Loss of life expectancy in patients with myeloproliferative neoplasms in Sweden

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Supplementary materials

age	scenario	LE$_P$	LE$_C$	LLE
Women				
55	default	30.9	25.5 (24.2; 26.7)	5.4 (4.3; 6.7)
	constant	30.9	25.8 (24.7; 26.8)	5.2 (4.2; 6.2)
	zero	30.9	27.7 (27.0; 28.3)	3.3 (2.7; 3.9)
65	default	21.9	16.0 (15.3; 16.6)	5.9 (5.3; 6.6)
	constant	21.9	16.2 (15.5; 16.8)	5.7 (5.1; 6.3)
	zero	21.9	17.5 (17.0; 18.0)	4.4 (3.9; 4.9)
75	default	13.7	9.7 (9.4; 9.9)	4.1 (3.8; 4.3)
	constant	13.7	9.7 (9.4; 10.0)	4.0 (3.8; 4.3)
	zero	13.7	9.9 (9.6; 10.2)	3.8 (3.5; 4.1)
85	default	7.0	5.1 (4.9; 5.3)	1.9 (1.7; 2.0)
	constant	7.0	5.1 (4.9; 5.3)	1.9 (1.7; 2.0)
	zero	7.0	5.1 (5.0; 5.3)	1.9 (1.7; 2.0)
Men				
55	default	28.2	22.5 (21.4; 23.6)	5.7 (4.6; 6.8)
	constant	28.2	22.6 (21.6; 23.6)	5.5 (4.6; 6.6)
	zero	28.2	24.2 (23.5; 24.9)	3.9 (3.2; 4.6)
65	default	19.4	13.5 (13.0; 14.1)	5.9 (5.3; 6.5)
	constant	19.4	13.6 (13.1; 14.2)	5.8 (5.2; 6.4)
	zero	19.4	14.6 (14.1; 15.1)	4.9 (4.4; 5.4)
75	default	11.8	7.8 (7.6; 8.1)	4.0 (3.7; 4.3)
	constant	11.8	7.8 (7.6; 8.1)	4.0 (3.7; 4.3)
	zero	11.8	8.0 (7.7; 8.2)	3.9 (3.6; 4.2)
85	default	5.7	3.8 (3.6; 4.0)	1.9 (1.8; 2.1)
	constant	5.7	3.8 (3.7; 4.0)	1.9 (1.8; 2.1)
	zero	5.7	3.8 (3.7; 4.0)	1.9 (1.7; 2.1)

Table S1: Estimates of Life Expectancy in the absence of Myeloproliferative Neoplasms (MPN) (LE$_P$), Life expectancy for individuals with MPN (LE$_C$) and the Loss in Life Expectancy (LLE) with 95% Confidence Intervals for women and men aged 55, 65, 75, and 85 years at MPN diagnosis based on a period analysis with period window 2012-2021, using diagnoses from 2002-2021 in Sweden. The results are obtained with three assumptions about the behaviour of the extrapolated excess hazard. Default refers to linear log cumulative excess hazard, constant and zero refer to a constant and a zero value of the excess hazard, respectively, after the follow-up period. The values are presented in years.

age	$RMST_P$	PV		ET		PMF		all subtypes combined	
		$RMST_C$	LRMST	$RMST_C$	LRMST	$RMST_C$	LRMST	$RMST_C$	LRMST
Women									
55	14,6	13.8	0.8 (0.5; 1.1)	14.0	0.6 (0.4; 0.9)	11.4	3.2 (1.9; 4.4)	13.6	1.0 (0.8; 1.1)
65	13,8	12.3	1.5 (1.2; 1.9)	12.8	1.1 (0.8; 1.3)	9.2	4.6 (3.5; 5.6)	12.1	1.8 (1.6; 2.0)
75	11,6	9.3	2.4 (2.0; 2.7)	10.0	1.6 (1.3; 1.9)	6.5	5.2 (4.3; 5.9)	9.1	2.6 (2.4; 2.8)
85	6,9	5.2	1.6 (1.4; 1.9)	5.7	1.20 (0.9; 1.5)	3.9	3.0 (2.4; 3.5)	5.1	1.8 (1.6; 1.9)
Men									
55	14,35	13.4	1.0 (0.7; 1.3)	13.5	0.8 (0.5; 1.2)	10.4	4.0 (2.5; 5.2)	13.0	1.3 (1.1; 1.6)
65	13,27	11.5	1.8 (1.5; 2.1)	12.0	1.3 (1.0; 1.7)	8.0	5.3 (4.3; 6.3)	11.0	2.31 (2.1; 2.6)
75	10,60	8.1	2.5 (2.1; 2.8)	8.8	1.8 (1.4; 2.2)	5.4	5.2 (4.6; 5.8)	7.6	3.0 (2.8; 3.2)
85	5,68	4.1	1.6 (1.3; 1.8)	4.5	1.2 (0.9; 1.5)	3.1	2.6 (2.1; 3.0)	3.8	1.9 (1.7; 2.0)

Table S2: 15-year restricted mean survival time in the absence of Myeloproliferative Neoplasms (MPN) ($RMST_P$), 15-year restricted mean survival time for individuals with MPN ($RMST_C$), and the loss in RMST (LRMST) with 95% Confidence Intervals. Results are presented for women and men diagnosed at ages 55, 65, 75 and 85 years and based on a period analysis with period window 2012-2021, using diagnoses from 2002-2021 in Sweden. The estimates are presented in years. The estimates are given by MPN subtypes: essential thrombocythemia (ET), polycythaemia vera (PV), and primary myelofibrosis (PMF) as well as for all MPN subtypes combined (including MPN-U).

	The Inpatient Registry				
	ET	**MPN-UNS**	**PMF**	**PV**	**Total**
N	775 (30.8%)	342 (13.6%)	65 (2.6%)	1,332 (53.0%)	2,514 (100.0%)
Age at diagnosis	76.0 (67.7-83.7)	77.1 (69.5-85.8)	75.4 (68.9-81.9)	74.9 (67.7-82.3)	75.6 (68.0-83.4)
sex					
men	298 (38.5%)	170 (49.7%)	39 (60.0%)	794 (59.6%)	1,301 (51.8%)
women	477 (61.5%)	172 (50.3%)	26 (40.0%)	538 (40.4%)	1,213 (48.2%)
Categories of age					
[50;60]	79 (10.2%)	26 (7.6%)	6 (9.2%)	143 (10.7%)	254 (10.1%)
[60;70]	165 (21.3%)	64 (18.7%)	13 (20.0%)	294 (22.1%)	536 (21.3%)
[70;80]	233 (30.1%)	110 (32.2%)	25 (38.5%)	437 (32.8%)	805 (32.0%)
[80;99]	298 (38.5%)	142 (41.5%)	21 (32.3%)	458 (34.4%)	919 (36.6%)
	The Outpatient Registry				
	ET	**MPN-UNS**	**PMF**	**PV**	**Total**
N	572 (44.3%)	175 (13.6%)	35 (2.7%)	509 (39.4%)	1,291 (100.0%)
Age at diagnosis	69.7 (61.6-76.9)	72.6 (65.2-79.1)	69.2 (61.5-74.3)	70.1 (61.9-77.4)	70.1 (62.0-77.1)
sex					
men	185 (32.3%)	68 (38.9%)	21 (60.0%)	279 (54.8%)	553 (42.8%)
women	387 (67.7%)	107 (61.1%)	14 (40.0%)	230 (45.2%)	738 (57.2%)
Categories of age					
[50;60]	121 (21.2%)	21 (12.0%)	8 (22.9%)	102 (20.0%)	252 (19.5%)
[60;70]	174 (30.4%)	53 (30.3%)	11 (31.4%)	152 (29.9%)	390 (30.2%)
[70;80]	182 (31.8%)	64 (36.6%)	14 (40.0%)	178 (35.0%)	438 (33.9%)
[80;99]	95 (16.6%)	37 (21.1%)	2 (5.7%)	77 (15.1%)	211 (16.3%)
	The Swedish Cancer Registry (SCR)				
	ET	**MPN-UNS**	**PMF**	**PV**	**Total**
N	2,004 (40.4%)	668 (13.5%)	612 (12.3%)	1,682 (33.9%)	4,966 (100.0%)
Age at diagnosis	71.8 (63.7-78.8)	74.0 (66.6-81.1)	73.3 (65.8-79.7)	71.3 (64.4-77.3)	72.1 (64.6-78.9)
sex					
men	824 (41.1%)	329 (49.3%)	359 (58.7%)	813 (48.3%)	2,325 (46.8%)
women	1,180 (58.9%)	339 (50.7%)	253 (41.3%)	869 (51.7%)	2,641 (53.2%)
Categories of age					
[50;60]	327 (16.3%)	76 (11.4%)	72 (11.8%)	265 (15.8%)	740 (14.9%)
[60;70]	536 (26.7%)	155 (23.2%)	159 (26.0%)	480 (28.5%)	1,330 (26.8%)
[70;80]	705 (35.2%)	249 (37.3%)	236 (38.6%)	625 (37.2%)	1,815 (36.5%)
[80;99]	436 (21.8%)	188 (28.1%)	145 (23.7%)	312 (18.5%)	1,081 (21.8%)

Table S3: Demographic characteristics of individuals diagnosed with Myeloproliferative Neoplasms (MPN) and reported to the Swedish Cancer Registry (SCR), Outpatient Registry, or Inpatient Registry.

scenario	LE$_P$	LE$_C$	LLE
default	16.4	12.0 (11.6; 12.4)	4.4 (4.0; 4.8)
constant	16.4	12.1 (11.8; 12.4)	4.3 (4.0; 4.6)

Table S4: Marginal estimates of Life Expectancy in the absence of Myeloproliferative Neoplasms (MPN)(LE$_P$), Life expectancy for individuals with MPN (LE$_C$) and the Loss in Life Expectancy (LLE) with 95% Confidence Intervals, obtained with two assumptions about the behaviour of the extrapolated excess hazard. Default refers to linear log cumulative excess hazard, constant refers to a constant excess hazard after the follow-up period. Individuals diagnosed with MPN were identified through the Swedish Cancer Register (SCR) between 2002 and 2021. The results are for MPN cases aged 50 and above based on a period analysis with period window 2012-2021 using diagnoses from 2002 to 2021 in Sweden. The values are presented in years.

MPN subtype	RMST$_P$	RMST$_C$	LRMST
PV	11.5	10.1 (9.9; 10.3)	1.4 (1.2; 1.6)
ET	11.4	10.5 (10.3; 10.7)	0.9 (0.7; 1.1)
PMF	10.9	6.6 (6.2; 7.0)	4.3 (3.9; 4.7)
All subtypes combined	11.4	9.4 (9.3; 9.6)	2.0 (1.8; 2.1)

Table S5: Marginal 15-year restricted mean survival time in the absence of Myeloproliferative Neoplasms (MPN) (RMST$_P$), 15-year restricted mean survival time for individuals with MPN (RMST$_C$) and the loss in 15-year RMST (LRMST) with 95% Confidence Intervals for MPN cases aged 50 and above based on a period analysis with period window 2012-2021 using diagnoses from 2002-2021 in Sweden. The estimates are presented in years. Individuals diagnosed with MPN were identified through the Swedish Cancer Register (SCR) between 2002 and 2021. The estimates are given by MPN subtypes: polycythaemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF) as well as for all MPN subtypes combined (including MPN-U).

age	scenario	LE$_P$	LE$_C$	LLE
Women				
55	default	31	26.0 (24.0; 27.7)	5.0 (3.2; 6.9)
	constant	31	26.4 (24.8; 27.7)	4.6 (3.2; 6.7)
65	default	21.9	15.8 (15.0; 16.8)	6.1 (5.1; 6.9)
	constant	21.9	16.2 (15.3; 16.9)	5.7 (5.0; 6.6)
75	default	13.7	9.9 (9.5; 10.2)	3.9 (3.5; 4.2)
	constant	13.7	9.9 (9.5; 10.3)	3.8 (3.5; 4.2)
85	default	7.0	5.6 (5.3; 5.9)	1.4 (1.1; 1.7)
	constant	7.0	5.6 (5.3; 5.9)	1.4 (1.1; 1.7)
Men				
55	default	28.2	22.5 (20.8; 24.0)	5.7 (4.2; 7.4)
	constant	28.2	22.7 (21.3; 24.2)	5.5 (4.0; 7.0)
65	default	19.4	13.0 (12.3; 13.9)	6.4 (5.6; 7.1)
	constant	19.4	13.2 (12.4; 13.8)	6.3 (5.6; 7.1)
75	default	11.8	7.8 (7.5; 8.2)	4.0 (3.6; 4.3)
	constant	11.8	7.8 (7.5; 8.2)	4.0 (3.7; 4.7)
85	default	5.8	4.3 (4.0; 4.6)	1.5 (1.2; 1.7)
	constant	5.8	4.3 (4.0; 4.6)	1.5 (1.2; 1.8)

Table S6: Estimates of Life Expectancy in the absence of Myeloproliferative Neoplasms (MPN) (LE$_P$), Life expectancy for individuals with MPN (LE$_C$) and the Loss in Life Expectancy (LLE) with 95% Confidence Intervals for women and men aged 55, 65, 75, and 85 years at MPN diagnosis based on a period analysis with period window 2012-2021, using diagnoses from 2002-2021 in Sweden. The results are obtained with two assumptions about the behaviour of the extrapolated excess hazard. Default refers to linear log cumulative excess hazard and constant refers to a constant excess hazard after the follow-up period. Individuals diagnosed with MPN were identified through the Swedish Cancer Register (SCR) between 2002 and 2021. The values are presented in years.

		PV		ET		PMF		all subtypes combined	
age	$RMST_P$	$RMST_C$	LRMST	$RMST_C$	LRMST	$RMST_C$	LRMST	$RMST_C$	LRMST
Women									
55	14.6	14.2	0.4 (0.1; 0.6)	14.2	0.4 (0.2; 0.7)	11.5	3.1 (1.7; 4.3)	13.8	0.8 (0.5; 1.0)
65	13.8	13.1	0.8 (0.5; 1.0)	12.7	1.1 (0.8; 1.4)	9.2	4.6 (3.5; 5.6)	12.2	1.7 (1.4; 1.9)
75	11.6	10.5	1.2 (0.9; 1.5)	9.8	1.8 (1.4; 2.3)	6.5	5.1 (4.1; 5.9)	9.3	2.3 (2.0; 2.6)
85	6.9	6.2	0.7 (0.4; 0.9)	5.9	1 (0.6; 1.4)	4.1	2.8 (2.1; 3.4)	5.6	1.3 (1.0; 1.6)
Men									
55	14.4	13.8	0.5 (.2; .8)	13.7	0.6 (0.3; 1.0)	10.6	3.8 (2.3; 5.1)	13.2	1.2 (0.9; 1.5)
65	13.3	12.2	1.1 (0.7; 1.4)	11.7	1.6 (1.2; 1.9)	8	5.2 (4.2; 6.2)	10.9	2.4 (2.1; 2.7)
75	10.6	9.1	1.5 (1.0; 1.9)	8.4	2.3 (1.8; 2.7)	5.5	5.1 (4.4; 5.7)	7.6	3.0 (2.7; 3.3)
85	5.7	5.0	0.7 (0.4; 1.1)	4.7	1.0 (0.5; 1.4)	3.3	2.4 (1.8; 2.8)	4.3	1.4 (1.2; 1.7)

Table S7: 15-year restricted mean survival time in the absence of Myeloproliferative Neoplasms (MPN) ($RMST_P$), 15-year restricted mean survival time for individuals with MPN ($RMST_C$), and the loss in RMST (LRMST) with 95% Confidence Intervals. Results are presented for women and men diagnosed at ages 55, 65, 75 and 85 years and based on a period analysis with period window 2012-2021, using diagnoses from 2002-2021 in Sweden. Individuals diagnosed with MPN were identified through the Swedish Cancer Register (SCR) between 2002 and 2021. The estimates are presented in years. The estimates are given by MPN subtypes: essential thrombocythemia (ET), polycythaemia vera (PV), and primary myelofibrosis (PMF) as well as for all MPN subtypes combined (including MPN-U).
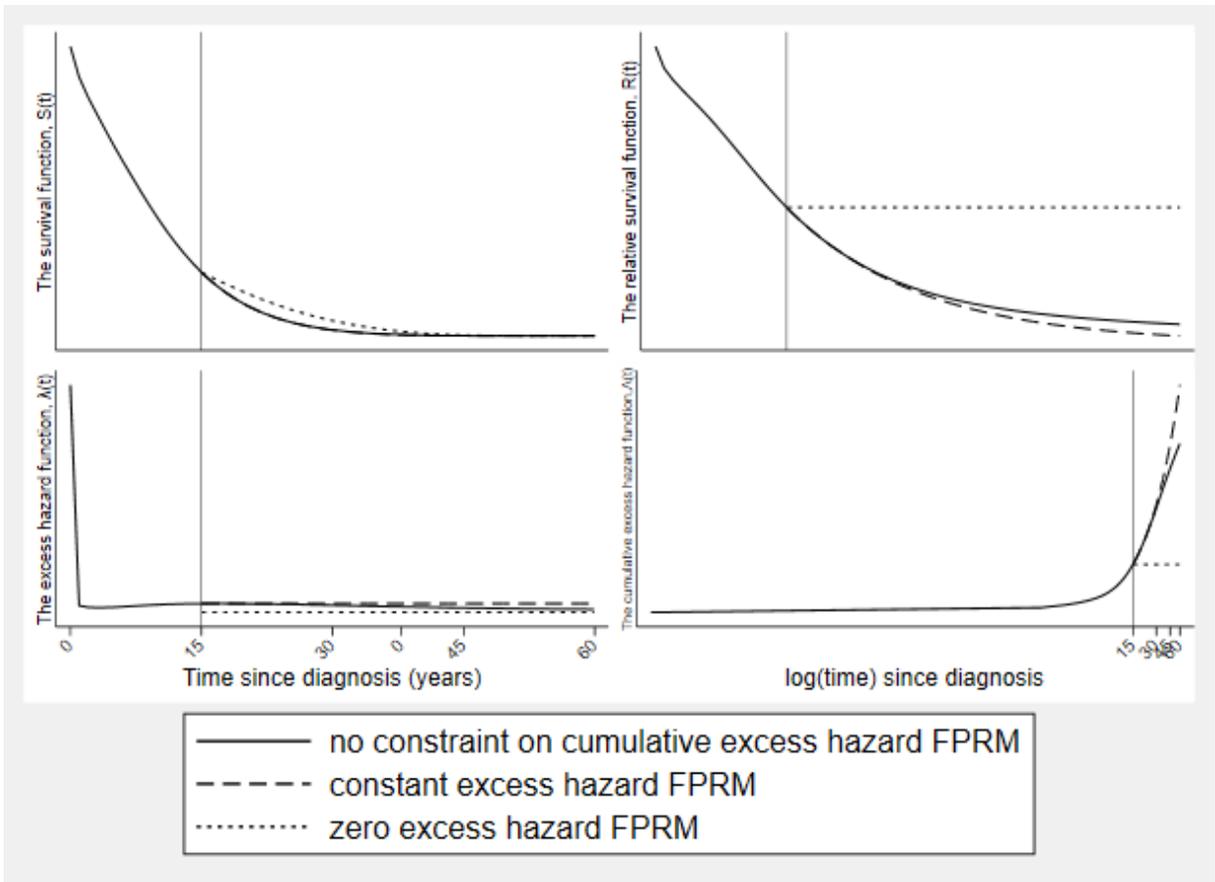
Figure S1: Graphical illustration of extrapolation of different functions beyond the 15-year follow-up period with various assumptions of the behaviour of the excess hazard in the extrapolation. No constraint refers to a standard Flexible Parametric Relative Survival Model (FPRM) when extrapolation of the excess hazard is based on the model parameters and is the default. Constant excess hazard FPRM has a constant value of the excess hazard function after the follow-up period, which equals the value of the excess hazard at 15 years. Zero excess hazard FPRM has 0 excess hazard from the last follow-up.
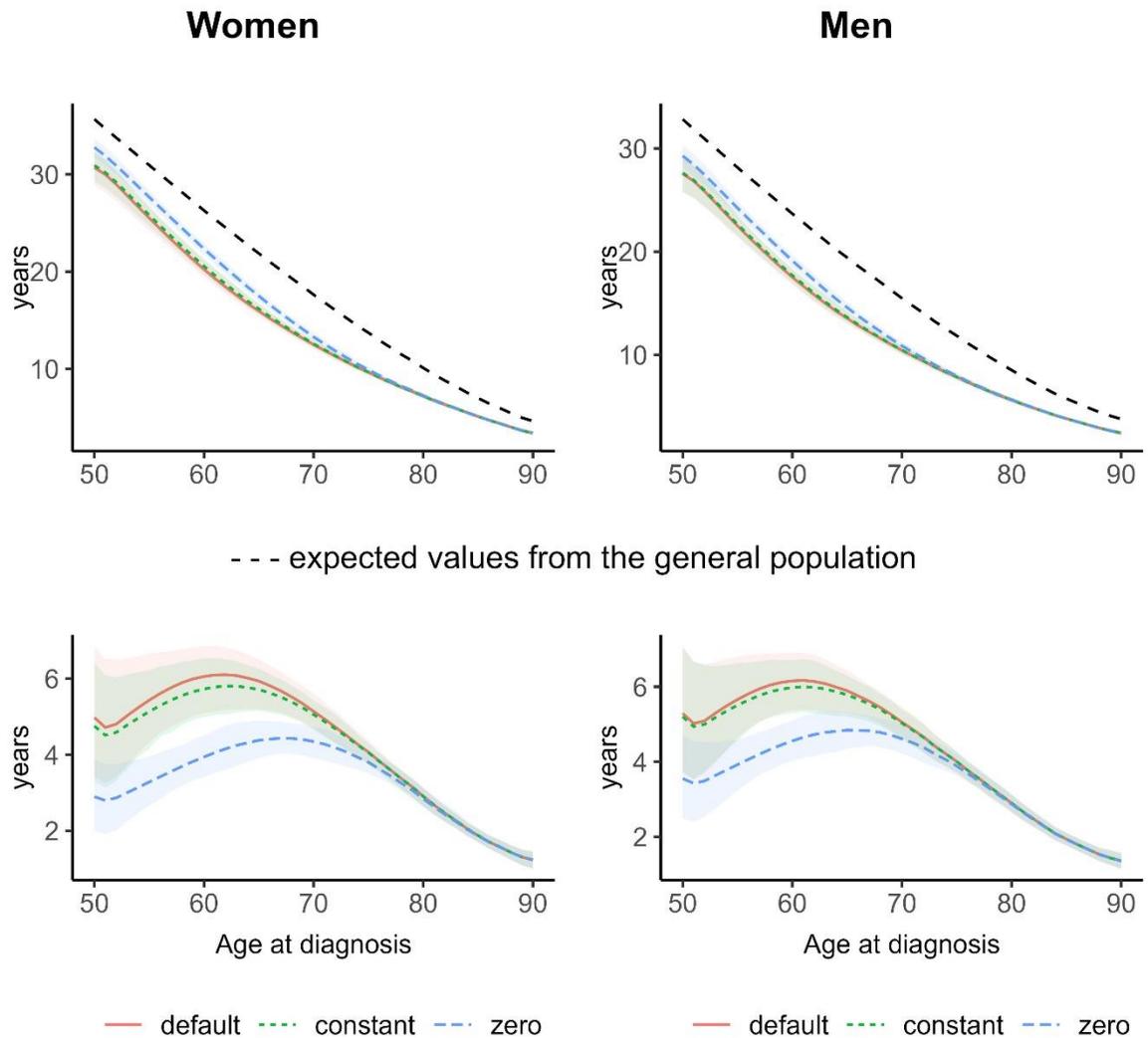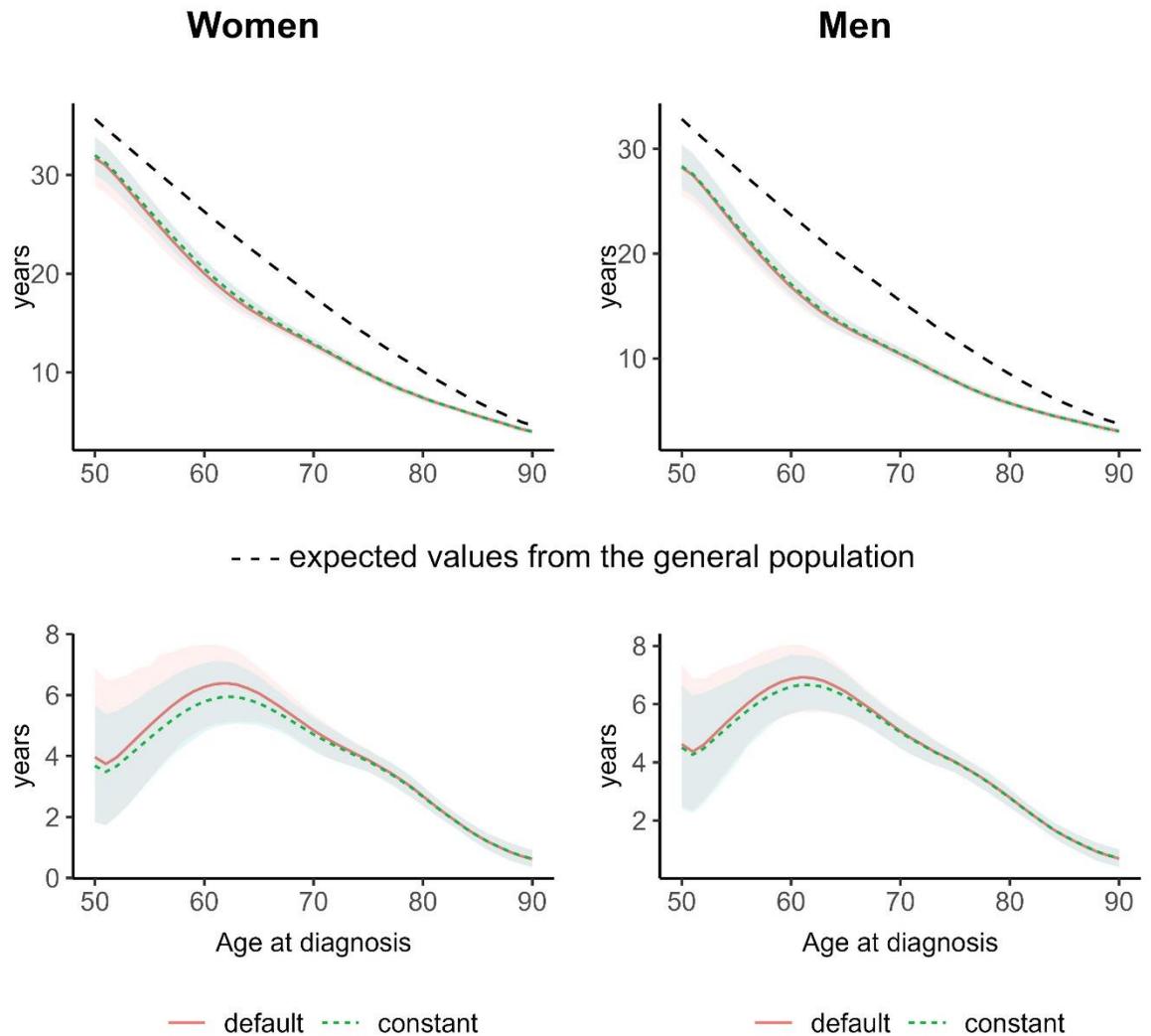
Figure S2: Life expectancy LE_C (above) and Loss in life expectancy LLE (below) in Myeloproliferative Neoplasms (MPN), with 95% confidence intervals, obtained with three assumptions about the behaviour of the extrapolated excess hazard. Default refers to linear log cumulative excess hazard, constant and zero refer to a constant and a zero-excess hazard, respectively, after the follow-up period. Results are shown for women (left) and men (right) based on a period analysis with period window 2012-2021, using diagnoses from 2002-2021 in Sweden. The values are presented in years.

Figure S3: Life expectancy LE$_C$ (above) and Loss in life expectancy LLE (below) in Myeloproliferative Neoplasms (MPN), with 95% confidence intervals, obtained with two assumptions about the behaviour of the extrapolated excess hazard. Default refers to linear log cumulative excess hazard and constant refers to a constant excess hazard after the follow-up period. Individuals diagnosed with MPN were identified through the Swedish Cancer Register (SCR) between 2002 and 2021. Results are shown for women and men based on a period analysis with period window 2012-2021, using diagnoses from 2002-2021 in Sweden. The values are presented in years.
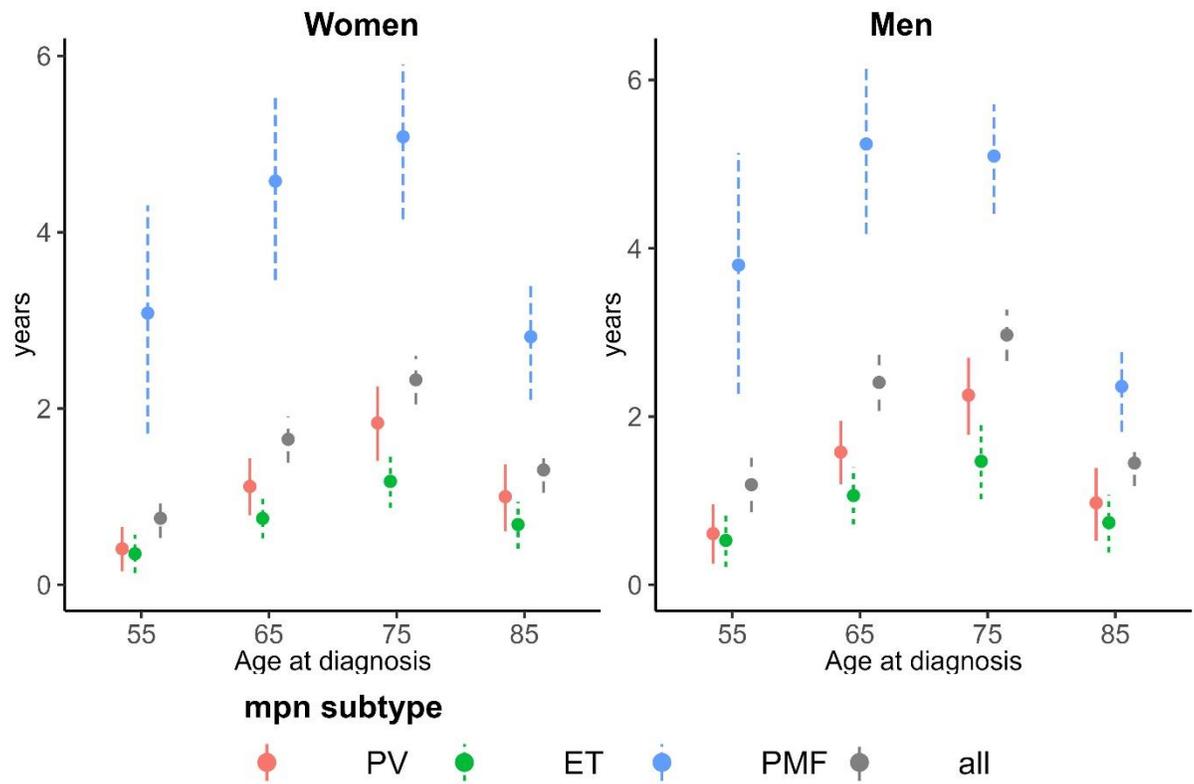
Figure S4: Loss in 15-year restricted mean survival time (LRMST) in Myeloproliferative Neoplasms (MPN), with 95% confidence intervals. Results are shown for women and men aged 55, 65, 75 and 85 years at MPN diagnosis based on a period analysis with period window 2012-2021, using diagnoses from 2002-2021 in Sweden. Individuals diagnosed with MPN were identified through the Swedish Cancer Register (SCR) between 2002 and 2021. LRMST is presented in years. The results are presented by MPN subtypes: polycythaemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF) as well as for all MPN subtypes combined (including MPN-U).
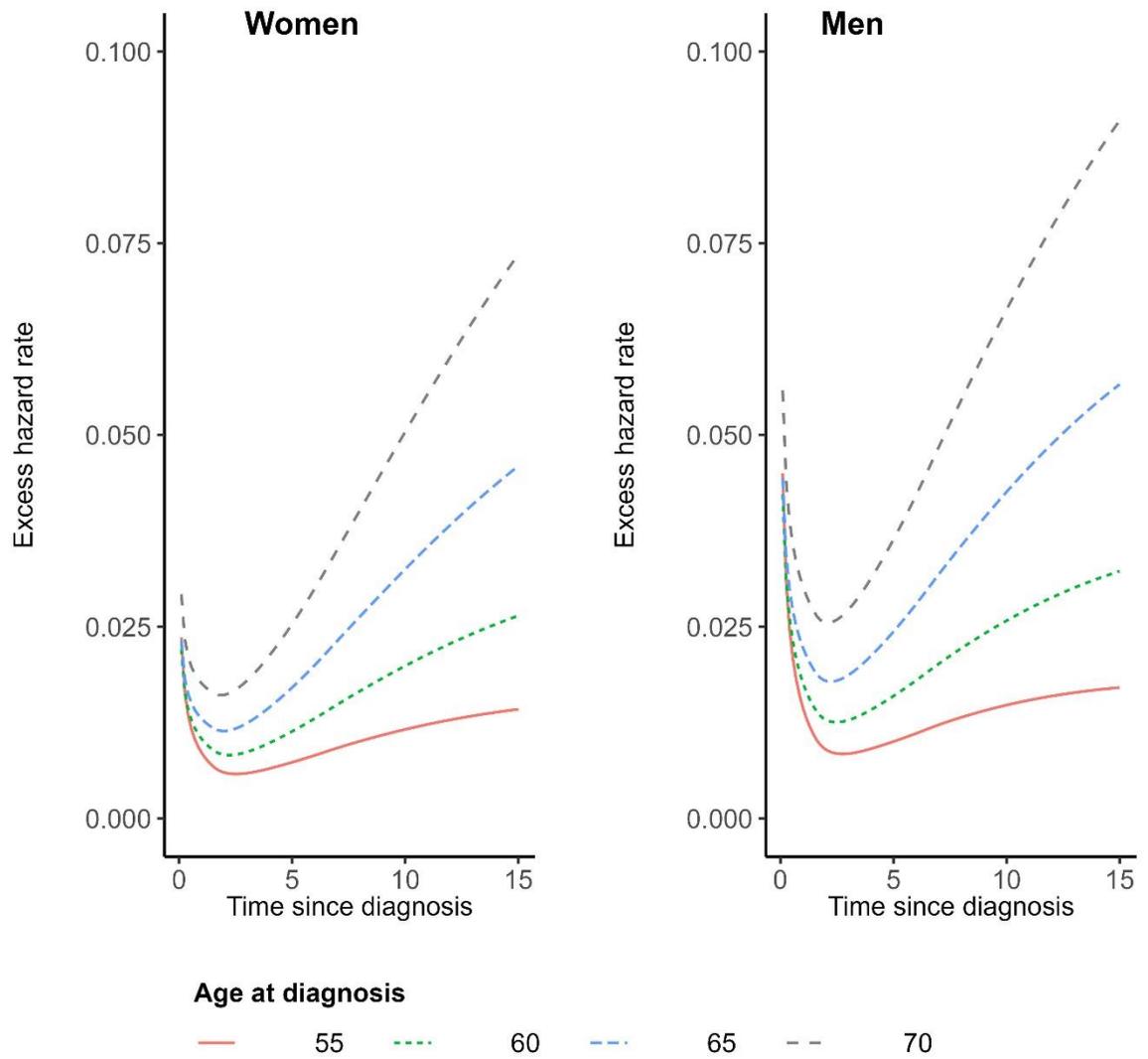
Figure S5*:* 15-year excess hazard rates for women (left figure) and men (right figure) diagnosed with Myeloproliferative Neoplasms (MPN) at specific ages: 55, 60, 65, and 70. Results are shown based on a period analysis with period window 2012-2021, using diagnoses from 2002-2021 in Sweden.

Excess hazard assumptions

The flexible parametric relative survival model (FPRM) is fitted on the log cumulative excess hazard scale using restrictive cubic splines of log time:

$$\ln(\Lambda(t)) = s(\ln(t)\,|\gamma, k) + X\beta + \sum_{d=1}^{D} s(\ln(t)\,|\gamma_d, k_d) \cdot x_d \qquad (1)$$

where X is a vector of covariates, $s(\ln(t)\,|\gamma, k)$ is a restricted cubic spline function of $\ln(t)$ with knot location vector k; D is the number of covariates allowed to have a time-dependent effect, and k_d is a vector of knots for a specific covariate, x_d, with a time-dependent effect.

The splines are restricted in the sense that the fitted function is forced to be linear before the first knot and after the final knot.

For a vector of knots $k = (k_1, \ldots, k_K)$, a restricted cubic spline function can be written as:

$$s(\ln(t)\,|\gamma, k) = \gamma_0 + \gamma_1 z_1 + \cdots + \gamma_{K-1} z_{K-1} \qquad (2)$$

The derived variables, z_j (known as the basis functions) are calculated as follows:

$$z_1 = \ln(t)$$

$$z_j = \left(\ln(t) - k_j\right)_+^3 - \phi_j(\ln(t) - k_1)_+^3 - \left(1 - \phi_j\right)(\ln(t) - k_K)_+^3,$$

where K is the number of knots, $j = 2, \ldots, K - 1$ and $\phi_j = \left(k_K - k_j\right)/(k_K - k_1)$.

We considered the following three possible scenarios for the extrapolation from model (1):

1. **Default (standard FPRM)** Beyond 15 years from cancer diagnosis, the log cumulative excess hazard is a linear function of log time, given by the model parameters.

2. **Constant** Beyond 15 years from cancer diagnosis, the excess hazard remains constant, maintaining the value it reaches at 15 years after cancer diagnosis.

3. **Zero** Beyond 15 years from cancer diagnosis, the excess hazard becomes zero, i.e., the mortality rate for cancer patients returns to that of the general population.

The first assumption is the default from fitting a FPRM on the log cumulative excess hazard scale since restricted cubic splines are linear beyond the boundary knots. This assumption is equivalent to the excess hazard behaving like a Weibull distribution in the tail. This can be seen below, since all variables z_j except z_1 take the value zero 0 after the last knot, model (1) can be rewritten for $t > k_K$:

$$\ln(\Lambda(t)) = \boldsymbol{X\beta} + \gamma_0 + \gamma_1 ln(t) + \sum_{d=1}^{D}(\gamma_{d0} + \gamma_{d1} \ln(t))x_d \tag{3}$$

If we put

$$a = \boldsymbol{X\beta} + \gamma_0 + \sum_{d=1}^{D} \gamma_{d0} x_d$$

and

$$b = \gamma_1 + \sum_{d=1}^{D} \gamma_{d1} x_d,$$

then

$$\Lambda(t) = \exp(a + b \cdot \ln(t)) = \exp(a) \cdot \exp(b \cdot \ln(t)) = \exp(a)\, t^b$$

and

$$\lambda(t) = \frac{d\Lambda(t)}{dt} = b \exp(a) t^{b-1},$$

which is the hazard function for the Weibull distribution.

To incorporate an assumption of constant excess hazard beyond the last knot, i.e., $\lambda(t) = c$, we rewrite the cumulative excess hazard as the sum of the cumulative excess hazard within the follow-up and beyond the follow-up. If we set the last follow-up time to t^*, then for $t > t^*$:

$$\Lambda(t) = \Lambda(t^*) + \int_{t^*}^{t} \lambda(s) \, ds = \Lambda(t^*) + \int_{t^*}^{t} c \, ds = \Lambda(t^*) + c(t - t^*)$$

Then

$$\ln(\Lambda(t)) = \ln\big(\Lambda(t^*) + c(t - t^*)\big), t > t^* \tag{4}$$

When excess hazard is zero beyond the last knot $\lambda(t) = 0$, the cumulative excess hazard stays constant. Thus, like incorporating the assumption of constant excess hazard, we rewrite:

$$\Lambda(t) = \Lambda(t^*) + 0, t > t^*$$

$$\ln(\Lambda(t) = \ln\big(\Lambda(t^*)\big), t > t^*$$