



A one-mutation mathematical model can explain the age incidence of acute myeloid leukemia with mutated nucleophosmin (NPM1)

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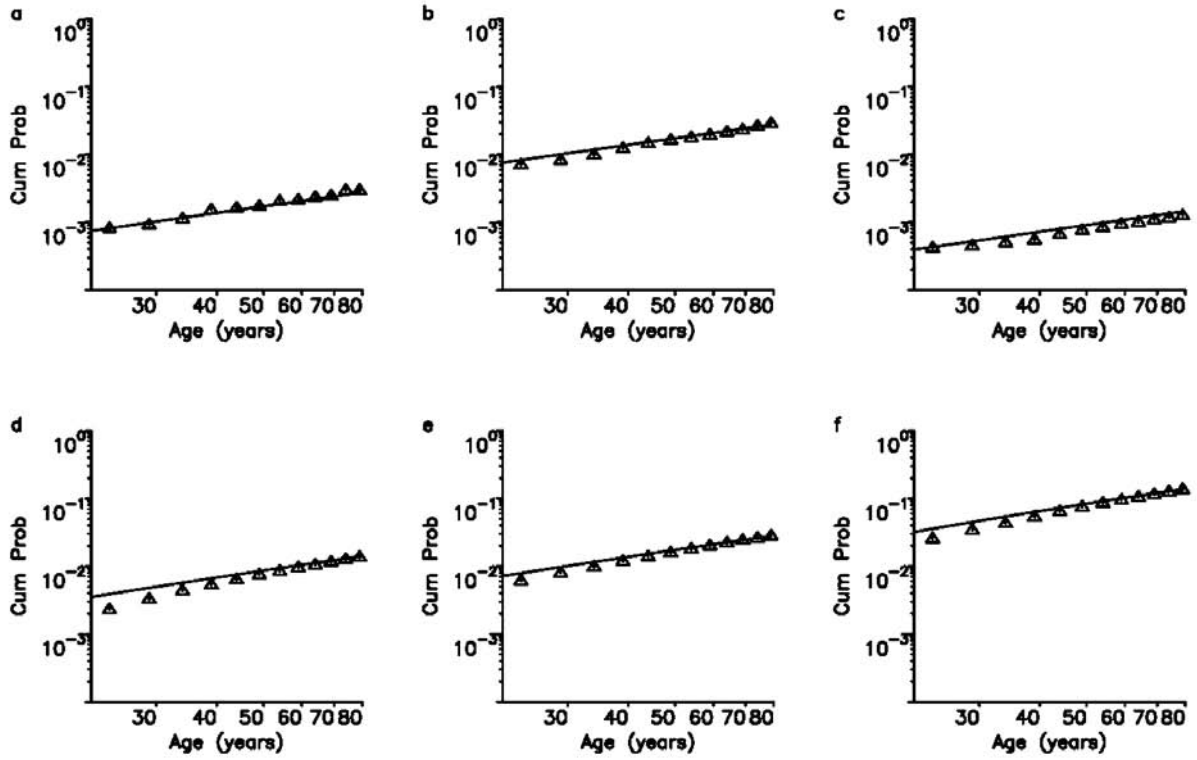
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Supplementary Table 1. Poisson regression models.

Variable	Model	95%		Model	95%	
	1	CI	U	2	CI	U
	IRR	L		IRR	L	
Age						
20-24	ref			ref		
25-29	1.6	0.90	2.7	1.8	1.1	2.8
30-34	2.2	1.4	3.7	2.5	1.7	3.8
35-39	4.1	2.5	6.5	4.2	2.8	6.1
40-44	5.3	3.3	8.5	5.9	4.0	8.6
45-49	6.9	4.3	11.0	7.3	5.0	10.7
50-54	7.5	4.7	12.0	8.8	6.0	12.9
55-59	9.8	6.2	15.5	10.5	7.2	15.4
Country						
Germany	ref			ref		
Italy	0.75	0.28	2.0	1.2	1.04	1.3
Netherlands	0.49	0.17	1.4	0.46	0.38	0.55
Age x Country						
age classxGermany		ref				
25-29xItaly		2.0	0.65	6.1		
30-34xItaly		1.7	0.58	5.0		
35-39xItaly		1.2	0.43	3.5		
40-44xItaly		1.6	0.57	4.5		
45-49xItaly		1.4	0.52	4.0		
50-54xItaly		1.8	0.65	5.0		
55-59xItaly		1.6	0.56	4.4		
25-29xNetherland		0.73	0.17	3.0		
30-34xNetherland		1.0	0.30	3.6		
35-39xNetherland		0.85	0.26	2.8		
40-44xNetherland		1.0	0.32	3.2		
45-49xNetherland		0.81	0.26	2.6		
50-54xNetherland		1.2	0.40	3.6		
55-59xNetherland		0.74	0.23	2.3		

LR test $p=0.85$

Poisson regression models with and without AGExCOUNTRY interaction terms respectively. IRR Incidence rate ratio; 95%CI 95% confidence interval; L: lower bound; U: upper bound; LR: likelihood ratio.



Supplementary Figure 1. Comparison of the probability of diagnosis with AML, equation (1), with the direct stochastic computer simulation, system (2). The panels show the cumulative probability of being diagnosed with AML before a certain age. Parameter values are: a) $\tau=30$, $\mu=10^9$, $q=10^{-4}$, $N=10^4$, $N=10^{13}$, $r=14$; b) $\tau=3$, $\mu=1^9$, $q=10^6$, $N=10^4$, $N=10^{13}$, $r=14$; c) $\tau=10$, $\mu=10^9$, $q=10^9$, $N=10^3$, $N=10^9$, $r=2$; d) $\tau=100$, $\mu=10^6$, $q=10^{-7}$, $N=100$, $N=10^9$, $r=2$; e) $\tau=50$, $\mu=10^6$, $q=10^{-10}$, $N=100$, $N=10^9$, $r=2$; f) $\tau=100$, $\mu=10^{-10}$, $q=10^{-10}$, $N=10^7$, $N=10^{10}$, $r=2$.

Supplementary Table 2. Mann-Witney u test.

	<i>Slope DE</i>	<i>Slope NL</i>	<i>Slope IT</i>
<i>NPM1</i> -mutated	4.038	4.096	4.332
<i>NPM1</i> -mutated/ <i>FLT3</i> -ITD	4.222	3.664	3.935
<i>NPM1</i> -mutated/ <i>FLT3</i> wt	3.927	4.657	4.752

The slopes of the three sets (*NPM1*-mutated, *NPM1*-mutated/*FLT3*-ITD, *NPM1*-mutated/*FLT3* wt) are not significantly different according to Mann-Witney U test ($p > 0.05$).