

Supplementary Table 2. Self-, and proxy-reported health in children with galactosemia diagnosed by means of family screening or newborn screening versus children with galactosemia diagnosed after clinical presentation according to both self-report and proxy-report on PROMIS domains.

	Children (age 8 – 18)						Parents or caregivers (age children 5 – 18)					
	FS/NBS			Clinical presentation			FS/NBS			Clinical presentation		
	N	Mean (SD)	N	Mean (SD)	P	d	N	Mean (SD)	N	Mean (SD)	P	d
Anxiety [^]	12	47.5 (7.5)	3	51.2 (11.5)	0.638	0.45	13	52.3 (7.7)	3	52.0 (10.9)	0.704 [#]	1.07 [§]
Depression [^]	11	47.5 (9.3)	3	49.0 (12.8)	0.867	0.15	13	46.9 (6.6)	3	46.2 (10.0)	0.924	0.09
Fatigue [^]	11	46.4 (8.4)	2	41.2 (16.7)	0.735	0.55	13	45.1 (6.6)	2	39.0 (8.1)	0.472	0.90
Cognition ⁺	11	46.3 (5.9)	3	48.5 (5.4)	0.585	0.37	13	45.6 (7.1)	3	49.8 (5.6)	0.328	0.61
Upper extremity function ⁺	11	45.2 (6.8)	2	46.0 (4.9)	0.870	0.11	13	44.9 (10.4)	2	50.4 (6.3)	0.591 [#]	0.23 [§]
Peer relations ⁺	11	48.9 (6.7)	3	43.3 (2.7)	0.056	0.90	13	43.9 (5.0)	3	43.3 (6.2)	0.901	0.10

N = Sample size. SD = Standard deviation. P = P-value. d = Cohen's D; ≥ 0.20 = small effect, ≥ 0.50 = medium effect, ≥ 0.80 = large effect. [^] Higher scores indicate more symptoms. ⁺Higher scores indicate better functioning. * P < 0.05, ** P < 0.01, *** P < 0.001. [§] Effect size calculated with median and median absolute deviation.

Supplementary Table 3. Self-reported health in adults with galactosemia diagnosed by means of family screening versus adults with galactosemia diagnosed after clinical presentation on PROMIS domains.

	Diagnosis after clinical presentation		Diagnosis after family screening		P	d
	N	Mean (SD)	N	Mean (SD)		
Anxiety [^]	25	54.3 (8.0)	5	57.3 (11.8)	0.607	0.35
Depression [^]	25	51.1 (7.6)	5	52.0 (10.1)	0.868	0.10
Fatigue [^]	25	52.4 (10.5)	5	60.4 (10.9)	0.190	0.75
Cognition ⁺	25	47.1 (9.0)	5	39.6 (13.0)	0.273	0.78
Physical functioning ⁺	25	52.3 (8.2)	5	47.6 (4.7)	0.152 [#]	0.32 [§]
Participation social roles ⁺	26	54.2 (6.8)	5	48.1 (8.8)	0.203	0.86
Satisfaction social roles ⁺	25	48.5 (8.2)	5	45.4 (6.2)	0.372	0.39
Companionship ⁺	25	50.7 (8.1)	5	47.5 (12.4)	0.603	0.36
Emotional support ⁺	25	53.4 (7.9)	5	51.0 (12.8)	0.705	0.27
Social Isolation [^]	25	46.8 (9.4)	5	55.8 (10.0)	0.120	0.94

N = Sample size. SD = Standard deviation. P = P-value. d = Cohen's D; ≥ 0.20 = small effect, ≥ 0.50 = medium effect, ≥ 0.80 = large effect. [^] Higher scores indicate more symptoms. ⁺Higher scores indicate better functioning. * P < 0.05, ** P < 0.01, *** P < 0.001. [§]Effect size calculated with median and median absolute deviation.

Supplementary Table 4. Self-, and proxy-reported health in children with the classical phenotype of galactosemia and good intellectual outcome versus poor intellectual outcome on PROMIS domains.

	Children (age 8 – 18)						Parents or caregivers (age children 5 – 18)					
	Good intellectual outcome			Poor intellectual outcome			Good clinical outcome			Poor clinical outcome		
	N	Mean (SD)	N	Mean (SD)	P	d	N	Mean (SD)	N	Mean (SD)	P	d
Anxiety [^]	5	49.2 (10.1)	4	49.5 (10.8)	0.968	0.03	5	54.9 (8.5)	5	51.4 (13.1)	0.324	0.32
Depression [^]	5	49.4 (11.0)	4	49.1 (12.4)	0.967	0.03	5	48.6 (4.1)	5	46.6 (10.9)	0.739	0.27
Fatigue [^]	4	52.3 (6.7)	4	46.2 (11.2)	0.340	0.66	4	46.7 (5.3)	5	43.6 (7.5)	0.524	0.48
Cognition ⁺	5	42.5 (3.3)	4	48.0 (7.7)	0.252	0.99	5	43.1 (5.8)	5	48.2 (8.1)	0.556 [#]	0.24 [§]
Upper extremity function ⁺	4	45.3 (8.7)	4	45.3 (7.8)	0.989	0.01	4	49.8 (10.0)	5	38.8 (11.5)	0.219 [#]	3.02 [§]
Peer relations ⁺	5	48.3 (5.8)	4	42.7 (2.7)	0.104	1.19	5	46.1 (15.4)	5	43.0 (11.5)	0.376	0.65

N = Sample size. SD = Standard deviation. P = P-value. d = Cohen's D; ≥ 0.20 = small effect, ≥ 0.50 = medium effect, ≥ 0.80 = large effect. [^] Higher scores indicate more symptoms. ⁺Higher scores indicate better functioning. [#] Non-parametric test. * P < 0.05, ** P < 0.01, *** P < 0.001. [§] Effect size calculated with median and median absolute deviation. Good intellectual outcome: Intelligence Quotient ≥ 85, poor intellectual outcome: Intelligence Quotient < 85.

Supplementary Table 5. Self-reported health in adults with galactosemia and good intellectual outcome versus poor intellectual outcome on PROMIS domains.

	Good intellectual outcome		Poor intellectual outcome		<i>P</i>	<i>d</i>
	N	Mean (SD)	N	Mean (SD)		
Anxiety [^]	4	47.8 (5.0)	14	58.3 (8.7)	0.014*	1.30
Depression [^]	4	43.8 (2.8)	14	54.2 (6.5)	0.003***	0.67 [§]
Fatigue [^]	4	43.4 (4.9)	14	58.4 (9.3)	0.001**	1.74
Cognition ⁺	4	57.1 (5.0)	14	41.8 (9.0)	0.001**	1.83
Physical functioning ⁺	4	58.3 (5.4)	14	49.9 (4.9)	0.044*	1.68
Participation social roles ⁺	4	59.3 (3.1)	14	50.9 (7.7)	0.006**	1.19
Satisfaction social roles ⁺	4	55.4 (7.0)	14	49.1 (6.2)	0.336 [#]	0.13 [§]
Companionship ⁺	4	49.3 (4.3)	14	53.2 (8.9)	0.243	0.48
Emotional support ⁺	4	58.5 (6.8)	14	52.9 (9.3)	0.230	0.62
Social Isolation [^]	4	36.0 (3.9)	14	50.4 (8.9)	0.010**	1.42 [§]

N = Sample size. SD = Standard deviation. *P* = P-value. *d* = Cohen's *D*; ≥ 0.20 = small effect, ≥ 0.50 = medium effect, ≥ 0.80 = large effect. [^] Higher scores indicate more symptoms. ⁺ Higher scores indicate better functioning. [#] Non-parametric test. * *P* < 0.05, ** *P* < 0.01, *** *P* < 0.001. [§] Effect size calculated with median and median absolute deviation. Good intellectual outcome: Intelligence Quotient ≥ 85 , poor intellectual outcome: Intelligence Quotient < 85.

Supplementary Table 6. Self-reported HRQoL (TAAQOL) between adults with galactosemia and good intellectual outcome versus poor intellectual outcome.

	Good intellectual outcome		Poor intellectual outcome		<i>P</i>	<i>r</i>
	N	Mean (SD)	N	Mean (SD)		
Gross motor [#]	4	87.5 (13.5)	14	76.8 (20.9)	0.362	-0.21
Fine motor [#]	5	93.8 (8.8)	14	93.3 (11.4)	1.000	0.00
Pain [#]	4	81.3 (13.5)	14	70.5 (22.1)	0.486	-0.16
Sleeping [#]	5	53.8 (36.3)	14	50.9 (33.7)	0.963	-0.01
Cognitive function [#]	5	85.0 (22.4)	14	54.5 (26.3)	0.045*	-0.46
Social function [#]	5	91.3 (7.1)	14	77.7 (25.3)	0.348	-0.22
Daily activities [#]	5	72.5 (41.1)	14	70.5 (29.5)	0.708	-0.09
Sexuality [#]	5	100.0 (0.0)	14	67.9 (28.9)	0.016*	-0.55
Vitality [#]	5	58.3 (33.3)	14	44.0 (24.1)	0.176	-0.31
Happiness [#]	5	73.3 (16.0)	14	63.1 (29.4)	0.779	-0.06
Depressive moods [#]	5	83.3 (16.7)	14	60.7 (29.5)	0.111	-0.37
Agressiveness [#]	5	97.8 (5.0)	14	88.1 (14.1)	0.059	-0.43

N = Sample size. SD = Standard deviation. *P* = P-value. *r* = Pearson *r* correlation; ≥ 0.10 = small effect, ≥ 0.30 = medium effect, ≥ 0.50 = large effect. Higher scores indicate a better quality of life. * *P* < 0.05, ** *P* < 0.01, *** *P* < 0.001. [#] Non-parametric test.