

SUPPLEMENTAL DATA

Table S1. Characteristics of retrieved articles

First Author	Year	Diagnosis	N	Risk groups	Type of event	Time of event	WBC time	Cut-off	RR	95% Low CI	95% Up CI	Model
OUTCOME: THROMBOSIS												
Abdulkarim	2017	ET	1284	All	All	First event	Diagnosis	$\geq 12.0 \times 10^9/L$	1,67	1,18	2,35	Multivariable
		PV	1105	All	All	First event	Diagnosis	$\geq 12.0 \times 10^9/L$	1,16	0,88	1,51	Multivariable
Alvarez-Larran	2010	ET	300	Low-risk	All	First event	Diagnosis	$\geq 8.7 \times 10^9/L$	0,8	0,4	1,8	Multivariable
Alvarez-Larran	2012	PV	261	All	All	First event	Diagnosis	$\geq 10.0 \times 10^9/L$	1,36	0,61	2,75	Multivariable
Andriani	2016	ET	1297	All	All	First event	Diagnosis	$\geq 8.7 \times 10^9/L$	1,52	1,03	2,22	Multivariable
Bai	2008	PV	320	All	All	First event	Diagnosis	Continuous	1	0,98	1,03	Univariate
Barbui	2015	PV	365	All	All	First event	Time-dependent	$\geq 11.0 \times 10^9/L$	3,9	1,24	12,3	Multivariable
Buxhofer-Ausch	2016	ET	620	All	All	First event	Time-dependent	$\geq 8.48 \times 10^9/L$	4,13	1,38	12,34	Univariate
Caramazza	2009	ET	88	All	All	First event	Diagnosis	$\geq 9.5 \times 10^9/L$	1,7	0,5	3,1	Multivariable
		PV	99	All	All	First event	Diagnosis	$\geq 9.5 \times 10^9/L$	1,6	0,4	2,8	Multivariable
Carobbio	2007	ET	439	All	All	First event	Diagnosis	$\geq 8.7 \times 10^9/L$	2,3	1,4	3,9	Multivariable
		ET	439	All	All	First event	Time-dependent	$\geq 8.7 \times 10^9/L$	1,6	0,9	2	Multivariable
Carobbio	2008	ET	657	All	All	First event	Diagnosis	$\geq 10.4 \times 10^9/L$	3	1,3	6,9	Multivariable
Carobbio	2008	ET	1063	All	All	First event	Diagnosis	$\geq 11.0 \times 10^9/L$	2	1,1	3,6	Multivariable
Carobbio	2009	PV+ET	1282	All	All	First event	Diagnosis	$\geq 11.3 \times 10^9/L$	1,93	1,01	2,77	Multivariable

First Author	Year	Diagnosis	N	Risk groups	Type of event	Time of event	WBC time	Cut-off	RR	95% Low CI	95% Up CI	Model
Carobbio	2011	ET	867	All	All	First event	Diagnosis	$\geq 11.0 \times 10^9/L$	1,14	0,72	1,79	Multivariable
		ET	867	All	Arterious	First event	Diagnosis	$\geq 11.0 \times 10^9/L$	1,66	1,01	2,72	Multivariable
Cerquozzi	2017	PV	587	All	All	First event	Diagnosis	$\geq 11.0 \times 10^9/L$	1,3	0,9	2	Multivariable
		PV	587	All	Venous	First event	Diagnosis	$\geq 11.0 \times 10^9/L$	2	1,1	3,8	Multivariable
De Stefano	2008	PV+ET	494	All	All	Recurrence	Diagnosis	$\geq 12.4 \times 10^9/L$	1,6	0,79	3,23	Multivariable
		PV+ET	109	Low-risk	All	Recurrence	Diagnosis	$\geq 12.4 \times 10^9/L$	3,55	1,02	12,25	Multivariable
De Stefano	2010	PV+ET	253	All	All	Recurrence	Diagnosis	$\geq 12.4 \times 10^9/L$	1,72	1	2,95	Multivariable
		PV+ET	253	All	Arterious	Recurrence	Diagnosis	$\geq 12.4 \times 10^9/L$	2,16	1,12	4,18	Multivariable
		PV+ET	253	All	Venous	Recurrence	Diagnosis	$\geq 12.4 \times 10^9/L$	1,14	0,43	2,98	Multivariable
De Stefano	2016	PV+ET+MF	181	All	All	Recurrence	Diagnosis	$\geq 14.0 \times 10^9/L$	2,8	1,32	6,28	Multivariable
Enblom-Larsson	2017	PV	217	All	All	First event	Diagnosis	$\geq 10.0 \times 10^9/L$	2,88	1,23	6,60	Univariate
Gangat	2009	ET	254	All	Arterious	First event	Diagnosis	$\geq 9.4 \times 10^9/L$	1,3	0,7	2,3	Univariate
		ET	254	All	Venous	First event	Diagnosis	$\geq 9.4 \times 10^9/L$	0,9	0,3	2,6	Univariate
		PV	153	All	Arterious	First event	Diagnosis	$\geq 15.0 \times 10^9/L$	0,7	0,3	1,8	Univariate
		PV	153	All	Venous	First event	Diagnosis	$\geq 15.0 \times 10^9/L$	0,5	0,5	1,2	Univariate
Haider	2016	ET	585	All	All	First event	Diagnosis	Continuous	1,02	0,99	1,06	Multivariable
Kaifie	2016	PV	141	All	All	First event	Diagnosis	$\geq 25 /nl$	1,7	0,50	5,77	Univariate
		PV+ET	278	All	All	First event	Diagnosis	$\geq 25 /nl$	1,28	0,41	3,98	Univariate
Landolfi	2007	PV	1638	All	All	First event	Enrollment	$\geq 15.0 \times 10^9/L$	1,24	0,78	1,96	Multivariable

First Author	Year	Diagnosis	N	Risk groups	Type of event	Time of event	WBC time	Cut-off	RR	95% Low CI	95% Up CI	Model
		PV	1638	All	Arterious	First event	Enrollment	$\geq 15.0 \times 10^9/L$	1,21	0,69	2,11	Multivariable
		PV	1638	All	Venous	First event	Enrollment	$\geq 15.0 \times 10^9/L$	1,28	0,56	2,92	Multivariable
		PV	1638	All	All	First event	Time-dependent	$\geq 15.0 \times 10^9/L$	1,71	1,1	2,65	Multivariable
		PV	1638	All	Arterious	First event	Time-dependent	$\geq 15.0 \times 10^9/L$	1,67	0,99	3,8	Multivariable
		PV	1638	All	Venous	First event	Time-dependent	$\geq 15.0 \times 10^9/L$	1,81	0,84	3,89	Multivariable
Lim	2015	PV+ET	102	All	All	First event	Diagnosis	$\geq 11.0 \times 10^9/L$	3,61	1,43	9,09	Univariate
Montanaro	2014	ET	1144	All	All	First event	Diagnosis	$\geq 15.0 \times 10^9/L$	1,42	0,61	3,29	Univariate
Ohyashiki	2008	ET	54	All	All	First event	Diagnosis	$\geq 12.0 \times 10^9/L$	5,95	1,49	23,70	Univariate
Palandri	2011	ET	532	All	All	First event	Diagnosis	$\geq 11.0 \times 10^9/L$	1,76	1,05	2,97	Multivariable
Passamonti	2010	PV	338	All	All	First event	Diagnosis	$\geq 11.0 \times 10^9/L$	1,1	0,4	3,4	Multivariable
Passamonti	2009	ET	359	Low-risk	All	Recurrence	Diagnosis	Positive delta	3,86	1,4	10,5	Univariate
Patriarca	2010	ET	106	All	All	First event	Diagnosis	$\geq 8.4 \times 10^9/L$	2,8	1,08	7,03	Multivariable
Piccin	2015	ET	136	Low-risk	All	Recurrence	Diagnosis	Continuous	1,08	1,02	1,15	Multivariable
Posfai	2014	PV+ET	128	All	All	First event	Diagnosis	$\geq 11.1 \times 10^9/L$	1,41	0,36	5,51	Multivariable
Wolanskyj	2006	ET	322	All	All	First event	Diagnosis	$\geq 15.0 \times 10^9/L$	1,74	1,15	2,66	Multivariable
Zhao	2016	ET	71	All	All	First event	Diagnosis	$\geq 10.0 \times 10^9/L$	0,73	0,19	2,75	Multivariable
OUTCOME: BLEEDING												
Alvarez-Larran	2010	ET	300	Low-risk	Bleeding	First event	Diagnosis	$\geq 8.7 \times 10^9/L$	3,8	0,8	17,8	Multivariable

First Author	Year	Diagnosis	N	Risk groups	Type of event	Time of event	WBC time	Cut-off	RR	95% Low CI	95% Up CI	Model
Alvarez-Larran	2012	PV	261	Under HU	Bleeding	First event	Diagnosis	$\geq 10.0 \times 10^9/L$	1,36	0,61	2,75	Univariate
Chou	2012	ET+PV	247	All	Bleeding	First event	Diagnosis	$\geq 16 \times 10^9/L$	3,19	1,62	6,25	Univariate
Finazzi	2011	ET+earlyPMF	1104	All	Bleeding	First event	Diagnosis	$\geq 10.0 \times 10^9/L$	1,74	1,02	2,97	Multivariable
OUTCOME: HEMATOLOGICAL TRANSFORMATIONS IN MF/AML OR SOLID TUMORS												
Bai	2008	PV	320	All	MMM	First event	Diagnosis	Continuous	1,05	1,02	1,08	Univariate
Passamonti	2010	PV	338	All	MF	First event	Diagnosis	$\geq 11.0 \times 10^9/L$	0,3	0,6	1,1	Multivariable
		PV	338	All	AML	First event	Diagnosis	$\geq 11.0 \times 10^9/L$	1,6	0,3	9,3	Multivariable
OUTCOME: DEATH												
Alvarez-Larran	2012	PV	261	Under HU	Death	-	Diagnosis	$\geq 10.0 \times 10^9/L$	2,9	1,5	5,9	Multivariable
Barbui	2013	mPV	140	All	Death	-	Diagnosis	$\geq 15.0 \times 10^9/L$	3,96	1,01	15,9	Univariate
Barraco	2017	PV	267	All	Death	-	Diagnosis	$\geq 15.0 \times 10^9/L$	3,04	1,4	6,62	Multivariable
Gangat	2007	PV	459	All	Death	-	Diagnosis	$\geq 15.0 \times 10^9/L$	1,79	1,28	2,5	Multivariable
Jeryczynski	2017	ET	225	All	Death	-	Diagnosis	$\geq 11.0 \times 10^9/L$	2,6	1,3	5,3	Multivariable
Montanaro	2014	ET	1144	All	Death	-	Diagnosis	$\geq 15.0 \times 10^9/L$	2,11	1,05	4,25	Multivariable
Mudireddi	2017	ET	183	All	Death	-	Diagnosis	$\geq 15.0 \times 10^9/L$	4,7	1,5	14,6	Univariate
Passamonti	2010	PV	338	All	Death	-	Diagnosis	$\geq 11.0 \times 10^9/L$	2,1	0,6	7,7	Multivariable
Tefferi	2017	ET	904	All	Death	-	Diagnosis	$\geq 11.0 \times 10^9/L$	1,5	1,2	1,9	Multivariable
		ET	590	All	Death	-	Diagnosis	$\geq 11.0 \times 10^9/L$	1,8	1,1	2,8	Multivariable
Wolanskyj	2006	ET	322	All	Death	-	Diagnosis	$\geq 15.0 \times 10^9/L$	1,7	1,09	2,65	Multivariable

MF=myelofibrosis; AML=acute myeloid leukemia; MMM= myelofibrosis with myeloid metaplasia; HU=hydroxyurea; mPV=masked polycythemia vera

Table S2. Newcastle - Ottawa quality assessment scale of publications included

Publication	Selection	Comparability	Outcome	TOTAL SCORE	STUDY QUALITY
Abdulkarim, 2017	4	2	3	9	GOOD
Alvarez-Larran, 2010	3	1	2	6	GOOD
Alvarez-Larran, 2012	3	1	2	6	GOOD
Andriani, 2016	4	2	3	9	GOOD
Bai, 2008	2	0	2	4	FAIR
Barbui, 2014	3	2	3	8	GOOD
Barbui, 2015	4	2	3	9	GOOD
Barraco, 2017	4	2	3	9	GOOD
Buxhofer-Ausch, 2016	4	2	3	9	GOOD
Caramazza, 2009	3	1	2	6	GOOD
Carobbio, 2007	4	2	3	9	GOOD
Carobbio, 2008	3	2	3	8	GOOD
Carobbio, 2008	4	2	3	9	GOOD
Carobbio, 2009	3	2	3	8	GOOD
Carobbio, 2010	4	2	3	9	GOOD
Carobbio, 2011	4	2	3	9	GOOD
Cerquozzi, 2017	4	2	3	9	GOOD
Chou, 2012	3	1	2	6	GOOD
De Stefano, 2008	3	2	3	8	GOOD
De Stefano, 2010	3	2	3	8	GOOD
De Stefano, 2016	3	2	3	8	GOOD
Enblom-Larsson, 2017	3	0	1	4	FAIR
Finazzi, 2012	4	2	2	8	GOOD
Gangat, 2007	4	2	3	9	GOOD
Gangat, 2009	3	2	3	8	GOOD
Haider, 2016	4	2	3	9	GOOD

Publication	Selection	Comparability	Outcome	TOTAL SCORE	STUDY QUALITY
Jeryczynski, 2017	3	2	2	7	GOOD
Kaifie, 2016	2	2	2	6	GOOD
Landolfi, 2007	4	2	3	9	GOOD
Montanaro, 2014	4	2	3	9	GOOD
Mudireddi, 2017	3	2	2	7	GOOD
Ohyashiki, 2008	3	0	1	4	FAIR
Palandri, 2011	4	2	2	8	GOOD
Passamonti, 2009	4	2	2	8	GOOD
Passamonti, 2010	4	2	2	8	GOOD
Patriarca, 2010	3	1	2	6	GOOD
Piccin, 2015	3	2	3	8	GOOD
Posfai, 2014	2	0	2	4	FAIR
Tefferi, 2017	4	2	3	9	GOOD
Wolanskyj, 2006	4	2	3	9	GOOD
Zhao, 2016	3	1	2	6	GOOD

Table S3. Meta-regression analysis with MPN diagnosis and type of thrombosis as moderators

	RR (95% CI)	p-value
ET+PV	1 (ref)	-
ET only	0.83 (0.60-1.15)	0.251
PV only	0.71 (0.50-0.99)	0.043
All thrombosis	1 (ref)	-
Arterial only	0.89 (0.64-1.23)	0.465
Venous only	0.68 (0.47-0.99)	0.046

Figure S1. Funnel plot of the primary outcome (thrombosis)

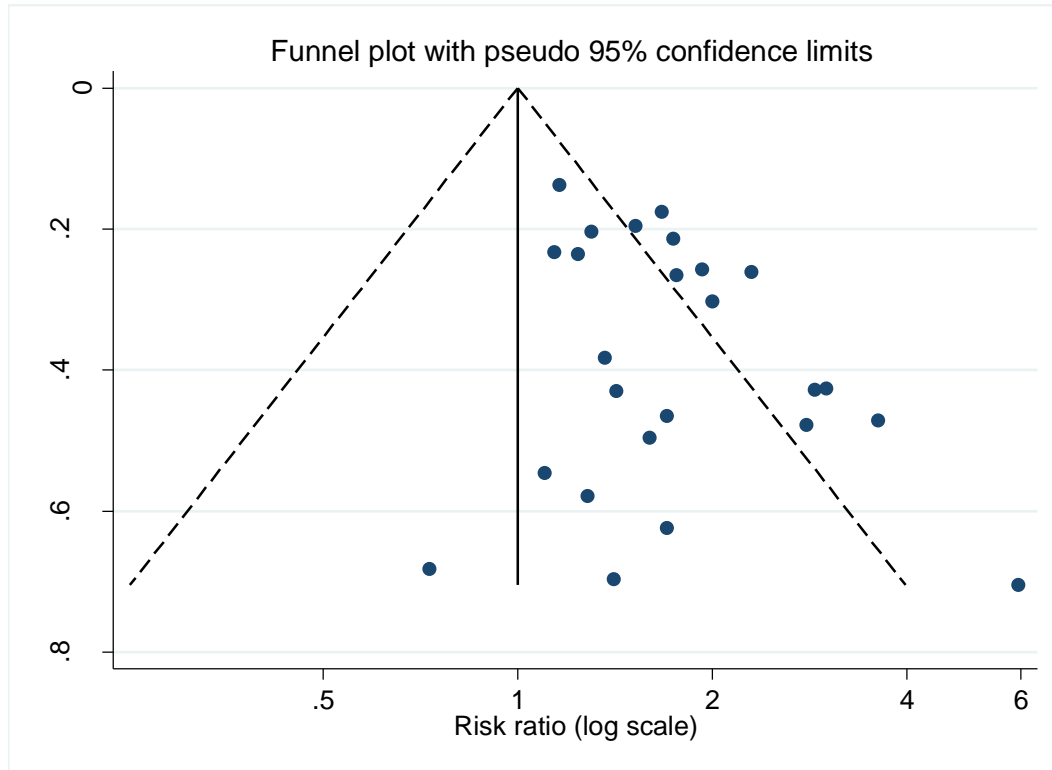


Figure S2. Forrest plot for the primary outcome according to Duval and Tweedie's trim and fill procedure. Four studies were added (fill 1 to 4), raising a concern that these left-hand studies may actually exist, and are missing from the original analysis. Duval and Tweedie's procedure finally re-compute the combined effect, with the diamond representing the adjusted RR.

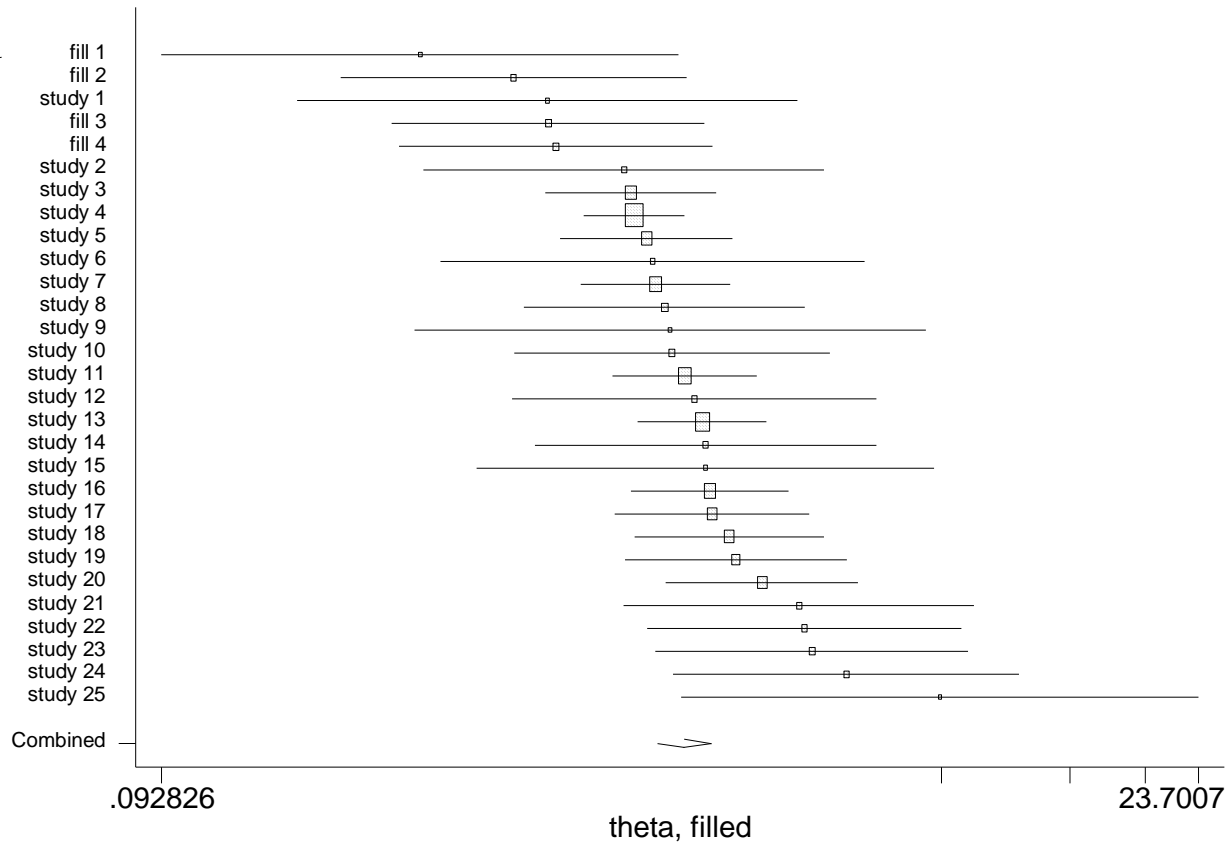


Figure S3. Funnel plot of the primary outcome. Circles are study actually included in the meta-analysis whereas squares represents studies potentially missing from the analysis according to Duval and Tweedie's procedure

