

## Supplementary Online Content

The Emerging Risk Factors Collaboration. Major lipids, apolipoproteins, and risk of vascular disease. *JAMA*. 2009;302(18):1993-2000.

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1.** Characteristics of the 68 prospective studies contributing data to the current analysis (references are listed in eAppendix 1)

Study abbreviation <sup>a</sup>	Year(s) of baseline survey	Population source	Participants, No.	Male, No. (%)	Age at Survey, mean (SD), y	Median follow-up (5th & 95th percentiles)	Log <sub>e</sub> triglyceride mean (SD)	HDL-C (mg/dL) mean (SD)	Non-HDL-C (mg/dL) mean (SD)
<b>Cohort studies</b>									
ARIC <sup>1</sup>	1987-89 <sup>f</sup>	Household lists	14544	6279 (43)	54 (6)	14.0 (4.9-15.7)	4.72 (0.51)	52 (17)	162 (44)
ATENA <sup>c 2</sup>	1983-97 <sup>f</sup>	Electoral rolls	4681	0 (0)	50 (7)	6.7 (5.2-8.1)	4.62 (0.43)	63 (16)	174 (47)
BHS <sup>3</sup>	1969-95 <sup>f</sup>	Electoral rolls	4183	1911 (46)	49 (16)	21.2 (6.9-24.2)	4.56 (0.54)	58 (15)	167 (49)
BRHS <sup>4</sup>	1978-80	GP lists	4883	4883 (100)	50 (6)	22.3 (4.5-23.6)	5.03 (0.56)	44 (11)	198 (42)
BRUN <sup>5</sup>	1990	Pop. register	817	398 (49)	58 (11)	15.3 (3.9-15.5)	4.74 (0.52)	57 (14)	165 (41)
BUPA <sup>6</sup>	1975-82	Medical centre list	5288	5288 (100)	47 (8)	21.0 (11.6-21.9)	4.76 (0.54)	51 (12)	206 (46)
BWHHS <sup>7</sup>	1999-01	Pop. register	3118	0 (0)	69 (5)	4.6 (2.0-5.6)	4.98 (0.45)	65 (17)	194 (48)
CaPS <sup>8</sup>	1979-83 <sup>f</sup>	Electoral rolls	2011	2011 (100)	52 (4)	13.0 (4.0-13.0)	5.01 (0.55)	44 (13)	176 (45)
CASTEL <sup>9</sup>	1983-87 <sup>f</sup>	Pop. screening	2367	913 (39)	73 (5)	11.2 (2.5-14.0)	4.71 (0.44)	59 (16)	160 (43)
CHS-1 <sup>b 10</sup>	1989-93 <sup>f</sup>	Medicare lists	3862	1481 (38)	72 (5)	12.1 (2.0-12.9)	4.84 (0.43)	55 (16)	157 (39)
CHS-2 <sup>b 10</sup>	1989-93 <sup>f</sup>	Medicare lists	455	174 (38)	72 (5)	9.1 (1.6-9.5)	4.64 (0.43)	58 (15)	150 (38)
COPEN <sup>11</sup>	1991-94	Pop. register	7698	3285 (43)	59 (13)	7.4 (2.3-8.9)	4.95 (0.53)	62 (19)	179 (51)
DRECE <sup>12</sup>	1992-94	Pop. register	2541	1236 (49)	41 (10)	15.4 (14.5-15.6)	4.64 (0.55)	54 (14)	153 (44)
DUBBO <sup>13</sup>	1988-89	Electoral rolls	2049	862 (42)	68 (7)	14.1 (1.8-14.9)	4.88 (0.48)	54 (15)	199 (47)
EAS <sup>14</sup>	1987-88 <sup>f</sup>	GP lists	1002	499 (50)	64 (6)	15.2 (2.8-15.8)	4.77 (0.44)	57 (16)	211 (47)
EPESEBOS <sup>15</sup>	1982-83 <sup>f</sup>	Pop. register	732	252 (34)	77 (4)	4.0 (1.1-4.5)	5.05 (0.51)	48 (15)	168 (41)
EPESEIOW <sup>15</sup>	1981-83 <sup>f</sup>	Pop. register	1182	352 (30)	78 (5)	4.8 (1.6-4.9)	5.02 (0.52)	51 (15)	167 (43)
EPESENCA <sup>15</sup>	1986-87 <sup>f</sup>	Pop. register	998	328 (33)	77 (5)	4.0 (1.3-4.6)	5.04 (0.51)	50 (17)	163 (41)
EPESENHA <sup>15</sup>	1982	Pop. register	572	217 (38)	78 (5)	4.3 (1.5-4.7)	4.97 (0.50)	50 (15)	168 (42)
ESTHER <sup>16</sup>	2000-02	GP lists	4663	2005 (43)	62 (7)	2.0 (1.9-2.7)	4.76 (0.57)	55 (18)	169 (50)
FINE-FIN <sup>d 17</sup>	1985 <sup>f</sup>	Survivors of existing cohort	271	271 (100)	76 (5)	7.0 (1.3-10.0)	4.75 (0.42)	46 (13)	174 (41)
FINE-IT <sup>d 17</sup>	1985 <sup>f</sup>	Survivors of existing cohort	458	458 (100)	72 (4)	9.8 (1.9-21.4)	4.79 (0.50)	51 (13)	175 (43)
FINRISK-92 <sup>18</sup>	1992 <sup>f</sup>	Pop. register	5260	2436 (46)	46 (10)	11.8 (7.1-11.9)	4.75 (0.55)	54 (14)	166 (45)
FINRISK-97 <sup>18</sup>	1997	Pop. register	6306	3126 (50)	51 (11)	6.8 (6.0-6.9)	4.75 (0.53)	54 (14)	165 (40)
FRAMOFF <sup>19</sup>	1991-95	Offspring & spouse to FHS	2699	1183 (44)	60 (9)	5.2 (3.1-7.0)	4.74 (0.53)	54 (17)	147 (36)
GOH <sup>20</sup>	1969-73 <sup>f</sup>	Pop. register	1277	626 (49)	56 (11)	24.8 (0.8-28.6)	4.73 (0.49)	46 (13)	173 (52)
GOTO43 <sup>21</sup>	1993-94	Pop. register	736	736 (100)	50 (0)	10.0 (8.0-10.7)	4.80 (0.49)	51 (13)	175 (41)
GOTOW <sup>22</sup>	1968-70	Pop. register	710	0 (0)	70 (6)	8.2 (2.8-8.7)	4.75 (0.43)	56 (27)	190 (43)
GRIPS <sup>23</sup>	1982	Occup.	5785	5785 (100)	48 (5)	9.8 (4.8-10.0)	4.95 (0.42)	48 (12)	169 (39)
HONOL <sup>24</sup>	1991-93	Service registration cards	2425	2425 (100)	78 (4)	6.3 (1.5-7.6)	4.86 (0.49)	52 (13)	140 (33)
HOORN <sup>25</sup>	1989-91	Pop. register	2198	971 (44)	61 (7)	8.8 (3.6-9.9)	4.82 (0.47)	52 (14)	206 (48)
IKNS <sup>26</sup>	1989-96	Pop. screening	4436	2081 (47)	57 (10)	11.5 (4.8-13.6)	4.75 (0.52)	57 (14)	140 (37)

**eTable 1.** Characteristics of the 68 prospective studies contributing data to the current analysis (continued)

Study abbreviation <sup>a</sup>	Year(s) of baseline survey	Population source	Participants, No.	Male, No. (%)	Age at Survey, mean (SD), y	Median follow-up (5th & 95th percentiles)	Log <sub>e</sub> triglyceride mean (SD)	HDL-C (mg/dL) mean (SD)	Non-HDL-C (mg/dL) mean (SD)
KIHD <sup>27</sup>	1984-89 <sup>f</sup>	Pop. register	2001	2001 (100)	52 (5)	19.3 (3.1-23.1)	4.58 (0.50)	51 (11)	176 (43)
MATISS-83 <sup>c 2</sup>	1983-97 <sup>f</sup>	Electoral rolls	2552	1194 (47)	52 (10)	18.6 (6.7-19.5)	4.84 (0.53)	51 (13)	174 (45)
MATISS-87 <sup>c 2</sup>	1983-97 <sup>f</sup>	Electoral rolls	2025	902 (45)	52 (9)	15.6 (6.8-16.2)	4.85 (0.48)	53 (13)	166 (40)
MATISS-93 <sup>c 2</sup>	1983-97 <sup>f</sup>	Electoral rolls	1177	576 (49)	49 (9)	8.3 (7.0-9.3)	4.93 (0.55)	50 (14)	168 (42)
MICOL <sup>e 28</sup>	1977-87	Electoral rolls, Occup.	18375	10351 (56)	51 (10)	5.9 (4.5-7.1)	4.73 (0.53)	53 (15)	167 (48)
MONFRI-94 <sup>c 2</sup>	1983-97 <sup>f</sup>	Electoral rolls	1279	623 (49)	49 (8)	8.5 (7.0-8.8)	4.64 (0.54)	58 (15)	165 (44)
MOSWEGOT <sup>29</sup>	1985-95	Pop. register	4030	1903 (47)	47 (11)	12.9 (7.7-18.6)	4.69 (0.49)	56 (16)	171 (47)
NFR <sup>e 28</sup>	1977-87	Electoral rolls, Occup.	2825	2825 (100)	55 (5)	10.2 (6.1-11.2)	4.83 (0.51)	47 (11)	167 (40)
NHANES III <sup>30</sup>	1988-94 <sup>f</sup>	Census list	5931	2732 (46)	54 (16)	8.8 (3.7-11.7)	4.84 (0.57)	51 (16)	161 (44)
NPHS II <sup>31</sup>	1989-94 <sup>f</sup>	GP lists	1882	1882 (100)	61 (4)	3.3 (1.2-5.6)	5.08 (0.51)	32 (10)	184 (38)
OSAKA <sup>32</sup>	1990-98	Occup. & Pop. register	11184	7502 (67)	53 (9)	5.1 (1.5-8.1)	4.77 (0.56)	58 (14)	146 (36)
PRIME <sup>33</sup>	1991-94	General Pop.	9521	9521 (100)	55 (3)	5.2 (5.0-7.3)	4.87 (0.50)	49 (13)	173 (39)
PROCAM <sup>34</sup>	1975-01	Occupational	20120	14575 (72)	44 (10)	10.0 (3.9-18.9)	4.74 (0.57)	49 (14)	169 (45)
QUEBEC <sup>35</sup>	1985-86	Pop. register	622	622 (100)	57 (7)	5.3 (3.1-5.6)	5.01 (0.45)	40 (10)	182 (41)
RANCHO <sup>36</sup>	1984-87	Household listings	1775	738 (42)	68 (11)	14.2 (2.0-18.1)	4.59 (0.55)	63 (19)	156 (41)
REYK <sup>37</sup>	1967-91	Pop. register	1427	351 (25)	62 (7)	16.6 (4.6-19.3)	4.60 (0.43)	57 (16)	198 (47)
SHHEC <sup>38</sup>	1984-95	GP lists	9203	4654 (51)	49 (7)	10.0 (6.9-10.0)	4.96 (0.55)	59 (16)	188 (47)
SHS <sup>39</sup>	1989-92 <sup>f</sup>	Tribal rolls	4065	1588 (39)	56 (8)	12.4 (2.1-14.3)	4.81 (0.57)	46 (14)	145 (40)
SPEED <sup>8</sup>	1979-82 <sup>f</sup>	GP lists	2007	2007 (100)	55 (4)	16.7 (3.5-18.2)	4.80 (0.49)	43 (14)	183 (47)
TARFS <sup>40</sup>	1990 <sup>f</sup>	Household lists	1794	864 (48)	50 (11)	5.2 (0.5-6.4)	4.86 (0.52)	42 (13)	148 (39)
TROMSØ <sup>41</sup>	1986-87 <sup>f</sup>	Household lists	16893	8541 (51)	40 (9)	13.9 (10.3-14.3)	4.66 (0.52)	59 (15)	167 (49)
ULSAM <sup>42</sup>	1970-74	Pop. register	1808	1808 (100)	54 (9)	21.7 (4.2-35.6)	4.96 (0.46)	52 (15)	209 (54)
WHITE II <sup>43</sup>	1985-88 <sup>f</sup>	Civil servant	8114	5563 (69)	49 (6)	7.8 (4.1-12.2)	4.76 (0.56)	56 (16)	192 (47)
WHS <sup>44</sup>	1993-04	Health professionals	22827	0 (0)	55 (7)	10.2 (8.4-10.8)	4.84 (0.55)	53 (15)	160 (41)
ZARAGOZA <sup>45</sup>	1994	GP lists	1995	859 (43)	60 (11)	5.1 (3.4-5.1)	4.74 (0.46)	55 (14)	175 (38)
ZUTE <sup>46</sup>	1990	Pop. register	350	350 (100)	75 (4)	8.9 (1.1-10.1)	4.71 (0.47)	45 (11)	190 (43)
<i>Subtotal</i>			<i>255989</i>	<i>137004 (54)</i>	<i>58 (9)</i>	<i>9.6 (2.6-20.4)</i>	<i>4.81 (0.53)</i>	<i>52 (15)</i>	<i>172 (44)</i>
<b>Clinical Trials</b>									
AFTCAPS <sup>47</sup>	1990-93 <sup>f</sup>	Pop. screening	5600	4765 (85)	58 (7)	5.1 (4.5-6.7)	5.05 (0.38)	37 (6)	184 (21)
ALLHAT <sup>48</sup>	1994-98 <sup>f</sup>	Pop. register	15297	7716 (50)	66 (7)	4.3 (0.9-6.7)	4.96 (0.55)	47 (14)	171 (40)
LEADER <sup>49</sup>	1993-98 <sup>f</sup>	GP lists	921	921 (100)	68 (9)	4.2 (0.8-6.2)	5.23 (0.48)	47 (15)	171 (38)
MRFIT <sup>50</sup>	1973-76 <sup>f</sup>	Pop. screening	12825	12825 (100)	47 (6)	6.9 (4.4-7.8)	5.10 (0.56)	42 (12)	198 (38)
PROSPER <sup>51</sup>	1998 <sup>f</sup>	Primary Care screening	3252	1350 (42)	75 (3)	3.2 (1.1-3.8)	4.81 (0.42)	51 (14)	169 (35)
WOSCOPS <sup>52</sup>	1989-91	Heart screening clinic	6213	6213 (100)	55 (6)	4.8 (2.9-6.0)	5.00 (0.40)	44 (9)	227 (23)
<i>Subtotal</i>			<i>44108</i>	<i>33790 (77)</i>	<i>61 (6)</i>	<i>5.0 (1.6-7.5)</i>	<i>5.0 (0.5)</i>	<i>45 (12)</i>	<i>187 (35)</i>

**eTable 1.** Characteristics of the 68 prospective studies contributing data to the current analysis (continued)

Study abbreviation <sup>a</sup>	Year(s) of baseline survey	Population source	Participants, No.	Male, No. (%)	Age at Survey, mean (SD), y	Median follow-up (5th & 95th percentiles)	Log <sub>e</sub> triglyceride mean (SD)	HDL-C (mg/dL) mean (SD)	Non-HDL-C (mg/dL) mean (SD)
<b>Nested Case-Control Studies</b>									
EPICNOR <sup>53</sup>	1993-98 <sup>f</sup>	GP lists	1233	844 (68)	66 (8)	7.2 (2.1-9.3)	4.99 (0.46)	51 (15)	192 (45)
FIA <sup>54</sup>	1985-99 <sup>f</sup>	Pop. register	325	244 (75)	54 (8)	5.6 (1.5-10.7)	4.87 (0.50)	49 (14)	206 (47)
GLOSTRUP <sup>55</sup>	1976-84	Pop. register	199	164 (82)	51 (9)	4.5 (0.5-10.5)	4.86 (0.52)	48 (15)	208 (58)
NHS <sup>56</sup>	1990 <sup>f</sup>	Occup.	576	0 (0)	60 (7)	8.0 (1.3-8.8)	4.77 (0.56)	57 (17)	172 (42)
<i>Subtotal</i>			<i>2333</i>	<i>1252 (54)</i>	<i>58 (8)</i>	<i>7.1 (1.5-9.3)</i>	<i>4.87 (0.50)</i>	<i>51 (16)</i>	<i>195 (46)</i>
<b>Total</b>			<b>302430</b>	<b>172046 (57)</b>	<b>59 (8)</b>	<b>8.1 (2.3-19.0)</b>	<b>4.83 (0.52)</b>	<b>52 (15)</b>	<b>175 (43)</b>

Median (interquartile range) values were: 120 (85-175) mg/dL for triglyceride; 50 (41-61) mg/dL for HDL-C; 169 (140-201) mg/dL for non-HDL-C.

Abbreviations: Pop = Population; Occup.= Occupation based cohort; GP = General Practitioner.

<sup>a</sup> eAppendix 2 lists study acronyms.

<sup>b</sup> CHS was analysed as 2 different studies (ie, CHS-1 and CHS-2).

<sup>c</sup> Progetto CUORE was analysed as 5 different studies (ie, ATENA, MATISS-83, MATISS-87, MATISS-93 and MONFRI-94).

<sup>d</sup> FINE was analysed as 2 different studies (ie, FINE-FIN and FINE-IT).

<sup>e</sup> RIFLE was analysed as 2 different studies (ie, MICOL and NFR).

<sup>f</sup> These studies have contributed data on baseline and re-survey measurements.

**eTable 2.** Blood handling, storage and assay characteristics at first measurement of triglyceride and HDL-cholesterol in studies contributing to the current analysis.

Study abbreviation <sup>a</sup>	Fasting status at blood sampling & duration	Sample source	HDL-C				Triglyceride <sup>b</sup>		
			Time between collection and measurement	Sample state before analysis, storage temperature (°C) if frozen	Assay Method	Assay Source (Standard)	Time between collection and measurement	Sample state before analysis, storage temperature (°C) if frozen	Assay Source (Standard)
AFTCAPS	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	NS (WHO LRC)	<1 week	Fresh	NS (WHO LRC)
ALLHAT	Fasted >8 hrs	Serum	<1 week	Fresh	NS	NS (NS)	<1 week	Fresh	NS (NS)
ARIC	Fasted >8 hrs	Plasma	1 week - 1 yr	-70	P-I	Boehringer (CDC)	1 week - 1 yr	-70	Boehringer (CDC)
ATENA	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	Boehringer (WHO LRC)	<1 week	Fresh	Boehringer (CDC)
BHS	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	Abbott (Boehringer)	1 week - 1 yr	-20	Calbiochem (Commercial)
BRHS	Non-fasted	Serum	<1 week	Fresh	P-I	Technicon (Manuf.)	1 week - 1 yr	-20	Abbott (Manuf.)
BRUN	Fasted >8 hrs	Plasma	1 week - 1 yr	-70	P-I	Merck (Manuf.)	1 week - 1 yr	-70	Merck (Manuf.)
BUPA	Fasted NS	Serum	<1 week	NS	NS	NS (NS)	> 10 yrs	-40	Sigma (CAPRMSL)
BWHHS	Fasted >8 hrs	Serum	<1 week	-20	P-I	Roche (Manuf.)	<1 week	-20	Roche (Manuf.)
CaPS	Fasted >8 hrs	Plasma	<1 week	Fresh	P-I	Boehringer (Manuf.)	<1 week	Fresh	Boehringer (Manuf.)
CASTEL	Fasted >8 hrs	Serum	1 week	-20	P-I	Boehringer (NS)	1 week - 1 yr	-20	In-house (Commercial)
CHS-1	Fasted >8 hrs	Plasma	<1 week	-70	P-I	Olympus (CDC)	<1 week	-70	Olympus (NS)
CHS-2	Fasted >8 hrs	Plasma	<1 week	-70	P-I	Olympus (CDC)	<1 week	-70	Olympus (NS)
COPEN	Non-fasted	Serum	<1 week	Fresh	P-I	Boehringer (Manuf.)	1 week - 2 yr	-80	Boehringer (Manuf.)
DRECE	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	Boehringer (Manuf.)	<1 week	Fresh	Boehringer (Manuf.)
DUBBO	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	Boehringer (Manuf.)	<1 week	Fresh	Boehringer (Manuf.)
EAS	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	Roche (Manuf.)	<1 week	Fresh	Roche (Wellcome Scheme)
EPESEBOS	Non-fasted	Serum	<1 week	Fresh	P-I	Hitachi (Manuf.)	<1 week	Fresh	Technicon (Manuf.)
EPESEIOW	Non-fasted	Serum	<1 week	Fresh	P-I	Hitachi (Manuf.)	<1 week	Fresh	Technicon (Manuf.)
EPESENCA	Non-fasted	Serum	<1 week	Fresh	P-I	Hitachi (Manuf.)	<1 week	Fresh	Technicon (Manuf.)
EPESENHA	Non-fasted	Serum	<1 week	Fresh	P-I	Hitachi (Manuf.)	<1 week	Fresh	Technicon (Manuf.)
EPICNOR	Non-fasted	Serum	<1 week	Fresh	NS	Bayer (NS)	<1 week	Fresh	Bayer (NS)
ESTHER	Fasted NS	Serum	1 week - 1 yr	-80	P-I	Beckman (Manuf.)	1 week - 1 yr	-80	Beckman (Manuf.)
FIA	Fasted 4 hrs	Plasma	<1 week	-80	NS	NS (NS)	<1 week	Fresh	Boehringer (NS)
FINE-FIN	Non-fasted	Serum	1 week - 1 yr	-20	P-I	Boehringer (WHO LRC)	1 week - 1 yr	-20	Boehringer (WHO LRC)
FINE-IT	Non-fasted	Serum	1 week - 1 yr	-20	P-I	Boehringer (WHO LRC)	1 week - 1 yr	-20	Boehringer (WHO LRC)

**eTable 2.** Blood handling, storage and assay characteristics at first measurement of triglyceride and HDL-cholesterol in studies contributing to the current analysis (continued)

Study abbreviation <sup>a</sup>	Fasting status at blood sampling & duration	Sample source	HDL-C				Triglyceride <sup>b</sup>		
			Time between collection and measurement	Sample state before analysis, storage temperature (°C) if frozen	Assay Method	Assay Source (Standard)	Time between collection and measurement	Sample state before analysis, storage temperature (°C) if frozen	Assay Source (Standard)
FINRISK92	Fasted 4-8 hrs	Serum	<1 week	Fresh	P-I	Boehringer (Manuf.)	<1 week	Fresh	Boehringer (Manuf.)
FINRISK97	Fasted 4-8 hrs	Serum	<1 week	Fresh	P-I	Boehringer (Manuf.)	<1 week	Fresh	Boehringer (Manuf.)
FRAMOFF	Fasted >8 hrs	Plasma	<1 week	Fresh	P-I	CDC (NS)	<1 week	Fresh	Technicon (CDC)
GLOSTRUP	Fasted >8 hrs	Serum	<1 week	Fresh	P-NS	Boehringer (Manuf.)	<1 week	Fresh	Boehringer (Manuf.)
GOH	Fasted >8 hrs	Plasma	<1 week	Fresh	P-II	Boehringer (CDC)	<1 week	Fresh	Boehringer (CDC)
GOTO43	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	Roche (Manuf.)	<1 week	Fresh	Boehringer (Manuf.)
GOTOW	Fasted >8 hrs	Serum	<1 week	Fresh	NS	NS (NS)	<1 week	Fresh	Boehringer (Manuf.)
GRIPS	Fasted 4-8 hrs	Serum	<1 week	Fresh	P-I	Immuno (Manuf.)	1-5 yrs	-90	Boehringer (Manuf.)
HONOL	Fasted >8 hrs	Plasma	1 week - 1 yr	-70	P-I	Olympus (CDC)	1 week - 1 yr	-70	Olympus (CDC)
HOORN	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	Boehringer (Manuf.)	<1 week	Fresh	Boehringer (Manuf.)
IKNS	Non-fasted	Serum	1 week - 1 yr	Fresh	P-I	Technicon (CDC)	1 week - 1 yr	-70	Technicon (CDC)
KIHD	Fasted >8 hrs	Serum	<1 week	Fresh	P-II	Boehringer (Orion)	1 week - 1 yr	-70	Boehringer (CAPRMSL)
LEADER	Non-fasted	Serum	<1 week	Fresh	P-I	NS (NS)	<1 week	Fresh	Wako (Manuf.)
MATISS-83	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	Boehringer (WHO LRC)	<1 week	Fresh	Boehringer (CDC)
MATISS-87	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	Boehringer (WHO LRC)	<1 week	Fresh	Boehringer (CDC)
MATISS-93	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	Boehringer (WHO LRC)	<1 week	Fresh	Boehringer (CDC)
MICOL	Fasted >8 hrs	Serum	NS	NS	P-I	NS (WHO LRC)	NS	NS	Multiple (WHO LRC)
MONFRI-94	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	Boehringer (WHO LRC)	<1 week	Fresh	Boehringer (CDC)
MOSWEGOT	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	Roche (Manuf.)	<1 week	Fresh	NS (NS)
MRFIT	Fasted >8 hrs	Plasma <sup>c</sup>	NS	NS	P-I & II	Technicon (CDC)	NS	NS	Technicon (CDC)
NFR	Fasted >8 hrs	Serum	NS	NS	P-I	NS (WHO LRC)	NS	NS	Multiple (WHO LRC)
NHANES III	Fasted >6 hrs	Serum	1 week - 1 yr	-20	P-I	CDC (NS)	1 week - 1 yr	-20	Boehringer (CDC)
NHS	Fasted Variable	Plasma	10 yrs	-130	Homo	Roche (Manuf.)	10 yrs	-130	Roche (Manuf.)
NPHS II	Non-fasted	Serum	1 week - 1 yr	-40	P-I	Sigma Poole (NS)	1 week - 1 yr	-40	Wako (Precinorm & Precilip)
OSAKA	Non-fasted	Serum	<1 week	-70	P-NS	CDC (NS)	1 week - 1 yr	-70	Daiichi (NS)
PRIME	Fasted >8 hrs	Plasma	<1 week	Fresh	P-I	Boehringer (NS)	<1 week	Fresh	Boehringer (Manuf.)
PROCAM	Fasted >8 hrs	Serum	<1 week	Fresh	P-?	Roche (NS)	<1 week	Fresh	Boehringer (Manuf.)
PROSPER	Fasted >8 hrs	Plasma	<1 week	Fresh	P-I	Roche (cFas calibrator)	<1 week	Fresh	Roche (cFas calibrator)

**eTable 2.** Blood handling, storage and assay characteristics at first measurement of triglyceride and HDL-cholesterol in studies contributing to the current analysis (continued)

Study abbreviation <sup>a</sup>	Fasting status at blood sampling & duration	Sample source	HDL-C				Triglyceride <sup>b</sup>		
			Time between collection and measurement	Sample state before analysis, storage temperature (°C) if frozen	Assay Method	Assay Source (Standard)	Time between collection and measurement	Sample state before analysis, storage temperature (°C) if frozen	Assay Source (Standard)
QUEBEC	Fasted >8 hrs	Plasma	<1 week	Fresh	P-I	Technicon (In-house)	<1 week	Fresh	Technicon (In-house)
RANCHO	Fasted >8 hrs	Plasma	<1 week	Fresh	P-II	LRC (NS)	<1 week	Fresh	Abbot (CDC)
REYK	Fasted >8 hrs	Serum <sup>d</sup>	<1 week	Fresh	P-I	NS (NS)	<1 week	Fresh	Technicon (NS)
SHHEC	Non-fasted	Serum	<1 week	-20	P-NS	COBAS Bio (NS)	<1 week	Fresh	COBAS Bio (WHO LRC)
SHS	Fasted >8 hrs	Plasma	<1 week	-70	P-I	Boehringer (CDC)	NS	-70	Boehringer (CDC)
SPEED	Fasted >8 hrs	Plasma	<1 week	Fresh	P-I	NS (NS)	<1 week	Fresh	Boehringer (NS)
TARFS	Fasted >8 hrs	Plasma	<1 week	Fresh	P-I	Roche (Manuf.)	<1 week	Fresh	Roche (Manuf.)
TROMSØ	Non-fasted	Serum	<1 week	Fresh	P-I	Boehringer (NS)	<1 week	Fresh	Boehringer (NS)
ULSAM	Fasted >8 hrs	Serum	>10 yrs	-150	P-I	Technicon (Manuf.)	> 10 yrs	-150	Technicon (Manuf.)
WHITEII	Fasted NS	Serum	<1 week	Fresh	P-I	Boehringer (NS)	<1 week	Fresh	Boehringer (Manuf.)
WHS	Non-fasted	Plasma	<1 week	-150	Homo	Roche (NS)	NS	NS	NS (NS)
WOSCOPS	Fasted >8 hrs	Plasma	<1 week	Fresh	P-II	LRC (NS)	<1 week	Fresh	Boehringer (LRC)
ZARAGOZA	Fasted >8 hrs	Serum	<1 week	Fresh	P-I	NS (NS)	<1 week	Fresh	NS
ZUTE	Fasted >8 hrs	Serum	<1 month	-20	P-I	Boehringer (NS)	1-5 yrs	-20	Boehringer (CDC)

Abbreviations: NS = Not Stated; Homo=Homogenous; Manuf.= Manufacturer; P = precipitation; P-I : HDL-C measured following precipitation of apo-B containing particles; P-II : As for P-I, but precipitation is preceded by preparative ultracentrifugation to remove triglycerides containing particles i.e. VLDL & Chylomicrons; CDC = Centers for Disease Control and Prevention; LRC = Lipid Research Clinic; CAPRMSL = College of American Pathologists' Reference Material for Serum Lipids.

<sup>a</sup> eAppendix 2 lists study acronyms.

<sup>b</sup> All the studies used enzymatic assay methods to measure triglyceride concentration except for OSAKA, which used a non-enzymatic method.

<sup>c</sup> serum for triglyceride.

<sup>d</sup> plasma for HDL-C.



**eTable 3.** Cross-sectional associations of triglyceride, HDL-C, and non-HDL-C with various baseline characteristics

	Summary of available data			Correlates of log <sub>e</sub> triglyceride		Correlates of HDL-C		Correlates of non-HDL-C	
	No of studies	No of participants	Mean (SD) or %	Pearson Correlation r (95% CI) <sup>a</sup>	Percentage difference (95%CI) in triglyceride levels per 1 SD increase or compared to reference category <sup>b</sup>	Pearson Correlation r (95% CI) <sup>a</sup>	Difference (95%CI) in HDL-C levels per 1 SD increase or compared to reference category <sup>b</sup> mg/dL	Pearson Correlation r (95% CI) <sup>a</sup>	Difference (95%CI) in non-HDL-C levels per 1 SD increase or compared to reference category <sup>s</sup> mg/dL
<b>Age at survey (yrs)</b>	68	302430	59 (8)	0.04 (0.02, 0.06)	2 (0, 3)	0.04 (0.02, 0.05)	0.52 (0.32, 0.72)	0.06 (0.02, 0.10)	1.89 (0.20, 3.57)
<b>Sex</b>	68	302430							
Male	63	172046	57%	-	Ref	-	Ref	-	Ref
Female	49	130384	43%	-	-12 (-16, -8)	-	8.97 (8.01, 9.94)	-	0.69 (-2.59, 3.96)
<b>Race</b>	51	206798							
White	47	171564	83%	-	Ref	-	Ref	-	Ref
Asian	7	18665	9%	-	8 (-2, 19)	-	-1.29 (-4.91, 2.33)	-	0.36 (-6.28, 7.00)
Black	13	14050	7%	-	-23 (-28, -18)	-	4.34 (2.58, 6.09)	-	-5.93 (-8.91, -2.96)
Other	14	2519	1%	-	1 (-3, 6)	-	-0.26 (-1.38, 0.87)	-	-2.18 (-5.64, 1.28)
<b>Smoking status</b>	68	302430							
Other	68	208793	69%	-	Ref	-	Ref	-	Ref
Current	67	93637	31%	-	5 (4, 7)	-	-2.15 (-2.63, -1.67)	-	2.32 (1.11, 3.53)
<b>Alcohol status</b>	57	255009							
Other	57	94882	37%	-	Ref	-	Ref	-	Ref
Current	50	160127	63%	-	-2 (-4, 0)	-	4.38 (3.87, 4.89)	-	-2.12 (-3.43, -0.81)
<b>History of diabetes</b>	68	302430							
Other	68	281405	93%	-	Ref	-	Ref	-	Ref
Definite diabetic	66	21025	7%	-	20 (18, 23)	-	-4.27 (-5.13, -3.40)	-	0.25 (-1.51, 2.02)
<b>Lipid markers</b>									
Total cholesterol, mg/dL	68	302430	226 (42)	0.36 (0.34, 0.38)	18 (17, 20)	0.12 (0.11, 0.14)	1.57 (1.31, 1.83)	0.94 (0.94, 0.95)	40.56 (40.30, 40.83)
Non-HDL-C, mg/dL	68	302430	175 (43)	0.49 (0.47, 0.50)	25 (23, 26)	-0.22 (-0.24, -0.20)	-3.39 (-3.70, -3.07)	-	-
HDL-C, mg/dL	68	302430	52 (15)	-0.40 (-0.43, -0.37)	-22 (-24, -20)	-	-	-0.22 (-0.24, -0.20)	-10.18 (-10.80, -9.56)
Log <sub>e</sub> triglyceride, mg/dL	68	302430	4.83 (0.52)	-	-	-0.40 (-0.43, -0.37)	-5.60 (-6.74, -4.46)	0.49 (0.47, 0.50)	21.02 (19.67, 22.36)
LDL-C, mg/dL	8	44243	147 (33)	0.10 (-0.04, 0.23)	5 (-1, 11)	-0.05 (-0.11, 0.00)	-0.91 (-1.77, -0.04)	0.86 (0.80, 0.90)	31.58 (27.29, 35.87)
Apolipoprotein B, mg/dL	24	93524	112 (29)	0.49 (0.45, 0.53)	24 (22, 26)	-0.22 (-0.26, -0.19)	10.78 (9.55, 12.01)	0.86 (0.83, 0.88)	37.53 (33.93, 41.13)
Apolipoprotein AI, mg/dL	24	96771	149 (29)	-0.18 (-0.21, -0.14)	-9 (-8, -11)	0.75 (0.72, 0.77)	-3.39 (-4.06, -2.72)	-0.04 (-0.07, -0.01)	-2.46 (-3.88, -1.03)

**eTable 3.** Cross-sectional associations of triglyceride, HDL-C, and non-HDL-C with various baseline characteristics (continued)

<b>Non-lipid markers</b>									
Systolic blood pressure, mmHg	68	302430	137 (18)	0.15 (0.13, 0.17)	6 (6, 7)	-0.01 (-0.03, 0.01)	-0.19 (-0.39, 0.01)	0.11 (0.09, 0.13)	3.51 (3.00, 4.03)
Diastolic blood pressure, mmHg	67	300906	82 (11)	0.15 (0.13, 0.17)	6 (6, 7)	-0.05 (-0.06, -0.03)	-0.37 (-0.55, -0.20)	0.12 (0.09, 0.14)	4.08 (3.53, 4.64)
Body mass index <sup>c</sup>	68	302430	26 (4)	0.26 (0.23, 0.28)	13 (12, 15)	-0.21 (-0.23, -0.19)	-3.13 (-3.59, -2.67)	0.14 (0.12, 0.17)	6.07 (5.06, 7.07)
<b>Geographical location</b>	68	302430							
Western Europe	44	180520	60%	-	Ref	-	Ref	-	Ref
North America	18	96987	32%	-	15 (8, 23)	-	-11.52 (-13.51, -9.54)	-	-30.58 (-36.57, -24.59)
Other	6	24923	8%	-	-9 (-17, -2)	-	-5.97 (-8.07, -3.87)	-	-37.63 (-43.96, -31.30)
<b>Fasting status</b>	68	302430							
Non-fasted/random/<8hrs	20	103354	34%	-	Ref	-	Ref	-	Ref
>=8hrs/fasted NS	48	199076	66%	-	37 (32, 42)	-	-14.96 (-16.30, -13.62)	-	20.27 (16.23, 24.32)
<b>Sample type</b>	68	302159							
Serum	48	221092	73%	-	Ref	-	Ref	-	Ref
Plasma	19	81067	34%	-	-41 (-46, -36)	-	15.54 (14.20, 16.89)	-	-42.62 (-46.68, -38.56)
<b>Study design</b>	68	302430							
Cohort	58	255989	85%	-	Ref	-	Ref	-	Ref
Case-control	4	2333	1%	-	27 (18, 36)	-	2.05 (-0.52, 4.63)	-	55.37 (47.60, 63.13)
Clinical trial	6	44108	14%	-	42 (36, 49)	-	-9.47 (-11.19, -7.75)	-	24.79 (19.61, 29.96)

SI conversions: To convert total cholesterol, HDL-C, non-HDL-C and LDL-C to mmol/L, multiply by 0.0259; triglyceride to mmol/L, multiply by 0.0113; apolipoproteins to g/L, multiply by 0.01.

Abbreviations: CI, confidence interval; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol.

<sup>a</sup> Pearson correlation coefficient between HDL-C, log<sub>e</sub> triglycerides or non-HDL-C and the row variable pooled across studies using random effects meta-analyses.

<sup>b</sup> Adjusted for sex and age, allowing for random effects across studies.

<sup>c</sup> Body mass index is calculated as weight in kilograms divided by height in meters squared.

**eTable 4.** Summary of vascular outcomes recorded in the 68 prospective studies contributing data to the current analysis

Study abbreviation <sup>a</sup>	Non-fatal MI & coronary death	Non-fatal MI	Ischaemic stroke	Haemorrhagic stroke	Unclassified stroke	Other CV deaths
<b>Cohort studies</b>						
ARIC	871	673	452	53	16	198
ATENA <sup>c</sup>	17	16	1*	2*	0	7*
BHS	248	0	10	8*	80	85
BRHS	838	476	4*	11	298	85
BRUN	54	23	24	15	0	7*
BUPA	157	0	3*	6*	15	34
BWHHS	55	31	19	4*	14	14
CaPS	236	130	3*	2*	8*	19
CASTEL	91	0	0	0	100	298
CHS-1 <sup>b</sup>	593	380	367	62	37	55
CHS-2 <sup>b</sup>	52	31	35	5*	4*	6*
COPEN	278	245	179	36	85	82
DRECE	13	0	0	1*	3*	7*
DUBBO	281	220	75	19	85	66
EAS	77	38	0	3*	59	18
EPESEBOS	35	28	17	6*	1*	23
EPESEIOW	53	32	21	6*	25	35
EPESENCA	47	28	30	5*	15	21
EPESENHA	20	16	10	2*	9*	42
ESTHER	27	21	2*	0	51	2*
FINE-FIN <sup>d</sup>	70	33	8*	1*	16	12
FINE-IT <sup>d</sup>	67	18	4*	5*	83	39
FINRISK-92	150	119	83	36	0	22
FINRISK-97	107	74	73	19	0	20
FRAMOFF	52	48	23	1*	0	0
GOH	32	0	0	0	9*	19
GOTO43	24	23	9*	1*	1*	2*
GOTOW	29	15	0	0	58	7*
GRIPS	299	299	0	0	103	47
HONOL	149	108	12	39	67	23
HOORN	73	60	3*	4*	46	44
IKNS	16	13	82	28	1*	2*
KIHD	383	372	103	34	3*	26
MATISS-83 <sup>c</sup>	83	46	14	7*	48	162
MATISS-87 <sup>c</sup>	44	20	6*	4*	30	73
MATISS-93 <sup>c</sup>	14	11	0	0	3*	12
MICOL <sup>e</sup>	96	0	7*	2*	20	10

**eTable 4.** Summary of vascular outcomes recorded in the 68 prospective studies contributing data to the current analysis (continued)

MONFRI-94 <sup>c</sup>	11	11	3*	7*	2*	13
MOSWEGOT	139	101	63	17	15	20
NFR <sup>e</sup>	86	0	2*	7*	10	7*
NHANES III	216	0	0	0	74	96
NPHS II	73	66	16	4*	4*	5*
OSAKA	30	26	42	14	3*	11
PRIME	145	128	33	6*	3*	20
PROCAM	486	367	77	22	7*	149
QUEBEC	20	19	0	0	2*	5*
RANCHO	221	219	0	1*	175	100
REYK	159	97	12	8*	20	16
SHHEC	291	218	32	10	52	19
SHS	439	297	8*	10	185	113
SPEED	237	92	64	2*	5*	22
TARFS	59	23	1*	0	16	17
TROMSØ	470	402	136	29	19	42
ULSAM	435	327	151	39	27	73
WHITE II	197	167	1*	1*	3*	14
WHS	226	219	212	20	2*	74
ZARAGOZA	43	30	6*	0	27	0
ZUTE	52	35	1*	1*	29	24
<i>Subtotal</i>	<b>9766</b>	<b>6491</b>	<b>2467</b>	<b>513</b>	<b>2000</b>	<b>2407</b>
<b>Clinical Trials</b>						
AFTCAPS	107	104	16	0	1*	16
ALLHAT	613	611	0	0	275	0
LEADER	99	36	51	3*	12	16
MRFIT	765	581	5*	4*	61	49
PROSPER	266	201	0	0	115	14
WOSCOPS	371	300	0	0	73	9*
<i>Subtotal</i>	<b>2221</b>	<b>1833</b>	<b>67</b>	<b>0</b>	<b>536</b>	<b>95</b>
<b>Nested Case-Control Studies</b>						
EPICNOR	434	233	0	0	0	0
FIA	95	71	0	0	0	0
GLOSTRUP	68	52	0	0	0	0
NHS	201	177	0	0	0	0
<i>Subtotal</i>	<b>798</b>	<b>533</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
<b>Total</b>	<b>12785</b>	<b>8857</b>	<b>2534</b>	<b>513</b>	<b>2536</b>	<b>2502</b>

\* studies with fewer than 10 events do not contribute to the subtotals and overall total for each endpoint

<sup>a</sup>Appendix 2 lists study acronyms.

<sup>b</sup>CHS was analysed as 2 different studies (ie, CHS-1 and CHS-2).

<sup>c</sup>Progetto CUORE was analysed as 5 different studies (ie, ATENA, MATISS-83, MATISS-87, MATISS-93 and MONFRI-94).

<sup>d</sup>FINE was analysed as 2 different studies (ie, FINE-FIN and FINE-IT).

<sup>e</sup>RIFLE was analysed as 2 different studies (ie, MICOL and NFR).

**eTable 5.** Associations of usual levels of triglyceride, HDL-C and non-HDL-C with coronary heart disease and ischaemic stroke risk, adjusted for usual levels of potential confounding factors.

	Triglyceride Per 68% (1-SD) higher			HDL-C Per 15 mg/dL (1-SD) higher			Non-HDL-C Per 43 mg/dL (1-SD) higher		
	HR (95% CI)	Wald $\chi^2_1$	I <sup>2</sup> (95% CI)	HR (95% CI)	Wald $\chi^2_1$	I <sup>2</sup> (95% CI)	HR (95% CI)	Wald $\chi^2_1$	I <sup>2</sup> (95% CI)
<b>Coronary heart disease</b> (68 studies, 302 430 individuals, 12785 cases)									
Adjusted for age and sex	1.51 (1.44, 1.59)	258	66 (56, 73)	0.67 (0.63, 0.71)	174	70 (62, 77)	1.63 (1.54, 1.74)	244	79 (74, 83)
Plus systolic blood pressure	1.43 (1.37, 1.50)	253	53 (39, 65)	0.68 (0.64, 0.72)	177	66 (57, 74)	1.57 (1.48, 1.67)	224	77 (71, 81)
Plus smoking status	1.41 (1.35, 1.47)	255	47 (30, 60)	0.69 (0.66, 0.73)	170	64 (53, 72)	1.56 (1.47, 1.65)	229	75 (68, 80)
Plus body mass index	1.40 (1.34, 1.46)	234	45 (27, 59)	0.70 (0.66, 0.74)	162	61 (50, 70)	1.55 (1.47, 1.65)	221	75 (68, 80)
Plus history of diabetes	1.37 (1.31, 1.42)	214	42 (22, 57)	0.71 (0.68, 0.75)	149	60 (48, 69)	1.56 (1.47, 1.66)	229	74 (68, 80)
Plus non-HDL-C	1.13 (1.07, 1.19)	23	39 (18, 54)	0.78 (0.74, 0.82)	96	48 (31, 61)	-	-	-
Plus HDL-C	0.99 (0.94, 1.05)	0	35 (12, 52)	-	-	-	1.48 (1.40, 1.57)	171	73 (66, 79)
Plus log <sub>e</sub> triglyceride	-	-	-	0.78 (0.74, 0.82)	84	40 (20, 55)	1.50 (1.39, 1.61)	122	73 (66, 79)
<b>Ischaemic stroke</b> (32 studies, 173 312 individuals, 2534 cases)									
Adjusted for age and sex	1.26 (1.18, 1.34)	47	10 (0, 40)	0.84 (0.77, 0.92)	14	41 (9, 61)	1.21 (1.14, 1.28)	37	3 (0, 41)
Plus systolic blood pressure	1.17 (1.11, 1.24)	29	1 (0, 40)	0.86 (0.79, 0.93)	13	38 (5, 59)	1.15 (1.08, 1.22)	21	0 (0, 40)
Plus smoking status	1.17 (1.10, 1.24)	27	0 (0, 40)	0.87 (0.80, 0.95)	9	39 (7, 60)	1.14 (1.08, 1.21)	20	0 (0, 40)
Plus body mass index	1.17 (1.08, 1.28)	13	27 (0, 53)	0.87 (0.80, 0.95)	10	36 (2, 58)	1.14 (1.08, 1.21)	20	0 (0, 40)
Plus history of diabetes	1.12 (1.05, 1.19)	14	0 (0, 40)	0.89 (0.82, 0.97)	7	33 (0, 57)	1.14 (1.08, 1.21)	19	0 (0, 40)
Plus non-HDL-C	1.08 (0.99, 1.17)	3	10 (0, 41)	0.91 (0.84, 1.00)	4	31 (0, 56)	-	-	-
Plus HDL-C	1.02 (0.94, 1.11)	0	0 (0, 40)	-	-	-	1.12 (1.05, 1.19)	13	0 (0, 40)
Plus log <sub>e</sub> triglyceride	-	-	-	0.93 (0.84, 1.02)	2	27 (0, 53)	1.12 (1.04, 1.20)	9	0 (0, 40)

Regression analyses were stratified, where appropriate, by sex and trial arm.

Studies with fewer than 10 cases were excluded from analysis of each outcome.

There was evidence of considerable heterogeneity among the studies of non-HDL-C, however sensitivity analyses that excluded the 10 most discrepant studies (FINE-FIN, CHS-2, EPESENHA, GOH, AFTCAPS, PROSPER, CHS-1, IKNS, GRIPS, MONFRI-94) yielded broadly similar results (HRs 1.50 [95% CI 1.46, 1.55]), with the I<sup>2</sup> reduced to 49% (95% CI 30%-62%).

**eTable 6.** Associations of usual levels of triglyceride, HDL-C and non-HDL-C with coronary heart disease and ischaemic stroke risk, adjusted for usual levels of classical risk factors and inflammatory markers.

	Adjustment for conventional risk factors plus fibrinogen			Adjustment for conventional risk factors plus C-reactive protein		
	HR (95% CI)			HR (95% CI)		
	Triglyceride Per 68% (1-SD) higher	HDL-C Per 15 mg/dL (1-SD) higher	Non-HDL-C Per 43 mg/dL (1-SD) higher	Triglyceride Per 68% (1-SD) higher	HDL-C Per 15 mg/dL (1-SD) higher	Non-HDL-C Per 43 mg/dL (1-SD) higher
<b>Coronary heart disease</b>	<i>33 studies, 144 118 individuals, 6067 cases</i>			<i>30 studies, 80719 individuals, 4497 cases</i>		
Adjusted for age and sex	1.52 (1.41, 1.63)	0.66 (0.61, 0.71)	1.64 (1.49, 1.81)	1.49 (1.35, 1.63)	0.68 (0.62, 0.76)	1.52 (1.38, 1.68)
Plus systolic blood pressure	1.44 (1.35, 1.54)	0.67 (0.62, 0.72)	1.58 (1.44, 1.74)	1.41 (1.30, 1.54)	0.70 (0.63, 0.76)	1.47 (1.34, 1.62)
Plus smoking status	1.41 (1.33, 1.50)	0.68 (0.63, 0.73)	1.56 (1.43, 1.71)	1.38 (1.28, 1.49)	0.71 (0.64, 0.78)	1.46 (1.33, 1.60)
Plus body mass index	1.41 (1.32, 1.50)	0.68 (0.64, 0.73)	1.56 (1.42, 1.70)	1.37 (1.27, 1.49)	0.71 (0.65, 0.78)	1.46 (1.33, 1.60)
Plus history of diabetes	1.37 (1.29, 1.45)	0.70 (0.66, 0.75)	1.56 (1.43, 1.71)	1.34 (1.24, 1.45)	0.72 (0.66, 0.80)	1.47 (1.34, 1.62)
Plus other lipid markers†	0.98 (0.90, 1.06)	0.76 (0.71, 0.82)	1.50 (1.34, 1.68)	1.04 (0.97, 1.12)	0.80 (0.73, 0.88)	1.36 (1.24, 1.50)
Plus fibrinogen	1.00 (0.92, 1.09)	0.80 (0.75, 0.86)	1.37 (1.23, 1.52)	-	-	-
Plus log <sub>e</sub> C-reactive protein	-	-	-	1.03 (0.96, 1.10)	0.81 (0.74, 0.89)	1.34 (1.22, 1.46)
<b>Ischaemic stroke</b>	<i>21 studies, 110 732 individuals, 1834 cases</i>			<i>13 studies, 50870 individuals, 1099 cases</i>		
Adjusted for age and sex	1.26 (1.18, 1.35)	0.86 (0.78, 0.95)	1.20 (1.12, 1.28)	1.20 (1.04, 1.38)	0.90 (0.79, 1.04)	1.12 (0.98, 1.28)
Plus systolic blood pressure	1.18 (1.11, 1.26)	0.87 (0.79, 0.96)	1.14 (1.07, 1.22)	1.14 (1.00, 1.30)	0.92 (0.80, 1.05)	1.07 (0.94, 1.23)
Plus smoking status	1.18 (1.10, 1.26)	0.89 (0.81, 0.98)	1.14 (1.07, 1.22)	1.13 (0.99, 1.28)	0.94 (0.82, 1.07)	1.07 (0.94, 1.22)
Plus body mass index	1.18 (1.10, 1.26)	0.90 (0.81, 0.99)	1.14 (1.06, 1.22)	1.14 (1.00, 1.30)	0.92 (0.81, 1.04)	1.09 (0.96, 1.23)
Plus history of diabetes	1.13 (1.05, 1.21)	0.92 (0.84, 1.01)	1.14 (1.06, 1.22)	1.11 (0.98, 1.25)	0.94 (0.83, 1.05)	1.10 (0.98, 1.23)
Plus other lipid markers†	1.06 (0.96, 1.16)	0.97 (0.88, 1.07)	1.09 (1.00, 1.19)	1.05 (0.91, 1.19)	0.97 (0.87, 1.08)	1.09 (0.97, 1.22)
Plus fibrinogen	1.07 (0.97, 1.17)	0.99 (0.91, 1.07)	1.06 (0.97, 1.15)	-	-	-
Plus log <sub>e</sub> C-reactive protein	-	-	-	1.02 (0.90, 1.16)	0.96 (0.86, 1.08)	1.09 (0.98, 1.21)

Regression analyses were stratified, where appropriate, by sex and trial arm.

† Analyses of analyses of log<sub>e</sub> triglyceride were adjusted for HDL-C and non-HDL-C levels, analyses of HDL-C were adjusted for non-HDL-C and log<sub>e</sub> triglyceride levels, and analyses of non-HDL-C were adjusted for HDL-C and log<sub>e</sub> triglyceride levels. Studies with fewer than 10 cases were excluded from analysis of each outcome.

**eTable 7.** Associations of usual levels of measured LDL-C and non-HDL-C with coronary heart disease, adjusted for usual levels of potential confounding factors, in the subset of participants with available measurements.

	LDL-C Per 33 mg/dL (1-SD) higher			Non-HDL-C Per 39 mg/dL (1-SD) higher		
	HR (95% CI)	Wald $\chi^2_1$	I <sup>2</sup> (95% CI)	HR (95% CI)	Wald $\chi^2_1$	I <sup>2</sup> (95% CI)
<b>Coronary heart disease</b> (8 studies, 44234 individuals, 2076 cases)						
Adjusted for age and sex	1.39 (1.09, 1.78)	7	94 (91, 96)	1.55 (1.23, 1.95)	14	93 (88, 96)
Plus systolic blood pressure	1.37 (1.08, 1.74)	7	94 (90, 96)	1.48 (1.19, 1.85)	12	92 (87, 95)
Plus smoking status	1.34 (1.03, 1.73)	5	93 (89, 96)	1.46 (1.18, 1.82)	12	91 (86, 95)
Plus body mass index	1.40 (1.10, 1.80)	7	93 (89, 96)	1.48 (1.19, 1.84)	12	92 (86, 95)
Plus history of diabetes	1.41 (1.11, 1.81)	8	93 (89, 96)	1.49 (1.20, 1.86)	13	91 (86, 95)
Plus log <sub>e</sub> triglyceride	1.37 (1.09, 1.73)	7	92 (87, 95)	1.39 (1.04, 1.87)	5	92 (87, 95)
Plus HDL-C	1.38 (1.09, 1.73)	7	92 (86, 95)	1.42 (1.06, 1.91)	5	92 (87, 95)

Regression analyses were stratified, where appropriate, by sex and trial arm.  
Studies with fewer than 10 cases were excluded from analysis of each outcome.

**eTable 8.** Associations of usual levels of non-HDL-C, HDL-C, apolipoprotein B and apolipoprotein AI with coronary heart disease and ischaemic stroke, adjusted for usual levels of potential confounding factors.

	<b>Non-HDL-C</b> Per 43 mg/dL (1-SD) higher	<b>ApoB</b> Per 29 mg/dL (1-SD) increase	<b>HDL-C</b> Per 15 mg/dL (1-SD) higher	<b>ApoAI</b> Per 29 mg/dL (1-SD) increase	<b>Non-HDL-C / HDL-C</b> Per 1.53 unit (1-SD) increase	<b>ApoB / ApoAI</b> Per 0.27 unit (1-SD) increase
	<b>HR</b> <b>(95% CI)</b>	<b>HR</b> <b>(95% CI)</b>	<b>HR</b> <b>(95% CI)</b>	<b>HR</b> <b>(95% CI)</b>	<b>HR</b> <b>(95% CI)</b>	<b>HR</b> <b>(95% CI)</b>
<b>Coronary heart disease</b> (22 studies, 91307 individuals, 4499 cases)						
Adjusted for age and sex	1.73 (1.52, 1.96)	1.71 (1.51, 1.95)	0.66 (0.59, 0.73)	0.70 (0.63, 0.77)	1.63 (1.45, 1.83)	1.59 (1.46, 1.74)
Plus systolic blood pressure	1.65 (1.46, 1.86)	1.64 (1.46, 1.85)	0.67 (0.61, 0.74)	0.72 (0.66, 0.69)	1.58 (1.42, 1.76)	1.56 (1.44, 1.71)
Plus smoking status	1.63 (1.46, 1.83)	1.62 (1.44, 1.82)	0.69 (0.63, 0.76)	0.74 (0.67, 0.81)	1.55 (1.40, 1.72)	1.53 (1.41, 1.66)
Plus body mass index	1.62 (1.45, 1.82)	1.60 (1.43, 1.80)	0.70 (0.63, 0.77)	0.75 (0.69, 0.83)	1.54 (1.39, 1.71)	1.52 (1.40, 1.65)
Plus history of diabetes	1.55 (1.34, 1.80)	1.61 (1.44, 1.80)	0.71 (0.65, 0.79)	0.81 (0.74, 0.88)	1.52 (1.37, 1.68)	1.51 (1.39, 1.63)
Plus lipid markers†	1.59 (1.36, 1.85)	1.58 (1.39, 1.79)	0.77 (0.72, 0.83)	0.78 (0.72, 0.86)	1.50 (1.38, 1.62)	1.49 (1.39, 1.60)
<b>Ischaemic stroke</b> (8 studies, 60571 individuals, 1192 cases)						
Adjusted for age and sex	1.16 (1.06, 1.26)	1.19 (1.03, 1.38)	0.88 (0.79, 0.97)	0.90 (0.82, 0.99)	1.23 (1.11, 1.36)	1.23 (1.13, 1.34)
Plus systolic blood pressure	1.10 (1.01, 1.20)	1.13 (0.99, 1.30)	0.90 (0.81, 1.00)	0.90 (0.82, 0.99)	1.19 (1.10, 1.28)	1.19 (1.10, 1.28)
Plus smoking status	1.10 (1.01, 1.20)	1.12 (0.98, 1.28)	0.91 (0.82, 1.01)	0.91 (0.83, 1.00)	1.17 (1.09, 1.27)	1.16 (1.08, 1.26)
Plus body mass index	1.10 (1.00, 1.20)	1.11 (0.97, 1.28)	0.92 (0.84, 0.99)	0.93 (0.84, 1.02)	1.16 (1.08, 1.26)	1.15 (1.07, 1.25)
Plus history of diabetes	1.09 (1.00, 1.19)	1.13 (1.00, 1.27)	0.95 (0.87, 1.03)	0.96 (0.87, 1.06)	1.12 (1.04, 1.22)	1.13 (1.04, 1.23)
Plus lipid markers†	1.08 (0.97, 1.20)	1.19 (1.05, 1.34)	0.96 (0.90, 1.02)	0.97 (0.88, 1.08)	1.14 (1.05, 1.24)	1.13 (1.05, 1.21)

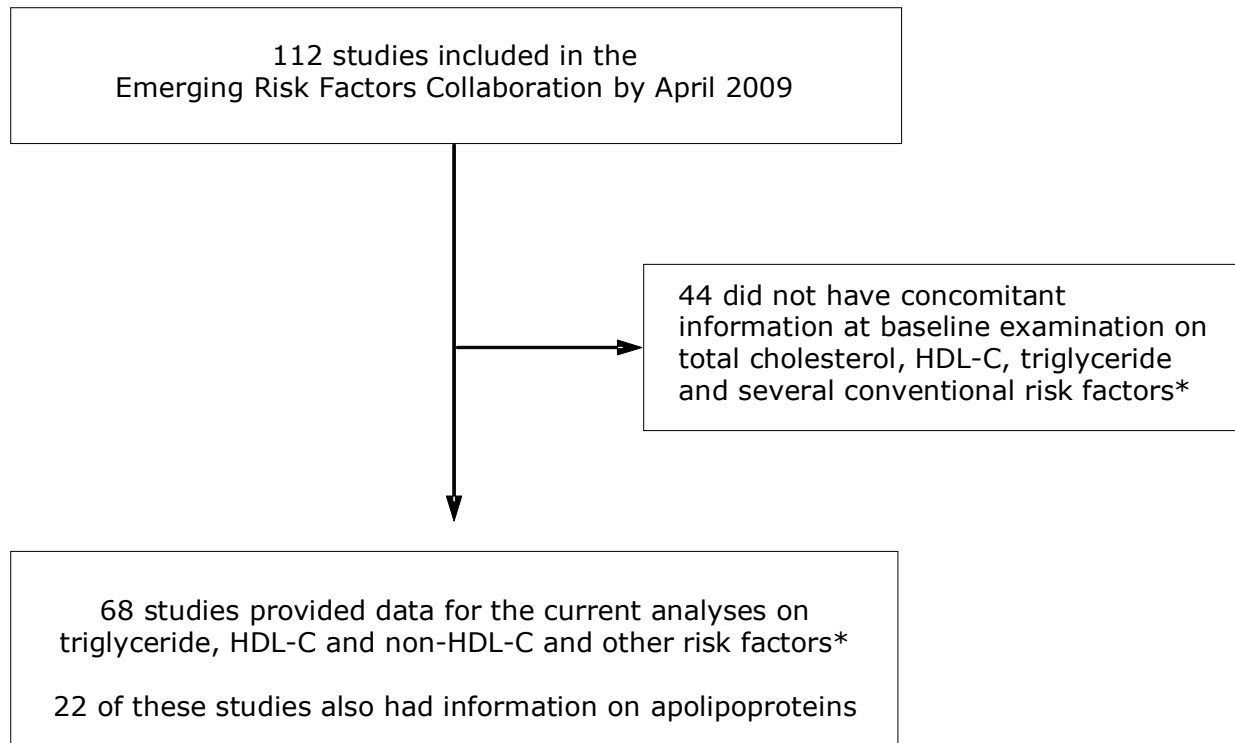
Regression analyses were stratified, where appropriate, by sex and trial arm.

Studies with fewer than 10 cases were excluded from analysis of each outcome.

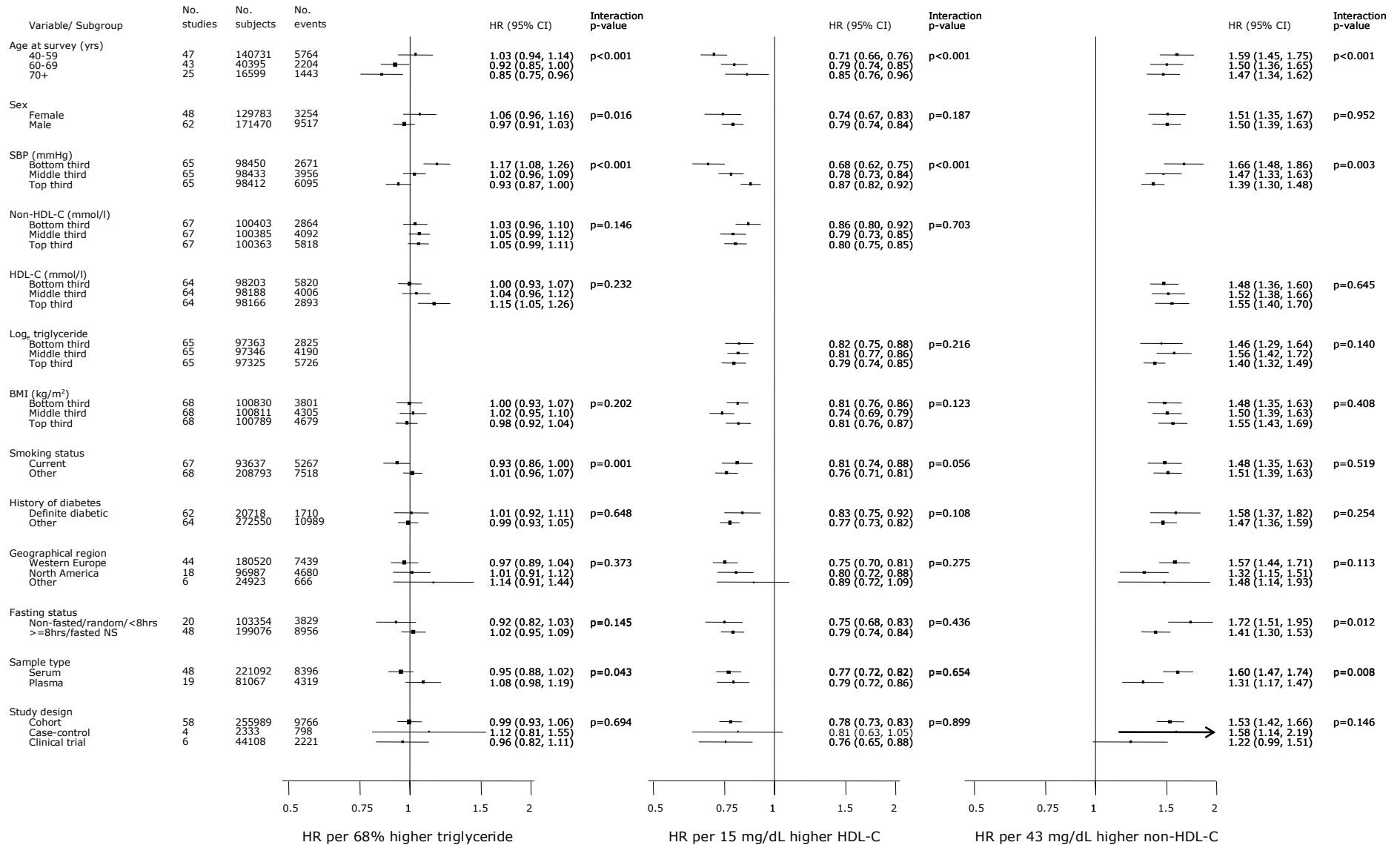
† Analyses of non-HDL-C were adjusted for HDL-C and log<sub>e</sub> triglyceride, analyses of apolipoprotein B were adjusted for apolipoprotein AI and log<sub>e</sub> triglyceride, analyses of HDL-C were adjusted for non-HDL-C and log<sub>e</sub> triglyceride, and analyses of apolipoprotein AI were adjusted for apolipoprotein B and log<sub>e</sub> triglyceride; analyses of non-HDL-C / HDL-C and apoB / apoA were adjusted for log<sub>e</sub> triglyceride.



**eFigure 1.** Study Flow Diagram

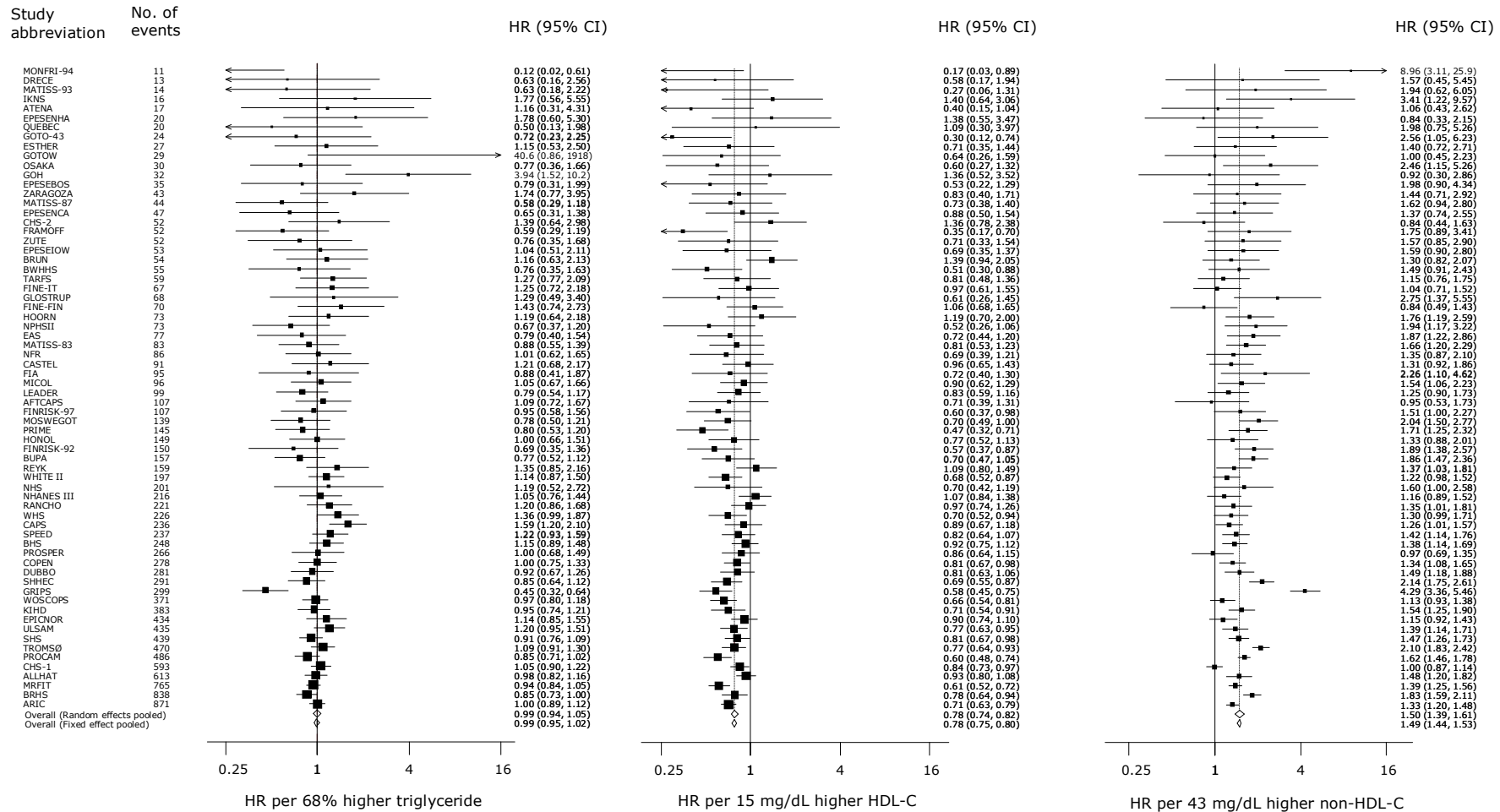


**eFigure 2.** Adjusted hazard ratios for coronary heart disease per 1-SD increase in usual triglyceride, HDL-C and non-HDL-C according to various characteristics



Regression analyses were stratified, where appropriate, by sex and trial arm and adjusted for age, systolic blood pressure, smoking status, history of diabetes, body mass index; furthermore analyses of log<sub>e</sub> triglyceride were adjusted for HDL-C and non-HDL-C levels, analyses of HDL-C were adjusted for non-HDL-C and log<sub>e</sub> triglyceride levels, and analyses of non-HDL-C were adjusted for HDL-C and log<sub>e</sub> triglyceride levels, analyses. Studies with fewer than 10 cases were excluded from analysis. P-values for interaction were calculated from analyses using continuous variables where appropriate. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios.

**eFigure 3.** Study-specific hazard ratios for CHD per 1 SD higher of usual triglyceride, HDL-C and non-HDL-C levels adjusted for usual levels of potential confounding factors\*.



Test for heterogeneity ( $I^2$  [95% CI]): 35% (12%, 52%) triglyceride, 40% (20%, 55%) HDL-C, and 73% (66%, 79%) non-HDL-C, but the heterogeneity was not significantly explained by study size as measured by the number of CHD cases recorded ( $p > 0.1$  for meta-regression of log HR on the number of CHD cases).

\*Adjusted for age, systolic blood pressure, smoking status, history of diabetes, body mass index; furthermore analyses of  $\log_e$  triglyceride were adjusted for HDL-C and non-HDL-C levels, analyses of HDL-C were adjusted for non-HDL-C and  $\log_e$  triglyceride levels, analyses of non-HDL-C were adjusted for HDL-C and  $\log_e$  triglyceride levels. Sizes of data markers are proportional to the inverse of the variance of the hazard ratios.

## eAppendix 1. Reference list of the contributing studies (56 references represent the 68 studies)

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## eAppendix 2

Because direct measurement of low density lipoprotein cholesterol (LDL-C) has been relatively uncommon in long-term prospective studies, most studies have tended to use the Friedewald equation<sup>1</sup> to estimate LDL-C values from the measured concentrations of total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), and triglycerides (divided by a constant):

$$\text{Calculated LDL-C} = \text{TC} - \text{HDL-C} - (\text{triglycerides}/2.2) \quad (1)$$

where triglycerides/2.2 approximates the concentration of cholesterol carried in very low density lipoprotein (VLDL-C) when the units of measurement are mmol/l (if mg/dl are used, the constant is 5.0).

Non-HDL-C (calculated as the difference between TC and HDL-C) can be substituted into equation 1:

$$\text{Calculated LDL-C} = \text{non-HDL-C} - (\text{triglycerides}/2.2) \quad (2)$$

As a consequence, any regression model (eg, Cox proportional hazards model for survival data, or logistic regression model for case-control data) that concomitantly includes calculated LDL-C, HDL-C and triglycerides, is simply a mathematical rearrangement of a model that includes non-HDL-C, HDL-C and triglycerides, as shown below.

Consider a survival model for the log hazard ratio (HR) including non-HDL-C, HDL-C and triglycerides (TG), where the mutually adjusted coefficients for each term are given by  $\beta_1$ ,  $\beta_2$  and  $\beta_3$ , respectively:

$$\log\text{HR} = \beta_1 \text{ non-HDL-C} + \beta_2 \text{ HDL-C} + \beta_3 \text{ TG} \quad (3)$$

Adding and subtracting  $(\beta_1/2.2)$  TG and simplifying yields:

$$\begin{aligned} \log\text{HR} &= \beta_1 \text{ non-HDL-C} + \beta_2 \text{ HDL-C} + \beta_3 \text{ TG} + (\beta_1/2.2 - \beta_1/2.2) \text{ TG} \\ &= \beta_1 (\text{non-HDL-C} - \text{TG}/2.2) + \beta_2 \text{ HDL-C} + (\beta_3 + \beta_1/2.2) \text{ TG} \end{aligned}$$

Substituting calculated LDL-C for  $(\text{non-HDL-C} - \text{TG}/2.2)$  as in equation 2 gives:

$$\log\text{HR} = \beta_1 \text{ calculated LDL-C} + \beta_2 \text{ HDL-C} + (\beta_3 + \beta_1/2.2) \text{ TG} \quad (4)$$



Comparing equations 3 and 4 demonstrates that:

- the calculated LDL-C parameter ( $\beta_1$  in equation 4) equals the non-HDL-C parameter ( $\beta_1$  in equation 3) in any model that also includes HDL-C and triglycerides. Indeed, any of the coefficients in equation 4 can be calculated from those in equation 3, should the need arise.
- when calculated LDL-C, HDL-C and triglycerides are included in the same model (equation 4), the coefficient for triglycerides is biased by  $\beta_1/2.2$  (or  $\beta_1/5.0$  if mg/dl are used) compared to equation 3. This means that even if triglycerides concentration was not associated with the outcome of interest in equation 3 (ie.  $\beta_3 = 0$ ), then it would appear to have an association of ( $\beta_1/2.2$ ) when adjusted for calculated LDL-C and HDL-C in equation 4.

In the current ERFC analyses,  $\log_e$  triglycerides concentration has been used rather than triglycerides concentration, but a similar bias as described above for triglycerides concentration applies with use of calculated LDL-C. Hence, non-HDL-C concentration has been used in the current report rather than calculated LDL-C.

#### Reference

1) Friedewald WT, Levy RI and Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972;18(6):499-502

### **eAppendix 3. List of studies' acronyms**

**AFCAPS**, Air Force/Texas Coronary Atherosclerosis Prevention Study

**ALLHAT**, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial

**AMORIS**, Apolipoprotein Related Mortality Risk Study

**ARIC**, Atherosclerosis Risk in Communities Study

**ATTICA**, ATTICA Study

**ATENA**, cohort of Progetto CUORE

**BHS**, Busselton Health Study

**BIP**, Bezafibrate Infarction Prevention Registry Study

**BRHS**, British Regional Heart Study

**BRUN**, Bruneck Study

**BUPA**, BUPA Study

**BWHHS**, British Women's Heart and Health Study

**CaPS**, Caerphilly Prospective Study

**CASTEL**, Cardiovascular Study in the Elderly

**CHARL**, Charleston Heart Study

**CHS-1**, cohort of Cardiovascular Health Study

**CHS-2**, cohort of Cardiovascular Health Study

**COPEN**, Copenhagen City Heart Study

**CUORE**, Progetto CUORE

**DRECE**, Diet and Risk of Cardiovascular Disease in Spain

**DUBBO**, Dubbo Study of the Elderly

**EAS**, Edinburgh Artery Study

**EPESEBOS**, The Established Populations for the Epidemiologic Study of the Elderly Studies, Boston

**EPESEIOW**, The Established Populations for the Epidemiologic Study of the Elderly Studies, Iowa

**EPESENCA**, The Established Populations for the Epidemiologic Study of the Elderly Studies, North Carolina

**EPESENHA**, The Established Populations for the Epidemiologic Study of the Elderly Studies, New Haven

**EPICNOR**, EPIC Norfolk Study

**ESTHER**, Epidemiologische Studie zu Chancen der Verhütung, Früherkennung und Therapie chronischer Erkrankungen in der älteren Bevölkerung

**FIA**, First myocardial infarction in Northern Sweden

**FINE-FIN**, Finland, Italy and Netherlands Elderly Study - Finland cohort

**FINE-IT**, Finland, Italy and Netherlands Elderly Study - Italian cohort

**FINRISK-92**, Finrisk Cohort 1992

**FINRISK-97**, Finrisk Cohort 1997

**FLETCHER**, Fletcher Challenge Blood Study

**FRAMOFF**, Framingham Offspring Study

**GLOSTRUP**, Glostrup Study

**GOH**, The Glucose Intolerance, Obesity and Hypertension Study

**GOTO33**, Göteborg 1933 Study

**GOTO43**, Göteborg 1943 Study

**GOTOW**, Population Study of Women in Göteborg, Sweden

**GRIPS**, Göttingen Risk Incidence and Prevalence Study

**HELSINAG**, Helsinki Aging Study

**HONOL**, Honolulu Heart Program

**HOORN**, Hoorn Study  
**HPFS**, Health Professionals Follow-up Study  
**IKNS**, Ikawa, Kyowa, and Noichi Study  
**ISRAEL**, Israeli Ischaemic Heart Disease Study  
**NORTH KARELIA**, North Karelia Project  
**KIHD**, Kuopio Ischaemic Heart Disease Study  
**LASA**, Longitudinal Aging Study Amsterdam  
**LEADER**, Lower Extremity Arterial Disease Event Reduction Trial  
**MALMO**, Malmö Study  
**MATISS-83**, cohort of Progetto CUORE  
**MATISS-87**, cohort of Progetto CUORE  
**MATISS-93**, cohort of Progetto CUORE  
**MCVDRFP**, Monitoring of CVD Risk Factors Project  
**MICOL**, cohort of Risk Factors and Life Expectancy Pooling Project  
**MOGERAUG1**, MONICA/KORA Augsburg Surveys S1  
**MOGERAUG2**, MONICA/KORA Augsburg Surveys S2  
**MOGERAUG3**, MONICA/KORA Augsburg Surveys S3  
**MONFRI-94**, cohort of Progetto CUORE  
**MORGEN**, Monitoring Project on Chronic Disease Risk Factors  
**MOSWEGOT**, MONICA Göteborg Study  
**MRFIT**, Multiple Risk Factor Intervention Trial 1  
**NCS**, Norwegian Counties Study  
**NFR**, cohort of Risk Factors and Life Expectancy Pooling Project  
**NHANES I**, National Health and Nutrition Examination Survey I  
**NHANES II**, National Health and Nutrition Examination Survey II  
  
**NHANES III**, National Health and Nutrition Examination Survey III  
**NHS**, Nurses Health Study  
**NPHSI**, Northwick Park Heart Study I  
**NPHSII**, Northwick Park Heart Study II  
**OSAKA**, Osaka Study  
**OSLO**, Oslo Study  
**OYABE**, Oyabe study  
**PARIS1**, Paris Prospective Study I  
**PRHHP**, Puerto Rico Heart Health Program  
**PRIME**, Prospective Epidemiological Study of Myocardial Infarction  
**PROCAM**, Prospective Cardiovascular Münster Study  
**PROSPER**, Prospective Study of Pravastatin in the Elderly at Risk  
**QUEBEC**, Quebec Cardiovascular Study  
**RANCHO**, Rancho Bernardo Study  
**REYK**, Reykjavik Study  
**RIFLE**, Risk Factors and Life Expectancy Pooling Project  
**ROTT**, The Rotterdam Study  
**SHHEC**, Scottish Heart Health Extended Cohort  
**SHS**, Strong Heart Study

**SPEED**, Speedwell Study  
**TARFS**, Turkish Adult Risk Factor Study  
**TPT**, Thrombosis Prevention Trial  
**TROMSØ**, Tromsø Study  
**ULSAM**, Uppsala Longitudinal Study of Adult Men  
**USPHS**, U.S. Physicians Health Study  
**USPHS2**, U.S. Physicians Health Study 2  
**VHMPP**, Vorarlberg Health Monitoring and Promotion Programme  
**VITA**, Vicenza Thrombophilia and Atherosclerosis Project  
**WHITE I**, Whitehall I Study  
**WHITE II**, Whitehall II Study  
**WHS**, Womens Health Study  
**WOSCOPS**, West of Scotland Coronary Prevention Study  
**XIAN**, Xi'an Cohort Study  
**ZARAGOZA**, Zaragosa study  
**ZUTE**, Zutphen Elderly Study