Clinical Studies

The following table summarizes key studies that have been conducted in people with Duchenne. The table has been organized in accordance with the different levels of evidence based on the types of study designs used.

Summary of studies using different supplements in people with Duchenne								
Supplement	***Dose used in study***	***Participants***	***Steroids***	***Study Duration***	***Results***	***Well tolerated***	***Study***	***Comments***
Systematic Review (Level 1 Evidence)								
Creatine monohydrate	Characteristics of included studies listed below				Across the 5 studies listed below, there was an average increase in strength (8.5%), lean body mass (0.63kg), and bone mineral density (3%)	Yes	Kley *et al.* (2013)	This study combined all outcomes from the individual trials listed below. Although the average increase is encouraging, there was some variation in the results which means individuals may experience very modest effects from creatine monohydrate.
Randomised controlled trials (Level 2 Evidence)								
Creatine monohydrate	5 g/day	8 boys Average 10 years	No	8 weeks	Modest but significant improvement in muscle strength and daily-life activities	Yes	Walter *et al.* (2000)	See above comments. The summary of these studies gives the best indication of evidence for creatine monohydrate.
	0.1 g/kg/day	31 boys Average 10 years	50%	4 months	Decrease bone breakdown, increased grip strength, and increased fat free mass	Yes	Tarnopolsky *et al.* (2004)	
	3 g/day	12 boys Average 11 years	No	3 months	Increase in muscle strength, resistance to fatigue, and bone mineral density	Yes	Louis *et al.* (2003)	
	5 g/day	33 boys 3-12 years	No	8 weeks	Muscle strength was preserved in short term	Yes	Banerjee *et al.* (2010)	
	5 g/day	50 boys 4-10 years	No	6 months	No change in muscle strength or function	Yes	Escolar *et al.* (2005)	
L-Glutamine	0.6g/kg/day	50 boys 4-10 years	No	6 months	No change in muscle strength or function	Yes	Escolar *et al.* (2005)	There is mixed evidence for glutamine. There have been no significant differences found in function after glutamine supplementation. However, the study by Escolar et al. (2005) stated that they could not rule out a positive effect of glutamine because the control group did not decline as much as they expected. The study by Mok et al. (2009) potential improvements when glutamine is used together with corticosteroids.
	0.5 g/kg/day	30 boys 2-10 years	15%	4 months	No differences in muscle mass and protein breakdown were observed; small improvements when used in conjunction with steroids.	Yes	Mok *et al.* (2009)	
	0.5 g/kg/day	26 boys 7-15 years	No	10 days	Decrease in whole-body protein degradation.	Yes	Mok *et al.* (2006)	

L-Leucine	0.2 g/kg/day	96 boys Average 10 years	No	12 months	Small increase in muscle strength observed in the treatment group.	Yes	Mendell *et al.* (1984)	The researchers state that the difference may have been due to an unexpected decline in the control group.
L-Carnitine	0.05 g/kg/day twice a day	20 boys 4-9 years	No	12 months	No effect on muscle function.	Yes	Escobar-Cedillo *et al.* (2013)	Whilst this study was conducted well, there were very few descriptive results presented in the study (eg. mean function) so it is difficult to completely understand these findings.
Coenzyme-Q10	3-5 mg/kg/day	25 boys Average age 9 years	95%	6 months	No change in cardiac performance.	Not reported	Salehi *et al.* (2017)	Note this study measured heart outcomes only. Functional / strength outcomes were not measured. There may be some positive effects on strength following Coenzyme Q10 supplementation as outlined in the next section of the table .
Omega-3 long chain fatty acids	2.9 g/day	36 boys Average age 8 years	No	6 months	Improved markers of inflammation.	Yes	Rodríguez-Cruz et al. (2017)	Again, functional / strength outcomes not measured.
Other studies (Lower Level Evidence)								
Vitamin D	0.8 ug/kg/day of calcifediol (vitamin D) in addition to keeping calcium intake to 1 g/day through dietary counselling	33 boys 5-15 years	100%	24 months	Decrease in bone breakdown, increased bone mineral density, no change in motor function.	Yes	Bianchi *et al.* (2011)	Maintaining adequate blood Vitamin D levels and calcium intake are a very important component of optimizing bone health especially in the context of corticosteroids therapy. Vitamin D levels and calcium intake should be continually monitored in your neuromuscular clinic or by your managing physician. A dietitian can help you improve your dietary intake.
L-Carnitine	0.05 g/kg	5 boys Age 6-21 years	No	Single injection	Increased ketosis in dystrophic patients.	Not reported	Paulson *et al.* (1998)	This study has limited clinical application.
Coenzyme-Q10	>90 mg/day	12 boys Average age 8 years	100%	6 months	Improved muscle strength in most participants by 8.5%; no change in cardiac parameters.	Yes	Spurney *et al.* (2011)	Initial dose was 90 mg/day, but dosing ranged between 90 to 510 mg/day. Individuals were dosed to meet a level of Coenzyme-Q10 in the blood (2.5µg/ml).

Studies in the DMD-mouse model

The following table summarizes some of the studies conducted in the DMD-mouse model on additional supplements that are yet to be investigated in clinical studies. Caution is recommended when interpreting these results as findings in the mouse model do not always translate to the same effects within humans. These studies are considered preliminary findings.

Summary of studies using different supplements in DMD mouse models				
Supplement	***Dose used in study***	***Results***	***Study Duration***	***Study***
1) L-Arginine	200 mg/kg/day (5 days/week)	Decrease in skeletal muscle necrosis, and decrease in serum creatine kinase; increase in diaphragm specific force	6 weeks	Voisin et al. (2005)
	200 mg/kg/day	Decrease in markers of skeletal muscle inflammation; increase in centrally nucleated fibers (indirect marker of muscle damage)	2 weeks	Hnia et al. (2008)
	5 mg/mL in drinking water	Increased fibrosis in heart and muscle	17 months	Wehling-Henricks et al. (2010)
2) L-Glutamine	500 mg/kg/day	Increase in antioxidant capacity	3 days	Mok et al. (2008)
3) Taurine	10 % of daily chow	Increase in forelimb strength; improvement in markers of muscle regeneration	4–8 weeks	De Luca et al. (2003)
	1 g/kg/day	Decrease in plasma lactate dehydrogenase	4–8 weeks	Cozzoli et al. (2011)
4) Green tea extract	0.01–0.05 % of daily chow	Decrease in skeletal muscle necrosis and regenerative cycling	4 weeks	Buetler et al. (2002)
	0.50 % of daily chow	Decrease in serum creatine kinase and increase in voluntary running performance	3 weeks	Call et al. (2008)
	0.25–0.50 % of daily chow	Decrease in the percentage of regenerating fibers	6 weeks	Evans et al. (2010)
5) Omega-3's	Eicosapentaenoic acid (EPA) only (300 mg/kg/day)	Decrease in the percentage of centrally nucleated fibers; decrease in inflammatory biomarkers	16 days	Machado et al. (2011)
	EPA and docosahexaenoic (DHA) - (300 and 150 mg/kg/day, respectively)	Decrease in the percentage of centrally nucleated fibers; decrease in inflammatory biomarkers; decrease in serum creatine kinase	16 days	Mauricio et al. (2013)
	EPA only (300 mg/kg/day)	Promoted anti- inflammatory M1 to M2 macrophage shift	16 days	de Carvalho et al. (2013)
6) L -Carnitine	75 mg/kg/day	Decrease in serum creatine kinase	6 weeks	Oh et al. (2005)
7) Resveratrol	100 mg/kg/day	Decrease in the percentage of centrally nucleated fibers and oxidative stress in skeletal muscle; increase in skeletal muscle strength; no change in inflammatory biomarkers	8 weeks	Gordon et al. (2014)
	100 mg/kg/day	8 week treatment increased skeletal muscle strength but not fatigue resistance	10 day or 8 weeks	Kostek et al. (2011)
	4 g/kg/day	Decrease in skeletal muscle oxidative stress and fibrosis; decrease in maintained muscle mass	32 weeks	Hori et al. (2011)
8) N-acetylcysteine	1 % of drinking water (60 mM)	Improved in various markers of cardiac pathology; Decrease in centrally nucleated fibers and NFk-β; Increase in utrophin levels	6 weeks	Whitehead et al. (2008)
	150 mg/kg/day	Decrease in inflammatory areas in muscle and TNF-α in the diaphragm muscle	2 weeks	Pinto et al. (2013)
9) Protandim	457 mg/m2	Improves some markers of oxidative stress, but did not improve motor function.	6 weeks 6 months	Qureshi et al. (2010)

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