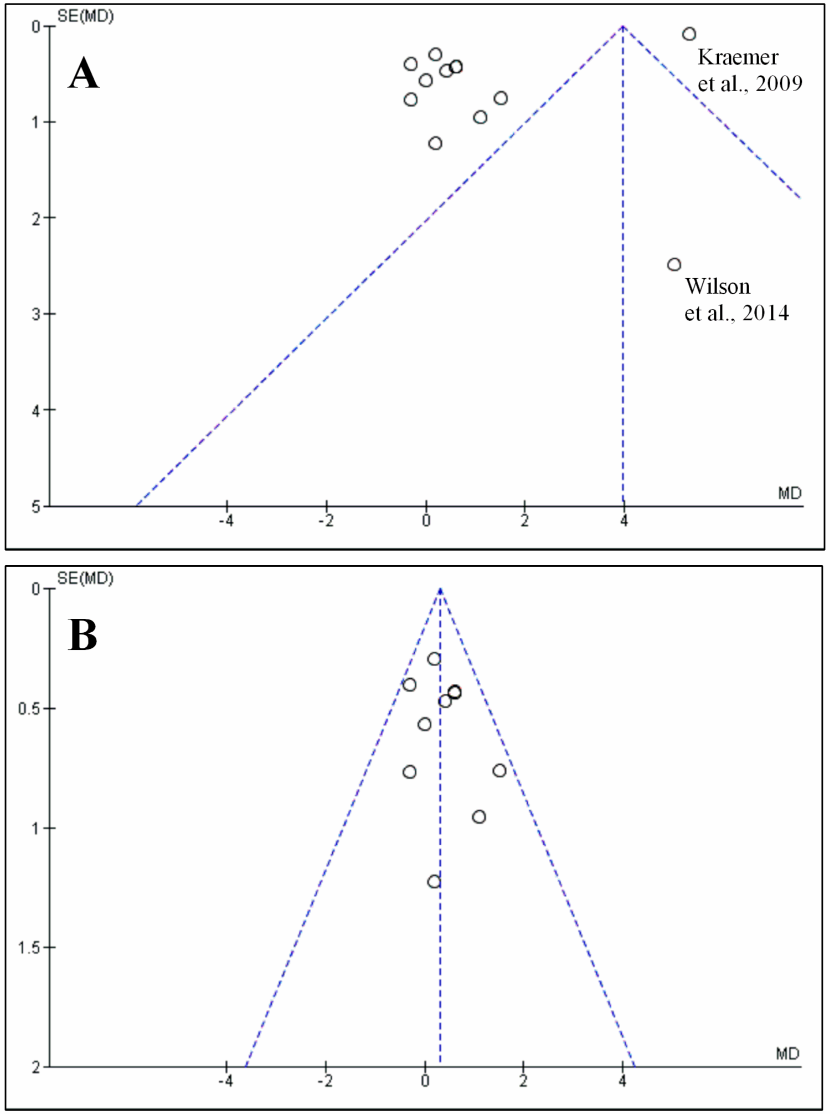
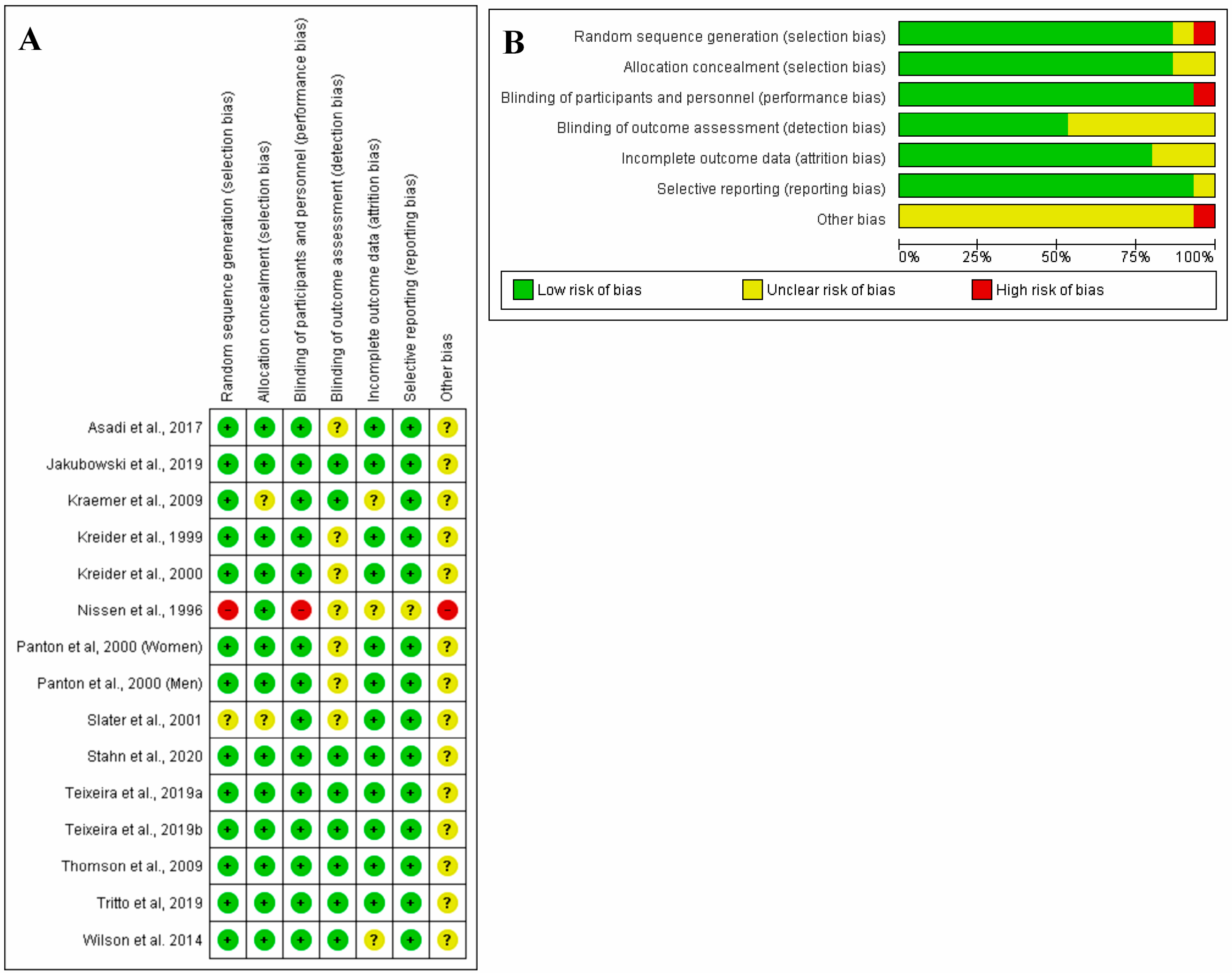


Figure S1: Funnel plots showing relation between mean differences (MD) in x axis and standard errors (SE) for mean differences.



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Asadi et al., 2017	+	+	+	?	+	+	?
Jakubowski et al., 2019	+	+	+	+	+	+	?
Kraemer et al., 2009	+	?	+	+	?	+	?
Kreider et al., 1999	+	+	+	?	+	+	?
Kreider et al., 2000	+	+	+	?	+	+	?
Nissen et al., 1996	−	+	−	?	?	?	−
Panton et al, 2000 (Women)	+	+	+	?	+	+	?
Panton et al., 2000 (Men)	+	+	+	?	+	+	?
Slater et al., 2001	?	?	+	?	+	+	?
Stahn et al., 2020	+	+	+	+	+	+	?
Teixeira et al., 2019a	+	+	+	+	+	+	?
Teixeira et al., 2019b	+	+	+	+	+	+	?
Thomson et al., 2009	+	+	+	+	+	+	?
Tritto et al, 2019	+	+	+	+	+	+	?
Wilson et al. 2014	+	+	+	+	?	+	?

Figure S2: Risk of bias summary for selected studies.

Table S1 **- Characteristics of the studies eligible for inclusion**

Study	Country	Design	Participants			Intervention					Outcome Measure			
			Sex	Age	Training Status	Dose	Duration (Weeks)	Training	HMB n	Control n	Strength		Body composition	
											Upper Body	Lower Body	FFM	FM
Asadi et al., 2017[10]	Japan	RCT DB	M	21.4±0.7	Not Described	3g HMB-FA	6	2x /w 3 sets of 8–12 rep at 75–85% of 1RM	8	8	Bench press	Leg Press	---	---
Jakubowski et al., 2019[9]	Canada	RCT DB	M	22.5±2.2	TR	3g HMB-Ca + 50g Whey Protein	12	3-5x /w Phase 1: 8w UPRT Phase 2: 2w overreaching Phase 3: 2w	13	13	Bench press	Squat	DXA	DXA
Kraemer et al (2009)[35]	USA	RCT DB	M	22.9 ± 2.8	TR	3 g HMB-Ca 10g Glycine, 11.5g Alanine, 1.5g Glutamic Acid, 1.5 g Serine	12	3x /w UPRT	8	9	Bench press	Squat	DXA	DXA
Kreider et al (1999)[3]	USA	RCT DB	M	25.1 ± 1	TR	3 g HMB-CA Drink: 81g CHO,75g PRO, 3g FAT	4	6.9 ± 0.5 hr/w	?	?	Bench press	Leg Press	DXA	DXA
Kreider et al (2000)[5]	USA	RCT DB	M	20.0±1.5	TR	3g HMB-Ca, 99 g/d of glucose, and 3 g/d of taurine.	4	4x/w , 1 to 3 sets of 2-8 rep, 60 to 95% of 1 RM (+ 3x week of agility /sprint training)	14	14	Bench Press	Squat	DXA	DXA

Nissen et al., 1996[2]	USA	RCT DB?	M	19-29	UT (at least 3 months)	3 g HMB-Ca +MET-Rx TM (37g milk protein)	7	3x /w 3 sets of 3–5 rep at 90% of 1 RM.	14	14	Several upper body exercises	Several lower body exercises	TOBEC	TOBEC
Panton et al (2000)[4]	USA	RCT DB	M/F	25 ± 1.2 (M) 23 ± 0.6 (F)	TR	3 g HMB-Ca	4	3 x/w. 3-6 rep 90% 1RM.	39 (21M/18F)	36 (18M/18F)	Bench press	Leg Press (M) Leg Extension (F)	UWW	UWW
Slater et al (2001)[6]	Australia	RCT DB	M	24.5±1.7	TR	3 g HMB-Ca (Standard encapsulation vs. Time Release)	6	2-3x /w. 4-6 repetitions for 3-5 sets (24 to 32 sets per session)	7	7	Bench press	Leg Press	DXA	DXA
Stahn et al (2020)[39]	USA	RCT DB	M	22.1±1.5	UT (for the past 6 months)	3 g HMB-Ca + 30g Whey Protein (daily). +30g carbohydrate supplement only on training days.	12	4x /w upper/lower body split routine. Weeks 1-6: linear periodization. Week 7 tapering. Weeks 8-12: undulating periodization	8	7	Bench Press	Leg Press	BIA	BIA
Teixeira et al., 2019a[8]	Portugal	RCT DB	M	31.7±7.6	TR	3g HMB-Ca or 3g HMB-FA	8	3x /w Weeks 1-3, 3-4 sets 12RM Weeks 4-6, 3-4 sets 10RM Weeks 7-8, 4 sets 8RM	20	10	---	---	DXA	DXA

Teixeira et al., 2019b[12]	Portugal	RCT DB	M	31.7±7.6	TR	3g HMB-Ca or 3g HMB-FA	8	3x /w Weeks 1-3, 3-4 sets 12RM Weeks 4-6, 3-4 sets 10RM Weeks 7-8, 4 sets 8RM	20	10	Bench Press	Squat	---	---
Thomson et al (2009)[37]	New Zealand	RCT DB	M	24 ± 4	TR	3 g HMB-Ca	9	3x /w	13	9	Bench press	Leg extension	BIA	BIA
Tritto et al, 2019[38]	Brazil	RCT DB	M	25.3±3.7	TR	3g HMB-Ca or 3g HMB-FA	12	2x /w 3-4 sets 8-10RM	29	15	Bench press	Leg Press	DXA	DXA
Wilson et al., 2014[36]	USA	RCT DB	M	21.6±0.5	TR	3g HMB-FA	12	3-5x /w Phase 1: 8w UPRT Phase 2: 2w overreaching Phase 3: 2w	11	9	Bench Press	Squat	DXA	DXA

BIA: bioelectrical impedance; CHO: Carbohydrates; DB: Double blinded; DXA: dual x-ray absorptiometry; FAT: Lipids; FFM: Free fat mass; FM: Fat mass; PRO: Protein; RCT: Randomized controlled trial; rep: repetitions per set; RM; Repetition maximum; TOBEC: Total body electrical conductivity; TR: Trained; UPRT: undulating periodized resistance-training; UT: Untrained; UWW: Under water weighting

Table S2 **– List of studies removed from the meta-analysis after data collection and asymmetry with reason for exclusion**

Study	**Reason for analysis exclusion**
Kraemer et al., 2009[35]	excluded based on funnel plot analysis of lean body mass data
Kreider et al., 1999[3]	missing data for performing meta-analysis, subjects per group
Wilson et al., 2014[36]	excluded based on funnel plot analysis of lean body mass data

Supplementary information – Search Strategy

Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:
----
beta-hydroxy, beta-methylbutyrate
beta-hydroxy-beta-methylbutyrate
beta-hydroxy beta-methylbutyrate
beta-hydroxy-beta methylbutyrate
HMB.tw,kf
HMB-Ca.tw,kf
HMB-Fa.tw,kf
((calcium or free acid) adj2 beta-hydroxy-beta-methylbutyrate).tw,kf
(beta-hydroxy-beta-methylbutyrate adj2 supplem*).tw,kf

Skeletal Muscle
Body composition
((lean or muscle) adj2 mass).tw,kf
Musc* adj2 Hypertrophy

Resistance Training
((resistance) adj2 (exercise or training)).tw,kf
Muscle strength

Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:
----
1 beta-hydroxy, beta-methylbutyrate.mp. (336)
2 hmb.mp. (2855)
3 HMB-Ca.mp. (12)
4 HMB-Fa.mp. (26)
5 1 or 2 or 3 or 4 (2917)
6 exp Muscle, Skeletal/ (263893)
7 muscle*.mp. (917658)
8 exp Muscle Strength/ (19245)
9 ((musc* or hand or grip) adj2 strength).mp. (55981)

10 Creatine Kinase/ (24181)
11 creatine kinase.mp. (37126)
12 Resistance Training/ (8337)
13 ((strength) adj2 training).mp. (5715)
14 Hypertrophy/ (22822)
15 muscular.mp. (125396)
16 Inflammation/ (153552)
17 inflam*.mp. (1030839)
18 exp Muscular Atrophy/ (14667)
19 sarcopenia.mp. (8626)
20 atroph*.mp. (137154)
21 or/6-20 (2129243)
22 5 and 21 (810)
23 remove duplicates from 22 (803)
24 animals/ not (humans/ and animals/) (4651948)
25 23 not 24 (721)
26 limit 25 to English language (667)

Database: Embase <1974 to 2020 April 02>
Search Strategy:
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1 beta-hydroxy, beta-methylbutyrate.mp. (437)
2 HMB.mp. (5163)
3 HMB-Ca.mp. (8)
4 HMB-Fa.mp. (21)
5 1 or 2 or 3 or 4 (5266)
6 exp skeletal muscle/ (335102)
7 muscle*.mp. (1534153)
8 muscle strength/ (61491)
9 ((musc* or hand or grip) adj2 strength).mp. (93810)
10 Creatine kinase.mp. or creatine kinase/ (68995)
11 muscle strength/ or muscle hypertrophy/ or resistance training/ (78812)
12 ((resistance or strength) adj2 training).mp. (24119)
13 hypertrophy/ (28416)
14 muscular.mp. (123936)
15 inflammation/ (430088)
16 inflam*.mp. (1499389)
17 muscle atrophy/ (31358)

18 sarcopenia.mp. (14170)
19 atroph*.mp. (225839)
20 musculoskeletal system inflammation/ (164)
21 or/6-20 (3213445)
22 5 and 21 (1489)
23 remove duplicates from 22 (1473)
24 animals/ not (humans/ and animals/) (955029)
25 23 not 24 (1452)
26 limit 25 to english language (1370)