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Original Article

From Lived Experiences to Systemic Change: Patient Perspectives on the Diagnostic Journey of Loeys-Dietz Syndrome

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ABSTRACT

Background: Loeys-Dietz syndrome (LDS) is a rare genetic connective tissue disorder characterized by early-onset aortic aneurysms and dissections, making early diagnosis crucial for patients' survival. Due to its rarity and overlap with other conditions, LDS is often challenging to diagnose. This study explored the diagnostic experiences of Canadians with LDS to identify perceived barriers, supports, and patient-informed gaps for improving diagnosis and care.

Methods: In-depth semi-structured interviews were conducted with 9 adults across Canada who were the first in their family to receive a confirmed diagnosis of LDS. Transcripts were generated, reviewed for accuracy, de-identified, and analyzed thematically using an inductive approach with iterative coding and team-based consensus around themes.

Results: Five themes emerged: (i) patient role—individuals demonstrated self-advocacy and persistence; (ii) clinician role—clinicians acted as either catalysts or constraints; (iii) system role—healthcare was perceived as reactive and unequal, with limited consistency; (iv) impact of diagnosis—receiving a diagnosis of LDS brought clarity but also emotional challenges; and (v) patient-identified gaps—participants recognized challenges and emphasized enhanced education, proactive detection, ongoing support, and centralized care pathways to improve the diagnostic journey.

RÉSUMÉ

Contexte : Le syndrome de Loeys-Dietz (SLD) est une maladie génétique rare du tissu conjonctif caractérisée par des anévrismes et des dissections aortiques précoces, de sorte qu'un diagnostic rapide est crucial pour la survie des patients. Compte tenu de sa rareté et de son tableau clinique qui se recoupe avec celui d'autres troubles, le SLD est souvent difficile à diagnostiquer. Cette étude visait à évaluer l'expérience diagnostique de Canadiens atteints du SLD pour déterminer les obstacles, les services de soutien et les lacunes telles que perçues par les patients, afin d'améliorer le diagnostic et les soins.

Méthodologie : Neuf adultes canadiens qui étaient les premiers de leur famille à recevoir un diagnostic confirmé de SLD ont participé à des entretiens approfondis semi-structurés. La transcription des entretiens a été générée dans Microsoft Teams. L'exactitude des transcriptions a été vérifiée avant que celles-ci soient dépersonnalisées et analysées par thème, selon une approche inductive avec codage itératif, les thèmes ayant été sélectionnés de manière consensuelle par l'équipe.

Résultats : Cinq thèmes ont émergé : (1) le rôle du patient — les patients se sont montrés capables de défendre leurs intérêts et ont fait preuve de persévérance; (2) le rôle du clinicien — les cliniciens

Loeys-Dietz syndrome (LDS) is a rare autosomal dominant connective tissue disorder characterized by a high risk of aortic aneurysm, dissection, and multisystem involvement.[1] LDS is currently known to be associated with 6 genes—*TGFBR1*, *TGFBR2*, *SMAD3*, *TGFB2*, *TGFB3*, and *SMAD2*.[1] Hallmark features of LDS include hypertelorism, bifid uvula or cleft palate, and aortic/arterial aneurysms with tortuosity, though clinical presentation is highly variable.[1]

Keywords: qualitative research; patient advocacy; genetic testing; connective tissue diseases; aortic diseases; diagnosis; rare disease

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Conclusions: The timeliness and accuracy of LDS diagnosis are shaped by interactions among patient persistence, clinician awareness, and coordination, with delays driven by limited knowledge, fragmented care, and system barriers, despite the life-threatening risk involved. Patients identified gaps in clinician awareness, diagnostic pathways, psychosocial support, and care coordination. These findings emphasize cardiologists' central role in integrated multidisciplinary cardiology–genetics models to improve timely care and recognition of rare cardiovascular conditions.

ont soit facilité le processus soit nui au processus; (3) le rôle du système — les soins de santé ont été perçus comme réactifs et inégaux, et peu constants; (4) l'impact du diagnostic — recevoir un diagnostic de SLD a permis de clarifier la situation, mais s'est aussi accompagné de défis émotionnels; (5) lacunes perçues par le patient — les participants ont reconnu les défis et souligné la nécessité d'une meilleure information, d'un dépistage proactif, d'un suivi continu et d'un parcours de soins centralisé pour améliorer le processus diagnostique.

Conclusions : La rapidité et la précision du diagnostic de SLD dépendent d'une conjonction de facteurs, soit la persévérance des patients, la sensibilisation des cliniciens et la coordination, tandis que les retards de diagnostic sont dus à la limitation des connaissances, à la fragmentation des soins et aux obstacles imposés par le système, malgré le risque mortel que pose ce syndrome. Les patients ont reconnu des lacunes dans la sensibilisation des cliniciens, le processus diagnostique, le soutien psychosocial et la coordination des soins. Ces résultats mettent l'accent sur le rôle central des cardiologues dans les modèles de soins intégrés multidisciplinaires en cardiologie-génétique, pour offrir des soins en temps opportun et améliorer la reconnaissance des maladies cardiovasculaires rares.

Additional manifestations may involve skeletal, craniofacial, cutaneous, ocular, and allergic or inflammatory systems.[1] The true prevalence of LDS remains unknown and likely is underestimated.[2]

Definitive diagnosis of LDS requires molecular genetic testing to identify the causative variant.[3] Early diagnosis is crucial, as individuals with LDS have a significantly elevated risk for aortic dissections and aneurysms, compared to the general population.[3,4] Early interventions, including serial surveillance, medication, lifestyle modification, and prophylactic surgery, are key to decreasing morbidity and mortality.[3,4] Despite the importance of early diagnosis, identifying LDS remains challenging due to its broad phenotypic spectrum and clinical overlap with other connective tissue disorders, such as Marfan syndrome (MFS) and Ehlers-Danlos syndrome (EDS), which may lead to misdiagnosis or delayed diagnosis.[1-3,5,6] Although management guidelines exist for heritable aortopathies, specific diagnostic criteria for LDS remain comparatively underdeveloped.[3,5,7,8] Notably, approximately 75% of LDS cases involve *de novo* variants without a related family history,[5,9] further highlighting the importance of clinical awareness to support timely recognition and diagnosis.

These challenges are compounded by systematic barriers within the Canadian healthcare system. A 2023 report by the Canadian Organization for Rare Disorders (CORD) reported that rare disease patients in Canada face significant diagnostic challenges, including prolonged timelines, information gaps, barriers to genetic testing, and a lack of coordinated care.[10] Over 3 million Canadians live with rare diseases, often consulting multiple healthcare providers and waiting several years for a diagnosis.[10] Diagnostic delays frequently are driven by limited frontline clinician awareness and reliance on referral-based pathways, placing an added burden on patients to self-advocate.[10,11] For individuals with LDS, such delays may have particularly serious consequences, given the risk of life-threatening events.[3]

Given the critical importance of timely and accurate diagnosis, a better understanding of the diagnostic experiences of individuals with LDS is needed. Although diagnostic delays in rare diseases have been studied broadly, no studies to date have specifically examined how individuals with LDS in Canada experience the diagnostic process. Patient perspectives are essential, as lived experiences can illuminate gaps in care, reveal system-level barriers, and highlight the active role patients play in navigating fragmented healthcare systems.[10,12] This qualitative study aims to explore the diagnostic experiences of individuals with LDS in Canada and how their perspectives can inform improvements in care.

Methods

Study design

This retrospective, phenomological study used semi-structured interviews to capture participants' past experiences. An interpretivist paradigm was employed throughout, focusing on understanding the lived experiences of LDS patients through the meanings they assign to their experiences.[13] The Consolidated Criteria for Reporting Qualitative Studies were followed (Supplemental Appendix S1).[14] The study protocol was approved by the University of Toronto Research Ethics Board (#00046866).

Sample and recruitment

Eligible for inclusion were English-speaking participants with a recently confirmed molecular diagnosis of LDS ($\leq$ 5 years) within Canada, and no known family history of LDS at the time of diagnosis. Posters linking to a screening survey were distributed via the Loeys-Dietz Syndrome Foundation Canada (LDSFC) network. Study data from the screening survey were collected and managed using REDCap electronic data capture tools hosted at the University of Toronto.[15,16] Further recruitment was conducted

at the University Health Network in Toronto, Ontario, Canada, as posters were placed in genetics, cardiac, and vascular clinics. Interested individuals completed a brief survey, providing contact information, demographic details, and responses to questions regarding inclusion criteria. All eligible participants were contacted via e-mail to schedule an interview.

Data collection

The interview guide (Supplemental Appendix S2) was informed by the CORD report "Experiences of Rare Disease Patients"[10] (with permission from Ipsos and CORD) and adapted to the LDS diagnostic context and study objectives. The guide included questions addressing diagnostic pathways, healthcare interactions, system navigation, and perceived impacts across life domains. The interview guide was reviewed by the research team and refined for clarity and relevance prior to data collection. Interviews were conducted via Microsoft Teams (Redmond, WA) between November 2024 and April 2025. Each session was recorded and transcribed through the platform. Transcripts were reviewed for accuracy, edited, and de-identified by S.A.1 (Sally Al-Mufty). To preserve participant anonymity, unique study identifiers (eg, ID1) were assigned. Informed consent was obtained prior to conducting interviews.

Data analysis

Data were analyzed thematically, employing an inductive approach, highlighting participant insights, attitudes, and lived experiences.[17] First, 2 study authors (S.A.1 and L.P.) independently coded 2 transcripts in duplicate in a nonrestricted manner. Together with a third author (M.P.M.), preliminary coding was discussed, with conflicts resolved and a codebook devised (Supplemental Appendix S3). Two further interviews were coded in duplicate by S.A.1 and L.P. to ensure consistency in coding. Finally, S.A.1 independently coded the remaining 5 interviews using Dedoose (Sociocultural Research Consultants, LLC, www.dedoose.com). Throughout the process, S.A.1, M.P.M., and L.P. periodically met to discuss emerging themes. Based on the grouping of codes, the study team arrived at higher-level themes. Finally, transcripts were re-read to verify concordance with the data and choose illustrative quotations, which are presented below.

Results

Nine individuals participated in this study, with demographic and clinical characteristics summarized in Table 1. Participants were drawn from 4 provinces, with most residing in Ontario (67%), and with diagnoses made across multiple clinical centres; 2 individuals received care at the same site. Given the rarity of LDS and the targeted inclusion criteria, the sample size was determined by participant response to recruitment invitations. Despite these constraints, interviews yielded rich, in-depth data that enabled identification of consistent patterns across participants and were sufficient to address the study objectives. Later interviews largely reinforced previously identified themes, indicating a degree of thematic convergence.

Table 1. Participant demographics (n = 9)

Characteristic	Value
Age, Y	
Mean	43
Range	31–73
Gender	
Male	5 (56)
Female	3 (33)
Non-binary	1 (11)
Racial/ethnic group	
White	7 (78)
South Asian	1 (11)
Mixed—Indigenous and White	1 (11)
Province of residence (also of diagnosis)	
Ontario	6 (67)
British Columbia	1 (11)
Quebec	1 (11)
New Brunswick	1 (11)
Education level	
College/university graduate	7 (78)
Some college/university	1 (11)
Postgraduate	1 (11)
Year of diagnosis	
2019	2 (22)
2021	1 (11)
2022	2 (22)
2023	1 (11)
2024	1 (11)
2025	2 (22)
LDS subtype	
LDS1 (*TGFBR1*)	2 (22)
LDS2 (*TGFBR2*)	1 (11)
LDS3 (*SMAD3*)	4 (44)
LDS4 (*TGFB2*)	1 (11)
LDS5 (*TGFB3*)	1 (11)
History of acute aortic syndrome (aortic dissection) exposure	
Personal history	2 (22)
Family history	2 (22)
None	5 (56)

Values are n (%), unless otherwise indicated. LDS, Loeys-Dietz syndrome.

The findings are organized into 5 interrelated themes that describe how interviewees experienced and made sense of their diagnostic journeys with LDS. Participants portrayed diagnosis not as a single event, but as an evolving process shaped by patient actions, clinician involvement, and healthcare system structures. Collectively, the themes trace how diagnosis often initiated an ongoing effort to interpret symptoms, identity, and future care needs.

The role of the patient: navigating crisis, persistence, and chance

Acting as seeker and self-advocate. Interviewees described navigating a prolonged and challenging path to diagnosis, often taking on dual roles as seekers and self-advocates. For many, the process began not with clinical recognition, but with a personal sense of concern: "I wasn't gonna leave the emergency room until they told me what was wrong" (ID1). This effort was often felt to be dismissed by healthcare professionals (HCPs)—"I've been fighting . . . just years of pushback" (ID7)—or deprioritized: "I had to advocate for myself because they have thousands and thousands of

patients, and I'm just a number in the line waiting for that MRI [magnetic resonance imaging]." (ID9)

Diagnosis sometimes occurred only because the participant, or someone close to them, took proactive steps. One participant recounted recognizing symptoms and seeking care: "I essentially self-diagnosed myself . . . put myself on a cardiac monitor . . . checked myself into the ER" (ID3). In some cases, personal connections expedited the process: "My dad's a doctor . . . he sent my echo [echocardiogram] to his surgeon . . . I'd still be waiting if I had been alone" (ID6).

Several interviewees turned to online resources, tracked symptoms, and attempted to explore family history to interpret their condition. One noted, "I linked the ASD [atrial septum defect] and my arm condition . . . looked it up and found they could be genetic" (ID5). Despite these efforts, the process often felt isolating and emotionally taxing. One participant described it as "quite a lonely journey" (ID5), and another recalled feeling dismissed: "I've had a really hard time with our medical system . . . constantly gaslit, told I was too young . . . that it was just my period" (ID7).

Responding to an unexpected pathway to diagnosis. Not all interviewees sought a diagnosis themselves. Although for some interviewees, the process was initiated by a clinician, their own role quickly became active. Once they learned of the potential for a genetic condition, a sense of urgency set in, making the implications of testing feel immediate:

> *We had to let him [my father] go…the cardiac surgeon said with his brother's dissection and me being tall, we should do genetic testing…Having gone through two personal tragedies, it was like—I need to know. (ID2)*

Interviewees quickly thought of family members (eg, children) in response to implications of a potential genetic condition after a lack of suspicion before diagnosis:

> *My father having an aneurysm at 29 . . . and his brother had a dissection . . . they started monitoring me and my sister when we were really young . . . My cardiologist, same one I've had for 30 years, said it might be time we do a genetic screen after I already have four children . . . and the way he treated me my whole life, I fully expected it to be negative. (ID8)*

The role of the clinician: catalysts and constraints

Clinicians as catalysts. Interviewees described clinicians as crucial in advancing the diagnostic process when they were attentive, proactive, and open to possibilities. Clinicians acted as catalysts when they were thorough and responsive, whether or not they had specific expertise in LDS. One participant valued their general practitioner's willingness to make referrals despite limited specialty knowledge: "Anytime I want a referral for anything, she's great for that" (ID7). Another shared gratitude to the emergency doctors for covering all bases:

> *I interacted with the emerge (sic) docs. They did the standard cardiac work up . . . and they didn't find anything . . . but it was the echocardiogram that thankfully they sent me for . . . that's what found the aneurysm . . . then it was another four months before I received the diagnosis of LDS, and that was fairly quick. (ID3)*

Cardiac specialists were frequently credited as the first to raise suspicion of an underlying and unifying issue. Their recognition of unusual findings, such as atypical imaging or relevant family history, often prompted genetic referrals. One interviewee described their cardiologist as "phenomenal" (ID8) for their knowledge, and another noted the specialist's curiosity about an aneurysm at a young age as a key factor in pursuing further investigation (ID3). Interviewees valued these clinicians' instincts, attention to detail, and sense of urgency:

> *My daughter at that point was being checked out for EDS . . . they began to put two and two together . . . and my cardiac surgeon set me up with the genetic counsellor . . . and was proceeding on the assumption that there was something that I had going on in addition to just normal heart failure . . . he took me seriously. (ID4)*

Genetics specialists were valued for their thoroughness and support in navigating the healthcare system. One participant noted that their medical geneticist, despite initially diagnosing hypermobility EDS, was "astute enough to determine that it could be LDS" (ID3) and arranged genetic testing. Another (ID5) praised their genetic counsellor for clearly explaining "how the system has been put in place… and how to navigate it," adding that they were "very impressed" by the guidance.

Interviewees emphasized how meaningful the experience of coordinated care was, especially when clinicians kept each other informed and worked as a team:

> *My thoracic surgeon was the one that was doing the intermediate between the two programs [Northern Ontario and Toronto]. I had answers so that was a big relief . . . The communication between the doctors was great. There was always a fax or a note." (ID9)*

Clinicians as constraints. Although some clinicians facilitated diagnosis, others delayed it by dismissing symptoms or neglecting follow-up, leaving patients feeling invalidated and forced to take action themselves. One interviewee discovered their aortic aneurysm only after independently reviewing medical records: "I wasn't told . . . I've been walking around with an aortic aneurysm" (ID6). Another found out about their LDS diagnosis through a self-requested file, as they felt there was inadequate follow-up: "I never had an actual consultation where [the geneticist] explained to me what LDS was" (ID5). Similarly, one interviewee learned only recently that a physiatrist had suspected a connective tissue disease years earlier: "I didn't even know they had actually considered that until I was reading my medical file yesterday . . . I had a big aortic root, but was still treated like a normal person" (ID8).

Beyond clinical oversights, some interviewees described feeling "uncomfortable" (ID9) with how certain clinicians communicated or handled their concerns:

> *Previously I went to my vascular doctor at [center] because I had very bad varicose veins. I mentioned the tortuous veins [likely referring to arteries] and he just dismissed it. I was a bit miffed . . . I think tortuous veins are part of the LDS profile (ID4).*

Several interviewees emphasized that these delays carried consequences, sometimes impacting treatment decisions and outcomes. One participant noted that their atrial septum defect was very large and had already caused damage to their heart (ID5).

"If I would have known I had LDS, I might have waited to do the hysterectomy . . . some of the adverse reactions I'm having, like the neuropathy in the foot, could have been avoided if the practitioner took me seriously. (ID7)

The role of the system: reactive and unequal

The system as reactive, not proactive. Interviewees frequently described the healthcare system as reactive, addressing issues only after symptoms escalated or complications occurred. Many were taken seriously only after a critical event: "When the echocardiogram found the aortic root aneurysm . . . that was the beginning of my journey" (ID3). Others described living for decades with overlooked symptoms: "I've had a lot of the physical presentations like scoliosis, flat feet. I have like bad chronic pain. I don't think I've had a pain free day in like 25 years." (ID2)

Every time I've had to go into hospital, 'you know oh well you'll be here for five days' well I'm here for 10 days . . . all my life I've had symptoms of LDS now that I know more about it. Just nobody recognized it." (ID4)

Barriers to timely care often stemmed from systemic issues, such as long wait times and referral backlogs, leaving patients in limbo: "I contacted a geneticist . . . it was going to be a year and a half to two years . . . I just said forget it. Because I didn't know [I had LDS] right?" (ID3). Even when care was available, it was fragmented, with specialists working independently:

I kept saying that it's all interconnected, but people [clinicians] aren't looking at me as a holistic thing. You keep sending me to specialists for different things . . . I feel like Pokémon—like I collect all these specialists and they don't always intermingle with each other. (ID7)

Care influenced by location and access. Interviewees described stark differences in care based on location and available services. Those in urban centres with robust infrastructure benefited from streamlined referrals, co-located specialists, multidisciplinary teams, and shorter wait times:

They had an occupational therapist, a pain specialist, they've got a few cardiologists. They had a few genetic counsellors . . . We had a case worker at the hospital . . . she really helped with everything. She didn't have every answer, but she got every answer for us. (ID2)

It does help that her [cardiologist] and the genetic counsellor work together and in the same building. (ID1)

In contrast, those in smaller communities faced delays due to limited services and an overburdened system:

They told me I had a dissected aorta and so then we drove 8 hours to Winnipeg to go and see the doctor there. (ID9)

A lot of the people from my [old, rural] area might also have something similar and they might never know . . . moving to the city has removed a few of these barriers. (ID7)

LDS diagnosis: more than a label

For most interviewees, an LDS diagnosis was a turning point, bringing clarity and recontextualizing previously dismissed symptoms. For many, what once seemed like coincidence now made sense: "I've always thought it was connected to something bigger . . . It's nice to know I was right" (ID7). The diagnosis often offered comfort and answers: "It is kind of a relief to know there's a reason why these things are happening" (ID4). One interviewee noted that the diagnosis explained lingering medical issues: "They still didn't know why I had a dissected aorta or the aneurysms, but this LDS answers those questions" (ID9).

On the other hand, some interviewees described a sense of identity loss, especially when LDS forced changes in social functioning, leading to significant lifestyle changes following their diagnosis. As one interviewee noted, "I walked into that [diagnosis] meeting feeling like a very healthy person and walked out of it like I've always had Loeys-Dietz" (ID6).

My own identity was formed towards pushing my own boundaries physically . . . now I sort of cannot enjoy that part of my identity, and I think I'm still mourning that. (ID5)

When she found out what I did for a living, [the geneticist] said, that might not be something that . . . you should continue doing . . . it was a pretty difficult time (ID3)

Interviewees also described stepping into protective roles, trying to ensure their relatives would not go through the same diagnostic delays:

I immediately said to my geneticist . . . what about [my daughter] because she was five or six months pregnant at that time. (ID3)

Our conversations are now turning to the young kids . . . there are severe expressions of LDS that can affect children and teenagers much earlier than what has affected us. (ID6)

Some also spoke about the intergenerational emotional weight of passing on a genetic condition. One interviewee noted that it was "a concern from day one" in terms of family planning (ID2). "For dad, I think it's been difficult . . . he feels the pain it's causing me . . . and then I feel the same way. I passed it to some of my children." (ID8)

Mental health and emotional well-being were woven throughout these reflections. Some interviewees described grief or trauma: "The 'what-ifs' were exceptionally hard to take . . . dealing with the knowledge that I probably would've dropped by 45 . . . that was very difficult to grapple with." (ID6)

For many, diagnosis sparked a motivation to help others. Some became educators and advocates: "I just started working with an aortic dissection collaborative" (ID2) and "If any patients come through here [genetics clinic] that want to talk . . . please give them my number." Engaging in online groups also provided a therapeutic outlet: "It was very cathartic . . . I found myself trying to help others" (ID3).

Recognizing the challenge, demanding the change

Recognizing the challenge. Interviewees acknowledged that LDS remains largely invisible in medical training. One noted, "It wouldn't have even been on anyone's radar until the last 20 years" (ID8). Many reported that most healthcare providers they encountered had little to no familiarity with LDS:

The majority of doctors that I meet have never heard of it (ID4).

My father-in-law who was a family doctor for 38 years said he had never heard of LDS. (ID6)

There tends to be a lack of awareness with some doctors around diseases that are rare or not well-known . . . despite even people's requests for such. (ID3)

Interviewees recognized LDS as a rare condition but questioned whether it is "underdiagnosed," noting that it "doesn't express in very visible ways" (ID1), or is "misdiagnosed as MFS [Marfan syndrome] or EDS" (ID7).

They noted gaps in LDS research, such as the risks of physical activity—"there is not enough good information on risks in sports" (ID5)—and the variability in disease severity—"why some people have a really terrible expression . . . and why some people . . . get it off scot-free (sic)" (ID6).

Demanding the change

Interviewees emphasized the need for greater clinician training and broader awareness to improve recognition and care for LDS. They recommended education initiatives, noting that "a practitioner that's well versed in this is needed, even if they could do like online training for folks that are curious" (ID7), and stressed that "education is certainly a big part of this" (ID3).

Interviewees described the integration of screening approaches, including genetic testing, digital tools, and public health initiatives, as central to proactive detection. As one explained, "if Canadians as a whole were broadly screened . . . it could be taken into account from an earlier age" (ID1). Another noted that "if there was just a way to put in all of my symptoms . . . that will reduce so much strain off (sic) the healthcare system" (ID2). A third emphasized, "If there's something so obviously genetic, like two brothers with the same disease, then maybe pursuing genetic testing sooner would be smart" (ID8).

Interviewees emphasized the need for comprehensive post-diagnostic support delivered through centralized systems that integrate mental health services, patient advocacy, care navigation, and community resources. They pointed to gaps in guidance and counselling, sharing, "If I have to go in for surgery . . . if there was somebody we could just call and say, hey, is there anything the surgeon should be aware of?" (ID4) and "A lot of the government-run [mental health] clinics are six months to a year . . . or they don't access after 30" (ID7). Online communities were also viewed as valuable sources of connection when moderated for accuracy: "Facebook could be utilized to create a really accessible way for people to reach others . . . but there could be moderators with knowledge" (ID8).

At the same time, interviewees called for broader structural reforms to unify fragmented services into coordinated, multidisciplinary hubs. They expressed frustration with the burden on patients to navigate multiple organizations:

"We're expecting a lot from the public . . . to decipher all these different organizations that can help . . . We don't have a centralized system. I wish Canada, or even provincially, could just get behind one group." (ID2)

One envisioned collaborative models to bring research and clinical care together: "All researchers should be intercommunicating . . . so that we're all looking for the common goal" and "I would love for LDS to have their own clinic . . . a hub that people are able to access" (ID7). Ultimately, they rejected the idea that action should come only after crisis, stressing: "Tragedy should not be the prerequisite for an LDS diagnosis" (ID2).

Discussion

We report here a qualitative study exploring the diagnostic journey of LDS patients in Canada, highlighting perceived supports, barriers, and areas for improvement. As the first of its kind in this population, the study shows that although patients recognize the need for timely diagnosis and intervention, the system does not consistently meet this need.

An LDS diagnosis represents more than a medical label. Participants described diagnosis as validating previously unexplained symptoms while introducing challenges including identity disruption, mental health impacts, and intergenerational concerns. These experiences align with existing rare disease literature showing that diagnosis can both reduce uncertainty and introduce new psychosocial burdens.[10]

Diagnostic pathways were influenced by the interplay of patients, clinicians, and the healthcare system, each acting at times as a facilitator, and at other times as a hindrance. First, patients frequently played a proactive role in their own diagnostic process. As in reports in other rare disease populations,[10,11] participants described navigating fragmented systems and persisting despite encountering dismissive attitudes. Self-advocacy could accelerate recognition and testing; however, difficulty articulating symptoms, repeated invalidation, and self-doubt delayed progress. These findings emphasize that LDS patients carry a burden in driving their diagnostic journey, reflecting both resilience and vulnerability.

Clinicians were central in either advancing or deterring diagnostic pathways. Several participants noted that the curiosity and suspicion of their specialist (eg, cardiologist) led to timely genetic testing, echoing literature showing the positive role of clinician awareness in rare disease recognition.[12] In contrast, lack of familiarity with LDS, limited genetic training, and dismissive encounters compounded delays. Participants reported repeated misdiagnoses and inappropriate management, similar to findings reported across other rare conditions, with clinicians minimizing concerns or lacking knowledge.[10-12] Despite growth in genomic medicine, many clinicians remain underprepared to identify or manage rare genetic conditions such as LDS, leading to symptom misinterpretation and delayed interventions.

At the health system level, access to multidisciplinary and well-coordinated care was a key support for participants, reinforcing findings from broader rare disease literature.[2] Those who received coordinated care, most often through urban healthcare centres, reported having greater confidence in their diagnosis and management, as collaboration among specialties such as cardiology and genetics streamlined the diagnostic process and reduced patient burden. This finding aligns with existing literature and current American Heart Association (AHA) and Canadian Journal of Cardiology (CJC) guidance emphasizing the importance of multidisciplinary approaches to aortic diseases such as LDS.[2,7,8] Geography also influenced access to care, with prior studies documenting barriers in rural regions, including long travel distances, a limited workforce, and reduced awareness.[18] Consistent with these findings, participants in urban areas reported having more reliable access to multidisciplinary

teams, whereas those in rural communities experienced delayed referrals, limited expertise, and a lack of specialized clinics. These disparities often forced patients to navigate fragmented systems independently, with the absence of centralized care contributing to information loss among clinicians and unclear diagnostic pathways.

Peer support networks and rare disease organizations also played a vital role, helping participants feel less isolated and more empowered in managing their health. Online communities and advocacy groups provided practical advice and emotional connection, fostering community and resilience among those living with LDS. In the Canadian context, the LDSFC has been instrumental in building such peer networks and promoting awareness, advocacy, and education for affected families.[19] These findings align with studies of other connective tissue disorders showing that online support groups provide medical information, emotional support, daily living strategies, and a sense of belonging.[20]

The Central Illustration in this study shows how the LDS diagnostic journey ultimately extends beyond naming the condition, and is shaped by the interconnected roles of key players, including patients, clinicians, and the system. This model highlights the value of integrating patient perspectives to enhance healthcare, potentially offering a framework that is applicable to other rare diseases.

This study highlights the significant consequences of delayed diagnosis in LDS. Prolonged diagnostic timelines were perceived to heighten the risk of complications, such as scoliosis, chronic pain, large atrial septum defect, neuropathy, and aortic dissection. Beyond medical risks, the diagnostic process carried a profound emotional toll for interviewees—particularly, feelings of helplessness, frustration, and isolation—reflecting the burden of repeatedly advocating for themselves in the face of clinical uncertainty. This finding aligns with the broader rare disease literature, which shows that prolonged searches for diagnosis erode patient confidence, contribute to mental health strain, and reduce quality of life.[11,12]

Patient-identified gaps in LDS diagnosis and care

Participants entered the diagnostic process through different initial circumstances, including, for some, personal or family experiences of acute aortic syndrome, and for others, the absence of such events but the presence of persistent or unexplained symptoms. Although these differing entry points influenced perceptions of urgency, participants across groups described similar challenges navigating the diagnosis process. Participants with prior personal or family histories of acute aortic events often reflected that diagnosis should have occurred earlier given the known risk, whereas those without such histories emphasized the prolonged effort required to have their symptoms be taken seriously. Despite these differing perspectives, both groups converged on a shared view that diagnosis should not depend on crisis or extraordinary persistence. This convergence suggests that interventions aimed at improving LDS care should focus less on how patients enter the diagnostic pathway and more on reducing systemic barriers that delay diagnosis across presentations, whether driven by acute events, family history, or ongoing symptoms.

Across interviews, participants described a range of challenges encountered throughout their diagnostic journeys. Although these experiences were captured within several themes, including patient self-advocacy, clinician interactions, and healthcare system structures, they collectively highlighted recurring areas in which recognition, support, and coordination were limited. Drawing on these cross-cutting insights across our thematic findings, the gaps described by participants were grouped into 4 overarching domains, as follows: clinician knowledge and awareness; diagnostic recognition and pathways; psychosocial support;

Table 2. Synthesis of cross-cutting patient-identified gaps in the Loeys-Dietz syndrome (LDS) diagnostic journey, and potential strategies to address them

Domain of need	Key patient-identified gaps	Potential strategies
1. Clinical knowledge and awareness	• Limited familiarity with LDS among general and nonspecialist clinicians • Delays in recognition of rare genetic conditions • Gaps in training related to genetics, inherited aortopathies, and connective tissue disorders	• Integrate genetics education more broadly within clinical training programs • Expand continuing education on recognition of rare genetic diseases • Develop clinical decision-support tools to help clinicians identify potential genetic aortopathies and initiate appropriate referrals
2. Diagnostic recognition and pathways	• Delayed diagnosis in the absence of acute events or clear family history • Inconsistent documentation and consideration of family history and symptom patterns • Fragmented diagnostic pathways across specialties	• Implement standardized approaches to documenting and flagging family history • Establish clearer referral pathways for suspected genetic aortopathies • Integrate genetic consultation within cardiac and aortopathy care
3. Psychosocial support	• Lack of guidance for navigating lifestyle changes and long-term uncertainty • Limited access to mental health and emotional support following diagnosis • Reliance on informal or peer-led support networks	• Integrate psychosocial services within multidisciplinary aortopathy or cardiogenetics programs • Expand access to structured peer-support and patient education services
4. System-level coordination	• Fragmentation among specialties involved in LDS care • Challenges accessing coordinated or multidisciplinary services • Burden placed on patients to navigate complex healthcare systems	• Strengthen coordination through multidisciplinary clinics and regional expertise networks • Support centralized registries (eg, CAN-ACT) for care coordination and research

CAN-ACT, Canadian Aortopathy and Connective Tissue Disorders Registry.

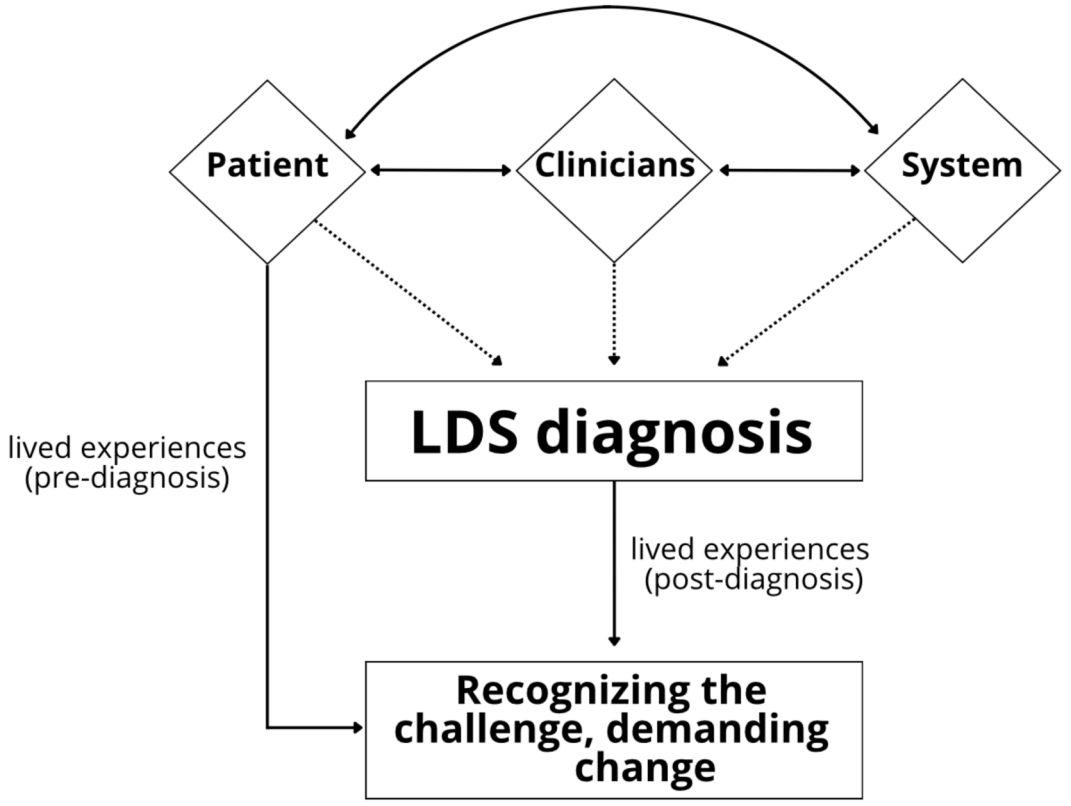
and system-level coordination of care. Table 2 summarizes these domains and outlines potential strategies that may help address them.

Overall, patient-identified gaps align with challenges described more broadly in the rare disease, aortopathy, and cardiogenetics literature. Prior work highlights limited clinician awareness of rare conditions and the need for improved genetics literacy across general and specialty care settings.[21,22] Participants'emphasis on diagnostic uncertainty, psychosocial burden, and fragmented care similarly reflects concerns raised in studies of other rare genetic conditions, including the importance of access to psychosocial supports and of coordinated, multidisciplinary models of care.[7,8,10-12] Recent Canadian Cardiovascular Society guidance on cardiogenetic testing also identifies system-level challenges related to education, care coordination, and access to specialized expertise, reinforcing the relevance of these patient-identified needs within the current Canadian healthcare context.[22]

In Canada, related efforts to strengthen coordination and longitudinal monitoring for genetic aortopathies are underway through national initiatives such as the Canadian Aortopathy and Connective Tissue Disorders Registry (CAN-ACT),[23] which provides a centralized framework to support care coordination and research for heritable aortic conditions. In parallel, the Canadian Cardiovascular Society emphasizes health-system planning approaches, such as establishing regional cardiogenetics expertise networks and strengthening provider genetics literacy, along with outlining delivery models that connect local clinicians with specialized expertise, including multidisciplinary clinics and "hub-and-spoke" frameworks to support equitable access across geographic settings.[22] Complementing these system-level initiatives, organizations such as the LDSFC work to advance national coordination across research, clinical care, and patient communities by supporting initiatives including CAN-ACT, funding research, and developing educational and community resources for individuals and families affected by LDS.[19]

Limitations and future directions

The self-selection sampling method used here may have biased the sample toward individuals who are proactive in seeking care and engaged in advocacy, potentially excluding those with fewer resources, limited access, or less capacity to self-advocate. Relatedly, although it is sufficient and consistent with similar qualitative research in rare disease, the small sample size may impact the representativeness of the findings. Future research with larger and even more diverse samples, recruited through registries or healthcare networks rather than self-selection alone, would help strengthen transferability and prioritize outreach strategies that engage harder-



Central Illustration. Conceptual pathways shaping the Loeys-Dietz syndrome (LDS) diagnostic process. Patients, clinicians, and the healthcare system continuously influence one another throughout the diagnostic journey (**bidirectional arrows**). Factors arising from patient lived experiences, clinician practices, and healthcare system structures shape progress toward an LDS diagnosis (**dotted arrows**), either facilitating or constraining whether and how a diagnosis is achieved. An LDS diagnosis itself creates new lived experiences, requiring ongoing medical management, psychosocial adjustment, and acknowledgment of hereditary risk. Both the patient and the diagnosis inform the recognition of challenges, which in turn drive calls for systemic change.

to-reach populations. In addition, no *de novo* cases of LDS were represented in the sample, omitting the perspectives of patients whose lack of family history may shape a distinct diagnostic trajectory. Targeted recruitment of such cases would offer valuable insights into how diagnosis unfolds when family history does not serve as a prompt. All participants were also English-speaking, meaning the experiences of non-English speakers were not captured, which likely underrepresents individuals who face additional barriers related to language and healthcare access in Canada. As well, by focusing solely on adults, this study does not capture how the LDS diagnostic journey unfolds in pediatric settings; future research including pediatric patients would provide a more complete understanding of the diagnostic trajectory across the lifespan.

Beyond broadening representation, this study examined diagnostic pathways and the perceived impacts of the diagnostic journey across life domains. Because the interview guide (adapted from the CORD rare disease framework) emphasized experiences leading up to and around diagnosis, we did not explore the longer-term postdiagnosis impacts of living with LDS, including how outcomes may unfold over time as a result of participants' diagnostic journeys (eg, sustained vocational, functional, or lifestyle changes). Future postdiagnosis focused or longitudinal qualitative studies could better characterize longer-term adaptation and evolving patient priorities. Comparative studies involving LDS and other connective tissue disorders could also clarify which challenges are shared vs condition-specific, and support examination of the transferability of the patient-clinician-system framework (Central Illustration).

Future work should evaluate how the patient-identified gaps highlighted in this study (Table 2) can be addressed in real-world settings, using implementation-focused designs that assess feasibility, acceptability, and potential unintended consequences. Building on the domains outlined in Table 2, future research could examine the potential strategies to strengthen clinician knowledge and diagnostic recognition, improve psychosocial and postdiagnosis support, and evaluate system-level approaches to enhance coordination and continuity of care.

Conclusion

This study provides the first examination of the diagnostic journey for patients with LDS in Canada, illustrating how patient persistence, clinician initiative, and system coordination supported diagnosis, whereas limited clinician awareness, fragmented care, and delayed recognition posed significant barriers. Given the potentially life-threatening nature of LDS, diagnostic delays may prolong exposure to preventable risk and delay access to appropriate surveillance and management.

Patients identified gaps across 4 interconnected domains: clinician knowledge and awareness, diagnostic recognition and pathways, psychosocial support, and system-level coordination. An important point to note is that cardiologists were consistently identified as central to diagnosis, referral, and care coordination, emphasizing their critical role within a multidisciplinary model that integrates cardiology and clinical genetics. These patient-identified priorities align with broader Canadian efforts to strengthen cardiogenetics expertise and collaborative care pathways for genetic aortopathies.

Together, these findings highlight the need for increased clinician awareness of LDS and more formalized multidisciplinary diagnostic pathways. By centring patient voices, this study provides a patient-informed framework to guide future research and health system planning aimed at improving timely diagnosis and coordinated care for rare genetic cardiovascular conditions.

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Data Availability

Due to the sensitive nature of the questions asked in the study, participants were assured that raw data would remain confidential and would not be shared. If you would like to request access to de-identified transcripts, please contact the corresponding author, who will then seek permission from the participant to release the requested data.

Ethics Statement

This study was approved by the University of Toronto research ethics board (#00046866), ensuring the ethical acceptability of the research. A data transfer agreement between the University of Toronto and the Loeys-Dietz Syndrome Foundation Canada granted L.P. access to de-identified data.

Patient Consent

The authors confirm that patient consent forms have been obtained for this article (in both the screening survey and interview stages).

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Disclosures

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2026.03.009