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Surrogates for functional improvement in neuromuscular diseases



Linda Pax Lowes, PT PhD Lindsay Alfano, PT, DPT, PCS



**Parent Project
Muscular Dystrophy**

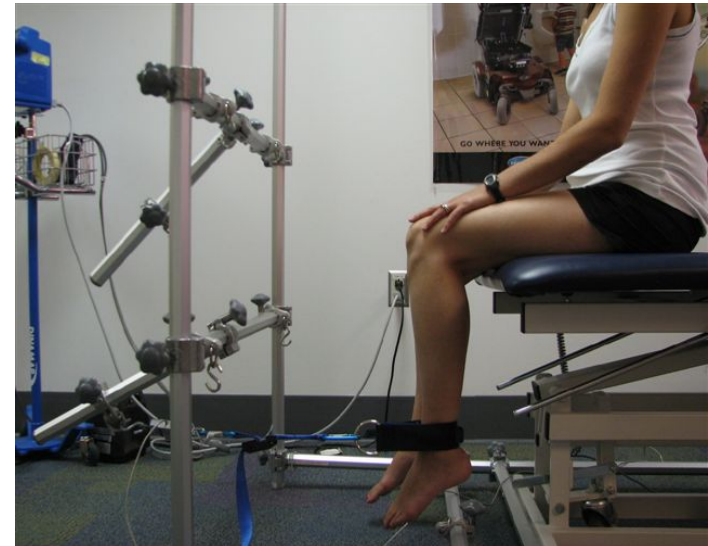
WHO / International Classification of Functioning, Disability and Health

Body Structures and function

Activity

Participation

- Maximal Voluntary Isometric Contraction
 - strength
- Modified Timed Up and Go
 - Getting out of a chair walking 3 m
- Timed 4 stairs
- Progressive Step Ups
 - 2, 4, 6, 8 inches
- IBM Functional Rating Scale
 - 10 questions 0-4 response
- Timed walking
 - 10m , 1-6 minutes
- Berg Balance Scale
 - 14 0-4 response



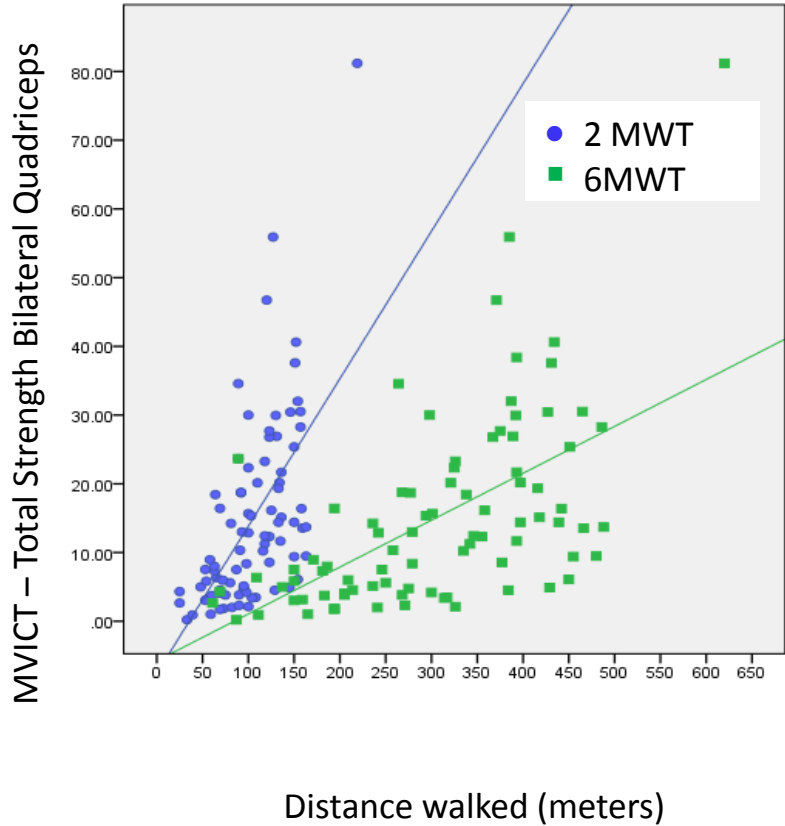
IBM	N	Range	Mean(SD)	Quad "r"	p value
IBMFRS	80	12 - 37	26.3 (\pm 5.7)	0.375 *	0.001
mTUG (sec)	63	5.6 - 35.2	12.2 (\pm 6.1)	-0.419 *	0.001
Stairs - Up (sec)	58	2.0 - 21.5	6.3 (\pm 3.7)	-0.307 *	0.019
Stairs - Down (sec)	58	1.6 - 22.9	6.1 (\pm 4.2)	-0.380 *	0.003
Height of curb (inches)	52	0 - 8	4.4 (\pm 3.3)	0.506 *	<0.001
2MWT Distance (meters)	84	25 - 219	104. 0(\pm 38.2)	0.603 *	<0.001
6 MWT Distance (meters)	85	61 - 620	304.2 (\pm 116.5)	0.578 *	<0.001



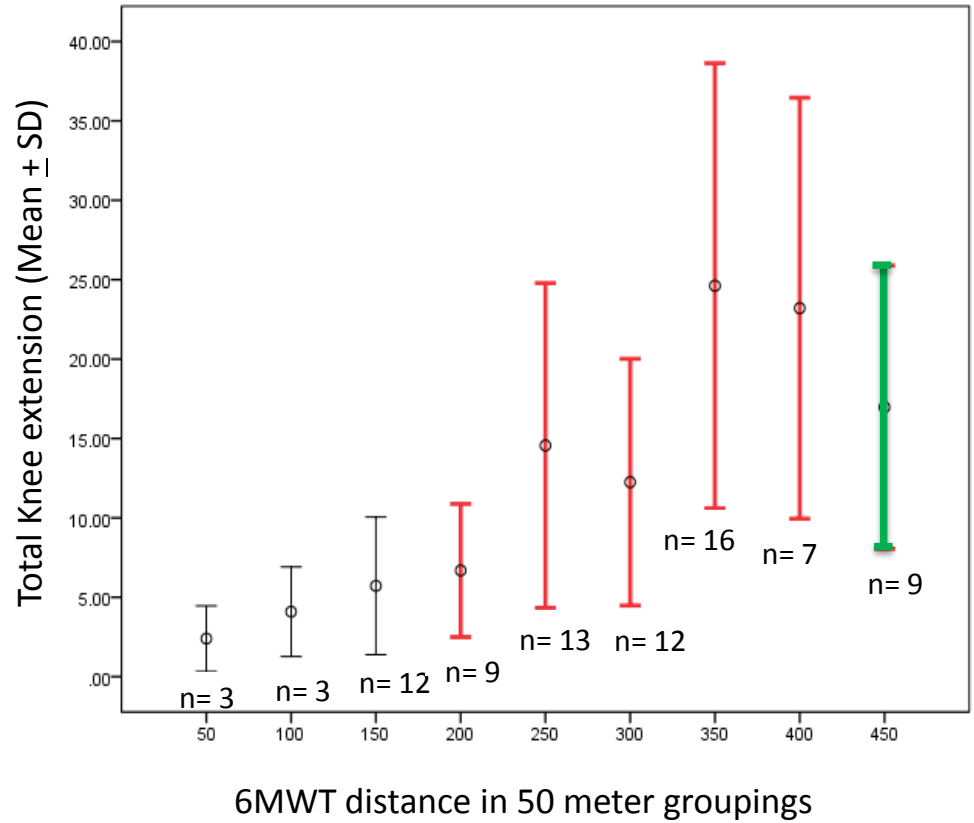
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Correlation between quad strength and distance walked in 2 and 6 minutes



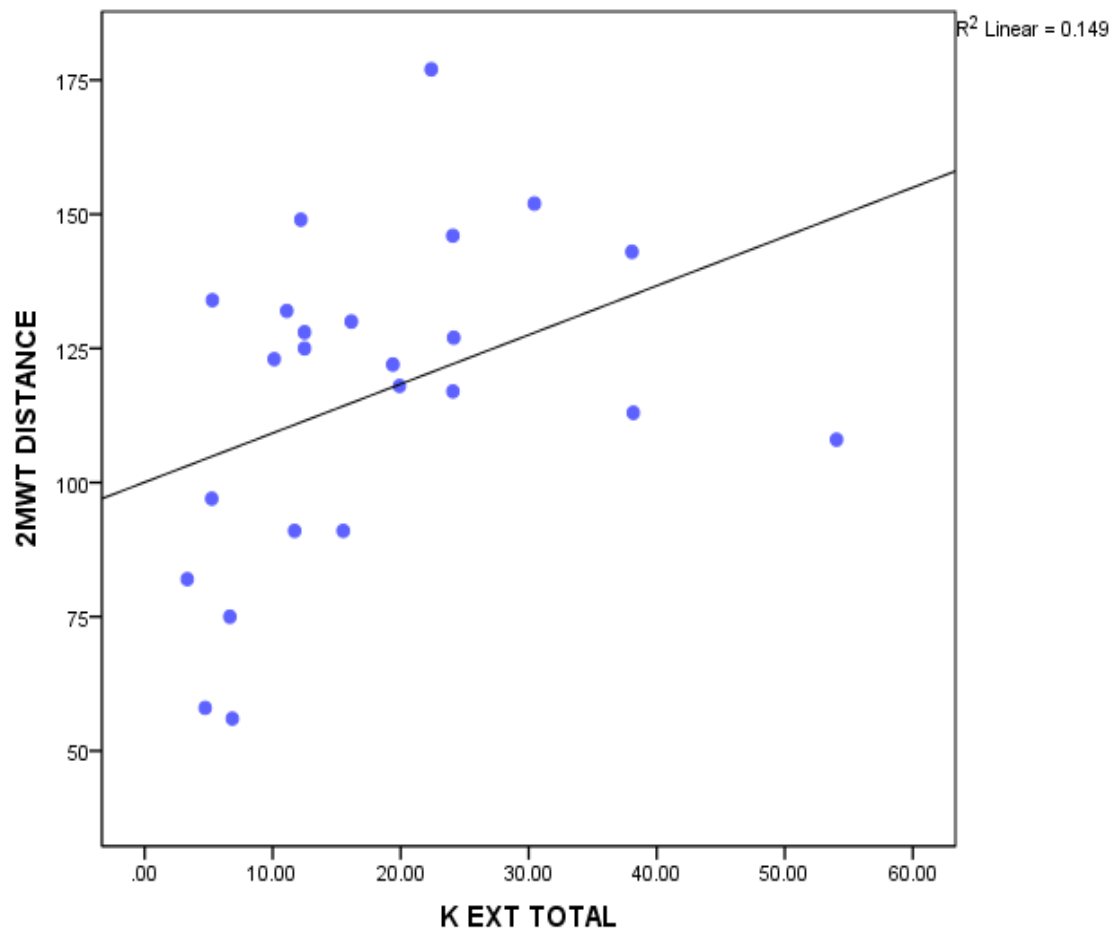
Relationship between quadriceps strength and distance walked in 6 minutes



Becker Muscular Dystrophy

BMD	N	Range	Mean(SD)	Quad "r"	p value
Berg	14	20-56	(46.6± 12.2)	0.648 *	0.012
mTUG (sec)	22	6 – 27.6	11.9 (± 7.2)	-0.41 *	0.001
Stairs - Up (sec)	16	2.0 - 23	6.5 (± 5.6)	-0.307 *	0.019
Stairs - Down (sec)	16	1.3 – 243.7	6.0 (± 10.3)	-0.380 *	0.003
Height of curb (inches)	14	0 - 8	5.0 (± 3.2)	0.612 *	0.02
2MWT Distance (meters)	24	56 - 177	116.4(± 29.8)	0.385	0.063
6 MWT Distance (meters)	24	154-548	345.2 (± 94.8)	0.378	0.068

Timed walking is not correlated to quad strength in this sample of individuals with BMD

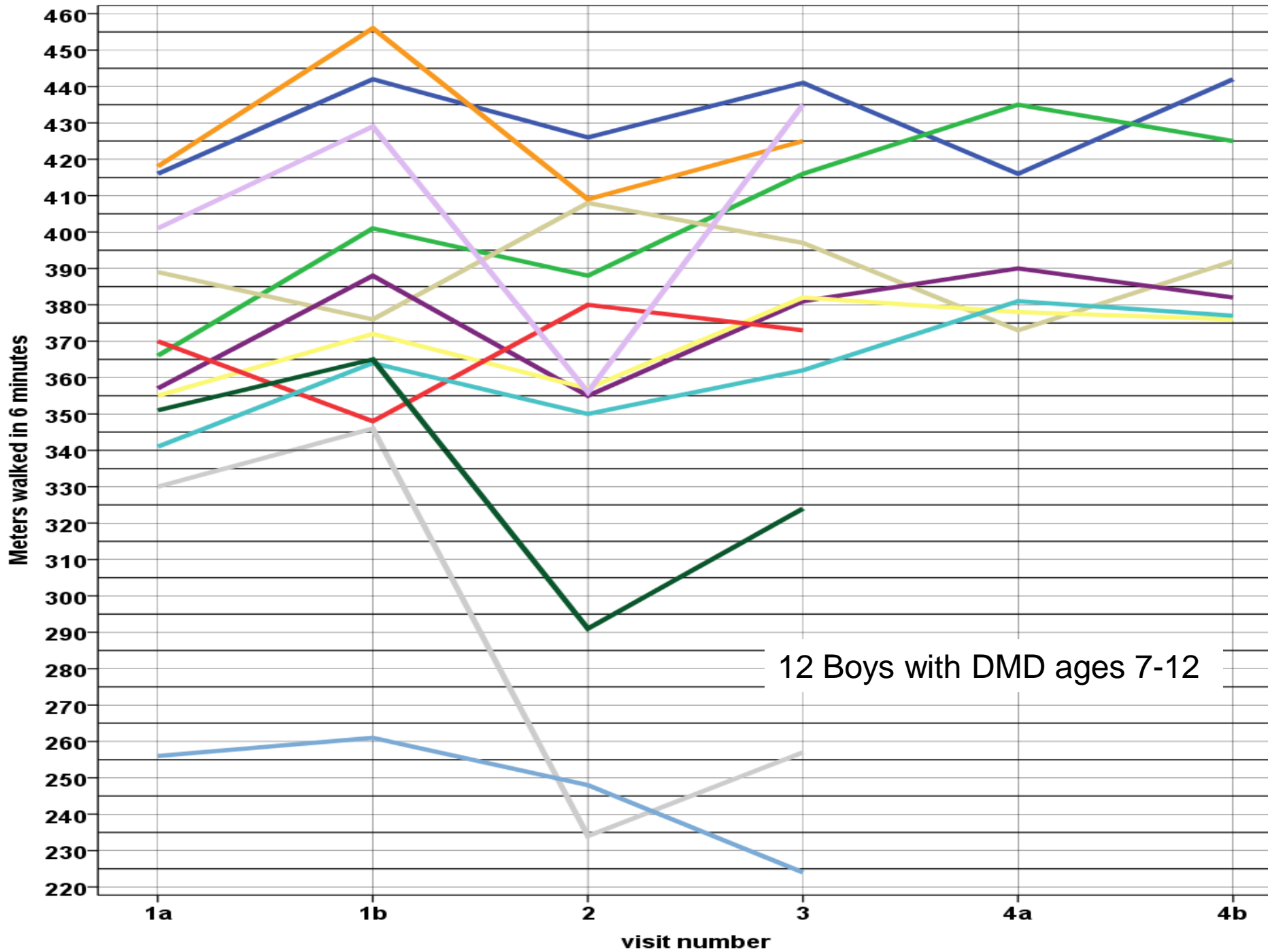


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Duchenne Muscular Dystrophy

DMD	N	Range	Mean(SD)	Quad "r"	p value
10 m WT (sec)	32	3.4-16.4	(6.0± 2.9)	0.586 *	0.000
NSAA	34	8-34	23.3 (± 8.2)	0.631*	0.000
Stairs - Up (sec)	31	1.4-19.1	4.7 (± 4.2)	-0.490 *	0.005
Stairs - Down (sec)	31	1.4 – 19.1	4.2 (± 3.9)	-0.403 *	0.024
2MWT Distance (meters)	35	25 - 171	119.1(± 31.9)	0.597*	0.063
6 MWT Distance (meters)	35	51-500	337.8 (± 101.6)	0.598*	0.000

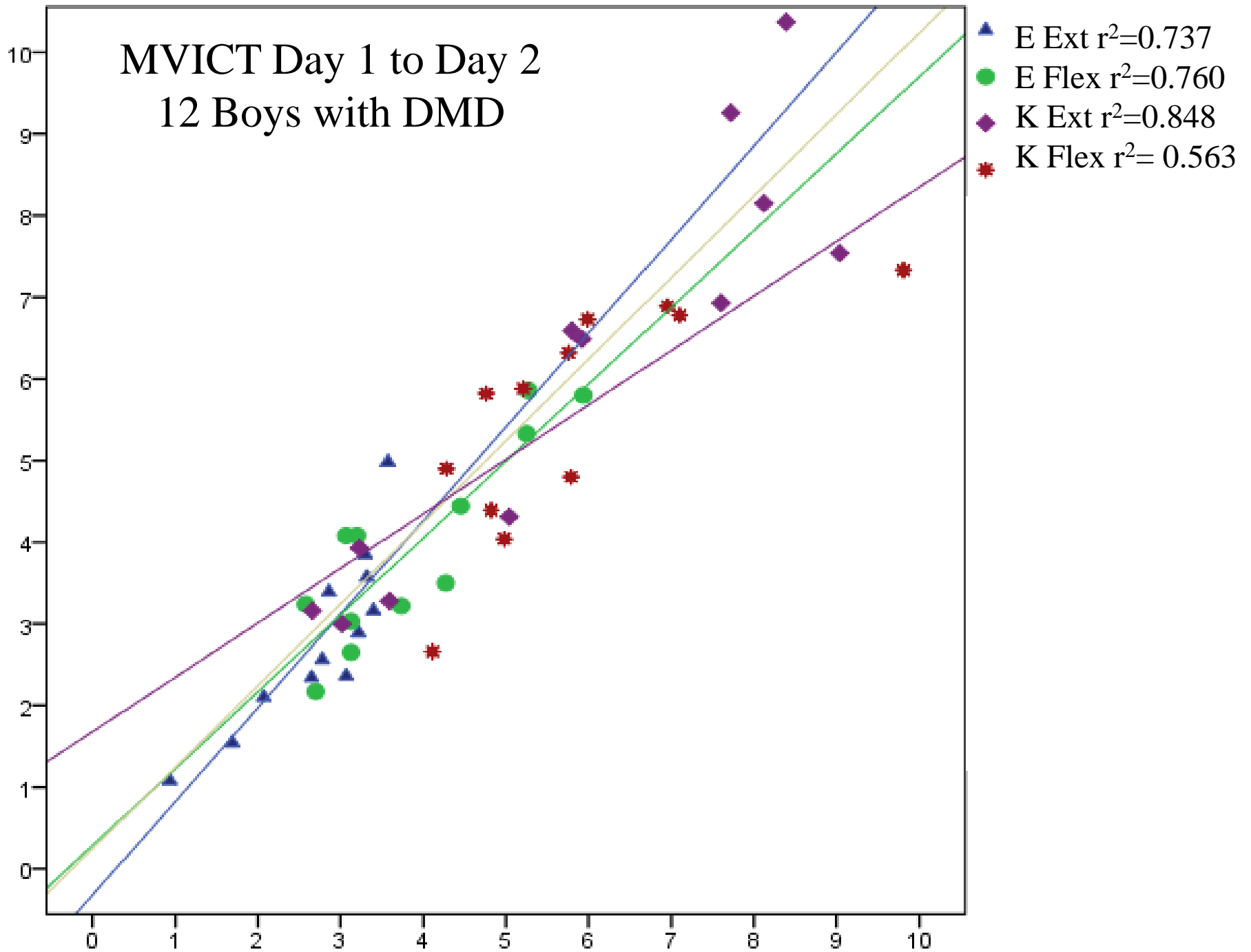


% Variability within each minute of 6MWT

	N	MINIMUM	MAXIMUM	AVERAGE	SD
MINUTE 1	10	1.45	27.94	11.9341	9.98
MINUTE 2	10	.00	10.85	3.0465	3.11
MINUTE 3	12	.00	8.81	1.9924	2.37
MINUTE 4	12	.00	4.58	1.7622	1.57
MINUTE 5	12	.00	10.34	1.8826	2.81
MINUTE 6	12	.28	7.10	2.6248	2.12

Learning effect? (Trial 1a and 1b)

MVICT Day 1 to Day 2 12 Boys with DMD



Summary

- Surrogates for function appear to be disease specific
- Single level interventions may not change all aspects of function
- Walking distance in small, short studies should be selected carefully
- Human performance is variable