Physical Fitness and Exercise Training on individuals with Spina Bifida: a systematic review

Ana Oliveira[a], Cristina Jácome[a], Alda Marques[a, b]

[a] School of Health Sciences, University of Aveiro (ESSUA), 3810-193 Aveiro, Portugal

[b] Unidade de Investigação e Formação sobre Adultos e Idosos (UniFAI), 4050-313 Porto, Portugal

1[st] Author:
Name: Ana Oliveira
email: alao@ua.pt

2[nd] Author:
Name: Cristina Jácome
email: cristinajacome@ua.pt

3[rd] Author (Corresponding author):
Name: Alda Marques
School of Health Sciences, University of Aveiro (ESSUA), Agras do Crasto - Campus Universitário de Santiago - Edifício 30, 3810-193 Aveiro, Portugal; Tel.: +351 234 372 462; Fax: +351 234 401 597; E-mail address: amarques@ua.pt

RESEARCH HIGHLIGHTS

- Individuals with SB have impaired physical fitness;
- Data on body composition, flexibility and neuromotor fitness in SB are scarse;
- Exercise training improve cardiorespiratory endurance and muscle strength.

Physical Fitness and Exercise Training on individuals with Spina Bifida: a systematic review

ABSTRACT

Spina Bifida (SB) is characterised by several physical impairments; however data on physical fitness and on the benefits of exercise training in individuals with SB are dispersed in the literature. Thus, this systematic review aimed to describe i) physical fitness components (cardiorespiratory endurance, muscle strength, body composition, flexibility and neuromotor) and ii) exercise training effects on the physical fitness of individuals with SB. CINAHL, MEDLINE and EMBASE were searched from January to March 2013 and updated in December 2013. Twenty-three studies were included. A summary of the results was performed using a best-evidence synthesis. Participants with SB had lower cardiorespiratory endurance (- 32-54% in VO_2peak) and muscle strength (- 58-90%) and higher body fat (159%) than their healthy peers. Mobility restrictions were present in 26.3-61% of participants. No data on neuromotor fitness were found. Aerobic and strength training improved participants' cardiorespiratory endurance (effect sizes 0.78-1.4) and muscle strength (effect sizes 0-0.59). Individuals with SB have impaired cardiorespiratory endurance, muscle strength, body composition and flexibility when compared to healthy peers. Exercise training seems to improve two of these fitness components (cardiorespiratory endurance and muscle strength). Nevertheless, the heterogeneity of the studies' designs, methods and instruments used limits the establishment of firm conclusions and highlights the need for further research.

Key Words: Spina Bifida; Physical Fitness; Exercise Training.

1. Introduction

Spina Bifida (SB) is a consequence of a malformation in the caudal neural tube, which results in a heterogeneous range of structural defects affecting the spinal cord, cerebrum and brainstem (Botto, Moore, Khoury, & Erickson, 1999; Mitchell, et al., 2004). The worldwide incidence is on average 2-8 per 10000 live births, and, due to medicine advances, aproximetly 60% of individuals with SB are expected to survive until early adulthood (Chamberlain & Kent, 2005; Kondo, Kamihira, & Ozawa, 2009). The four most common types of SB are SB occulta, SB cystica, meningocele, lipomyelomeningocele (LMMC) and myelomeningocele (MMC), being MMC the most severe and common presentation of the disease (Botto, et al., 1999; Jenkinson, et al., 2011; National Health Service, 2011).

Depending on the type and level of the lesion, impairments related to defits in cognition, motor function and sensory function may arise (Özek, Cinalli, & Maixner, 2008; Vinck, et al., 2010). These imparments place individuals with SB at an increased risk of developing inactive lifestyles (Roebroeck, Jahnsen, Carona, Kent, & Chamberlain, 2009). Recent studies have shown that individuals with SB have reduced physical fitness levels compared with their healthy peers, potentiating the risk of developing obesity and cardiovascular diseases (Buffart, Roebroeck, et al., 2008; Buffart, van den Berg-Emons, Burdorf, et al., 2008). However, data on physical fitness components (cardiorespiratory endurance, muscle strength, body composition, flexibility and neuromotor fitness) in individuals with SB are dispersed in the literature, which makes difficult to draw strong conclusions (American College of Sports Medicine, 2009; Garber, et al., 2011).

Exercise training has been recommended to improve physical fitness components in individuals with SB, aiming at enhancing their health and overall well-being (Buffart, van den Berg-Emons, van Wijlen-Hempel, Stam, & Roebroeck, 2008; Dickens & McMillen, 2003). In other neurological diseases, such as Cerebral Palsy and Spinal Cord Injury, previous reviews concluded that there is high evidence that exercise training improves participants' physical fitness (Hicks, et al., 2011; Papavasiliou, 2009; Verschuren, Ketelaar, Takken, Helders, & Gorter, 2008). Regarding SB, one review from Dagenais, et al. (2009) reported muscle strength improvements after electrical stimulation, exercise training and/or motor skills training. However, the effect of these interventions was analyzed only in one physical fitness component - muscle strength – and in one SB subtype - MMC. Therefore, the benefits of exercise training on the main components of physical fitness are not systematically documented. A systematic review would be valuable to provide health professionals with the best evidence available on exercise training and guide interventions for individuals with SB. The present systematic review provides a critical synthesis on physical fitness components and on the effects of exercise training on these components in individuals with SB.

2. METHODS

2.1. Data Sources and Searches

A systematic literature search, restricted to articles published in Portuguese, English and French, was conducted from January to March 2013 and updated in December 2013. The following electronic databases were searched: CINAHL (1982-present), MEDLINE (1980-present) and EMBASE (1980-present). A specific search was conducted in the Cochrane Library to exclude the existence of reviews with the same objective as the present one. For the purpose of this review, physical fitness was defined as: cardiorespiratory endurance (ability to perform large muscle, dynamic, moderate-to-high intensity exercise for prolonged periods, assessed by maximal or submaximal exercise tests), muscle strength (ability of a muscle to exert force), body composition (relative amount of muscle, fat, bone and other vital parts of the body), flexibility (range of motion of a specific joint) and neuromotor fitness (motor skills like balance, coordination, gait and agility) (American College of Sports Medicine, 2009; Garber, et al., 2011).

The following search terms were applied: [(Spina Bifida OR Meningomyelocele OR Meningocele OR Spina Bifida Occulta OR Spina Bifida Cystica OR Spinal Dysraphism) AND (cardiorespiratory fitness OR respiratory fitness OR aerobic capacity OR aerobic fitness OR aerobic exercises OR physical activity OR fitness OR physical fitness OR physiotherapy OR muscle strength OR body composition OR body fat OR flexibility OR neuromotor fitness OR balance OR coordination OR gait OR agility)]. The reference lists of the selected studies were also scanned for potential eligible articles. Articles were included if they i) were experimental (participants are randomly assigned to experimental and control groups), quasi-experimental (participants are not randomly assigned to experimental and control groups) or observational studies (studies that make observations of human behavior) (Jackson, 2009; Marczyk, DeMatteo, & Festinger, 2005); ii) included individuals with SB; iii) assessed physical fitness (including at least one of the following parameters: cardiorespiratory endurance, muscle strength, body composition, flexibility and neuromotor fitness) and/or exercise training effects on physical fitness. Articles published before 1980, not providing quantitative data on physical fitness and not individualizing the results of participants with SB, as well as case reports and expert opinions, were excluded.

This review was reported according to the systematic review method proposed by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) (Liberati, et al., 2009; Moher, Liberati, Tetzlaff, Altman, & PRISMA group, 2009).

2.2. Study selection

Two reviewers independently assessed all the potential studies identified. A third reviewer was consulted to solve any disagreements. The studies were selected based on their titles and abstracts; when the title and abstract were relevant to the purpose of the review, the full-text article was read carefully to decide its inclusion.

2.3. Quality Assessment and Data Extraction

Two independent reviewers assessed the methodological quality of the studies with a checklist adapted by Petticrew and Roberts (2006) based on the 'Crombie criteria' to assess cross-sectional studies (Crombie, 1996). This checklist has been used in previous systematic reviews (Barnard, Thomas, Royle, Noyes, & Waugh, 2010). The checklist comprises 8 quality criteria: research design, recruitment strategy, response rate, sample representativeness, measures and statistics used and power. The methodological quality of the studies is directly proportional to the number of quality criteria met (i.e., a high number of quality criteria met indicates high methodological quality). A consensus method was used to solve disagreements between reviewers. The consistency of the quality assessment performed by the two reviewers was explored with an inter-rater agreement analysis using the Cohen's kappa. The value of Cohen's kappa ranges from 0 to 1 and can be categorized as slight (0-0.2), fair (0.21-0.4), moderate (0.41-0.6), substantial (0.61-0.8) or almost perfect (≥0.81) agreement (Landis & Koch, 1977). The statistical analysis was performed using PASW Statistics (version 18.0, SPSS Inc., Chicago, IL).

Data from the selected studies were independently extracted by two reviewers. Disagreements were discussed until a consensus was reached. If no consensus could be reached, a third reviewer was consulted. A data extraction form was designed to record the following characteristics for each study: publication details (authors, year of publication); study design; participants' characteristics (total number, % male and age range); setting and country; details of the assessment tools (studies without interventions) or of the intervention (type of intervention and comparison groups, if existed; type of training - cardiorespiratory, resistance, or mixed, training mode - treadmill walking, weight training, dose - intensity, frequency of delivery, timing - during or after usual care, length of training - duration and program length); outcome measures and results.

2.4. Data Syntheses and Analysis

Data from the physical fitness components of participants with SB were, whenever possible, compared with values from age-matched healthy peers.

This was possible for peak oxygen consumption (VO_2peak) and six minute walk distance (6MWD), since the included studies assessed participants with SB and healthy participants. However for muscle strength, flexibility and body fat (BF), data from healthy peers was not always available. In the absence of these data, comparisons with established reference values were performed.

Due to the great amount of diverse measures used in the selected studies, a meta-analysis was not possible to conduct. Instead, a summary of the results was performed using a best-evidence synthesis (Slavin, 1995; van Tulder, Furlan, Bombardier, & Bouter, 2003). This rating system takes into account the number, methodological quality and consistency of outcomes of the studies, in 5 levels of evidence: i) strong evidence, provided by generally consistent findings in multiple (≥2) high-quality studies; ii) moderate evidence, provided by generally consistent findings in 1 high-quality study and 1 or more low-quality studies or in multiple low-quality studies; iii) limited evidence, when only 1 study is available or findings are inconsistent in multiple (≥2) studies; iv) conflicting evidence, provided by conflicting findings in case-control studies (<75% of the studies reported consistent findings) and v) no evidence, when no case-control studies are found (Slavin, 1995; van Tulder, et al., 2003).

To analyze the effects of exercise training on physical fitness, effect sizes were computed for the outcomes of interest. Effect sizes (ES), calculated using Comprehensive Meta-Analysis (CMA) software, version 2 (Borenstein, Hedges, Higgins, & Rothstein, 2005), were interpreted as low (0.2), medium (0.5) and high (0.8) effect magnitudes (Cohen, 1988).

3. RESULTS

3.1. Study selection

The databases search identified 1196 records. After duplicates removal, 587 records were screened for relevant content. During the title and abstract screening, 537 articles were excluded. The full-text of 50 potentially relevant articles was assessed and 28 articles were excluded due to the following reasons: i) did not provide quantitative data on physical fitness (n=15); ii) did not individualize the results of participants with SB (n=7); iii) assessed the validity and reliability of outcome measures in physical fitness (n=3); iv) did not include participants with SB (n=2) and v) were systematic reviews (n=1). Therefore, 22 original articles were selected. The search for relevant articles within the reference list of the selected articles retrieved 1 study. Therefore, a total of 23 studies were included in this review (figure 1).

(insert figure 1 about here)

3.2. Study characteristics

All studies assessing physical fitness were cross-sectional (n=20), seventeen studies provided information on cardiorespiratory endurance, nine on muscle strength, seven on body composition and three on flexibility. No studies on neuromotor fitness were found. In total, 625 participants with SB (52% male) enrolled in the included studies, 475 diagnosed with MMC, 28 with LMMC and 122 not specified. All studies included children (≤18yrs old) and eight also included adults. Most studies described the participants' ambulatory status according to the classification of Hoffer, Feiwell, Perry, Perry, and Bonnett (1973), which defines 4 levels: i) community - independent outdoor ambulation with or without use of braces or assistive devices and/or use of wheelchair for longer distances; ii) household - use of braces or assistive devices for indoor ambulation and/or use of wheelchair for outdoor locomotion; iii) nonfunctional - walking only in therapeutic situations and iv) none - wheelchair dependent. Two studies have strictly followed this classification, seven studies have grouped nonfunctional participants and wheelchair dependents in one level (non-ambulators), six studies have added a new ambulatory status level (normal) to describe participants who walked without the use of aids and one study have grouped household participants, nonfunctional participants and wheelchair dependents in one single level (non-ambulators). Additionally, seven studies have not used this classification to describe participants' ambulatory status. Therefore, to facilitate comparisons, participants were, whenever possible, divided in two categories: ambulators (including normal, community and household ambulators) and non-ambulators (including nonfunctional ambulators and wheelchair dependents). Accordingly, 296 participants were ambulators and 180 non-ambulators.

From the three studies analyzing the exercise training effects on physical fitness, 2 were quasi-experimental [A1- one group pretest-posttest design (Widman, McDonald, & Abresch, 2006) and B1- untreated-control group design that uses dependent pretest-posttest samples designs (Andrade, Kramer, Garber, & Longmuir, 1991)] and one was a true experimental (de Groot, Takken, van Brussel, et al., 2011). A total of 53 participants with SB (55% male), age ranging from 8 to 17.5 years old, were included in these studies.

3.3. Quality assessment

As presented in table 1, all studies presented an appropriate research design, used objective measures and appropriate statistical analysis. One study failed in reporting the recruitment strategy used (Agre, et al., 1987) and eleven did not report the response rate. Only the studies conducted by de Groot, et al. used a representative sample (de Groot, Takken, van Brussel, et al., 2011) and performed a power calculation (de Groot, et al., 2009; de Groot, Takken, van Brussel, et al., 2011) (table 1). The agreement between the two reviewers was substantial (k=0.78; 95% CI 0.54-1; $p<0.001$).

(insert table 1 about here)

3.4. Synthesis of the results

3.4.1. Physical fitness

Results on physical fitness components are summarized in table 2.

3.4.1.1. Cardiorespiratory endurance

Cardiorespiratory endurance was assessed using supramaximal, maximal or submaximal tests. Only de Groot, et al. (2009) used a supramaximal test consisting of walking in a treadmill for 3 minutes at 110% of participants' maximum speed (achieved in a maximal test). Maximal tests included arm or cycle ergometry and graded treadmill. Submaximal tests, specifically the six minute walk test (6MWT), were also used.

Participants with SB present a reduction of 32-54% in VO_2peak (13.8-46.3mL·Kg^{-1}·min^{-1}) compared with age-matched healthy participants (21-

51mL·Kg^{-1}·min^{-1}). Conflicting evidence regarding VO_2peak levels and ambulatory status was found. Five studies reported that participants with higher levels of ambulatory status had significantly higher VO_2peak. Three other studies, however, did not reach a statistically significant difference. Similarly to healthy population, male participants had a higher VO_2peak than female participants (table 2).

The maximum workload capacity (maximum workload achieved during an exercise test) found in participants with SB was 48.9-158W, 13-25% lower than values from healthy peers (table 2).

Five studies reported the distance walked in the 6MWT. In this test, a higher distance walked indicates higher cardiorespiratory endurance. Results ranged from 391 to 424m (approximately 60–62% of the predicted for healthy peers). Studies found significant i) lower 6MWD in participants with SB compared to reference values and ii) higher 6MWD in participants with SB with normal ambulation compared with community ambulation (408.5-473m vs. 333.4-357m). Schoenmakers, et al. (2009) also found that the 6MWD was higher in participants with LMMC than in those with MMC (424m vs. 353m) (table 2).

According to a best-evidence synthesis, there is moderate evidence on decreased cardiorespiratory endurance in individuals with SB compared to healthy peers.

3.4.1.2. Muscle strength

The methods and protocols used to evaluate muscle strength varied considerably across studies, i.e., manual muscle testing, using scales ranging from 1 to 5 and from 0 to 5 (higher scores imply high strength); maximal handgrip strength; isometric strength, “break” testing method and peak dynamic strength (table 2).

Muscle groups assessed also varied. The upper extremity group muscles assessed were: shoulder flexors and extensors, elbow flexors and extensors and hand flexors. Participants with SB presented lower strength on shoulder flexors (- 10-23%) and on shoulder extensors (- 23-34%) than reference values from healthy peers (Danneskiold-Samsoe, et al., 2009; Widman, Abresch, Styne, & McDonald, 2007). Regarding elbow muscles, no differences were observed between participants with SB and reference values of healthy peers (Danneskiold-Samsoe, et al., 2009). For all these muscles groups, males presented higher values than females, both in healthy participants and participants with SB (Widman, et al., 2007). Hand grip strength was assessed in three studies and varied from 38N to 686N. Norrlin, Strinnholm, Carlsson, and Dahl (2003) found that hand grip strength of participants with MMC was 71.03±23.3% of the predicted for healthy peers (table 2).

Regarding the lower extremity muscles, strength was measured in: hip extensors, abductors and flexors, knee extensors and flexors, calf muscles and plantar and dorsal ankle flexors. Hip extensors strength ranged from 2 to 5 in manual testing and from 9±36N to 161±31N during isometric contractions (normative values range from 202N in females and 326N in males (Danneskiold-Samsoe, et al., 2009)). Hip flexors and hip abductors were only evaluated through manual testing and presented values between 4-5 and 2-5, respectively. Knee extensors strength was generally above 4 in manual testing and between 4±16N and 161±31N during isometric contractions (normative values range from 96.6N in females and 424N in males (Danneskiold-Samsoe, et al., 2009)). Knee flexors (≥4), calf muscles (2.9-4), plantar (0-5) and dorsal (2-5) ankle flexors were only assessed through manual testing (table 2).

Conflicting evidence regarding muscle strength and ambulatory status was found. Danielsson, et al. (2008) and Norrlin, et al. (2003) reported higher levels of muscle strength in ambulators (≥4 in manual testing and 74.5±25.2N in dynamometry) than in non-ambulators (≤3 in manual testing and 57.9±13.6N in dynamometry). Conversely, Buffart, van den Berg-Emons, van Wijlen-Hempel, et al. (2008) found subnormal muscle strength in 79% of the ambulators and in 54% of the non-ambulators. Another study from Buffart, van der Ploeg, et al. (2008) also showed that subnormal muscle strength was more common in participants with SB not enrolled in sport activities (52% in sport practitioners vs 81% in non-practitioners).

Studies comparing muscle strength of participants with SB with healthy peers reported that upper and lower extremity muscle strength were in general significantly reduced in approximately 64-90% ofin females and 58-77% in males (table 2).

According to a best-evidence synthesis, there is moderate evidence that individuals with SB have decreased muscle strength compared with healthy peers.

3.4.1.3. Body composition

Body composition was assessed with thickness of skinfolds and dual energy x-ray absorptiometry (table 2). Four studies reported on the sum of 4 skinfolds (biceps, triceps, subscapular and suprailiac) presenting values between 74.4-74.8mm, corresponding to approximately 159% of the reference values for healthy peers. The percentage of BF varied between 23.1% and 46.2%

(normative values range from 16.5-25.9% in females and 9.2-20.6% in males (American College of Sports Medicine, 2009)) and was higher in females, non-ambulators and in those with no participation in sports. Widman, et al. (2007) compared the percentage of BF between participants with SB and healthy participants and concluded that BF among participants with SB was significantly higher (table 2).

Moderate evidence supports that individuals with SB have higher values of BF when compared with healthy peers.

3.4.1.4. Flexibility

Studies provided data on flexibility through three different procedures: i) passive mobilization of the hip and knee joints while participants were lying supine and passive mobilization of the ankle joint while participants were sitting, ii) hip and knee joints degrees according to Cole (1982) recommendations and iii) hip, knee and ankle joints degrees according to the American Academy of Orthopedic Surgeons (table 2). Approximately, 26.3-61% of the participants had mobility restrictions in at least one of the following joints: hip, knee or ankle. Non-ambulators were those with more contractures and flexibility was more impaired in females (females 67% vs. males 54%).

Moderate evidence exists on decreased flexibility in individuals with SB compared to healthy peers (table 2).

3.4.1.5. Neuromotor fitness

None of the included studies assessed neuromotor fitness.

(insert table 2 about here)

3.4.2. Effects of exercise training

The effects of exercise training on physical fitness components are summarized in table 3. The VO_2peak was used in one study to compare a home based treadmill training protocol (2 times a week during 12 weeks with incremental speed and duration based on participant's reports of fatigue and heart rate peak) and usual care. It was found that treadmill training has a moderate/large effect on VO_2peak (mean change in experimental group 1.4±3.7mL·Kg^{-1}·min^{-1}; ES=0.78). Maximum workload capacity was analyzed by Widman, et al. (2006) through a ramp protocol on a magnetically braked arm ergometer. After the upper extremity exercise training (at least 20 minute per session, 3 times a week during 16 weeks), participants' maximum workload capacity increased significantly (pre 65.5±9.7W vs. post 77.7±7.1W; p<0.015; ES=1.40). Functional exercise capacity after exercise training was measured by Andrade, et al. (1991) using the 9' run modified form and by de Groot, Takken, van Brussel, et al. (2011) using the 6MWT. The distance travelled increased significantly within the exercise training groups (9' run: pre 683±330m vs. post 887±322m; 6MWD: pre 344.8±125.3m, mean change of 38.7+34.6m; p<0.05). However only in the study from de Groot, Takken, van Brussel, et al. (2011), the distance was significantly different from the control group (ES=1.08) (table 3).

Muscle strength significantly increased (ES 0-0.59) after a 10 week exercise training protocol (90 minutes of aerobic and strength exercises performed once a week) (Andrade, et al., 1991). BF did not change significantly after exercise training (ES=0.05)(Andrade, et al., 1991; de Groot, Takken, van Brussel, et al., 2011) (table 3).

There is moderate evidence that exercise training increase cardiorespiratory endurance and muscle strength and that it does not change body composition in participants with SB. No studies were found regarding exercise training effects on flexibility or neuromotor fitness.

(insert table 3 about here)

4. DISCUSSION

The purpose of the present systematic review was to provide a critical synthesis on physical fitness components and on the effects of exercise training on these components in individuals with SB. Two moderate findings emerged from this systematic review: i) individuals with SB have impaired cardiorespiratory endurance, muscle strength, body composition and flexibility compared with healthy peers/normative data and ii) cardiorespiratory endurance and muscle strength components seem to improve with exercise training.

Cardiorespiratory endurance was found to be lower in individuals with SB compared with age-matched healthy peers. Some of the included studies also shown that individuals with high levels of ambulatory status (normal or community ambulators) have better levels of cardiorespiratory endurance. Poor cardiorespiratory endurance in childhood has been described as having important consequences for the development of cardiovascular disease in later life (Berenson, 2002). Moreover, moderate and high levels of cardiorespiratory fitness have been associated with lower risk of mortality from all-causes regardless of gender, age and body composition (Lee, Artero, Sui, & Blair, 2010). Therefore, to prevent cardiovascular diseases and reduce mortality rates, it is crucial to enhance cardiorespiratory endurance in individuals with SB since early childhood. This review found moderate evidence that exercise training programs increase cardiorespiratory fitness in individuals with SB. Therefore, a key factor to enhance cardiorespiratory endurance in this population, and thus their survival, might be the integration of aerobic training in their treatment plans since early life.

Lower levels of muscle strength, in both upper and lower extremities, were found in individuals with SB when compared with age-matched healthy peers. As expected, muscle strength was higher in individuals with better ambulatory status, nevertheless conflicting evidence was found. The relatively better performance of non-ambulators compared to ambulators, together with similar elbow muscle strength in individuals with SB and healthy peers, might be explained by the relatively higher muscle strength in the upper extremities due to their routine use for wheelchair propulsion (Buffart, van den Berg-Emons, van Wijlen-Hempel, et al., 2008). Nevertheless, lower levels in hand grip strength were found in individuals with SB, regardless of ambulatory status. This is an important result, because upper extremity limbs are essential to perform daily life activities independently and grip strength is a powerful predictor of disability and morbidity (Bohannon, 2008; Syddall, Cooper, Martin, Briggs, & Aihie Sayer, 2003). Exercise training programs, including upper extremity strength training, significantly improved the muscle strength of the upper extremity muscle groups (Andrade, et al., 1991; de Groot, Takken, van Brussel, et al., 2011). Therefore, upper extremity strength training should be added to the health management of individuals with SB to prevent functional deterioration and physical dependence.

Subnormal muscle strength in hip abductors, knee extensors and ankle dorsal flexors tended to be linked with non-ambulators, whereas normal strength was more frequently observed in ambulators. One of the main reasons of low muscle strength in individuals with SB is muscles disuse, causing deconditioning (Buffart, van den Berg-Emons, van Wijlen-Hempel, et al., 2008). Therefore, strength training of the lower extremity muscles could be a strategy to preserve and improve muscle strength. This specific training might prevent non-ambulatory status and potentiate independent ambulation.

Body composition was assessed mainly with thickness of skinfolds. This measure is one of the most recommended as it provides an estimate of the total amount of subcutaneous fat and has been considered a better predictor of high BF than body mass index (Bedogni, et al., 2003; Nooyens, et al., 2007). However, controversy exists regarding reliability and accuracy of thickness of skinfolds. Some studies reported good accuracy (Grogan & Ekvall, 1999; Shurtleff, Walker, Duguay, Peterson, & Cardenas, 2010), while others showed poor test-retest and inter-rater reliability (Shurtleff, 1986). More research should, therefore, be conducted to test the reliability of skinfold measures and to develop useful regression equations. An increased BF in individuals with SB was found. As expected, BF was higher in female, non-ambulators and in those with no participation in sports. Several factors may contribute to these findings, such as i) physiologic mechanisms associated with the disorder itself (e.g., excessive BF has been linked to hormonal and metabolic imparments) (Buffart, Roebroeck, et al., 2008; Mita, et al., 1993); ii) decreased levels of sport participation and iii) reduced self-efficacy toward physical exercise (Bandini, Schoeller, Fukagawa, Wykes, & Dietz, 1991; Cairney, et al., 2005; Kelly, Altiok, Gorzkowski, Abrams, & Vogel, 2011). The conjugation of these factors may result in an energy imbalance, whereby energy expended is less than energy consumed, leading to accumulation of BF (Tsiotra, Nevill, Lane, & Koutedakis, 2009). It is not clear if exercise training influences BF, as only one study assessed its effects in this fitness component. However the participation in sports activities and exercise training programs with adequate intensities may aid to control this energy imbalance and therefore, reduce BF and improve overall health. More studies addressing the influence of these activities in BF are needed to provide evidence based recommendations.

Considering that only three studies provided data on flexibility through different measuring instruments, assumptions on this fitness component are limited. This lack of data is also observed in other chronic diseases such as Cerebral Palsy (Hombergen, et al., 2012). Nevertheless, in this review, a tendency for decreased flexibility, ultimately resulting in rigidity, was found (Agre, et al., 1987; Norkin & Levangie, 1992). As flexibility is essential to move efficiently and to perform daily activities independently, such as personal hygiene and transfer abilities (Agre, et al., 1987), studies assessing flexibility with standardized measures are needed. A best-evidence synthesis on the five physical fitness components in individuals with SB is presented in table 4.

(insert table 4 about here)

Moderate evidence shows that exercise training improves cardiorespiratory endurance and muscle strength in individuals with SB and that it has no impact on body composition. However, these conclusions are based in only three studies, which presented small sample sizes, differed in the training implemented (including type of exercise training, duration, frequency and intensity) and in the outcome measures reported. Also, the effects of exercise training on flexibility and neuromotor fitness components were not assessed in these studies and therefore, further research is required to draw specific recommendations regarding exercise training for individuals with SB. A best-evidence synthesis on the effects of exercise training on physical fitness in individuals with SB is presented in table 5.

(insert table 5 about here)

5. LIMITATIONS

This systematic review has some limitations that need to be acknowledged. Firstly, the different study designs, measures used to assess the physical fitness components hampered the results synthesis and impaired the conduction of a meta-analysis. Secondly, different ambulatory classifications were used, which weakens the associations between physical fitness and the ambulatory levels of individuals with SB. Thirdly, the same sample appears to have been used in more than one study and thus the results need to be interpreted with caution. Fourthly, the studies mainly included young participants and with MMC. These limitations restrict the extent to which the conclusions of this review are applicable to adult/elderly individuals and presenting other types of SB. Finally, studies comparing exercise training programs with standard care did not clearly describe the treatments implemented in the standard care groups. Thus, advantages of exercise training programs over other interventions cannot be pulled out.

6. IMPLICATIONS FOR PRACTICE AND RESEARCH

Cardiorespiratory endurance and muscle strength of children with SB seems to be well understood in the literature. However, further studies exploring other physical fitness components (body composition, flexibility and neuromotor fitness) and integrating adults/elderly with SB are needed to establish reference values and comparisons with healthy peers. This knowledge will allow health professionals to conduct their interventions based on objective data.

Currently, it appears that exercise training is valuable for increasing cardiorespiratory endurance and muscle strength in individuals with SB. However, due to the methodological limitations of the available studies, this review cannot draw recommendations regarding type, duration, frequency, and intensity of exercise training programs. Well-designed randomized control trials are needed to provide stronger evidence about the effects of exercise training on the physical fitness, mobility, independence and health of individuals with SB.

7. CONCLUSIONS

Individuals with SB have reduced physical fitness (cardiorespiratory endurance, muscle strength, body composition and flexibility) compared with healthy peers. These findings are a red flag as it is widely recognized that poor physical fitness leads to cardiovascular diseases, obesity and therefore, increases morbidity and mortality risks. Aerobic and strength training seem to improve cardiorespiratory endurance and muscle strength in individuals with SB. Therefore, exercise training might constitute a key component in the health management of this population to enhance physical fitness and prevent functional deterioration. Further research is needed to draw firm conclusions on the physical fitness of this population and to provide recommendations regarding exercise training programs.

Acknowledgments

The authors gratefully thank the contributions of Dr. Sara Demain, for her judgment on the search strategy and Marta Vieira, PT, for her helpful comments in the preparation of this manuscript.

Conflict of interest

The authors have no conflict of interest.

REFERENCES:

Agre, J. C., Findley, T. W., McNally, M. C., Habeck, R., Leon, A. S., Stradel, L., Birkebak, R., & Schmalz, R. (1987). Physical activity capacity in children with myelomeningocele. *Archives of Physical Medicine and Rehabilitation, 68*, 372-377.

American College of Sports Medicine. (2009). *ACSM's Guidelines for Exercise Testing and Prescription* (8th ed.): Lippincott Williams & Wilkins.

Andrade, C. K., Kramer, J., Garber, M., & Longmuir, P. (1991). Changes in self-concept, cardiovascular endurance and muscular strength of children with spina bifida aged 8 to 13 years in response to a 10-week physical-activity programme: a pilot study. *Child: Care, Health and Development, 17*, 183-196.

Bandini, L. G., Schoeller, D. A., Fukagawa, N. K., Wykes, L. J., & Dietz, W. H. (1991). Body composition and energy expenditure in adolescents with cerebral palsy or myelodysplasia. *Pediatric Research, 29*, 70-77.

Barnard, K., Thomas, S., Royle, P., Noyes, K., & Waugh, N. (2010). Fear of hypoglycaemia in parents of young children with type 1 diabetes: a systematic review. *BMC Pediatrics, 10*, 50.

Bedogni, G., Iughetti, L., Ferrari, M., Malavolti, M., Poli, M., Bernasconi, S., & Battistini, N. (2003). Sensitivity and specificity of body mass index and skinfold thicknesses in detecting excess adiposity in children aged 8-12 years. *Annals of Human Biology, 30*, 132-139.

Berenson, G. S. (2002). Childhood risk factors predict adult risk associated with subclinical cardiovascular disease. The Bogalusa Heart Study. *American Journal of Cardiology, 90*, 3L-7L.

Bohannon, R. W. (2008). Hand-grip dynamometry predicts future outcomes in aging adults. *Journal of Geriatric Physical Therapy, 31*, 3-10.

Borenstein, M., Hedges, L., Higgins, J., & Rothstein, H. (2005). *Comprehensive Meta-analysis Version 2.0.* Englewood NJ: Biostat Inc.

Botto, L. D., Moore, C. A., Khoury, M. J., & Erickson, J. D. (1999). Neural-tube defects. *New England Journal of Medicine, 341*, 1509-1519.

Bruinings, A. L., van den Berg-Emons, H. J., Buffart, L. M., van der Heijden-Maessen, H. M., Roebroeck, M. E., & Stam, H. J. (2007). Energy cost and physical strain of daily activities in adolescents and young adults with myelomeningocele. *Developmental Medicine and Child Neurology, 49*, 672-677.

Buffart, L. M., Roebroeck, M. E., Rol, M., Stam, H. J., van den Berg-Emons, H. J., & Transition Res Grp. (2008). Triad of physical activity, aerobic fitness and obesity in adolescents and young adults with myelomeningocele. *Journal of Rehabilitation Medicine, 40*, 70-75.

Buffart, L. M., van den Berg-Emons, R. J., Burdorf, A., Janssen, W. G., Stam, H. J., & Roebroeck, M. E. (2008). Cardiovascular Disease Risk Factors and the Relationships With Physical Activity, Aerobic Fitness, and Body Fat in Adolescents and Young Adults With Myelomeningocele. *Archives of Physical Medicine and Rehabilitation, 89*, 2167-2173.

Buffart, L. M., van den Berg-Emons, R. J., van Meeteren, J., Stam, H. J., & Roebroeck, M. E. (2009). Lifestyle, participation, and health-related quality of life in adolescents and young adults with myelomeningocele. *Developmental Medicine and Child Neurology, 51*, 886-894.

Buffart, L. M., van den Berg-Emons, R. J. G., van Wijlen-Hempel, M. S., Stam, H. J., & Roebroeck, M. E. (2008). Health-related physical fitness of adolescents and young adults with myelomeningocele. *European Journal of Applied Physiology, 103*, 181-188.

Buffart, L. M., van der Ploeg, H. P., Bauman, A. E., Van Asbeck, F. W., Stam, H. J., Roebroeck, M. E., & van den Berg-Emons, R. J. G. (2008). Sports Participation in Adolescents and Young Adults with Myelomeningocele and Its Role in Total Physical Activity Behaviour and Fitness. *Journal of Rehabilitation Medicine, 40*, 702-708.

Cairney, J., Hay, J. A., Faught, B. E., Wade, T. J., Corna, L., & Flouris, A. (2005). Developmental coordination disorder, generalized self-efficacy toward physical activity, and participation in organized and free play activities. *Journal of Pediatrics, 147*, 515-520.

Chamberlain, M. A., & Kent, R. M. (2005). The needs of young people with disabilities in transition from paediatric to adult services. *Europa medicophysica, 41*, 111-123.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences.* Hillsdale, NJ: Lawrence Earlbaum Associates.

Cole, T. M. (1982). Measurement of musculoskeletal function. In F. J. Kottke, G. K. Stillwell & J. F. Lehamann (Eds.), *Krusen's Handbook of Physical Medicine and Rehabilitation* (3rd ed.). Philadephia: WB Saunders Co.

Coutts, K., McKenzie, D., Loock , C., Beauchamp, R., & Armstrong, R. (1993). Upper body exercise capacity in youth with spina bifida. *Adapted physical activity quarterly : APAQ, 10*, 22-28.

Crombie, I. (1996). *The pocket guide to critical appraisal*. London: BMJ Publishing Group.

Dagenais, L. M., Lahay, E. R., Stueck, K. A., White, E., Williams, L., & Harris, S. R. (2009). Effects of Electrical Stimulation, Exercise Training and Motor Skills Training on Strength of Children with Meningomyelocele: A Systematic Review. *Physical & Occupational Therapy in Pediatrics, 29*, 445-463.

Danielsson, A., Bartonek, A., Levey, E., McHale, K., Sponseller, P., & Saraste, H. (2008). Associations between orthopaedic findings, ambulation and health-related quality of life in children with myelomeningocele. *Journal of Children's Orthopaedics, 2*, 45-54.

Danneskiold-Samsoe, B., Bartels, E. M., Bulow, P. M., Lund, H., Stockmarr, A., Holm, C. C., Watjen, I., Appleyard, M., & Bliddal, H. (2009). Isokinetic and isometric muscle strength in a healthy population with special reference to age and gender. *Acta Physiologica, 197 Suppl 673*, 1-68.

de Groot, J., Takken, T., de Graaff, S., Gooskens, R. H. J. M., Helders, P. J. M., & Vanhees, L. (2009). Treadmill testing of children who have spina bifida and are ambulatory: does peak oxygen uptake reflect maximum oxygen uptake? *Physical Therapy, 89*, 679-687.

de Groot, J., Takken, T., Gooskens, R. H. J. M., Schoenmakers, M. A. G. C., Wubbels, M., Vanhees, L., & Helders, P. J. M. (2011). Reproducibility of maximal and submaximal exercise testing in "normal ambulatory" and "community ambulatory" children and adolescents with spina bifida: which is best for the evaluation and application of exercise training? *Physical Therapy, 91*, 267-276.

de Groot, J., Takken, T., Schoenmakers, M. A., Vanhees, L., & Helders, P. J. (2008). Limiting factors in peak oxygen uptake and the relationship with functional ambulation in ambulating children with spina bifida. *European Journal of Applied Physiology, 104*, 657-665.

de Groot, J., Takken, T., van Brussel, M., Gooskens, R., Schoenmakers, M., Versteeg, C., Vanhees, L., & Helders, P. (2011). Randomized controlled study of home-based treadmill training for ambulatory children with spina bifida. *Neurorehabilitation and Neural Repair, 25*, 597-606.

Dickens, P., & McMillen, J. S. (2003). Growing Up with Spina Bifida: what we have learned. *The North Carolina Office on Disability and Health*.

Garber, C. E., Blissmer, B., Deschenes, M. R., Franklin, B. A., Lamonte, M. J., Lee, I. M., Nieman, D. C., Swain, D. P., & Amer Coll Sports Med. (2011). Quantity and Quality of Exercise for Developing and Maintaining Cardiorespiratory, Musculoskeletal, and Neuromotor Fitness in Apparently Healthy Adults: Guidance for Prescribing Exercise. *Medicine and Science in Sports and Exercise, 43*, 1334-1359.

Grogan, C. B., & Ekvall, S. M. (1999). Body composition of children with myelomeningocele, determined by 40K, urinary creatinine and anthropometric measures. *Journal of the American College of Nutrition, 18*, 316-323.

Hassan, J., van der Net, J., Helders, P. J., Prakken, B. J., & Takken, T. (2010). Six-minute walk test in children with chronic conditions. *British Journal of Sports Medicine, 44*, 270-274.

Hicks, A. L., Ginis, K. A. M., Pelletier, C. A., Ditor, D. S., Foulon, B., & Wolfe, D. L. (2011). The effects of exercise training on physical capacity, strength, body composition and functional performance among adults with spinal cord injury: a systematic review. *Spinal Cord, 49*, 1103-1127.

Hoffer, M. M., Feiwell, E., Perry, R., Perry, J., & Bonnett, C. (1973). Functional Ambulation in Patients with Myelomeningocele. *Journal of Bone and Joint Surgery. American Volume, 55*, 137-148.

Hombergen, S. P., Huisstede, B. M., Streur, M. F., Stam, H. J., Slaman, J., Bussmann, J. B., & van den Berg-Emons, R. J. (2012). Impact of Cerebral Palsy on Health-Related Physical Fitness in Adults: Systematic Review. *Archives of Physical Medicine and Rehabilitation, 93*, 871-881.

Jackson, S. (2009). *Research Methods and Statistics: A Critical Thinking Approach*. Belmont: Wadsworth Cengage Learning.

Jenkinson, M. D., Campbell, S., Hayhurst, C., Clark, S., Kandasamy, J., Lee, M. K., Flynn, A., Murphy, P., & Mallucci, C. L. (2011). Cognitive and functional outcome in spina bifida-Chiari II malformation. *Child's Nervous System, 27*, 967-974.

Kelly, E. H., Altiok, H., Gorzkowski, J. A., Abrams, J. R., & Vogel, L. C. (2011). How does participation of youth with spina bifida vary by age? *Clinical Orthopaedics and Related Research, 469*, 1236-1245.

Klimek-Piskorz, E., & Piskorz, C. (2002). Physiological responses to graded exercise in young boys with flaccid paresis of lower limbs in the course of meningomyelocele. *Biology of Sport, 19*, 365-372.

Kondo, A., Kamihira, O., & Ozawa, H. (2009). Neural tube defects: prevalence, etiology and prevention. *International Journal of Urology, 16*, 49-57.

Landis, J. R., & Koch, G. G. (1977). The Measurement of Observer Agreement for Categorical Data. *Biometrics, 33*, 159-174.

Lee, D. C., Artero, E. G., Sui, X., & Blair, S. N. (2010). Mortality trends in the general population: the importance of cardiorespiratory fitness. *Journal of Psychopharmacology, 24*, 27-35.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gotzsche, P. C., Ioannidis, J. P. A., Clarke, M., Devereaux, P. J., Kleijnen, J., & Moher, D. (2009). The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. *Annals of Internal Medicine, 151*, W65-W94.

Marczyk, G., DeMatteo, D., & Festinger, D. (2005). *Essentials of Research Design and Methodology*. New Jersey: John Wiley & Sons, Inc.

Mita, K., Akataki, K., Itoh, K., Ono, Y., Ishida, N., & Oki, T. (1993). Assessment of obesity of children with spina bifida. *Developmental Medicine and Child Neurology, 35*, 305-311.

Mitchell, L. E., Adzick, N. S., Melchionne, J., Pasquariello, P. S., Sutton, L. N., & Whitehead, A. S. (2004). Spina bifida. *Lancet, 364*, 1885-1895.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D., & PRISMA group. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *Annals of Internal Medicine, 151*, 264-269.

National Health Service. (2011). Spina Bifida. In (Vol. 2011): National Health Services.

Nooyens, A. C., Koppes, L. L., Visscher, T. L., Twisk, J. W., Kemper, H. C., Schuit, A. J., van Mechelen, W., & Seidell, J. C. (2007). Adolescent skinfold thickness is a better predictor of high body fatness in adults than is body mass index: the Amsterdam Growth and Health Longitudinal Study. *American Journal of Clinical Nutrition, 85*, 1533-1539.

Norkin, C., & Levangie, P. (1992). *Joint Structure and Function: A Comprehensive Approach.* Philadelphia: Davis FA.

Norrlin, S., Strinnholm, M., Carlsson, M., & Dahl, M. (2003). Factors of significance for mobility in children with myelomeningocele. *Acta Paediatrica, 92*, 204-210.

Özek, M. M., Cinalli, G., & Maixner, W. J. (2008). Spina Bifida: Management and Outcome. In. Milan: Springer.

Papavasiliou, A. S. (2009). Management of motor problems in cerebral palsy: A critical update for the clinician. *European Journal of Paediatric Neurology, 13*, 387-396.

Petticrew, M., & Roberts, H. (2006). *Systematic reviews in the social sciences: a practical guide*. Oxford: Blackwell.

Roebroeck, M. E., Jahnsen, R., Carona, C., Kent, R. M., & Chamberlain, M. A. (2009). Adult outcomes and lifespan issues for people with childhood-onset physical disability. *Developmental Medicine and Child Neurology, 51*, 670-678.

Schoenmakers, M. A., Groot, J. F. d., Gorter, J. W., Hillaert, J. L., Helders, P. J., & Takken, T. (2009). Muscle strength, aerobic capacity and physical activity in independent ambulating children with lumbosacral spina bifida. *Disability and Rehabilitation, 31*, 259-266.

Schoenmakers, M. A., Gulmans, V. A. M., Gooskens, R. H. J. M., & Helders, P. J. M. (2004). Spina bifida at the sacral level: more than minor gait disturbances. *Clinical Rehabilitation, 18*, 178-185.

Sherman, M. S., Kaplan, J. M., Effgen, S., Campbell, D., & Dold, F. (1997). Pulmonary dysfunction and reduced exercise capacity in patients with myelomeningocele. *Journal of Pediatrics, 131*, 413-418.

Shurtleff, D. (1986). *Myelodysplasias and Exstrophies: Significance, Prevention, and Treatment*: Grune & Stratton.

Shurtleff, D., Walker, W. O., Duguay, S., Peterson, D., & Cardenas, D. (2010). Obesity and myelomeningocele: anthropometric measures. *Journal of Spinal Cord Medicine, 33*, 410-419.

Slavin, R. E. (1995). Best evidence synthesis: an intelligent alternative to meta-analysis. *Journal of Clinical Epidemiology, 48*, 9-18.

Syddall, H., Cooper, C., Martin, F., Briggs, R., & Aihie Sayer, A. (2003). Is grip strength a useful single marker of frailty? *Age and Ageing, 32*, 650-656.

Tsiotra, G. D., Nevill, A. M., Lane, A. M., & Koutedakis, Y. (2009). Physical fitness and developmental coordination disorder in Greek children. *Pediatric exercise science, 21*, 186-195.

van den Berg-Emons, H. J., Bussmann, J. B., Meyerink, H. J., Roebroeck, M. E., & Stam, H. J. (2003). Body fat, fitness and level of everyday physical activity in adolescents and young adults with meningomyelocele. *Journal of Rehabilitation Medicine, 35*, 271-275.

van Tulder, M., Furlan, A., Bombardier, C., & Bouter, L. (2003). Updated method guidelines for systematic reviews in the cochrane collaboration back review group. *Spine (Phila Pa 1976), 28*, 1290-1299.

Verschuren, O., Ketelaar, M., Takken, T., Helders, P. J., & Gorter, J. W. (2008). Exercise programs for children with cerebral palsy: a systematic review of the literature. *American Journal of Physical Medicine and Rehabilitation, 87*, 404-417.

Vinck, A., Nijhuis-van der Sanden, M. W., Roeleveld, N. J., Mullaart, R. A., Rotteveel, J. J., & Maassen, B. A. (2010). Motor profile and cognitive functioning in children with spina bifida. *European Journal of Paediatric Neurology, 14*, 86-92.

Widman, L. M., Abresch, R. T., Styne, D. M., & McDonald, C. M. (2007). Aerobic fitness and upper extremity strength in patients aged 11 to 21 years with spinal cord dysfunction as compared to ideal weight and overweight controls. *Journal of Spinal Cord Medicine, 30*, S88-S96.

Widman, L. M., McDonald, C. M., & Abresch, R. T. (2006). Effectiveness of an upper extremity exercise device integrated with computer gaming for anaerobic training in adolescents with spinal cord dysfunction. *Journal of Spinal Cord Medicine, 29*, 363-370.

Figure legends

Figure 1- PRISMA Flowchart of the included studies

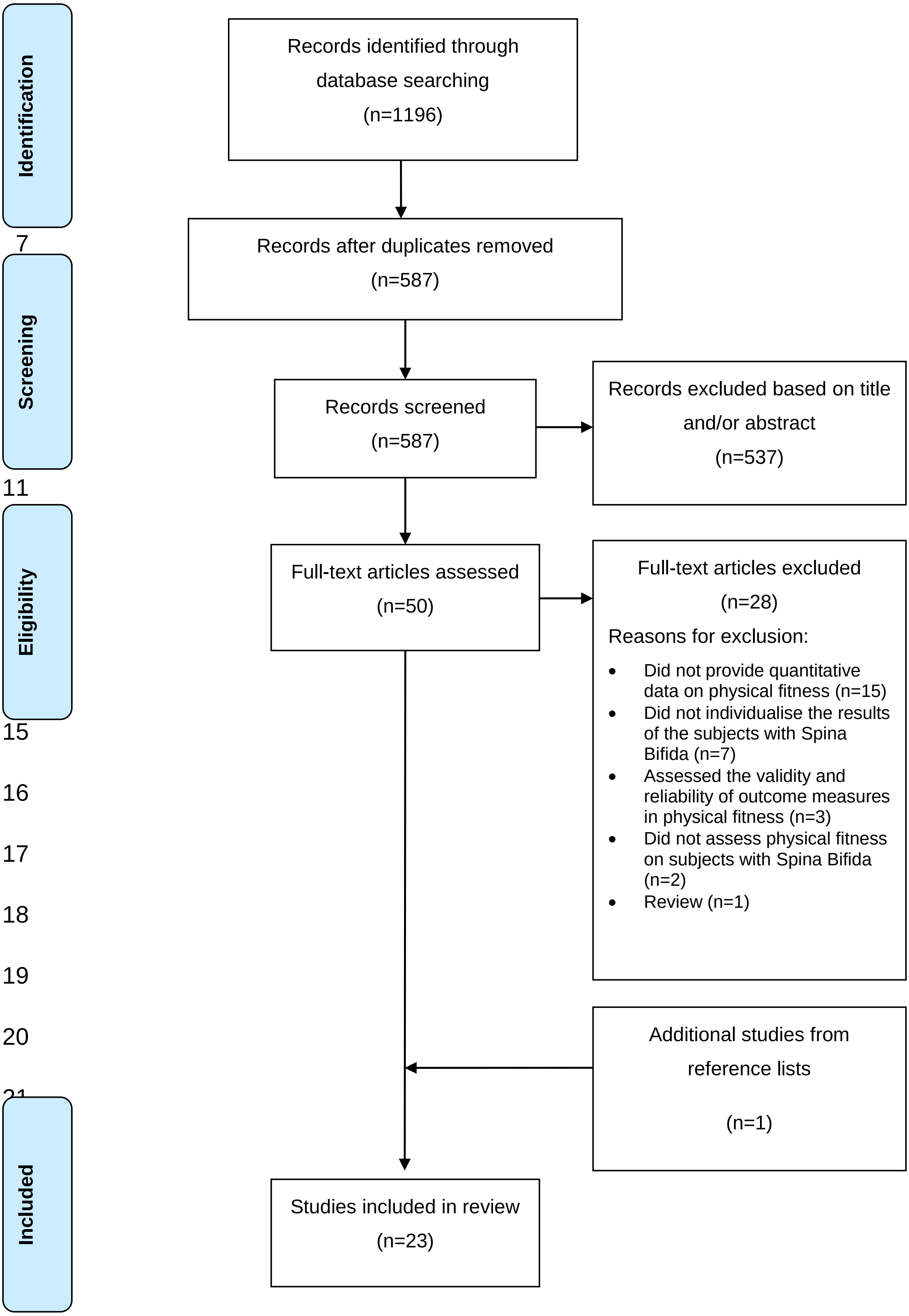

Table captions

Table 1- Quality assessment based on the 'Crombie criteria'.

Author (year)	**Appropriate Research Design**	**Appropriate Recruitment Strategy**	**Response Rate (%)**	**Sample Representa-tiveness**	**Objective and Reliable Measures**	**Power Calculation/ Justification of Numbers**	**Appropriate Statistical Analysis**	**Evidence of Bias**	**Quality Indicators Met**
Agre, et al. (1987)	♦				♦		♦	♦	3
Coutts, McKenzie, Loock, Beauchamp, and Armstrong (1993)	♦	♦	35		♦		♦	♦	5
Andrade, Kramer, Garber, and Longmuir (1991)	♦	♦	40.6		♦		♦	♦	6
Sherman, Kaplan, Effgen, Campbell, and Dold (1997)	♦	♦	50		♦		♦	♦	5
Klimek-Piskorz and Piskorz (2002)	♦	♦			♦		♦	♦	4
van den Berg-Emons, Bussmann, Meyerink, Roebroeck, and Stam (2003)	♦	♦	58		♦		♦	♦	5
Norrlin, Strinnholm, Carlsson, and Dahl (2003)	♦	♦	84		♦		♦	♦	5
Schoenmakers, Gulmans, Gooskens, and Helders (2004)	♦	♦			♦		♦	♦	4
Widman, McDonald, and Abresch (2006)	♦	♦			♦		♦	♦	4
Widman, Abresch, Styne, and McDonald (2007)	♦	♦			♦		♦	♦	4

Bruinings, et al. (2007)	♦	♦	35.3		♦		♦	♦	5
Buffart, van den Berg-Emons, van Wijlen-Hempel, Stam, and Roebroeck (2008)	♦	♦	29		♦		♦	♦	5
Buffart, van den Berg-Emons, Burdorf, et al. (2008)	♦	♦	61		♦		♦	♦	5
Buffart, van der Ploeg, et al. (2008)	♦	♦	30		♦		♦	♦	5
Buffart, Roebroeck, et al. (2008)	♦	♦	30		♦		♦	♦	5
Buffart, van den Berg-Emons, van Meeteren, Stam, and Roebroeck (2009)	♦	♦	30		♦		♦	♦	5
Danielsson, et al. (2008)	♦	♦			♦		♦	♦	4
de Groot, Takken, Schoenmakers, Vanhees, and Helders (2008)	♦	♦			♦		♦	♦	4
de Groot, et al. (2009)	♦	♦			♦	♦	♦	♦	5
Schoenmakers, et al. (2009)	♦	♦			♦		♦	♦	4
Hassan, van der Net, Helders, Prakken, and Takken (2010)	♦	♦			♦		♦	♦	4
de Groot, Takken, Gooskens, et al. (2011)	♦	♦			♦		♦	♦	4
de Groot, Takken, van Brussel, et al. (2011)	♦	♦	78	♦	♦		♦		7

Table 2–Assessment of physical fitness components in subjects with Spina Bifida.

Author (Year)	**Design**	**Participants**	**Setting (country)**	**Assessment tools and protocols**	**Outcome Measures**	**Results**
Agre, et al. (1987)	Cross-sectional	33 subjects with MMC 60% males 10-15y	NS	Treadmill test Isometri muscle strength ROM measure	VO_2peak HRpeak Muscle strength ROM	VO_2peak between 17.7±3.8 and 41.6±5.35mL·Kg^{-1}·min^{-1}; Males 29.4±2.6mL·Kg^{-1}·min^{-1}; Females 23.7±4.5mL·Kg^{-1}·min^{-1}; HRpeak between 167±9 and 202±12bpm; Males 179±5bpm; Females 184±6bpm Strength Hand grip between 199±35 and 236±14N Knee extension between 4±16 and 161±31N Hip extension between 9±36 and 118±22N ROM Hip extension: CA 174±13º; A 162±1º; NA 157±3º Knee extension: CA 175±3º; A 166±3º; NA 158±4º
Coutts, McKenzie, Loock , Beauchamp, and Armstrong (1993)	Cross-sectional	42 subjects with SB 45% males 7-18y	Outpatient (Canada)	A Wingate 30-s anaerobic power test, and a continuous, progressive maximal oxygen uptake test on an electronically brake arm or cycle ergometer Handgrip strength	VO_2peak Maximum workload HR Muscle strength	VO_2peak 7-12y: Males 0.81 L·min^{-1}; Females 1.03L·min^{-1}; 13-18y: Males1.47L·min^{-1}; Females 1.05L·min^{-1} Maximum workload 7-12y: Males 56W; Females 59W; 13-18y: Males 158W; Females 79W HRpeak 7-12y: Males 178bpm; Females 174bpm; 13-18y: Males 185bpm; Females 183bpm Handgrip strength 7-12y: Males 353N; Females 392N; 13-18y: Males 686N; Females 471N
Sherman, Kaplan, Effgen, Campbell, and Dold (1997)	Cross-sectional	12 subjects with MMC 33% males 10-17y 12 healthy subjects,	NS	Cardiopulmonary exercise testing	VO_2peak HRpeak	VO_2peak MMC 13.8±4.8mL·Kg^{-1}·min^{-1}; CG 21.3±7.5mL·Kg^{-1}·min^{-1}; p=0.02 HRpeak MMC 153.5±21.4bpm; CG 127.6±22.1bpm; p=0.09

		age, gender and arm span matched				
Klimek-Piskorz and Piskorz (2002)	Cross-sectional	10 subjects with MMC 100% males 17.6±0.6y	Outpatient	Upper limb graded cycle ergometer test	VO_2peak Maximum workload HRpeak	VO_2peak 46.3±2.2 $mL \cdot Kg^{-1} \cdot min^{-1}$ Maximum workload 157.5±38W HRpeak 191±6bpm
van den Berg-Emons, Bussmann, Meyerink, Roebroeck, and Stam (2003)	Cross-sectional	14 subjects with MMC 57% male 14-26y	Outpatient (Netherlands)	Progressive maximal exercise test in an electronically braked arm or cycle ergometer Thickness of 4 skinfolds (biceps, triceps, subscapular, suprailiac)	VO_2peak HRpeak BF	VO_2peak 27.3±7.4$mL \cdot Kg^{-1} \cdot min^{-1}$ A 30.1±6.2 $mL \cdot Kg^{-1} \cdot min^{-1}$; NA 22.5±7.5$mL \cdot Kg^{-1} \cdot min^{-1}$; p=0.15 HRpeak 185±18bpm A 193±5bpm; NA 171±25bpm; p=0.15 BF 23.1±7.1% A 22.3±8.1%; NA 25.0±4.4%; p=0.60
Norrlin, Strinnholm, Carlsson, and Dahl (2003)	Cross-sectional	32 subjects with MMC 59% male 6-11y	Outpatient (Sweden)	Isometric hand strength with hand-held dynamometry	Muscle strength	Hand strength CA 74.5±25.2N; HA 62.5±25.7N; NFA 79.6±25.2N; NA 57.9±13.6N 71.03±23.30% of reference values
Schoenmakers, Gulmans, Gooskens, and Helders (2004)	Cross-sectional	30 subjects with MMC 47% male 1-17y 14 subjects with LMMC 57% male 1-17y	Outpatient (Netherlands)	Manual muscle testing	Muscle strength	Hip flexor muscles: MMC 4.9±0.5; LMMC 4.9±0.3; p=0.98 Hip abductor muscles: MMC 4.5±0.9; LMMC 4.6±0.7;p=0.59 Hip extensor muscles: MMC 3.5±1.5; LMMC 4.4±1.1;p=0.01 Knee extensor muscles: MMC 4.9±0.5; LMMC 5.0±0.0;p=0.50 Ankle dorsal-flexor muscles: MMC 4.4±1.2; LMMC 4.07±1.6;p=0.49 Calf-muscles: MMC 2.9±1.5; LMMC 4.0±1.6;p=0.01
Widman, Abresch, Styne, and	Cross-sectional	37 subjects with SB 49% male	Outpatient (USA)	Ramp protocol with a magnetically	VO_2peak Maximum workload	VO_2peak SB: Males 20.6±7.6$mL \cdot Kg^{-1} \cdot min^{-1}$; Females 14.2±4.2$mL \cdot Kg^{-1} \cdot min^{-1}$; CG: Males 30.8±6.0$mL \cdot Kg^{-1} \cdot min^{-1}$; Females

McDonald (2007)		11-21y 34 healthy subjects, matched by age		braked arm ergometry Peak dynamic muscle strength using LIDO dynamometer Dual energy x-ray absorptiometry	HRpeak Muscle strength BF	21.0±4.8mL·Kg^{-1}·min^{-1}; p<0.05 Maximum workload SB: Males 61.9±17.9W; Females 48.9±15.3W; CG: Males 83.0±21.0W; Females 56.4±11.4W SB Males vs CG Males p<0.05 HRpeak SB: Males 163.4±18.7bpm; Females 167.3±19.3bpm; CG: Males 169.7±24.2bpm; Females 159.2±20.2bpm Shoulder flexion strength SB: Males 0.54±0.14N-m·Kg^{-1}; Females 0.46±0.14N-m·Kg^{-1}; CG: Males 0.70±0.14N-m·Kg^{-1}; Females 0.51±0.07N-m·Kg^{-1} SB Males vs CG Males p<0.05 Shoulder extension strength SB: Males 0.62±0.14N-m·Kg^{-1}; Females 0.52±0.18N-m·Kg^{-1}; CG: Males 0.94±0.19N-m·Kg^{-1}; Females 0.67±0.14N-m·Kg^{-1} (p<0.05) Elbow flexion strength SB: Males 0.58±0.20N-m·Kg^{-1}; Females 0.38±0.11N-m·Kg^{-1}; CG: Males 0.61±0.15N-m·Kg^{-1}; Females 0.37±0.05N-m·Kg^{-1} Elbow extension strength SB: Males 0.56±0.14N-m·Kg^{-1}; Females 0.43±0.12N-m·Kg^{-1}; CG: Males 0.57±0.10N-m·Kg^{-1}; Females 0.45±0.09N-m·Kg^{-1} BF SB: Males 36.3±9.3%; Females 46.2±5.0%; CG: Males 16.1±5.2%; Females 25.7±4.1% SB vs CG p<0.05
Bruinings, et al. (2007)	Cross-sectional	18 subjects with MMC 72% males 16-30y 18 healthy subjects, age and gender matched	Outpatient (Netherlands)	Progressive maximal exercise test on an electronically braked arm or cycle ergometer	VO_2peak	VO_2peak A 31.4±8.3mL·Kg^{-1}·min^{-1}, 34% lower than healthy subjects (p=0.02) NA 23.5±5.33mL·Kg^{-1}·min^{-1}, 54% lower than healthy subjects (p<0.001)

Buffart, van den Berg-Emons, Burdorf, et al. (2008)	Cross-sectional	31 subjects with MMC 58% males 16-30y	Outpatient (Netherlands)	Progressive maximal exercise Test in an electronically braked arm or cycle ergometer Thickness of 4 skinfolds (biceps, triceps, subscapular, suprailiac)	VO_2peak BF	VO_2peak 1.47±0.51L·min^{-1} A 1.62±0.59L·min^{-1}; NA 1.36±0.45L·min^{-1}; p=0.18 Males 1.76±0.47L·min^{-1}; Females1.07±0.27L·min^{-1}; p=0.001 BF 74.4±40.6mm A 59.1±33.4mm; NA 88.6±42mm; p=0.05 Males 50.7±24.2mm; Females 110.4±32.6mm; p<0.001
Buffart, van den Berg-Emons, van Wijlen-Hempel, Stam, and Roebroeck (2008)	Cross-sectional	50 subjects with MMC 50% males 16-30y	Outpatient (Netherlands)	Progressive maximal exercise test on an electronically braked arm or cycle ergometer Strength of hip flexors, knee extensors , shoulder abductors and elbow extensors through the “Break” Testing Method with hand-held dynamometry Thickness of 4 skinfolds (biceps, triceps, subscapular, suprailiac) ROM measure	VO_2peak Maximum workload HRpeak Muscle strength BF ROM	VO_2peak 22.6±8.2mL·Kg^{-1}·min^{-1} 67±15% of reference values Males 1.78±0.51L·min^{-1}, 71±13% of reference values; Females 1.18±0.30L·min^{-1}, 61±18% of reference values; p<0.001 Males 28.1±7.0mL·Kg^{-1}·min^{-1}; Females 17.0 ±4.7mL·Kg^{-1}·min^{-1} CA 29.0±7.7mL·Kg^{-1}·min^{-1}; HA 22.3±6.6mL·Kg^{-1}·min^{-1}; NA 19.2±6.8mL·Kg^{-1}·min^{-1}; p<0.001 Maximum workload 91±42W CA 123±42W; HA 97±35W; NA 73±34W Males 113±43W; Females 69±28W HRpeak 174±19bpm, 90±10% predicted maximum CA 173±21bpm, 87±10% of predicted maximum; HA183±14bpm, 95±8% of predicted maximum; NA 172±18bpm, 91±10% of predicted maximum Males 179±16bpm, 92±8% of predicted maximum; Females 169±20bpm, 89±10% of predicted maximum Subnormal muscle strength 61% subjects CA: 79%; A: 57%; NA: 54% Males 58%; Females 64% BF 74.8±38.8mm, 159±77% of reference values Males 51.2±24.6mm, 146±79% of reference values; Females 100.4±35.1mm, 173±73% of reference values Mobility restrictions in one or more joints 61% CA 79%; HA 57%; NFA 54%

						Males 54%; Females 67%
Buffart, van der Ploeg, et al. (2008)	Cross-sectional	51 patients with MMC 51% males 16-30y	Outpatient (Netherlands)	Progressive maximal exercise test on an electronically braked arm or cycle ergometer Muscle strength of hip flexors, knee extensors, shoulder abductors and elbow extensors through the “Break” Testing Method with hand-held dynamometry Thickness of 4 skinfolds (biceps, triceps, subscapular, suprailiac)	VO_2peak Muscle strength BF	VO_2peak $0.19L\cdot min^{-1}$ Participating in sports $1.58\pm0.53L\cdot min^{-1}$; No participation in sports $1.27\pm0.5L\cdot min^{-1}$; p=0.13 Muscle strength Sports 52% with subnormal muscle strength; No sports 81% with subnormal muscle strength; p=0.08 BF Sports 74±36.8mm; No sports 75.5±39.4mm; p=0.48
Buffart, Roebroeck, et al. (2008)	Cross-sectional	51 subjects with MMC 51% males 16-30y	Outpatient (Netherlands)	Progressive maximal exercise test on an electronically braked arm or cycle ergometer Thickness of 4 skinfolds (biceps, triceps, subscapular, suprailiac)	VO_2peak BF	VO_2peak $22.6\pm8.2mL\cdot Kg^{-1}\cdot min^{-1}$ CA $29\pm7.7mL\cdot Kg^{-1}\cdot min^{-1}$; HA $22.3\pm6.6mL\cdot Kg^{-1}\cdot min^{-1}$; NA $19.2\pm6.8mL\cdot Kg^{-1}\cdot min^{-1}$ Average VO_2peak 42% lower than normative values ($1.48\pm0.522mL\cdot Kg^{-1}\cdot min^{-1}$ vs. $2.56\pm0.412mL\cdot Kg^{-1}\cdot min^{-1}$respectively) Persons with a higher level of ambulatory status had higher VO_2peak (1.85±0.572ml/kg/min vs. 1.29±0.402ml/kg/min, p<0.001) BF 74.4±38.5mm Persons with a higher level of ambulatory status had less BF (p=0.03) compared with less ambulatory persons (CA

						59.1±29.2mm; HA 65.5±32.3mm; NA 86.0±42.0mm)
Buffart, van den Berg-Emons, van Meeteren, Stam, and Roebroeck (2009)	Cross-sectional	51 subjects with MMC 51% males 16-30y	Outpatient (Netherlands)	Progressive maximal exercise test on an electronically braked arm or cycle ergometer Thickness of 4 skinfolds (biceps, triceps, subscapular, suprailiac)	VO$_2$peak BF	VO$_2$peak 1.48±0.52L·min^{-1} CA 1.85±0.57L·min^{-1}; HA 1.44±0.45L·min^{-1}; NA 1.29±0.40L·min^{-1} BF 74.4±38.5mm CA 59.1±29.2mm; HA 65.5±32.3mm; NA 86.0±42.0mm
Danielsson, et al. (2008)	Cross-sectional	38 subjects with MMC 53% males 3.8-16.8y	Outpatient (Sweden)	Manual muscle testing ROM measure	Muscle strength ROM	Knee extensors muscle strength 36.8% graded 0-3; 63.3% graded 4-5 A 100% graded 4-5; NA 26.3% graded 4-5; $p<0.0001$ ROM Hip flexion contracture ≥20º: 32.4% A 5.3%; NA 61.1%; $p=0.0007$ Knee flexion contracture ≥20º:31.6% A 0%; NA 63.1%; $p<0.0001$ Equinus ≥15º: 26.3% A10.5%; NA 57.9%; $p=0.042$
de Groot, Takken, Schoenmakers, Vanhees, and Helders (2008)	Cross-sectional	23 subjects with SB 57% males 6-17y	Outpatient (Netherlands)	Graded treadmill test 6MWT	VO$_2$peak HRpeak 6MWD	VO$_2$peak; 33.14mL·Kg^{-1}·min^{-1} A 34.77mL·Kg^{-1}·min^{-1}; CA 26.2mL·Kg^{-1}·min^{-1}; $p<0.05$ 85% reached critical values HRpeak 172.2±21.2bpm A 175.5±20.8bpm; CA 158.5±19.1bpm; $p<0.05$ 6MWD 391.4±61m, 48.5±8.3% of the predicted A 408.5±57.2m, 50.2±8.3% of the predicted; CA 333.4±30.6m, 41.1±2.7% of the predicted; $p<0.05$
de Groot, et al. (2009)	Cross-sectional	20 subjects with SB 45% male 10.3±4.9y	Outpatient (Netherlands)	Graded treadmill test 3-minute supramaximal	VO$_2$peak HRpeak VO$_2$supramaximal	VO$_2$peak 34.1±8.3mL·Kg^{-1}·min^{-1} A 39.4±5.7mL·Kg^{-1}·min^{-1}; CA, 28.7±7mL·Kg^{-1}·min^{-1}; $p>0.05$ VO$_2$supramaximal 34.8ml/kg/min; No significant differences with VO$_2$peak ($p=0.274$)

				test 6MWT	6MWD	HRpeak 183.8±19.9bpm A 184.7±20.4bpm; CA 182.3±20.3bpm; p>0.05 6MWD 418±95 m A 473±45.5m; CA 357±100m; p<0.05
Schoenmakers, et al. (2009)	Cross-sectional	16 subjects with MMC 9.9±3.2y 7 subjects with LMMC 11.6±2.7y	Outpatient (Netherlands)	Maximal exercise test in a treadmill Manual muscle testing Isometric muscle strength 6MWT	VO_2peak HRpeak 6MWD Muscle strength	VO_2peak and HRpeak lower compared to reference values (p<0.05) 6MWD MMC 353±108m; LMMC 424±65m; p=0.07 Lower compared to reference values (p=0.03) Muscle strength > 25% hip abductors and the plantar flexors <3 grade. < 50% hip extensors = 5 grade Muscle strength of upper and lower extremity muscles lower compared to reference values (p<0.01)
Hassan, van der Net, Helders, Prakken, and Takken (2010))	Cross-sectional	22 subjects with SB (15 with MMC;7 with LMMC) 59% male 10.3±3.1y	Outpatient (Netherlands)	6MWT	6MWD	6MWD 391±61m 60.0±9.4% of the predicted distances derived from Li et al. (p<0.001) 62.2±9.4% of the predicted distances derived from Geiger et al. (p<0.001)
de Groot, et al. (2011)	Cross-sectional	23 subjects with MMC 48% male 10.7±3.5y	Outpatient (Netherlands)	Graded treadmill exercise test 6MWT	VO_2peak HRpeak 6MWD	VO_2peak 1.27±0.6L·min^{-1} HRpeak 185±21.1bpm 6MWD 408±94.7m

Data are Mean±Standard Deviation.

6MWT: six minute walk test; 6MWD: six minute walk distance; A: ambulatory; BF: Body Fat; CA: community ambulatory; CG: control group; HA: household ambulator; HRpeak: peak heart rate; LMMC: Lipomyelomeningocele; MMC: Myelomeningocele; NA: non-ambulator; NFA: non-functional ambulator; NS: not stated; ROM: range of movement; SB: Spina Bifida; USA: United States of America; VO_2peak: peak oxygen consumption.

Table 3–Exercise training effects in subjects with Spina Bifida

Author (Year)	Design	Participants	Setting (Country)	Intervention	Outcome Measures	Results
Andrade, Kramer, Garber, and Longmuir (1991)	B1	EG 8 subjects with SB 50% male 8-13y CG 5 subjects with SB 60% male 8-13y	Outpatient (Canada)	10 weeks 1 time/week 90’ per session (60’ exercise + 30’ housekeeping activities) Each exercise session was composed by: Warm up and cool down (slow rhythmical exercises; slow sustained stretching of the major muscle groups) Aerobic training through aerobic games (co-operative games, team sports and running/wheeling laps) Strength training (isotonic and dynamic exercises of shoulder flexors and abductors, elbow flexors and extensors and abdominals; each muscle group was exercised in 1 set of 10 repetitions)	Distance travelled in the 9’ run modified form HR Isometric hand held strength	Distance travelled in the 9’ run: EG Post 887±322m; CG Post: 752±171m; p<0.1; ES=1.09 HR during the 9’ run EG Post 158±14bpm; CG Post 160±10bpm; p<0.40; ES=0.33 Shoulder flexion strength EG Post 10.3±2.4Nm; Post 12.5±7.8Nm; p<0.25; ES=0.26 Shoulder extension strength EG Post 7.6±1.9Nm; CG Post 10±7.3Nm; p<0.25; ES=0.15 Shoulder abduction strength Post 11.3±4.7Nm; CG Post 13±7.8Nm; p<0.40; ES=0.0 Elbow flexion strength EG Post 20.3±7.6Nm; CG Post 21.2±4.3; p<0.01; ES=0.59 Elbow extension strength

						EG Post 19.2±8.7Nm; CG Post 22.2±4.3Nm; ES=0.12
Widman, McDonald, and Abresch (2006)	A1	8 subjects with SB: 4 males with 17.5±0.9y 4 females with 15.5±0.6y	Home-based (USA)	16 weeks 3 sessions/week At least 20 minutes per session Aerobic training though upper extremity exercise integrated with video game at anaerobic threshold.	**Maximum workload**	**Maximum workload** Pre 65.5±9.7W; Post 77.7±7.1W; p<0.015; ES=1.40
de Groot, et al. (2011)	Randomised controlled trial	EG: 18 patients with SB 50% male 10.3±2.9y CG: 14 patients with SB 64% male 11.1±2.6y	Home-based (Netherlands)	12 weeks 2 times/week Increasing time from 18 to 30 minutes Aerobic training (treadmill training) at 66% of HRpeak and gradually progressed from 70% to 140% of their individual walking speed.	VO_2peak 6MWD Isometric hand held strength BF	Mean change of VO_2peak EG 1.4±3.7mL·Kg-1·min-1; CG -3.0±7.5mL·Kg-1·min-1; p=0.034; ES=0.78 Mean change of 6MWD EG 38.7±34.6m; CG 2.1±27.8m; p=0.002; ES=1.08 Handgrip strength EG 1.6±9.9N; CG -3.0±7.6N; p=0.2; ES=0.51 Quadriceps strength EG -8.7±71.7N; CG -27.2±27.2N; p=0.7; ES=0.33 BF EG -1.7±17.5; CG -2.4±8.2; p=0.9; ES=0.05

Data are Mean±Standard Deviation.
6MWT: six minute walk test; 6MWD: six minute walk distance; BF: Body Fat; CG: control group; EG: experimental group; ES: effect size; HRpeak: peak heart rate; LMMC: Lipomyelomeningocele; MMC: Myelomeningocele; SB: Spina Bifida; USA: United States of America; VO_2peak: peak oxygen consumption.

Table 4 – Evidence for physical fitness in people with Spina Bifida compared with age matched healthy peers/normative values.

Fitness Measure	Increase in SB	Decrease in SB
VO_2peak		Widman, Abresch, Styne, and McDonald (2007), p≤0.05
		Bruinings, et al. (2007), p≤0.05
		Sherman, Kaplan, Effgen, Campbell, and Dold (1997), p≤0.05
		Schoenmakers, et al. (2009), p≤0.05
		Buffart, van den Berg-Emons, van Wijlen-Hempel, Stam, and Roebroeck (2008)
		Buffart, Roebroeck, et al. (2008)
Muscle strength		Widman, et al. (2007), p≤0.05
		Schoenmakers, et al. (2009), p≤0.05
		Buffart, van den Berg-Emons, et al. (2008)
		Buffart, van der Ploeg, et al. (2008)
		Norrlin, Strinnholm, Carlsson, and Dahl (2003)
ROM		Buffart, van den Berg-Emons, et al. (2008)
		Danielsson, et al. (2008)
Body fat	Widman, et al. (2007), p≤0.05	
	Buffart, van den Berg-Emons, et al. (2008)	
Maximum workload		Widman, et al. (2007), p≤0.05
6MWD		Schoenmakers, et al. (2009), p≤0.05
		de Groot, Takken, Schoenmakers,

		Vanhees, and Helders (2008)
		Hassan, van der Net, Helders, Prakken, and Takken (2010), $p \leq 0.05$
Neuromotor	No studies found	

SB: Spina Bifida; VO_2peak: peak oxygen consumption; ROM: range of movement; 6MWD: six minute walk distance.

Table 5 - Evidence for the effect of exercise training on the physical fitness of people with Spina Bifida.

Fitness Measure	**Significantly improved with exercise training**	**Not different with exercise training**
VO_2peak	de Groot, et al. (2011)	
Heart rate		Andrade, Kramer, Garber, and Longmuir (1991)
Muscle strength	Andrade, et al. (1991)	
	de Groot, et al. (2011)	
Body fat		de Groot, et al. (2011)
Maximum workload	Widman, McDonald, and Abresch (2006)	
6MWD	de Groot, et al. (2011)	
9' run modified form	Andrade, et al. (1991)	
Neuromotor	No studies found	

VO_2peak: peak oxygen consumption; 6MWD: six minute walk distance.