Supplementary Material

	Vitamin E	group	Control	group		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Belch et al., 2008 (POPADAD)	48	640	39	636	2.2%	1.22 [0.81, 1.84]	
Catalano et al., 2007 (CLIPS)	6	185	5	181	0.3%	1.17 [0.36, 3.78]	
CG of the Primary Prevention Project, 2001 (PPP)	22	2231	18	2264	1.0%	1.24 [0.67, 2.31]	
Cook et al., 2007 (WACS)	137	4083	161	4088	7.3%	0.85 [0.68, 1.07]	
GISSI-Prevenzione Investigators, 1999 (GISSI)	83	5660	95	5664	4.3%	0.87 [0.65, 1.17]	
Heart Protection Study CG, 2002 (HPS)	511	10269	518	10267	25.8%	0.99 [0.88, 1.11]	-
Hodis et al., 2002 (VEAPS)	0	177	2	176	0.0%	0.20 [0.01, 4.11]	•
Lee et al., 2005 (WHS)	241	19937	246	19939	11.7%	0.98 [0.82, 1.17]	
Leppala et al., 2000 (ATBC)	509	14238	548	14281	26.1%	0.93 [0.83, 1.05]	
Sesso et al., 2008 (PHS II)	237	7315	227	7326	11.4%	1.05 [0.87, 1.25]	
Steiner et al., 1995	3	52	6	48	0.2%	0.46 [0.12, 1.74]	·
Yusuf et al., 2000 (HOPE)	209	4761	180	4780	9.6%	1.17 [0.96, 1.42]	+
Total (95% CI)		69548		69650	100.0%	0.98 [0.92, 1.04]	•
Total events	2006		2045				
Heterogeneity: Tau ² = 0.00; Chi ² = 10.41, df = 11 (P	= 0.49); ² =	0%					
Test for overall effect: Z = 0.57 (P = 0.57)							0.2 0.5 1 2 5 Vit E reduces stroke Vit E increases stroke

Figure S1. Forest plot for the relative risks of the effect of vitamin E on total stroke for individual trials and for the pooled population.

	Vitamin E	group	Control	group		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.2.1 Subgroup primary prevention							
Belch et al., 2008 (POPADAD)	48	640	39	636	2.2%	1.22 [0.81, 1.84]	
Catalano et al., 2007 (CLIPS)	6	185	5	181	0.3%	1.17 [0.36, 3.78]	
CG of the Primary Prevention Project, 2001 (PPP)	22	2231	18	2264	1.0%	1.24 [0.67, 2.31]	
GISSI-Prevenzione Investigators, 1999 (GISSI)	83	5660	95	5664	4.3%	0.87 [0.65, 1.17]	
Hodis et al., 2002 (VEAPS)	0	177	2	176	0.0%	0.20 [0.01, 4.11]	•
Lee et al., 2005 (WHS)	241	19937	246	19939	11.7%	0.98 [0.82, 1.17]	
Leppala et al., 2000 (ATBC)	509	14238	548	14281	26.1%	0.93 [0.83, 1.05]	
Subtotal (95% CI)		43068		43141	45.6%	0.96 [0.87, 1.05]	
Total events	909		953				
Heterogeneity: Tau ² = 0.00; Chi ² = 3.84, df = 6 (P =	0.70 ; $l^2 = 0$?	%					
Test for overall effect: Z = 0.98 (P = 0.33)							
1.2.2 Subgroup secondary prevention							
Cook et al., 2007 (WACS)	137	4083	161	4088	7.3%	0.85 [0.68, 1.07]	
Heart Protection Study CG, 2002 (HPS)	511	10269	518	10267	25.8%	0.99 [0.88, 1.11]	-
Sesso et al., 2008 (PHS II)	237	7315	227	7326	11.4%	1.05 [0.87, 1.25]	
Steiner et al., 1995	3	52	6	48	0.2%	0.46 [0.12, 1.74]	·
Yusuf et al., 2000 (HOPE)	209	4761	180	4780	9.6%	1.17 [0.96, 1.42]	+
Subtotal (95% CI)		26480		26509	54.4%	1.00 [0.90, 1.12]	◆
Total events	1097		1092				
Heterogeneity: Tau ² = 0.00; Chi ² = 5.91, df = 4 (P =	0.21); I ² = 32	2%					
Test for overall effect: Z = 0.08 (P = 0.93)							
Total (95% CI)		69548		69650	100.0%	0.98 [0.92, 1.04]	•
Total events	2006		2045				
Heterogeneity: Tau ² = 0.00; Chi ² = 10.41, df = 11 (F	$P = 0.49$; $ ^2 =$	0%					0.2 0.5 1 2 5
Test for overall effect: Z = 0.57 (P = 0.57)							U.2 U.5 1 2 5 Vit E reduces stroke Vit E increases stroke
Test for subgroup differences: Chi ² = 0.47, df = 1 (l	^o = 0.49), ² =	:0%					VILE reduces shoke VILE Increases shoke

Figure S2. Forest plot for the relative risks of the effect of vitamin E on total stroke for individual trials and for the pooled population (Type of prevention subgroup).

	Vitamin E	group	Control	group		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.3.1 Subgroup synthetic vitamin E							
Catalano et al., 2007 (CLIPS)	6	185	5	181	0.3%	1.17 [0.36, 3.78]	
CG of the Primary Prevention Project, 2001 (PPP)	22	2231	18	2264	1.0%	1.24 [0.67, 2.31]	
GISSI-Prevenzione Investigators, 1999 (GISSI)	83	5660	95	5664	4.4%	0.87 [0.65, 1.17]	
Heart Protection Study CG, 2002 (HPS)	511	10269	518	10267	26.5%	0.99 [0.88, 1.11]	
Hodis et al., 2002 (VEAPS)	0	177	2	176	0.0%	0.20 [0.01, 4.11]	•
Leppala et al., 2000 (ATBC)	509	14238	548	14281	26.8%	0.93 [0.83, 1.05]	
Sesso et al., 2008 (PHS II)	237	7315	227	7326	11.7%	1.05 [0.87, 1.25]	_ _
Subtotal (95% CI)		40075		40159	70.6 %	0.97 [0.90, 1.04]	•
Total events	1368		1413				
Heterogeneity: Tau ² = 0.00; Chi ² = 3.44, df = 6 (P =	0.75); I ² = 09	6					
Test for overall effect: Z = 0.82 (P = 0.41)							
1.3.2 Subgroup natural vitamin E							
Cook et al., 2007 (WACS)	137	4083	161	4088	7.5%	0.85 [0.68, 1.07]	
Lee et al., 2005 (WHS)	241	19937	246	19939	12.0%	0.98 [0.82, 1.17]	-+-
Yusuf et al., 2000 (HOPE)	209	4761	180	4780	9.8%	1.17 [0.96, 1.42]	+
Subtotal (95% CI)		28781		28807	29.4%	1.00 [0.84, 1.18]	•
Total events	587		587				
Heterogeneity: Tau ² = 0.01; Chi ² = 4.39, df = 2 (P =	0.11); P= 54	96					
Test for overall effect: Z = 0.04 (P = 0.97)							
Total (95% CI)		68856		68966	100.0%	0.98 [0.92, 1.04]	•
Total events	1955		2000				
Heterogeneity: Tau ² = 0.00; Chi ² = 8.05, df = 9 (P =	0.53); I ² = 09	6					ttttttttt
Fest for overall effect: Z = 0.67 (P = 0.51)							
Test for subgroup differences: Chi ² = 0.08, df = 1 (F	P = 0.77), P =	0%					Vit E reduces stroke Vit E increases stroke

Figure S3. Forest plot for the relative risks of the effect of vitamin E on total stroke for individual trials and for the pooled population (Source of vitamin E subgroup).

	Vitamin E	group	Control	group		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.4.1 Subgroup high dose							
Catalano et al., 2007 (CLIPS)	6	185	5	181	0.3%	1.17 [0.36, 3.78]	
CG of the Primary Prevention Project, 2001 (PPP)	22	2231	18	2264	1.0%	1.24 [0.67, 2.31]	
Cook et al., 2007 (WACS)	137	4083	161	4088	7.3%	0.85 [0.68, 1.07]	
GISSI-Prevenzione Investigators, 1999 (GISSI)	83	5660	95	5664	4.3%	0.87 [0.65, 1.17]	
Heart Protection Study CG, 2002 (HPS)	511	10269	518	10267	25.8%	0.99 [0.88, 1.11]	
Hodis et al., 2002 (VEAPS)	0	177	2	176	0.0%	0.20 [0.01, 4.11]	•
Lee et al., 2005 (WHS)	241	19937	246	19939	11.7%	0.98 [0.82, 1.17]	
Steiner et al., 1995	3	52	6	48	0.2%	0.46 [0.12, 1.74]	·
Yusufetal., 2000 (HOPE)	209	4761	180	4780	9.6%	1.17 [0.96, 1.42]	_ -
Subtotal (95% CI)		47355		47407	60.3%	0.99 [0.91, 1.07]	•
Total events	1212		1231				
Heterogeneity: Tau ² = 0.00; Chi ² = 8.06, df = 8 (P = 0	0.43); I ² = 19	6					
Test for overall effect: Z = 0.35 (P = 0.72)							
1.4.2 Subgroup low dose							
Belch et al., 2008 (POPADAD)	48	640	39	636	2.2%	1.22 [0.81, 1.84]	
Leppala et al., 2000 (ATBC)	509	14238	548	14281	26.1%	0.93 [0.83, 1.05]	
Sesso et al., 2008 (PHS II)	237	7315	227	7326	11.4%	1.05 [0.87, 1.25]	_
Subtotal (95% CI)		22193		22243	39.7%	0.99 [0.88, 1.10]	•
Total events	794		814				
Heterogeneity: Tau ² = 0.00; Chi ² = 2.34, df = 2 (P = 0	0.31); I ² = 14	%					
Test for overall effect: Z = 0.25 (P = 0.80)							
Total (95% CI)		69548		69650	100.0%	0.98 [0.92, 1.04]	•
Total events	2006		2045			- / *]
Heterogeneity: Tau ² = 0.00; Chi ² = 10.41, df = 11 (P		0%					t <u> t</u> t t t
Test for overall effect: Z = 0.57 (P = 0.57)							0.2 0.5 1 2 5 Vit E reduces stroke Vit E increases stroke
Test for subgroup differences; Chi ² = 0.00, df = 1 (P	= 1.00), l ² =	0%					VILE reduces stroke VILE Increases stroke

Figure S4. Forest plot for the relative risks of the effect of vitamin E on total stroke for individual trials and for the pooled population (Dosage of vitamin E subgroup).

	Vitamin E	group	Control	group		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
GISSI-Prevenzione Investigators, 1999 (GISSI)	39	2830	41	2828	9.5%	0.95 [0.62, 1.47]	
Hodis et al., 2002 (VEAPS)	0	177	2	176	0.2%	0.20 [0.01, 4.11] 🔸	
Leppala et al., 2000 (ATBC)	251	7120	252	7153	60.8%	1.00 [0.84, 1.19]	
Sesso et al., 2008 (PHS II)	133	3659	113	3653	29.5%	1.18 [0.92, 1.50]	+
Total (95% CI)		13786		13810	100.0%	1.04 [0.91, 1.19]	◆
Total events	423		408				
Heterogeneity: Tau ² = 0.00; Chi ² = 2.45, df = 3 (F	= 0.49); I ² =	0%				-	
Test for overall effect: Z = 0.59 (P = 0.56)							Vit E reduces stroke Vit E increases stroke

Figure S5. Forest plot for the relative risks of the effect of vitamin E on total stroke for individual trials and for the pooled population (Vitamin E alone).

	Vitamin E	group	Control	group		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Belch et al., 2008 (POPADAD)	12	640	5	636	3.9%	2.38 [0.85, 6.73]	
Catalano et al., 2007 (CLIPS)	3	185	0	181	0.5%	6.85 [0.36, 131.67]	
CG of the Primary Prevention Project, 2001 (PPP)	2	2231	5	2264	1.7%	0.41 [0.08, 2.09]	
Cook et al., 2007 (WACS)	18	4083	15	4088	7.8%	1.20 [0.61, 2.38]	
Heart Protection Study CG, 2002 (HPS)	108	10269	107	10267	22.6%	1.01 [0.77, 1.32]	-+-
Lamas et al., 2013 (TACT)	8	853	15	855	5.5%	0.53 [0.23, 1.25]	
Lee et al., 2005 (WHS)	21	19937	24	19939	9.8%	0.88 [0.49, 1.57]	
Leppala et al., 2000 (ATBC)	90	14238	70	14281	20.1%	1.29 [0.94, 1.76]	
Li et al., 1993 (Linxian)	22	1657	35	1661	11.3%	0.63 [0.37, 1.07]	
Sesso et al., 2008 (PHS II)	45	7315	56	7326	16.2%	0.80 [0.54, 1.19]	
Stephens et al., 1996 (CHAOS)	1	1035	1	967	0.6%	0.93 [0.06, 14.92]	· · · · · · · · · · · · · · · · · · ·
Total (95% CI)		62443		62465	100.0%	0.96 [0.77, 1.20]	•
Total events	330		333				
Heterogeneity: Tau ² = 0.04; Chi ² = 14.70, df = 10 (P	= 0.14); l ² =	32%					
Test for overall effect: Z = 0.35 (P = 0.73)							Vit E reduces stroke Vit E increases stroke
							VILL reduces subke VILL increases subke

Figure S6. Forest plot for the relative risks of the effect of vitamin E on fatal stroke for individual trials and for the pooled population.

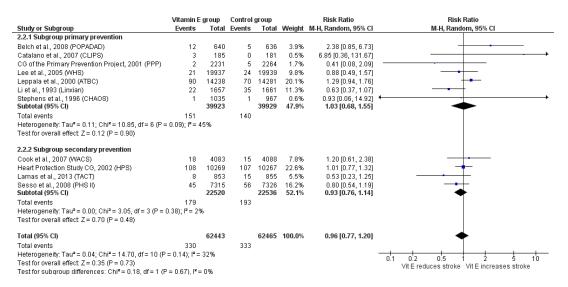


Figure S7. Forest plot for the relative risks of the effect of vitamin E on fatal stroke for individual trials and for the pooled population (Type of prevention subgroup).

	Vitamin E		Control			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
2.3.1 Subgroup synthetic vitamin E							
Catalano et al., 2007 (CLIPS)	3	185	0	181	0.5%	6.85 [0.36, 131.67]	
CG of the Primary Prevention Project, 2001 (PPP)	2	2231	5	2264	1.5%	0.41 [0.08, 2.09]	
Heart Protection Study CG, 2002 (HPS)	108	10269	107	10267	25.7%	1.01 [0.77, 1.32]	
Leppala et al., 2000 (ATBC)	90	14238	70	14281	22.0%	1.29 [0.94, 1.76]	+ - -
Li et al., 1993 (Linxian)	22	1657	35	1661	11.1%	0.63 [0.37, 1.07]	
Sesso et al., 2008 (PHS II)	45	7315	56	7326	16.9%	0.80 [0.54, 1.19]	
Subtotal (95% CI)		35895		35980	77.7%	0.94 [0.72, 1.24]	•
Total events	270		273				
Heterogeneity: Tau ² = 0.05; Chi ² = 9.45, df = 5 (P = 1	0.09); I ² = 47	'%					
Test for overall effect: Z = 0.43 (P = 0.67)							
2.3.2 Subgroup natural vitamin E							
Cook et al., 2007 (WACS)	18	4083	15	4088	7.3%	1.20 [0.61, 2.38]	
Lamas et al., 2013 (TACT)	8	853	15	855	5.0%	0.53 [0.23, 1.25]	
Lee et al., 2005 (WHS)	21	19937	24	19939	9.5%	0.88 [0.49, 1.57]	+
Stephens et al., 1996 (CHAOS)	1	1035	1	967	0.5%	0.93 [0.06, 14.92]	
Subtotal (95% CI)		25908		25849	22.3%	0.88 [0.59, 1.29]	
Total events	48		55				
Heterogeneity: Tau ² = 0.00; Chi ² = 2.11, df = 3 (P = I	0.55); I ² = 09	6					
Test for overall effect: Z = 0.66 (P = 0.51)							
Total (95% CI)		61803		61829	100.0%	0.94 [0.77, 1.15]	•
Total events	318		328				
Heterogeneity: Tau ² = 0.02; Chi ² = 11.86, df = 9 (P =	0.22); I ² = 2	24%					
Test for overall effect: Z = 0.63 (P = 0.53)							0.1 0.2 0.5 1 2 5 10 VitEreduces stroke VitEincreases stroke
Test for subgroup differences: Chi ² = 0.09, df = 1 (P	= 0.77), l ² =	:0%					VILE reduces stroke VILE Increases stroke

Figure S8. Forest plot for the relative risks of the effect of vitamin E on fatal stroke for individual trials and for the pooled population (Source of vitamin E subgroup).

	Vitamin E		Control			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
2.4.1 Subgroup high dose							
Catalano et al., 2007 (CLIPS)	3	185	0	181	0.5%	6.85 [0.36, 131.67]	
CG of the Primary Prevention Project, 2001 (PPP)	2	2231	5	2264	1.7%	0.41 [0.08, 2.09]	
Cook et al., 2007 (WACS)	18	4083	15	4088	7.8%	1.20 [0.61, 2.38]	
Heart Protection Study CG, 2002 (HPS)	108	10269	107	10267	22.6%	1.01 [0.77, 1.32]	
Lamas et al., 2013 (TACT)	8	853	15	855	5.5%	0.53 [0.23, 1.25]	
Lee et al., 2005 (WHS)	21	19937	24	19939	9.8%	0.88 [0.49, 1.57]	
	1		1				· · · · · · · · · · · · · · · · · · ·
		38593		38561	48.5%	0.96 [0.77, 1.19]	•
			167				
	0.52); I² = 09	Ко					
Test for overall effect: Z = 0.36 (P = 0.72)							
2.4.2 Subgroup low dose							
Belch et al., 2008 (POPADAD)	12	640	5	636	3.9%	2.38 [0.85, 6.73]	
Leppala et al., 2000 (ATBC)	90	14238	70	14281	20.1%	1.29 [0.94, 1.76]	+
Li et al., 1993 (Linxian)	22	1657	35	1661	11.3%	0.63 [0.37, 1.07]	
Sesso et al., 2008 (PHS II)	45	7315	56	7326	16.2%	0.80 [0.54, 1.19]	
Subtotal (95% CI)		23850		23904	51.5%	1.01 [0.66, 1.55]	•
Total events	169		166				
Heterogeneity: Tau ² = 0.12; Chi ² = 9.35, df = 3 (P = 0	0.02); I ² = 68	3%					
Test for overall effect: Z = 0.04 (P = 0.97)							
Total (95% CI)		62443		62465	100.0%	0.96 [0.77, 1.20]	
Total events	330		333				
Heterogeneity: Tau ² = 0.04; Chi ² = 14.70, df = 10 (P	= 0.14); 2=	32%					
Test for overall effect; Z = 0.35 (P = 0.73)		-					
Test for subgroup differences: Chi ² = 0.04, df = 1 (P	= 0.84), l ² =	:0%					VILE reduces stroke VILE Increases stroke
Lee et al., 2005 (WHS) Stephens et al., 1996 (CHAOS) Subtotal (55% CI) Total events Heterogeneily: Tau ² = 0.00; Chi ² = 5.21, df = 6 (P = (Test for overall effect Z = 0.36 (P = 0.72) 2.4.2 Subgroup low dose Beich et al., 2008 (POPADAD) Leppala et al., 2008 (POPADAD) Leppala et al., 2008 (PHB II) Subtotal (95% CI) Total events Heterogeneily: Tau ² = 0.12; Chi ² = 9.35, df = 3 (P = (Test for overall effect Z = 0.04 (P = 0.97) Total events Heterogeneily: Tau ² = 0.04; Chi ² = 14.70, df = 10 (P Test for overall effect Z = 0.35 (P = 0.73)	21 161 1.52); = 0' 12 20 22 45 169 0.02); = 6(330 = 0.14); =	19937 1035 38593 % 640 14238 1657 7315 23850 3% 62443 32%	24 1 167 5 70 35 56 166	19939 967 38561 636 14281 1661 7326 23904	9.8% 0.6% 48.5% 20.1% 11.3% 16.2% 51.5%	0.88 [0.49, 1.57] 0.93 [0.06, 14.92] 0.96 [0.77, 1.19] 2.38 [0.85, 6.73] 1.29 [0.94, 1.76] 0.63 [0.37, 1.07] 0.80 [0.54, 1.19] 1.01 [0.66, 1.55]	0.1 0.2 0.5 12 5 10 Vit E reduces stroke

Figure S9. Forest plot for the relative risks of the effect of vitamin E on fatal stroke for individual trials and for the pooled population (Dosage of vitamin E subgroup).

	Vitamin E	group	Control	group		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Belch et al., 2008 (POPADAD)	36	640	34	636	3.5%	1.05 [0.67, 1.66]	
Catalano et al., 2007 (CLIPS)	3	185	5	181	0.4%	0.59 [0.14, 2.42]	·
CG of the Primary Prevention Project, 2001 (PPP)	20	2231	13	2264	1.6%	1.56 [0.78, 3.13]	
Cook et al., 2007 (WACS)	119	4083	146	4088	11.2%	0.82 [0.64, 1.04]	
Heart Protection Study CG, 2002 (HPS)	430	10269	435	10267	25.8%	0.99 [0.87, 1.13]	
Lee et al., 2005 (WHS)	220	19937	222	19939	16.4%	0.99 [0.82, 1.19]	
Leppala et al., 2000 (ATBC)	419	14238	478	14281	26.1%	0.88 [0.77, 1.00]	
Milman et al., 2008 (ICARE)	6	726	11	708	0.8%	0.53 [0.20, 1.43]	
Sesso et al., 2008 (PHS II)	192	7315	171	7326	14.3%	1.12 [0.92, 1.38]	+•
Total (95% CI)		59624		59690	100.0%	0.96 [0.88, 1.05]	•
Total events	1445		1515				
Heterogeneity: Tau ² = 0.00; Chi ² = 10.03, df = 8 (P =	0.26); I ² = 2	20%					
Test for overall effect: Z = 0.94 (P = 0.35)							Vit E reduces stroke Vit E increases stroke

Figure S10. Forest plot for the relative risks of the effect of vitamin E on non-fatal stroke for individual trials and for the pooled population.

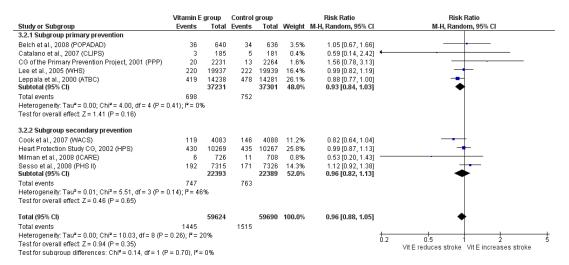


Figure S11. Forest plot for the relative risks of the effect of vitamin E on non-fatal stroke for individual trials and for the pooled population (Type of prevention subgroup).

	Vitamin E	group	Control	group		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
3.3.1 Subgroup synthetic vitamin E							
Catalano et al., 2007 (CLIPS)	3	185	5	181	0.5%	0.59 [0.14, 2.42]	·
CG of the Primary Prevention Project, 2001 (PPP)	20	2231	13	2264	1.9%	1.56 [0.78, 3.13]	
Heart Protection Study CG, 2002 (HPS)	430	10269	435	10267	25.7%	0.99 [0.87, 1.13]	-+-
Leppala et al., 2000 (ATBC)	419	14238	478	14281	26.0%	0.88 [0.77, 1.00]	
Sesso et al., 2008 (PHS II) Subtotal (95% CI)	192	7315 34238	171	7326 34319	15.4% 69.4%	1.12 [0.92, 1.38] 0.99 [0.87, 1.12]	 ◆
Total events	1064		1102				
Heterogeneity: Tau ² = 0.01; Chi ² = 6.60, df = 4 (P = Test for overall effect: Z = 0.21 (P = 0.83)	0.16); I ^z = 3!	3%					
3.3.2 Subgroup natural vitamin E							
Cook et al., 2007 (WACS)	119	4083	146	4088	12.3%	0.82 [0.64, 1.04]	
Lee et al., 2005 (WHS)	220	19937	222	19939	17.4%	0.99 [0.82, 1.19]	-+-
Milman et al., 2008 (ICARE) Subtotal (95% CI)	6	726 24746	11	708 24735	0.9% 30.6 %	0.53 [0.20, 1.43] 0.89 [0.74, 1.08]	
Total events	345		379				
Heterogeneity: Tau ² = 0.01; Chi ² = 2.75, df = 2 (P = 1) Test for overall effect: $Z = 1.14$ (P = 0.25)	0.25); I² = 2)	7%					
Total (95% CI)		58984		59054	100.0%	0.96 [0.87, 1.05]	•
Total events	1409		1481				
Heterogeneity: Tau ² = 0.01; Chi ² = 9.85, df = 7 (P = Test for overall effect: $Z = 0.91$ (P = 0.36) Test for subgroup differences: Chi ² = 0.70, df = 1 (F							0.2 0.5 1 2 Vit E reduces stroke Vit E increases stroke

Figure S12. Forest plot for the relative risks of the effect of vitamin E on non-fatal stroke for individual trials and for the pooled population (Source of vitamin E subgroup).

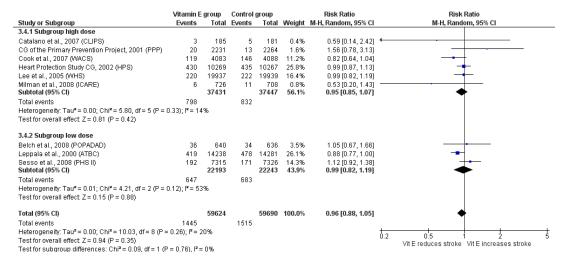


Figure S13. Forest plot for the relative risks of the effect of vitamin E on non-fatal stroke for individual trials and for the pooled population (Dosage of vitamin E subgroup).

	Vitamin E	group	Control	group		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Cook et al., 2007 (WACS)	15	4083	10	4088	4.8%	1.50 [0.68, 3.34]	
Heart Protection Study CG, 2002 (HPS)	51	10269	53	10267	20.6%	0.96 [0.66, 1.41]	
Lee et al., 2005 (WHS)	44	19937	48	19939	18.2%	0.92 [0.61, 1.38]	
Leppala et al., 2000 (ATBC)	108	14238	89	14281	38.8%	1.22 [0.92, 1.61]	
Sesso et al., 2008 (PHS II)	39	7315	23	7326	11.5%	1.70 [1.02, 2.84]	
Steiner et al., 1995	2	52	0	48	0.3%	4.62 [0.23, 93.91]	
Yusuf et al., 2000 (HOPE)	17	4761	13	4780	5.8%	1.31 [0.64, 2.70]	
Total (95% CI)		60655		60729	100.0%	1.17 [0.98, 1.39]	•
Total events	276		236				
Heterogeneity: Tau ² = 0.00; Chi ² = 5.74, d	f= 6 (P = 0.	45); I² = 0)%				0.01 0.1 1 10 100
Test for overall effect: Z = 1.73 (P = 0.08)							Vit E reduces stroke Vit E increases stroke

Figure S14. Forest plot for the relative risks of the effect of vitamin E on haemorrhagic stroke for individual trials and for the pooled population.

	Vitamin E	group	Control	group		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Boaz et al., 2000 (SPACE)	5	97	6	99	0.5%	0.85 [0.27, 2.70]	· · · · · · · · · · · · · · · · · · ·
Cook et al., 2007 (WACS)	121	4083	150	4088	11.0%	0.81 [0.64, 1.02]	
Heart Protection Study CG, 2002 (HPS)	345	10269	354	10267	27.0%	0.97 [0.84, 1.13]	_
Lee et al., 2005 (WHS)	194	19937	197	19939	15.4%	0.98 [0.81, 1.20]	
Leppala et al., 2000 (ATBC)	373	14238	434	14281	30.4%	0.86 [0.75, 0.99]	
Sesso et al., 2008 (PHS II)	191	7315	196	7326	15.5%	0.98 [0.80, 1.19]	
Steiner et al., 1995	1	52	6	48	0.1%	0.15 [0.02, 1.23]	•
Total (95% CI)		55991		56048	100.0%	0.92 [0.85, 0.99]	•
Total events	1230		1343				
Heterogeneity: Tau ² = 0.00; Chi ² = 6.31, d	f= 6 (P = 0.3	39); I ² = 6	5%				
Test for overall effect: Z = 2.10 (P = 0.04)							0.5 0.7 1 1.5 2 Vit E reduces stroke Vit E increases stroke

Figure S15. Forest plot for the relative risks of the effect of vitamin E on ischaemic stroke for individual trials and for the pooled population.

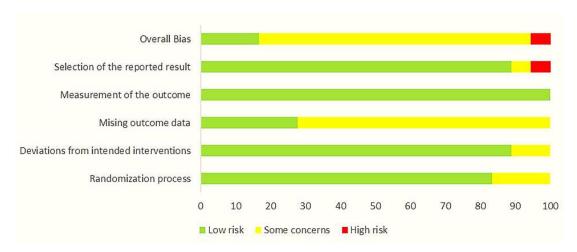


Figure S16. Risk of bias graph shows review authors' judgements about each risk of bias items presented as percentages across all included studies.

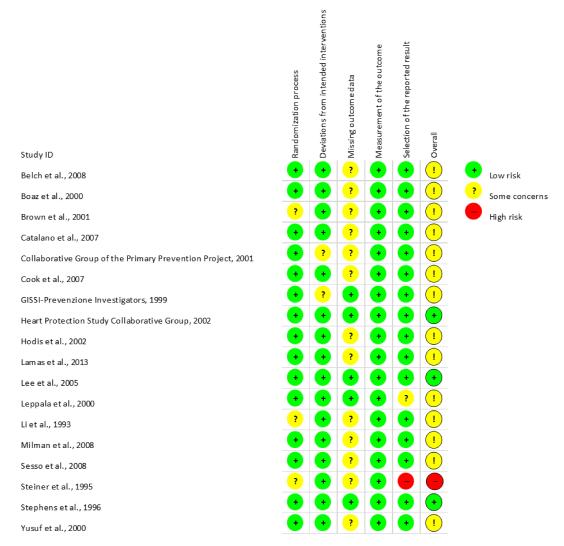


Figure S17. Risk of bias summary shows review authors' judgements about each risk of bias items for each included study.

Table S1. GRADE quality assessment for the study findings was summarised as follows.

	Certainty assessment							Nº of patients		Effect		Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vitamin E	Control	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
The effec	t of vitamin E	on total strok	e									
40							0000000540	0045/00050	DD 000		-	

12	randomised trials	serious	not serious	not serious	not serious	none	2006/69548 (2.9%)	2045/69650 (2.9%)	RR 0.98 (0.92 to 1.04)	1 fewer per 1,000 (from 2 fewer to 1 more)			
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The effect of vitamin E on fatal stroke

11	randomised trials	not serious	not serious	not serious	not serious	none	330/62443 (0.5%)	333/62465 (0.5%)	RR 0.96 (0.77 to 1.20)	0 fewer per 1,000 (from 1 fewer to 1 more)	⊕⊕⊕⊕ _{HIGH}	
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The effect of vitamin E on non fatal stroke

9	randomised trials	not serious	not serious	not serious	not serious	none	1445/59624 (2.4%)	1515/59690 (2.5%)	RR 0.96 (0.88 to 1.05)	1 fewer per 1,000 (from 3 fewer to 1 more)	⊕⊕⊕⊕ _{HIGH}		
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The effect of vitamin E on haemorrhagic stroke

7	randomised trials	serious	not serious	not serious	very serious	none	276/60655 (0.5%)	236/60729 (0.4%)	RR 1.17 (0.98 to 1.39)	1 more per 1,000 (from 0 fewer to 2 more)		
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The effect of vitamin E on ischaemic stroke

7	randomised trials	serious	not serious	not serious	not serious	none	1230/55991 (2.2%)	1343/56048 (2.4%)	RR 0.92 (0.85 to 0.99)	2 fewer per 1,000 (from 4 fewer to 0 fewer)		
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CI: Confidence interval; RR: Risk ratio