Wearable Inertial Devices in Duchenne Muscular Dystrophy: A Scoping Review

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# Wearable Inertial Devices in Duchenne Muscular Dystrophy: A Scoping Review

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**Abstract:** In clinical practice and research, innovative digital technologies have been proposed for the characterization of neuromuscular and movement disorders through objective measures. Among these, wearable devices prove to be a suitable solution for tele-monitoring, tele-rehabilitation, and daily activities monitoring. Inertial Measurement Units (IMUs) are low-cost, compact, and easy-to-use wearable devices that evaluate kinematics during different movements. Kinematic variables could support the clinical evaluation of the progression of some neuromuscular diseases and could be used as outcome measures. The current review describes the use of IMUs for the biomechanical assessment of meaningful outcome measures in individuals affected by Duchenne muscular dystrophy (DMD). The PRISMA methodology was used and the search was conducted in different databases (Scopus, Web of Science, PubMed). A total of 23 articles were examined and classified according to year of publication, ambulatory/non-ambulatory subjects, and IMU positioning on human body. The analysis points out the recent regulatory identification of Stride Velocity 95th Centile as a new endpoint in therapeutic DMD trials when measured continuously from a wearable device, while only a few studies proposed the use of IMUs in non-ambulatory patients. Clinical recognition of reliable and accurate outcome measures for the upper body is still a challenge.

**Keywords:** Duchenne muscular dystrophy; inertial measurement units; wearable devices; outcome measures; movement disorders



**Citation:** Panero, E.; D'Alessandro, R.; Cavallina, I.; Davico, C.; Mongini, T.; Gastaldi, L.; Ricci, F. Wearable Inertial Devices in Duchenne Muscular Dystrophy: A Scoping Review. *Appl. Sci.* **2023**, *13*, 1268. https://doi.org/10.3390/app13031268

Academic Editors: Maria Luisa Lorusso, Sara Mascheretti and Francesca Borasio

Received: 20 December 2022
Revised: 12 January 2023
Accepted: 14 January 2023
Published: 17 January 2023



## 1. Introduction

Duchenne muscular dystrophy (DMD) is a progressive, critical, muscle-degenerative pathology caused by mutations in the encoding dystrophin DMD gene, which inhibit production of the muscle dystrophin isoform [1]. DMD has an incidence of 1 in 5000 boys, with clinical symptoms appearing in early childhood (between 3 and 5 years of age). Even though the majority of female DMD patients are asymptomatic, up to 20% of them show moderate muscle weakness [2]. In DMD, the most common symptoms are delayed motor development, muscle weakness, gait alterations, and recurrent risk of falls. Untreated patients may become wheelchair dependent before age 10–12 and need assisted ventilation by age 20. Associated complications requiring monitoring and management include lung disease, cardiomyopathy, scoliosis, corticosteroid side effects, and educational and psychosocial issues. Patients with DMD die between the third and fourth decades of life from cardiac and/or respiratory failure. Due to its complexity and strong impact on patient wellbeing, a coordinated and multidisciplinary clinical approach is essential for an early diagnosis of DMD and for the optimal management of the primary manifestations and secondary complications [3]. The current availability of more sensitive diagnostic techniques and the early adoption of therapeutic interventions [4,5] have the potential to improve patients' length and quality of life [6].

Several clinical scales and scores are currently used to assess and monitor the functional changes in neuromuscular disorders. In children with DMD, one of the most important therapeutic goals is to maintain independent ambulation for as long as possible, postponing spinal deformities and muscle contractures. Gait pattern and potential gait impairments are generally assessed by the 6-minute walk test (6MWT) [7,8], also used to assess treatment effect in clinical trials [9], or by the North Star Ambulatory Assessment (NSAA) scale, which includes 17 items and was developed specifically for ambulatory DMD patients [8,10,11]. The Brooke Upper Extremity Functional scale [12] and the Performance of Upper Limb (PUL) scale [13,14] were designed specifically to measure upper-body motor performance. Tasks are targeted at weaker ambulatory patients as well as non-ambulatory patients when upper limb weakness becomes more evident. While functional motor scales are currently the most widely used assessment methods, they have some limitations, including the learning effect, limited repeatability, and lack of sensitivity to highlight relevant changes in slowly progressive diseases.

During the last few decades, several innovative technologies have been proposed and adopted for the biomechanical assessment and monitoring of human movement disorders in different clinical fields [15–17]. Among these technologies, wearable inertial devices have gained prominence in recent years [18–20]. Inertial Measurement Units (IMUs) are portable, easy to use, low-cost systems that allow continuous monitoring of human movements during outdoor and daily activities. Wearable sensors are composed of a single accelerometer, a single gyroscope, and a single magnetometer, or a combination of them for three-axis measurement, and can measure several kinematic parameters, such as acceleration, angular velocity, and magnetic field. Each system can measure data in a specific direction (one-axis) or along three different directions (three-axis). Based on human motion, the units can be positioned on several human body parts, with sensor placement able to affect data measurement [21]. The interpretation of the data obtained from the three-dimensional movement analysis allows the quantification of the functional alterations related to the disease, guiding decisions such as surgical interventions and therapeutic indications. Moreover, IMUs have the potential to be widely used in tele-rehabilitation and tele-monitoring [22]. The clinical relevance of movement analysis has motivated researchers to develop indexes capable of synthesizing data and facilitating their comprehension and clinical interpretation. A technological outcome measure can be defined as "the outcome of instrumented clinical tests performed in standardized settings to objectively measure specific movements or self-administered by patients to detect and monitor impairments during specific daily activities" [23]. In DMD, several previous studies focused on the biomechanical analysis of human movement impairments through objective and technological measures [24–26], proposed the potential use of indexes and scores as clinical descriptors [27,28], and correlated the objective outcomes with the clinical functional assessment [29]. Nevertheless, only a few recent studies have proposed the application of IMU sensors and the identification of suitable outcome measures.

The principal aim of this review is on the current applications of wearable inertial systems for the definition and detection of significant motor outcome measures in Duchenne muscular dystrophy. Meaningful articles are discussed, highlighting the most significant content from a technical, biomechanical, and clinical point of view. The manuscript is structured as follows. Section 2 describes the adopted methodology, presenting the main research questions, the literature search strategy, and the inclusion criteria defined to filter the articles. Section 3 summarizes the search results, presenting the most relevant content. Section 4 discusses the main content from a technical, biomechanical, and clinical point of view. Section 5 concludes the paper with a summary of the literature search, the main findings, and some challenges that can be addressed in future work.

## 2. Methodology

The literature search was conducted in October 2022 by two individuals (E.P. and F.R.). The literature research was conducted through several steps:

- Definition of the principal aim of the search and research questions;
- Formulation of relevant keywords;
- Selection of search databases;
- Identification of specific inclusion/exclusion criteria for article selection;
- Elimination of duplicates and unrelated articles;
- In-depth analysis and investigation of selected articles.

The adopted methodology is in line with the "Preferred Reporting Items for Systematic reviews and Meta-Analyses" (PRISMA) [30,31]. The PRISMA flowchart is reported in Appendix A. No a priori protocol was registered. Additional information about the process can be obtained from the corresponding author on request.

### 2.1. Research Questions

The following main questions were proposed: (i) How are wearable inertial measurement devices currently used for the identification of meaningful outcome measures in Duchenne muscular dystrophy? (ii) Are there any clinical guidelines describing how experimental tests should be conducted and normative data of parameters of interest defined? (iii) What is the correlation between IMU variables and the current clinical scales?

### 2.2. Search Schemes

Starting from the main questions, four different fields were identified for the formulation of suitable keywords according to the PICOS framework: (1) Population; (2) Intervention; (3) Comparison; and (4) Outcome. The search focused on patients affected by Duchenne muscular dystrophy and articles dealing with pediatric populations were included in the review without any cultural, gender, race, or age restrictions. Due to the principal question on the use of wearable inertial sensors for the identification of meaningful outcomes, the intervention was identified in the experimental application of IMUs for the monitoring and evaluation of patients' motor performance, without any limits on the environment. Studies dealing with the comparison of results with a control group and those focusing on the comparison with other neuromuscular diseases were included in the analysis. No restrictions were imposed on the objective outcomes obtained with the sensors. Moreover, clinical functional scales were not included in the keywords to avoid too many strict restrictions. The following keywords were defined:

- Duchenne muscular dystrophy, neuromuscular disease;
- Wearable, inertial systems, IMU, accelerometer, gyroscope, magnetometer;
- Outcome measures.

The following search string was formulated: "((duchenne OR duchenne muscular dystrophy OR neuromuscular disease)) AND ((wearable) OR (inertial) OR (imu) OR (accelerometer) OR (gyroscope) OR (magnetometer)) AND ((outcome))".

For the article selection, the Scopus, Web of Science, and PubMed electronic databases were explored. The search strategy and search string used for all three databases were the same. The three lists of articles were uploaded on Mendeley and all duplicates were automatically eliminated.

### 2.3. Inclusion Criteria

Only articles published from 2000–2022 were included. The following eligibility criteria were considered for article selection: (i) studies presenting IMU sensors for monitoring human motion in DMD; (ii) reviews discussing the use of IMU sensors in clinical analysis of DMD; (iii) studies focusing on human/pediatric populations; (iv) studies presenting current and innovative outcome measures in DMD obtained by the use of IMU sensors; (v) studies investigating the correlation between IMU outcomes and clinical scales; and (vi) articles written in English.

Finally, the presence of the keyword "Duchenne" within the title, among keywords, or in the abstract was defined as the discriminating request.

### *2.4. Study Characteristics and Classification*

Several data were extracted from the identified manuscripts. The main characteristics are summarized in Table 1: the year of publication, the journal, the aim of the study, the subjects enrolled in the experimental tests, the instrumentations used, and the objective variables investigated. Each article has been analyzed and main results highlighted. Articles were grouped and classified based on the positioning of the wearable sensors on specific human body parts, the year of publication, and the discrimination between ambulatory and non-ambulatory DMD subjects.

**Table 1.** Summary of selected articles.

| Paper | Subjects | Instruments | Variables |
|---|---|---|---|
| Jeannet et al. [32], 2011 | 5 DMD (age: 4–6 years) | Non-commercialized ASUR monitor with 3D accelerometer and gyroscope positioned on the chest | Posture parameters, no. of walking episodes, cadence, maximum duration of walking, total steps |
| Ganea et al. [33], 2012 | 25 DMD (age: 5–12 years) 20 healthy children as control group | 2 ASUR units with a 1-axis gyroscope fixed on the shank, 1 BioAGM unit with 3-axis accelerometer fixed on the trunk | Stride length, shank peak angular velocity, stride velocity, cadence, double support, power spectral entropy |
| Davidson et al. [34], 2015 | 16 DMD (age: 5–13 years) 13 healthy children as control group | StepWatch accelerometer worn at the ankle joint | Time inactivity, time in low activity, time in high activity, total steps |
| Le Moing et al. [35], 2016 | 7 non-ambulatory DMD (around 18 years) | ActiMyo (3 axis-MIMU) worn on the wrist | Rotation rate, ratio of the vertical component in the overall acceleration, hand elevation rate, power |
| Jacques et al. [36], 2018 | 15 DMD, 16 healthy, 46 other dystrophies (mean age 24) | GENEActiv with a 3-axis accelerometer worn on the wrist | Daily average minutes being physically active, % sedentary behavior |
| Straub et al. [37], 2018 | / | / | Stride length, cadence, knee extension strength, heart rate, PUL, 6MWT, NSAA |
| Fujii et al. [38], 2019 | 7 non-ambulatory DMD (age: 12–24 years) | Silmee Bar-type Lite 3-axis accelerometer worn on the dominant wrist | Cumulative sum of jerk, Brooke Upper Extremity Scale, muscle strength |
| Van der Geest et al. [39], 2019 | 16 DMD (age: 7–17 years) | 3-axis accelerometer MOX worn on upper arm and lower arm | Intensity (activity counts), level of arm elevation, elevation rate, Brooke Upper Extremity Scale, PUL |
| Haberkamp et al. [40], 2019 | / | / | Stride Velocity 95th Centile (SV95C) defined as a new endpoint in therapeutic DMD trials |
| Siegel et al. [41], 2020 | 54 DMD (age: 5–17 years) | Actigraphy Actiwatch 2 worn on the wrist | Rest activity, sleep quality, and 6-minute walk test (6MWT) |
| Ann et al. [42], 2020 | 100 DMD and 100 healthy controls (age: 2–13 years) | 5 APDM OPAL accelerometers applied on forearms, shanks, chest | Relative coupling coefficient (RCC) |
| Arteaga et al. [43], 2020 | 49 DMD (mean age 13 years) | Accelerometer Actigraph GT3X worn on wrist and ankle | Total vector magnitude (VM), awake vector magnitude |
| Killian et al. [44], 2020 | 48 DMD (mean age 13 years) | Accelerometer Actigraph GT3X worn on wrist and ankle | Total vector magnitude, awake vector magnitude |
| Lott et al. [45], 2021 | 70 DMD (age: 8 years) and 10 controls | Accelerometer Actigraph GT3X worn on waist | Daily steps count |
| McErlane et al. [46], 2021 | 8 DMD (age: 6–16 years) | Wrist-worn accelerometer | Average daily maximum, average daily steps, average steps per epochs |
| Poleur et al. [47], 2021 | 91 healthy subjects (mean age: 16 years) | ActiMyo (3 axis-MIMU) worn on the wrist and ankle | Stride length, stride velocity, meters walked per hour |
| Servais et al. [48], 2021 | / | ActiMyo (3 axis-MIMU) worn on the wrist and ankle | Stride Velocity 95th Centile (SV95C) defined as a new endpoint in therapeutic DMD trials |
| Youn et al. [49], 2021 | / | / | Several activity biomarkers based on previous studies |
| Jacques et al. [50], 2022 | 15 DMD (mean age: 25 years) | GENEActiv with a 3-axis accelerometer worn on the wrist | Percentage of time spent sedentary (SB%), total time spent physically active |
| Kaslow et al. [51], 2022 | 49 DMD (mean age: 13 years) | Accelerometer Actigraph GT3X worn on wrist and ankle | Minutes per day of wearing, minutes per day of wearing and awake, VMs generated while wearing, VMs generated per minute while wearing, VMs generated per minute while wearing and awake |
| Servais et al. [52], 2022 | - | ActiMyo (3 axis-MIMU) worn on the ankle | Stride length, stride velocity, no. of meters walked per hour |
| Morse et al. [53], 2022 | 53 MD men (mean age: 40 years) | GENEActiv with a 3-axis accelerometer worn on the wrist | Sleep time, sleep efficiency, activity periods, activity times |
| Nair et al. [54], 2022 | 114 DMD (age:5–15 years) and 24 healthy controls | Accelerometer Actigraph GT3X worn on waist | Step activity, quality of muscle health |

## 3. Results

Figure 1 schematizes the flowchart of the performed research. Based on the search string and after eliminating the duplicates, a total of 350 articles were found. Only research dealing with DMD in the human population and with the keyword "Duchenne" in the title, keywords, or abstract fields were considered, for a final result of 49 articles. All of these manuscripts were analyzed, with some excluded as they were not directly related to the use of IMU sensors for human movement investigation. No restrictions were imposed on the type of article. Finally, the full text of the remaining 23 research articles was examined and included in the qualitative and quantitative syntheses.

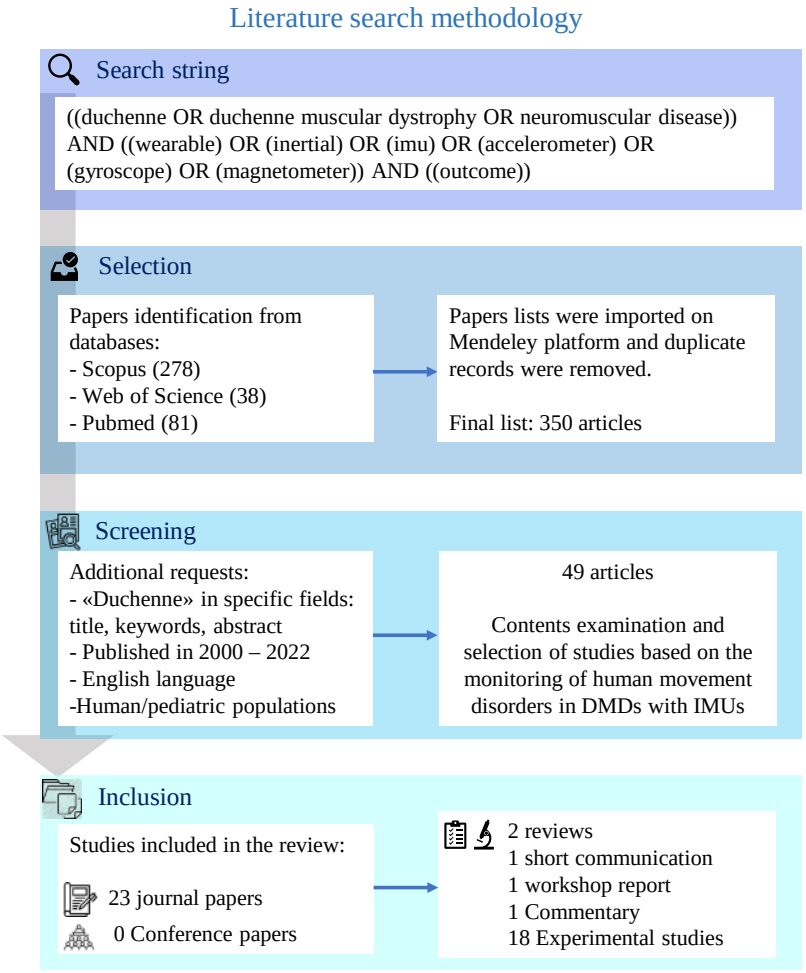


**Figure 1.** Flowchart describing the several paper selection steps in the literature search.

Relevant data have been extracted from the selected articles. Papers were classified based on the IMU sensors' positioning on human body parts (Figure 2A). Three studies positioned the IMU on the chest; only one study proposed the positioning on the waist; regarding the upper limb, two studies positioned the IMUs on the forearm and seven studies on the wrist; as for the lower limb, two studies positioned the IMUs on the shanks and six studies on the ankles. Moreover, the articles were grouped considering the year of publication. Figure 2B shows that all articles were published after 2010, the majority after 2018. Only one article was published per year in 2011, 2012, 2015, and 2016, while in 2018 two articles were published and in 2020 there were three. Four manuscripts were registered for the year 2019; the years 2021 and 2022 saw 5 articles per year.

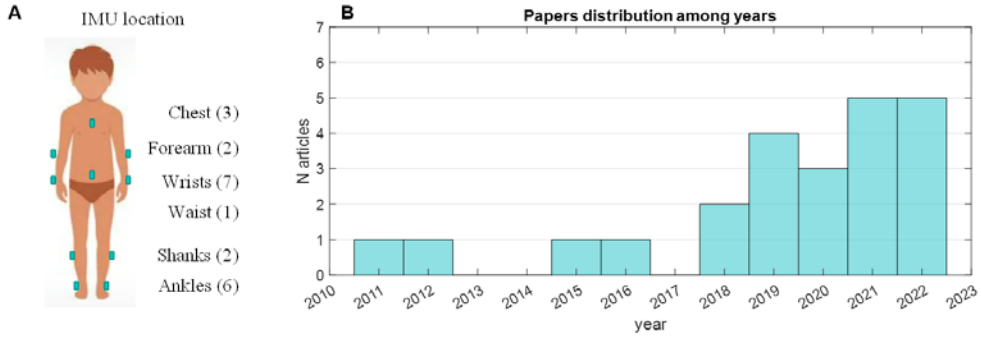


**Figure 2.** (**A**) Report of the different human body positions of the wearable inertial units described in the selected articles; (**B**) Classification of the articles based on the year of publication.

Finally, articles dealing with experimental tests were classified as differentiating ambulatory (15 articles) and non-ambulatory (10 articles) subjects, as reported in Figure 3. It must be noted that most of the studies enrolled both ambulatory and non-ambulatory patients, while only a few studies considered walking an inclusion/exclusion criterion. Several types of wearable inertial sensors were presented and used in the studies; Table 2 summarizes their main characteristics. All sensors present a 3-axis accelerometer to measure the segment acceleration in the 3D space, while only a few systems integrate a 3-axis gyroscope and a 3-axis magnetometer, which is fundamental for the analysis of segment orientation. Among these sensors, ActiMyo has been established as a Class I medical device for the continuous measurement of acceleration, velocity, and angular movements over prolonged periods in a domestic environment.

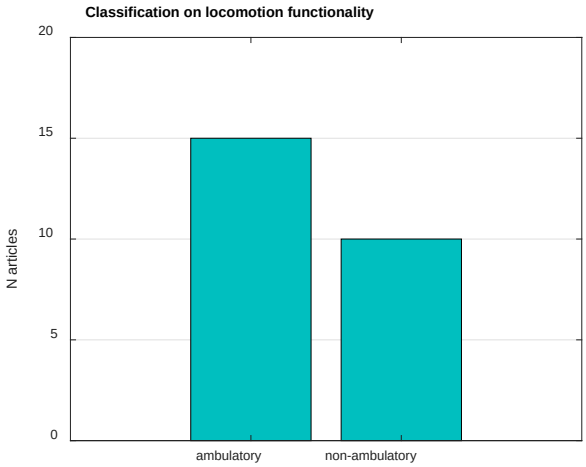


**Figure 3.** Experimental studies classification based on ambulatory and non-ambulatory patients.

In 2011, Jeannet and colleagues [32] tested the accuracy and reliability of daily physical activity using a miniaturized wearable sensor during home monitoring. Experimental tests were conducted for two consecutive days and 5 DMD patients (age 4–6 years) were included in the study. Body movements and activities were monitored by a customized wearable sensor (ASUR-Autonomous Sensing Unit Recorder) composed of a 3D accelerometer and a 3D gyroscope. The unit was positioned on the chest of the patient. A customized algorithm for daily activity recognition (sitting, standing, laying, walking) was proposed and validated in a preliminary test. Moreover, as a second aim of the study, patients started prednisolone therapy and the experimental test was repeated after one month. Two types of objective parameters were considered and discussed: posture parameters, quantifying the percentage of time at rest, the percentage of time in motor activity, the percentage of time spent during specific daily activity, such as sitting, standing, lying down, and walking; and

walking parameters, quantifying common gait parameters (step, cadence, duration). The study highlighted the suitability of objectively measuring DMD children's activity in their everyday environment. Results demonstrated that all patients spent more time in activity after one month of treatment (55.8% at follow-up, 51.9% at baseline). Relevant differences between the two acquisitions (before and after one month of treatment) were observed in parameters showing endurance, such as the maximum duration of quasi-continuous walking episodes (1087 s at follow-up versus 789 s at baseline). A follow-up study [33] was presented by the same authors and dealt with the analysis of gait alteration in 25 DMD children (age 5–12 years) during long-distance walking. The study included 20 healthy children identified as a control group. Two ASUR units were fixed on patients' shanks and the datalogger Physiolog BioAGM was attached on the trunk for activity monitoring. Spatio-temporal parameters were obtained from the angular velocity monitored by the IMU on the shanks. In addition, the smoothness of trunk movement was assessed based on the spectral entropy of the acceleration norm. The Motor Function Measure scale was used to clinically evaluate DMD patients, who were grouped into two different classes: mildly and moderately affected patients. A traditional statistical classifier was proposed to categorize patients in the two groups. Results depicted a significant decrease in stride velocity and stride length in DMD patients compared to controls. Moreover, a significantly higher stride velocity variability and shank peak angular velocity variability was depicted in DMD patients. A moderate and significant (probability value $p$ with level of significance $p < 0.05$) correlation (Spearman's rank correlation coefficient rho) was obtained between gait parameters and the clinical score obtained with the Motor Function Measure (rho(25) = 0.59, $p = 0.002$ for the stride velocity; rho(25) = 0.6, $p = 0.001$ for the cadence; rho(25) = $-0.51$, $p = 0.008$ for the spectral entropy). The statistical classifier enabled the different clinical states of DMD to be distinguished.

**Table 2.** Description of wearable sensors used in the studies.

| Sensor | Component Description | Technical Data |
| --- | --- | --- |
| ASUR-Autonomous Sensing Unit Recorder | 3-axis accelerometer3-axis gyroscope | Sample rate = 25 HzNon-commercialized sensor |
| Physiolog BioAGM | 3-axis accelerometer3-axis gyroscope 3-axis magnetometer | Sample rate = 1–500 HzAcc range = ±2 g/±10 g |
| StepWatch | 3-axis accelerometer | Sample rate = 200 Hz |
| ActiMyo | 3-axis accelerometer3-axis gyroscope3-axis magnetometer | Sample rate = 100 Hz |
| GENEActiv | 3-axis accelerometer | Sample rate = 10–100 HzAcc range = ±8 g |
| Silmee Bar-type Lite | 3-axis accelerometer | Sample rate = 15–125 HzAcc range = ±2 g |
| MOX | 3-axis accelerometer | Sample rate = 25–100 HzAcc range = ±8 g |
| Actiwatch 2 | 3-axis accelerometer | Sample rate = 32 Hz |
| OPAL | 3-axis accelerometer3-axis gyroscope 3-axis magnetometer | Sample rate = 20–128 HzAcc range = ±16 g Gyr range = ± 2000 deg/sMagn range = ±8 Gauss |
| Actigraph GT3X/GT3X+ | 3-axis accelerometer | Sample rate = 30–100 HzAcc range = ±6 g |

In 2015, Davidson and colleagues [34] proposed a preliminary investigation on the relationship between the clinical evaluation of gait alteration (6MWT) and the acceleration

data obtained with the StepWatch activity monitor. The StepWatch accelerometer is a small device used to monitor the number of steps while performing walking tasks. The unit was positioned at the ankle joint. The experimental study involved 16 DMD patients and 13 healthy controls. Both clinical and instrumental analysis highlighted locomotion dysfunctions in DMD patients (6MWT mean results: 600 m control group, and 400 m DMD patients; mean total steps/day: 7000 steps for the control group, 5000 steps for DMD patients) and a strong correlation (Pearson's correlation coefficient r(16) = 0.7–0.8) was depicted between the two assessment methodologies.

Le Moing and colleagues [35] applied inertial sensors in the analysis of human movements in non-ambulatory DMD children (7 patients, mean age = 18 years). The aim of the study was to investigate any relationships between clinical and instrumental monitoring. The ActiMyo is an innovative inertial sensor (3-axis accelerometer, 3-axis gyroscope, and 3-axis magnetometer) used to record linear accelerations and angular velocities over a long period of time. The ActiMyo was positioned on patients' wrist and four outcome measures were evaluated during the performance of validated tasks: the rotation rate, the ratio of the vertical component in the overall acceleration, the hand elevation rate, and the estimated power of the upper limb. Results pointed out that all the ActiMyo variables were representative of human movements and well correlated with clinical scores. The norm of the angular velocity and the mean elevation rate provided the most promising outcomes, with strong Spearman's rank correlation and good reliability (range of correlation rho(7) = 0.6–0.8).

Jacques and colleagues [36] investigated the physical activity in 76 participants with different muscular dystrophies (MD, 15 patients with DMD, mean age = 24 years). Physical activity was measured on seven consecutive days with the GENEActiv 3-axis accelerometer. Motor activity was expressed as average daily minutes spent physically active or average daily percentage of sedentary waking hours. In addition, muscle weakness and impaired 10 m walking time were monitored. Maximum voluntary contraction during plantar flexion was significantly associated with the anatomical cross-sectional area of the gastrocnemius medialis in DMD (Pearson's r(15) = 0.429, $p = 0.026$) and controls (Pearson's r(16) = 0.553, $p = 0.015$). Results pointed to a significant relationship between muscle weakness and sedentary behavior in MD patients. MD groups were 14–38% more sedentary than control groups, while DMD were more sedentary than Becker MD (14%), limb-girdle MD (8%), and facioscapulohumeral MD (14%). Sedentary behavior was associated with the lean body mass in DMD participants (Pearson's r(15) = $-0.45$, $p = 0.021$).

In January 2017, clinicians, physiotherapists, imaging experts, and patient advocacy group representatives participated in a two-day workshop discussing which outcome measures are relevant as primary and secondary endpoints in clinical trials for DMD patients. Straub and Mercuri [37] synthesized the principal concepts pointed out in the discussions and described outcome parameters that were considered for both ambulatory (6MWT, NSAA, stride length, cadence, knee extension strength, heart rate, step activity) and non-ambulatory (PUL, respiratory function, MyoGrip, MyoPinch, MoviPlate) DMD patients. In particular, the inertial sensors were confirmed as suitable and reliable instruments for the monitoring of motion activity over a long time period, for both lower and upper limbs.

In 2019, Fujii et al. [38] monitored the activity of seven non-ambulatory patients by means of one Silmee Bar-type Lite accelerometer, positioned on the wrist of the dominant arm. Physical activity was monitored for 8 consecutive hours. The jerk (rate of change of acceleration) was considered as an outcome measure of interest and the cumulative jerk along the 8 h of monitoring was estimated. Arm muscle strength was measured by a hand-held dynamometer during elbow flexion-extension movement. Clinical scales and subjective questionnaires were applied to the participants in the functional evaluation of the upper extremities. Results pointed to a strong and significant correlation between the cumulative jerk and the clinical score (Spearman's rho(7) = $-0.97$, $p < 0.001$ for the Brooke Upper Extremity Scale, Spearman's rho(7) = 0.81, $p < 0.03$ with the arm function scores for the DMD Functional Ability Self-Assessment Tool). Jerk values also had a very strong or

strong correlation with elbow flexion strength (non-dominant arm: Pearson's r(7) = 0.931, $p = 0.002$; dominant arm: Spearman's rho(7) = 0.75, $p = 0.052$).

Similar promising results were obtained by van der Geest and colleagues [39] in the home monitoring of 16 DMD patients (age 7–17 years). Physical activity was monitored for 1–3 days. Three MOX accelerometers were used for monitoring, positioned on the patient's wheelchair, the upper arm and the lower arm. Three principal outcome variables were analyzed: the intensity of activity, the level of arm elevation, and the elevation rate. The intensity of activity was calculated by integrating the acceleration during 1-minute episodes and summing this outcome over all three axes. The level of elevation was referred to the orientation of the arm during a period of 1 s. Data were categorized as low (<45°), middle (45°–90°), or high (>90°) elevation of the arm according to the upper arm sensor. The elevation rate was referred to the frequency of elevation of the arm from low to middle elevation and from middle to high elevation. Clinical scores were registered with the Brooke and PUL scales. A remarkably high correlation was obtained between the intensity of activity monitored at the upper arm and the lower arm (Spearman's rho(15) = 0.95, $p < 0.01$). Moreover, there was a significantly high correlation between intensity and PUL scale score (lower arm: Spearman's rho(15) = 0.82, $p < 0.01$; upper arm: Spearman's rho(15) = 0.84, $p < 0.01$). There was a moderate correlation between number of transfers per hour and PUL scale score from low–middle (Spearman's rho(15) = 0.59, $p < 0.05$) to middle–high (Spearman's rho(15) = 0.69, $p < 0.01$) and a high correlation between the total number of transfers per hour and the PUL scale score (Spearman's rho(15) = 0.76, $p < 0.01$).

The short communication written by Haberkamp and colleagues [40] pointed out and discussed the fact that European regulators provided an update on the recent regulatory consideration of a new endpoint that could be used in DMD therapeutic trials. Previously, regulators recognized the loss of ambulation as an important DMD milestone and the 6MWT as an endpoint. Five Gait Variables were assessed for their validity in measuring a patient's locomotion ability: the 95th centile of the stride velocity (SV95C), the median stride velocity, the 95th centile of the stride length, the median stride length, and the distance walked/recorded hour. Accuracy, reliability, and sensitivity of the Gait Variables were tested and discussed. European regulators considered that, for ambulatory DMD patients (5 years of age and above), SV95C is a reliable secondary endpoint when measured continuously in a home environment by a valid and suitable wearable device.

In 2020, Siegel and colleagues [41] used a wearable device to assess the sleep and motor function in DMD patients. The aim of the study was to describe the sleep impairment and its relationship with quality of life, and to evaluate relationships between rest-activity parameters, sleep quality, and 6MWT performance. A total of 54 DMD patients participated in the experimental study, but only 23 patients were enrolled in the actigraphy monitoring. The actigraphy Actiwatch 2 was used to quantify activity parameters. Participants wore the Actiwatch 2 for up to 10 days on their non-dominant wrist. Non-ambulatory participants had significantly lower sleep efficiency (percentage of time scored as sleep during time spent in bed), less wake time after sleep onset (minutes scored as wake during a sleep period), and less daytime activity than those in the ambulatory group. In contrast with previous research, there were no significant correlations between rest-activity data, SDSC (a questionnaire designed to identify sleep disturbances in pediatric populations during the previous 6 months) and PedsQL (a questionnaire adopted to register health-related QOL in both healthy children and pediatric patients).

Ann and colleagues [42] proposed a new relative coupling coefficient RCC to evaluate walking coordination and to distinguish between DMD and control children. 100 DMD patients and 100 control children were involved in the experimental study. Five APDM accelerometers were used for acceleration monitoring and units were positioned on forearms, shanks, and chest. The phase space reconstruction method was used to extract the non-linear dynamic feature of the monitored signals and the Local Manifold Structure Mapping method was used to estimate the RCC. Results verified the sensitivity of the proposed index to distinguish between DMD and control participants ($p < 0.001$). Moreover,

in accordance with clinical experience, the RCC showed that the coordination ability of DMD children during gait gradually declines with age.

Arteaga and colleagues [43] monitored the total physical activity in 49 DMD patients (mean age = 13 years) for 7 consecutive days. The Actigraph GT3X accelerometer was positioned on the wrist and the ankle of participants. Results pointed to significant differences ($p < 0.001$) in physical activity measures between DMD patients and control groups, and between ambulatory and non-ambulatory DMD patients. Moreover, results showed that locomotion ability and age can influence activity measures. The authors proposed a follow-up investigation [44] for the assessment of correlation between accelerometry measures and quantitative muscle testing (QMT). Accelerometer outcomes considered in the study were total vector magnitudes and awake vector magnitude. Results evaluated a strong Spearman's rank correlation for several variables combinations: indexed arm QMT with total wrist vector magnitude (rho(43) = 0.85, $p < 0.001$), total indexed QMT with total wrist vector magnitude (rho(43) = 0.8, $p < 0.001$), and indexed leg QMT with total ankle vector magnitude (rho(43) = 0.69, $p < 0.001$). Finally, all measures significantly declined over time.

In 2021, Lott et al. [45] registered the step activity for 7 days in ambulatory DMD boys (70 patients, mean age = 9 years) and compared the results with a control group (10 healthy subjects, mean age = 9 years). The Actigraph GT3X accelerometer was used to monitor the activity. Results demonstrated that, if wearing the accelerometer for at least 10 h/day for two consecutive days, the collected data can predict the average weekly amount (multiple linear regression model, strength prediction represented by the adjusted $R^2 = 0.80$). On average, the 70 DMD children took 63% of daily steps compared with unaffected control boys (5147 and 8138 steps, respectively; $p < 0.01$). To examine step activity across ages, the DMD subjects were classified into four groups based on 2-year age ranges: 5 to 6.9 years (n = 18); 7 to 8.9 years (n = 20); 9 to 10.9 years (n = 20); and 11 to 12.9 years (n = 12). An overall decline was noted with increasing age, with the three older age groups being significantly different from the first group.

McErlane and colleagues [46] investigated the utility of wearable technologies in physical activity assessment in three pediatric diseases: Niemann-Pick C (NPC), Juvenile Idiopathic Arthritis (JIA), and Duchenne muscular dystrophy (DMD). All patients completed the 6MWT with median results of 450 m, 325 m, and 434.5 m for the NPC, DMD, and JIA respectively. Accelerometric data were monitored with a wrist-worn accelerometer and three principal outcomes were evaluated: average daily maximum, average daily steps, and average steps per epoch. Results were compared among groups and the relationship between the 6MWT and wearable metrics was assessed. A moderate correlation was obtained between 6MWT and the average daily steps in JIA patients (Spearman's rho(8) = 0.68).

Poleur and colleagues [47] recruited 91 healthy volunteers (mean age = 16 years) for monitoring stride length, stride velocity, and walked distance per hour in different motion tasks (4-stair climb, 6MWT, 10-m walk test, and rise from floor assessments) at baseline and 12 months later. Parameters were obtained from ActiMyo accelerometers worn at the wrist and ankle of participants. The aim of the study was to obtain normative data for validating the new outcome measures. Results pointed out significant positive correlations (Spearman's rank correlation coefficient) of stride length with age and height of participants, and a significant increase in children's median stride length after the period. The 95th centile stride velocity was not correlated with age and was unchanged after one year.

Servais and colleagues [48] wrote a review article discussing the potential effect of novel digital endpoints on the drug development standard for DMD patients. The study underlined that suitable and reliable objective endpoints calculated with wearable devices may decrease the time required to perform clinical assessment. Moreover, the comparison between objective and clinical data could provide support in the clinical decisions to continue, stop, or change the therapy. Finally, objective monitoring across different periods of time could quantify the change of outcomes at different stages of the disease. Similarly, Youn et al. [49] proposed a systematic scoping review describing significant

digital biomarkers for neuromuscular disorders. A total of 10 studies were included in the analysis. Observational studies included research on patients with amyotrophic lateral sclerosis, Duchenne muscular dystrophy, and spinal muscular atrophy. The review pointed to the potential use of digital biomarkers for several pathologies, the current initial stage of their analysis, and possible future investigations for the verification of digital biomarker effectiveness.

In 2022, different studies on DMD patients were conducted. Jacques et al. [50] assessed 15 DMD patients at baseline and after 12 months in terms of body composition, isometric maximum voluntary contraction, plantar flexion, and physical activity. Daily physical activity was monitored using a tri-axial accelerometer (GENEActiv, Kimbolton, Cambs, United Kingdom). Accelerometric units were worn 24 h a day and continuously for 7 days on the participants' preferred wrist. Results pointed to significant changes in muscular strength, but no significant alteration of physical activity. Kaslow et al. [51] investigated the correlation between imaging metrics from cardiac magnetic resonance imaging (CMR) and functional valuations, including quantitative muscle testing (QMT), spirometry, and accelerometry. A total of 49 patients with DMD were evaluated at different time intervals (baseline, after 1 year, after 2 years). DMD patients wore an Actigraph GT3X accelerometer (Actigraph, Pensacola, FL, USA) on their dominant wrist and ankle for 7 days, 24 h per day. Participants were classified as awake for their accelerometer recordings between 6:00 am and 9:00 pm. The physical activity outcomes obtained for the wrist and ankle accelerometers were: minutes per day of wearing an accelerometer (min/day wear), minutes per day of wearing and awake (min/day awake), vector magnitude generated while wearing (VM total), vector magnitude generated per minute while wearing (VM/min wear), and vector magnitude generated per minute while wearing and awake (VM/min awake). Among the results, the imaging of the upper extremity musculature showed the most robust and reliable correlations with accelerometry (Spearman's rho(49) > 0.5, $p < 0.03$). Servais and colleagues [52] discussed the SV95C parameter as a new digital endpoint. The study highlighted some fundamental previous results concerning the decrease of spatial and temporal gait parameters (stride length, stride velocity, SV95C) after a short period of time and the relationship of these parameters with the clinical scores obtained from the 6MWT and NSAA. Finally, the recent studies of Morse and colleagues [53] and Nair and colleagues [54] focused on investigating any relationships of accelerometric data with sleep quality and magnetic resonance measures, respectively. Both these studies stressed promising results that can support the validity and reliability of accelerometric measures to investigate the progression of pathology in Duchenne patients.

Table 3 summarizes the principal results and limitations of the analyzed articles.

**Table 3.** Summary of main results and limitations of each study.

| Study | Results | Limitations |
| --- | --- | --- |
| Jeannet et al. [32] | A wide range of detailed parameters of daily activity can be reliably measured and quantified in DMD patients using a single monitoring device worn on the patient's chest | Small number of patients, no statistical analysis, no information about activity organization throughout the day, possible extrinsic factors that may have influenced the measure |
| Ganea et al. [33] | Significant differences in stride velocity, stride length, and variability of stride velocity. Moderate correlation between spatio-temporal parameters and clinical scale. Possibility to recognize and classify DMD patients with different levels of motor dysfunction | Small numbers of investigated gait parameters, only one clinical scale and only two groups characterizing the functional status |
| Davidson et al. [34] | Strong correlation between clinical 6MWT and accelerometry data | Small sample size, no investigation into the sensitivity of accelerometry data on the natural history of change in DMD |
| Le Moing et al. [35] | No difference between dominant and non-dominant hands, strong correlation of instrumental outcomes with clinical scores | Small sample of patients and large heterogeneity among them, difficult to establish reliability of results |

**Table 3.** *Cont.*

| Study | Results | Limitations |
| --- | --- | --- |
| Jacques et al. [36] | Significant relationship between muscle weakness and sedentary behavior in MD patients | No different level of physical activities |
| Straub et al. [37] | Inertial sensors were confirmed as suitable and reliable instruments for the monitoring of motion activity both in ambulatory and non-ambulatory DMD patients | Previous studies suffered from the lack of natural history data available at the time the trails were scheduled, no ideal outcome that can be used for all the studies |
| Fujii et al. [38] | Strong and significant correlation between the cumulative jerk of the acceleration norm and the clinical score | Small sample size, only 8 h of monitoring, small sample rate (15 Hz) of data acquisition |
| Van der Geest et al. [39] | Strong and significant correlation between objective outcomes and the clinical score | Small sample size, not all data available for all patients, no specific inclusion criteria for the selection of patients |
| Haberkamp et al. [40] | Stride Velocity 95th Centile continuously monitored in home environment was recognized as a new endpoint in DMD patients by European regulators | - |
| Siegel et al. [41] | Non-ambulatory participants had significantly lower sleep efficiencies, less wake time after sleep onset, and less daytime activity than those in the ambulatory group. There were no significant correlations between rest-activity data and SDSC and PedsQL questionnaires | Small sample size and limited statistical power to detect significant association with clinical data |
| Ann et al. [42] | The proposed RCC is a sensitive index to distinguish children with DMD and controls at the same age in terms of motor coordination | The complex methodology for the formulation of the coordination index |
| Arteaga et al. [43] | DMD patients spent most of their time in sedentary and low-intensity activities. Age and locomotion ability affected the monitoring of acceleration results | Small sample size and unequal distribution of participants among ambulatory, non-ambulatory, and control. No inclusion of anthropometric and clinical data |
| Killian et al. [44] | Moderate–strong correlation between QMT and acceleration measures | No analysis of correlation between the accelerometric measures and locomotion clinical tests (6MWT) |
| Lott et al. [45] | 2 to 5 days of activity monitoring predicted weekly step activity | Waist-worn device, large natural history of participants |
| McErlane et al. [46] | Utility of remote and continuous monitoring of physical activity in different pediatric diseases | Small sample size |
| Poleur et al. [47] | Significant positive correlations of the stride length with age and height of participants, significant increase of the median stride length. 95th centile stride velocity stable after one year | No upper limb movement analysis |
| Servais et al. [48] | Reliability, sensitivity, and efficacy of objective endpoints for DMD patients evaluated with wearable inertial devices | - |
| Youn et al. [49] | Potential use of digital biomarkers for several neuromuscular disorders | - |
| Jacques et al. [50] | No significant differences after 12 months from baseline in physical activity monitored with the accelerometer | Sample size, short time monitoring |
| Kaslow et al. [51] | Imaging of the upper extremity musculature (triceps and biceps) demonstrated the most robust correlations with accelerometry | No distinction between ambulatory and non-ambulatory patients, limitations in the CMR protocol |
| Servais et al. [52] | Significant decrease of stride length 95th percentile, median stride velocity, and SV95C after 6 months. All variables have moderate–strong correlations with clinical scores | - |
| Morse et al. [53] | Possibility to differentiate sleep and activity phases through measuring the accelerometer data; no significant differences among different groups of muscular disease | Small sample size for each pathological groups, patients from the same clinical center |
| Nair et al. [54] | Significant correlation between accelerometry, magnetic resonance, and functional measures. Significant decrease of step activity in older patients | No covariation with external factors, different genetic mutations among DMD patients, no examination of intensity of physical activity |

## 4. Discussion

The literature search focuses on analyzing the current use of inertial measurement devices for the objective evaluation of meaningful outcome measures in Duchenne muscular dystrophy. The wearable instrumentation has been described in terms of principal characteristics, positioning, and measured variables. Significant clinical discoveries and results related to the pathology are highlighted, to identify clinical guidelines for experimental tests and normative data of parameters of interest, and to underline a possible relationship between instrumental and clinical analysis.

The discussion of the selected articles is presented from three main points of view: technical, biomechanical, and clinical.

### *4.1. Technical Perspective*

In all research, the compact and easy-to-use configuration of wearable sensors has proved to be a positive and crucial advantage for physical activity monitoring during daily routine, home monitoring, and tele-rehabilitation. This solution allows possible limitations to be overcome, namely those due to clinical analysis in laboratory settings and indoor environments, and the alteration of movements caused by the consciousness of being observed. Moreover, continuous and prolonged monitoring allows the registration of a large amount of data, which increases the robustness and reliability of the final results. Instruments' small dimensions and their lack of invasiveness contribute to acceptance of wearing them for a long interval of time for both patients and caregivers. Several typologies of wearable devices were used in the current research (Table 2), both customized systems [32,33] and commercial products [41,42,47,50]. The configuration of a 3-axis accelerometer was shown to be the most widespread in the past, but in the last few years studies have proposed the use of inertial sensors, including accelerometers, gyroscopes, and magnetometers. Most of the studies used the accelerometric measurement system as actigraphy, in particular to monitor patients' physical activity levels [34,43], to differentiate the type of activity performed (walking, sitting, lying) [33], to distinguish between sedentary and active behavior [36,50], to represent sleep quality [41,53], and to assess the total amount of steps during walking in ambulatory subjects [45,46]. The integration of a 3-axis gyroscope and a 3-axis magnetometer contributes to the definition and calculation of objective outcomes suitable for measuring the human segment's orientation and for describing more complex movements, also involving the upper body part of the human [35,39,42].

It is important to underline that, among the different wearable devices, the ActiMyo sensor has been recognized as a Class I medical device [48]. It is composed of a base station for charging units and data transmission, and two wearable units. ActiMyo units continuously measure acceleration, velocity, and orientation over prolonged intervals of time and with high accuracy. The device can be worn by the subject both at the wrist and ankle joints. Moreover, studies demonstrated its potential in the identification of meaningful clinical improvements. Based on European regulatory requirements, the wearable sensor ActiMyo is currently the only suitable and validated device for gathering SV95C data in clinical gait trials. Other acquired endpoints are likely to be identified and verified in both ambulatory and non-ambulatory neuromuscular diseases [48].

Based on the performed motion, sensors have been positioned in correspondence to different human body parts (Figure 2A). In particular, results pointed out that the most suitable configurations for monitoring lower-body activities and evaluating walking steps require the positioning of sensors on the pelvis and/or ankle joints of the patient. When monitoring upper-body motions, sensors must be referred to the chest, the upper arm, and/or the lower arm. The positioning of inertial sensors on the wrist joints (dominant and/or non-dominant arm) revealed themselves as suitable for movements involving both upper- and lower-body segments.

### 4.2. Biomechanical Perspective

Several biomechanical variables were obtained from acceleration and angular velocities raw data. These variables were selected and investigated with a strong dependence on the human task performed. The first and most commonly proposed analysis dealt with the differentiation between sedentary behavior and physical activity, followed by recognition of the activity (walking, sitting, lying down) in a home environment. These analyses can be conducted for all DMD patients, without considering walking ability as possible inclusion/exclusion criteria. Nevertheless, significant differences were stressed in the comparison between ambulatory and non-ambulatory DMD patients [43].

In case of ambulatory patients, both posture and walking parameters have been analyzed. Due to the crucial treatment goal of maintaining walking ability as long as possible, several studies focused on the evaluation of gait parameters, such as stride velocity, stride length, cadence, number of meters walked per hour, and average daily steps. Among them, as already stressed, European regulators considered SV95C to be an acceptable secondary endpoint in pivotal or exploratory drug therapeutic studies for regulatory purposes, when measured continuously and in a home environment by a valid and suitable wearable device [40]. This crucial result has been reached after numerous investigations on accuracy, reliability, and sensitivity of the selected parameter. It is not only an important and recognized assessment of the potential of objective biomechanical parameters as outcome measures, but also a fundamental milestone in the recognition of wearable devices as suitable instrumentation for clinical trial assessments. Despite the numerous studies and the confirmation of significant differences in walking ability between MD patients and healthy controls, the lack of investigation into spatio-temporal parameters describing the different phases and subphases of a gait cycle, such as stance duration, swing duration, single and double support, step length, and step width, must be stressed. Moreover, despite large interest in the evaluation of gait symmetry and the application in other clinical circumstances, only one study proposed the investigation of gait smoothness based on the spectral entropy of the acceleration norm monitored at the trunk [33], while another proposed a new relative coupling coefficient index (RCC) for assessing motor coordination during the walking trial [42]. Additional future investigations might be conducted to enhance the biomechanical description of gait characteristics.

Only a few studies focused on the evaluation of objective measures in non-ambulatory DMD patients [35,38,39]. Indeed, it is more difficult to define and describe repetitive and cyclic movement for the investigation of upper limb dysfunctions. Acceleration and angular velocity data were combined and post-processed to define parameters of interest, such as the rotation rate, the hand elevation rate, the ratio between the vertical and the overall acceleration, the estimated mechanical power of the upper limb, the jerk, and the cumulative jerk of acceleration norm. All these parameters were preliminarily investigated and discussed, stressing their correlation with clinical and functional scales (PUL, Brooke). Nevertheless, the majority of studies proposed instrumental evaluation with IMUs during long periods of home monitoring [38,39], while only one study [35] used instrumental monitoring in combination with the functional scale during the simulation of daily activities in a laboratory setting. Moreover, the kinematic orientation of different human body parts (trunk, upper arm, lower arm) performed during validated tasks of the functional scales were not investigated. The definition and validation of suitable biomechanical parameters that can be simultaneously combined with clinical evaluation and recognized as clinical outcome measures for DMD patients are still open challenges and under research.

### 4.3. Clinical Perspective

All articles demonstrated meaningful relationships between clinical and instrumental evaluations. Experimental tests focused on the estimation of correlation between objective outcomes monitored by the inertial sensors and the clinical scores assigned through functional scales, revealing moderate (“r” or “rho” > 0.5) and strong correlations (“r” or

"rho" > 0.7). These promising results were obtained for tasks involving both upper and lower limbs.

An important aspect that should be emphasized is the complementary relationship between clinical and instrumental evaluation. In fact, wearable sensors and related outcome measures can be used to support the functional analysis conducted by the physiotherapist, not to replace it. Functional outcome measures for DMD patients in clinical trials have traditionally consisted of timed tests and motor scales performed during hospital visits (6MWT, NSAA, Brooke, PUL) and they proved to be reliable and reproducible. A common disadvantage of traditional scales is that they may not capture real-world conditions. Additionally, multiple external factors such as motivation, fatigue, time of day, age, developmental stage, and behavior are known to influence performance in these clinical assessments. Moreover, clinical evaluation could be affected by the physiotherapist's subjective opinion. Innovative, technological, and wearable tools provide the opportunity to identify outcome measures that are objective and clinically relevant. The implementation and validation of qualified, digitally measured endpoints enables accurate and continuous assessment of the progression of the pathology and related motor dysfunctions, the evolution and effect of endurance during different periods of the day, or the potential benefits of an investigational treatment in a real-world setting.

## 5. Conclusions

The current study presents an overall review of inertial sensors' use in the identification of outcome measures in the DMD. The search was conducted on different literature databases and with specific inclusion/exclusion criteria. A total of 23 articles were selected and analyzed. Results confirmed the suitability and reliability of IMU outcomes to describe DMD motor dysfunctions, especially in the home environment. Moreover, a strong correlation between instrumental home monitoring and clinical assessment was depicted in several analyses and with different clinical scales. The majority of previous studies used IMU sensors for the differentiation of time spent in different physical activities during the day and/or for the quantification of parameters distinctive of human locomotion. Regulators stipulated the Stride Velocity 95th Centile as the first validated and suitable digital endpoint when continuously measured by a wearable device. Nevertheless, only a few studies have focused on the movement analysis of the upper body and the identification of objective parameters for the characterization of motor dysfunctions. This review identified the current research trends, results, and limitations of previous studies and the open challenges that might be discussed in future research.

**Author Contributions:** Conceptualization, E.P., I.C., T.M. and F.R.; methodology, E.P., R.D., I.C. and C.D.; validation, E.P., I.C. and F.R.; formal analysis, E.P., I.C. and F.R.; investigation, E.P., R.D., I.C. and C.D.; resources, E.P.; data curation, E.P.; writing—original draft preparation, E.P.; writing—review and editing, E.P., R.D., I.C., C.D., T.M. and F.R.; visualization, T.M., L.G. and F.R.; supervision, L.G. and F.R. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** Not applicable.

**Conflicts of Interest:** The authors declare no conflict of interest.

## Appendix A

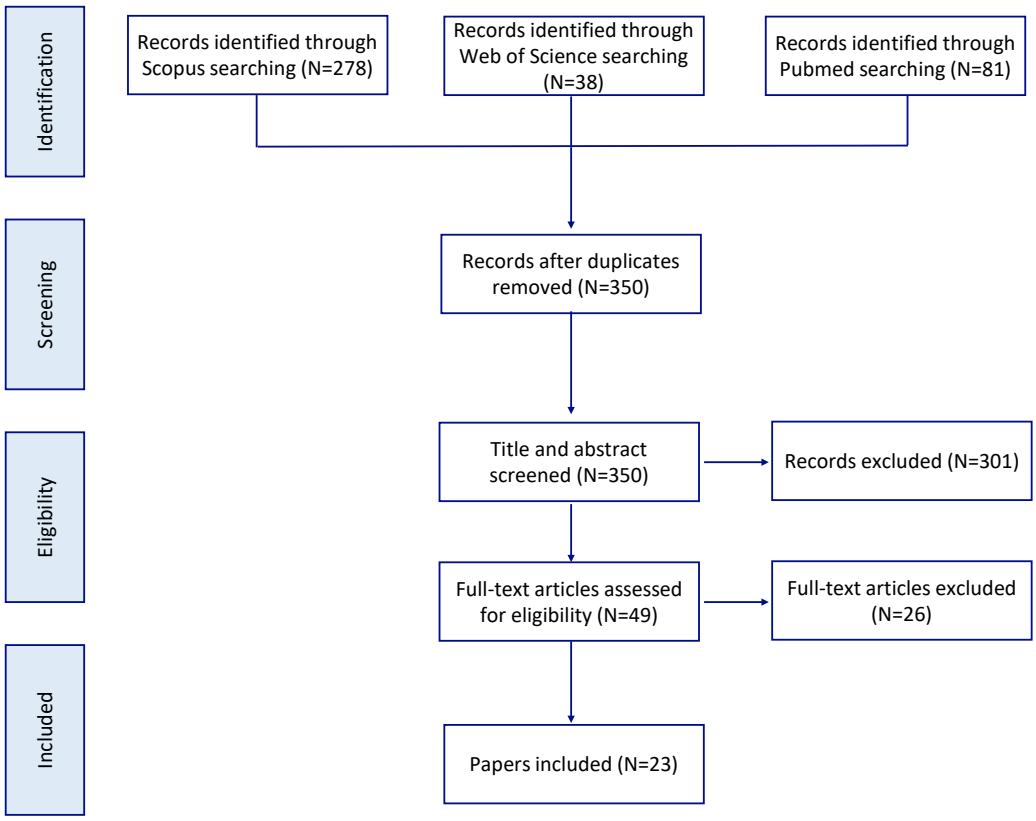


**Figure A1.** Literature search scheme based on PRISMA flowchart.

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