

Table S1. Lathosterol levels (μmol/mmol cholesterol) of the included studies.

First author	Intervention	Day 1 (hours)																	
		06:30	07:00	07:30	08:00	08:30	09:00	09:30	10:00	10:30	11:00	11:30	12:00	12:30	13:00	13:30	14:00	14:30	15:00
Al-Khaifi [1]	No treatment					0.9			0.7			0.7			0.6			0.6	
	CME					0.9			0.8			0.7			0.6			0.6	
	CME+STAT					0.3			0.3			0.2			0.2			0.2	
Gälman [2]	No treatment						0.6			0.6			0.5			0.5			0.5
Persson [3]	CME					1.1			1.0			0.9			0.8			0.9	

First author	Intervention	Day 1 (hours)																	
		15:30	16:00	16:30	17:00	17:30	18:00	18:30	19:00	19:30	20:00	20:30	21:00	21:30	22:00	22:30	23:00	23:30	00:00
Al-Khaifi [1]	No treatment		0.6			0.6			0.5			0.6			0.6			0.6	
	CME		0.6			0.6			0.7			0.8			0.9			1.0	
	CME+STAT		0.3			0.3			0.3			0.3			0.3			0.3	
Gälman [2]	No treatment			0.5			0.5			0.5			0.5			0.6			0.7
Persson [3]	CME		1.1			0.9			1.0			1.1			1.0			1.3	

First author	Intervention	Day 1 (hours)															Day 2			
		00:30	01:00	01:30	02:00	02:30	03:00	03:30	04:00	04:30	05:00	05:30	06:00	06:30	07:00	07:30	08:00	08:30	09:00	
Al-Khaifi [1]	No treatment		0.6			0.7			0.7			0.7			0.7			0.7		
	CME		1.1			1.2			1.5			1.3			1.3			1.3		
	CME+STAT		0.3			0.4			0.4			0.4			0.5			0.4		
Gälman [2]	No treatment			0.9			0.8			0.8			0.8			0.7			0.6	
Persson [3]	CME		1.5			1.7			1.8			1.8			1.8			1.8		

First author	Intervention	Day 2 (hours)																	
		09:30	10:00	10:30	11:00	11:30	12:00	12:30	13:00	13:30	14:00	14:30	15:00	15:30	16:00	16:30	17:00	17:30	18:00
Al-Khaifi [1]	No treatment		0.6			0.6			0.6			0.6			0.7				
	CME		1.3			1.2			1.2			1.4			1.5				
	CME+STAT		0.4			0.4			0.4			0.4			0.4				
Gälman[2]	No treatment			0.5															
Persson[3]	CME		1.7			1.6			1.6			1.7			1.9			1.8	

Values are means. CME = cholestyramine; STAT = statins. N/A = data unknown.

Table S2. Mevalonate concentrations (pmol/mL) of the included studies.

[illegible]

Table S2. Cont.

First author	Intervention	Day 1 (hours)																	
		15:30	16:00	16:30	17:00	17:30	18:00	18:30	19:00	19:30	20:00	20:30	21:00	21:30	22:00	22:30	23:00	23:30	00:00
Scoppola[4]	No treatment		6.1				8.1				10.8				10.8				14.2
Pappu[5]	No treatment		52.9		54.1		33.3		53.4		56.3		49.1		57.9		68.7		83.6
	No treatment ^a		59.0		65.8		45.3		66.7		67.8		66.2		68.0		87.2		86.5
Pappu[6]	No treatment		N/A		51.1		34.7		49.2		51.7		75.5		72.0		80.9		70.8
	Lovastatin		N/A		22.5		52.2		34.2		54.1		59.2		55.2		47.2		38.9
	Simvastatin		43.1		40.1		23.0		20.7		23.0		21.0		22.8		20.8		21.7
Parker[7]	No treatment						71.3						63.7						92.6
	No treatment		79.8		93.9		113.4		100.4		107.7		119.9		167.5		151.7		150.0
	No treatment		115.1		98.0		102.4		74.1		77.8		77.2		75.0		76.8		87.9
	Fasting		71.7		44.3		65.1		62.5		68.0		55.1		N/A		61.9		38.6
	HChol meals		41.4		51.5		61.8		69.7		66.5		84.4		N/A		91.0		51.7
Parker[8]	No treatment		40.0		36.5		38.1		37.9		40.0		50.2		63.6		59.7		76.0
	No treatment		56.9		62.3		63.4		70.9		70.9		75.3		83.5		70.4		63.4
	HChol meals		30.2		31.2		36.2		49.3		44.5		38.3		30.2		32.6		39.1
Jones[9]	No treatment						40.3								50.1				
Kopito[10]	One daily meal						10.9								10.3				
	Fasting						13.0								12.9				
Nozaki[11]	No treatment				89.2												84.0		
	Morning pravastatin																	84.1	
	Evening pravastatin				71.4												50.7		
Martin[12]	Pre-morning treatment						35.8								38.5				47.9
	Pre-evening treatment						37.2								35.3				43.5
	Morning rosuvastatin						19.8								26.6				33.0
	Evening rosuvastatin						32.9								11.7				13.4

Table S2. *Cont.*

First author	Intervention	Day 1 (hours)																	
		00:30	01:00	01:30	02:00	02:30	03:00	03:30	04:00	04:30	05:00	05:30	06:00	06:30	07:00	07:30	08:00	08:30	09:00
Scoppola[4]	No treatment				22.9				21.6						18.9				14.2
Pappu[5]	No treatment		129.3		101.8		93.2		84.7		84.5		66.0		94.0		71.0		
	No treatment ^a		87.8		92.1		85.4		101.8		87.4		79.1		81.3		83.6		
Pappu[6]	No treatment		89.1		59.1		81.7		80.9		87.5		56.3		N/A		N/A		
	Lovastatin		40.3		29.7		42.8		31.3		45.0		45.0		N/A		N/A		
	Simvastatin		22.3		22.4		17.5		23.9		33.5		37.9		26.6		N/A		
Parker[7]	No treatment						87.5						48.5						52.2
	No treatment		127.4		166.0		113.2		113.2		108.8		99.6		101.5		78.7		
	No treatment		147.1		196.0		129.8		117.3		95.2		104.2		94.5		79.6		79.2
	Fasting		56.1		47.8		45.4		57.9		80.3		56.4		55.3		61.9		
	HChol meals		63.2		61.8		71.3		65.8		57.9		49.6		55.7		56.8		73.5
Parker[8]	No treatment		68.2		62.6		62.4		56.3		55.3		45.2		N/A		N/A		
	No treatment		53.7		46.0		44.0		40.5		39.4		37.3		35.8		35.8		
	HChol meals		35.8		35.1		36.9		34.0		29.8		32.0		27.9		N/A		
Jones[9]	No treatment				66.6								68.4						
Kopito[10]	One daily meal				34.4								54.2						
	Fasting				10.6								8.1						
Nozaki[11]	No treatment																76.5		
	Morning pravastatin																82.4		
	Evening pravastatin																74.1		
Martin[12]	Pre-morning treatment				43.2								25.0						
	Pre-evening treatment				47.5								31.3						
	Morning rosuvastatin				33.4								30.1						
	Evening rosuvastatin				15.5								21.0						

Table S2. *Cont.*

First author	Intervention	Day 2 (hours)																	
		09:30	10:00	10:30	11:00	11:30	12:00	12:30	13:00	13:30	14:00	14:30	15:00	15:30	16:00	16:30	17:00	17:30	18:00
Parker[7]	No treatment						47.9						48.7						57.8
Jones[9]	No treatment		57.6								46.7								45.8
Kopito[10]	One daily meal		39.7								18.0								15.1
	Fasting		7.6								7.9								N/A
Nozaki[11]	No treatment																		
	Morning pravastatin																		
	Evening pravastatin							55.7									75.9		
First author	Intervention	Day 2 (hours)																	
		18:30	19:00	19:30	20:00	20:30	21:00	21:30	22:00	22:30	23:00	23:30	00:00	00:30	01:00	01:30	02:00	02:30	03:00
Parker[7]	No treatment						58.4						62.1						125.1
Jones[9]	No treatment								51.2								65.0		
Kopito[10]	One daily meal								12.2								32.2		
First author	Intervention	Day 2 (hours)																	
		03:30	04:00	04:30	05:00	05:30	06:00	06:30	07:00	07:30	08:00	08:30	09:00	09:30	10:00	10:30	11:00	11:30	12:00
Parker[7]	No treatment						56.5						65.7						87.8
Jones[9]	No treatment						58.4												
Kopito[10]	One daily meal						46.3								32.8				
First author	Intervention	Day 3 (hours)																	
		12:30	13:00	13:30	14:00	14:30	15:00	15:30	16:00	16:30	17:00	17:30	18:00	18:30	19:00	19:30	20:00	20:30	21:00
Parker[7]	No treatment						81.9						71.2						90.0
Kopito[10]	One daily meal				23.3														
First author	Intervention	Day 3 (hours)																	
		21:30	22:00	22:30	23:00	23:30	00:00	00:30	01:00	01:30	02:00	02:30	03:00	03:30	04:00	04:30	05:00	05:30	06:00
Parker[7]	No treatment						123.1						45.3						35.0

Values are means. HChol = high cholesterol. N/A = data unknown. ^aSubjects with phenotypic abetalipoproteinaemia.

Tabel S3. VLDL-squalene levels (μmol/mmol free cholesterol) of the included studies.

First author	Subgroup	Day 1 (hours)																	
		06:30	07:00	07:30	08:00	08:30	09:00	09:30	10:00	10:30	11:00	11:30	12:00	12:30	13:00	13:30	14:00	14:30	15:00
Miettinen [13]	Healthy subjects				3.0								1.5						
Miettinen [14]	Jejunioleal bypass				4.7								3.8						
	Ileal exclusion				1.7								1.6						

First author	Subgroup	Day 1 (hours)																	
		15:30	16:00	16:30	17:00	17:30	18:00	18:30	19:00	19:30	20:00	20:30	21:00	21:30	22:00	22:30	23:00	23:30	00:00
Miettinen [13]	Healthy subjects		1.4								2.3								3.2
Miettinen [14]	Jejunioleal bypass		2.1								2.1								2.6
	Ileal exclusion		1.5								1.9								1.7

First author	Subgroup	Day 1 (hours)																	
		00:30	01:00	01:30	02:00	02:30	03:00	03:30	04:00	04:30	05:00	05:30	06:00	06:30	07:00	07:30	08:00	08:30	09:00
Miettinen [13]	Healthy subjects								4.1										
Miettinen [14]	Jejunioleal bypass								3.5										
	Ileal exclusion								1.8										

Values are means.

Tabel S4. LDL+HDL-squalene levels ($\mu\text{mol}/\text{mmol}$ free cholesterol) of the included studies.

First author	Subgroup	Day 1 (hours)																	
		06:30	07:00	07:30	08:00	08:30	09:00	09:30	10:00	10:30	11:00	11:30	12:00	12:30	13:00	13:30	14:00	14:30	15:00
Mietinnen [13]	Healthy subjects				0.8								0.7						
Mietinnen [14]	Jejunioleal bypass				0.3								0.5						
	Ileal exclusion				0.1								0.3						

First author	Subgroup	Day 1 (hours)																	
		15:30	16:00	16:30	17:00	17:30	18:00	18:30	19:00	19:30	20:00	20:30	21:00	21:30	22:00	22:30	23:00	23:30	00:00
Mietinnen [13]	Healthy subjects		0.8								0.9								1.2
Mietinnen [14]	Jejunioleal bypass		0.4								0.4								0.3
	Ileal exclusion		0.2								0.2								0.2

First author	Subgroup	Day 1 (hours)																	
		00:30	01:00	01:30	02:00	02:30	03:00	03:30	04:00	04:30	05:00	05:30	06:00	06:30	07:00	07:30	08:00	08:30	09:00
Mietinnen [13]	Healthy subjects								1.2										
Mietinnen [14]	Jejunioleal bypass								0.3										
	Ileal exclusion								0.2										

Values are means.

Tabel S5. C4 levels (nmol/mmol cholesterol) of the included studies.

First author	Intervention	Day 1 (hours)																	
		06:30	07:00	07:30	08:00	08:30	09:00	09:30	10:00	10:30	11:00	11:30	12:00	12:30	13:00	13:30	14:00	14:30	15:00
Al-Khaifi [1]	No treatment					11.0			7.2			5.8			6.7			5.6	
	CME					9.4			5.9			8.6			10.4			12.2	
	CME + STAT					10.2			5.4			6.5			9.0			11.3	
Gälman [2]	No treatment						2.6			2.2			4.6			4.9			3.6
	No treatment ^a						3.4			2.7			8.3			5.3			4.5

First author	Intervention	Day 1 (hours)																	
		15:30	16:00	16:30	17:00	17:30	18:00	18:30	19:00	19:30	20:00	20:30	21:00	21:30	22:00	22:30	23:00	23:30	00:00
Al-Khaifi [1]	No treatment	4.8				5.9			6.4			6.1			7.2			5.3	
	CME	11.7				11.8			16.2			20.2			19.1			18.9	
	CME + STAT	10.3				11.9			15.1			19.4			19.0			22.0	
Gälman [2]	No treatment		2.8				2.4			3.8			5.6			5.4			3.5
	No treatment ^a		3.8				3.2			3.2			5.1			5.7			4.5

First author	Intervention	Day 1 (hours)																Day 2	
		00:30	01:00	01:30	02:00	02:30	03:00	03:30	04:00	04:30	05:00	05:30	06:00	06:30	07:00	07:30	08:00	08:30	09:00
Al-Khaifi [1]	No treatment	5.2				4.4			4.7			7.0			6.5			5.1	
	CME	19.7				23.0			24.2			36.5			37.6			35.1	
	CME + STAT	20.5				17.3			19.7			22.3			24.4			22.3	
Gälman [2]	No treatment			2.8			2.7			2.2			1.9			2.2			2.1
	No treatment ^a			5.3			4.6			7.4			5.2			5.0			3.2

First author	Intervention	Day 2 (hours)																	
		09:30	10:00	10:30	11:00	11:30	12:00	12:30	13:00	13:30	14:00	14:30	15:00	15:30	16:00	16:30	17:00	17:30	18:00
Al-Khaifi [1]	No treatment	3.9				5.6			6.8			6.2			4.2				
	CME	38.7				49.3			46.6			41.3			29.3			49.3	
	CME + STAT	20.7				24.5			27.8			25.7			20.3			24.5	
Gälman [2]	No treatment			1.8															
	No treatment ^a			2.6															

Values are means. CME = cholestyramine; STAT = statins. ^a Cholecystectomized subjects.