Appendix 1: Electronic search strategy used to search Medline

1. exp ethanol/
2. exp alcoholic beverages/
3. exp alcohol drinking/
4. 1 or 2 or 3
5. (drink or drinks or drinking or drinker$).ti,ab.
6. (liquor or liquors).ti,ab.
7. ethanol intake.ti,ab.
8. ethanol.ti,ab.
9. "alcohol drink$".ti,ab.
10. "ethanol drink$".ti,ab.
11. 5 or 6 or 7 or 8 or 9 or 10
12. 4 or 11
13. exp biological markers/
14. exp inflammation mediators/
15. exp C-reactive protein/
16. exp leukocyte/
17. exp leukocyte count/
18. exp Interleukin-6/
19. exp platelet aggregation/
20. exp blood coagulation/
21. exp Antithrombins/
22. exp Plasminogen Activator Inhibitor 1/
23. exp von Willebrand Factor/
24. exp Intercellular Adhesion Molecule-1/
25. exp E-Selectin/
26. exp Vascular Cell Adhesion Molecule-1/
27. exp Natriuretic Peptide, Brain/
28. exp Troponin T/
29. exp "Lipoprotein(a)"/
30. exp leptin/
31. exp adiponectin/
32. exp cholesterol, hdl/
33. exp lipoprotein, ldl/
34. exp tumor necrosis factor alpha/
35. exp cholesterol, ldl/
36. exp triglycerides/
37. exp apoprotein$/
38. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37
39. c-reactive protein.ti,ab.
40. leukocyte.ti,ab.
41. interleukin-6.ti,ab.
42. plasminogen activator inhibitor-1.ti,ab.
43. D-dimer.ti,ab.
44. exp tissue plasminogen activator/
45. tissue plasminogen activator.ti,ab.
46. von Willebrand Factor.ti,ab.
47. intracellular adhesion molecule-1.ti,ab.
48. E-selectin.ti,ab.
49. vascular cell adhesion molecule-1.ti,ab.
50. brain natriuretic peptide.ti,ab.
51. Troponin T.ti,ab.
52. "lipoprotein a".ti,ab.
53. (biomarker or biomarkers or biological marker or biological markers).ti,ab.
54. ((inflammatory or inflammation) adj (marker$ or biomarker$ or biological marker$)).ti,ab.

55. ((serological or serum) adj (marker or markers)).ti,ab.
56. adipocyte hormone$.ti,ab.
57. (prothrombotic adj (marker$ or biomarker$ or biological marker$)).ti,ab.
58. (fibrinolytic adj (marker$ or biomarker$ or biological marker$)).ti,ab.
59. "platelet aggregation".ti,ab.
60. "blood coagulation".ti,ab.
61. "platelet function".ti,ab.
62. (("endothelial cell adhesion" or lipid) adj (biomarker$ or marker$ or biological marker$)).ti,ab.
63. leptin.ti,ab.
64. adiponectin.ti,ab.
65. triglycerides.ti,ab.
66. apoliprotein$.ti,ab.
67. 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66
68. 38 or 67
69. randomized controlled trial.pt.
70. controlled clinical trial.pt.
71. random$.ti,ab.
72. placebo$.ti,ab.
73. clinical trials as topic.sh.
74. (trial or trials).ti,ab.
75. (subjects or groups or volunteers).ti,ab.
76. exp cross-over studies/
77. comparative study.pt.
78. cross-over.ti,ab.
79. crossover.ti,ab.
80. (before adj after).ti,ab.
81. (pre adj post).ti,ab.
82. (control or controls or controlled).ti,ab.
83. 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82
84. limit 83 to animals
85. limit 84 to (animals and humans)
86. 84 not 85
87. 83 not 86
88. 12 and 68 and 87

No limits were placed on the search.

Appendix 2: Explanation for excluding studies from meta-analysis

Biomarker	**# articles in systematic review**	**# articles meta-analyzed**	**Number of articles not included in meta analysis: Reasons for excluding**
High density lipoprotein cholesterol	44	33	11: (1) Data reported as least mean squares, (1)Data reported as % change, (4)Error measurements not reported, (5)Data in graph format
Low density lipoprotein cholesterol	28	24	4: (1) Data reported as least mean squares, (1) Error measurements not reported, (2) Data in graph format
Total cholesterol	32	26	6: (1) Data reported as least mean squares, (2) Error measurements not reported, (3) Data in graph format
Triglycerides	39	31	8: (1) Data reported as least mean squares, (3) Error measurements not provided, (4) Data in graph format only
Apoprotein	22	16	6: (1)Data reported as least mean squares, (1)Data

A1			reported as % change, (1)Data reported as density fractions, (1)Error measurements not reported, (2)Data in graph format
lipoprotein(a)	5	3	2: (1) Units reported are incorrect, (1) Error measurements not reported
C-reactive protein	8	5	3: (1): Data reported as a correlation with leptin, (1) Data in graph form, (1): Data presented as median change.
Leukocytes	1	0	1: Only study reporting on this biomarker
Interleukin-6	4	2	2: (1): Data presented as median difference, (1): Data presented as percent change in graph format
Tumour necrosis factor alpha	7	3	4: (1) Reports a "non-detectable change", (1) Data reported as median difference, (1)Data in graph form, (1) Error measurements not reported
Plasminogen activator inhibitor-1	3	3	--
von Willebrand factor	2	0	1: (1) data presented as a percent of normal, the other study was the only one to report usable data on this biomarker
Tissue plasminogen activator	4	3	(1) Error measurements not reported
Plasminogen	1	0	1: Only study reporting on this biomarker
Fibrinogen	8	7	1: Data in graph format
Thromboxane	1	0	1: Only study reporting on this biomarker
e-selectin	2	0	
Intracellular adhesion molecule-1	3	0	(1): data presented as percent change, (1) reports on other cellular adhesion molecule, the third study was the only one to report usable data on this biomarker
Vascular cellular adhesion molecule-1	2	0	(1) reports on other cellular adhesion molecule, the other study was the only one to report usable data on this biomarker
Adiponectin	7	4	3: (1) Error measurements not reported, (2) Data reported as % change
Leptin	2	0	1: (1) data presented as geometric mean, the other study was the only one to report usable data on this biomarker

Appendix 3: Restricted Analyses by study type or alcohol type

Analysis	All studies mean change (95% confidence interval) test for heterogeneity (n)	By Study Design mean change (95% confidence interval) test for heterogeneity (n)		By Alcohol Type mean change (95% confidence interval) test for heterogeneity (n)		
Biomarker		Pre-Post design only	Cross-over design only	Wine	Beer	Spirits
high density lipoprotein cholesterol	0.094 (0.064 to, 0.123) P=0.005 (n=33*)	0.089 (0.039 to 0.138) P=0.007 (n=15)	0.100 (0.072 to 0.128) P=0.975 (n=16)	0.104 (0.069 to 0.138) P=0.588 (n=17)	0.102 (0.028 to 0.177) P=0.989 (n=7)	0.015 (-0.004 to 0.034) P=0.275 (n=7)
low density lipoprotein cholesterol	-0.11 (-0.22 to 0.006) P<0.001 (n= 24*)	-0.089 (-0.252 to 0.075) P<0.001 (n=12)	-0.064 (-0.141 to 0.012) P=0.871 (n=10)	-0.053 (-0.147 to 0.041) P=0.915 (n=13)	-0.043 (-0.246 to 0.159) P=0.650 (n=5)	-0.175 (-0.383 to 0.032) P<0.001 (n=7)
Total cholesterol	0.00 (-0.066 to 0.067) P=0.995 (n=26†)	0.011 (-0.149 to 0.172) P=0.995 (n=9)	-0.004 (-0.078 to 0.070) P=0.872 (n=16)	-0.040 (-0.136 to 0.057) P=0.883 (n=15)	0.076 (-0.205 to 0.357) P=0.982 (n=4)	0.019 (-0.036 to 0.074) P=0.993 (n=7)
Triglycerides	0.016 (-0.018 to 0.051) P=0.353 (n =31*)	-0.007 (-0.060 to 0.045) P=0.419 (n=1)	0.030 (-0.016 to 0.076) P=0.256 (n=16)	0.031 (-0.013 to 0.074) P=0.111 (n=16)	0.00 (-0.141 to 0.140) P=0.915 (n=6)	0.031 (-0.039 to 0.102) P=0.789 (n=7)
Fibrinogen	-0.20 (-0.29 to -0.11) P=0.713 (n =7)	-0.175 (-0.410 to 0.060) (test for heterogeneity n/a)	-0.208 (-0.308 to -0.109) P=0.598 (n=6)	-0.172 (-0.275 to -0.068) P=0.920 (n=5)	-0.460 (-0.832 to -0.088) (test for heterogeneity	-0.300 (-0.555 to -0.045) (test for heterogeneity

		n=1			n/a) n=1	n/a) n=1

* 2 studies in this group were prospective two-arm controlled studies; † 1 study in this group was a prospective two-arm controlled study.

Appendix 4: Quality Assessment for studies included in Meta-analyses

Source	Study design	Randomized	Randomization described	Measures compliance with alcohol consumption and/or abstinence	Any losses to attrition described	Relevant confounders described*	Included in Meta-analyses for which biomarker?
Bantle 2008[21]	Random crossover	Y	N	Y	Y	Y	Triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, C-reactive protein
Bertiere 1986[24]	Pre-post	N	N	N	N	Y	Triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, apoprotein A1
Beulens 2008[28]	Random crossover	Y	N	Y	Y	Y	Adiponectin
Beulens 2007[26]	Random crossover	Y	N	Y	N	Y	Adiponectin
Beulens 2006[25]	Random crossover	Y	N	Y	Y	Y	Adiponectin
Burr 1986[29]	Random crossover	Y	N	Y	Y	N	Triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, fibrinogen
Cartron 2003[30]	Random crossover	Y	N	N	N	Y	Triglycerides, total cholesterol, apoprotein A1
Clevidence 1995[31]	Random crossover	Y	N	N	Y	Y	Triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, apoprotein A1, Lp(a)
Contaldo 1989[32]	crossover	N	N	N	N	Y	Triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, apoprotein A1
Couzigou	Pre-post						high density

1984[33]		N	N	N	Y	Y	lipoprotein cholesterol, low density lipoprotein cholesterol, apoprotein A1
Crouse 1984[34]	Pre-post	N	N	Y	N	Y	Triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol
Davies 2002[35]	Random crossover	Y	N	N	Y	Y	Triglycerides
De Oliveira e Silva 2000[36]	crossover	N	N	N	Y	Y	Triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol
Djurovic 2007[35]	Random crossover	Y	N	N	Y	Y	Interleukin-6
Estruch 2004[38]	Random crossover	Y	N	Y	Y	Y	C-reactive protein, fibrinogen
Fraser 1983[39]	crossover	N	N	N	Y	Y	high density lipoprotein cholesterol, apoprotein A1
Frimpong 1989[40]	Pre-post	N	N	N	N	Y	Triglycerides, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol
Glueck 1980[41]	Pre-post	N	N	Y	N	Y	Triglycerides, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol
Goldberg 1996[42]	crossover	N	N	N	N	Y	Triglycerides, total cholesterol, high density lipoprotein cholesterol, apoprotein A1
Gottrand 1999[43]	Random crossover	Y	N	Y	N	Y	Triglycerides, total cholesterol, high density lipoprotein cholesterol, apoprotein A1, lipoprotein (a)
Hagiage 1992[44]	Pre-post	N	N	N	N	Y	Triglycerides, low density lipoprotein cholesterol, high density lipoprotein cholesterol,

							apoprotein A1, lipoprotein (a)
Hansen 2005[45]	Random crossover	Y	N	N	Y	Y	Total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, fibrinogen
Hartung 1983[46]	Pre-post	N	N	Y	N	Y	Triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol
Hartung 1986[47]	Pre-post	N	N	Y	N	Y	Triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, apoprotein A1
Hartung 1990[48]	Pre-post	N	N	N	Y	Y	high density lipoprotein cholesterol, apoprotein A1
Jensen 2006[50]	Random crossover	Y	Y	N	Y	Y	fibrinogen
Joosten 2008[51]	Cross over	N	N	Y	N	Y	Triglycerides, low density lipoprotein cholesterol, high density lipoprotein cholesterol, adiponectin
Malmendier 1985[53]	Pre-post	N	N	N	Y	Y	Total cholesterol, Triglycerides, high density lipoprotein cholesterol, low density lipoprotein cholesterol, apoprotein A1
McConnell 1997[54]	Pre-post	N	N	Y	Y	Y	Triglycerides, high density lipoprotein cholesterol, low density lipoprotein cholesterol, apoprotein A1, lipoprotein (a)
Mezzano 2001[55]	Pre-post	N	N	N	Y	Y	c-reactive protein, fibrinogen
Retterstol 2005[61]	Random crossover	Y	N	N	Y	Y	Triglycerides, total cholesterol, high density lipoprotein cholesterol, c-reactive protein, fibrinogen
Romeo	Pre-post						Interleukin-6,

2007[60]		N	N	Y	Y	Y	tumor necrosis factor alpha
Senault 2000[66]	Random crossover	Y	N	N	N	Y	Triglycerides, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol , apoprotein A1, lipoprotein (a)
Sharpe 1995[67]	Pre-post	N	N	N	N	Y	Triglycerides, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, apoprotein A1, lipoprotein (a)
Sierksma 2004[71]	Random crossover	N	N	Y	Y	Y	Triglycerides, total cholesterol, high density lipoprotein cholesterol apoprotein A1
Sierksma 2002[70]	Random crossover	Y	N	Y	Y	Y	Triglycerides, high density lipoprotein cholesterol, fibrinogen
Suzukawa 1994[73]	Random prospective two-arm control	Y	N	N	Y	Y	Triglycerides, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol
Thornton 1983[74]	Pre-post	N	N	N	N	Y	Triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol
Tsang 2005[75]	Random prospective two-arm control	Y	N	Y	N	Y	Triglycerides, high density lipoprotein cholesterol, low density lipoprotein cholesterol
Valimaki 1991[77]	Pre-post	N	N	Y	N	Y	Triglycerides, total cholesterol, high density lipoprotein cholesterol, apoprotein A1
Valimaki 1988[76]	Pre-post	N	N	Y	N	Y	Triglycerides, total cholesterol, high density lipoprotein cholesterol
Van der	Random						high density

Gaag 2001[78]	crossover	Y	N	Y	Y	Y	lipoprotein cholesterol, apoprotein A1
Van Golde 2002[78]	Pre-post	N	N	N	N	Y	plasminogen activator inhibitor-1, tissue plasminogen activator
Watzl 2004[80]	Random crossover	Y	N	N	Y	Y	tumor necrosis factor alpha