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Bridging the Neurological Misdiagnosis Gap in Myotonic Dystrophies: A Comprehensive Review

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ABSTRACT

Background. Myotonic dystrophy types 1 (DM1) and 2 (DM2) occur due to pathogenic repeat expansions; DM1 due to a repeat expansion in the DMPK gene and DM2 due to a repeat expansion in the CNBP gene. Myotonic dystrophy (DM) is an autosomal dominant multisystem disorder characterized by increasing muscle weakness, myotonias (muscle stiffness), cataracts, abnormalities in cardiac conduction, and endocrine dysfunction. Although the molecular mechanisms that lead to DM are well defined, its diagnosis is often delayed by many years due to the broad phenotype of the conditions and their overlap with other neuromuscular and metabolic disorders.

Objectives. This review examines DM from a clinical, molecular, and diagnostic perspective in order to examine what causes diagnostic mistakes and how recent advances in DM detection techniques and multidisciplinary approaches to its diagnosis may have contributed to reducing these errors.

Methods. A scoping review of the literature has been conducted to determine what was known prior to 1993 about clinical variability, molecular testing methods, and new diagnostic methods for DM type 1 and type 2 (DM1 and DM2). We evaluated studies published in the peer-reviewed and non-peer-reviewed literature between January 1993 and June 2025, focusing specifically on studies that document delays in diagnosis, patterns of accuracy, and awareness of physicians. In addition, high-quality pre-print articles were also included when they provided significant new information regarding novel approaches to the diagnosis of DM1 and DM2 using the same type of research methodologies as typically used in peer-reviewed journals.

Results. Previous studies indicated that diagnostic delay was found for both DM1 (5-7 year delay) and DM2 (10-14 year delay), with some regional differences influenced by clinicians' familiarity with these diagnoses. The utility of electrophysiological methods of diagnosis varies; however, both triplet-primed PCR and long-read sequencing provide increased accuracy with regard to identifying atypical and/or large repeat expansions. Other

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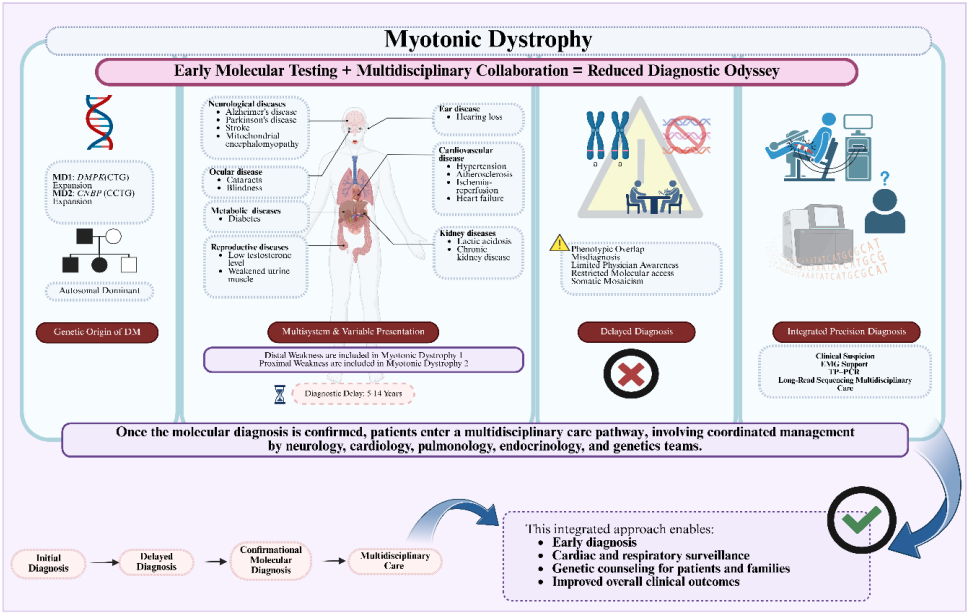
barriers to timely diagnosis include phenotypic variability, limited physician knowledge about these diagnoses outside of neuromuscular specialties, limited access to advanced molecular testing, and the lack of standardized diagnostic pathways.

Conclusion. Overlapping clinical features, inconsistent levels of physician awareness, and unequal access to molecular diagnostics within various healthcare settings are all factors that contribute to the persistent difficulty in diagnosing both DM1 and DM2. As such, it is critical to develop strong multidisciplinary collaboration, enhance the infrastructure for molecular diagnostics, and establish global harmonized standards for the diagnosis of DM in order to ensure that patients can be accurately identified promptly.

Keywords: clinical variability, diagnostic delay, molecular genetics, myotonic dystrophy (DM), triplet-repeat disorders, TP-PCR, nanopore sequencing

GRAPHICAL ABSTRACT



Highlights

- Diagnostic delays of up to 5-14 years in DM are driven by phenotypic variability, limited physician awareness, and inconsistent access to molecular testing.
- Integration of clinical assessment with modern molecular diagnostics, particularly TP-PCR and long-read sequencing, substantially improves the detection of complex and atypical repeat expansions in DM1 and DM2.
- A multidisciplinary and standardized diagnostic pathway is essential to reduce misdiagnosis, enable timely surveillance for systemic complications, and improve patient outcomes in DM.

1. INTRODUCTION

Myotonic dystrophy (DM) is a type of autosomal dominant genetic disorder that affects many different parts of the body. The two main types of DM are DM type 1 (DM1) and DM type 2 (DM2), caused by unstable repeat expansions in the DMPK gene and the CNBP gene, respectively [1, 2]. Both of these types of DM have some similarities in terms of how they affect the body, including causing weakness of skeletal muscle, cataract formation, disruption of electrical conduction in the heart, endocrine dysfunction, cognitive impairment, and progressive myotonia [1-3]. Although the molecular basis of DM1 was established many years ago (after Steinert's original description), accurate diagnosis remains difficult due to the large degree to which these two disease processes vary in their presentation and overlap with other neuromuscular and metabolic diseases [4, 5].

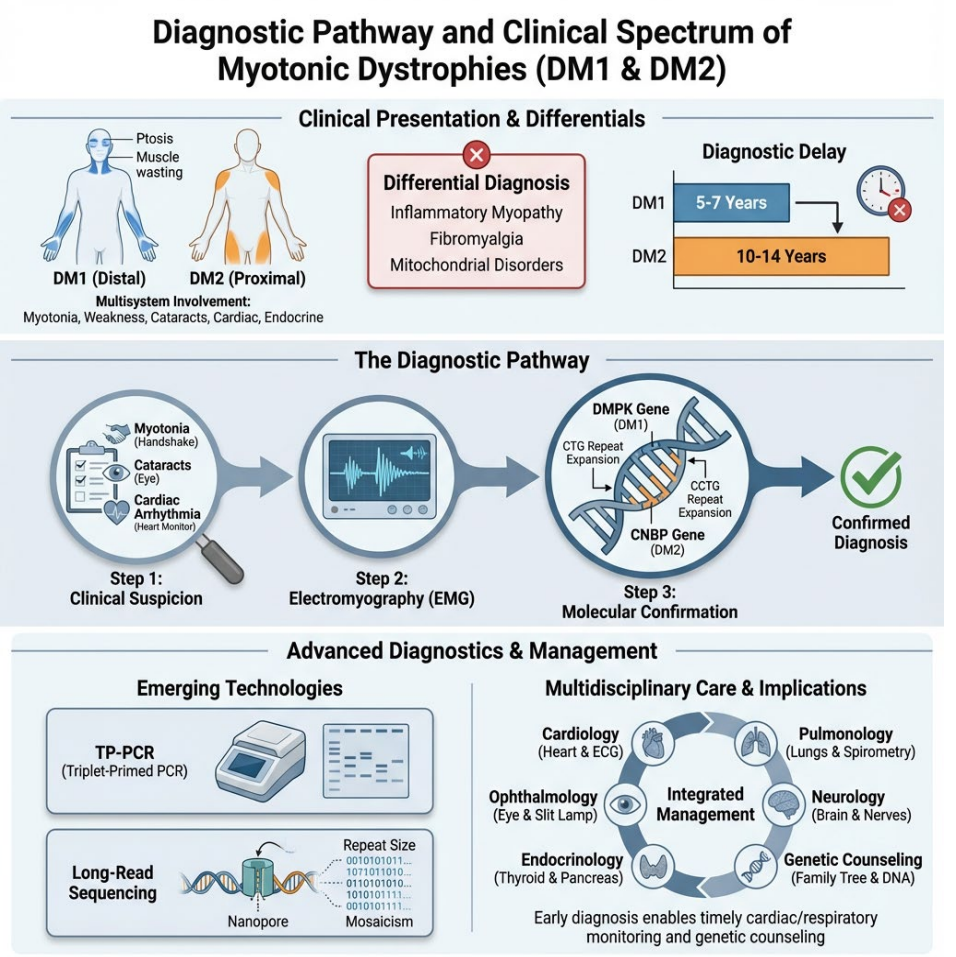


Figure 1. Clinical Spectrum, Diagnostic Delay, and Diagnostic Pathway in Myotonic Dystrophies (DM1 and DM2)

According to epidemiological studies, approximately 1 in 8,000 people have DM1, globally [6-8]. DM2 is much less frequently diagnosed than DM1, may go undetected due to later onset and more varied presentations. Thus, when diagnosed later, the patient cannot receive cardiac/respiratory evaluations and genetic counseling, which could help reduce the risk of morbidity and intergenerational transmission [9-11].

Fast-moving advances in PCR-based diagnostics and next-generation sequencing still leave many patients misdiagnosed. Commonly, patients are misdiagnosed with inflammatory myopathies or fibromyalgia, or disorders of mitochondria, resulting in inappropriate intervention and prolonged uncertainty [12-14]. This review provides a synthesis between the clinical and molecular evidence used for diagnostic confusion in DM and supports clinical improvements in the methods of detection based on evidence.

2. METHODOLOGY

2.1. Study Design

This review was developed as a narrative scoping review that examined the scope of problems associated with the diagnosis, patterns of misdiagnosis, and newer technologies available for the molecular diagnosis of DM1 and DM2. For this exercise, PRISMA guidelines developed for scoping reviews (PRISMA-ScR) were used to provide transparency in the identification and selection of studies. We did not conduct quantitative synthesis or meta-analysis of the reviewed studies due to the heterogeneity of the studies with respect to methodology and outcome measurement.

2.2. Search Strategy

Systematic searches were performed in PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar for studies published between 1993 and 2025 that were pertinent to the area of interest. Supplemental searches were made in SpringerLink, Elsevier, Oxford Academic, and bioRxiv. Search terms included various combinations of the following words/phrases: myotonic dystrophy, DM1, DM2, delay in diagnosis, misdiagnosis, triplet repeat, DMPK, CNBP, PCR, nanopore sequencing, and electromyography. We also reviewed the reference lists of relevant articles to identify additional potentially suitable publications.

2.2.1. Inclusion Criteria. Both original peer-reviewed research articles and clinical case studies that explored the diagnostic routes, molecular testing, or misdiagnosis of DM1/DM2 were included. English-language publications were considered as a primary source of evidence, supplemented with non-English significant publications only if they presented unique clinical information or provided a translation for their abstract into English, where possible. High-quality preprints were included if they contained new information on developing technologies to diagnose diseases/environments not yet published in a peer-reviewed publication (these types of studies are labelled as ‘preprints’ in the body of work and reference section).

2.3. Data Extraction and Synthesis

We extracted 1) author details; 2) year of publication; 3) type of research conducted; 4) method of diagnosis; 5) number of days taken between the time of diagnosis and report; and 6) author-reported accuracy of their respective diagnosis. Data were synthesized with minimal effort and as narrative summary (one group of findings represented one theme) with no attempts to conduct cross-study statistical analyses.

2.4. Quality Assessment

The methodological quality of observational/review studies was evaluated using the Joanna Briggs Institute (JBI) Critical Appraisal Instrument - Observational and Review Studies. Studies were assigned three categories (high, moderate, and low). The quality of each study was determined by a) clarity of research objectives; b) clarity of methodology goals; and c) reproducibility of study results. The interpretation of lower-quality studies was made using cautionary language and, in most cases, low-quality studies provided context to arrive at better absolute conclusions.

3. CLINICAL SPECTRUM AND SYMPTOM VARIABILITY

3.1. Phenotypic Range

DM1 typically begins earlier in life and presents with distal muscle weakness, prominent myotonia, and extensive multisystem complications, whereas DM2 tends to appear later with proximal muscle weakness and a slower, more variable clinical course [5, 15]. In DM1, early manifestations may include reduced muscle tone in infancy, breathing difficulties, and delayed developmental milestones, while adults commonly develop cataracts, hormonal irregularities, and cardiac rhythm disturbances [2, 16].

The more subtle early presentation of DM2 often leads clinicians to consider inflammatory or metabolic myopathies first. Patients may experience fatigue or mild muscle pain for years before more obvious weakness develops, resulting in substantial delays before genetic testing is pursued [10, 12, 17].

3.2. Atypical and Systemic Manifestations

DM can present with atypical symptoms, making diagnosis more difficult. For some patients, their initial medical contact may not be for muscle symptoms, but other medical problems such as respiratory failure, isolated eye symptoms, and cardiac arrhythmias [18, 19]. There have been reports of acute respiratory failure diagnosed later as being the result of DM. This correlates with the need to evaluate neuromuscular conditions as possible causes of acute respiratory failure and provide options for these patients to be transferred to an intensive care unit [17, 20]. Some patients with posterior subcapsular cataracts may be diagnosed with DM at their first eye doctor visit due to subtle signs and symptoms [18, 21, 22].

3.3. Genotype-Phenotype Discordance

There have been several documented cases of patients with DM who exhibited symptoms consistent with diagnosis but showed no detectable CTG or CCTG repeat expansions using the standard methods. This indicates either pathophysiological mechanisms or failure of conventional detection methods [11, 16, 23, 24]. This variability in diagnostic results emphasizes the need for molecular diagnostic technologies which provide a high level of resolution, in addition to careful clinical correlation with diagnostic results. This variability underscores the need for high-resolution molecular diagnostic approaches and careful clinical correlation. Table 1 summarizes representative studies illustrating the range of clinical presentations and associated diagnostic delays in DM1 and DM2.

Table 1. Representative Studies Illustrating Clinical Variability and Diagnostic Delay

Study	Year	Key Phenotypic Features	Reported Diagnostic Delay	Diagnostic Challenges	Key Insight
Eymard & Dobon [1]	2004	High multisystem involvement; variable presentation	5-10 years	Limited awareness outside neurology; overlapping symptoms	Misdiagnosis is common due to insufficient familiarity with physicians
Turnpenny & Kelly [4]	1993	Classical DM1 features: family history is often present	Variable	Clinical and EMG findings are non-specific	Need for molecular confirmation emphasized
Meola et al. [12]	2014	DM2 mild and heterogeneous presentation	10-14 years	Subtle early symptoms; overlap with inflammatory myopathies	DM2 is significantly underdiagnosed compared to DM1
Wenninger et al. [2]	2018	Overlapping DM1/DM2 features; proximal vs distal weakness	5-8 years	Phenotypic overlap between subtypes	Integrated diagnostics reduce misclassification
AlNawaiseh [18]	2020	Ophthalmic findings as the presenting feature	2-4 years	Cataracts and ocular symptoms often precede muscle involvement	Ophthalmology can enable earlier detection
Yamada et al. [19]	2023	Respiratory presentation without obvious muscle weakness	Variable	Neuromuscular causes are not considered in ICU settings	Requires high clinical suspicion in critical care
Nishihara et al. [17]	2020	Acute respiratory failure as the first manifestation	Previously undiagnosed	Atypical presentation, delayed recognition	ICU awareness essential for timely diagnosis
Meola & Cardani [13]	2015	Distinct pathomolecular mechanisms DM1 vs DM2	8-10 years	DM2-specific featurses are poorly recognized	Need for subtype-specific physician training
Silvestri & Modoni [5]	2023	Wide phenotypic spectrum; multisystem involvement	Variable	Clinical heterogeneity complicates diagnosis	Comprehensive phenotyping improves accuracy

Table 2. Diagnostic Methods and Relative Performance

Diagnostic Method	Sensitivity/Specificity	Primary Advantages	Principal Limitations	Clinical Utility	Key References
Clinical Examination	Moderate sensitivity; variable specificity	Non-invasive; widely available; guides further testing	Non-specific; depends on examiner expertise; variable presentation	Initial screening; raises clinical suspicion	Turnpenny & Kelly [4]; Quinn & Salajegheh [25]
Electromyography (EMG)	Moderate sensitivity (60-70%); low-moderate specificity	Can detect myotonic discharges; widely available	Non-specific; variable with disease stage; requires expertise	Supports clinical diagnosis; differential diagnosis	Miller [26]; Quinn & Salajegheh [25]
Conventional PCR + Southern Blot	High for moderate expansions (85-90%)	Established standard; reliable for typical expansions	Cannot reliably detect very large repeats; labor-intensive	Gold standard for decades; still widely used	Longman [6]; Savić Pavićević et al. [36]
Triplet-Primed PCR (TP-PCR)	Very high (>95%)	Rapid; cost-effective; detects large expansions; high sensitivity	Limited quantitation of exact repeat size	Current preferred molecular method for screening	Meng et al. [28]; Dryland et al. [30]
Repeat-Primed PCR (RP-PCR)	Very high (>95%)	Detects expansions regardless of size; rapid	Does not provide precise sizing	Excellent screening tool; confirms presence of expansion	Meng et al. [28]
Nanopore Sequencing	Near-complete (≈99%)	Direct sizing; detects interruptions; reveals mosaicism; full characterization	Expensive; requires specialized expertise; limited availability	Research and complex cases; most comprehensive characterization	Alfano et al. [29]
Muscle Biopsy	Variable; supportive evidence	Reveals histopathologic changes; rules out other myopathies	Invasive; non-specific findings; variable sampling	Adjunct when molecular testing is ambiguous	Raheem [34]; Schüller et al. [35]
Cardiac Evaluation (ECG/Echo)	Detects cardiac involvement	Identifies conduction defects; prognostic value	Not diagnostic for DM; findings are non-specific	Essential for management; not for diagnosis	Wenninger et al. [2]
Ophthalmologic Examination	High for detecting cataracts	Non-invasive; cataracts are highly characteristic	Not specific to DM; requires correlation	Early detection opportunity; supports diagnosis	AlNawaiseh [18]
Combined Clinical + Molecular	Highest overall accuracy	Holistic assessment confirms diagnosis; guides management	Resource-intensive; requires coordination	Optimal diagnostic strategy	Schüller et al. [35]; Ashizawa & Harper [19]

4. DIAGNOSTIC CRITERIA AND MOLECULAR APPROACHES

4.1. Evolution of Diagnostic Standards

Historically, the diagnosis of DM has been based on clinical examination and electromyography (EMG) for the detection of myotonic discharge. However, both of these methods are based on subjective interpretation of the associated signs or symptoms. Such an interpretation lacks any diagnostic specificity. Hence, the results may vary depending on the patient's stage of disease and the muscle sampled for EMG evaluation [25, 26]. The two-step approach currently favored by experts is a combination of clinical examination and EMG evaluation. The former aims to establish clinical suspicion for indicative signs and symptoms before proceeding to molecular testing for repeat expansions [18, 27].

4.2. Molecular Techniques

The first reliable methods of confirming the diagnosis of DM1 were polymerase chain reaction (PCR) and Southern blotting[6]. Since PCR, refinements to molecular genetic testing methods, such as triplet-primed PCR (TP-PCR), repeat-primed PCR, and long-read nanopore sequencing, have improved the ability to accurately size and identify even large or interrupted repeat expansions [28, 29]. Current PCR methods are very sensitive and specific, with significantly fewer false negatives than older techniques [30].

4.3. Challenges in Molecular Diagnosis

Although there has been a huge progress in developing molecular diagnostic technologies, challenges still remain. Somatic mosaicism leads to a significant amount of variability between tissues of the same individual, making it difficult to correlate genotype with phenotype [22, 31]. Many advanced molecular assays remain prohibitively expensive and are thus not available in the majority of healthcare settings worldwide, especially in developing countries with limited resources and diagnostic capabilities [15, 32, 33]. Additionally, the lack of standardized molecular diagnostic procedures across laboratories contributes to variability in test performance, data interpretation, and inter-laboratory comparison of results. This variability can diminish the reliability of diagnostic test results.

4.4. Integration of Multimodal Diagnostics

Combining molecular findings with EMG, histopathology, and imaging results provides greater confidence in the accuracy of a diagnosis. Muscle biopsies can reveal type I fiber atrophy and central nuclei, which correlates with genetic testing results [34, 35]. When molecular testing initially remains unclear or negative, EMG can provide further information to assist in differentiating DM from other neuromuscular disorders. Table 2 provides an overview of the various diagnostic methods and their relative performance characteristics, as described in the reviewed literature.

5. CLINICAL CONSEQUENCES OF MISDIAGNOSES

The consequences resulting from the misdiagnosis or delayed diagnosis of DM include their clinical, psychological, and economic effects. Many patients are given inaccurate diagnoses, such as chronic fatigue syndrome, fibromyalgia, and psychosomatic illnesses due to this misdiagnosis, leaving them to receive inappropriate treatment for years [1, 12].

5.1. Impact on Patient Care and Prognosis

Late diagnosis can prevent the timely recognition of life-threatening cardiac arrhythmias and respiratory failure. Many of

the aforementioned problems result from misdiagnosis and documentation of respiratory muscle dysfunction associated with DM. Complications that were documented in postoperative or critical care cases can be attributed in part to the lack of recognition of DM respiratory muscle dysfunction [17, 19]. Untreated endocrine and metabolic manifestations, which may include, but are not limited to, insulin resistance, thyroid dysfunction, and hypogonadism, are associated with increased morbidity [2, 12].

Psychologically, the extended period from when a patient becomes symptomatic until diagnosis causes significant anxiety, delay in planning for a family, and emotional distress1. These observations indicate that the clinical consequences of an accurate and timely diagnosis of DM1 and DM2 are considerable and have implications for clinical outcome and future treatment.

5.2. Health System and Research Implications

The effects of misdiagnosis on the healthcare system are multifactorial and include increased costs to the healthcare system from the patient due to the fact that misdiagnosed patients continuously present to the healthcare provider and have unnecessary diagnostic tests or inappropriate treatment[1,12]. Patients who are misdiagnosed also may not be able to participate in clinical trials of new therapeutic approaches, such as gene-targeted and antisense therapies, which may affect both the research for treatment options and the epidemiologic data related to DM patients [9, 10].

6. EMERGING DIAGNOSTIC TECHNOLOGIES

Recent technological developments have greatly advanced the accuracy of diagnosing DM through improved methods.

6.1. Advanced Molecular Tools

Innovative PCR technologies, especially triplet primed PCR (TP-PCR), allow for much higher sensitivity in detecting so-called CTG and CCTG repeats [20, 22]. Recent advances in long-read sequencing using both nanopore technology and Cas9 methods allow the identification of repeat length, interruptions within a repeat, and somatic mosaicism with nearly total diagnostic success [29].

6.2. Integrative and Omics Approaches

Emerging omics technologies (genomics, transcriptomics, and proteomics) provide insight into the molecular underpinnings of disease and may ultimately be used to predict genotype to phenotype in a more precise manner. By combining omics data with advanced clinical phenotyping, there is a real potential to create more personalized methods of diagnosing diseases; however, research in this area is still in infancy.

6.3. Implementation Challenges

Advanced diagnostic technologies have significant potential but their implementation is limited by the lack of economic and physical resources, as well as the requirement for highly qualified staff [15, 37]. The absence of standardized guidelines further constrains interlaboratory reproducibility. Table 3 compares traditional and emerging diagnostic techniques, highlighting their respective advantages, limitations, and current accessibility as reported in various studies [38-41].

Table 3. Comparison of Traditional and Emerging Diagnostic Techniques

Technique	Technology Type	Approximate Turnaround Time	Primary Strengths	Primary Weaknesses	Complexity Level	Cost Level	Current Availability	Best Use Case
Clinical Evaluation + EMG	Electrophysiology	1-2 days	Widely accessible; non-invasive; established workflow	Low specificity; variable accuracy; operator-dependent	Low-Moderate	Low	Universal	Initial screening and differential diagnosis
Conventional PCR + Southern Blot	First-generation molecular	3-5 days	Reliable for moderate expansions; established method; well-validated	Cannot detect very large expansions; labor-intensive; technically demanding	Moderate-High	Moderate	Widespread	Standard confirmation in many centers
Triplet-Primed PCR (TP-PCR)	Second-generation molecular	1-2 days	Cost-effective; high sensitivity; rapid; detects large expansions	Limited precise quantitation; requires optimization	Moderate	Low-Moderate	Widely available	Current preferred screening/confirmation method
Repeat-Primed PCR (RP-PCR)	Second-generation molecular	1-2 days	Size-independent detection; rapid; reliable	No precise sizing; requires confirmation for exact length	Moderate	Low-Moderate	Widely available	Screening and initial confirmation
Long-Read Nanopore Sequencing	Third-generation sequencing	1-2 days (after prep)	Detects large repeats; reveals interruptions; characterizes mosaicism; most comprehensive	Expensive; requires expertise; limited availability; infrastructure-intensive	High	High	Limited (specialized centers)	Complex cases; research; full characterization
Cas9-Mediated Enrichment + Sequencing	Advanced molecular/sequencing	2-3 days (after prep)	Targeted approach; high resolution; detects structural variants	Highly specialized; expensive; limited accessibility	Very High	Very High	Very limited (research settings)	Research applications; refractory cases
Multi-Omics Integration	Systems biology approach	Variable (weeks)	Captures molecular complexity; potential for personalized medicine; mechanistic insights	Expensive; research phase; interpretation challenging; not clinically validated	Very High	Very High	Research only	Pathogenesis studies; future personalized diagnostics
Muscle Biopsy + Histopathology	Tissue analysis	3-7 days	Rules out other myopathies; provides tissue diagnosis; established method	Invasive; sampling variability; non-specific findings	Moderate	Moderate	Widespread	Differential diagnosis when molecular testing inconclusive
Combined Clinical-Molecular Protocol	Integrated workflow	Variable (3-7 days)	Highest diagnostic confidence; holistic assessment; best practice	Requires coordination; resource-intensive; depends on local infrastructure	Moderate-High	Moderate-High	Variable	Optimal comprehensive diagnostic pathway

EMG = electromyography; PCR = polymerase chain reaction; TP-PCR = triplet-primed PCR; RP-PCR = repeat-primed PCR; Cas9 = CRISPR-associated protein 9

7. PHYSICIAN AWARENESS AND MULTIDISCIPLINARY COLLABORATION

7.1. Physician Knowledge Gaps

The lack of physician knowledge has been recognized as a significant reason for slow diagnoses, especially for types of DM [21, 15, 42, 43]. Whereas, the lack of awareness is thought to be the main cause of missed diagnosis or delayed diagnosis. Many of the earlier signs (e.g., grip myotonia, early-onset cataracts, or insulin resistance) cannot be diagnosed by physicians who are non-specialists (e.g., GPs, pulmonologists, ophthalmologists, and endocrinologists) because these signs are subtle12,19.

7.2. Multidisciplinary Diagnostic Approach

Correct diagnosis can be improved through multidisciplinary diagnostic approaches, whereby combining expertise (e.g., neurology, cardiology, pulmonology, ophthalmology, and clinical genetics) has been shown to greatly enhance the ability to detect DM [9, 37, 44]. Also, cascade genetic testing and a detailed family history are important to identify asymptomatic carriers of the diagnosis [4, 36, 45].

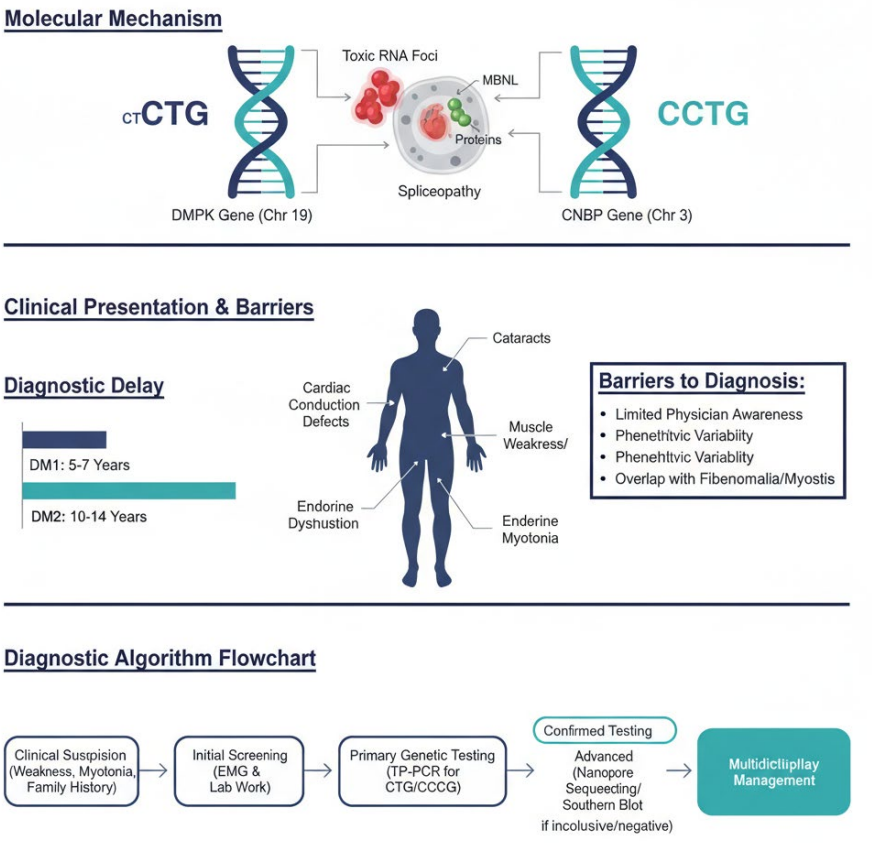


Figure 2. Molecular Pathogenesis of DM and Rationale for Molecular Diagnostics

7.3. Educational and Policy Implications

There is a need for standardized clinical practice guidelines and education programs to create globally focused physicians for equity (e.g., DM modules) in continuing medical education and graduate medical programs to help provide physicians with information regarding the disease [14, 46, 47].

8. DISCUSSION

This review highlights that diagnostic delay and misdiagnosis of DM remain persistent global challenges despite major advances in molecular genetics, consistent with earlier observations by Eymard et al. [48]. Delayed recognition is frequently attributed to phenotypic heterogeneity and limited awareness among non-neurologists. Similarly, Meola et al. demonstrated that DM2 remains particularly underdiagnosed due to its milder and more variable phenotype, as compared with DM112,15 .

Our findings align with Wenninger et al. [2], who emphasized the overlapping yet subtype-specific features between DM1 and DM2, which complicate clinical differentiation. The average diagnostic delay of 5-7 years in DM1 and up to 10-14 years in DM2 reported in prior studies [10, 12] is consistent with the trends synthesized in this review. Case-based evidence further supports this concern, particularly in atypical presentations such as acute respiratory failure [17, 19] or ophthalmologic manifestations preceding neuromuscular symptoms [18].

From a molecular perspective, the transition from conventional PCR and southern blotting to repeat-primed PCR and triplet-primed PCR significantly improves detection sensitivity [28, 30]. More recently, nanopore sequencing and Cas9-mediated enrichment approaches have demonstrated near-complete characterization of repeat expansions, including the detection of repeat interruptions and somatic mosaicism [29]. However, as previously discussed by Giordano et al. [22] and Morales et al. [31], somatic instability remains a critical factor limiting genotype–phenotype correlations.

Importantly, several studies stress that molecular tools alone remain insufficient without structured clinical pathways. Schneider-Gold et al. [37] and Rimoldi et al. [9] advocated for multidisciplinary diagnostic frameworks integrating neurology, cardiology, pulmonology, ophthalmology, and clinical genetics. This integrated approach not only enhances diagnostic accuracy but also facilitates early surveillance of systemic complications.

Collectively, the evidence supports a paradigm shift from symptom-based suspicion to integrated, early molecular confirmation, combined with multidisciplinary evaluation. Addressing physician awareness gaps and improving equitable access to advanced molecular diagnostics remain essential to reducing diagnostic inertia in both DM1 and DM2.

8.1. Conclusion

Myotonic dystrophy (DM) is a clinically heterogeneous multisystem disorder in which diagnostic delay and misdiagnosis remain common due to overlapping symptoms, phenotypic variability, limited physician awareness, and inconsistent access to molecular diagnostics. Although advances in PCR-based assays and long-read sequencing technologies have significantly improved the detection of repeat expansions, challenges such as somatic mosaicism, genotype–phenotype discordance, and limited availability of advanced testing continue to hinder timely diagnosis. Early integration of clinical suspicion, electrophysiological evaluation, and confirmatory

molecular testing—within a standardized multidisciplinary diagnostic framework—is essential to reduce misdiagnosis, enable proactive monitoring of systemic complications, and improve patient outcomes. Strengthening global diagnostic infrastructure and clinicians' education are critical steps toward bridging the neurological misdiagnosis gap in DM.

8.2. Future Directions

Research initiatives must concentrate on designing standardized, widely available, diagnostic algorithms that include clinical evaluations, electrophysiological evaluations, and molecular evaluations. The establishment of educational programs for healthcare providers, along with the provision of global access to advanced sequencing technology, are important steps in achieving equitable access to diagnostic testing for DM. The establishment of multicenter diagnostic registries and the use of artificial intelligence-based analysis to evaluate genetic and image data may also increase accuracy and decrease the time needed to obtain a diagnosis. The broader implementation of screening strategies would allow for the earlier identification of DM and the enhancement of patient outcomes across a variety of healthcare settings.

Author Contribution

Noman Ahmed: conceptualization, methodology, formal analysis, writing – original draft, data curation, software, resources, writing - review & editing. **Anas Saeed:** data curation, formal analysis, writing – original draft, validation. **Beena Gul:** writing – review & editing. **Danish Aizaz:** data curation, formal analysis, writing – original draft. **Zeeshan Siddique:** data curation, formal analysis, writing – original draft. **Hariz Riaz Khan:** data collection, visualization, validation. **Farakh Javaid:** data validation. **Usman Ayub Awan:** conceptualization, supervision, resources, software, data analysis, writing – review & editing.

Conflict of Interest

The authors declare no financial or non-financial conflict of interest related to this manuscript.

Data Availability Statement

Since this is a narrative scoping review, no primary datasets were generated or analyzed. Data supporting the findings will be made available by the corresponding author upon reasonable request.

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Generative AI Disclosure Statement

The authors did not use any type of generative artificial intelligence software for this research.

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