

SUPPLEMENTAL APPENDICES

Supplemental Appendix A: Complete List of Search Terms

Table 3

Search Terms

	Serum Lipid and Lip-lowering drugs	Tendon Structure and Pathology
MeSH	Lipids/ exp Lipoproteins/ Cholesterol/	exp Tendons/
Free text	Lipid*.ti,ab. Cholesterol*.ti,ab. Hyperlipid*.ti,ab. Hypercholesterol*.ti,ab. Triglyceride*.ti,ab. Hypertriglyceride*.ti,ab. High-density lipoprotein*.ti,ab. Low-density lipoprotein*.ti,ab.	Tendon structure*.ti,ab. Tendon thickness*.ti,ab.
MeSH	Hydroxymethylglutaryl-CoA Reductase Inhibitors/ exp Lovastatin/	exp Tendon Injuries/ exp Tendinopathy/ Xanthomatosis/ AND exp Tendons/
Free text	Statin*.ti,ab. Hydroxymethylglutaryl-CoA Reductase Inhibitor*.ti,ab. HMG-CoA.ti,ab. Atorvastatin.ti,ab. Fluvastatin.ti,ab. Lovastatin.ti,ab. Pitavastatin.ti,ab. Pravastatin.ti,ab. Rosuvastatin.ti,ab. Simvastatin.ti,ab.	Tendon pain.ti,ab. Tendon tear*.ti,ab. Tendon strain*.ti,ab. Tendon rupture*.ti,ab. Tend#nopath*.ti,ab. Tend#nitis.ti,ab. Tend#nos#s.ti,ab. Tenosynovitis.ti,ab. Achillodynia.ti,ab. Achilodynia.ti,ab. Jumper* Knee.ti,ab. Tennis Elbow.ti,ab. Golfer* Elbow.ti,ab. Epicondylitis.ti,ab. Xanthoma*.ti,ab. ADJ5 Tendon*.ti,ab.

MeSH = Medical Subject Heading

Supplemental Appendix B: Quality Assessment of Included Papers

Example: Abate et al., 2014

Abate et al., 2014			
No.	Criterion	Decision Rule	Score Y=1 N=0
STUDY POPULATION			
1	Is the method of recruitment and eligibility criteria reported?	Yes if the study states how participants were recruited, and clear eligibility criteria for participant inclusion and/or exclusion were reported	Y
2	Are the participants representative of the population from which they were recruited?	Yes if the study states that consecutive eligible patients were used, participants were randomly selected, or all participants were used from the source population	N
3	Is there evidence that the controls are free from disease?	Yes if evidence is supplied that the controls are not exposed to the disease	Y
4	Are both groups drawn from the same population?	Yes if both the case and control group were drawn from the same source population	Y
5	Are potential confounding factors identified?	Yes if the cases and controls were matched with respect to the potential confounding factors (age, sex, BMI)	N
OUTCOME			
6	Were lipid levels assessed identically?	Yes if the method for the collection and the analysis of the lipid levels were done in an identical way for the entire population	N
7	Valid definitions	Yes if the method used for assessing tendon structure or tendon pain was defined and explained with reference to its validity	Y
8	Was tendon structure or tendon pain assessed identically?	Yes if the methods for assessing tendon structure or tendon pain were measured in an identical way for the entire population	Y
9	Was assessor blinding reported?	Outcomes and variables were measured by assessors independently, without any knowledge of the key confounding outcome or grouping variables within the study	N
STUDY DESIGN			

10	Were data available for >80% of those enrolled?	Yes if data were available for at least 80% of all participants enrolled in the study	N
ANALYSIS			
11	Appropriate analysis	Yes if data are supplied that allows for the reader to determine if the relationship between abnormal lipid levels and change in tendon structure or pain is statistically significant	Y
		SCORE	6/11
		PERCENTAGE	55%

Supplemental Appendix C: Programs and formulas

Cholesterol Unit Conversion:

To convert milligrams per decileter (mg/dL) to millimole per litre (mmol/L), values should be divided by:

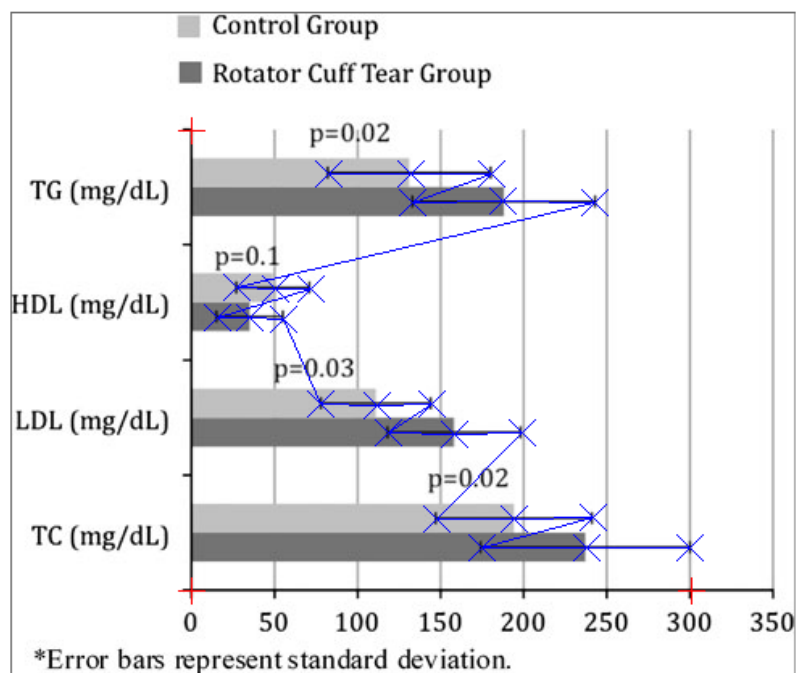
- 38.67 for total cholesterol, HDL and LDL
- 88.57 for triglycerides

*Figures taken from ‘Screening for Lipid Disorders in Children and Adolescents – Evidence Synthesis’ by Haney, E., Huffman, L., Bougatsos, C et al (2007). Agency for Healthcare Research and Quality (US).

Engauge Digitilizer 4.1:

Engauge Digitilizer 4.1 was developed by Mark Mitch in 2010.

Figure 6. Data extraction using Engauge Digitilizer



Supplemental Appendix D: Summary of Quality Assessment Results

Table 4

Summary of Quality Assessment Results

Author (Year)	1	2	3	4	5	6	7	8	9	10	11	Score
Abbate (2014)	✓	✗	✓	✓	✗	✗	✓	✓	✗	✗	✓	6/11 (55%)
Abboud (2010)	✓	✗	✓	✓	✓	✓	✓	✓	✗	✓	✓	9/11 (82%)
Beri (2009)	✓	✓	✓	✓	✓	N/A	✗	✗	✗	N/A	✓	6/9 (67%)
Descamps (2001)	✗	✗	✓	✗	✓	✗	✓	✓	✗	N/A	✓	5/10 (50%)
Durrington (1982)	✗	✗	✓	✗	✓	✗	✓	✓	✗	✓	✓	6/11 (55%)
Gaida (2009)	✓	✗	✓	✗	✓	✓	✓	✗	✓	N/A	✓	7/10 (70%)
Gattereau (1973)	✓	✗	✓	✗	✓	✗	✓	✓	✗	N/A	✓	6/10 (60%)
Junyent (2005)	✓	✓	✓	✗	✓	✓	✓	✓	✗	N/A	✓	8/10 (80%)
Klemp (1993)	✓	✓	✓	✗	✓	✗	✓	✓	✗	N/A	✓	7/10 (70%)
Kwak (2013)	✓	✗	✓	✓	✗	✗	✓	✓	✗	✓	✗	6/11 (55%)

Longo (2010)	✓	✗	✓	✓	✓	✓	✓	✓	✗	N/A	✓	8/10 (80%)
Mabuchi (1977)	✗	✗	✓	✗	✗	✗	✓	✓	✗	✓	✓	5/11 (45%)
Mabuchi (1978)	✓	✓	✓	✗	✗	✓	✓	✓	✗	✗	✓	7/11 (64%)
Ozgurtas (2003)	✗	✗	✗	✗	✗	✗	✓	✗	✗	N/A	✓	2/10 (20%)
Rechardt (2013)	✓	✓	N/A	N/A	N/A	✓	✓	✓	✗	✗	✓	6/8 (75%)
Tsouli (2009)	✓	✗	✓	✗	✓	✓	✓	✓	✗	✓	✓	8/11 (73%)
Yuzawa (1989)	✗	✗	✓	✗	✗	✓	✓	✓	✗	✓	✓	6/11 (55%)

✓ = yes, ✗ = no, N/A = not applicable

Supplemental Appendix E: Results Tables

Table 4
Participants

Author (Year)		Population	Setting	Number recruited	Age (years)	Gender (male/female)	BMI [†] (kg/m ²)
Abate (2014)	Case	Rotator cuff full-thickness tears (pre- and post-menopausal women)	Echography unit of department for lower limb disease	27	Mean = 50.9 SD = 4.1	0/27	Mean = 27.5 SD = 3.1
	Control	No rotator cuff full-thickness tears (pre- and post-menopausal women)	Echography unit of department for lower limb disease	205	Mean = 49.7 SD = 4.0	0/205	Mean = 23.7 SD = 3.0
Abboud (2010)	Case	Full-thickness rotator cuff tears	Outpatient tertiary care clinic	80 (6 excluded)	Mean = 66.1 Range = 21-93	44/30	Mean = 30.3
	Control	Shoulder complaint, normal rotator cuff	Outpatient tertiary care clinic	80 (7 excluded)	Mean = 67.2 Range = 21-93	39/34	Mean = 28.7
Beri	Case	Patients billed with a	University-based	93	Mean = 49.04	64/29	

(2009)		discharge diagnosis of tendon rupture	multispecialty group practice in East Lansing, MI.		SD = 17.2		-
	Control	Randomly selected patients who did not have tendon rupture	University-based multispecialty group practice in East Lansing, MI.	279	Mean = 49.04 SD = 17.2	192/87	-
Descamps (2001)	Case	Genetically ascertained FH individuals	Not stated	127	FH (excluded)	FH (excluded)	FH (excluded)
	Control	Individuals with a negative genetic test for ApoB3500 and LDL-R mutations	Not stated	160	Men: Mean = 50 SD = 11 Women: Mean = 51 SD = 13	88/72	Men: Mean = 28.7 SD = 3.4 Women: Mean = 28.3 SD = 4.8
Durrington (1982)	Case	Patients with primary hypercholesterolaemia	Patients attending either a Lipid Clinic or a Metabolic Clinic	32	FH (excluded)	FH (excluded)	FH (excluded)
	Control	Normolipidaemic volunteers	Volunteers	11	Mean = 44 SD = 4	4/7	Mean = 28.7 SD = 4
Gaida (2009)	Case	Diagnosed with mid-portion Achilles tendinopathy	Sports Medicine Unit, Umeå University, Sweden	60	Mean = 48 SD = 9.4	32/28	Mean = 25.4 SD = 2.8

	Control	No history of tendon injury	Member of the general community	60	Mean = 47 SD = 9.7	32/28	Mean = 25.4 SD = 2.7
Gattereau (1973)	Case	Classified as having type II hypercholesterolemia	Clinic of Nutrition, Metabolism and Atherosclerosis of the Clinical Research Institute of Montreal	32	Mean = 34.6 SD/R = -	13/19	Mean = 22.02 SD/R = -
	Control	Classified as normolipemic	Clinic of Nutrition, Metabolism and Atherosclerosis of the Clinical Research Institute of Montreal	32	Mean = 34.05 SD/R = -	18/14	Mean = 23.97 SD/R = -
Junyent (2005)	Case	Adults with a diagnosis of primary hypercholesterolaemia	Attending the Lipid Clinic of Hospital Clinic, Barcelona.	81	FH (excluded)	FH (excluded)	FH (excluded)
	Control	Normolipidaemic participants	Recruited from hospital personnel and lists of primary health physicians.	88	Mean = 48 Range = 26-81	37/51	Mean = 25.8 SD = 4.2
Klemp (1993)	Case	Patients with hyperlipidaemia	The lipid clinic at Tygerberg Hospital	88	Mean = 48 Range= 19-69	42/46	-
	Control	Volunteers with normal lipid profiles	Volunteers	88	-	-	-

Kwak (2013)	Case	Patients with dyslipidaemia	Cardiovascular Center of National Health Insurance Service (NHIS) Ilsan hospital	19	Mean = 60.0 SD = 12.5	6/13	Mean = 25.2 SD = 1.9
	Control	Normolipidaemic controls	Cardiovascular Center of National Health Insurance Service (NHIS) Ilsan hospital	96	Mean = 62.3 SD = 8.5	62/34	Mean = 24.2 SD = 2.6
Longo (2010)	Case	Patients who underwent arthroscopic repair of rotator cuff tear	University teaching hospital	120	Mean = 64.86 Range = 40-83	45/75	Mean = 27.62 SD/R = -
	Control	Patients who underwent arthroscopic meniscectomy	University teaching hospital	120	Mean = 63.91 Range = 38-78	45/75	Mean = 27.32 SD/R = -
Mabuchi (1977)	Case	Familial hypercholesterolaemic patients	Not stated	18	FH (excluded)	FH (excluded)	FH (excluded)
	Control	Normal participants	Not stated	36	Not stated	Not stated	Not stated
Mabuchi (1978)	Case	Familial hypercholesterolaemic patients	Not stated	112	FH (excluded)	FH (excluded)	FH (excluded)
	Control	Normal participants with no disease associated with lipid	Not stated	36	Mean = 56 SD = 12	Not stated	Not stated

metabolism

Ozgurtas (2003)	Case	Patients with Achilles tendon rupture	Department of Orthopedics and Traumatology of Gu'lhane Military Medical Academy	47	Mean = 25.7 SD/R = -	41/6	-
	Control	Individuals without Achilles tendon rupture	-	26	Mean = 32.6 SD/R = -	20/6	-
Rechartd (2013)	Case	Patients seeking medical advice for incipient upper extremity pain	Three occupational healthcare units in Helsinki	163	Mean = 45 SD = 9.8	23/140	Mean = 25.5 SD = 4.3
	Control	*Cross-sectional study – no control group*					
Tsouli (2009)	Case	Unrelated patients with herterozygous familial hypercholesterolaemia	Not stated	80	FH (excluded)	FH (excluded)	FH (excluded)
	Control	Normolipidemic, sex- and age-matched, apparently healthy volunteers with no history of hypercholesterolemia	Not stated	80	Mean = 43.0 SD = 9.7	30/50	Mean = 25.1 SD = 6.5
Yuzawa (1989)	Case	Japanese patients with heterozygous familial	Not stated	15	FH (excluded)	FH (excluded)	FH (excluded)

hypercholesterolaemia

Control	Normocholesterolaemic participants	University staff	34	Mean = 45 SD = 11	17/17	Not stated
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† BMI = Body Mass Index

Table 5
Lipid Assessment

Author (Year)		Fasting (Yes/No)	Total cholesterol Mean (SD or Range) mmol/L	HDL [†] Mean (SD or Range) mmol/L	LDL [†] Mean (SD or Range) mmol/L	Triglycerides Mean (SD or Range) mmol/L	Statin use
Abate (2014)	Case	Yes	5.15 (0.62)	1.23 (0.15)	-	1.50 (0.59)	Not stated
	Control	Yes	4.88 (0.67)	1.44 (0.22)	-	1.27 (0.45)	Not stated
Abboud (2010)	Case	-	6.13 (1.63)	0.91 (0.52)	4.09 (1.03)	2.11 (0.61)	-
	Control	-	5.02 (1.22)	1.29 (0.57)	2.87 (0.85)	1.49 (0.54)	No
Beri (2009)	Case	-	-	-	-	-	24.7 %
	Control	-	-	-	-	-	24.7 %
Descamps (2001)	Case	FH (excluded)	FH (excluded)	FH (excluded)	FH (excluded)	FH (excluded)	FH (excluded)
	Control	Not stated	Men = 7.16 (1.66) Women = 7.32 (1.37)	Men = 1.24 (0.36) Women = 1.40 (0.47)	Men = 4.78 (1.60) Women = 5.07 (1.34)	Men = 3.06 (2.36) Women = 2.26 (2.01)	Not stated
Durrington (1982)	Case	FH (excluded)	FH (excluded)	FH (excluded)	FH (excluded)	FH (excluded)	FH (excluded)
	Control	Not stated	5.2 (0.30)	-	-	-	Not stated
Gaida (2009)	Case	Yes	5.47 (1.02)	1.44 (0.39)	3.37 (0.86)	1.22 (0.77)	6 %
	Control	Yes	5.16 (1.00)	1.58 (0.48)	3.14 (0.93)	0.96 (0.47)	No
Gattereau (1973)	Case	-	Men = 7.9 (1.06) Women = 9.69 (1.72)	-	-	Men = 1.3 (0.30) Women = 1.14 (0.21)	-
	Control	-	Men = 4.42 (0.40)	-	-	Men = 0.96 (0.21)	-

(2009)	Control	Yes	5.22 (0.83)	1.32 (0.23)	3.52 (0.67)	0.90 (0.50)	No
Yuzawa (1989)	Case Control	FH (excluded) Not stated	FH (excluded) 4.55 (0.78)	FH (excluded) 1.32 (0.28)	FH (excluded) -	FH (excluded) 1.29 (0.61)	FH (excluded) Not stated

† HDL = High-density lipoprotein, LDL = Low-density lipoprotein

Table 6
Results

Author (Year)	Relationship investigated	Effect size (95% CI)	Univariate Odds Ratio (95% CI)	Multivariate Odds Ratio (95% CI)	Other
Abate (2014)	Rotator cuff tears and lipid levels	-	-	-	Predictor coefficient (of RC tears): HDL = -0.228 (p = 0.001)
Abboud (2010)	Rotator cuff tear and lipid levels	TC† = 1.11 (0.64 to 1.58) HDL† = -0.38 (-0.56 to -0.20) LDL† = 1.22 (0.91 to 1.53) TG† = 0.62 (0.43 to 0.81)	-	-	-
Beri (2009)	Statins and tendon rupture	-	All = 1.00 (0.54 to 1.84), p = 1.0 Men = 0.62 (0.30 to 1.30), p = 0.20 Women = 3.09 (1.04 to 9.75), p = 0.04	All = 1.1 (0.57 to 2.13), p = 0.76 Men = 0.66 (0.29 to 1.51), p = 0.32 Women = 3.76 (1.11 to 12.75), p = 0.03	-
Descamps (2001)	No relevant analyses were conducted	-	-	-	-
Durrington (1982)	No relevant analyses were conducted	-	-	-	-
Gaida (2009)	Achilles tendinopathy and lipid levels	TC = 0.31 (-0.06 to 0.66) HDL = -0.32 (-0.68 to 0.04) LDL = 0.26 (-0.1 to 0.61)	-	-	-

TG = 0.41 (0.4 to 0.77)

Gattereau (1973)	Non-familial hyperlipidemia and tendon thickness	Men = 0.95 (0.19 to 1.71) Women = 0.86 (0.13 to 1.58)	-	-	-
Junyent (2005)	No relevant analyses were conducted	-	-	-	-
Klemp (1993)	Musculoskeletal manifestations and Mixed hyperlipidemia	-	-	-	-
Kwak (2013)	ATT and lipid levels	-	-	-	Pearson's correlation (r) for: ATT and TC = -0.09 ATT and HDL = -0.06 ATT and LDL = -0.03 ATT and TG = -0.04 *all results not sig (p>0.05)
Longo (2010)	RC tears and lipid levels	TC = 0.08 (-0.18 to 0.33) TG = 0.20 (-0.05 to 0.46)	-	-	-
Mabuchi (1977)	ATT and serum cholesterol	-	-	-	r = 0.454, p<0.01

Mabuchi (1978)	No relevant analyses were conducted	-	-	-	-	-
Ozgurtas (2003)	Achilles tendon rupture and lipid levels	TC = 2.13 (1.52 to 2.7) HDL = -0.49 (-0.97 to 0) LDL = 2.13 (1.42 to 2.69) TG = 0.55 (0.06 to 1.03)	-	-	-	-
Rechardt (2013)	Pain intensity and lipid levels	-	-	OR	CI	-
				TC > 5.3:	1.8 0.8-4.0	
				HDL < 1.48:	2.7 1.2-6.3	
				LDL > 3.3:	1.7 0.7-4.2	
				TG > 1.08:	2.8 1.2-6.6	
				Statin	0.9 0.2-4.3	
Tsouli (2009)	No relevant analyses were conducted	-	-	-	-	-
Yuzawa (1989)	No relevant analyses were conducted	-	-	-	-	-

†TC = total cholesterol, HDL = high-density lipoprotein, LDL = low-density lipoprotein, TG = triglycerides

Supplemental Appendix F: Pooled mean and SD calculation

The excel formula for calculating pooled mean is

$$=(D3*B3+D4*B4)/(D3+D4)$$

Where B3 and D3 are the mean and sample size of one study, and B4 and D4 are the mean and sample size of another study

The excel formula for calculating pooled standard deviation (SD) is

$$=SQRT((((D3-1)*C3^2)+((D4-1)*C4^2)+((D3*D4)/(D3+D4))*(B3-B4)^2)/(D3+D4-1))$$

Where B3, C3 and D3 are the mean, SD and sample size of one study and B4,C4, D4 are the mean, SD and sample size of another study