Data supplement

Contents

Search strategy:

In this section we describe the search-strategy used for our systematic review for the separate databases. The number designates the number of hits per database.

Embase.com	932	921
Medline Ovid	679	152
Web of science	869	402
Cochrane	15	4
Google scholar	200	106
Total	**2695**	**1585**

Embase.com

('pregnancy'/exp OR 'pregnant woman'/de OR 'pregnancy outcome'/de OR 'pregnancy disorder'/de OR 'pregnancy complication'/de OR 'puerperal disorder'/de OR 'puerperium'/de OR 'high risk pregnancy'/de OR (pregnan* OR puerper* OR postpartum* OR 'post partum*' OR antenatal):ab,ti) AND ('venous thromboembolism'/exp OR 'vein thrombosis'/exp OR thrombosis/de/mj OR thromboembolism/de/mj OR (((venous OR vein) NEAR/3 (thrombo*)) OR ((lung OR pulmonar*) NEAR/3 embolism*)):ab,ti) AND ('risk'/exp OR 'incidence'/de OR 'high risk pregnancy'/de OR (risk OR incidence*):ab,ti) AND ('thrombophilia'/de OR 'antithrombin'/de OR 'blood clotting factor 5 Leiden'/de OR 'protein S'/de OR 'protein C'/de OR 'protein C deficiency'/de OR 'protein S deficiency'/de OR 'antithrombin deficiency'/de OR 'antithrombin III deficiency'/de OR 'prothrombin'/de OR (thrombophil* OR Hypercoagulabilit* OR antithrombin* OR '5 Leiden' OR 'V Leiden' OR 'protein S' OR 'protein C' OR (natural* NEAR/3 anticoagulant*) OR prothromb* OR g20210a OR 20201A):ab,ti) AND ('observational study'/exp OR 'cohort analysis'/exp OR 'longitudinal study'/exp OR 'retrospective study'/exp OR 'prospective study'/exp OR 'epidemiological data'/de OR 'case control study'/de OR 'cross-sectional study'/de OR 'correlational study'/de OR 'population research'/de OR 'family study'/de OR 'major clinical study'/de OR 'multicenter study'/de OR 'comparative study'/de OR 'follow up'/de OR 'clinical study'/de OR 'clinical article'/de OR 'clinical trial'/exp OR 'randomization'/exp OR 'intervention study'/de OR 'population based case control study'/de OR (((observation* OR epidemiolog* OR famil* OR comparativ*) NEAR/6 (stud* OR data OR research)) OR cohort* OR longitudinal* OR retrospectiv* OR prospectiv* OR population* OR (national* NEAR/3 (stud* OR survey)) OR ((case OR cases OR match*) NEAR/3 control*) OR (cross NEXT/1 section*) OR correlation* OR multicenter* OR (multi* NEXT/1 center*) OR 'follow up' OR followup* OR clinical* OR trial OR random*):ab,ti) NOT ([Conference Abstract]/lim OR [Letter]/lim OR [Note]/lim OR [Editorial]/lim) AND [english]/lim

Medline Ovid

(exp "pregnancy"/ OR exp "pregnant women"/ OR "pregnancy outcome"/ OR "Pregnancy Complications"/ OR "Puerperal Disorders"/ OR "Postpartum Period"/ OR "Pregnancy, High-Risk"/ OR (pregnan* OR puerper* OR postpartum* OR "post partum*" OR antenatal).ab,ti.) AND ("Venous Thromboembolism"/ OR "Venous Thrombosis"/ OR * thrombosis/ OR * thromboembolism/ OR (((venous OR vein) ADJ3 (thrombo*)) OR ((lung OR pulmonar*) ADJ3 embolism*)).ab,ti.) AND ("risk"/ OR "incidence"/ OR "Pregnancy, High-Risk"/ OR (risk OR incidence*).ab,ti.) AND (exp "thrombophilia"/ OR "antithrombins"/ OR "protein S"/ OR "protein C"/ OR "protein C deficiency"/ OR "protein S deficiency"/ OR "prothrombin"/ OR (thrombophil* OR Hypercoagulabilit* OR antithrombin* OR "5 Leiden" OR "V Leiden" OR "protein S" OR "protein C" OR (natural* ADJ3 anticoagulant*) OR prothromb* OR g20210a OR 20201A).ab,ti.) AND ("observational study"/ OR exp "Cohort Studies"/ OR "Epidemiologic Studies"/ OR "Epidemiological Monitoring"/ OR "Case-Control Studies"/ OR "Cross-Sectional Studies"/ OR "multicenter study"/ OR "comparative study"/ OR exp "clinical study"/ OR "Random Allocation"/ OR (((observation* OR epidemiolog* OR famil* OR comparativ*) ADJ6 (stud* OR data OR research)) OR cohort* OR longitudinal* OR retrospectiv* OR prospectiv* OR population* OR (national* ADJ3 (stud* OR survey)) OR ((case OR cases OR match*) ADJ3 control*) OR (cross ADJ section*) OR correlation* OR multicenter* OR (multi* ADJ center*) OR "follow up" OR followup* OR clinical* OR trial OR random*).ab,ti.) NOT (letter OR news OR comment OR editorial OR congresses OR abstracts).pt. AND english.la.

Cochrane

((pregnan* OR puerper* OR postpartum* OR 'post partum*' OR antenatal):ab,ti) AND ((((venous OR vein) NEAR/3 (thrombo*)) OR ((lung OR pulmonar*) NEAR/3 embolism*)):ab,ti) AND ((risk OR incidence*):ab,ti) AND ((thrombophil* OR Hypercoagulabilit* OR antithrombin* OR '5 Leiden' OR 'V Leiden' OR 'protein S' OR 'protein C' OR (natural* NEAR/3 anticoagulant*) OR prothromb* OR g20210a OR 20201A):ab,ti)

Web of science

TS=(((pregnan* OR puerper* OR postpartum* OR "post partum*" OR antenatal)) AND ((((venous OR vein) NEAR/2 (thrombo*)) OR ((lung OR pulmonar*) NEAR/2 embolism*))) AND ((risk OR incidence*)) AND ((thrombophil* OR Hypercoagulabilit* OR antithrombin* OR "5 Leiden" OR "V Leiden" OR "protein S" OR "protein C" OR (natural* NEAR/2 anticoagulant*) OR prothromb* OR g20210a OR 20201A)) AND ((((observation* OR epidemiolog* OR famil* OR comparativ*) NEAR/5 (stud* OR data OR research)) OR cohort* OR longitudinal* OR retrospectiv* OR prospectiv* OR population* OR (national* NEAR/2 (stud* OR survey)) OR ((case OR cases OR match*) NEAR/2 control*) OR (cross NEAR/1 section*) OR correlation* OR multicenter* OR (multi* NEAR/1 center*) OR "follow up" OR followup* OR clinical* OR trial OR random*)))

Google scholar

pregnant|pregnancy|puerperal|postpartum "venous|vein thromboembolism|thrombosis"|"lung|pulmonary embolism" risk|incidence thrombophilia|Hypercoagulability|antithrombins|"5|V Leiden"|"protein S|C"|"natural anticoagulants"|prothrombin|g20210a|20201A

List of excluded studies:

Author	year	Main reason for exlcusion (more than 1 reason may apply)
Adachi[1]	2001	Review
Allaart[2]	1993	Lacks requirements for VTE diagnosis
Antovic[3]	2003	No pregnancy risk data
Bergrem[4]	2010	No separate thrombophilia data
Bergrem[5]	2012	Other study on same dataset included
Blanco-Molina[6]	2007	No separate thrombophilia data
Bombeli[7]	2001	Lacks requirements for VTE diagnosis
Brouwer[8]	2006	No Pregnancy data
Chopra[9]	2002	No separate thrombophilia data
Conard[10]	1990	Lacks requirements for VTE diagnosis
Coppens[11]	2006	VTE prophylaxis
Coriu[12]	2014	Lacks requirements for VTE diagnosis
Couturaud [13]	2006	Other study on same dataset included
Danilenko[14]	2001	No separate thrombophilia data
Dargaud[15]	2009	VTE prophylaxis
De Stefano[16]	1994	No Pregnancy data
De Stefano[17]	2003	no pregnancy risk data
De Stefano[18]	2006	Recurrent VTE
DeSancho[19]	2010	no pregnancy risk data
Dulicek[20]	2000	no pregnancy risk data
Emmerich[21]	1997	No pregnancy risk data
Faioni[22]	1997	no pregnancy risk data
Finazzi[23]	1994	No Pregnancy data
Gadelha[24]	2010	no pregnancy risk data
Gat[25]	2014	VTE prophylaxis
Gerhardt[26]	2000	Other study on same dataset included
Gerhardt [27]	2003	Other study on same dataset included
Grandone[28]	2008	VTE prophylaxis
Hallak[29]	1997	no pregnancy risk data
Hellgren[30]	1995	Lacks requirements for VTE diagnosis
Hiltunen[31]	2007	Lacks requirements for VTE diagnosis

Hirsh[32]	1996	no pregnancy risk data
Hvas[33]	2009	Lacks requirements for VTE diagnosis
Ilonczai[34]	2015	VTE prophylaxis
Jacobsen[35]	2008	No separate thrombophilia data
James[36]	2006	Lacks requirements for VTE diagnosis
Khalafallah[37]	2014	Recurrent VTE
Knight[38]	2008	No separate thrombophilia data
Koster [39]	1995	No Pregnancy data
Kovac[40]	2010	Other study on same dataset included
Laroche[41]	2001	Various
Lensen[42]	2000	Lacks requirements for VTE diagnosis
Lenz[43]	2016	Lacks requirements for VTE diagnosis
Lim[44]	2016	Various
Lindqvist[45]	1999	No separate thrombophilia data
Lindqvist[46]	2002	Review
Linnemann[47]	2014	no pregnancy risk data
Lykke [48]	2012	Lacks requirements for VTE diagnosis
Mahmoodi [49]	2010	Other study on same dataset included
McColl [50]	2000	Recurrent VTE
McColl [51]	1997	no pregnancy risk data
Middeldorp[52]	2001-1	Lacks requirements for VTE diagnosis
Noboa[53]	2008	No separate thrombophilia data
Pabinger[54]	1994	Other study on same dataset included
Pabinger[55]	2000	proband selection
Pabinger[56]	1996	proband selection
Pabinger[57]	2005	Recurrent VTE
Pabinger[58]	2002	Recurrent VTE
Pai[59]	2011	Various
Philipp[60]	2014	Lacks requirements for VTE diagnosis
Pomp [61]	2008	Lacks requirements for VTE diagnosis
Procare[62]	2004	no pregnancy data
Procare[63]	2000	no pregnancy data
Rodger [64]	2015	VTE prophylaxis
Rodger [65]	2014	Lacks requirements for VTE diagnosis
Rodger [66]	2014-2	Review
Rogenhofer[67]	2014	proband selection
Rouse[68]	2003	Review
Sabadell[69]	2010	proband selection
Said[70]	2010	Lacks requirements for VTE diagnosis
Samama[71]	2004	language
Samama[72]	2003	proband selection

Sanson[73]	1999	VTE prophylaxis
Selmeczi[74]	2015	VTE prophylaxis
Simioni[75]	1999	No separate thrombophilia data
Simpson[76]	2001	No separate thrombophilia data
Tormene [77]	2012	VTE prophylaxis
Trauscht[78]	1992	Lacks requirements for VTE diagnosis
Vavrinkova[79]	2014	VTE prophylaxis
Vicente[80]	1994	proband selection
Villani[81]	2015	Various
Villani[82]	2012	No pregnancy risk data

Appendix figures

Appendix Table 1: Study characteristics

1st Author	Year	Study type	Study design	Family study	Ante/postpartum	Antithrombin	Protein C	Protein S	Heterozygous fVL	Homozygous fVL	Heterozygous fII	Homozygous fII	Compound fVL & fII	NOS score
Bank[83]	2004	cohort	retrospective	+	+	-	-	-	-	-	+	-	-	8
Bucciarelli[84]	1999	cohort	retrospective	+	+	+	+	+	-	-	-	-	-	6
Clark[85]	2008	cohort	prospective	-	+	-	-	-	+	+	-	-	-	8
Cochery[86]	2007	cohort	prospective	-	-	-	-	-	+	+	+	+	-	8
Cordoba[87]	2012	cohort	retrospective	+	-	-	-	-	+	-	+	-	-	9
Couturaud[88]	2008	cohort	retrospective	+	+	-	-	-	+	-	-	-	-	9
Dilley[89]	2000	case-control	NA	-		-	-	-	+	-	+	-	-	9
Dizon[90]	2005	cohort	prospective	-	-	-	-	-	+	-	-	-	-	9
Eichinger[91]	1999	cohort	prospective	-	-	-	-	-	+	-	-	-	-	9
Folkeringa[92]	2007	cohort	retrospective	+	+	+	+	+	-	-	-	-	-	9
Friederich[93]	1996	cohort	retrospective	+	+	+	+	+	-	-	-	-	-	8
Gerhardt [94]	2016	case-control	NA	-		+	+	+	+	+	+	-	+	8
Grandone[95]	1998	case-control	NA	-		+	-	+	+	-	+	+	+	8
Hammerova[96]	2011	cohort	prospective	-	-	-	-	-	+	-	-	-	-	7
Heit[97]	2005	cohort	retrospective	-	-	-	-	-	+	-	-	-	-	7
Jacobsen[98]	2010	case-control	NA	-		-	-	-	+	+	+	+	+	9
Kjellberg[99]	2010	cohort	prospective	-	+	-	-	-	+	-	-	-	-	9
Klai[100]	2012	case-control	NA	-		+	+	+	+	+	+	-	-	7
Lindqvist[101]	1999	cohort	prospective	-	-	-	-	-	+	+	-	-	-	8
Martinelli[102]	2001	cohort	retrospective	+	+	-	-	-	-	+	-	-	+	9
Martinelli[103]	2002	case-control	NA	-		+	+	+	+	+	+	-	+	8
Martinelli[104]	2008	cohort	retrospective	+	+	-	-	-	+	-	+	-	+	9
Meglic[105]	2003	case-control	NA	-		+	+	+	+	-	+	-	-	8
Middeldorp[106]	1998	cohort	retrospective	+	+	-	-	-	+	-	-	-	-	9
Middeldorp[107]	2001	cohort	prospective	+	-	-	-	-	+	-	-	-	-	6
Mitic[108]	2011	case-control	NA	-		+	+	+	+	+	+	+	+	6
Murphy[109]	2000	cohort	prospective	-	-	-	-	-	+	-	-	-	-	8
Ogunyemi[110]	2003	case-control	NA	-		-	+	-	+	-	+	-	-	7
Samama[111]	1996	cohort	retrospective	+	+	-	-	-	+	+	-	-	-	7
Simioni[112]	2002	cohort	prospective	+	+	-	-	-	+	-	-	-	-	9
Tam[113]	2012	case-control	NA	-		+	+	+	-	-	-	-	-	6
Tormene[114]	2001	cohort	retrospective	+	+	-	-	-	+	+	-	-	+	8

Tormene[115]	2007	cohort	retrospective	+	+	-	-	-	-	-	+	-	-	9
Van Boven[116]	1999	cohort	retrospective	+	+	+	-	-	-	-	-	-	-	8
Vora[117]	2007	case-control	NA	-		-	+	+	+	-	-	-	-	8
Yilmazer[118]	2003	case-control	NA	-		-	-	-	+	+	+	-	-	8

Table: Study characteristics

Study characteristics of the 43 studies included in the systematic review and meta-analysis: + indicates yes, - indicates no. NA: not applicable. Pregnancies, n refers to the number of pregnancies reported in individual studies, the total number of pregnancies is 41297. NOS score: Newcastle-Ottawa scale assessment score

Appendix Table 2 and 3: Quality assessment of studies.

Quality assessment was performed using the Newcastle-Ottawa scale (NOS). It was used for all cohort studies, including those that lack a non-carrier group. As can be appreciated from the items scored, cohort studies that lack a non-carrier group can only get a maximum score of 6.

Appendix Table 2: Quality assessment of cohort studies

Study	Year	Selection of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Exclusion of the outcome at start	Comparability of cases and controls	Assessment of outcome	Adequate of follow-up length	Adequacy of follow up of cohorts	Quality
Bank	2004	*	*	*	*	**	**NO**	*	*	**8**
Bucciarelli	1999	*	**NA**	*	*	**NA**	*	*	*	**6**
Clark	2008	*	*	*	*	**	**NO**	*	*	**8**
Cochery	2007	*	*	*	*	**	**NO**	*	*	**8**
Cordoba	2012	*	*	*	*	**	*	*	*	**9**
Couturaud	2008	*	*	*	*	**	*	*	*	**9**
Dizon	2005	*	*	*	*	**	*	*	*	**9**
Eichinger	1999	*	*	*	*	**	*	*	*	**9**
Folkeringa	2007	*	*	*	*	**	*	*	*	**9**
Friederich	1996	*	*	*	*	**	*	*	**NO**	**8**
Hammerova	2011	*	*	*	*	*	**NO**	*	*	**7**
Heit	2005	*	*	*	*	*	*	*	**NO**	**7**
Kjellberg	2010	*	*	*	*	**	*	*	*	**9**

Lindqvist	1999	*	*	*	*	**	**NA**	*	*	**8**
Martinelli	2001	*	*	*	*	**	*	*	*	**9**
Martinelli	2008	*	*	*	*	**	*	*	*	**9**
Middeldorp	1998	*	*	*	*	**	*	*	*	**9**
Middeldorp	2001	*	**NA**	*	*	**NA**	*	*	*	**6**
Murphy	2000	*	*	*	*	*	*	*	*	**8**
Samama	1996	*	*	*	*	**NO**	*	*	*	**7**
Simioni	2002	*	*	*	*	**	*	*	*	**9**
Tormene	2001	**NO**	*	*	*	**	*	*	*	**8**
Tormene	2007	*	*	*	*	**	*	*	*	**9**
Van Boven	1999	*	*	*	*	**	**NO**	*	*	**8**

* Indicates points awarded. NO denotes points not awarded. NA denotes that information was not available (leading to not awarding of points).

Appendix Table 3: Quality assessment of case-control studies

Study	Year	Definition of cases	Representativeness of cases	Selection of controls	Definition of controls	Comparability of cases and controls	Ascertainment of Exposure	Same method of ascertainment	Non-response rate	Quality
Dilley	2000	*	*	*	*	**	*	*	*	**9**
Gerhardt	2016	*	*	*	*	**	*	*	**NO**	**8**
Grandone	1998	*	*	*	*	**	**NO**	*	*	**8**

Jacobsen	2010	*	*	*	*	**	*	*	**NO**	**8**
Klai	2012	*	*	*	*	*	*	*	**NO**	**7**
Martinelli	2002	*	*	*	*	**	*	*	**NO**	**8**
Meglic	2003	*	*	*	*	**	*	*	**NO**	**8**
Mitic	2011	**NO**	*	**NO**	*	**	*	*	**NO**	**6**
Ogunyemi	2003	*	*	*	*	*	*	*	**NO**	**7**
Tam	2012	**NO**	*	*	*	*	*	*	**NO**	**6**
Vora	2007	*	*	*	*	**	*	*	**NO**	**8**
Yilmazer	2003	*	*	*	*	**	*	*	**NO**	**8**

* Indicates points awarded. NO denotes points not awarded.

Appendix Table 4: Recommendations for prophylaxis based on thresholds.

Threshold	Family history	LMWH Antepartum	LMWH Postpartum
AR >1	Yes	AT, PC, Hom FVL	AT, PC, PS, Hom FVL, FVL&FII, het FVL
	No	Hom FVL	Hom FVL
AR >3	Yes	AT, PC, (Hom FVL?)	AT, PC, PS, (Hom FVL?)
	No		

Treatment thresholds and recommendations following from thresholds and family history. Based on expert-consensus the threshold chosen for treatment with low-molecular-weight heparin was 3%. This table shows this threshold of 3% is clearly more restrictive than the threshold of 1% in regard to whom should be treated.

AR: Absolute risk, % of ante- or postpartum periods. Hom: homozygous. Het: heterozygous

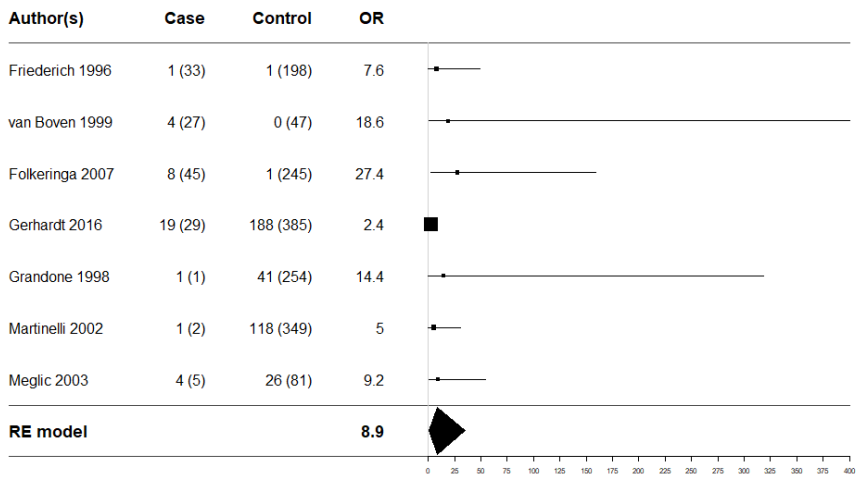
LMWH: Low-molecular-weight heparin.

The question mark in homozygous FVL reflects the following: The probability of antepartum VTE risk being >3% is 47%, and the probability of postpartum risk being >3% is 46%. In family studies the absolute risk estimates are higher than in non-family studies. Due to the limited data no ante- and postpartum analysis could be made for family studies on homozygous FVL could be made. Individual risk factors such as family history, but also other common risk factors for VTE may help guide clinical decision making.

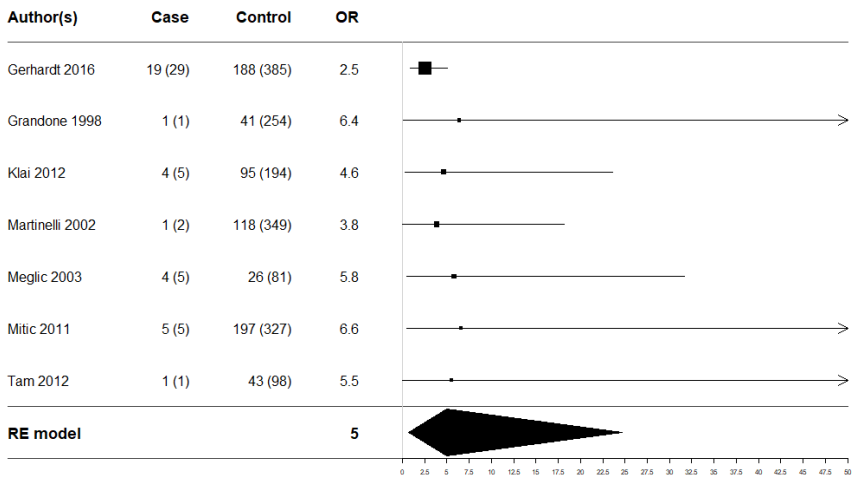
Results of the individual studies and their meta-analyses

Antithrombin deficiency

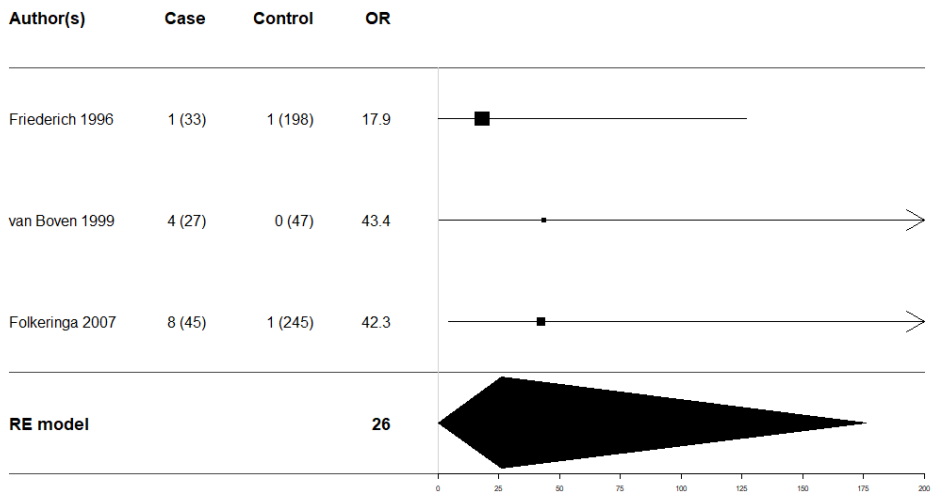
OR All studies



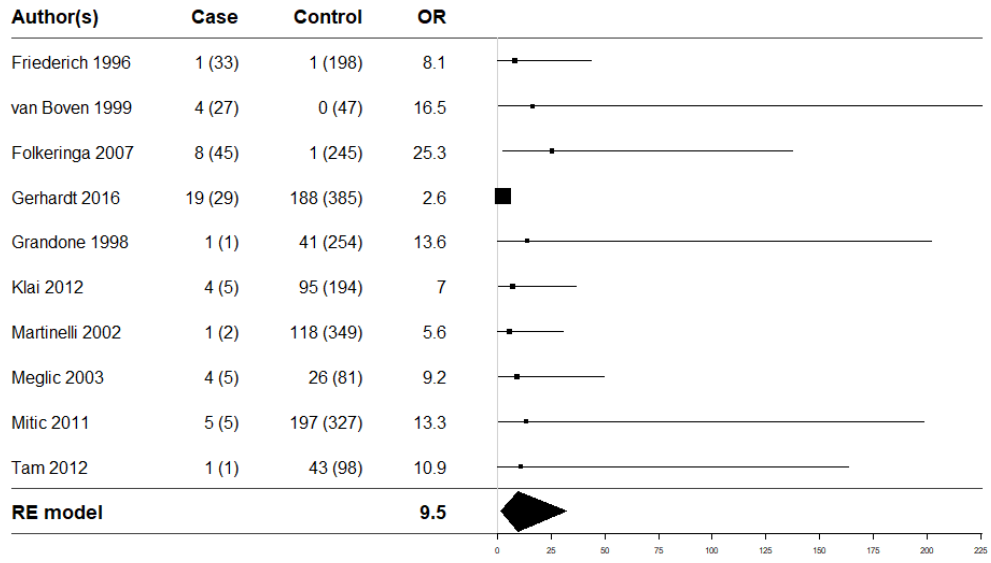
OR case-control studies



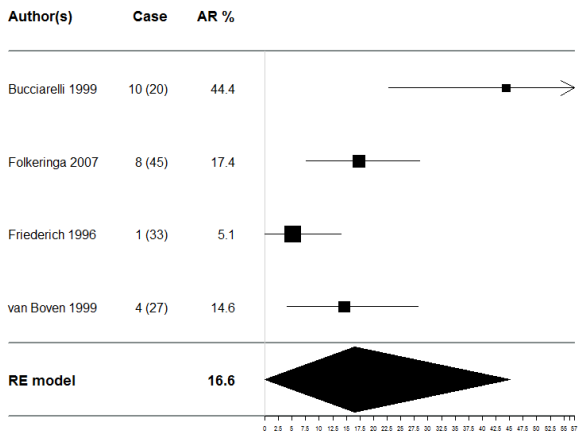
OR cohort studies



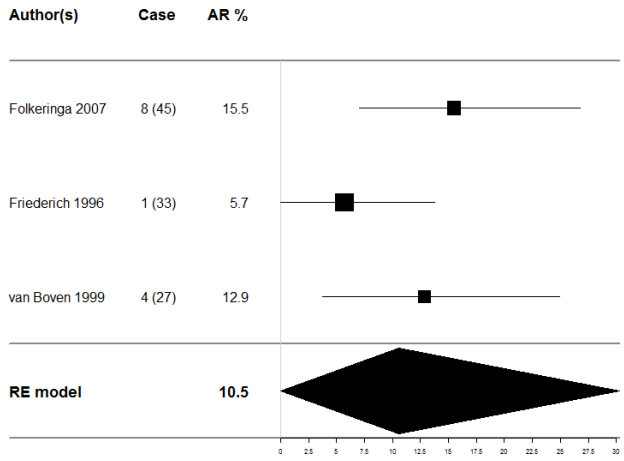
OR NOS ≥8



Absolute risk all studies

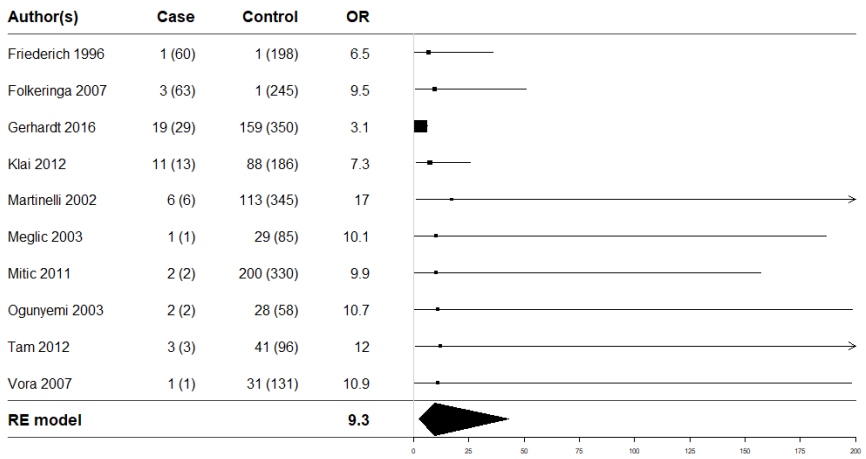


Absolute risk NOS ≥8

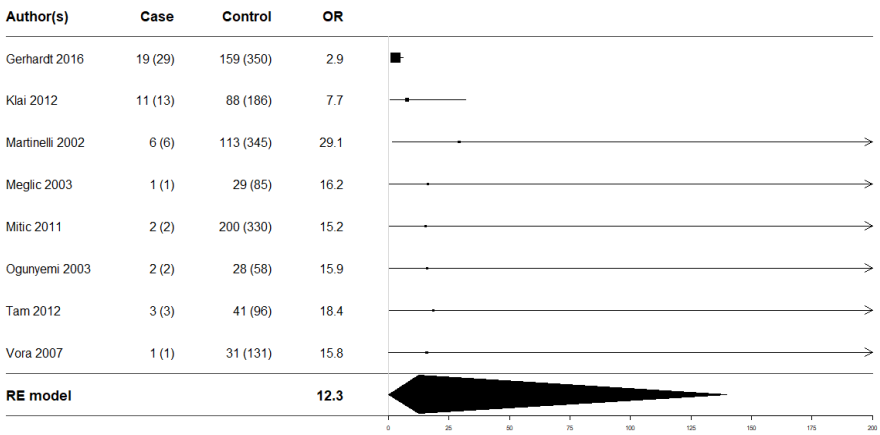


Protein C deficiency

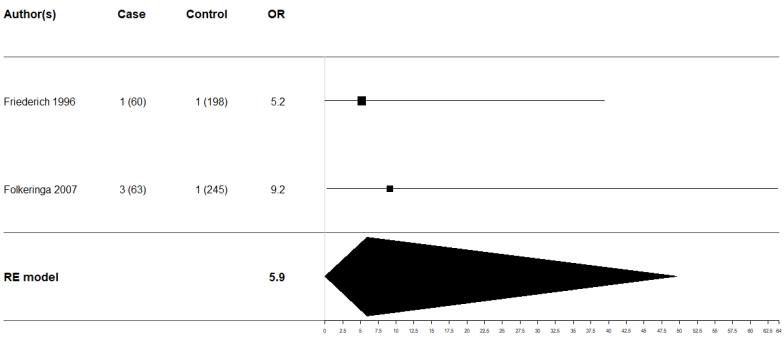
OR All studies



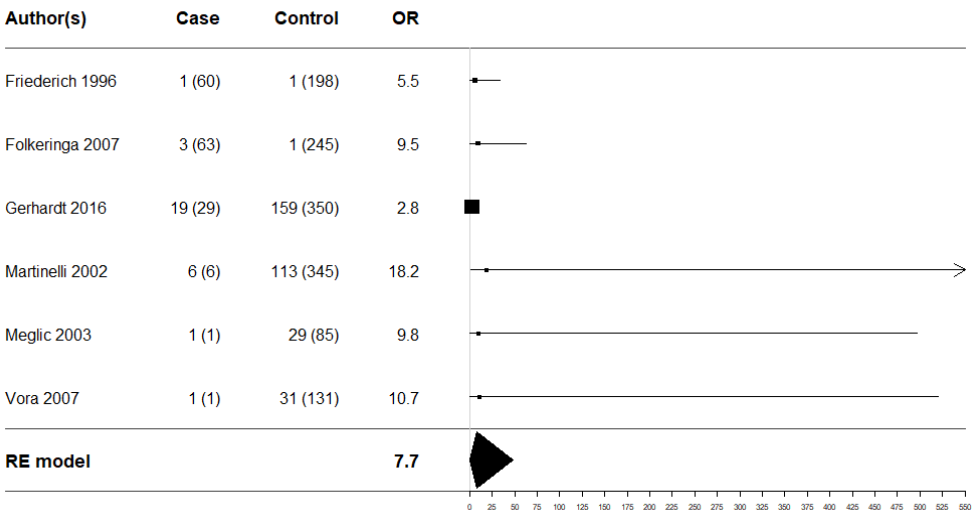
OR case-control studies



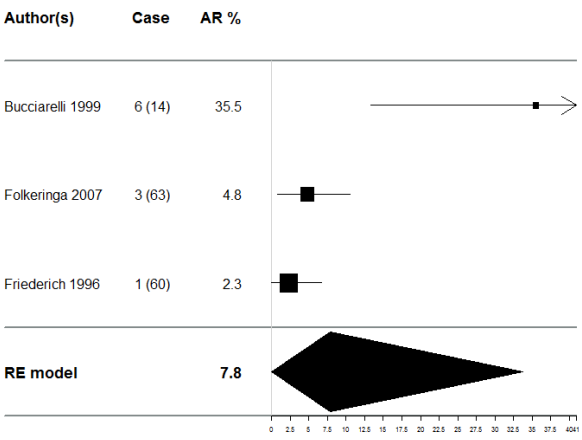
OR cohort studies



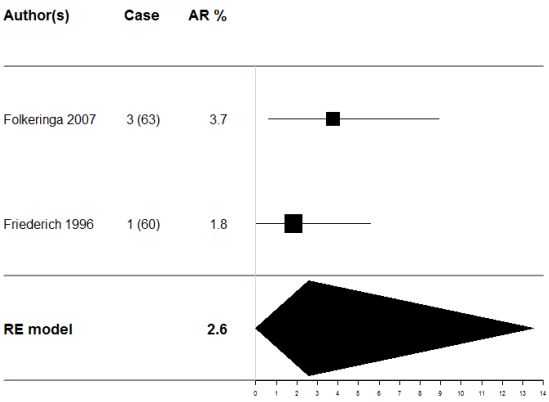
OR NOS ≥8


Author(s)
Case
Control
OR
Friederich 1996
1 (60)
1 (198)
5.5
Folkeringa 2007
3 (63)
1 (245)
9.5
Gerhardt 2016
19 (29)
159 (350)
2.8
Martinelli 2002
6 (6)
113 (345)
18.2
Meglic 2003
1 (1)
29 (85)
9.8
Vora 2007
1 (1)
31 (131)
10.7
RE model
7.7
0 25 50 75 100 125 150 175 200 225 250 275 300 325 350 375 400 425 450 475 500 525 550

Absolute risk all studies

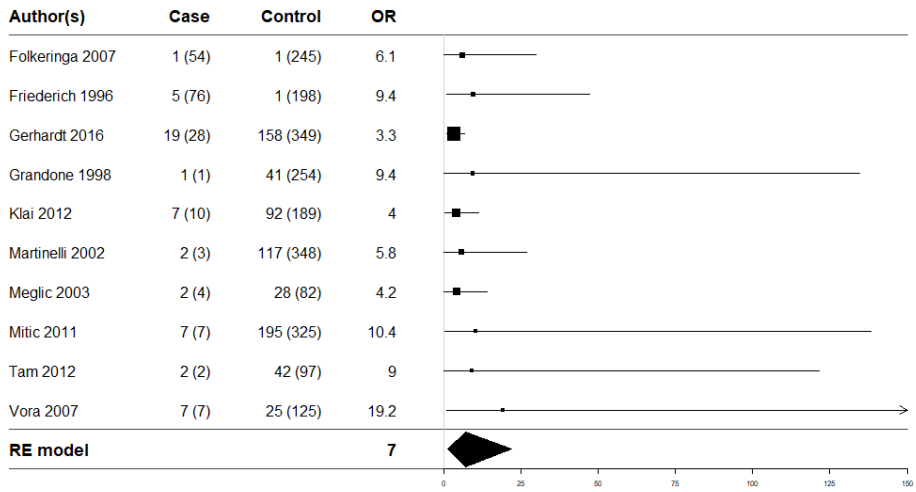


Absolute risk NOS ≥8

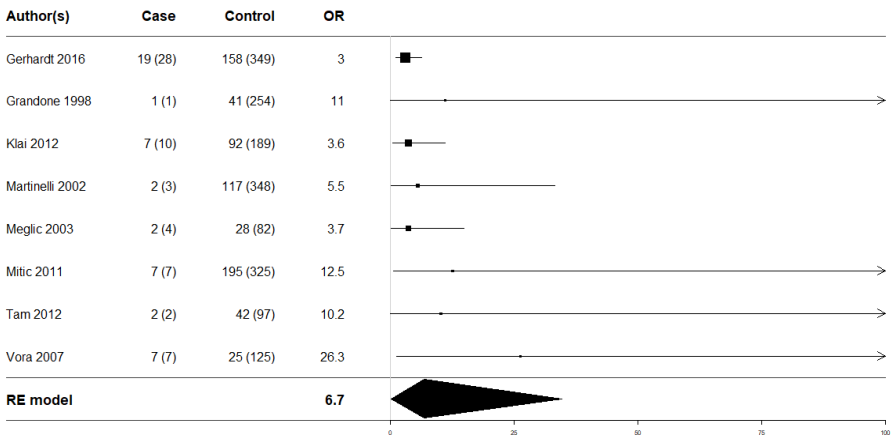


Protein S deficiency

OR All studies



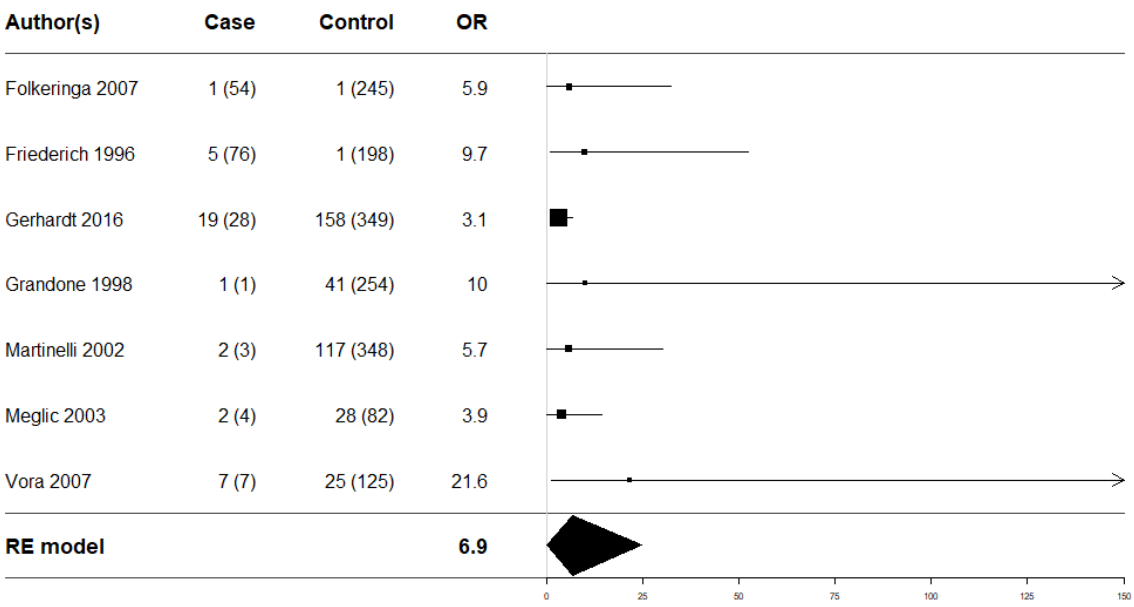
OR case-control studies



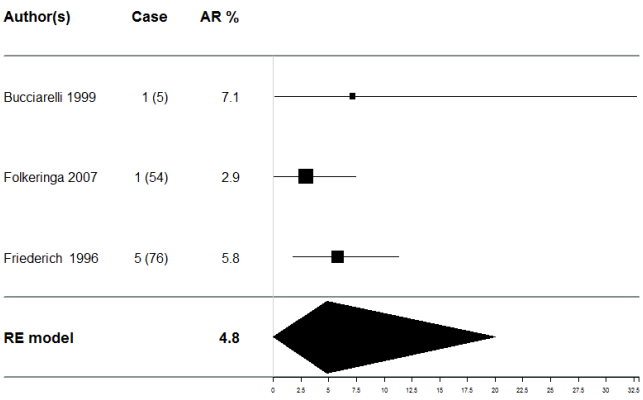
OR cohort studies

N=2, no forest-plot was constructed.

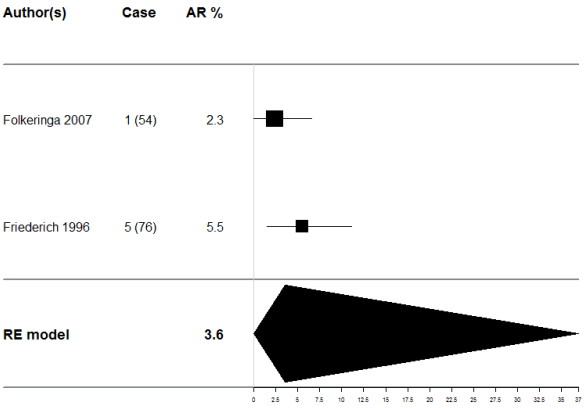
OR NOS ≥8


Author(s)
Case
Control
OR
Folkeringa 2007
1 (54)
1 (245)
5.9
Friederich 1996
5 (76)
1 (198)
9.7
Gerhardt 2016
19 (28)
158 (349)
3.1
Grandone 1998
1 (1)
41 (254)
10
Martinelli 2002
2 (3)
117 (348)
5.7
Meglic 2003
2 (4)
28 (82)
3.9
Vora 2007
7 (7)
25 (125)
21.6
RE model
6.9
0
25
50
75
100
125
150

Absolute risk All studies

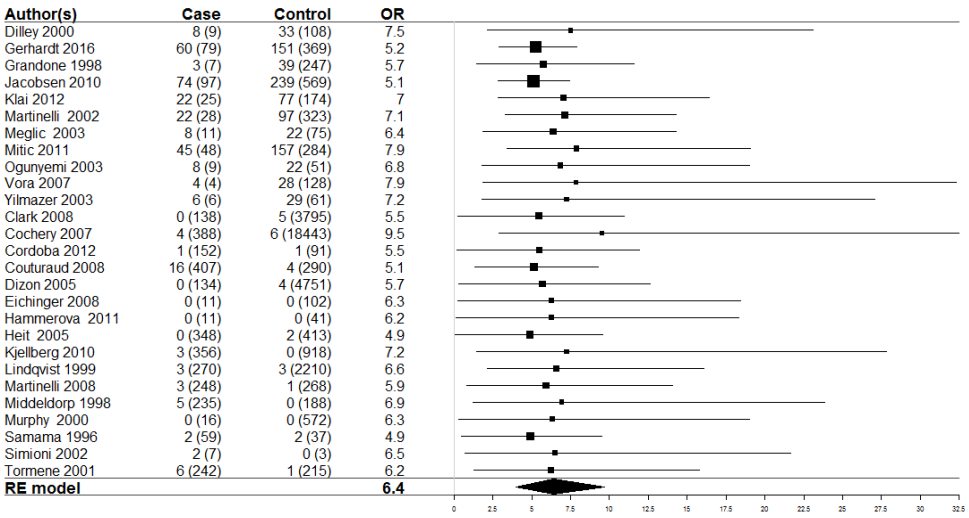


Absolute risk NOS ≥8



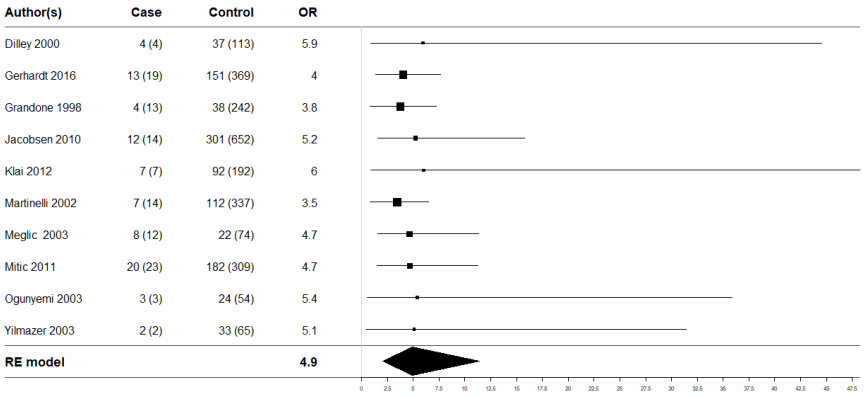
Heterozygous Factor V Leiden (FVL) mutation

OR All studies



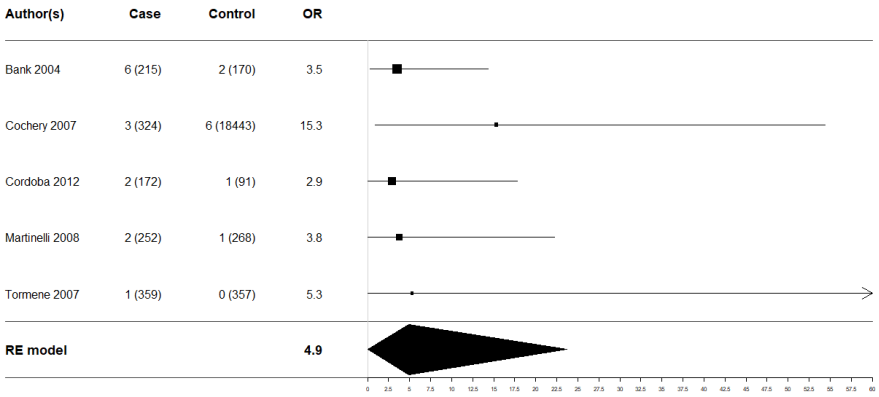
Author(s)	Case	Control	OR
Dilley 2000	8 (9)	33 (108)	7.5
Gerhardt 2016	60 (79)	151 (369)	5.2
Grandone 1998	3 (7)	39 (247)	5.7
Jacobsen 2010	74 (97)	239 (569)	5.1
Klai 2012	22 (25)	77 (174)	7
Martinelli 2002	22 (28)	97 (323)	7.1
Meglic 2003	8 (11)	22 (75)	6.4
Mitic 2011	45 (48)	157 (284)	7.9
Ogunyemi 2003	8 (9)	22 (51)	6.8
Vora 2007	4 (4)	28 (128)	7.9
Yilmazer 2003	6 (6)	29 (61)	7.2
Clark 2008	0 (138)	5 (3795)	5.5
Cochery 2007	4 (388)	6 (18443)	9.5
Cordoba 2012	1 (152)	1 (91)	5.5
Couturaud 2008	16 (407)	4 (290)	5.1
Dizon 2005	0 (134)	4 (4751)	5.7
Eichinger 2008	0 (11)	0 (102)	6.3
Hammerova 2011	0 (11)	0 (41)	6.2
Heit 2005	0 (348)	2 (413)	4.9
Kjellberg 2010	3 (356)	0 (918)	7.2
Lindqvist 1999	3 (270)	3 (2210)	6.6
Martinelli 2008	3 (248)	1 (268)	5.9
Middeldorp 1998	5 (235)	0 (188)	6.9
Murphy 2000	0 (16)	0 (572)	6.3
Samama 1996	2 (59)	2 (37)	4.9
Simioni 2002	2 (7)	0 (3)	6.5
Tormene 2001	6 (242)	1 (215)	6.2
RE model			**6.4**

OR case-control studies



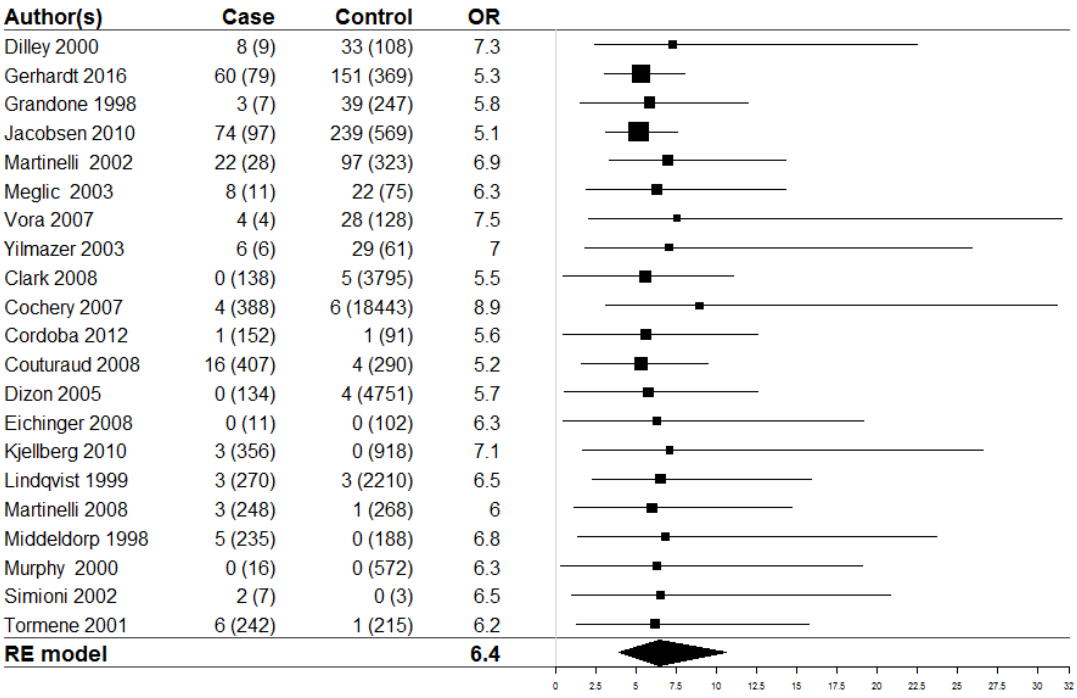
Author(s)	Case	Control	OR
Dilley 2000	4 (4)	37 (113)	5.9
Gerhardt 2016	13 (19)	151 (369)	4
Grandone 1998	4 (13)	38 (242)	3.8
Jacobsen 2010	12 (14)	301 (652)	5.2
Klai 2012	7 (7)	92 (192)	6
Martinelli 2002	7 (14)	112 (337)	3.5
Meglic 2003	8 (12)	22 (74)	4.7
Mitic 2011	20 (23)	182 (309)	4.7
Ogunyemi 2003	3 (3)	24 (54)	5.4
Yilmazer 2003	2 (2)	33 (65)	5.1
RE model			**4.9**

OR cohort studies

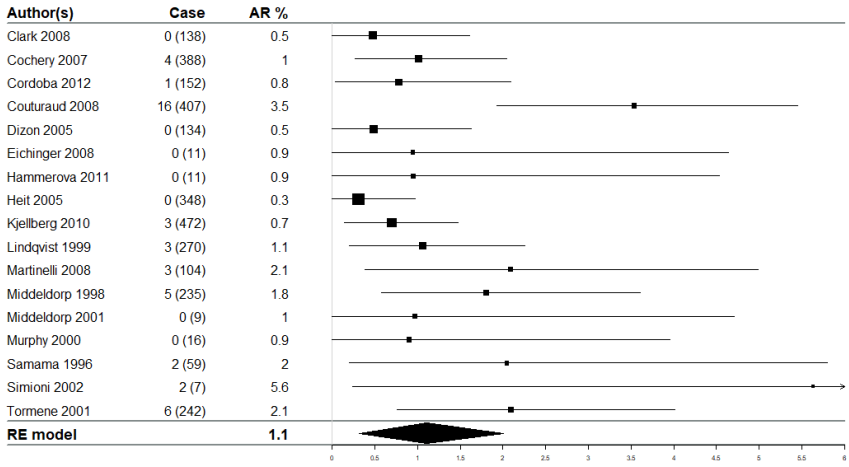


Author(s)	Case	Control	OR
Bank 2004	6 (215)	2 (170)	3.5
Cochery 2007	3 (324)	6 (18443)	15.3
Cordoba 2012	2 (172)	1 (91)	2.9
Martinelli 2008	2 (252)	1 (268)	3.8
Tormene 2007	1 (359)	0 (357)	5.3
RE model			**4.9**

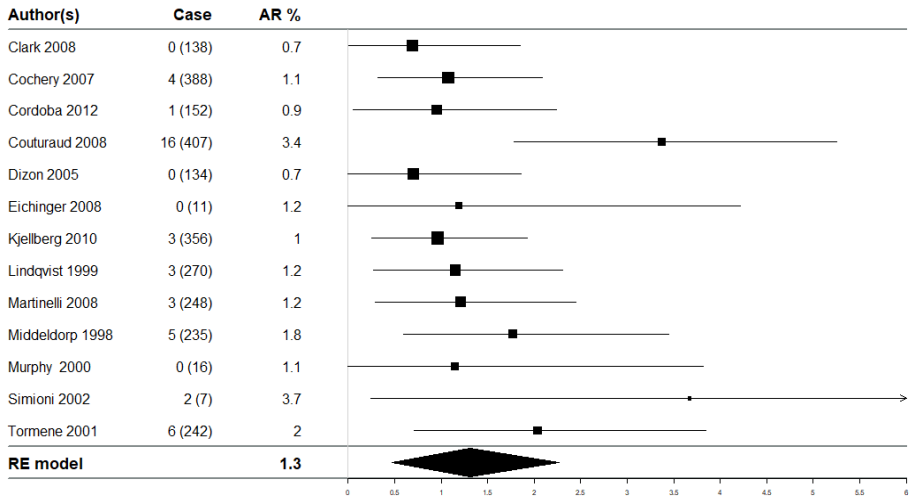
OR NOS ≥8


Author(s) Case Control OR
Dilley 2000 8 (9) 33 (108) 7.3
Gerhardt 2016 60 (79) 151 (369) 5.3
Grandone 1998 3 (7) 39 (247) 5.8
Jacobsen 2010 74 (97) 239 (569) 5.1
Martinelli 2002 22 (28) 97 (323) 6.9
Meglic 2003 8 (11) 22 (75) 6.3
Vora 2007 4 (4) 28 (128) 7.5
Yilmazer 2003 6 (6) 29 (61) 7
Clark 2008 0 (138) 5 (3795) 5.5
Cochery 2007 4 (388) 6 (18443) 8.9
Cordoba 2012 1 (152) 1 (91) 5.6
Couturaud 2008 16 (407) 4 (290) 5.2
Dizon 2005 0 (134) 4 (4751) 5.7
Eichinger 2008 0 (11) 0 (102) 6.3
Kjellberg 2010 3 (356) 0 (918) 7.1
Lindqvist 1999 3 (270) 3 (2210) 6.5
Martinelli 2008 3 (248) 1 (268) 6
Middeldorp 1998 5 (235) 0 (188) 6.8
Murphy 2000 0 (16) 0 (572) 6.3
Simioni 2002 2 (7) 0 (3) 6.5
Tormene 2001 6 (242) 1 (215) 6.2
RE model 6.4
0 2.5 5 7.5 10 12.5 15 17.5 20 22.5 25 27.5 30 32

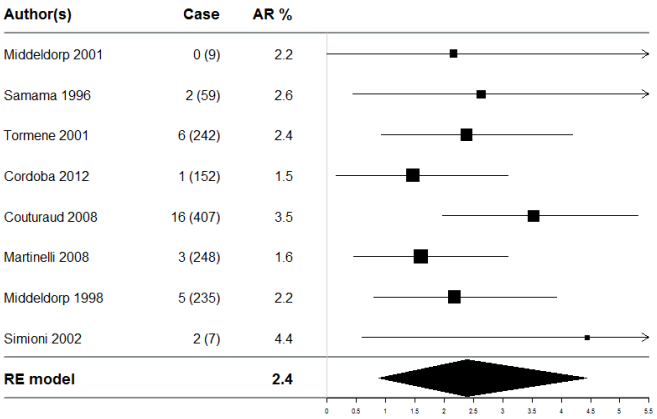
Absolute risk all studies



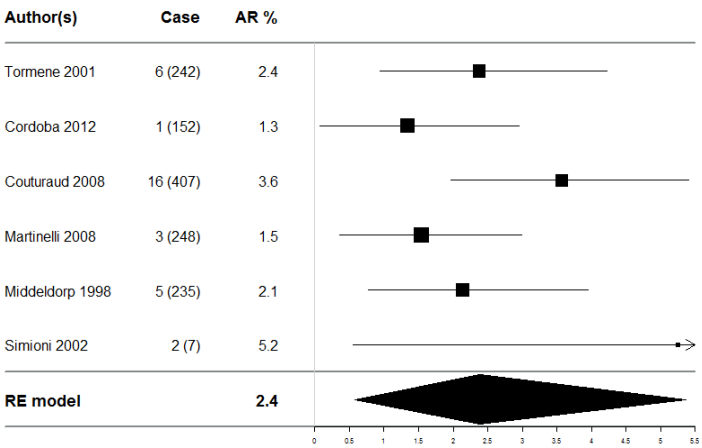
Absolute risk all studies NOS ≥8



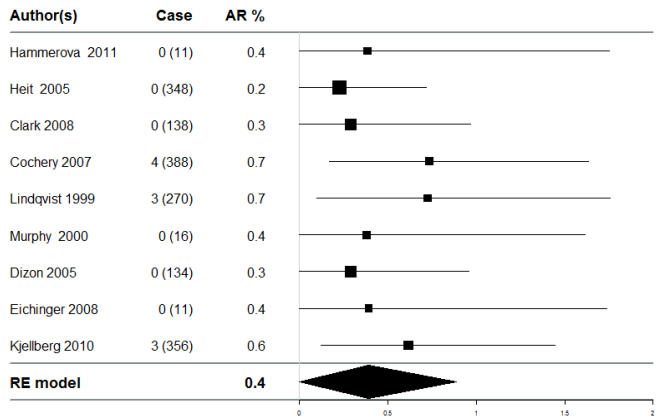
Absolute risk family studies



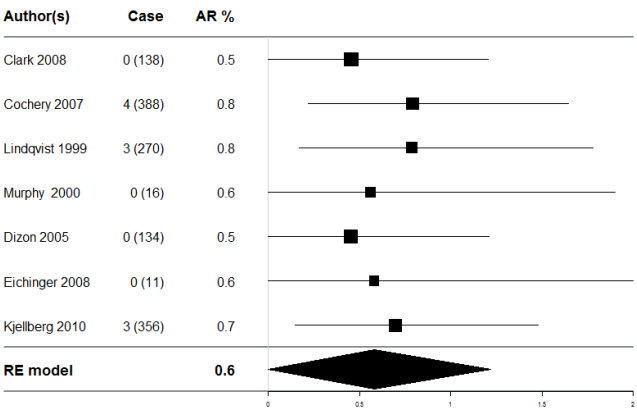
Absolute risk family studies NOS ≥8



Absolute risk non-family studies

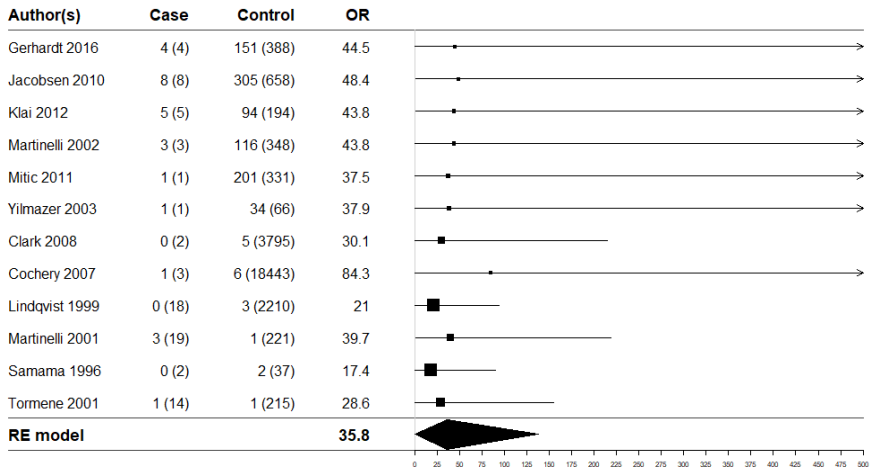


Absolute risk non-family studies NOS ≥8

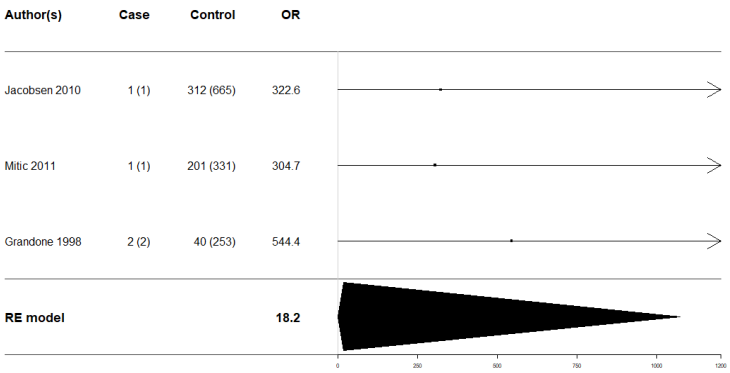


Homozygous FVL mutation

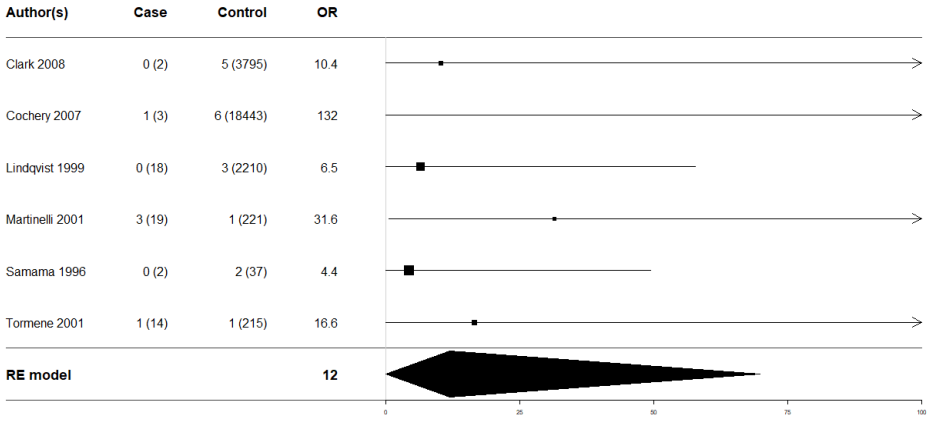
OR All studies



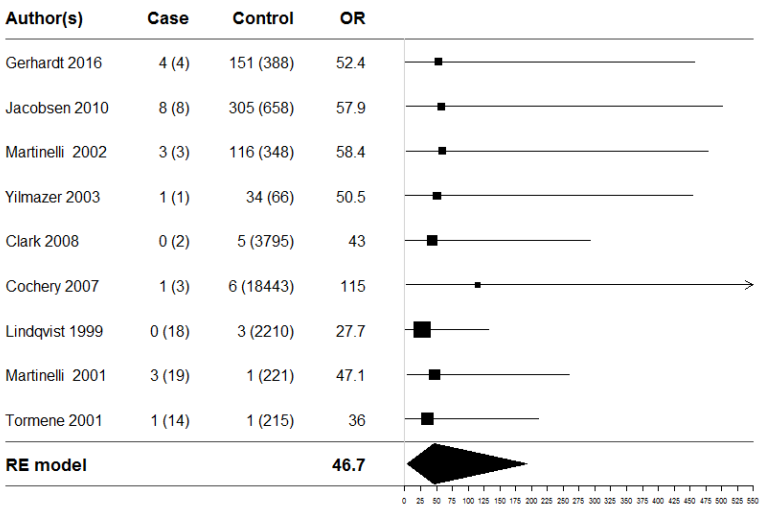
OR case-control studies



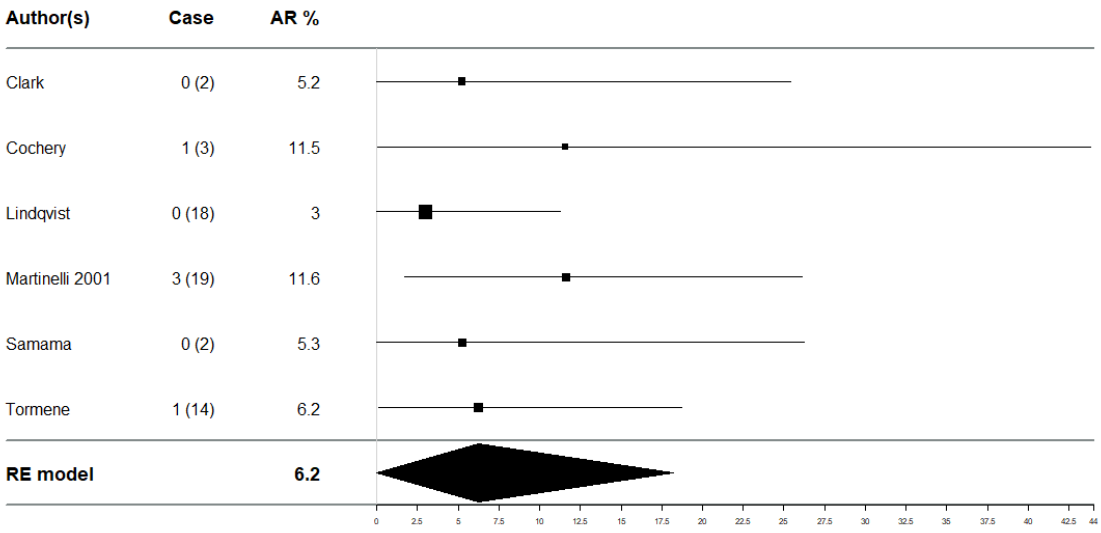
OR cohort studies



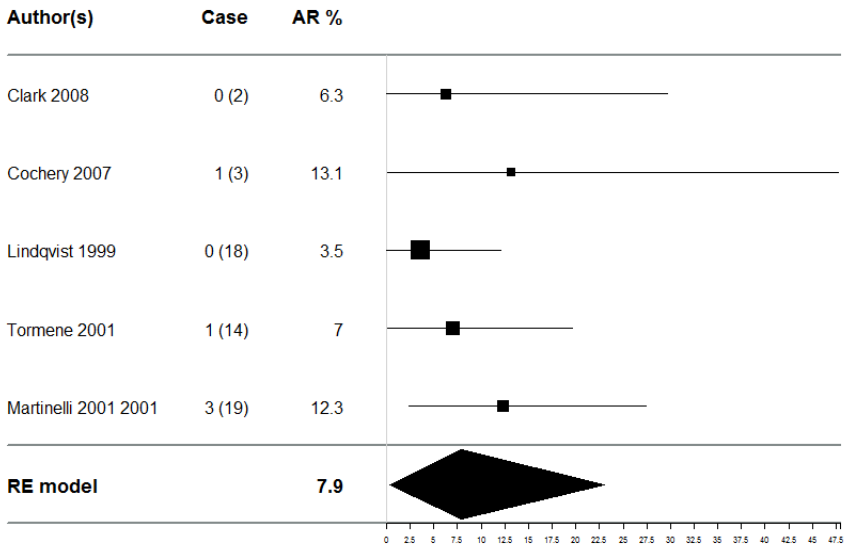
OR NOS ≥8


Author(s) Case Control OR
Gerhardt 2016 4 (4) 151 (388) 52.4
Jacobsen 2010 8 (8) 305 (658) 57.9
Martinelli 2002 3 (3) 116 (348) 58.4
Yilmazer 2003 1 (1) 34 (66) 50.5
Clark 2008 0 (2) 5 (3795) 43
Cochery 2007 1 (3) 6 (18443) 115
Lindqvist 1999 0 (18) 3 (2210) 27.7
Martinelli 2001 3 (19) 1 (221) 47.1
Tormene 2001 1 (14) 1 (215) 36
RE model 46.7
0 25 50 75 100 125 150 175 200 225 250 275 300 325 350 375 400 425 450 475 500 525 550

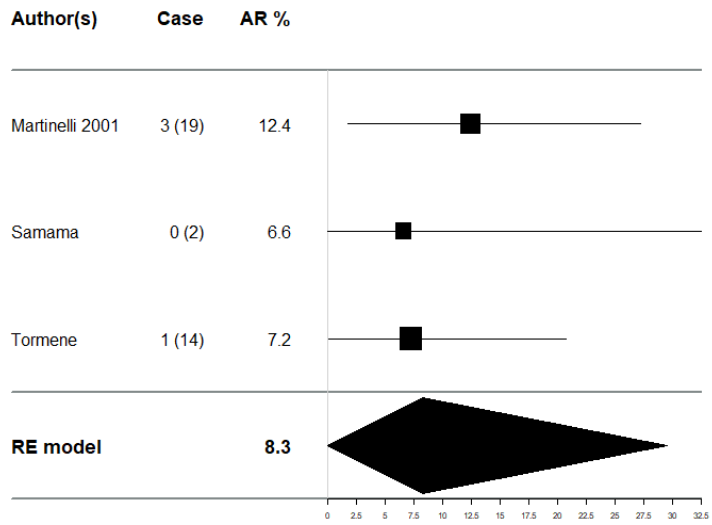
Absolute risk all studies



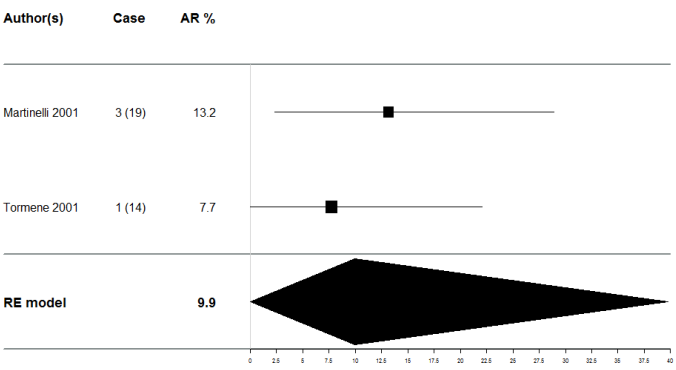
Absolute risk all studies NOS ≥8



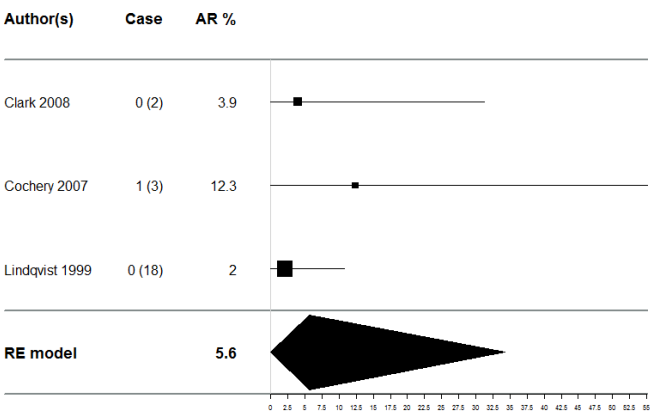
Absolute risk family studies



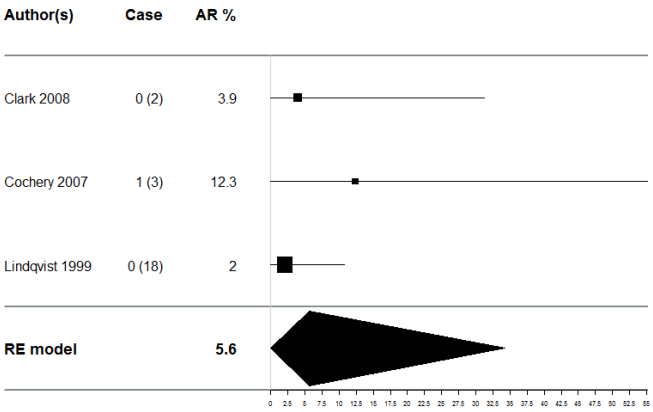
Absolute risk family studies NOS ≥8



Absolute risk non-family studies

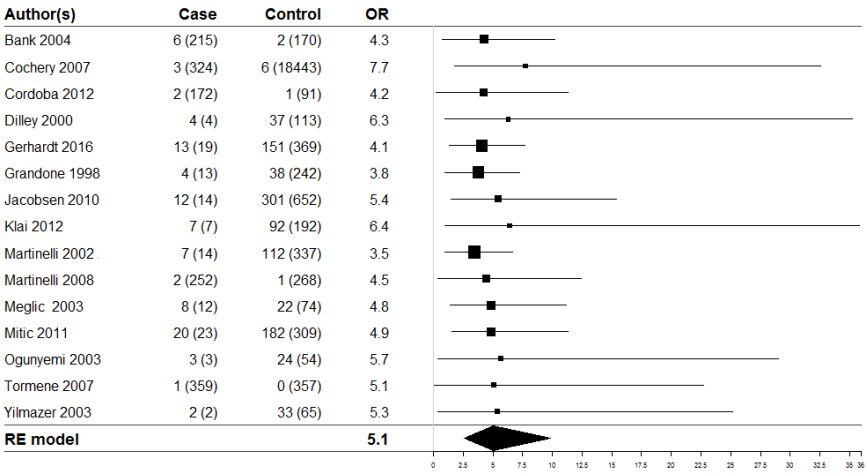


Absolute risk non-family studies (only NOS ≥8)

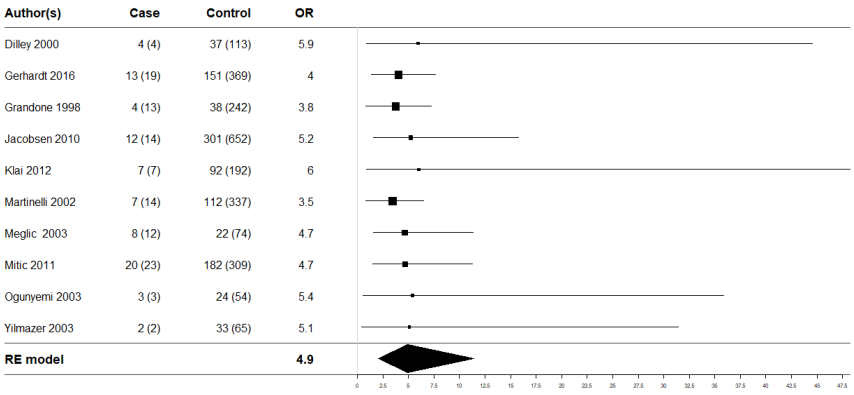


Heterozygous prothrombin G20210A (FII) mutation

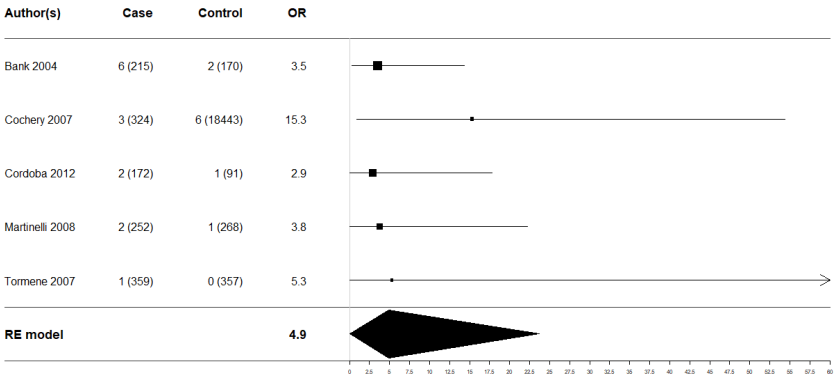
OR All studies



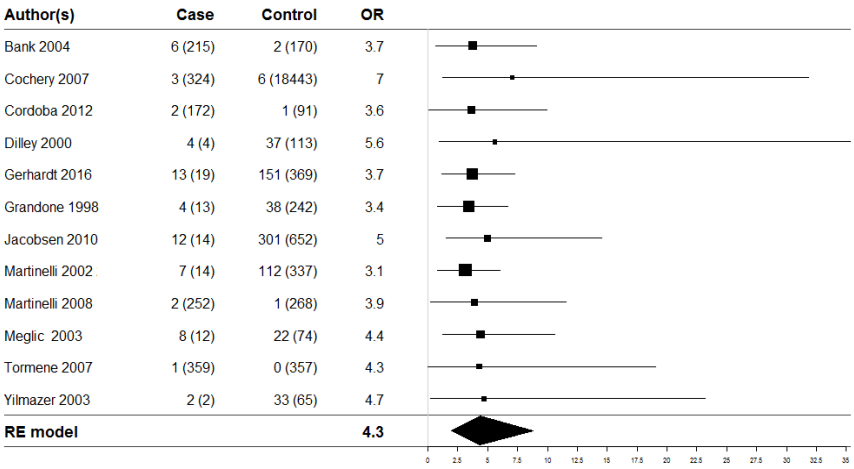
OR case-control studies



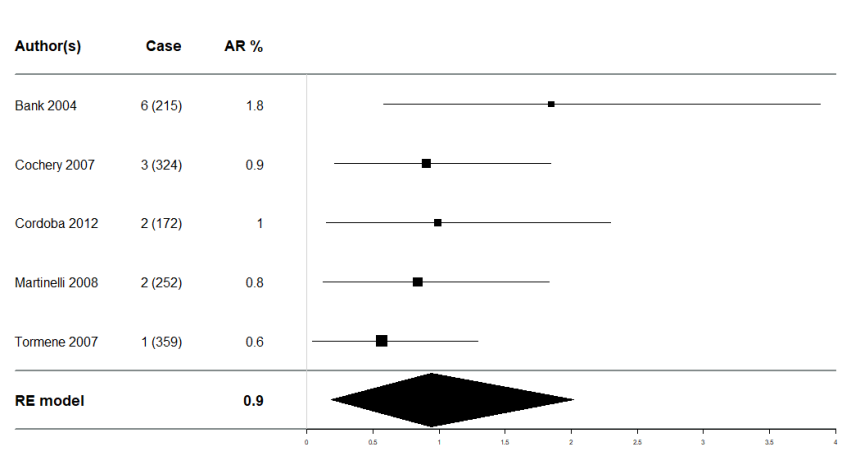
OR cohort studies



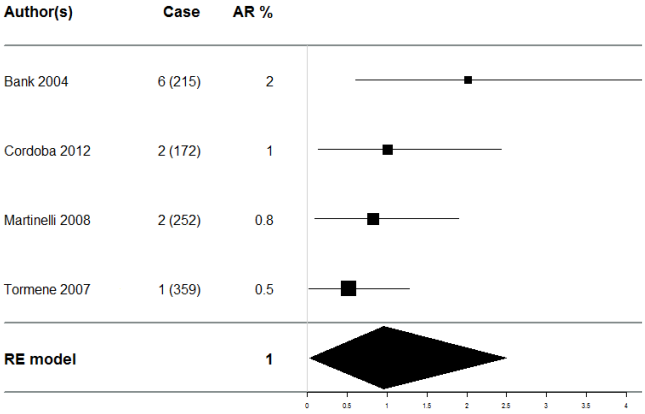
OR NOS ≥8


Author(s) Case Control OR
Bank 2004 6 (215) 2 (170) 3.7
Cochery 2007 3 (324) 6 (18443) 7
Cordoba 2012 2 (172) 1 (91) 3.6
Dilley 2000 4 (4) 37 (113) 5.6
Gerhardt 2016 13 (19) 151 (369) 3.7
Grandone 1998 4 (13) 38 (242) 3.4
Jacobsen 2010 12 (14) 301 (652) 5
Martinelli 2002 7 (14) 112 (337) 3.1
Martinelli 2008 2 (252) 1 (268) 3.9
Meglic 2003 8 (12) 22 (74) 4.4
Tormene 2007 1 (359) 0 (357) 4.3
Yilmazer 2003 2 (2) 33 (65) 4.7
RE model 4.3
0 2.5 5 7.5 10 12.5 15 17.5 20 22.5 25 27.5 30 32.5 35

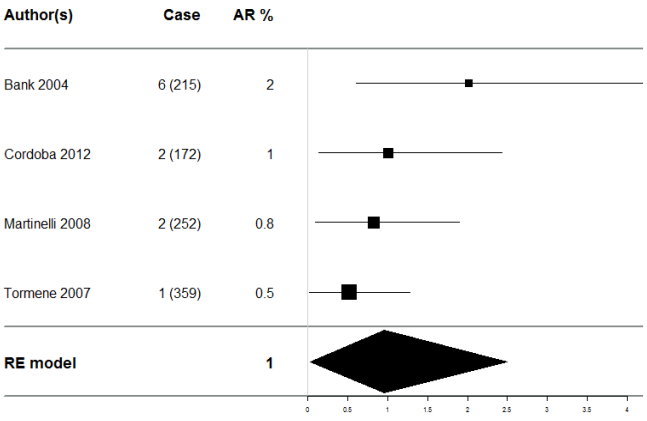
Absolute risk all studies



Absolute risk family studies



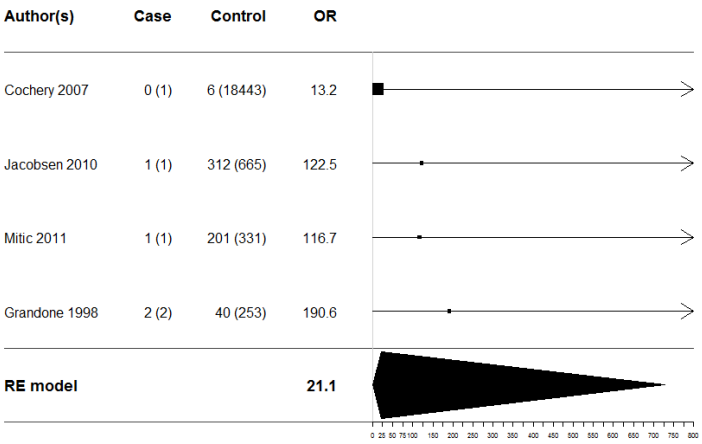
Absolute risk family studies NOS ≥8



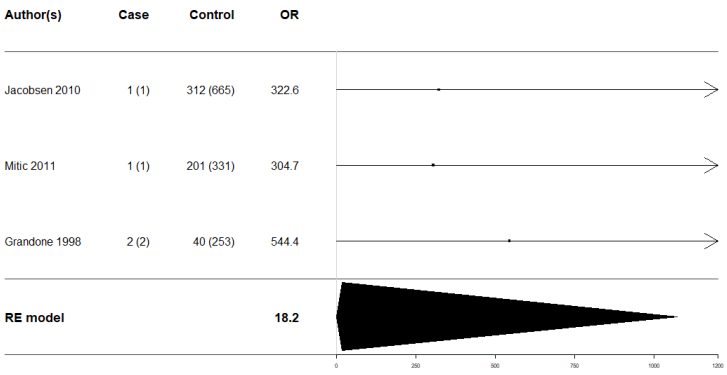
Absolute risk non-family studies: Only 1 non-family study, no forest-plot

Homozygous FII mutation

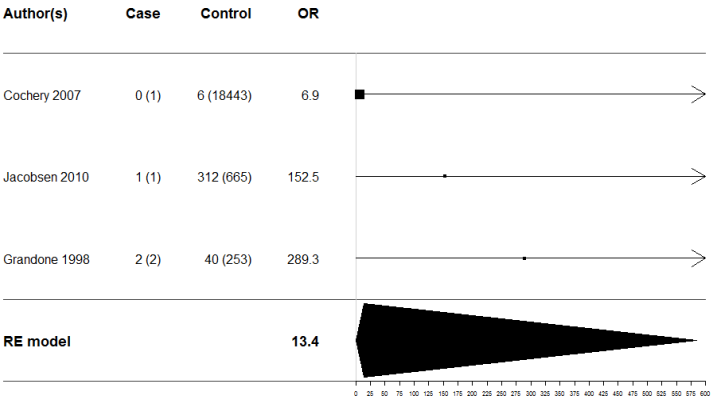
OR All studies



OR case-control studies



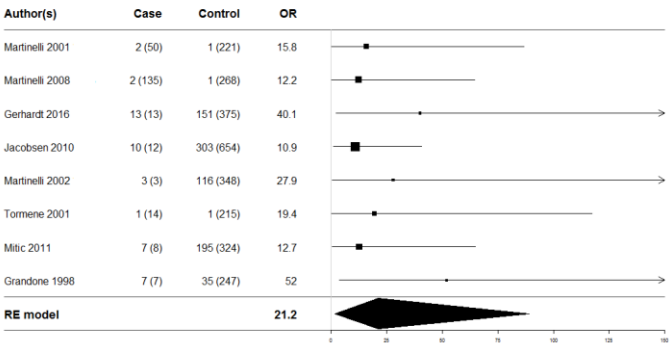
OR NOS ≥8:



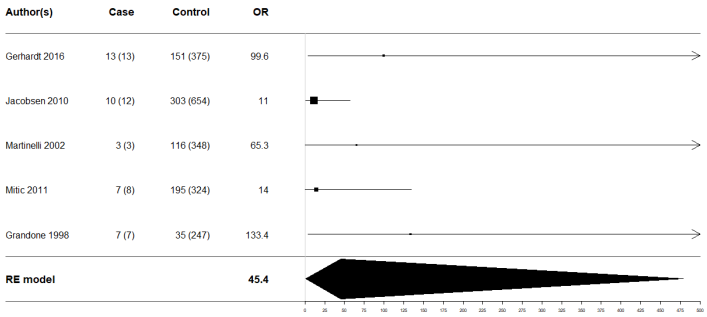
Absolute risk all studies: Insufficient data (n=1)

Compound heterozygous FVL&FII mutation

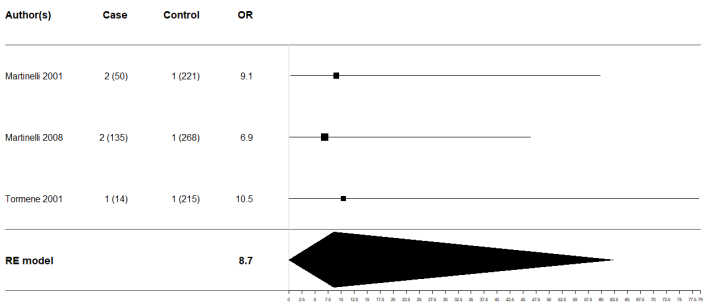
OR All studies



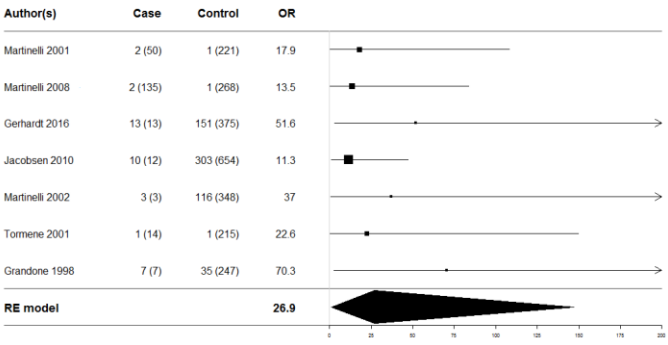
OR case-control studies



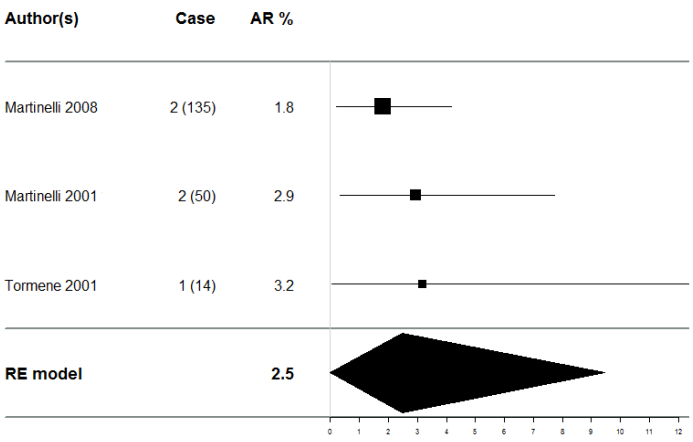
OR cohort studies



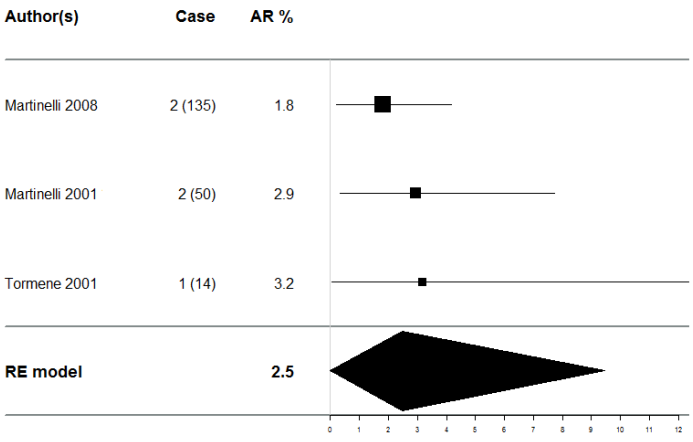
OR NOS ≥8


Author(s)
Case
Control
OR
Martinelli 2001
2 (50)
1 (221)
17.9
Martinelli 2008
2 (135)
1 (268)
13.5
Gerhardt 2016
13 (13)
151 (375)
51.6
Jacobsen 2010
10 (12)
303 (654)
11.3
Martinelli 2002
3 (3)
116 (348)
37
Tormene 2001
1 (14)
1 (215)
22.6
Grandone 1998
7 (7)
35 (247)
70.3
RE model
26.9
0
25
50
75
100
125
150
175
200

Absolute risk all studies

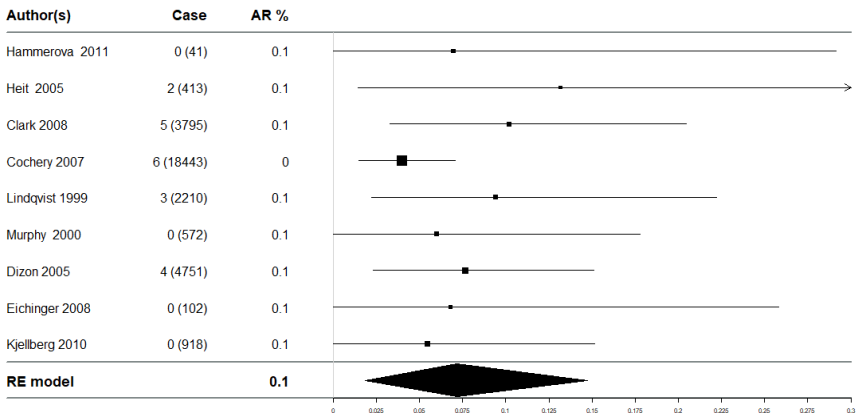


Absolute risk NOS ≥8

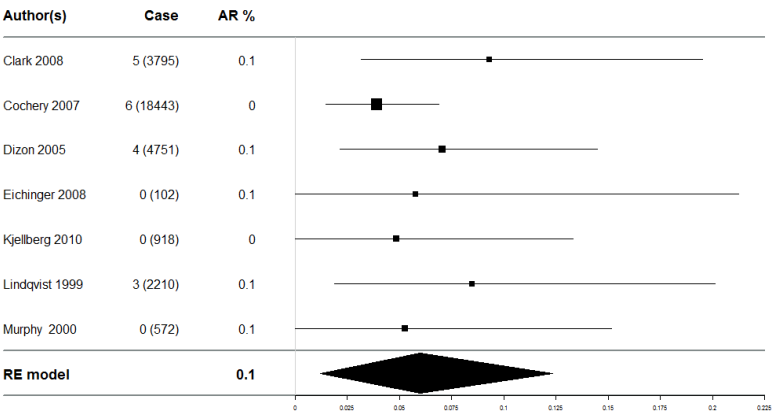


Non-carriers

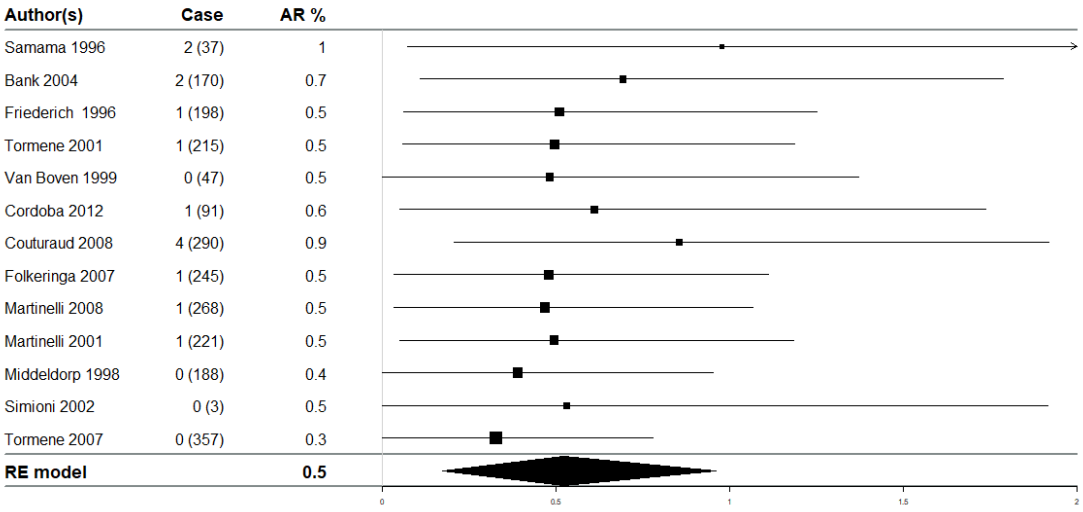
Absolute risk in non-family study non-carriers



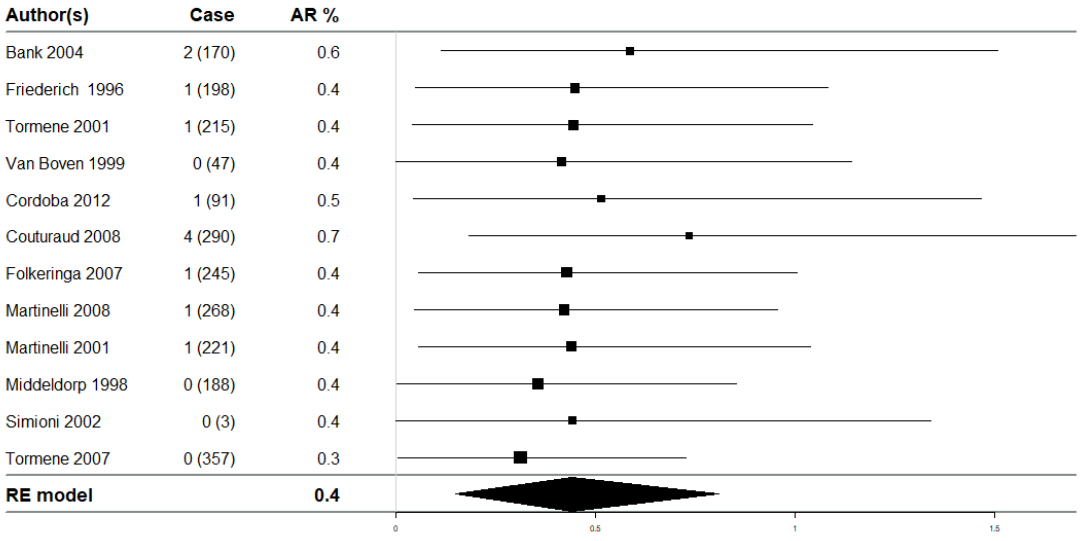
Absolute risk in non-family study non-carriers, NOS≥8



Absolute risk in family studies controls



Absolute risk in family studies controls, NOS≥8



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