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					95% CI				
LnRR	Coefficient	SE	t	P-value	Lower limit	Upper limit			
age	-0.008	0.003	-2.28	0.036	-0.015	-0.0006			
constant	0.522	0.233	2.24	0.039	0.028	1.015			
Number of o	Number of observations=18; Adjusted R ² =100%								

Table S1: Meta-regression for CVD events by age in Randomized controlled trial

Table S2: Meta-regression for CVD deaths by age in Randomized controlled trial

					95% CI		
LnRR	Coefficient	SE	t	P-value	Lower limit	Upper limit	
age	-0.014	0.006	-2.30	0.036	-0.027	-0.001	
constant	0.921	0.414	2.22	0.042	0.038	1.804	
Number of obs	servations=17; A	djusted R ² =100	%				

				Risk of bia			
		D1	D2	D3	D4	D5	Overall
	Virtanen 2022	+	+	+	+	<u>+</u>	+
	Naele 2022	+	+	+	+	+	+
	Chatterjee 2021	+	+	+	+	+	+
	Manson 2019	+	+	+	+	+	+
	Shoji 2018	+	+	+	+	+	+
	Scragg 2017	+	+	+	+	+	+
	Zittermann 2017	+	+	+	+	+	+
	Jorde 2016	-	+	+	+	-	-
	Baron 2015	+	+	+	+	+	+
	Martineau 2014	+	+	+	+	+	+
	Ford 2014	+	+	+	+	+	+
	Wang 2014	+	+	+	+	-	-
	Witham 2013	+	+	+	+	+	+
	Gallagher 2012	+	+	+	+	+	+
Study	Lehouchk 2012	+	+	+	+	+	+
	Sanders 2010	+	+	+	+	+	+
	Prince 2008	+	+	+	+	+	+
	Zhu 2008	+	+	+	+	-	-
	Berggren 2007	+		+	+	-	\mathbf{x}
	Hsia 2007	-	+	+	\mathbf{X}	-	\mathbf{X}
	Jackson 2006	+	+	+	+	+	+
	Brazier 2005	-	+	+	\mathbf{X}	-	\mathbf{X}
	Grant 2005	+	+	+	+	+	+
	Trivedi 2003	+	+	+	+	-	-
	Komulainen 1999	-	+	+	-	-	\mathbf{x}
	Ott 1989	-	-	+	\mathbf{X}	-	\mathbf{x}
	Aloia 1988	-	-	+	\mathbf{X}	-	\mathbf{X}
	Inkovaara 1983	-	-	+	×	-	\mathbf{x}
	Brohult 1973	-	-	+	$\mathbf{\times}$	+	
		D2: Bias due D3: Bias due D4: Bias in r	sing from the r e to deviations e to missing or measurement selection of the	from intendeo utcome data. of the outcom	d intervention. e.		ement High Some concerns Low

Figure S1: Risk of bias in Randomized Controlled Trial

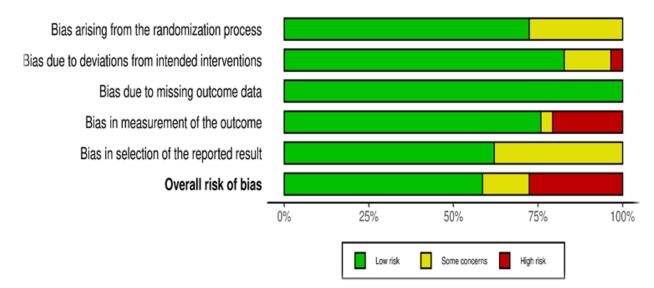


Figure S2: Risk of Bias in Randomized Controlled Trials

		Vitam	in D	Plac	00		%
study	Sex	Events	Total	Events	otal	RR (95% CI)	Weig
Ayocardial Infarc	tion						
Artanen 2022*	both	18	832	18	30 -	1.00 (0.52, 1.90)	0.82
Artanen 2022**	both	20	833	18	30 -	1.11 (0.59, 2.08)	0.86
Artanen 2022***	both	38	1665	18	30	1.05 (0.60, 1.83)	1.11
Manson 2019	both	169	12927	176	2944 🔶	0.96 (0.78, 1.19)	7.80
shoji 2018	both	10	488	11	76	0.89 (0.38, 2.07)	0.48
Scragg 2017	both	28	2558	31	550	- 0.90 (0.54, 1.50)	1.33
Baron 2015	both	8	1130	7	129	1.14 (0.42, 3.14)	0.34
Martineau 2014	both	0	125	1	25	0.33 (0.01, 8.10)	0.03
ord 2014	both	114	2649	117	643 🔶	0.97 (0.76, 1.25)	5.39
Nang 2014	both	0	30	1	0	0.33 (0.01, 7.87)	0.03
Vitham 2013	both	2	80	2	9	0.99 (0.14, 6.84)	0.09
Gallagher 2012	Female	9	245	6	44	1.49 (0.54, 4.13)	0.33
ehouchk 2012	both	1	81	3	1	0.37 (0.04, 3.53)	0.07
Sanders 2010	Female	3	1131	2	125	1.49 (0.25, 8.91)	0.11
Prince 2008	Female	2	151	3	51	0.67 (0.11, 3.93)	0.11
2008 Dhu	Female	1	39	0	1	 6.15 (0.26, 147.62 	0.03
Berggren 2007	Female	47	102	40	7	1.12 (0.81, 1.53)	3.41
Isia 2007	Female	411	18176	390	8106 +	1.05 (0.92, 1.20)	18.26
lackson 2006	Female	659	18176	637	8106 +	1.03 (0.93, 1.15)	29.97
Grant 2005	both	114	2649	117	643 🔶	0.97 (0.76, 1.25)	5.39
Trivedi 2003	both	224	1345	233	341 +	0.96 (0.81, 1.13)	12.28
frivedi 2003	Male	191	1345	193	341 +	0.99 (0.82, 1.19)	9.99
rivedi 2003	Female	33	1345	40	341	0.82 (0.52, 1.30)	1.66
Komulainen 1999	Female	1	112	0	15	\$ 3.08 (0.13, 74.81)	0.03
Dtt 1989	Female	0	43	1	3	0.33 (0.01, 7.96)	0.03
Voia 1988	Female	1	17	1	7	1.00 (0.07, 14.72)	0.05
Subtotal (I-squar	ed = 0.09	6, p = 1.0	00)		•	1.01 (0.95, 1.07)	100.0
Overall (I-square	d = 0.0%	p = 1.00	0)			1.01 (0.95, 1.07)	100.0

Figure S3: Forrest plot for Myocardial Infarction in Randomized Controlled Trials

		Vitam	nin D	Plac	00		%
Study	Sex	Events	Total	Events	otal	RR (95% CI)	Weig
Stroke events							
Virtanen 2022*	both	20	832	18	30 —	1.11 (0.59, 2.08)	0.99
Virtanen 2022**	both	16	833	18	30	0.89 (0.45, 1.72)	0.89
Virtanen 2022***	both	36	1665	18	30	1.00 (0.57, 1.74)	1.26
Naele 2022	both	10	250	15	61	0.70 (0.32, 1.52)	0.64
Manson 2019	both	141	12927	149	2944 -	← 0.95 (0.75, 1.19)	7.50
Shoji 2018	both	28	488	14	76	1.95 (1.04, 3.66)	0.99
Scragg 2017	both	26	2558	27	550	0.96 (0.56, 1.64)	1.37
Jorde 2016	both	4	256	2	55	1.99 (0.37, 10.78)	0.14
Baron 2015	both	9	1130	5	129	1.80 (0.60, 5.35)	0.33
Ford 2014	both	160	2649	149	643	➡ 1.07 (0.86, 1.33)	8.39
Wang 2014	both	0	30	2	•	0.20 (0.01, 4.00)	0.04
Witham 2013	both	3	80	1	9	2.96 (0.31, 27.88)	0.08
Gallagher 2012	Female	10	245	7	44	1.42 (0.55, 3.68)	0.44
Sanders 2010	Female	8	1131	6	125	1.33 (0.46, 3.81)	0.35
Prince 2008	Female	3	151	3	51	1.00 (0.21, 4.88)	0.16
Zhu 2008	Female	1	39	2	1	1.04 (0.10, 11.11)	0.07
Berggren 2007	Female	27	102	15	7	1.71 (0.97, 3.02)	1.22
Hsia 2007	Female	362	18176	377	8106	♦ 0.96 (0.83, 1.10)	19.30
Jackson 2006	Female	690	18176	659	8106	 1.04 (0.94, 1.16) 	35.84
Brazier 2005	Female	1	95	2	7 — •	0.51 (0.05, 5.54)	0.07
Grant 2005	both	160	2649	149	643	➡ 1.07 (0.86, 1.33)	8.39
Trivedi 2003	both	105	1345	101	341	➡ 1.04 (0.80, 1.35)	5.71
Trivedi 2003	Male	86	1345	85	341	1.01 (0.75, 1.35)	4.67
Trivedi 2003	Female	19	1345	16	341	1.18 (0.61, 2.29)	0.90
Inkovaara 1983	both	8	45	3	2 –	2.49 (0.71, 8.76)	0.25
Subtotal (I-squar	ed = 0.09	%, p = 0.8	56)			1.04 (0.97, 1.10)	
Overall (I-square	d = 0.0%	, p = 0.85	6)			1.04 (0.97, 1.10)	100.0
NOTE: Weights a	re from r	andom eff	fects anal	vsis			

Figure S4: Forrest plot for Stroke in Randomized Controlled Trials

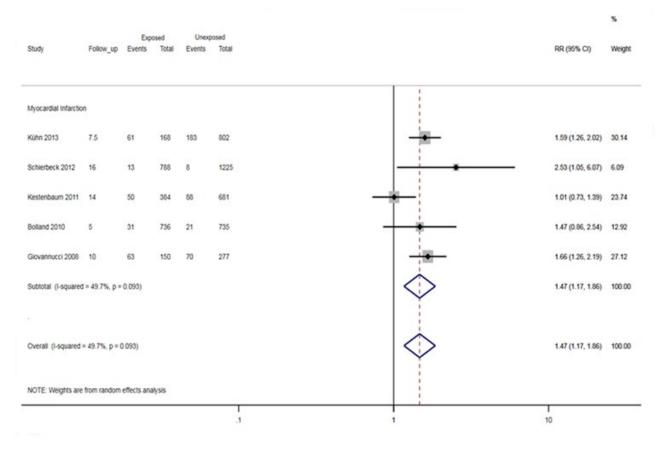


Figure S5: Forest plot for Myocardial Infarction in Prospective Cohort Studies

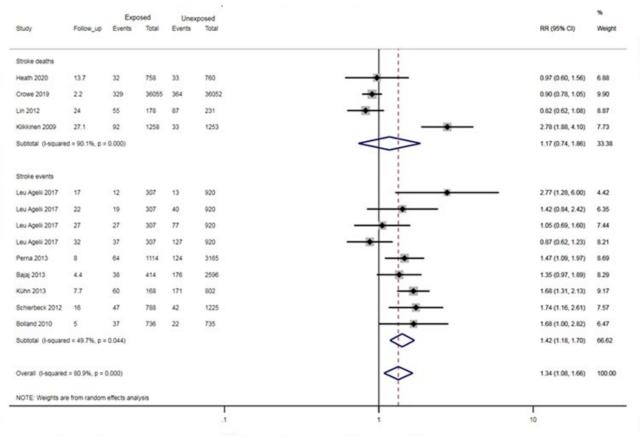


Figure S6: Forest plot for Stroke in Prospective Cohort Studies