Royal Free	1 (3)
Royal Papworth Hospital	5 (14)
Sheffield, Royal Hallamshire Hospital	10 (29)
Age at diagnosis, years (n=31)	45 (34–54)
Age current, years	55 (50–62)
Length of diagnostic journey, months (n=31)[#]	18 (10–36)
Time lived with PAH, years (n=31)	11 (9–16)
Sex	
Female	27 (77)
Male	8 (23)
Mutation	
No	22 (63)
Unknown	1 (3)
Yes	12 (34)
Gene (n=12)	
BMPR2	10 (83)
GDF2	1 (8)
KCNK3	1 (8)
Number of research studies in 5 years (n=34)	1 (1–3)
Education (n=34)	
Higher degree	10 (29)
Secondary	12 (35)
Sixth form/college	12 (35)
Income (n=34)	
<GBP 12 000	6 (18)
GBP 12 000–50 000	18 (53)
GBP 51 000–150 000	2 (6)
I prefer not to answer	8 (24)

Data are presented as n (%) or median (interquartile range). PAH: pulmonary arterial hypertension. [#]: defined as the number of months from first contact with general practitioner to diagnosis. Reproduced with amendment, from [2, 8] with permission.

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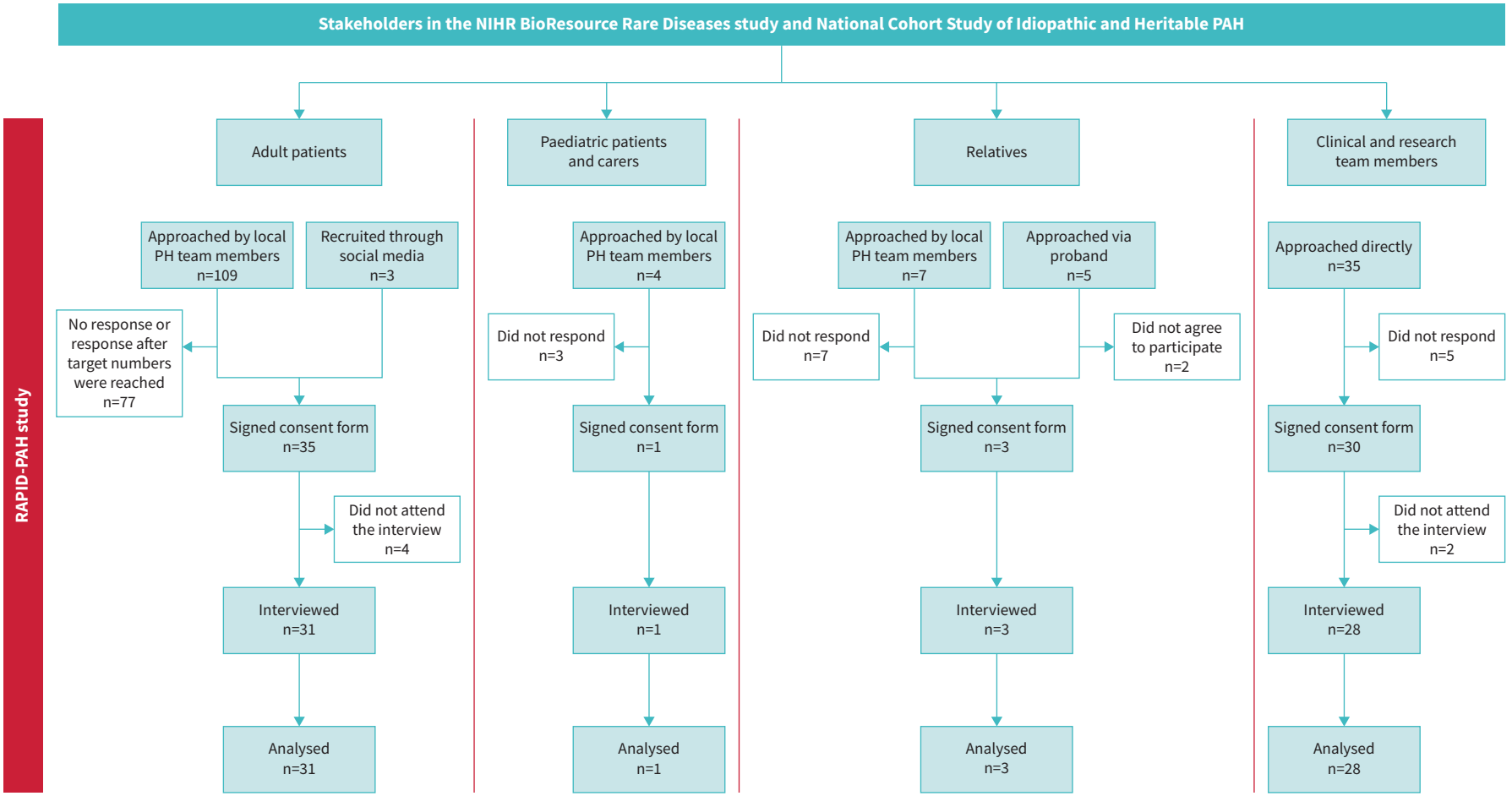

FIGURE 1 CONSORT (Consolidated Standards of Reporting Trials) flow diagram of RAPID-PAH. NIHR: National Institute for Health Research; PAH: pulmonary arterial hypertension; PH: pulmonary hypertension. Reproduced with amendment, from [2, 8] with permission.

TABLE 2 Themes and subthemes

Themes and subthemes	Segments[#]	Percentage[¶]
Complexities of family life	354	100
Family dynamics and impact/implications	275	77.68
Family planning and advice	44	12.43
Family background/disease history	35	9.89
Moral and ethical issues	94	100
Autonomy	27	28.72
Reproductive choices	21	22.34
Sampling at various stages of the life cycle	19	20.21
Informed consent	9	9.57
Duty of care	6	6.38
Psychological impact	6	6.38
Privacy and transparency	6	6.38

[#]: segment refers to the fragment of text that is isolated for analysis; [¶]: percentage refers to the proportion (%) of segments within a given subtheme, expressed as a fraction of the diagnostic theme or the proportion of subsubsegments within a given subtheme (Moral and ethical issues).

> "When she got to about 19, she got to the, I'm an adult. You still treat me like a child age. And I do remember having a conversation with her then, "Right, sweetheart. This is me treating you like an adult. Pulmonary hypertension is life-shortening, and I should not still be here." And I was as blunt as that. And she burst into tears. But it was a changing point." (Patient DS300)

Experience of the familial disease, even in the face of lack of firm genetic diagnosis, shaped attitudes to doing and displaying family and genetic thinking. A mother of an affected child shared "[My husband] he's much the same as me; we want to be able to help as much as we can, you know, anything we can do, we will." (Carer DS310), and expressed frustration with external assumptions about their capacity to cope with genetic information. These assumptions were perceived as intrusive and unnecessary, as families often have a better understanding of their own dynamics and resilience.

Disclosure of information to children and genetic testing of relatives

The study found a strong desire among participants to contribute to scientific progress and benefit future generations, regardless of familial ties. However, willingness to share personal genetic results with family varied significantly (figure 3). Currently, the responsibility for informing relatives about genetic testing often falls on the proband, but this approach can be ineffective in reaching all family members.

Advocates for testing

Some participants preferred involving their relatives in genetic testing and placing their care in the hands of healthcare professionals. They believed that having greater knowledge about their family's genetic makeup would provide a sense of control and enable more proactive healthcare management. One participant exemplified this viewpoint:

> "When my genetic test revealed a faulty gene likely causing my pulmonary hypertension, I knew I had to act. My 16-year-old daughter has a 50% chance of inheriting it, so getting her tested became a priority. My parents also wanted to be tested." (Patient DS331)

Participants acknowledged the importance of individual autonomy regarding genetic information disclosure to adult children. They emphasised allowing their children to make informed choices about genetic testing without undue influence. One participant described their approach:

> "So, all I could give them was all the information that I had regarding going through with genetic testing so they could make that decision themselves. I didn't influence them, and I don't think they were influenced, I think they made their own decisions." (Patient DS296)

The role of genetic diagnosis in guiding targeted management, especially for paediatric patients, was also emphasised. Participants recognised the limitations of current therapies and stressed the importance of research in improving care. A clinician highlighted this point:

FIGURE 2 Insights into family life amidst the diagnosis. Three primary themes surfaced, encompassing the consequences of the diagnosis on family dynamics, the considerations related to family planning, and the genetic testing of relatives. Each of these themes revealed various moral and ethical dilemmas that individuals encountered.

> "One of the reasons people say "yes" [to research] is because when you're diagnosed with, or your child is diagnosed with idiopathic PH, that is not a curable disease … even the best care at the moment is not what you would want to accept for your child, and the only way out of that trap is research." (Clinician DS317)

This underscores the critical need for ongoing research to develop personalised treatments and translate findings into clinical practice.

Gatekeeping and its complexities

While the desire for testing and confronting risk factors is understandable, the reasons behind a "gatekeeping" attitude, where disclosure is delayed or avoided, are more nuanced. Three key themes emerged: protecting children from the burden of knowledge, fear of blame for illness or emotional burden, and loose family connections.

Protecting children from the burden of knowledge. During interviews, discussions with parents often focused on the appropriate amount and timing of information to share with children. Parents recognised individual and age-related differences in their children's coping abilities and the need to tailor information accordingly. A parent of a teenage son shared their perspective:

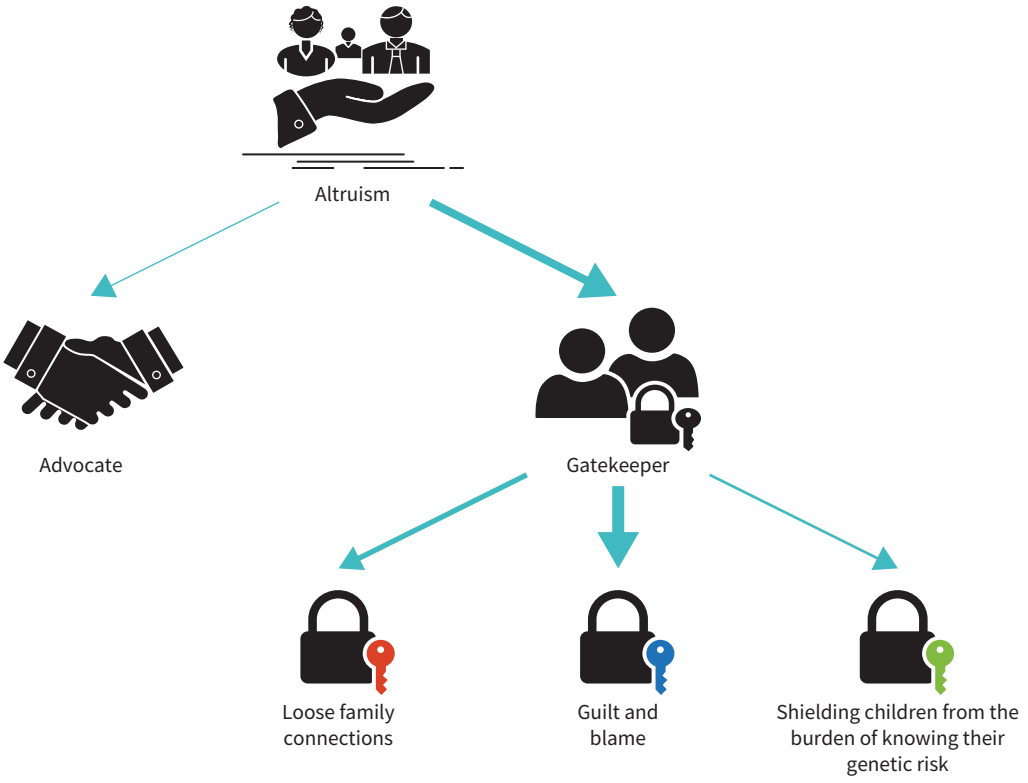

FIGURE 3 Attitudes toward genetic research and testing: altruism, advocacy and gatekeeping perspectives. Most patients engaged in genetic research due to altruistic motives. Among those with mutations in pulmonary arterial hypertension risk genes, two distinct attitudes toward testing offspring emerged: proactive advocates and gatekeepers. The gatekeeper perspective stemmed from three primary factors: a responsibility to protect children from the weight of genetic risk awareness, feelings of guilt or a desire to evade blame for disease transmission, and the influence of limited family connections on the decision to involve relatives in testing. The width of the arrow reflects the weight of the theme, with thicker arrows signifying a stronger and more prevalent sentiment.

> "Yes, when he's got a wife, and they're looking into having children, I think it's very important, then I do. 100% yes. Yeah. But then he's an adult then, and I haven't scarred him. He's got his own brain, and he'll work things out himself." (Patient DS315)

Fear of blame for illness or emotional burden. While acknowledging their adult children's autonomy to decide about genetic testing, some participants expressed a desire to avoid causing unnecessary anxiety. They worried that discussing the possibility of a genetic condition might burden their children, who already faced anxieties. As one participant explained:

> "Yes, if they wanted to [get tested], it would be up to them … But I haven't mentioned anything to them so far because I don't want them to be worrying unnecessarily …" (Patient DS324)

This quote highlights the tension between respecting adult family members' rights to make their own choices and safeguarding their emotional wellbeing.

Furthermore, some participants felt a sense of concern for their family members' health but struggled to initiate conversations about testing. One patient expressed this dilemma:

> "I'm a wee bit concerned that my daughter might have it [the genetic condition] because she has chest problems … so I'm worried she might end up in the position that I'm in." (Patient DS316)

This reflects the internal conflict between wanting to protect the patient's daughter and the fear of causing distress by bringing up the possibility of testing.

Loose family connections. The absence of strong family ties and limited personal experience with the disease hindered genetic testing uptake. Conversely, close familial connections encouraged engagement in testing and research. Relatives in the RAPID-PAH study had closer bonds with the proband and direct disease experience. Those who underwent genetic testing and received positive results reported minimal anxiety, valuing regular clinical screening and early diagnosis benefits over potential stress. Most relatives opted out of genetic testing, citing privacy concerns, insurance implications, emotional distress, inconvenience and low personal stakes. While these reasons were inferred from probands' interviews, it is important to note that probands respected their relatives' autonomy in testing decisions. Additionally, some relatives might have been unaware of the research opportunity and its benefits. Addressing these factors and providing clearer information could increase future participation rates.

Family planning considerations

Challenges faced by women receiving a diagnosis before starting a family

Receiving the diagnosis before starting a family proved to be a major setback, especially for women. This was primarily due to the advice against having children, which, in some cases, was delivered insensitively and without regard for the profound emotional impact it could have. One participant recounted:

> "As soon as I was diagnosed. I was just about to get married, and I was told that I wasn't even allowed to get a week pregnant, and they wanted to sterilise me. So that was more devastating than being diagnosed. It was always my plan to have children." (Patient DS304)

Another participant described encountering pressure to use contraception, stating:

> "Once I had the right heart cath and they confirmed it, then they were all about contraception. It was this big thing. They brought in this gynaecologist who wanted me to have the coil. I remember them being quite full on about that and I was very adamant that that wasn't something I wanted to do. I guess they wanted to make sure that I didn't fall pregnant because of the high risk of it. But I stood my ground with that because I said, "I've got no interest in that whatsoever"." (Patient DS342)

Others had a chance to discuss family planning with their clinical teams and felt well supported. One participant expressed:

> "I wasn't advised not to [have children]; they just said that it carries a significant risk. […] They did talk to me about it very well. It was definitely not a blanket, no." (Patient DS338)

This testimony highlights the importance of open and supportive communication between healthcare providers and patients regarding family planning decisions in the context of pulmonary hypertension.

Reflections of parents with children of childbearing age

Patients who already had children at the time of (genetic) diagnosis reflected on the impact this had on their children's reproductive health and family planning. Two main attitudes emerged: apprehension about passing the disease on and a pragmatic and optimistic approach. The first perspective can be illustrated by the following quote:

> "My daughter, I think if she thought it was a gene thing that she had, and she could pass on, she would be okay about having it herself, but she would potentially abstain from having children for fear of passing it on. And that would be, in my opinion, tragic." (Patient DS300)

On the contrary, the second perspective offers a pragmatic and optimistic outlook:

> "My daughter got married last year, and it looks to me like she's going to have kids, I think, and she knows the risks and she knows where she's at and how she feels and what she knows about her body. Maybe she will be fine, and everything will be fine and that verses the super-cautionary approach to life that you could have." (Patient DS296)

Overall, these perspectives illustrate the complex interplay between resilience, pragmatism, optimism and concern when individuals navigate family planning in the context of hereditary illnesses.

Abortion, adoption and surrogacy

Family planning discussions naturally centred around topics such as abortion, adoption and surrogacy.

Abortion

Lived experiences had a profound impact on attitudes toward abortion. Personal experiences, emotional attachment to the unborn child and the impact of personal loss played significant roles in shaping individuals' decisions not to pursue abortion, even when faced with potential health concerns or hereditary conditions. This is exemplified by a participant's statement:

> "If they'd said to me, "Yes, it's hereditary, yes, he could have it," I would not have had an abortion, no. Certainly not after losing my baby." (Carer DS310)

Other women, while grappling with moral dilemmas and emphasising individual choice, admitted that they could not bear the guilt of knowingly bringing a severely handicapped child into the world, especially if it posed a risk to maternal health and left the husband to care for the children alone. One participant reflected on this inner conflict, stating:

> "You want to give the best for your children, don't you, and if you're bringing a child into this world, and you know what you've done to it, I'd have guilt. I'd be looking at its eyes and thinking it's my fault you're in this world. I would have had an abortion. Sad to say." (Patient DS315)

Adoption

Despite the challenges encountered during the adoption process, adoption was seen as a viable choice for forming a family. The individuals reported that the joy of having a family outweighed the difficulties associated with the disease they were facing. One participant reflected:

> "The first thing we thought of was adoption, really. […] So I think we'd been together about 10 years by the time we adopted. Then we were going to adopt again, but my health deteriorated." (Patient DS338)

Additionally, some participants found profound meaning in their adoption experiences, with one individual expressing:

> "I don't even hate this disease because it got me, [adopted] daughter." (Patient DS315)

This sentiment highlights adoption's transformative power, offering comfort and meaning in the face of chronic illness. These quotes collectively portray adoption not only as a practical solution for building a family despite health challenges but also as a wellspring of deep joy and appreciation.

Surrogacy

While several women contemplated the idea of surrogacy, only a few ultimately chose to pursue this option. Those who decided against it expressed concerns about the commodification of children, legal complexities or unease with the idea. One participant said:

> "We didn't want to do surrogacy because it just doesn't sit well with me." (Patient DS338)

On the other hand, those who opted for surrogacy mentioned a sense of relief from potential risks and the fulfilment of their deep desire for parenthood. One participant shared their journey, revealing:

> "I always wanted to be a mum, but I wasn't going to be able to carry a child. So, we were lucky enough to do traditional surrogacy and had two children with the same lovely surrogate mum. That's been brilliant." (Patient DS304)

This highlights the diverse experiences and considerations surrounding surrogacy, from ethical qualms to the profound fulfilment it brings to individuals unable to carry pregnancy.

Ethical considerations and uncertainties in genetic decision making

Blameless guilt

Reproduction is a significant component of personal identity. Female patients with heritable PAH face increased reproductive risks, as pregnancy poses significant dangers for both the mother and the potential transmission of the disease to offspring. This can lead to feelings of guilt and blame, as captured in the following quote:

> "It was the guilt of, and it still is, it still is the guilt of … and I know it's not my fault and I know it's nothing that I could have prevented and I know I'm lucky to have had my child because obviously I was diagnosed when he was three and I wasn't allowed anymore." (Patient DS297)

Clinical teams are well aware of these emotional complexities and consider them when discussing genetic testing and relative screening with patients. They aim to address and mitigate these emotions by fostering open communication, providing education and showing empathy toward the patients' concerns.

Reservations surrounding embryo selection and prenatal diagnosis

Clinicians and some patients expressed reservations about recommending or choosing embryo selection, prenatal diagnosis or termination of pregnancy based on genetic results. These reservations were driven by moral concerns, the risk of miscarriage associated with prenatal testing and uncertainties regarding the penetrance of the genetic condition. This internal conflict is evident in one patient's quote:

> "There's a big bit of me that would say, "Don't select." But on the other side, could I bear to see a child of mine, because I'd be putting myself in her shoes, suffer like that? And I'm not sure that I can. So, in that sense, I would say, yes, do select. But then there's the moral side of it." (Patient DS338)

Additionally, the potential for future advancements in treatment was considered, leading to hesitations about making irreversible decisions based on current genetic information. One of the clinicians shared:

> "I struggle morally to suggest that that fetus that harbours a *BMPR2* mutation, you should recommend termination, particularly also when potentially the baby, 30 years down the line, develop a disease, we might well have a cure or at least good treatment." (Clinician DS305)

Several patients believed their daughters would choose embryo selection if they tested positive for the genetic mutation.

Posthumous sampling

We sought to explore stakeholders' perspectives regarding the expanded use of genomic testing across various stages of life. Clinicians in our study acknowledged that patients had provided consent for their samples to be utilised for research after their death. While all patients unanimously agreed to allow their blood samples to be used after their death, a majority of them also expressed willingness to donate other organs for research purposes upon their demise:

> "My body is going to research study research at [my hospital]. They can do anything to me, and I have actually declared and signed something." (Patient DS315)

Those who expressed hesitation admitted that they either had not given it much thought or were aware that their family members would be uncomfortable with it.

Similarly, the disclosure of the genetic results of a deceased person to their relatives, who may also be at risk of developing and passing down the disease, can present both moral and legal issues. These were succinctly summarised by one of the clinicians:

> "The seal of the confessional applies, and it's the same principle here. While you may possess critical information, nothing can often be done with it." (Clinician DS301)

Posthumous sampling and returning genetic results after death present similar ethical dilemmas. While the methods differ, the core conflict is the same: balancing respect for the deceased's autonomy with the potential to empower living relatives with knowledge that could impact their health.

Discussion

As genetic technology advances, understanding family dynamics is crucial [12, 13]. Studies highlight the social aspects, emphasising diverse family structures and shared activities shaping familial bonds. Recognising how families "display" their practices is vital for comprehending these relationships. Our interviews revealed participants viewing genetic research participation and attitudes toward knowledge advancement as part of family identity shared across generations. Genetic thinking permeates everyday family life, evident in discussions about family resemblances and inheritance. Genetic diagnoses strengthen familial bonds, fostering increased parental involvement and even roles for children as supporters and caregivers, enhancing familial resilience despite disease-related challenges.

Family planning considerations encompass various dimensions. First, challenges faced by women of childbearing age take precedence. Our analysis reveals that women diagnosed before starting a family often find the inability to have children more distressing than the diagnosis itself. They grapple with moral, ethical and legal dilemmas related to alternative family planning methods. Second, insights from parents with adult children shed further light on key aspects. The concept of autonomy was consistently emphasised by all participants with adult offspring. While opinions varied on genetic testing for their children, they unanimously stressed the importance of their children's autonomy in decision making regarding genetic testing and family planning.

There was a noticeable shift in normative expectations regarding "genetic reproductive responsibility" between parents and their adult children. Some mothers expressed concerns that their daughters, if carriers of risk mutations, might choose to refrain from having children or opt for pre-implantation diagnosis, a decision they considered "tragic". While these perspectives have not been extensively explored and involve individuals without direct disease experience, they could potentially have discriminatory effects on individuals and families living with diseases and disabilities [14]. Moreover, the first-hand experience of losing a child to the disease proved to alter attitudes toward abortion as a means to prevent the birth of potentially ill offspring.

Predictive DNA testing can determine if relatives have inherited the predisposition, and non-carriers can then be reassured that they do not carry the predisposition. At the same time, carriers can be assisted in making informed health decisions and possibly receive therapeutic and preventive interventions. However, knowledge about the increased risk of developing a hereditary disease may also have a profound psychological impact [15]. Studies suggest that the perceived importance of genetic risk fluctuates, becoming most prominent at key life stages [16]. This aligns with our study participants' experiences, as they carefully considered the timing of disclosing genetic information to their children.

In current clinical practice, genetic healthcare professionals typically rely on the proband to inform at-risk relatives about the genetic disease and the option of predictive DNA testing or clinical screening, often supported by a family letter provided by the professional [17–19]. However, only half of the at-risk relatives attend genetic counselling, indicating the approach's limited effectiveness [20, 21]. Barriers to informing at-risk relatives include family conflicts, the proband's reluctance to burden relatives and the complexity of genetic information. These barriers may hinder informed decision making about predictive DNA testing [22]. Our study identified two main groups regarding attitudes toward genetic testing of relatives: those actively advocating for testing and those assuming a gatekeeping role. Advocates of genetic testing demonstrated a strong understanding of genetics and were enthusiastic supporters of research overall. Their attitudes were proactive, driven by a sense of responsibility rather than guilt or fear. On the other hand, gatekeepers were influenced by factors such as a desire to protect children from the emotional burden of genetic risk awareness, feelings of guilt and limited family connections. Effective communication about the disease and genetic risk was facilitated by close family relationships, a sense of duty to others and support from healthcare practitioners. Conversely, barriers included a lack of understanding of the importance of sharing risk information with family members and feelings of guilt, anxiety, grief and blame, which is in keeping with published literature [23].

While there has been a notable improvement in patients' understanding of the genetic background of PAH over the last 16 years [24], going forward, geneticists and counsellors should focus on creating a supportive environment where patients and relatives can express feelings of guilt or blame, particularly in cases where genetic risk is passed down. This can be achieved by normalising these emotions and framing genetic testing not as deterministic, but rather as a probabilistic risk prediction tool, which offers an opportunity for preventive action rather than certainty of disease. Additionally, shifting the focus from individual health to the collective benefit, especially in a research setting, can help reduce the stigma associated with genetic diseases and foster more proactive attitudes. Finally, increasing disease awareness in the general population and among healthcare professionals, especially general practitioners, and

integrating genetic testing into routine clinical practice will enhance early detection and normalise its role in managing health, leading to improved outcomes.

The genetic research studies informing our interviews were closely integrated into routine NHS clinical care [2, 8]. While this facilitated rapid translation of genetic findings, it introduced complexity. In research settings, confidentiality agreements prohibit sharing information with third parties, but in clinical settings, healthcare professionals may feel a moral obligation to prevent harm to at-risk relatives [25, 26]. Nonetheless, breaching confidentiality, whether between healthcare professionals and patients or researchers and patients, is seen as harmful, outweighing potential benefits to at-risk relatives [7], although theoretical frameworks exist to cater to the needs of both patients and relatives [25].

Current recommendations, such as those from the American Medical Association [5] and the American Academy of Pediatrics [6], advise testing for actionable conditions, deferring to parental discretion for paediatric-onset conditions without effective interventions and postponing testing until adulthood for late-onset conditions lacking prevention or treatment. However, arguments for predictive testing of minors have gained traction, citing psychological benefits, positive impacts on family planning, the right to plan for the future, prevention of harm and the principle of autonomy. These arguments, as noted by Mand *et al.* [27], are empirically testable, emphasising the need for further research to establish guidelines in the predictive testing of minors. Similar ethical issues apply to consent for research involving underage offspring at risk of disease-causing variants [28].

It is important to note that while genetic screening and counselling for carriers of mutations in PAH risk genes are now widely available in the UK, evidence-based guidelines regarding the optimal timing, duration and intervals for clinical screening are lacking. Therefore, further studies are needed to inform the development of effective and cost-efficient best practices in this context [29].

This study delves into the rapidly evolving field of attitudes to genetic testing among patients and their families, focusing on its impact on family dynamics. Several important points warrant clarification. Previous research in this area was conducted shortly after the introduction of genetic testing for the *BMPR2* mutation, and primarily involved patients who were largely untested at the time of their interviews [24]. While these participants were enthusiastic about the idea of genetic testing, they often overstated their testing status, and the majority admitted to having limited knowledge about the genetic background of their disease. Furthermore, they reported minimal difficulty in deciding whether to undergo testing.

In contrast, our study, based on semi-structured interviews, allowed for a more in-depth exploration of these topics and specifically targeted patients and relatives who had already undergone genetic testing. Our findings demonstrated an improvement in self-reported knowledge and understanding of genetic testing, highlighting how increased genetic awareness and other factors influenced decision-making processes. Similar to earlier studies, many of our patients cited altruistic reasons for undergoing genetic testing, particularly for the benefit of their offspring [8, 30].

The attitudes toward genetic testing were shaped by multiple factors, which played a key role in decision making. While the RAPID-PAH study aimed to recruit both patients and relatives, who had undergone genetic testing, the number of relatives recruited was relatively small. Consequently, their attitudes were largely explored indirectly, through the probands. This has important implications. First, as was the case in the original genetic study [31] (from which the current sample was drawn), and in routine clinical practice, relatives were typically reached only through the probands. The gatekeeping role that probands assumed in involving their relatives in genetic research was also evident in this study. As a result, the relatives who participated in interviews were primarily those with probands who held an advocacy stance toward testing. Second, relatives with stronger familial ties to the proband were more likely to engage in the research, whereas those with weaker familial connections or no direct experience of the disease were less likely to participate. Finally, while parallels can be drawn with other works regarding participation in genetic testing [30, 32–34], it is important to emphasise that, in PAH, both genetic and environmental factors are likely to play a significant role in disease risk. The relatively low penetrance of the genetic mutations further complicates the picture, as it makes predicting who will develop the disease more challenging. This complexity underscores the need for a nuanced approach in both genetic counselling and risk communication, where potential outcomes and uncertainties are carefully discussed with patients and their families.

Conclusions

Our study highlights the significant impact of a PAH diagnosis on family dynamics. While genetic risk awareness can strengthen bonds, it also brings challenges such as disclosing information and deciding on

testing for at-risk relatives. We emphasise the importance of comprehensive genetic counselling and support systems to assist families. Addressing the medical and ethical dimensions of genetic testing is crucial for patient care and familial wellbeing in PAH.

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Data availability: Access to anonymised interview transcripts can be granted upon request, subject to ethical clearance. Please contact the corresponding author to discuss access and ethical considerations.

Ethics statement: The study was approved by the North of Scotland Research Ethics Service (REC: 22/NS/0127). All patients provided written informed consent before enrolment in the study.

Author contributions: E.M. Swietlik conceived the project, analysed the data and wrote the manuscript. M. Fay conducted the interviews and focus groups, and analysed the data. N.W. Morrell supervised the project.

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