

Additional table . Summary of published SMA Type I natural history studies

Legend: SS: single site study, MS: multiple site study, ERS: epidemiological registry survey, R: retrospective, P: prospective, M: mean (Standard Deviation), m: median (range, X-Y), IQR: interquartile range (25-75%ile)

Study Lead Author, Year of publication Years when data were collected Country	Study Type	Supportive Care Provided	Survival time	Age at death (months): Mean (M) and median (m) (range)
Descriptive case series. No or little genetic confirmation. Age of onset was generally less than 6 months of age. Little or no supportive care was provided				
Brandt, 1950 Denmark	ERS, R N=76 of 112	none		56% died by 12M of age 80% died by 4 years of age
Byers, 1961 1950-61 USA	SS, R N=52	none	2 survivors, M=17	Symptom onset < 2 months (Types IA and IB): 23/25 died, 2 sat, M=10 (0.5-52) Symptom onset 2-12 months (Types IC and II): 5 of 19 died, M=25 (7-73)
Pearn, 1973 1961-70, England	SS, R N= 76	none	None live >3 years	M=5.9, m= 7 95% died by 18 months
Thomas, 1994 1982-90 England	SS, R N=36	none	"few live beyond 2 years"	(n=29) M=9.6 , m=7 (1-24) Symptom onset <2 months: m=5.5 Symptom onset > 2 months: m=17
Ignatius, 1994 1960-88 Finland	ERS, R N=71	none	Uniformly poor if symptoms onset < 2 mos, variable if onset 2-6 mos	(n=69) M=8.75, m=7. Age at symptom onset and median age at death: birth, m=4; 1-2 months, m=7.5; 4-6 months, m=17.5
Zerres, 1995 1985-95 Germany	ERS, R N=197 + 90	minimal	2 years=32% 4 years=18% 10 years=8% 20 years =0	
Borkowska, 2002 Poland and Germany	ERS, R N=349	minimal	10% lived >5 years	(n=18) M=11 (3.4) years (5-24 years)
Case series with some genetic confirmation and SMN2 gene copy number. The extent of supportive care varied				
Chung, 2004 1984-2002 Hong Kong	SS, R N=22	Proactive	6 survivors, all NIV/TV dependent: 1Y=50% 2Y=40% 4Y,10Y,20Y =30%	16 of 22 (72%) died, m= approximately 2 years
loos, 2004 France	SS, R N=68	Proactive	IB: 18% alive with TV (8-17Y)	Age at symptom onset and median age at death:

			IC: 74% alive (? range)	IB: (n=27 of 33, 82% mortality), M=18 (29) IC: (n=9 of 35, 26% mortality), M=4 Years (3.75Y)
Barois, 2005 1997-2004 France	MS, P IB=14, IC=32	Proactive	IB: 100% at 4Y IC: 94% at 4Y	
Bach, 2007 1996-2006 USA	SS, R N=74 +18	Proactive	61 of 74 alive at M=66.1±44.8	Unsupported (n= 18), M=9.6±4.0 Supported (n=74), 13 died: M=32.9±50.4, one at 270
Oskoui 2007 1980-1994 (n=65) 1995-2006 (n-78) USA mainly	ERS, R N=143	2 cohorts: None Proactive	m=8.5 m=indeterminate	M=19.1, m=7.3 (1.0-193.5) M=22.1, m=10.0 m (2.5-112.0)
Cobben 2008 1996-99 Netherlands	SS/ESR, P N=34	Minimal	26% survive to 1Y	Entire group: M=6 (CI: 5-7), m=10 Those with SMN2CN of 2 (n=23): M=6.7
Mannaa, 2009 1989-2005 USA	SS, R N=15	Proactive	53% survivors: 2Y=62% 4Y=62% 10Y=8%	Data not available
Park, 2010 2000-09 Korea	SS, R N=14	57% with ventilation and feeding support	M=22.8 (2.0) 6M=93% 12M=93% 18M=76% 24M=76% 30M=65%	4 of 14 died, range 4-26
Rudnik-Schöneborn, 2009 2000-05 diagnosis Germany	ERS, R N=66	Variable NIV/TV, strong NG/GT support	Alive at 2Y: Overall: 6% SMN2CN2: 2% SMN2CN3: 67%	Mortality in 57 (86.3%): All patients: M=9.0 (few days-55 months), m=6.7 SMN2CN=2 (n=57): M=7.8, m=6.5 (0.5-30) SMN2CN=3 (n=5): M=28.9, m=19 (10.1-55.1)
Lemoine, 2012 2002-09 USA	SS, R N= 49	2 groups: proactive supportive	4 year survival: Proactive: 72% Supportive: 33%	Proactive care (n=23; 6 deaths): m=7.6 (IQR 6.5,10.5) Supportive care (n=26; 16 deaths), m=8.8 (IQR 4.7, 23.7).
Ge 2012 2003-08 birth year, followed to 2010 China	ERS, R	Minimal	31.8% alive m=10 (14-151) 1Y=45% 2Y=38% 4Y=33% 5Y=29%	68.2% died, M=11.3(15.0), m=7.0 Symptom onset <2 months (n=36), m= approx 6 Symptom onset ≥2 months (n=37), m= approx 36

			10Y=20%	
Farrar, 2013 1995-2010 Australia	SS, R N=20 Type I	Minimal 5% with GT and NIV	Survival at 1Y=40% 2Y=25% 4Y=6% 10Y=0	95% died, m=7.4 (3-56)
Petit, 2011 France	MS, R N=45 Type I	Minimal None of the survivors >2 years had prior GT or NIV/TV support	9/34 (26%) survived to 2 years SMN2CN=2 (n=1): 12% at 2Y SMN2CN=3 (n=8): 90% at 2Y	Mortality in 76%, M=10.7 (10 days - 6.5 years) SMN2CN=1: M=4 (1 day-11 months)
Finkel. 2014 2005-09 enrolment followed for up to 3Y	MS, P N=34	Proactive 76% with both GT and NIV/TV	Combined endpoint: Type IB, m=11.9 Type IC, m=13.6	Death (n=9): m=9 (2-14) Death or requiring >16 hours of BiPAP/day: Overall group: 13.5 m (IQR: 8.1-22) SNM2CN = 2: 10.5 m (IQR: 8.1-13.6 m)

Additional table: clinical meaningfulness of the HFMSE item

	HMFSE activities	Answers
1	ABLE TO SIT ON CHAIR OR WITH LEGS OFF BED WITH OR WITHOUT HAND SUPPORT	Sitting on normal school chair or public spaces (stools in restaurant)
		Sitting on toilet
		Sitting in car
		Independence out of the house
		Dress by herself/himself
2	ABLE TO SIT ON FLOOR CROSS LEGGED OR LEGS STRETCHED IN FRONT	Play on floor with siblings
		Sit on lounge chair, deck-chair
		Picnic
		Travel with less equipment
3	ABE TO BRING HANDS TO FACE AT EYE LEVEL	Inclusion in activities
		Wash face
		Brush and style
		Eat
		Put on eye glasses
		Answer telephone
4	ABE TO BRING HANDS TO HEAD	Blow nose
		Scratch head
		Wash, brush, style hair
		Put on hat
5	ROLL TO SIDE	Dress upper body
		Sleep by myself in my own room
		Caregiver does not have to wake up to turn him/her
		Help during dressing lying down
		Not having to turn head to see
6-7-8-9	ROLL	Play
		Sleep well
		Sunbathe
		Experience space
		Reach for something at sides when lying down
10	ABLE TO LYE DOWN FROM SITTING	Independence: lie down and rest when tired
		Fun movement when falling
		Rest on the back
		Safety: Fall in a controlled way (avoid head trauma)
11	ABLE TO RAISE HEAD WHEN LYING PRONE	Turn head react to stimulus, visual exploration of surroundings
		Read a book
		Not be afraid of choking
		Watch TV
		On beach not get sand in face
12-13	ABLE TO PROP ON FOREARMS OR EXTENDED ARMS	Read a book
		Watch TV
		Stretch back
		Sun bathe
14	ABLE TO SIT UP FROM LYING	No need for assistant
		Wake up and not have to wait for someone to sit me up
		Independence
		Sit up and drink at night
15	ABLE TO FOUR-POINT KNEEL	Play like an animal in school
		Hiding
		Be able to fit under small spaces
16	ABLE TO CRAWL	Move around
		Experience space
		Go get objects
		Play on floor
17	LIFT HEAD FROM SUPINE	Change head position
		Drink at night
		Read
		Watch TV
		Check the clock or alarm
18	STAND WITH SUPPORT	Use toilet standing (boy)
		Use full length mirror, perceive body dimensions and proportions
		Shower properly
		Climb in car
19	STAND WITHOUT SUPPORT	Use kitchen burners, cook
		Public spaces: wait for bus, stand in cue
		Cook
		Use normal sink
20	ABLE TO WALK	Dress
		Reach something on a shelf
		Freedom
		Go where and when you please
21-22	ABLE TO FLEX HIP FROM SUPINE	Get to places
		Not to have to rely on wheelchair batteries
		Dress (pants, socks)
		Scratch legs, kill mosquito
23-24-25-26	ABLE TO HALF KNEEL	Change position
		Pick up object on floor
		Tie shoe laces
		Put away object on low surfaces
		Pet a dog
		Play
		Make a proposal
		Kneel in church
		Talk with a kid
27	ABLE TO GO FROM STANDING TO SITTING	Not get hurt when falling or not fall in an embarrassing way
		Sit on grass or sand
		Pet a dog
		Sit beside a friend in same position/ play on floor
28	ABLE TO SQUAT	Pick up something from floor
		Sit when needed
		Pick up objects on floor
		Pee
29	ABLE TO JUMP	Tie shoes
		Pull up trousers
		Have fun, play
		Dance, gymnastics
		Avoid obstacles
		Normality
30-31-32-33	GO UP AND DOWN STAIRS	Go to friends' home regardless of where they live
		Stay and live in my own home
		Absence of barriers
		Normality