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BMJ INVESTIGATION

Rare diseases: NHS labs fail to share data vital for diagnosis and care, *BMJ* finds

Three of England's seven NHS Genomics Laboratory Hubs say they lack the resources to implement key guidance on information sharing, despite good intentions. Experts and families say the delay could be prolonging uncertainty and delaying treatment for patients with rare diseases, **Jennifer Richardson** reports

Jennifer Richardson *investigations and senior features editor*

When Sophie Muir's middle son Calvin was born, "Everything seemed fine." But then, "He didn't babble like babies babble. He just didn't do it."

Muir then noticed hypotonia, and by age 2 years Calvin had been referred for speech and language therapy and was wearing glasses. "He was delayed walking, he was delayed with everything," she says now, "and everyone just kept saying, 'Don't worry, he'll catch up, it'll be okay.'"

By the time he went to school, "It was clear that cognitively he was behind in everything," yet NHS genetic test results for conditions such as Angelman and fragile X syndromes all came back negative.

What followed was a 10 year "diagnostic odyssey" of seeking answers for a wide range of symptoms that progressed to include drooling, uncontrolled movements, and cardiac symptoms.

Calvin's participation in two research studies eventually revealed to Muir that he had a variant in his *CACNA1C* gene, which encodes part of a calcium channel. This later led to a diagnosis, when he was 15, of a *CACNA1C* related disorder, an umbrella term that includes Timothy syndrome.

Calvin's variant had not been found through previous testing because it had been interpreted in the NHS laboratory as a variant of uncertain significance (VUS), meaning it is not known whether the variant is pathogenic.

VUSs may not be reported to patients, their families, or even their clinicians through routine NHS genetic testing and counselling, because everyone has many of them and most are unlikely to explain the patient's symptoms; our genomes each contain 4-5 million variants when compared with the human genome reference sequence.

However, NHS genetics laboratories should be submitting variants—and their interpretation—to publicly accessible databases. This ensures that the knowledge is shared, feeds into future research development and literature, and ultimately helps patients access diagnosis and care.

Now, *The BMJ* can reveal that some NHS genetics laboratories are failing to routinely make these vital variant submissions. They say they lack the necessary

staff and technology to do so but intend to implement the requirement as soon as possible.

Experts and families say that this failure can lead to prolonged uncertainty for patients suspected of having a rare genetic disease, as well as raising questions about the management and sharing of publicly generated patient data and knowledge in the NHS ([box 1](#)).

"For rare disease families like ours, shared variant data is often the difference between prolonged uncertainty and diagnostic clarity," says Muir, now chair of the charity the Timothy Syndrome Alliance.

Information sharing inconsistent, incomplete, or absent

England has seven NHS Genomics Laboratory Hubs (GLHs) that coordinate clinical genomics services in their region, including testing, diagnosis, treatment, and counselling ([box 2](#)).¹ They are contractually required to submit genetic variants to public databases, as set out in professional guidance provided by the Association for Clinical Genomic Science (ACGS).^{2,3}

The guidance also sets out why these submissions are vital. Prompt and accurate molecular diagnosis is crucial, it says, for targeting treatment and optimising patient care. It is therefore the "professional responsibility of the clinical genomics community to ensure data is shared" appropriately and responsibly.

Information provided by the seven GLHs earlier this year in response to freedom of information (FOI) requests by Muir shows that there is a gap between this professional requirement and the operational reality in the NHS.

The responses indicate that variant sharing is inconsistent, incomplete, and in some cases absent.

Three of the GLHs—South East, South West, and North East and Yorkshire—said they were not routinely submitting variants to the ClinVar public database. This is the database that since the 2024 ACGS guideline it has been mandatory for NHS genetics laboratories to submit variants to ([box 3](#)).²

One of these three GLHs said it did not have any members of staff with assigned responsibility for ClinVar submissions.

Only the four GLHs that were making routine submissions to ClinVar—North Thames, East, North West, and Central and South—had any operational internal policies, standard operating procedures, or governance documents relating to ClinVar submission.

Even those hubs that routinely submit variants to ClinVar have significant backlogs of unsubmitted variants and inconsistencies and gaps in what is submitted.

Muir says, “ClinVar functions as a shared clinical evidence base for variant interpretation. Inconsistent submission practices create structural blind spots, selectively limiting the evidence available for rare disease diagnosis, variant reclassification, and research.

“Where governance and monitoring are absent, non-submission is invisible, unaccountable, and self-perpetuating.”

She adds, “The downstream consequences affect . . . the entire rare disease ecosystem, where case numbers are small and every data point carries disproportionate weight.”

Reclassification and the broken loop

A growing global evidence base of variants can lead to reclassification, as happened in Calvin’s case. On ClinVar, Muir found another patient, based in France, with the same variant as Calvin—except in their case it had been interpreted as “likely pathogenic.” Calvin’s variant was finally reclassified as “likely pathogenic” when he was 15, six years after Muir first learnt of its existence and 10 since he joined the first research study.

Reclassification can in turn lead to diagnosis and access to treatment.

“If [the GLHs] submit patients to ClinVar, then that provides a bigger body of evidence that speeds up diagnosis for everyone,” says John Sayer, an expert in rare inherited kidney diseases. “Patients ultimately are missing out because this isn’t happening.”

“Putting variants into ClinVar opens up treatment possibilities for different groups of patients,” agrees Jack Underwood, a forensic psychiatry registrar who works with Muir on the Timothy Syndrome Alliance. “There is a loop that is broken by not submitting to ClinVar.”

A decade long study (2006 to 2016) published in *JAMA* showed that the classification of most cancer predisposition genes in a large commercial laboratory remained unchanged, and most of those that were reclassified were downgraded.⁴ This rate of reclassification might differ, for example, with the disease setting or type of VUS being reviewed.

Sayer, clinical professor of renal medicine at Newcastle University, has also conducted research analysing how long it takes for a variant to be upgraded or downgraded from VUS: typically between two and four years, he found. “That sounds a reasonable length of time—but if you imagine you’re a family and you’re desperate for that information to inform testing of other children or helping you get a treatment, two years is a really long time to wait.”

However, experts also point out that long diagnostic journeys are not necessarily due to system failure. Diagnoses may come after many years because of new discoveries and knowledge that wasn’t previously available. “Data sharing is an enabler and facilitator of the potential to give diagnoses to people,” says Helen Firth, consultant in clinical genetics and genomic medicine at Cambridge University Hospitals, “[but] even with the most advanced tests we’ve got it’s often not possible to make a diagnosis at the moment.”

Labs blame insufficient resource

GLHs pointed to insufficient resourcing against a backdrop of a lack of semi-automation for export to ClinVar as a reason for the absence of routine submission.

Experts tell *The BMJ* that ClinVar is clunky to use, contains “very mixed quality” data, and is “unaccommodating” to submissions. The ACGS guidance was updated in July 2026 and now names three public databases, including ClinVar, that GLHs should share variants to “as relevant” (box 3).³

Clare Turnbull, professor of cancer genetics at the Institute of Cancer Research in London, points out that the laboratories also have to submit data to NHS England and the National Disease Registration Service, among other places, so “there’s quite an onus on them to submit all these different types of data to different people.”

“The systems have become increasingly complex,” she adds, “so there are issues around designing your workflows, and how the data are extracted, and what is or isn’t in the data.

“The labs lack flexibility to do those things in efficient ways.”

Staffing was the issue most cited by the GLHs as the reason for delays in implementing routine submissions to ClinVar. Some hubs blamed the time taken to develop policies and also technology and infrastructure issues.

Those GLHs that had not yet implemented routine ClinVar submission said they planned to do so this year. Guys’ and St Thomas’ NHS Foundation Trust (for the South East hub) said, “ClinVar submission is on the priority projects list.”

Great Ormond Street Hospital for Children NHS Foundation Trust (North Thames) and Cambridge University Hospitals NHS Foundation Trust (East) said they had developed their own software to automate ClinVar submission.

Cambridge University Hospitals said it had submitted more than 2500 variants to ClinVar. “It’s been particularly rewarding to assist clinical laboratories from around the world that have reached out after seeing one of the variants that we have submitted,” it said in its FOI submission.

Manchester University NHS Foundation Trust (North West) said in its FOI response: “There are several valid operational and technical reasons why full submission is not yet in place. Despite these barriers, the NWGLH is now routinely submitting highly curated variants biweekly.”

Non-submission reflects wider NHS IT problems

Turnbull says GLHs’ delay in variant sharing is part of the wider issue of lagging NHS IT systems hobbling progress and innovation. “You’ve got these sort of practical on-the-ground issues of people using quite frustrating systems in frustrating circumstances with frustrating IT systems on a day to day basis in the NHS labs to try to classify these variants,” she tells *The BMJ*.

“That lack of IT systems and lack of manpower resources is part of the reason they are not ahead of the game in terms of submitting.”

NHS England tells *The BMJ* that it is putting in place a new “contract and performance framework” for the NHS Genomic Medicine Service, which includes the seven GLHs. This will include “assurance meetings . . . to monitor delivery.”

In response to *The BMJ*’s findings, an NHS England spokesperson says, “While it is right that genomic laboratories prioritise their resources on the delivery of core services, genomic variant databases

nevertheless play an important role in supporting this, and we have recently reiterated the requirement for all NHS genomic laboratories to ensure relevant guidance is followed.”

Experts and families have concerns about how the backlog of historically discovered variants will be dealt with even once routine GLH submission is in place.

In the meantime, says Muir, the delay is causing harm to patients with rare diseases and families like hers: “Some of these individuals can be supported better if they know, their families know about it, and you can get them into therapies.”

Calvin is now 18 and in a special educational college. “We don’t have time on our side,” says Muir. “Our families, our children, our researchers and clinicians, our patient advocacy organisations, and our life sciences need this data.”

Box 1: Should private information be shared to generate public good?

The contractual and professional obligation on the seven NHS Genomics Laboratory Hubs (GLHs) to share genetic variants in publicly accessible databases raises questions over the management and sharing of publicly generated patient data and knowledge in the NHS.

The BMJ understands that there was a historical governance concern about sharing variant information to the ClinVar database but that this was resolved and is not considered a reason for GLHs now not to be making submissions. Guidance from the Association for Clinical Genomic Science (ACGS) in 2024 states: “Submission of variants to ClinVar by NHS laboratories in England is now a requirement following completion of the information governance review process.”

The GLHs are generating clinically interpreted data in a publicly funded system, points out Sophie Muir, chair of the rare disease charity the Timothy Syndrome Alliance: “Public funds are going in to pay for genetic testing and then it’s not being shared. It’s not right.”

John Sayer, clinical professor of renal medicine at Newcastle University, agrees that variant sharing maximises the value of public investment in genetic testing. “No system’s perfect, but I think if people are not even submitting variant data into that database to allow the community to think about it, interact with it, and confirm or refute it, then the power of doing that sequencing in the first place is kind of lost.”

He suggests that GLHs could be required to report their variant submission rates, although he adds that submission shouldn’t need to be incentivised, because “it’s like a duty of care.”

“It’s privileged information, knowing someone’s genetics,” Sayer says, “and if they’ve consented to that being used for the greater good then you’re betraying a patient’s trust by not allowing that information to be shared.”

However, others question whether this is indeed what patients are consenting to. Helen Firth, consultant in clinical genetics and genomic medicine at Cambridge University Hospitals NHS Foundation Trust, says she promotes data sharing, including through her clinical leadership of another publicly accessible genomics database, Decipher (see [box 3](#)).

But, she adds: “There’s a difference between encouraging somebody to share [their data] with an understanding of why it’s useful and just assuming that their data should be shared openly, worldwide, because they had a test.”

Box 2: England’s seven Genomics Laboratory Hubs

Since 2018 genomic testing in the NHS in England has been delivered through a national testing network comprising seven Genomic Laboratory Hubs that each coordinate genetic testing in their region[1]:

- North East and Yorkshire (led by Newcastle upon Tyne Hospitals NHS Foundation Trust)
- North West (Manchester University NHS Foundation Trust)
- Central and South (Birmingham Women’s and Children’s NHS Foundation Trust)

- East (Cambridge University Hospitals NHS Foundation Trust)
- North Thames (Great Ormond Street Hospital for Children NHS Foundation Trust)
- South East (Guy’s and St Thomas’ NHS Foundation Trust)
- South West (North Bristol NHS Trust)

Box 3: Why ClinVar? The network of databases

The seven NHS Genomics Laboratory Hubs may share data on variants to databases other than ClinVar, which may be preferred by different clinicians for many different reasons, such as the level and type of detail available.

These include gnomAD and Decipher—which, for example, says cancer genetics professor Clare Turnbull, is “better annotated and linked into other repositories”—and other databases specific to certain clinical areas, such as CanVIG and CanVar-UK for cancer.

The BMJ’s investigation focused on ClinVar because it is the publicly accessible database that was named as the one to which NHS genetics laboratories should submit variants since the 2024 professional guideline from the Association for Clinical Genomic Science (ACGS).²

The FOI responses on which this article was based were submitted at the beginning of 2026, except for that from North West GLH, which responded in July. The ACGS guidance was updated in July 2026 and now adds CanVar-UK and Decipher, along with ClinVar, as the public databases to which the GLHs should share variants, “as relevant.”

This proliferation of different locations where information on variants can be shared is a problem, some experts say. “You’ve got a spread of data in different databases that aren’t talking to each other,” says Jack Underwood, a forensic psychiatry registrar.

ClinVar is the “broadest one,” says John Sayer, clinical professor of renal medicine at Newcastle University. It is also, in common with Decipher, globally accessible—the “default international one,” says Clare Turnbull, professor of cancer genetics at the [Institute of Cancer Research in London](#).

“Variant interpretation is only as good as the databases [you are] comparing it to,” Sayer says. “Globally everyone does look to ClinVar, and if it’s not being updated in a timely manner then it’s less useful.”

In the US a June 2026 statement from the American College of Medical Genetics and Genomics also underlined the importance of variant sharing and specifically named ClinVar.⁵

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