

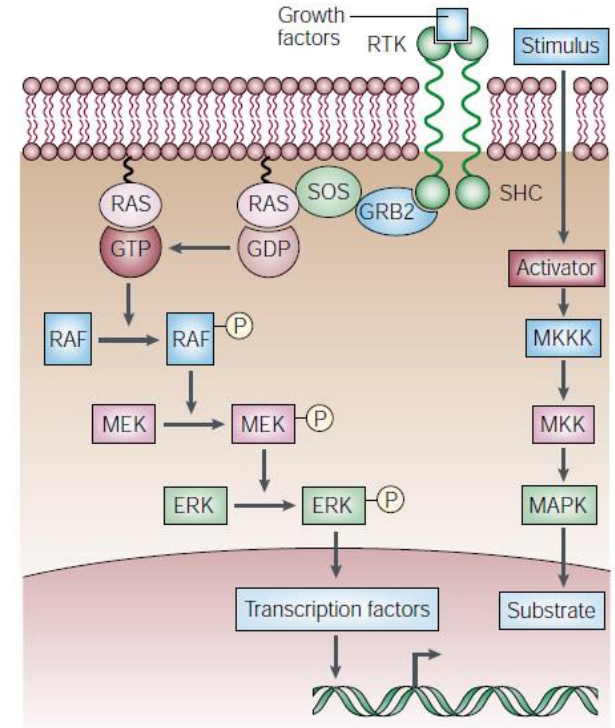
The Prognostic Value of *BRAF* Gene Mutation in Melanoma and colorectal Cancer: A Systematic Review and Meta-analysis

Reza Safaee

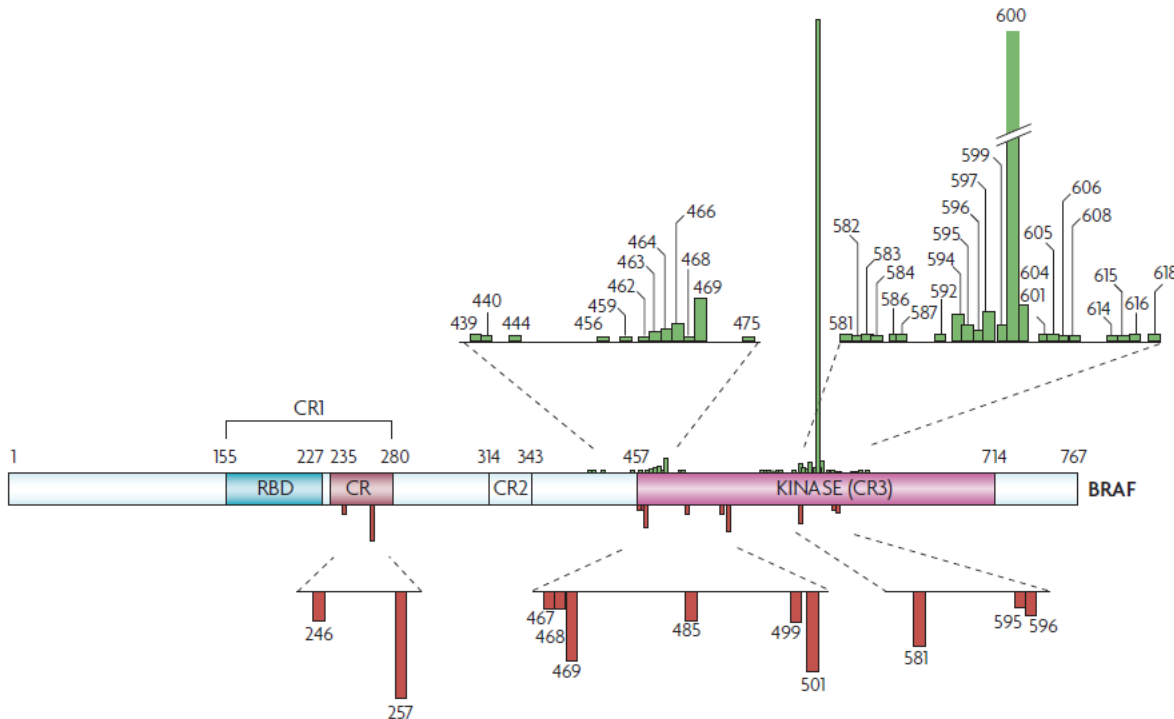
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BRAF mutations and MAPK pathway

- 7% of Cancers
- 60% of Melanoma



Chin L. Nat Rev Cancer. 2003 Aug;3(8):559-70



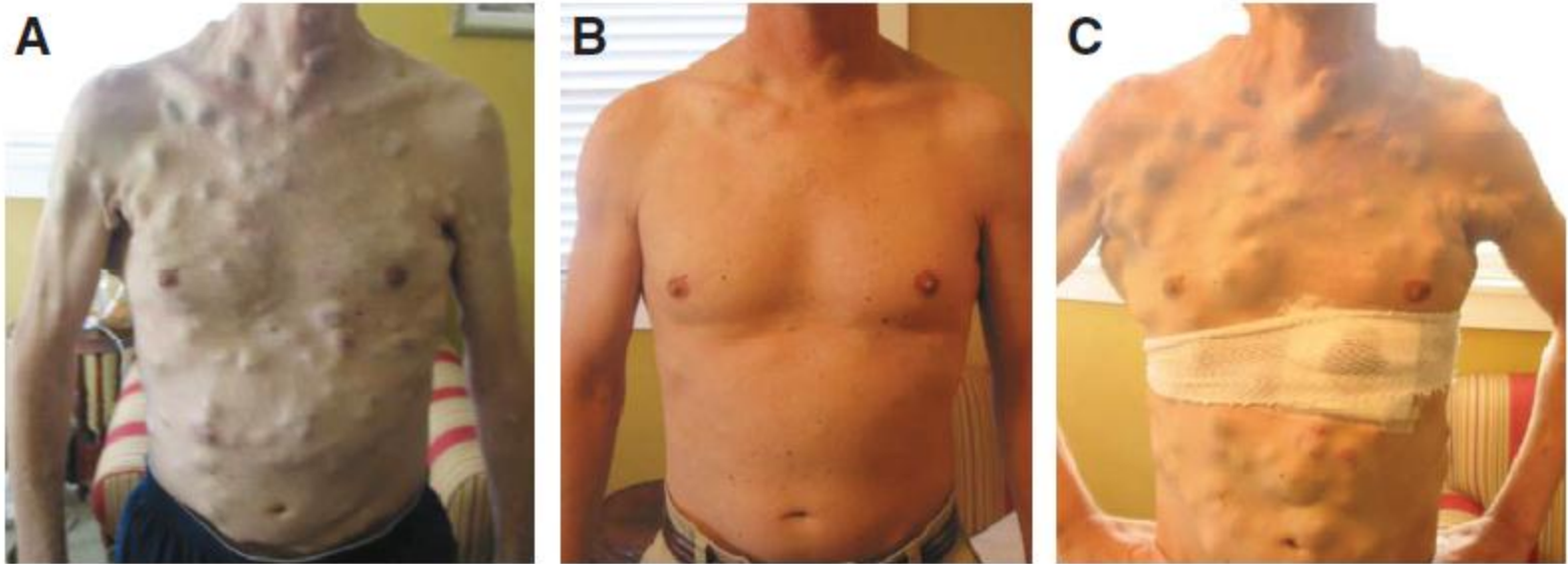
Schubert S. Nat Rev Cancer. 2007 Apr;7(4):295-308

***BRAF* mutation in different cancers**

Melanoma	50-60%
Papillary thyroid carcinoma	40%
Ovarian Cancer	15-30%
Colangiocarcinoma	20%
Colorectal Cancer	15-20%
NSCLC	3%

Davies H. et al. Nature. 2002 Jun 27;417(6892):949-54., Brose M. et al. Cancer Res 2002;62(23):6997, Kimura ET et al. Cancer Res 2003;63(7):1454., Tannapfel A et al. Gut 52(5):706., Rajagopalan H et al. Nature 418(6901):934., Singer G. JNCI 95(6):484

Targeting *BRAF-V600E* for melanoma treatment and its complications



Wagle N. et al. J Clin Oncol.. 2011 Aug 1;29(22):3085-96

***BRAF* mutation & patient survival**

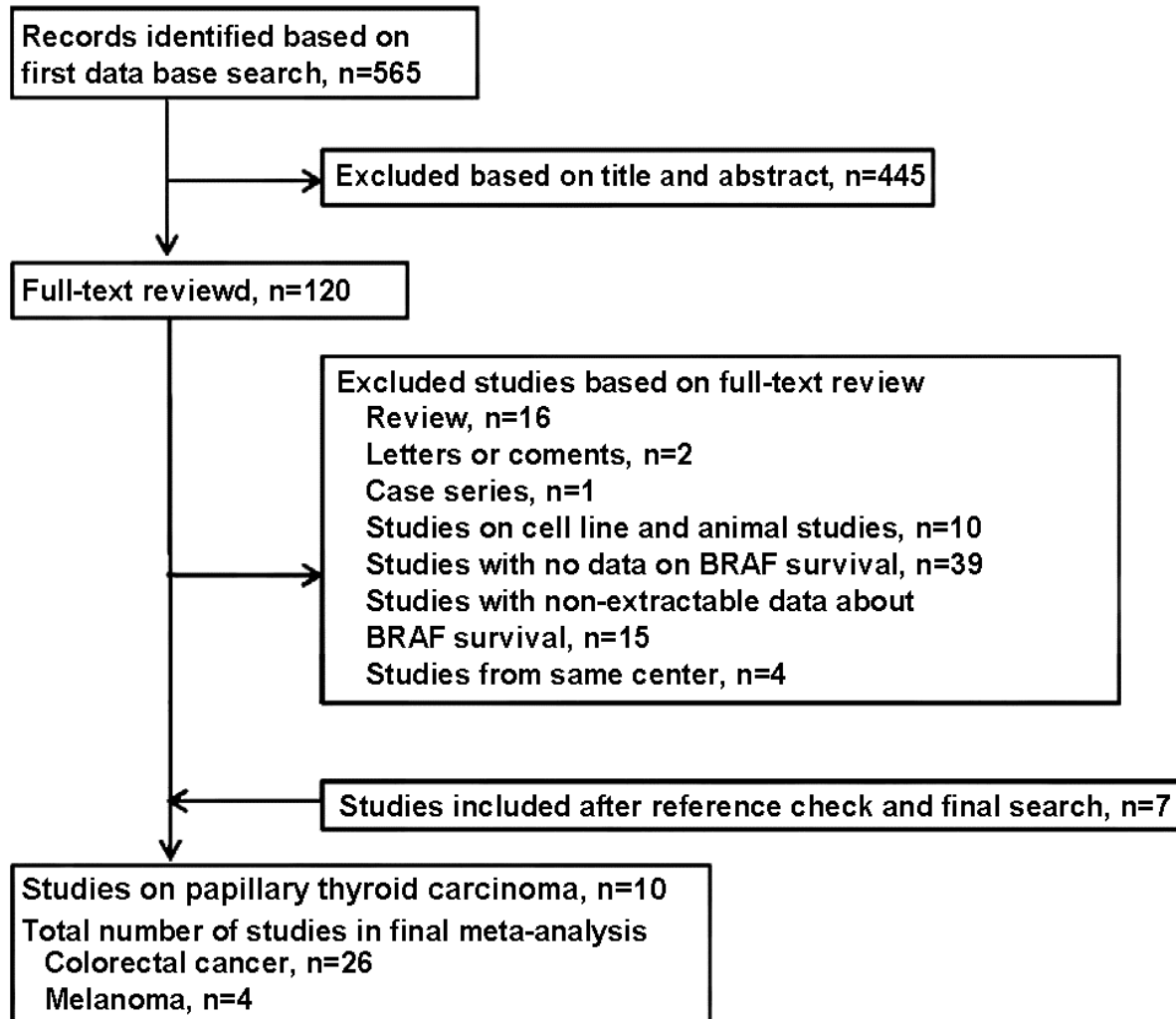
The correlation between *BRAF-V600E* mutation and cancer patient survival is still a matter of controversy in different reports.

- Reports with **negative** effect
- Reports with **no difference**
- And even reports for **protective effect** on patient survival

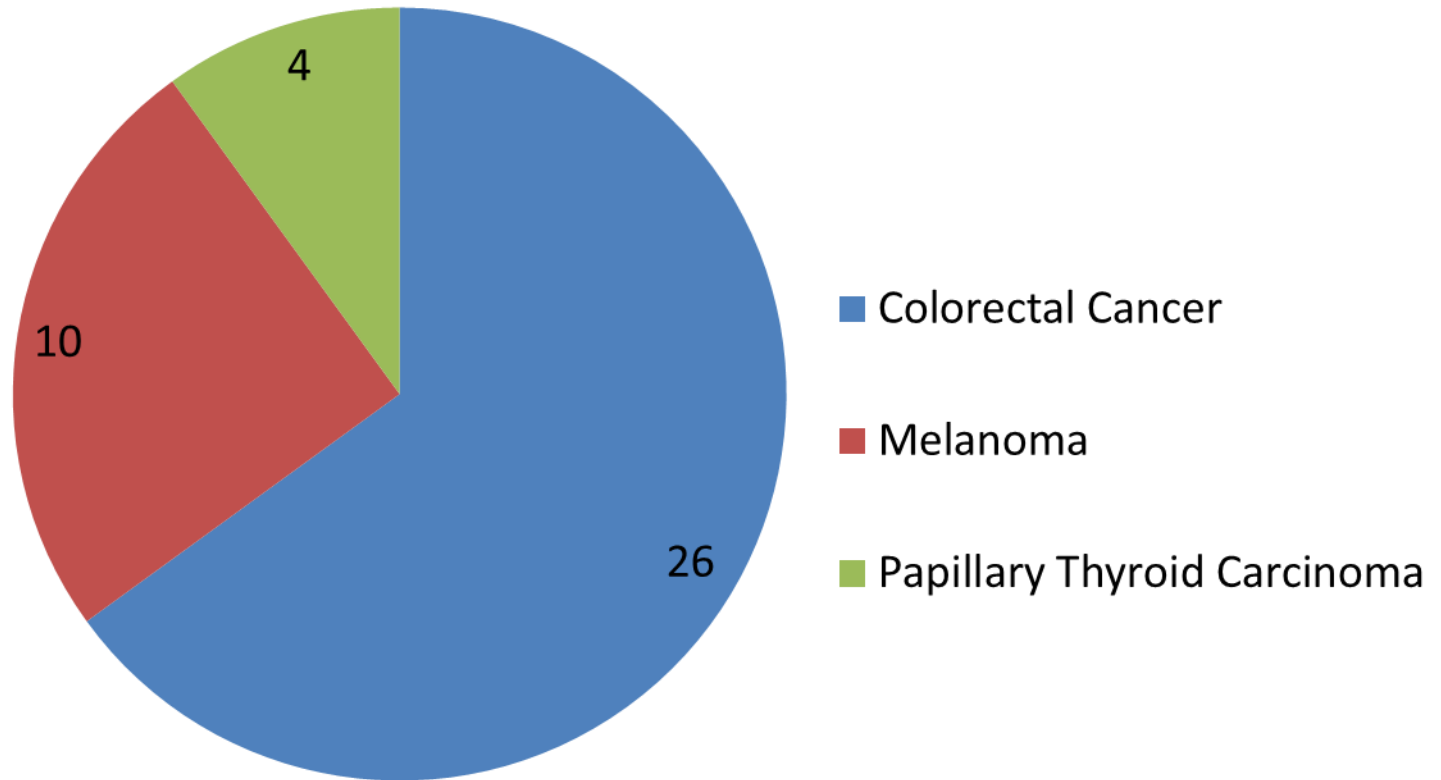
What we did?

- We searched MEDLINE and EMBASE using the terms “***BRAF***”, “***BRAF mutation***”, “***BRAF V600E***”, “***cancer***”, “***patient survival***”, “***colorectal cancer***”, “***melanoma***”, and “***papillary thyroid carcinoma***” in different combinations from June 2002 to December 2011.
- 120 relevant full text studies were categorized based on **study design** and **cancer type**.

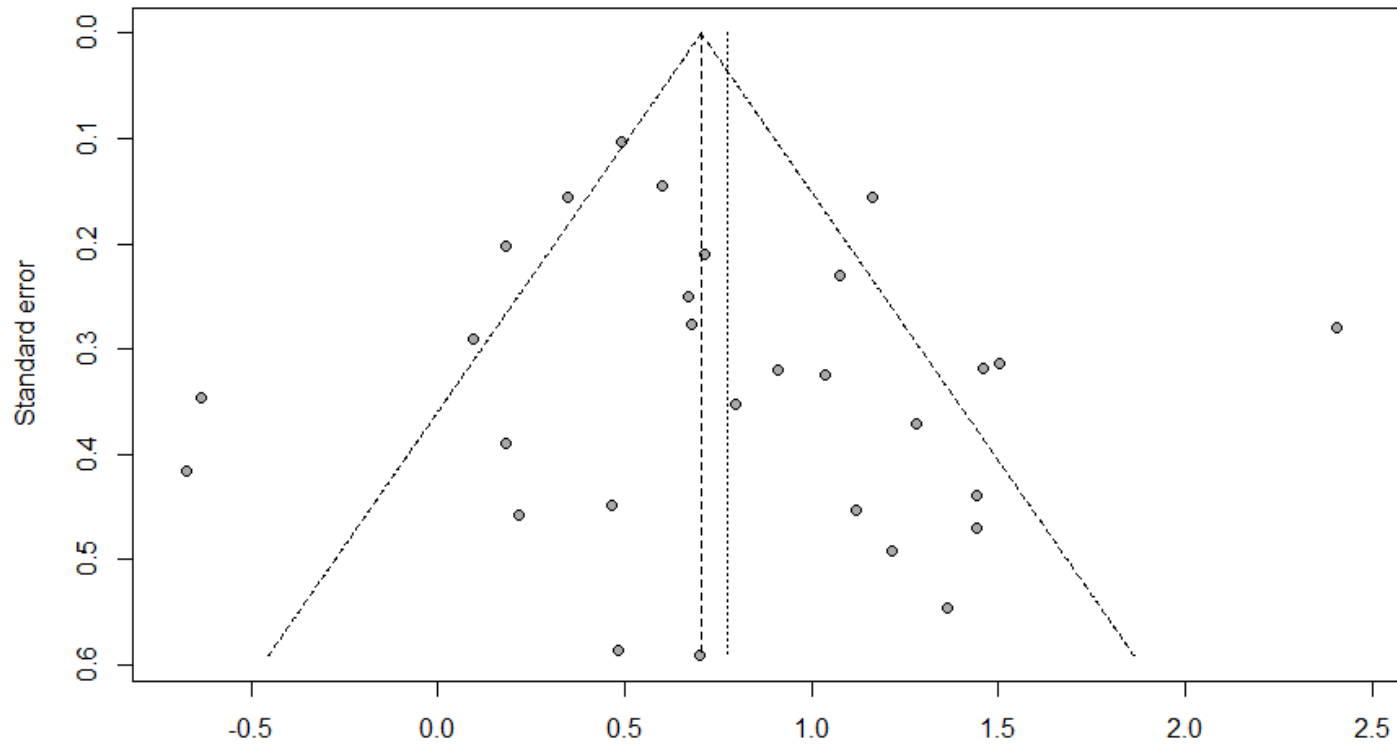
Study Selection Process



Studies included in final Meta-Analysis



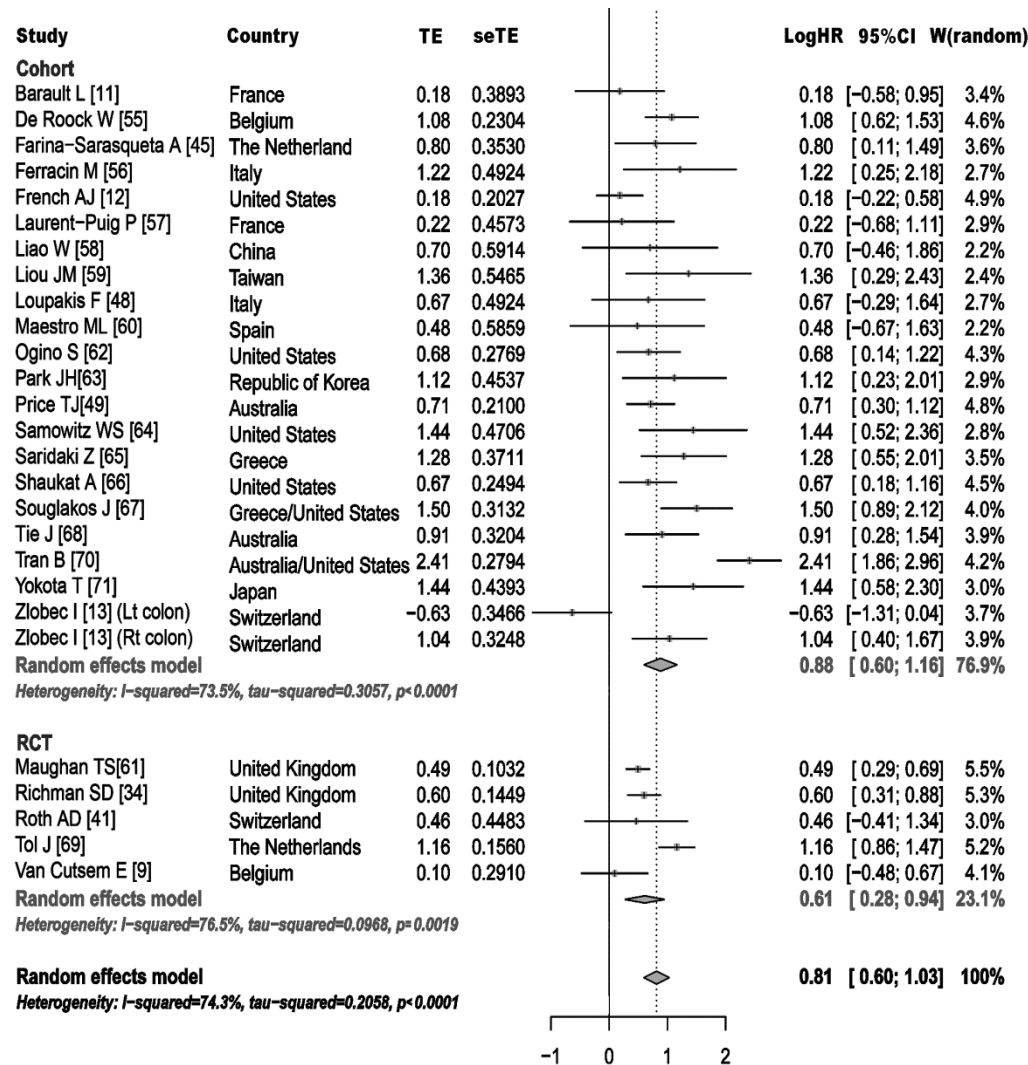
Colorectal Cancer Patient Survival



Heterogeneity was significant ($P < 0.0001$)

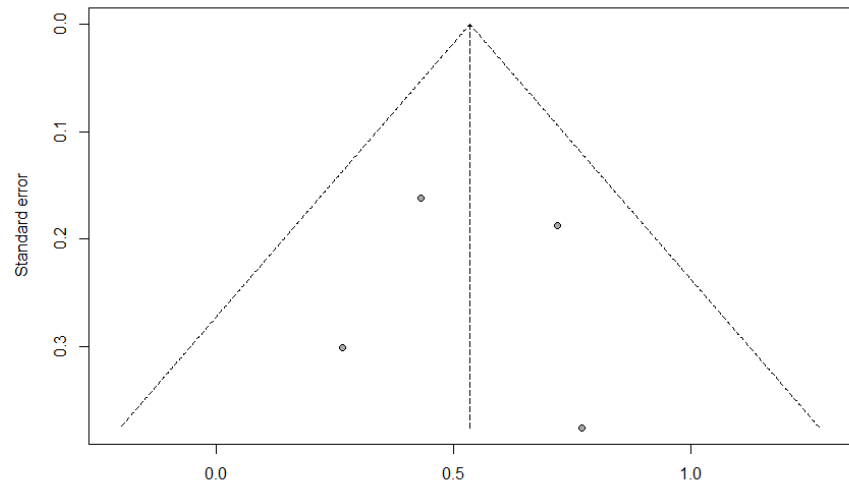
I^2 estimate of variation between analyzed studies was 74.3% .

Colorectal Cancer Patient Survival



26 studies (11,773 patients) HR 2.24 (1.82-2.83, 95% CI)

Melanoma Patient Survival

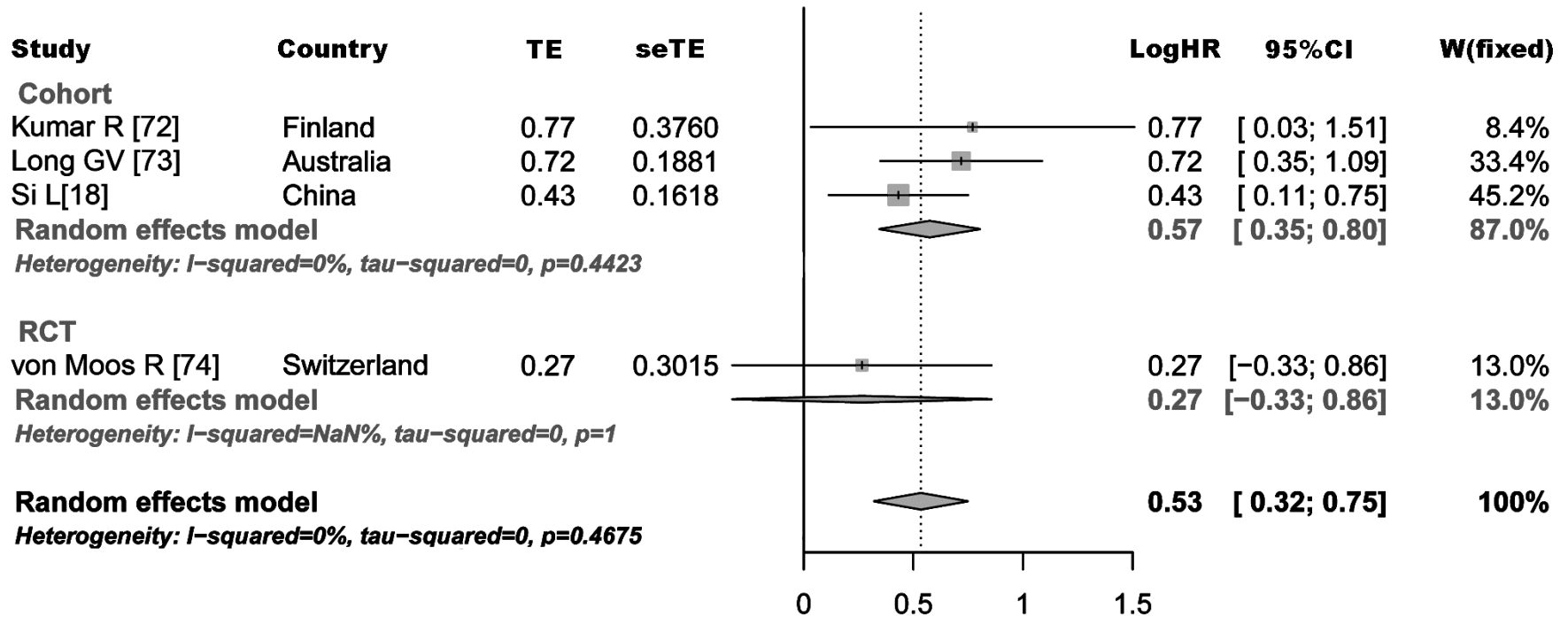


Kumar R [72]	Finland	Cohort	38	38	12	26 (68.4%)			2.16 (1.02-4.59)
Long GV [73]	Australia	Cohort	197	197	102	95 (48.2%)	11.1	46.1	
Si L [18]	China	Cohort	432	395	297	98 (24.8%)	33	53	1.54 (1.11-2.12)
von Moos R [74]	Switzerland	RCT	62	44	22	22 (50.0%)	9.2	12	

Heterogeneity was not significant ($P = 0.467$)

I^2 estimate of variation between analyzed studies was 0.0%.

Melanoma Patient Survival



4 studies (674 patients) HR of 1.70 (1.37-2.12, 95% CI)

Papillary Thyroid Carcinoma

		Number of study patients			Overall Survival		Hazard ratio	Progression free Survival		Hazard ratio	
		Overall	<i>BRAF</i> subgroup	<i>BRAF</i> WT	<i>BRAF</i> mutant	<i>BRAF</i> mutant	<i>BRAF</i> WT	<i>BRAF</i> mutant	<i>BRAF</i> WT		
Abubaker J [26]		536	296	143	153 (51.7%)			Poor			
Costa AM [27]		49	49	22	27 (55%)	No diff. Poor, when combined with other markers					
Elisei R [20]		102	102	64	38 (37.3%)	Sig. Lower	OR 14.63 (1.28-167.29)				
Ito Y [25]		631	631	389	242 (38.4%)			DFS No diff.			
Musholt TJ [19]		290	290	168	122 (42%)	No diff.	1.04				
Oler G [75]			120	62	57 (48%)			No data on survival			
O'Neill CJ [24]		104	101	41	60 (59%)			80%	75%		
Stanojevic B [10]			266	182	84 (31.6%)			DFS. No diff.		1.15 (0.42-3.19)	
Wang W [28]		891	208	93	115 (55.3%)	S <i>Bi</i> PTC with more <i>BRAF</i> mutation had lower survival compared to <i>Ui</i> PTC (<i>P</i> = 0.091)					
		177	67 (S <i>Bi</i> PTC)	23	44 (65.7%)						
		714	141 (<i>Ui</i> PTC)	70	71 (50.4%)						
Xing M [76]			219	112	107 (48.9%)	Recurrence free probability					

Take home message

- *BRAF*-V600E mutation increases the risk of mortality in **Colorectal Cancer** patients for more than two-fold.
- This mutation also significantly increases the risk of mortality in **melanoma** patients(HR:1.7).
- Data on **papillary thyroid carcinoma** are not conclusive enough and studies with larger sample size are required.
- There is **Hope** that with successful BRAF inhibition we could increase patient survival.

Acknowledgements

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CANADIAN DERMATOLOGY FOUNDATION

Thank you all for your attention!