Increased survival disparities among children and adolescents & young adults with acute myeloid leukemia: a Dutch population-based study

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Supplementary Table S1 Age-specific 5-year relative survival of children and AYAs (0-39 years) diagnosed with AML (excl. APL and ML-DS) in the Netherlands between 1990-2015, overall and by period of diagnosis

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Supplementary Table S3 Univariable and multivariable associations of alternative categories of age with excess mortality due to AML (excl. APL and ML-DS) in children and AYAs (0-39 years) until 5 years of follow-up, the Netherlands, 1990-2015

Supplementary Table S4 Five-year and 10-year relative survival of children (0-17 years) and AYAs (18-39 years) diagnosed with APL in the Netherlands between 1990-2015, overall and by subgroup

Supplementary Table S1 Age-specific 5-year relative survival[a] of children and AYAs (0-39 years) diagnosed with AML (excl. APL and ML-DS) in the Netherlands between 1990-2015, overall and by period of diagnosis

				5-year relative survival								
	1990-1999	2000-2009	2010-2015	1990-2015		1990-1999		2000-2009		2010-2015		
	N	N	N	%	SE	%	SE	%	SE	%	SE	p_{trend}
Age (years)												
0	27	31	18	47.6	5.8	29.8	8.8	55.1	9.0	61.4	11.5	**0.01**
1-9	110	117	64	60.8	2.9	53.7	4.8	54.7	4.6	84.3	4.6	**0.001**
10-17	92	96	57	56.6	3.2	48.5	5.2	58.4	5.0	66.7	6.2	**0.01**
18-29	226	177	110	42.9	2.2	35.5	3.2	46.9	3.8	51.9	4.8	**0.002**
30-39	296	263	137	42.9	1.9	35.3	2.8	44.3	3.1	56.7	4.3	**<0.001**
Age (years)												
0-14	193	208	119	57.9	2.2	49.8	3.6	55.8	3.4	74.8	4.0	**<0.001**
15-19	69	64	36	50.1	3.9	38.4	5.9	57.9	6.2	58.4	8.2	**0.01**
20-29	193	149	94	42.7	2.4	35.8	3.5	45.0	4.1	53.3	5.2	**0.003**
30-39	296	263	137	42.9	1.9	35.3	2.8	44.3	3.1	56.7	4.3	**<0.001**

AYAs adolescents and young adults, *AML* acute myeloid leukemia, *APL* acute promyelocytic leukemia, *ML-DS* myeloid leukemia associated with Down Syndrome, *SE* standard error.

[a] Expected probabilities of survival were estimated using the Ederer II method.

Supplementary Table S2 Multivariable associations[a] of age with excess mortality due to AML (excl. APL and ML-DS) in children and AYAs (0-39 years) until 5 years of follow-up stratified by period of diagnosis, the Netherlands, 1990-2015

	Until 5 years of follow-up (1990-2015)											
	1990-1999				2000-2009				2010-2015			
Variable	$N_{at\ risk}$	Excess HR	95% CI	p-value	$N_{at\ risk}$	Excess HR	95% CI	p-value	$N_{at\ risk}$	Excess HR	95% CI	p-value
Age												
Children (0-17 years)	229	1.00 (ref)			244	1.00 (ref)			139	1.00 (ref)		
AYAs (18-39 years)	522	1.41	(1.14-1.75)	**0.002**	440	1.49	(1.16-1.91)	**0.002**	247	2.62	(1.66-4.14)	**<0.001**
Age (years)												
0	27	2.74	(1.61-4.66)	**<0.001**	31	1.11	(0.61-2.01)	0.73	18	3.01	(1.13-7.98)	**0.03**
1-9	110	1.00 (ref)			117	1.00 (ref)			64	1.00 (ref)		
10-17	92	1.40	(0.94-2.09)	0.10	96	0.89	(0.59-1.34)	0.58	57	2.44	(1.13-5.26)	**0.02**
18-29	226	1.78	(1.28-2.46)	**0.001**	177	1.32	(0.93-1.88)	0.12	110	5.03	(2.45-10.33)	**<0.001**
30-39	296	1.84	(1.34-2.52)	**<0.001**	263	1.53	(1.09-2.14)	**0.01**	137	4.42	(2.11-9.23)	**<0.001**

AML acute myeloid leukemia, *APL* acute promyelocytic leukemia, *ML-DS* myeloid leukemia associated with Down Syndrome, *AYAs* adolescents and young adults, *excess HR* excess hazard ratio, *CI* confidence interval, *SCT* stem cell transplantation.

[a] Adjusted for follow-up time (years), sex (male, female), SCT (no, yes), and site of primary treatment (non-academic hospital, academic hospital).

Supplementary Table S3 Univariable and multivariable associations[a] of alternative categories of age with excess mortality due to AML (excl. APL and ML-DS) in children and AYAs (0-39 years) until 5 years of follow-up, the Netherlands, 1990-2015

		Until 5 years of follow-up (1990-2015)								
		Univariable			Adjusted 1[b]			Adjusted 2[c]		
Variable	$N_{at\ risk}$	Excess HR	95% CI	p-value	Excess HR	95% CI	p-value	Excess HR	95% CI	p-value
Age (years)										
0-14	520	1.00 (ref)			1.00 (ref)			1.00 (ref)		
15-19	169	1.25	(0.97-1.60)	0.09	1.24	(0.97-1.60)	0.09	1.30	(1.01-1.68)	**0.04**
20-29	436	1.50	(1.25-1.80)	**<0.001**	1.47	(1.23-1.77)	**<0.001**	1.61	(1.33-1.94)	**<0.001**
30-39	696	1.53	(1.30-1.80)	**<0.001**	1.51	(1.28-1.78)	**<0.001**	1.68	(1.41-2.00)	**<0.001**

AML acute myeloid leukemia, *APL* acute promyelocytic leukemia, *ML-DS* myeloid leukemia associated with Down Syndrome, *AYAs* adolescents and young adults, *excess HR* excess hazard ratio, *CI* confidence interval, *SCT* stem cell transplantation.

[a] All models were adjusted for follow-up time (years).

[b] Additionally adjusted for sex (male, female) and period of diagnosis (1990-1999, 2000-2009, 2010-2015).

[c] Additionally adjusted for sex (male, female), period of diagnosis (1990-1999, 2000-2009, 2010-2015), SCT (no, yes), and site of primary treatment (non-academic hospital, academic hospital).

Supplementary Table S4 Five-year and 10-year relative survival[a] of children (0-17 years) and AYAs (18-39 years) diagnosed with APL in the Netherlands between 1990-2015, overall and by subgroup

	5-year relative survival (1990-2015)									10-year relative survival (1990-2009)[b]								
	Total			Children (0-17 years)			AYAs (18-39 years)			Total			Children (0-17 years)			AYAs (18-39 years)		
	N	%	SE	N	%	SE	N	%	SE	N	%	SE	N	%	SE	N	%	SE
Overall	202	80.8	2.8	34	76.6	7.3	168	81.7	3.0	146	73.7	3.7	28	64.5	9.1	118	75.9	4.0
Sex																		
Male	83	83.3	4.1	18	83.4	8.8	65	83.2	4.7	60	75.5	5.6	15	66.9	12.2	45	78.4	6.3
Female	119	79.1	3.8	16	68.8	11.6	103	80.7	3.9	86	72.5	4.9	13	61.6	13.5	73	74.4	5.2
Period of diagnosis																		
1990-1999	74	73.2	5.2	15	73.4	11.4	59	73.2	5.8	74	70.8	5.4	15	66.8	12.2	59	71.8	6.0
2000-2009	72	77.9	4.9	13	69.3	12.8	59	79.8	5.3	72	76.7	5.1	13	61.7	13.5	59	80.0	5.3
2010-2015	56	94.8	3.0	6	NA	NA	50	94.2	3.4	NA	NA	NA	NA	NA	NA	NA	NA	NA
P_{trend}		**0.004**			0.34			**0.01**			0.44			0.75			0.32	
Site of primary treatment																		
Non-academic hospital	54	70.2	6.3	5	NA	NA	49	71.3	6.6	40	65.2	7.7	4	NA	NA	36	66.9	8.0
Academic hospital	148	84.7	3.0	29	79.4	7.5	119	86.0	3.2	106	76.9	4.2	24	66.8	9.6	82	79.9	4.5
Therapy																		
Chemo	190	84.9	2.6	33	78.9	7.1	157	86.2	2.8	135	78.2	3.6	27	66.8	9.1	108	81.1	3.9
SCT	12	75.2	12.5	5	NA	NA	7	NA	NA	12	67.2	13.7	5	NA	NA	7	NA	NA

AYAs adolescents and young adults, *APL* acute promyelocytic leukemia, *SE* standard error, *SCT* stem cell transplantation.

NA: N at risk <10

[a] Expected probabilities of survival were estimated using the Ederer II method.

[b] 10-year relative survival could not be estimated for the most recent period 2010-2015 due to incomplete follow-up.