The Bone Biomarker Response to an Acute Bout of Exercise:

A Systematic Review with Meta-Analysis

Supplementary File 1: PRISMA Checklist

Dolan E[1], Dumas A[1], Keane KM[2], Bestetti G[1], Freitas LHM[1], Gualano B[1,3], Kohrt WM[4], Kelley GA[5], Pereira RMR[6], Sale C[7], Swinton PA[8]*

[1] Applied Physiology & Nutrition Research Group; School of Physical Education and Sport; Rheumatology Division; Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[2] Department of Sport, Exercise and Nutrition, Galway Mayo Institute of Technology, Ireland.

[3] Food Research Centre, University of São Paulo, SP, BR.

[4] Department of Medicine, Division of Geriatric Medicine, University of Colorado Anschutz Medical Campus, USA.

[5] Department of Epidemiology and Biostatistics, West Virginia University, USA.

[6] Bone Metabolism Laboratory; Rheumatology Division, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[7] Musculoskeletal Physiology Research Group, Sport, Health and Performance Enhancement (SHAPE) Research Centre, School of Science and Technology, Nottingham Trent University, Nottingham, UK.

[8] School of Health Sciences, Robert Gordon University, Aberdeen, UK.

*Corresponding author:

Eimear Dolan:

Faculdade de Medicina FMUSP, Universidade de Sao Paulo – Av. Dr. Arnaldo, 455, 3º andar, ZIP code: 01246-903, Sao Paulo - SP, Brazil.

Phone: +55 11 2648-1337; Fax: +55 11 3061-7490; E-mail: eimeardol@gmail.com or eimeardolan@usp.br

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Line 2
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Lines 26 - 57
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Lines 100 - 143
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Lines 144 - 146
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Table 1 and Supplementary File 2
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Lines
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary File 4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Lines 173 – 177.
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Lines 179 – 190.
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Table 1 and Supplementary File 2.
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Table 1; Supplementary File 2 and Lines 188 – 190.
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Lines 236 – 243 and Supplementary File 4.
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Lines 193 – 230.
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Lines 179 – 190 and 219 – 224.

Section and Topic	Item #	Checklist item	Location where item is reported
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Lines 195 – 197.
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Supplementary File 5, 7 – 10.
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Lines 193 – 224.
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Lines 222 – 224.
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Lines 198 – 210.
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Lines 224 – 227.
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Lines 223 – 255.
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Lines 268 – 269 and Figure 1.
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	NA
Study characteristics	17	Cite each included study and present its characteristics.	Supplementary File 5.
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Lines 282 – 297 and Supplementary Files 7 – 10.
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Lines 302 – 307; Supplementary Files 7 – 10 and Figure 3.
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Lines 302 – 370 and Supplementary Files 7 – 10.
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Lines 302 – 370 and Supplementary Files 7 – 10.
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Lines 302 – 370;

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
			Supplementary Files 7 – 10.
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Supplementary Files 7 – 10.
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Lines 292 – 295; Figure 2 and Supplementary File 6.
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Lines 302 – 370 and Supplementary Files 7 – 10.
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Section 4.1 (Lines 397 – 494)
	23b	Discuss any limitations of the evidence included in the review.	Section 4.2 (Lines 496 – 522)
	23c	Discuss any limitations of the review processes used.	Section 4.2 (Lines 496 – 522)
	23d	Discuss implications of the results for practice, policy, and future research.	Section 4.3 (Lines 524 – 549)
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Lines 56 – 57.
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Lines 56 – 57 and 152.
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Lines 257 – 264.
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Lines 564 – 565.
Competing interests	26	Declare any competing interests of review authors.	Line 567.
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

PRISMA 2020 Checklist

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Supplementary File 2: Codebook

Dolan E[1]*, Dumas A[1], Keane KM[2], Bestetti G[1], Freitas LHM[1], Gualano B[1,3], Kohrt WM[4], Kelley GA[5], Pereira RMR[6], Sale C[7], Swinton PA[8]

[1] Applied Physiology & Nutrition Research Group; School of Physical Education and Sport; Rheumatology Division; Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

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*Corresponding author:

Eimear Dolan:

Faculdade de Medicina FMUSP, Universidade de Sao Paulo – Av. Dr. Arnaldo, 455, 3º andar, ZIP code: 01246-903, Sao Paulo - SP, Brazil.

Phone: +55 11 2648-1337; Fax: +55 11 3061-7490; E-mail: eimeardol@gmail.com or eimeardolan@usp.br

Column		Heading	Description
STUDY DETAILS	A	Study Number	Study number
	B	Author	First author surname *et al.,*
	C	Year	Year of publication
	D	Journal	Journal name
	E	Title	Study title
	F	Funding/COI	List all funding sources, and any declared conflict of interest.
	G	Aim	Study aim
	H	Design	Main study design, with brief description of conditions investigated.
	I	Design Code	Experimental Trials = 1; Observational Trials = 2
	J	Nutritional Intervention	0 = Studies without a nutritional intervention; 1 = Studies that include a nutritional intervention (e.g., exercise conducted with and without calcium supplementation)
	K	Nutritional Intervention	If column H is coded 1, provide a brief, free-text, description of the nutritional intervention under investigation.
POPULATION	L	Participant Overview	Brief descriptive overview of the participant population (age, sex, health and training status)
	M	Starting n	Number of individuals initially enrolled in the study.
	N	End n	Number of individuals who finished the study.
	O	Group	Number of independent groups who participated in the study.
	P	Training Status	1 = sedentary; 2 = recreationally trained; 3 = athlete.
	Q	Sex	1 = male, 2 = female, 3 = mixed male and female group.
	R	Age	Mean (yrs)
	S	Age	SD (yrs)

	T	Age	$1 = <18; 2 = 18 – 45; 3 = >45$
	U	Height	Mean (cm)
	V	Height	SD (cm)
	W	Weight	Mean (kg)
	X	Weight	SD (kg)
	Y	BMI	Mean
	Z	BMI	SD
	AA	Comments	Any additional information relevant information related to the participants investigated.
EXERCISE TEST DETAILS	AB	Exercise stimulus	Brief narrative description of the test undertaken.
	AC	Type	1 = resistance (defined as exercises that cause the body's muscles to work or hold against an applied force or weight, *e.g.,* weight lifting); 2 = aerobic (defined as activities whereby large muscle groups move in a rhythmic manner for a sustained period of time, *e.g.,* walking, running or cycling); 3 = multi-modal (defined as exercise bouts that comprise a combination of exercise modalities, *e.g.,* sessions that comprise a mixture of both resistance and aerobic exercises); 4 = plyometric (high-impact exercise types designed to develop muscular power, *e.g.,* jump based exercise bouts); 5 = calisthenics (systematic rhythmic body weight exercises, *e.g.,* yoga or pilates); 6 = no exercise control.
	AD	Aerobic type	1 = running; 2 = cycling; 3 = walking.
	AE	Aerobic type	1 = continuous; 2 = intermittent.
	AF	Aerobic Intensity	% (free text)
	AG	Aerobic Intensity	$1 = <80\%$ (low/moderate); $2 = >80\%$ (high/supramaximal). For studies that vary intensities throughout the test do not code, unless it is clear that the majority of the test was conducted at an intensity aligning to the categories (e.g., a brief warm-up at a lower intensity followed by fixed load test)
	AH	Aerobic Duration	Minutes
	AI	Resistance Intensity	$1 = <80\%$ (low/moderate); $2 = >80\%$ (high/supramaximal).

	AJ	Total reps	Sets*repetitions
	AK	Total work done (aerobic)	Intensity*Duration
	AL	Total work done (resistance)	Total reps*Intensity
	AM	Impact level	1 = low-impact/repetitive; 2 = moderate-impact/repetitive; 3 = low-impact with high muscular load; 4 = high-impact/multi-directional.
	AN	Active Versus Control	1 = Exercise; 2 = Non-exercise control
SAMPLING	AO	Samples	Brief narrative description of the number and timing of samples taken.
	AP	Baseline condition	Time of day (free text)
	AQ	Baseline condition	1 = fed; 2 = fasted
	AR	Bone biomarkers	List all bone biomarkers assessed.
	AS	Other biomarkers	List all other biomarkers assessed.
	AT	Bone biomarker	Name
	AU	Bone biomarker (code)	1 = bone specific alkaline phosphatase (B-ALP); 2 = dickkopf-1 (DKK-1); 3 = carboxyterminal propeptide of type 1 procollagen (P1CP); 4 = N-terminal propeptide of type 1 procollagen (P1NP); 5 = sclerostin; 6 = pyridinoline (Pyr); 7 = deoxypyridinoline (Dpd); 8 = carboxyterminal telopeptide of type-1 procollagen (ICTP); 9 = aminoterminaltelopeptide of type 1 collagen (NTx); 10 = cathepsin K; 11 = C-terminal telopeptide of type 1 collagen (β-CTX-1); 12 = tartrate resistance acid phosphatase isoenzyme 5b (TRAP5b), 13 = OPG/RANKL ratio, 14 = OPG, 15 = RANKL, 16 = hydroxylysine, 17 = hydroxylysine; 18 = osteopontin; 19 = total OC; 20 = ucOC 21 = iCa; 22 = Aca, 23 = PTH
	AV	Subtype	If information regarding specific biomarker subtype is provided, insert as free text.

	AW	Process	Free text
	AX	Process	1 = Formation (bone specific alkaline phosphatase (B-ALP (+)); dickkopf-1 (DKK-1 (-)); carboxyterminal propeptide of type 1 procollagen (P1CP (+)) and N-terminal propeptide of type 1 procollagen (P1NP (+)) and sclerostin (-); Undercarboxylated osteocalcin (ucOC (+)); 2 = Resorption (pyridinoline (Pyr (+)); deoxypyridinoline (Dpd (+)); carboxyterminal telopeptide of type-1 procollagen (ICTP (+)); aminoterminal telopeptide of type 1 collagen (NTx (+)); C-terminal telopeptide of type 1 collagen (β-CTX-1 (+)); tartrate resistance acid phosphatase isoenzyme 5b (TRAP5b (+)), osteoprotegerin (-); RANKL (+); the ratio of osteoprotegerin to receptor activator NF kappaB ligand (OPG/RANKL (-1)), hydroxylysine (+) and hydroxyproline (+)); 3 = General (osteopontin (+) and total osteocalcin (T-OC (+)); 4 = Ca Metabolism (ionized or albumin adjusted calcium (+) and parathyroid hormone (+))
	AY	Direction	1 = increase represents an increase in the relevant process; -1 = increase represents a decrease in the relevant process (e.g., sclerostin, DKK, OPG, OPG/RANKL).
	AZ	Sample type	Free text
	BA	Sample type code	1 = serum; 2 = plasma; 3 = urine.
	BB	Process	Brief narrative description of the assay used/assessment type.
	BC	Inter-assay variability	%
	BD	Intra-assay variability	%
	BE	Unit	Unit of measurement
MAIN DATA	BF	Baseline	Mean
	BG	Baseline	SD
	BH	Time	Exact time at which the measurement was taken

	BI	Time (code)	1 = sample taken immediately before the exercise bout (i.e., within 15 minutes before exercise commencement); 2 = samples taken within 15 minutes and 2 hours before exercise commencement); 3 = samples taken > 2 hours before exercise commencement); 4 = day before.
	BJ	Post Exercise	Mean
	BK	Post Exercise	SD
	BL	Time	Exact time at which the measurement was taken
	BM	Time	1 = sample taken immediately post exercise (i.e., within 15 minutes of exercise termination); 2 = samples taken within 15 minutes and 2 hours post exercise; 3 = samples taken within 2 and 8 hours post exercise; 4 = samples taken 1 day post exercise; 5 = samples taken 2 days post exercise; 6 = samples taken 3 days post exercise; 7 = samples taken 4 days post exercise, *etc*.
	BN	During/Post	1 = sample taken post exercise; 2 = sample taken during the exercise bout.
	BO	Comment	Any other relevant comments

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Supplementary File 3: Searches

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*Corresponding author:

Eimear Dolan:

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Phone: +55 11 2648-1337; Fax: +55 11 3061-7490; E-mail: eimeardol@gmail.com or eimeardolan@usp.br

MEDLINE = 1709

# ▲	Searches	Results	Type	Actions	Annotations
1	bone.mp. or "Bone and Bones"/	957226	Advanced	Display Results | More ▾	💬
2	Exercise/ or exercise.mp.	359857	Advanced	Display Results | More ▾	💬
3	physical activity.mp.	114381	Advanced	Display Results | More ▾	💬
4	biomarkers.mp. or Biomarkers/	539836	Advanced	Display Results | More ▾	💬
5	turnover.mp.	101121	Advanced	Display Results | More ▾	💬
6	Bone Remodeling/ or remodeling.mp.	125194	Advanced	Display Results | More ▾	💬
7	formation.mp.	1155930	Advanced	Display Results | More ▾	💬
8	Bone Resorption/ or resorption.mp.	62019	Advanced	Display Results | More ▾	💬
9	2 or 3	418547	Advanced	Display Results | More ▾	💬
10	4 or 5 or 6 or 7 or 8	1896333	Advanced	Display Results | More ▾	💬
11	1 and 9 and 10	2373	Advanced	Display Results | More ▾	💬
12	limit 11 to humans	1709	Advanced	Display Results | More ▾	💬

EMBASE = 3507

# ▲	Searches	Results	Type	Actions	Annotations
1	Bone.mp. or bone/	1372929	Advanced	Display Results | More ▾	💬
2	exercise/ or exercise.mp.	511133	Advanced	Display Results | More ▾	💬
3	physical activity.mp. or physical activity/	219864	Advanced	Display Results | More ▾	💬
4	biomarkers.mp. or biological marker/	467863	Advanced	Display Results | More ▾	💬
5	turnover.mp. or turnover rate/	122669	Advanced	Display Results | More ▾	💬
6	remodeling.mp. or bone remodeling/	192799	Advanced	Display Results | More ▾	💬
7	formation.mp.	1388334	Advanced	Display Results | More ▾	💬
8	resorption.mp.	61139	Advanced	Display Results | More ▾	💬
9	2 or 3	657767	Advanced	Display Results | More ▾	💬
10	4 or 5 or 6 or 7 or 8	2127106	Advanced	Display Results | More ▾	💬
11	1 and 9 and 10	4453	Advanced	Display Results | More ▾	💬
12	limit 11 to human	3507	Advanced	Display Results | More ▾	💬

Cochrane CENTRAL = 1012

(Reviews = 163; Protocols = 26; Trials = 823)

Bone Biomarker Review Search (21.11.20)

Last saved on: 21/11/2020 13:34:59

✔ Search saved.

#1	MeSH descriptor: [Bone and Bones] this term only		MeSH ▾	1461
#2	bone		Limits	59077
#3	MeSH descriptor: [Exercise] explode all trees		MeSH ▾	24409
#4	exercise		Limits	99716
#5	(physical activity):ti,ab,kw	S ▾	Limits	53374
	(Word variations have been searched)			
#6	biomarkers		Limits	33953
#7	MeSH descriptor: [Biomarkers] explode all trees		MeSH ▾	20199
#8	turnover		Limits	5758
#9	MeSH descriptor: [Bone Remodeling] explode all trees		MeSH ▾	2583
#10	remodeling		Limits	6533
#11	formation		Limits	20170
#12	MeSH descriptor: [Concept Formation] explode all trees		MeSH ▾	310
#13	resorption		Limits	4423
#14	(#1 OR #2) AND (#3 OR #4 OR #5) AND (#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13)		Limits	1012
	in Cochrane Reviews, Cochrane Protocols, Trials and Clinical Answers			

PEDro = 56

Same search terms but the system requires search terms be entered one by one, so couldn't record a screenshot. Results are available in a .ris file.

LILACS/Ibec = 35

Same search terms – used the title/abstract/subject option. Accessed via the Virtual Health Portal and restricted to LILACS and IBEC databases. Further filtered to controlled clinical trial, systematic review or observational study.

Copied from "study detail" option on the webpage.

(bone) AND (exercise OR physical activity) AND (biomarkers OR turnover OR remodeling OR formation OR resorption) AND (db:("LILACS" OR "IBECS") AND type_of_study:("clinical_trials" OR "systematic_reviews" OR "observational_studies"))

SPORT Discus = 438

Searching: SPORTDiscus with Full Text | Choose Databases

bone — Select a Field (optional) ▾ — Search

AND ▾ exercise OR physical activity — Select a Field (optional) ▾ — Create Alert

AND ▾ biomarkers OR turnover OR remodelling OF — Select a Field (optional) ▾ — Clear ?

Basic Search   Advanced Search   Search History ▸

Refine Results

Search Results: 1 - 10 of 438

Relevance ▾   Page Options ▾   Share ▾

Current Search

Boolean/Phrase:

bone AND (exercise OR physical activity) AND (biomarkers OR tu...

Expanders

Aplicar assuntos equivalentes ⊠

Source Types

Academic Journals ⊠

Limit To

☐ Full Text
☐ References Available
☐ English Abstract Available

1. Acute response of biochemical **bone turnover** markers and the associated ground reaction forces to high-impact **exercise** in postmenopausal women.

Prawiradilaga, Rizky S.; Madsen, Anders O.; Jørgensen, Niklas R.; Helge, Eva W., Biology of Sport 2020, Vol. 37 Issue 1, p41 (English Abstract Available)

Academic Journal

Subjects: BONE resorption; JUMPING, WOMEN'S health; **EXERCISE** intensity; WEIGHT-bearing (Orthopedics); RESISTANCE training; PROTEIN analysis; **BIOMARKERS**; DOSE-response relationship in biochemistry; GROUND reaction forces (Biomechanics); STATISTICAL sampling; RANDOMIZED controlled trials, POSTMENOPAUSE; DESCRIPTIVE statistics; OSTEOCALCIN

📄 PDF Full Text   ☁ Salvar PDF em Nuvem   (868KB)

2. The effect of intermittent running on **biomarkers** of **bone turnover**.

Evans, W.; Nevill, A.; McLaren, S. J.; Ditroilo, M., European Journal of Sport Science May2020, Vol. 20 Issue 4, p505 (English Abstract Available)

Academic Journal

Subjects: BONE remodeling; **BONE resorption**; BONE growth; CIRCADIAN rhythms; COLLAGEN; **EXERCISE** physiology; RUNNING; TREADMILLS; HIGH-intensity interval training; METABOLISM; **BIOMARKERS**; CONFIDENCE intervals; MEDICAL protocols; EMPLOYEES' workload; RANDOMIZED controlled trials

Cited References: (45)

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Supplementary File 4: Modified Downs & Black Checklist

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*Corresponding author:

Eimear Dolan:

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Phone: +55 11 2648-1337; Fax: +55 11 3061-7490; E-mail: eimeardol@gmail.com or eimeardolan@usp.br

Q.1. *Is the hypothesis/aim/objective of the study clearly described*? (Yes = 1; No = 0)

Q.2. *Are the main outcomes to be measured clearly described in the introduction or methods section?* If the main outcomes are first mentioned in the results section, answer no. (Yes = 1; No = 0).

Q.3. *Are the characteristics (e.g., age, height, weight, training and health status) of the participants included in the study clearly described?* (Yes = 1; No = 0).

Q.4. *Are the interventions of interest clearly described?* For exercise interventions, the type, intensity and duration should be described. If they provide a nutritional supplement the exact type and dose should be provided (Yes = 1, No = 0).

Q.5. *Are the main findings of the study clearly described?* Simple outcome data should be reported for all major findings so the reader can check the major analyses and conclusions. This does not cover statistical tests. (Yes = 1; No = 0).

Q.6. *Does the study provide estimates of the random variability in the data for the main outcomes?* In non-normal data, inter-quartile range should be reported. In normal data, standard deviation, standard error or confidence intervals should be reported. (Yes = 1; No = 0).

Q.7. *Have all important adverse events that may be a consequence of the intervention been reported.* Answer yes if they confirm they have ethical approval (Yes = 1; No = 0).

Q.8. *Was an attempt made to blind study subjects to the intervention they have received?* For exercise interventions where it is not possible to blind, answer yes. Answer no if the intervention contains a supplement/placebo arm, and this is not blinded. (Yes = 1, no = 0, unable to determine = 0)

Q.9. *Was an attempt made to blind those measuring the main outcomes of the intervention?* For exercise interventions where it is not possible to blind, answer yes. Answer no if the intervention contains a supplement/placebo arm, and this is not blinded. (Yes = 1, no = 0, unable to determine = 0)

Q.10. *If any of the results of the study were based on 'data dredging' was this made clear?* Any analyses that had not been planned at the outset should be clearly indicated. If no retrospective subgroup analyses were reported, then answer yes. (Yes = 1; No = 0; Unable to determine = 0).

Q.11. *Was the timing of blood sampling clearly described?* Answer yes if the precise time-points were provided. Answer no if it is not clear exactly when the blood samples were drawn (Yes = 1, no = 0, no = 0).

Q.12. *Were the statistical tests used to assess the main outcomes appropriate?* (Yes = 1, no = 0, Unable to determine = 0).

Q.13. *Were the main outcome measures used accurate (valid and reliable)?* For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work that demonstrates the outcome measures are accurate, or that use commonly used tests, the question should be answered yes (Yes = 1, No = 0; Unable to determine = 0).

Q.14. *Were study subjects randomised to intervention groups?* Answer yes if the order of treatment, or allocation to groups, was randomly assigned. If it was not possible for the study to be randomised (e.g., single-trial studies) answer yes. (Yes = 1; No = 0; Unable to determine = 0)

Q.15. *Was at least one familiarization session conducted prior to exercise testing?* Answer yes if they conducted a familiarization trial, or if familiarization was not necessary (*e.g.,* if the study uses a single, non-performance-based, exercise bout). (Yes = 1; No = 0; Unable to determine = 0).

Q.16. *Were the exercise test conditions adequately standardised and described?* Factors to consider include confirmation of the time of day that testing was conducted (score yes if the exact time of day that tests were conducted was reported, and this was the same for all participants), and control for unusual activity (score yes if they requested that participants avoid unusual or very strenuous activity for at least 24 hours prior to the test) or nutritional factors in the days prior to the exercise test (score yes if they request participants to maintain usual feeding habits the day before). Yes (all 3 factors considered) = 3; Yes (most factors (2 of the 3) considered) = 2; Yes (some (1 of the 3) factors considered) = 1; No = 0; Unable to determine = 0.

Q.17. *Was nutritional status for blood sampling adequately described*? Answer yes if the strategy for standardization was described in sufficient detail to allow for replication. (Yes = 1, No = 0, Unable to determine = 0)

Q.18. Were samples corrected for plasma volume changes? Yes = 1; No = 0.

Max attainable score = 20. The combined score will be used to categorise each study according to 4 categories, i.e., High (18 - 20), Moderate (15 - 17), Low (11 - 14) or Very Low (≤ 10)

Note: For any question where the response cannot be ascertained based on the information presented in the article, score 0 (unable to tell).

Original Reference:

Downs SG & Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health*. 1998; 52(6): 377 – 384.

The Bone Biomarker Response to an Acute Bout of Exercise:

A Systematic Review with Meta-Analysis

Supplementary File 5: Characteristics of Included Studies

Dolan E[1]*, Dumas A[1], Keane KM[2], Bestetti G[1], Freitas LHM[1], Gualano B[1,3], Kohrt WM[4], Kelley GA[5], Pereira RMR[6], Sale C[7], Swinton PA[8]

[1] Applied Physiology & Nutrition Research Group; School of Physical Education and Sport; Rheumatology Division; Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[2] Department of Sport, Exercise and Nutrition, Galway Mayo Institute of Technology, Ireland.

[3] Food Research Centre, University of São Paulo, SP, BR.

[4] Department of Medicine, Division of Geriatric Medicine, University of Colorado Anschutz Medical Campus, USA.

[5] Department of Epidemiology and Biostatistics, West Virginia University, USA.

[6] Bone Metabolism Laboratory; Rheumatology Division, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[7] Musculoskeletal Physiology Research Group, Sport, Health and Performance Enhancement (SHAPE) Research Centre, School of Science and Technology, Nottingham Trent University, Nottingham, UK.

[8] School of Health Sciences, Robert Gordon University, Aberdeen, UK.

*Corresponding author:

Eimear Dolan:

Faculdade de Medicina FMUSP, Universidade de Sao Paulo – Av. Dr. Arnaldo, 455, 3º andar, ZIP code: 01246-903, Sao Paulo - SP, Brazil.

Phone: +55 11 2648-1337; Fax: +55 11 3061-7490; E-mail: eimeardol@gmail.com or eimeardolan@usp.br

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Alkahtani et al. [1]	Saudi Arabia	To investigate the effects of flat versus downhill running on bone biomarkers.	Counterbalanced cross-over design, whereby participants took part in three experimental trials (flat running, downhill running or control).	Healthy, active men (n = 14)	Flat running: 5 X 8-minute stages conducted at 60% VO2 max, interspersed with 2 minutes of lower speed running. Downhill running: 5 X 8-minute stages conducted at 60% VO2 max, interspersed with 2 minutes of lower speed running.	P1NP, osteocalcin and β-CTX-1 measured pre, immediately and 24 hours post-exercise.
Ashizawa et al. [2]	Japan	To investigate if a single bout of resistance training induces hypercalciuria and how is it mediated.	Single-measure experimental design, whereby participants took part in a 9 day experimental trial with a controlled diet and a single session of resistance exercise	Healthy, recreationally trained oriental men (n = 10)	Resistance: 3 sets of 7 exercises: Bench press, back press, arm curl, double leg extension, bent-leg incline sit up, lateral pull down leg press Intensity = 60% 1RM, 80% 1 RM, 80% 1RM	Urine samples; DPYR, total ionized calcium and PTH. 30min samples before exercise bout, sample during exercise bout and 4 samples post exercise
Ashizawa et al. [3]	Japan	To investigate the effects of a single bout of resistance exercise on urinary calcium excretion and markers of bone metabolism in untrained male subjects.	Single-measure experimental design, whereby participants took part in a 9 day experimental trial with a controlled diet and a single session of resistance exercise	Healthy, untrained Oriental men (n = 14)	Resistance: 3 sets of 10 reps of bench press, back press, arm curl, double leg extension bent leg incline sit up Intensity = 60% 1RM, 80% 1 RM, 80% 1RM	Osteocalcin, B-ALP, TRAP, PICP, DPYR, urinary calcium. Fasted samples on day before exercise bout, day of exercise bout and 3 days after exercise bout
Banfi et al. [4]	Italy	To investigate the influence of rugby training on the OPG-RANK-RANKL system	Observational study Morning Rugby practice	Professional rugby players, men (10)	Morning practice during normal Rugby training session	OPG, RANK, RANKL 2 samples: one before and one after training.

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Barry et al. [5]	United States (Colorado)	To investigate the effects of calcium supplementation before and during exercise	Experimental study Randomized cross-over design whereby participants completed three 35-kilometer time trials under different conditions of Ca supplementation	Healthy, well-trained cyclists and triathletes, men (20)	35km time trial (on a cycle ergometer)	PTH, iCA, CTX, B-ALP Pre, every 15 min during and immediately on competition
Bemben et al. [6]	United States (Oklahoma)	To investigate the effects of low intensity resistance exercise on bone biomarkers	Randomized cross-over design where each subject performed both the restricted blood flow (KAATSU) condition and resistance exercise control condition in random order	Healthy recreationally active men (9)	Warm up of 30 repetitions at 20% 1RM, followed by 3 sets of 15 repetitions at 20%1RM.	B-ALP, NTx 3 samples (rest, immediately after and 30 min post)
Bemben et al. [7]	United States (Oklahoma)	To investigate the response of bone turnover markers to resistance exercise (RE) and to resistance exercise combined with WBV (WBV + RE) in young men	Randomized cross-over design Participants completed two exercise protocols in random order separated by a two week washout period	Healthy, recreationally active men (10)	RE only: 3 sets of 10 repetitions of each exercise at 80% 1RM (9 exercises)	B-ALP, TRAP5b, CTX-1 3 samples (rest, immediately after and 30 min post)
Bowtell et al. [8]	Sweden	To investigate whether a single bout of either football or body vibration would induce favorable responses in markers of bone turnover and muscle strain in premenopausal inactive women.	Randomized design whereby participants were assigned to one of three groups: short duration football (13.5 min small sided football) or longer duration (4x13.5 min small sided football) or or whole body vibration	Healthy, premenopausal inactive women (11) Healthy, premenopausal inactive women (13)	Long duration football Short duration football	CTX-1, P1NP, OC: Before, during (after 15 min), and immediately, 30min and 48hrs post CTX-1, P1NP, OC: Before, and immediately, 30min and 48hrs post

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Brahm et al. [9]	Sweden	To investigate the relationship between exercise intensity and bone biomarkers response	Single measure experimental design, whereby participants completed a single, standardized, running exercise test on a treadmill at varying intensities	Healthy men and women (20)	10 minute warm-up at 30% VO2 max, followed by 10 minutes of a submaximal load at 47, then 76% VO2 max followed by a maximal effort until exhaustion lasting for 4 - 5 minutes.	Osteocalcin, P1CP, ICTP, calcium, PTH. At rest, after 10 minutes at 47%, after 10 minutes at 76%, 5 minutes post exhaustion, after 30 mins of recovery and after 24 hours of recovery.
Brahm et al. [10]	Sweden	To investigate hormone, growth factors, bone and muscle metabolism response during exercise	Single-measure acute intervention whereby participants completed a single, standardized, exercise test comprising one legged knee extension.	Healthy, sedentary men and women (12)	One-legged dynamic work with the knee extensor on a modified Krogh bicycle ergometer - warm up 10 minutes, 15 minutes of submax work corresponding to 38 and 61% of peak one leg VO2 respectively then finishing with about 5 minutes of maximal work.	PTH, calcium, OC, PICP, B-ALP, ICTP Blood samples drawn at rest, after the different workloads (10 and 25 minutes), immediately after and 5, 30, and 60 minutes post exercise
Brown et al. [11]	United Kingdom (England)	To investigate the effect of exercise on indirect indices of skeletal damage	Single-measure, acute intervention whereby participants performed a single bout of 50 maximum voluntary eccentric muscle contractions using the knee extensors of a single leg	6 women and 2 men with no weight training for 6 months (8)	Single bout of 50 maximum voluntary eccentric muscle contractions using the knee extensors of a single leg.	hydroxylysine, hydroxyproline and PYD Samples at pre-exercise and on days 1, 2, 3, 5, 7 and 9 following the bout.

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Brown et al. [12]	United Kingdom (England)	To investigate the effects of concentric muscle action on muscle damage and collagen breakdown	Experimental design whereby all participants took part in 2 resistance sessions, the first session focused on concentric, the second on eccentric movements.	Men and women with no resistance training in the last 6 months (9)	50 maximum voluntary concentric and eccentric actions of the knee extensors of a randomly chosen leg	Plasma Hydroxyproline Samples before exercise, after exercise and on days 1, 2, 3, 7 and 9 after each exercise bout
Clifford et al. [13]	United Kingdom (England)	To investigate whether the consumption of collagen peptides after exercise could attenuate muscle damage	Double blind, placebo controlled, independent group, whereby participants were randomized to one of 2 experimental groups: supplementation with collagen peptides or placebo and performed a drop jump protocol.	Healthy recreationally active men (12)	150 drop jumps from a 60cm box - jumps were performed in sets of 6 x 25 separated by 2 mins rest - for each jump participants were instructed to land on 2 ft, squat to 90 degrees then jump vertically with maximal effort	B-CTX, P1NP Blood samples were collected pre supplementation, pre exercise, post exercise, and1.5h, 24h, and 48h post
de Sousa et al. [14]	Brazil (São Paulo)	To investigate the effect of CHP beverages on bone biochemical in elite runners	Independent, group, randomized, double-blind design, whereby participants were randomly assigned to either the CHO or the control group and took part in an intermittent running session	Elite runners, men (24)	Intermittent running protocol: participants underwent 13 training sessions over a period of 8 days. On day 9, athletes performed an intermittent running protocol which consisted of 10 series of 800 m (10x800 m) performed at 3-km time trial pace	CTX, P1NP, osteocalcin, PTH Samples at pre training (-9 days), 140 min before intermittent running protocol, after intermittent running protocol and 80 minutes after running protocol

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Dekker et al. [15]	Canada (Ontario)	To investigate the levels of anabolic and catabolic osteokinesis at rest, in pre and postmenarchal girls	Single-measure, acute intervention whereby participants took part in a single plyometric session with biomarkers measured both before and after this session	Recreational active premenarchal girls (14) Recreational active postmenarchal girls (12)	A minimum of 100 jumps organized into 5 circuit training stations (box jumps, lunge jumps, tuck jumps, single leg hopping and jumping jacks)	Sclerostin, DKK-1, OPG/RANKL Samples at pre exercise and 5min, 1h and 24h post
Diaz Castro et al. [16]	Spain	To investigate the effect of uiquinol prior to high intensity exercise on bone and energy levels	Parallel group, randomized, controlled trial, whereby participants were randomized into either the ubiquinol or placebo group, and performed two exercise tests (separated by 24 hours) after a 2 week supplementation period.	Healthy, well trained firemen (38)	Circuit composed of 10 resistance exercises (athletic press, chest press, seated oar, shoulder press, femoral bicep flexion, chest press, step with weight, surveyors pole chest, shove with weight, quad extension)	PTH, osteocalcin, osteopontin, OPG, sclerostin Samples at pre supplementation, pre exercise, post exercise, 24h post
Ehrnborg et al. [17]	Sweden	To investigate the effects of the serum concentrations of hormones in the GH/IGF-I axis and among bone markers in 117 elite athletes of both genders and different sports in relation to a maximum exercise test	Participants took part in a single maximum exercise bout - the nature of the exercise stimulus was specific to each athlete.	Elite athletes (84 men and 33 women) alpine skiers (21); cross-country skiers (23); long distance cyclists (9; sprint cyclists (3), decathletes (2) footballers (10); rowing (16); swimmers (1); tennis (3); triathlon (8); weight lifting (15). Elite.	Each athlete group did a test specific to their sport	Osteocalcin, PICP, ICTP Pre exercise, immediately after, and 15min, 30min, 60min, 90 min, 120 min after exercise bout

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Evans et al. [18]	United Kingdom (England)	To investigate the magnitude of the effect of both internal and external load-matched intermittent exercise protocols of varying exercise-to-rest durations, on traditional	Randomised repeated measures cross-over design, whereby each participant took part in 4 experimental trials, namely one control, and 3 45-minute exercise protocols with varying exercise to rest intervals.	Healthy men that participated in at least 3 impact exercises sessions per week (12)	Highly intermittent running with speed varying from 55 - 95% VO2 max Moderately intermittent running with speed varying from 55 - 95% VO2 max Low intermittent running with 80 seconds running at 75% max, interspersed with 80 seconds of recovery walking.	CTX-1, P1NP Samples pre exercise and 1h, 2h and 24h post
Falk et al. (2015) [19]	Canada (Ontario)	To investigate the acute response of sclerostin and PTH to a single exercise session of high mechanical loading in boys and men	Participants (boys and men) took part in a single plyometric exercise bout	Healthy nonobese boys (12)	Exercise circuit consisting of 6 jump stations for a total of 144 jumps (3 sets of 2 repetition with 3-min recovery between sets	Sclerostin, PTH Samples at pre-exercise and 5 min, 1 hr and 24 hour post exercise.

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Gombos et al. [20]	Hungary	To to investigate the direct effects of specific training and walking on bone metabolic markers, and to analyse if there is any difference between the effects of the two types of exercise.	Parallel group experimental design, whereby 2 groups of women took part in an acute exercise bout, with biomarkers measured pre and post.	Specific: healthy young women (25) Walking: healthy young women (25)	Specific: 10 minute warm-up followed by low/high impact exercises (mainly axial load) for 20 minutes. Then exercises performed in various positions (lying, high creeping, low creeping, sitting and standing) for 20 minutes. At the end there was a 10 minute cool down Walking: walking to a metronome set to 120bpm for 60 minutes	PTH, CTX-1, B-ALP Samples before and after training
Gombos et al. [21]	Hungary	To investigate the acute response of plasma markers of bone formation (BALP) and resorption (CTX and sclerostin) to a single session of either walking or resistance exercise.	Randomized, parallel-group study design. Participants were randomly allocated into one of three. groups: resistance exercise, walking or non-exercise control, with biomarkers measured pre and post this exercise bout.	Resistance: older adults with osteoporosis/osteopenia (50) Walking: older adults with osteoporosis/osteopenia (50) Walk training: older adults with osteoporosis/osteopenia (50)	Resistance: 8 minutes of dynamic exercises. Main body of session comprised approx. 30 minutes of muscle strengthening and core stabilization. Walking: moderate intensity brisk walking at a 100 steps per minute Walk training: no exercise, control group	B-ALP, CTX, SOST Samples at baseline and immediately after

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Grimston et al. [22]	Canada (Alberta)	To investigate the effect of treadmill running on calciotropic hormones	Repeated-measures, parallel group experimental design, whereby female distance runners undertook a 45 minute submaximal exercise test, with and without an oral calcium load. Control subjects (non-runners) sat stationary. Bloods taken pre and post the exercise bout. Runners are divided into those with normal or low BMD. The control subjects did not take part in the exercise trial.	Long distance runner with normal BMD (4) Long distance runner with low BMD (5)	45 minute run at self selected training pace	Osteocalcin, calcium, PTH Samples at pre exercise, immediately after exercise and 2.5 hours after exercise
Guerriere et al. [23]	United States (Massachusetts)	The investigate the influence of acute exercise on sclerostin under controlled diet	Randomized cross-over design, whereby participants took part in a plyometric exercise session or a non-exercise control period. All participants ingested a calcium controlled diet prior and throughout each study period.	Healthy young, active, on-duty army men (14)	10 sets of 10 repetitions of maximal effort jumps at 40% of their estimated 1RM.	B-ALP, TRAP5B, CTX, DKK-1, Sclerostin, PTH, Calcium Samples at baseline, 12h, 24h, 48h and 72h post

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Guillemant et al. [24]	France	To investigate the acute effects on bone metabolism of intensive endurance bicycling, and to determine whether the simultaneous intake of calcium could modify these effects	Randomized cross-over design whereby participants took part in two experimental sessions during which they did an exercise test with and without pre-supplementation calcium intake.	Well trained, endurance triathletes, men (12)	1 hour of cycling at 80% VO2 max	CTX, B-ALP, PTH, calcium Samples: immediately before exercise bout, 30 minutes into the exercise bout, and immediately, 30 60, 90, 120 and 180 minutes post-exercise
Haakonssen et al. [25]	Australia	To investigate the effects of consuming calcium rich foods pre exercise	Repeated-measures, counter-balanced, cross-over experimental design, whereby participants performed two experimental exercise trials separated by one day in which they undertook the same exercise trial each time, preceded by either a low or high calcium pre-exercise breakfast.	Competitive cyclists; female (32)	80min cycling at 60% VO2 max and a 10min time trial	CTX-1, P1NP, PTH, iCa Samples at fasted, immediately pre exercise, immediately post exercise and 40, 100 and 190 minutes after exercise bout
Hammond et al. [26]	United Kingdom (England)	To investigate the effect of CHO and caloric restriction on skeletal muscle cells	Randomized, repeated-measures, cross-over experimental design, whereby participants took part in three running high intensity interval training experimental conditions	Trained runners, male (9)	High intensity interval training session of 1 hour. 8 x 5-minute running bouts at a velocity corresponding to 85% VO2peak interspersed with 1min recovery at walking pace	B-CTX-1, P1NP 6 samples were taken, but only pre and post exercise were used

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Heikura et al. [27]	Australia	To investigate the bone response in endurance athletes on a ketogenic diet	Parallel group, single-measure acute intervention whereby two independent groups undertook a period of intensified training for 3.5 weeks, supported by either a high CHO or an isoenergetic LCHF diet. The experimental trial took place at baseline, after adaptation to the diet and after CHO restoration, and involved a strenuous exercise bout.	Elite race walker athletes (25 male, 5 female)	A hybrid laboratory/field test of 25km (males) or 19km (females) at around 50km race pace (75% VO2 max) RACE WALKING	CTX, P1NP, Osteocalcin Samples fasted at morning, pre exercise, post exercise and 3h after exercise
Hermann et al. [28]	Germany	To investigate if lactic acidosis exercise induced stimulates osteoclasts	Parallel-group, single-measure, acute intervention, whereby participants (separated into 4 separate groups, i.e., male athletes, female athletes, male sedentary controls and female sedentary controls) took part in three 60-minute exercise trials, i.e., at 75, 95 and 110% of their anaerobic threshold, with these trials occurring in a randomized order.	Male athletes (8) Sedentary male, control (7) Female athletes (8) Sedentary female control (9)	60 minutes cycling at 75% anaerobic threshold - intended not to create a pH shift 60 minutes cycling at 95% anaerobic threshold - at the anaerobic threshold so should shift pH 60 minutes cycling at 110% anaerobic threshold - intended to markedly shift pH	Trap5b, CTX, P1NP, osteocalcin Before, and 3h and 24h post

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Hiam et al. [29]	Australia (Victoria)	To investigate if GWAS SNPs that were previously identified to be associated with bone related phenotypes can predict circulatating tOC, ucOC and cOC at baseline and following an acute bout of high intensity interval exercise.	Single-measure, acute-intervention experimental design whereby blood samples were taken before and after a 24-minute cycling HIIT session.	Healthy, white men (73)	High intensity interval session on a cycle ergometer, consisting of 8x2 min intervals at 40% (Wpeak-LT)+LT with 1 minute of active recovery intervals at a power of 60W.	Total carboxylated and uncarboxylated osteocalcin Samples pre, immediately post and 3h after exercise
Hiam et al. [30]	Australia (Victoria)	To investigate if osteocalcin responds different between sexes at HIIT exercise	Based on the GeneSMART cohort. Single-measure, acute experimental design. Bone biomarkers were measured before, immediately after and 3 hours after an acute bout of experimental HIIE.	Healthy, premenopausal women (22)	High intensity interval session on a cycle ergometer, consisting of 8x2 min intervals at 40% (Wpeak-LT)+LT with 1 minute of active recovery intervals at a power of 60W.	Total carboxylated and uncarboxylated osteocalcin Samples pre, immediately post and 3h after exercise
Horswill et al. [31]	United States (Illinois)	To investigate whether urine levels of 3MH and OHP change as a result of a single bout of weight training.	Parallel group, single-measure acute intervention whereby participants performed a resistance training session. Control group did not perform exercise	Exercise group: moderately active (9: 5 women, 4 men) Control group (9: 6 women, 3 men)	Resistance exercise bout: consisted of three circuits. The first circuit involved doing a maximum number of repetitions, with approx. 80% 1RM for each respective exercise. The second and third circuits consisted of doing a maximum number of repetitions with a resistance of approx. 60% and 40% 1RM, respectively	Hydroxyproline 24 hour urine samples collected: pre sample collecged on day before exercise bout, second smple started after exercise bout. The third and final collection began at the end of POST1 and continued for the next 24 hours

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Huang et al. [32]	Taiwan	To investigate bone changes in men at knee exercises	Single-measure acute intervention whereby participants undertook an exercise bout (max eccentric contractions) with biomarkers measured pre and post.	Healthy, sedentary men (39)	10 sets of 10 MaxEC knee extensors and flexors respectively, on each leg with a counterbalanced order, thus the total number of max eccentric contractions was 400 for each participant.	Osteocalcin, CTX-1, P1NP Samples at baseline, immediately after exercise, and 1, 2, 4 and 7 days after exercise
Jurimae et al. [33]	Estonia	To investigate the influence of prolonged low-intensity single scull rowing exercise on plasma adipocytokine and ostekine concentrations	Quasi-experimental or observational experimental design whereby venous blood samples were obtained before and after an approximately 2h constant load on-water sculling training session.	National level rowers, male (9)	Long-distance on-water rowing in a single scull boat for 2h	Osteocalcin, ICTP. Samples before, after and 30 min post exercise
Kish et al. [34]	Canada (Ontario)	To investigate the acute response and recovery of biochemical markers of bone metabolism induced by a high-impact, plyometric exercise protocol	Single-measure acute intervention whereby bone biomarkers were assessed pre and post a plyometric training session in boys and men.	Men age 18-30, not athletes (14) Boys age 8-12, not athletes (12)	High impact weight bearing circuit session comprising drop jumps, lunge jumps, hurdle jumps, single leg hops and jumping jacks - 3 sett of 8 repetitions (144 jumps in total).	B-ALP, OPG, RANKL, NTx 4 blood samples taken: at rest before exercise bout, and 5 minutes,1 hour and, 24 hours post exercise bout
Klentrou et al. [35]	Canada (Ontario)	To investigate potential sex related differences in the Wnt signaling-related osteokines, at rest and in response to plyometric exercise in prepubertal and early pubertal children.	Single-measure, acute experimental intervention whereby bone biomarkers were measured in 12 girls and 12 boys before and after a plyometric exercise session.	Recreationally active, pre-menarchal girls (12) Recreationally active boys (12)	High impact weight bearing circuit session comprising drop jumps, lunge jumps, hurdle jumps, single leg hops and jumping jacks - 3 sets of 8 repetitions (144 jumps in total).	Sclerotisn, DKK-1, OPG, RANKL Samples at rest, and 5 minutes, 1 hour and 24 hours post-exercise

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Kohrt et al. [36]	United States (Colorado)	To investigate whether the increases in PTH and bone resorption during exercise are prevented when serum iCa concentration is maintained	Cross-over experimental design, whereby participants took part in 2 exercise sessions, namely an experimental condition where Ca was infused at a rate intended to maintain serum CA content. In the other volume matched saline was infused. The tests were done in a standardised order so that they could calculate the volume of saline required for the 2nd test.	Men aged 18-45 accustomed to cycling (11)	60 minutes of vigorous cycling at 80% HRM WITH SALINE INFUSION (CONTROL)	Total and ionized calcium, PTH, CTX, P1NP 12 samples - pre infusion, pre exercise, each 15 minutes during exercise, and throughout the 4 hour recovery period.
Kohrt et al. [37]	United States (Colorado)	To investigate whether varying the thermal conditions during cycling exercise at ~75% VO2 peak (warm vs. cool) to manipulate sweat rate and dermal Ca loss influences iCa, PTH and CTX response to exercise	Randomized, counter-balanced, repeated-measures experimental design whereby participants completed two identical exercise sessions, one in a cold and the other in a warm environment.	Active accustomed to cycling; men (12) Active accustomed to cycling; women (14)	60 min exercise bout at 75% VO2 and at self-selected cadence WARM	PTH, CTX, ionised calcium 10 sample, 15 and 0 minutes before, post 15, 30, 45 and 60 minutes during, and after 15, 30, 45 and 60 minutes post exercise

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Kouvellioti et al. [38]	Canada (Ontario)	To investigate and compare the response of sclerostin to two modes of high intensity exercise (impact, running versus noimpact, cycling) in young women and examined whether potential exercise-induced changes in sclerostin are accompanied by changes in bone resorption (CTXI) and formation (PINP) markers.	Randomized, repeated-measures, cross-over within subject experimental design, where each participant performed a running and a cycling HIIT trials	Healthy, recreationally active women (20)	High intensity interval RUNNING - 8 intervals of 1 minute running with 1 minute recovery High intensity interval CYCLING - 8 intervals of 1 minute cycling with 1 minute recovery	Sclerostin, CTX1, P1NP 5 samples - resting (pre-exercise) and 5 min, 1 hour, 24 hours and 48 hours post exercise
Kouvelioti et al. [39]	Canada (Ontario)	To investigate exercise induced changes in sclerostin and in bone turnover markers in young men two different modes of high-intensity interval exercise (impact running vs. no-impact cycling)	Participants took part in two, randomly ordered, exercise sessions (high-intensity interval running or high-intensity interval cycling) with biomarkers tested pre and post.	Healthy recreationally active men (20)	High intensity interval running - 8 intervals of 1 minute RUNNING with 1 minute recovery High intensity interval cycling - 8 intervals of 1 minute CYCLING with 1 minute recovery	Sclerostin, CTX1, P1NP 5 samples - resting (pre-exercise) and 5 min, 1 hour, 24 hours and 48 hours post exercise

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Kovárová et al. [40]	Bratislava	To investigate the acute response of serum bone turnover markers (B-ALP and sclerostin) to two single sessions of different resistance exercises in women.	Repeated measures, randomized, experimental design, whereby women took part in three experimental sessions, namely two single resistance exercise bouts and a non-exercise control.	Active women (7)	Reistance session: Constant resistance (ISOF) comprising 6 sets of 6 reps at 75% 1RM Resistance session comprising: Isokinetic mode. One loading cycle (repetition) represents 1 concentric and 1 eccentric phase of the movement Exercise protocol with serial stretch loading (SSL) Non-exercise control group:	B-ALP, sclerostin 3 Samples: pre exercise, and 24 and 48h post-exercise
Kristofersson et al. [41]	Sweden	To investigate whether short-term maximal exercise influences serum levels of calcium and PTH, and bone biomarkers.	Participants took part in a single experimental trial (wingate) with bone biomarkers assessed pre and post.	Healthy, ice hockey players; male (7)	modified wingate at 7.5% body weight	Total and ionized calcium, PTH, PICP, ICTP, osteocalcin 3 samples - during the hour before the test and 5 and 60 minutes post.

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Langberg et al. [42]	Denmark	To investigate local and circulating markers of T1 collagen synthesis and degradation after exercise.	Single-measure, acute intervention, whereby participants completed a 3 hour running bout. Samples were taken pre and post	Trained runners, 6 men and 1 women (7)	36km of running at a pace of 12km/hr.	PICP, ICTP Samples drawn every 30min during rest and recovery. The experiment consisted of a rest period of 60 min, an exercise period of 180 min and a recovery period of 120min
Lehrskov et al. [43]	Denmark	To assess the tole of IL-6 in regulating CTX and P1NP in a crossover design during an acute exercise bout	Single-measure, placebo-controlled, single blind, cross-over study whereby participants were infused with either saline or the IL-6 receptor antibody prior to an exercise bout in which they ran for 1hr at 75% VO2 max	Healthy men (5)	1 hr treadmill run at 75% of VO2 max.	CTX, P1NP 5 blood samples taken: immediately post-infusion, 20, 40, 60 minutes into the run, and after the run. After the run an MMTT was undertaken and more samples were taken but not used for meta-analysis.
Levinger et al. [44]	Australia (Victoria)	To investigate whether glucose loading reduces bone remodeling.	The study has both an in vivo and in vitro portion. Pre and postmenopausal women particpated in a rnadomized-control cross-over design. In one condition bone biomarkers were measured pre and post an OGTT. In the other an exercise test was done before the OGTT	Healthy, premenopausal women (8)	30 minutes on a cycle ergometer at an intensity of 70-75% VO2 peak.	Total and uOC, P1NP, B-CTX 4 samples taken: before exercise, immediately after exercise and, 30 and 60 minutes post exercise

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Lin et al. [45]	Taiwan	To investigate the acute responses of bone metabolism induced by two exercises (running and plyometric jumping)	Parallel group, randomized, controlled trial, whereby participants were randomly assigned to one of three groups, namely plyometric jumping, interval running or control.	Group 1: young men (8) Group 2: young men (8) Group 3: young men (8)	Group 1: plyometric jumping comprising a series of forward and lateral jumps Group 2: Interval Running, comprising 10 reps of 200m running Group 3: control, no exercise	Osteocalcin, TRAP, calcium 9 samples, i.e., fasted in the morning (and before a standardized breakfast) then 5 min, 15 min, 1, 3, 6, 24, 48 and 72 hours post exercise.
Maimoun et al. [46]	France	To investigate the extent to which a single session of brisk walking exercise affects bone metabolism related hormones in active elderly subjects.	Single-measure, acute, experimental study whereby participants performed a maximal incremental walking test.	Healthy, active, elder men and women (21)	Maximal incremental walking test conducted at their individually determined preferred walking speed	ionised calcium, intact PTH, CTX, OC, B-ALP. 2 samples: pre and post exercise
Maimoun et al. [47]	France	To analyze the effect of submaximal exercise intensity on bone turnover.	experimental study whereby participants took part in 2 experimental trials, i.e., one where they cycled below their individual ventilatory threshold.	Male competitive road cyclists (7)	submaximal exercise cycling test conducted at 15% below their individually determined	calcium, PTH, osteocalcin, B-ALP, CTX-1 4 samples, taken pre, after 30 minutes (during), after 50 minutes (post) and after 15 minutes of recovery.
Maimoun et al. [48]	France	To investigate the response of calciotropic hormones and bone turnover with participants of different activity levels of a similar age	Parallel group experimental design: with three groups:old active, old inactive and young inactive whereby participants performed a maximal incremental test	Healthy elderly, moderately active (18) Healthy young active (9)	maximal incremental walking test conducted at their individually maximal incremental test as previously described	Ionized calcium, intact PTH, osteocalcin, B-A:P, CTX, 2 blood samples, before exercise and post-exercise

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Mathis et al. [49]	United States (Alabama)	To investigate whether calcium lost through sweat causes a decrease in serum calcium, triggering a rise in PTH levels	Single-measure, acute intervention experimental feasibility study, whereby biomarkers related to calcium homeostasis and bone metabolism were measured before and after a 90 minute bikram yoga session,	Females aged 30-70 years (5)	90 minute sequence of 26 hatha yoga asana poses and 2 breathing exercises performed in a room heated to 105 F with 40% humidity.	Ionized calcium, serum PTH and serum calcium and CTX-1 2 blood samples, before exercise and post-exercise
Mezil et al. [50]	Canada (Ontario)	To investigate the response of the bone turnover and the cytokines on low impact high intensity exercise in the form of cycling	Quasi-experimental design whereby bone biomarkers participants completed an incremental cycling test followed by an HIE trial on the cycle ergometer	Healthy, recreationally active men (23)	12 minutes high intensity interval cycling session consisting of 6x1-min high intensity cycling intervals at 90% of max workload separated by six 1-min active rest periods	B-ALP, OPG, NTX, RANKL 4 samples, before exercise and 5 minutes, 1 hour and 24 hours after exercise
Morgan et al. [51]	United States (Washington)	To investigate the effect of different modes of exercise on changes in metabolic markers of bon turnover within the 24-hour period following the exercise bout in physically active women	Experimental cross-over design whereby participants underwent three trials with different ground impact forces, namely jogging, water aerobics and control.	Healthy active females (10)	Jogging on an indoor track at 60 - 70% predicted HRM40 mins total Water aerobics consisting of 40 minutes including warm-up and cool-down.	NTX, osteocalcin, B-ALP 4 samples, before, after, and 1 and 24 hours post-exercise

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Murphy and Koehler [52]	United States (Nebraska)	To investigate the impact of short term caloric restriction on the anabolic response to a bout of resistance exercise and quantify the impact of resistance exercise at calorie restriction on bone turnover	Randomized, single-blind, repeated measures crossover trial, whereby participants underwent 3-day conditions of caloric restriction with post-exercise carbohydrate or post-exercise protein and an energy balance control with post exercise carbohydrate	Healthy, recreational weight lifters, men and women (7)	5 sets of 5 repetitions of the barbell back squat exercise	P1NP, sclerostin 7 blood samples taken: pre, immediately post, and 1, 2, 4, 8, 24 hours post
Nelson et al. [53]	Canada (Ontario)	To investigate the serum concentrations of osteogenesis related to Wnt signaling pathways and markers of bone formation at rest and in response to single bout of high-impact exercise	Experimental trial whereby participants took part in a single exercise bout with samples taken before, after and 1 day after.	Healthy premenopausal women (20) Healthy postmenopausal women (20) Pre and post menopausal women (8)	128 jumps organized into 5 circuit exercise stations, with 3 minutes of rest between stations. Circuit included box jumps, lunge jumps, tuck jumps, single leg hops and jumping jacks. No exercise, control group	Sclerostin, CTX, P1NP, DKK-1 4 samples: baseline and 5 minutes, 1 hour and 24 hours post-exercise
Nishiyama et al. [54]	Japan	To investigate the differences in basal and postexercise osteocalcin levels in athletic and nonathletic humans.	Parallel group experimental design, whereby biomarkers were monitored in athletic and nonathletic university male students	Japanese, athletic men (9) Japanese, non-athletic men (10)	running on an ergometer for 30 minutes at a constant workload of 43 - 52% of the students maximum.	Calcium, PTH, osteocalcin 3 samples: before, immediately after, 60min after

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Oosthuyse et al. [55]	South Africa	To investigate the effect of multi-day cycling on bone turnover.	Participants completed 4 consecutive days of cycling for 3 hours per day, and biomarkers were measured before and immediately post exercise each day.	Well-trained cyclists, male (10)	3 hours of race-simulated indoor cycling	serum and sweat ionized calcium, intact PTH, CTX-1, B-ALP 2 samples: before and post on each day of cycling
Parker et al. [56]	Australia (Victoria)	To investigate whether LV-HIIE, or CMIE, performed during the postprandial period can minimize or prevent the meal-induced suppression of tOC and/or ucOC	Repeated measures, randomized, parallel-group experimental design. Participants took part in two trials, a rest control trial and an exercise trial (they were randomized into either the LI HIT or CMIE groups). Each trial started with breakfast.	Sedentary overweight or obese men and women (14) Sedentary overweight or obese men and women (13)	Low volume, high intensity exercise bout, consisting of 8x1 minute cycling bouts at 100% of Wmax interspersed with 1-min active recovery periods at 50W and including a 5 min warm-up and 3 min cool down at 50% Wmax. 38 minutes of continuous cycling at 50% Wmax	Total and ucOC 3 samples, pre exercise, immediately post-exercise and 1.5h post exercise
Pickering et al. [57]	France	To investigate the response of sclerostin to an acute bout of exercise.	Parallel group experimental design. On the day of the test volunteers had a standardized breakfast, and then they took part in a 45 minute treadmill run, with samples taken pre and post. Responses were compared to an independent control group.	Healthy young women (exercise group) (23) Healthy young women (control group) (9)	45 minute treadmill run comprising progressive 5 min warm-up, running at an established speed of 7.5km/hr, then a 3 min cool-down	CTX-1, B-ALP, sclerostin 2 samples, pre and post exercise

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Pomerants et al. [58]	Estonia	To investigate bone biomarker and IGF axis responses to an acute bout of aerobic exercise in boys at different pubertal stages.	Participants took part in a cycle ergometer test, with samples taken pre, post and 30 minutes post.	Healthy, non obese boys (60)	30 minute exercise on a cycle ergometer at 95% individual ventilatory threshold	P1NP, ICTP 3 samples, before, immediately after and 30 minutes after exercise
Prawiradilaga et al. [59]	Denmark	To investigate the acute bone biomarker response to jumps with different ground reaction forces in postmenopausal women.	Randomized, repeated-measures, controlled, cross-over study, whereby participants took part in 4 experimental sessions of jumps conducted in a randomized order	Healthy, sedentary, post menopausal women (29)	Participants completed a 7-minute standardized warm-up followed by 6 sets of 10 repetitions of jumps. Four types of jump were performed: countermovement jump, drop jump, diagonal drop jump and a resting control trial	P1NP, OC, CTX-1 3 samples, baseline, immediately after, 2 hours post-exercise
Rantalainen et al. [60]	Finland	To examine the response of bone biochemical markers to a single bout of high-impact exercise.	Single-measure, acute experimental study whereby participants took part in an exhaustive high-impact session with biomarkers measured pre and post.	Young male students (15)	Fatiguing bilateral jump routing conducted to exhaustion. Initially 10 - 20 jumps were performed and used to identify a steady max GRF. They then kept going until they dropped below 65% for 10 successive jumps	CTX, P1NP 5 samples, prior to warm-up and immediately after exercise, 2 hours after exercise and 1 and 2 days later.

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Rogers et al. [61]	United States (Missouri)	To investigate the acute response of a plasma marker of bone formation (BAP) and of resorption [tartrate-resistant acid phosphatase 5b (TRAP5b)] to a single bout of RT or PLY in the fed or fasted state

Follow up study toverify the results of Study 1: to investigate whether findings were due to the exercise or circadian rhythm (control condition) and to include extra biomarkers (OC and CTX) | STUDY ONE: experimental repeated measured, cross-over design, whereby participants took part in a single bout of resistanc or plyometric training

STUDY TWO: 5 of the 12 participants in study 1 took part in study 2. They took part in 3 trials, i.e., fasted no exercise control trial, fed resistance and fed plyometric. | Physically active men (12)

Physically active men (5) | Plyometric Session: squat jump, forward hop, split squat jump, lateral box push-off, bounding, lateral bounding, boz drill, lateral hurdle, zig-zag, single leg lateral hurdle, depth jump (10cm) and jump off a box (10cm)

Resistance session: 3 sets of 10 repetitions of 6 exercises (squat, military press, dead lift, bent over row, lunge and calf-raise). First set was performed at 60% 1RM while next 2 were at 80% 1RM. | B-ALP and TRAP5b, PTH 7 samples taken., pre-exercise, post-exercise, and 15, 30, 60 and 120 minutes post and 24 hours post |

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Rong et al. [62]	Sweden	Investigate the influence of acute endurance and strength exercise on the bone levels of calcitonin, PTH, PTHrP, and bone turnover markers osteocalcin and 1CTP on young non-athletic males	Randomized, repeated-measures experimental design whereby participants took part in three exercise sessions (2 cycling and 1 strength) and a control session	Healthy, active men (8)	E-55% endurance exercise at 55% VO2 max on a cycle ergometer for 45 minutes E 85% - endurance exercise at 85% of VO2 max on a cycle ergometer for 15 minutes. Strength session - 2 warm up sets of 10 reps pressing 40 kg (estimated as approx 20%), then they pressed for 5 sets of 8 repetitions at 85% of 3 RM (which I estimated as 90% 1RM) CONTROL GROUP	Calcium, PTH, osteocalcin, ICTP 5 samples, before exercise, in the last minute, and 1, 4, and 24h post-exercise
Rudberg et al. [63]	Sweden	To investigate whether exercise would cause observable changes of ALP bone isoforms in serum	Single-measure, acute experimental design, whereby biomarkers were measured pre and post an exercise bout - postmenopausal women did a non-weight bearing trial (cycle ergometer) while the young women did a jogging	Post menopausal women (8) Young healthy women (7)	Cycle ergometer, where workload increased and continued to exhaustion jogging for 30 - 40 min at an even pace just below subjective lactate accumulating effort level. They covered a mean of 4.7km (range 4 - 6)	Serum total and ionized calcium, bone Alp (three isoforms B/1, B1 and B), osteocalcin and ICTP. 3 samples - before exercise, immediately after exercise and 20 minutes after exercise.

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Sale et al. [64]	United Kingdom (England)	To investigate the immediate and short-term bone metabolic response to carbohydrate feeding during treadmill running	Randomized, repeated-measures, cross-over experimentaldesign, whereby men took part in 2 identical exercise trials, one where they were fed CHO immediately before, during and after exercise, and the other placebo.	Healthy physically active men (10)	120 minutes running at 70% VO2 max (PLACEBO TRIAL) Running exercise, with 3 submaximal stages, followed by a maximal	B-CTX, P1NP, OPG, OC, PTH, calcium 7 samples, i.e., pre and immediately post exercise, 60 and 120 mins post exercise, and 1, 2 and 3 days post exercise.
Salvesen et al. [65]	Sweden	To investigate the effect of exhaustive treadmill running on bone biomarkers.	Single-measure, acute intervention experimental design whereby participants took part in a single exercise bout, in which Each test consisted of 3 consecutive submaximal and one maximal with markers measured pre and post.	Healthy well trained cross country runners, man and women VO2 max of 60 (8) Healthy well trained cross country runners, man and women VO2 max of 73 (7)	Running exercise, with 3 submaximal stages, followed by a maximal. Submaximal tests were carried at 12, 14 and 16 km/h for 4 min on each load (correspond to 25±5%, 50±5% and 75±5% of maximal oxygen uptake). After a 15 min rest period, the maximal part was performed.	Osteocalcin, P1CP, ICTP 2 samples, before and 30min after exercise bout.
Scott et al. [66]	United Kingdom (England)	To investigate if training status influences the bone biomarker response to an acute bout of strenuous running exercise.	Independent group experimental design whereby bone biomarkers were measured in recreationally active or endurance trained participants before and after a strenuous endurance run. A third group of recreationally active men acted as a control group.	Healthy recreationally active men (11) Healthy endurance trained men (10) Control group, recreationally active (11)	60 minute run at 65% VO2 max (fixed duration test), then 15 minute rest, then run to exhaustion at 70% VO2 max, then rest for 5 minutes then continue until they can no longer perform at least 5 mins of continuous running, then they went down to work-rest patterns of 1:2 mins	OPG, PTH, albumin adjusted calcium (ACa), B-CTX-1, P1NP and B-ALP. 12 blood samples, before exercise, at 20, 40, 60 minutes during the exercise bout, immediately post exercise, 05, 1, 1.5, and 2 hours after exercise 1, 2 and 3 days post exercise.

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Scott et al. [67]	United Kingdom (England)	To investigate the effects of three different cardiovascular exercise intensities on changes in bone turnover markers	Repeated measures, counterbalanced, experimental design, whereby participants took part in 3 experiments, each one involving an exercise test conducted at a different intensity.	Healthy, in good physical condition; men(10)	60 minute bout of treadmill running at 55% of VO2 max. 60 minute bout of treadmill running at 65% of VO2 max. 60 minute bout of treadmill running at 75% of VO2 max.	B-CTX-1, P1NP, osteocalcin, OPG, B-ALP, PTH, albumin adjusted calcium 11 blood samples taken: pre-exercise, 20, 40 minutes into the exercise bout, immediately after, 05, 1, 2 and 3 hour post and 1, 2 and 3 days post.
Scott et al. [68]	United Kingdom (England)	To investigate the effect of an overnight fast, versus feeding, on the bone metabolic response to an acute bout of treadmill exercise.	Repeated measures, experimental design, whereby participants took part in two, counterbalanced, experiments comprising exercise conducted in either a fasted, or fed, state.	Physically active men (10)	60 minute treadmill run at 65% VO2 max - FASTED CONDITION 60 minute treadmill run at 65% VO2 max - FED CONDITION	B-CTX-1, P1NP, osteocalcin, OPG, B-ALP, PTH, albumin adjusted calcium 9 samples - pre exercise, 30 minutes into the bout, post-exercise, and after 1, 2 and 3 hours of recovery
Scott et al. [69]	United Kingdom (England)	To investigate the bone metabolic response to two consecutive bouts of exercise in young men when recovery duration was either 23 or 3h.	Repeated measures, cross-over design, whereby participants took part in two experimental trials, each one comprising 2 exercise bouts, one with 23 hours of recovery between bouts, the other with 3 hours of recovery between bouts	Healthy, physically active men (10)	60 minutes treadmill running at 65% VO2 max.	CTX-1, P1NP, OPG PTH); B-ALP, calcium 5 samples - pre exercise, post exercise and 1, 2 and 3 hours post exercise

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Sharma-Ghimire et al. [70]	United States (Oklahoma)	To investigate the response of sclerostin and PTH to a resistance exercise bout, with and without prior whole body vibration.	Randomized, repeated measure cross-over design whereby biomarkers were assessed pre and post 2 identical resistance training bouts, one of which was preceded by WBV	Healthy recreationally active women, OC users (9)	Resistance protocol - 5 min cycling warm-up at light intensity, followed by 3 sets of 10 repetitions of each exercise at 80% 1RM isotonic resistance exercises, namely leg press, hip extension, hip abduction, hip adduction, seated row, shoulder press)	Sclerostin, PTH 3 samples, pre-exercise, post-exercise and 30min after exercise
Shea et al. [71]	United States (Colorado)	To investigate whether vigorous walking increases PTH and CTX in older women	Randomized, double-blinded, cross-over trial, whereby participants took part in in two 60 minute bouts of treadmill walking, one as a control and the other a Ca supplementation condition.	Healthy post menopausal women (10) Healthy post menopausal women (23)	60 minute bout of treadmill walking at a workload corresponding to 75 - 80% VO2 peak.	iCa, PTH, CTX 3 samples, immediately before, immediately post and 30min after
Sherk et al. [72]	United States (Oklahoma)	To investigate the effect of WBV + RE and to RE alone on bone formation and bone resorption marker responses in untrained young women, taking oral contraceptives.	Randomized, repeated measure cross-over design whereby biomarkers were assessed pre and post 2 identical resistance training bouts, one of which was preceded by WBV	Healthy, recreationally active women, who were taking oral contraceptives 6 months prior (10)	Resistance protocol - 5 min cycling warm-up at light intensity, followed by 3 sets of 10 repetitions of each exercise at 80% 1RM isotonic resistance exercises (leg press, hip extension, hip abduction, hip adduction, seated row, shoulder press)	B-ALP, CTX, TRAP5b 3 samples: pre, post and 30 min after

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Sherk et al. [73]	United States (Colorado)	To investigate if the consume of chewable calcium 30min pre exercise attenuates the decrease of serum iCa and increases in serum PTH and bone resorption	Randomized, double-blind, placebo-controlled, parallel group design whereby participants were randomized to either the placebo or the calcium condition. Both groups took part in a 35 km time trial, with biomarkers measured pre and post.	Competitive road cyclists, male (28)	35 km time trial conducted in a fasted state.	ionized calcium, intact PTH, CTX 3 samples, before, immediately after and 30 min post
Taylor et al. [74]	United Kingdom (England)	To investigate bone turnover response to moderate-intensity, continuous physical exercise in people with T1 diabetes	Parallel group, single-measure, acute intervention. Case control study	T1 diabetes patients (15) Healthy control group (15)	45 mins of steady state incline walking on a treadmill with exercise intensity set at 60% VO2 peak.	Ionized and albumin calcium, PTH, B-CTX, P1NP 4 samples, baseline, post-exercise, and 30 and 60 min post-exercise
Theocharidis et al. [75]	Canada (Ontario)	To investigate the influence of post exercise whey protein intake, compared to an isocaloric carbohydrate beverage and water, consumed immediately after an intense swimming trial on bone turnover in adolescent swimmers.	Double blind, placebo controlled study, with participants stratified into 3 groups matched for age, body mass and sex. All participants took part in the an intensive swim trial, with their relevant supplementation consumed directly after	Competitive swimmers aged 11-17 (18)	Swim Trial: 1000 m warm up, followed by a maximal 200m front crawl swim, followed by a HIIS protocol consisting of 5 x 100m, 5 x 50m and 5 x 25m freestyle sprints at near maximal effort, with 1:1 work t rest ratio	CTX, P1NP 3 samples, baseline, 8 and 24h post

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Thorsen et al. [76]	Sweden	To investigate the acute effect of moderate endurance exercise on hormones and bone markers of metabolism in postmenopausal women	Experimental design, whereby a single group of postmenopausal women took part in an exercise session, with biomarkers measured before, and after.	Postmenopausal, not regularly trained women (12)	Outdoor brisk walking for 90 minutes at a temperature of 2°C.	Ionized calcium, PTH, osteocalcin, P1CP, ICTP 4 samples taken, 15min before, and 1-, 24- and 72-hours after exercise bout
Thorsen et al. [77]	Sweden	To investigate the short term effect of a simple bout of moderate, weight bearing, endurance exercise on calciotropic hormones and markers of bone metabolism in young females	Single-measure experimental, whereby participants took part in a single bout of exercise with biomarkers measured pre and post.	Young, untrained women (14)	Outdoor jogging (temperature +8°C) conducted at 50% HR max reserve and measured by pulse telemetry during exercise.	Ionized calcium, PTH, osteocalcin, P1CP, ICTP 4 samples taken, 15min before, and 1-, 24- and 72-hours after exercise bout
Tosun et al. [78]	Turkey	To investigate the acute effects of a single session of brisk walking on bone turnover and to determine whether additive weight-lifting would cause observable differences on bone metabolism	Experimental cross-over design, whereby participants took part in 3 trials, i.e., 2 exercise bouts (brisk walking and brisk walking while carrying 5kg of weight in a backpack) and one control condition.	Healthy, sedentary, premenopausal women (9)	Brisk treadmill walking for 30 minutes at a submax intensity Brisk treadmill walking for 30 minutes at a submax intensity while carrying 5kg of weight	PTH, osteocalcin, PICP, PINP, ICTP 3 samples, before, immediately after and 15 min after

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Townsend et al. [79]	United Kingdom (England)	To investigate whether feeding CHO and protein after a prolonged intense running bout will impact the bone biomarker response to that exercise bout .	Randomized, counterbalanced, placebo controlled and single blinded crossover study, whereby participants took part in 3 experimental trials, i.e., placebo control trial, immediate feeding (CHO/PRO) ingested straight after exercise and delayed feeding (CHO and PRO) ingested 2 hours post exercise.	Trained endurance runners, men (10)	Treadmill run at 75% VO2 max, conducted until exhaustion.	CTX, P1NP, PTH, calcium 7 samples - pre, immediately post and 1, 2, 3 and 4 and 24 hours post.
Virtanen et al. [80]	Finland	To Investigate the effects of an acute bout of high-intensity concentric exercise on muscle and connective tissue cells.	Single-measure, acute experimental design whereby the participants took part in a single high intensity exercise bout consisting of maximal concentric lower limb extensions, followed by isometric contractions and countermovement jumps with biomarkers measured pre and post.	Healthy, physical education students with training background, male (9)	3 countermovement jumps, then 3 isometric bilateral lower limb extension exercises, then a fatigue loading protocol of 50 maximal concentric successive bilateral lower limb extensions, followed by three isometric contractions and three countermovement jumps.	P1CP, hydroxyproline 8 blood samples taken the day before and 2 mins, 1 and 2 hours after and 1, 2, 3 and 4 days after.

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Wallace et al. [81]	Australia (Queensland)	Study 1: to investigate the influence of exercise on bone and collagen markers Study 2: to investigated the effect of GH administration on bone markers with and without exercise.	Study 1: Randomized, repeated-measures controlled trial, whereby participants took part in an exercise and rest condition, conducted in a random order Study 2: Parallel group, double-blind, placebo-controlled design whereby participants took either GH or placebo for 7 days, with response to the exercise assessed before and after treatment	Healthy, highly active men (17)	Submaximal exercise protocol, consisting of three executive stages. Stage 1 was 5 mins at 1 W/kg, stage 2 was 5 mins at 2 W/Kkg and stage 3 was 20 mins at 65% of predetermined VO2 peak.	PICP, ICTP, osteocalcin, B-ALP 8 blood samples taken: immediately pre, 15 minutes into the exercise bout, immediately after, and 15, 30, 45, 60 and 90 minutes post-exercise
Welsh et al. [82]	United Kingdom (England)	To investigate the short term effects of moderate exercise on the bone biomarkers in healthy sedentary males	Single-measure, acute experimental design whereby the participants took part in a single exercise trial with biomarkers measured pre and post.	Healthy, not trained, young men (10)	30 minute treadmill walk at 60% of predicted max heart rate.	serum osteocalcin, B-ALP, urinary Pyr ad Dpd. Three 24-hour urine samples were collected and volumes recorded on the day before. the day of the walk and the day after 7 blood samples taken: immediately before, after, and 0.5, 1, 8, 24 and 32 hours post exercise

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Wheat et al. [83]	United States (Texas)	To investigate whether urinary excretion of hydroxylysine is increased during the 4-day period following prolonged, down hill running.	Experimental design spanning a 9-day period, involving a single exercise bout on day 6 with hydroxylysine assessed pre and post.	Not highly trained, males (10)	Conducted in 2 parts, started with a VO2 max test, then after 15-20 minutes of recovery, they did a 60 minute intermittent running bout	Hydroxylysine and total urine excreted 8 hour urine samples: starting 48 hours before exercise and continuing until 4 days after exercise bout.
Wherry et al. [84]	United States (Colorado)	To investigate whether exercise in a warm environment exaggerates the decrease in serum iCa and increases in PTH and CTX compared with a cool environment.	Repeated-measures cross-over design, whereby participants took part in 2 identical 60 minute treadmill bouts under both warm and cool conditions.	Healthy recreationally active men and women (12)	60 minutes of treadmill walking at 70 - 80% of measured Hrmax-cool and warm condition	iCa, PTH, CTX 10 samples, i.e., 15 mins and immediately before the exercise bout, 15, 30 and 45 minutes during, 60 minutes post, and 15, 30, 45 and 60 minutes post.
Whipple et al. [85]	United States (Pennsylvania)	To investigate the effects of a single bout of moderately intense resistance exercise on biochemical markers of bone cell activity in untrained young male subjects	Randomized, repeated measures, cross-over, controlled design, whereby participants took part in both a resistance exercise and a control session, with biomarkers measured pre and post.	Healthy, young, active but not exercising men (9)	3 sets of 10 reps of 7 exercises (bench press, leg press, lateral pull down, seated row, leg curl, back extension and arm curl).	Serum B-ALP, PICP, NTx and urinary NTx 6 samples - before, after, and at 1, 8, 24, and 48 hours post exercise
Zanker and Swaine [86]	United Kingdom (England)	To investigate the effect of long treadmill runs under energy balance or energy restriction on bone turnover markers in trained runners	Repeated measures, cross-over design, whereby participants took part in two 3-day trials, under conditions of either energy balance or energy restriction and with an exercise trial on each day.	Well-trained, distance runners; men (8)	60 minutes of treadmill running divided in to 4 x 15 minute intervals	Two blood samples collected (on days 2 and 5) and two urine samples (on days 1 and 4)

Author (date)	Country	Primary Aim	Research Design	Participants (n)	Exercise Bout	Biomarkers and Sampling
Zerath et al. [87]	France	To investigate the effects of a maximal exercise test before and at the end of a 6 week endurance training program on serum levels on markers related to calcium	Two single-measure exercise bouts whereby subjects performed a maximal exercise test with blood samples collected pre and post this test were performed before the beginning and at the end of a 6 week endurance training period.	Healthy older men (24)	Incremental exercise test on a monark ergometer, with workload incremented by 20W per minute until exhaustion.	Albumin adjusted calcium, PTH, OC 2 samples, pre- and post-exercise
Zitterman et al. [88]	Germany	To investigate the consequences of an acute aerobic exercise bout on fractional Ca absorption and on bone turnover	Randomized, parallel-group, controlled design whereby participants were randomized to take part either in an exercise bout or resting condition	Healthy, nonsmoking, athletes; male (18)	60 minute run at the heart rate that corresponded to 70% of the speed at 4mmol blood lactate	Serum and urine Ca, PICP, protein, PTH, CTX 2 samples, 60 min before and 3 hours after exercise

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The Bone Biomarker Response to an Acute Bout of Exercise:

A Systematic Review with Meta-Analysis

Supplementary File 6: Funnel Plots and Eggers Test Results

Dolan E[1]*, Dumas A[1], Keane KM[2], Bestetti G[1], Freitas LHM[1], Gualano B[1,3], Kohrt WM[4], Kelley GA[5], Pereira RMR[6], Sale C[7], Swinton PA[8]

[1] Applied Physiology & Nutrition Research Group; School of Physical Education and Sport; Rheumatology Division; Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[2] Department of Sport, Exercise and Nutrition, Galway Mayo Institute of Technology, Ireland.

[3] Food Research Centre, University of São Paulo, SP, BR.

[4] Department of Medicine, Division of Geriatric Medicine, University of Colorado Anschutz Medical Campus, USA.

[5] Department of Epidemiology and Biostatistics, West Virginia University, USA.

[6] Bone Metabolism Laboratory; Rheumatology Division, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[7] Musculoskeletal Physiology Research Group, Sport, Health and Performance Enhancement (SHAPE) Research Centre, School of Science and Technology, Nottingham Trent University, Nottingham, UK.

[8] School of Health Sciences, Robert Gordon University, Aberdeen, UK.

*Corresponding author:

Eimear Dolan:

Faculdade de Medicina FMUSP, Universidade de Sao Paulo – Av. Dr. Arnaldo, 455, 3º andar, ZIP code: 01246-903, Sao Paulo - SP, Brazil.

Phone: +55 11 2648-1337; Fax: +55 11 3061-7490; E-mail: eimeardol@gmail.com or eimeardolan@usp.br

Resorption:
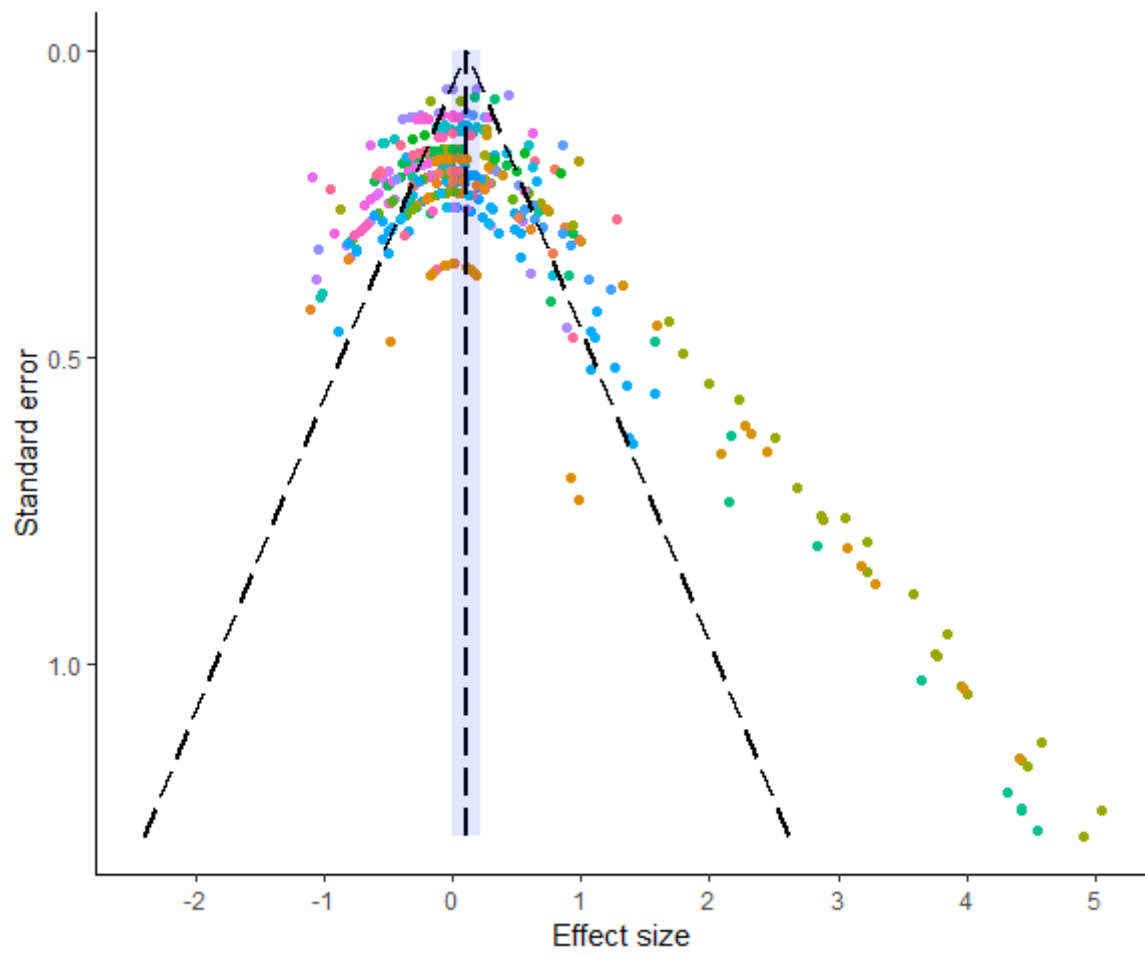
Egger Intercept$_{0.5}$ =-0.51 [95%CrI: -0.64 to -0.39].

Formation:
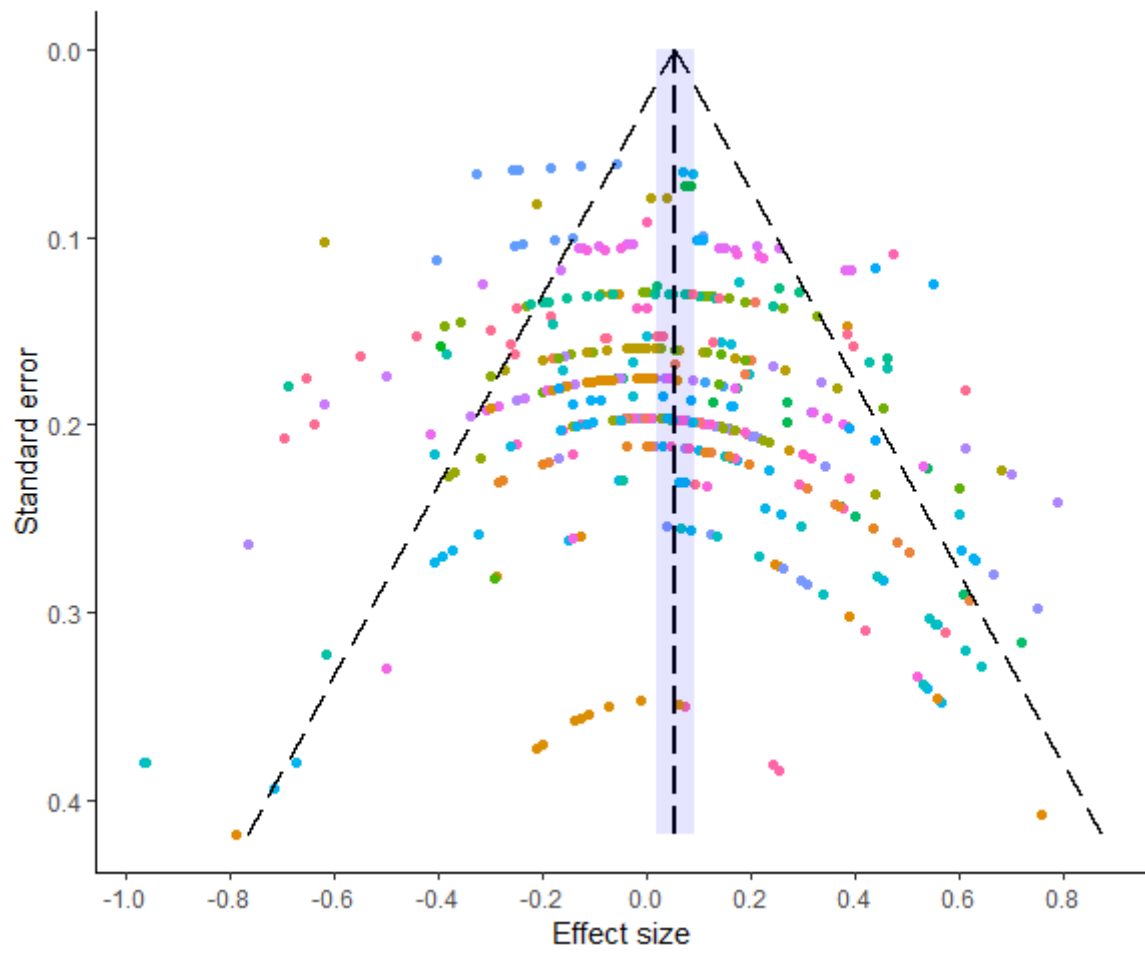
Egger Intercept$_{0.5}$ =-0.06 [95%CrI: -0.16 to 0.04].

General:
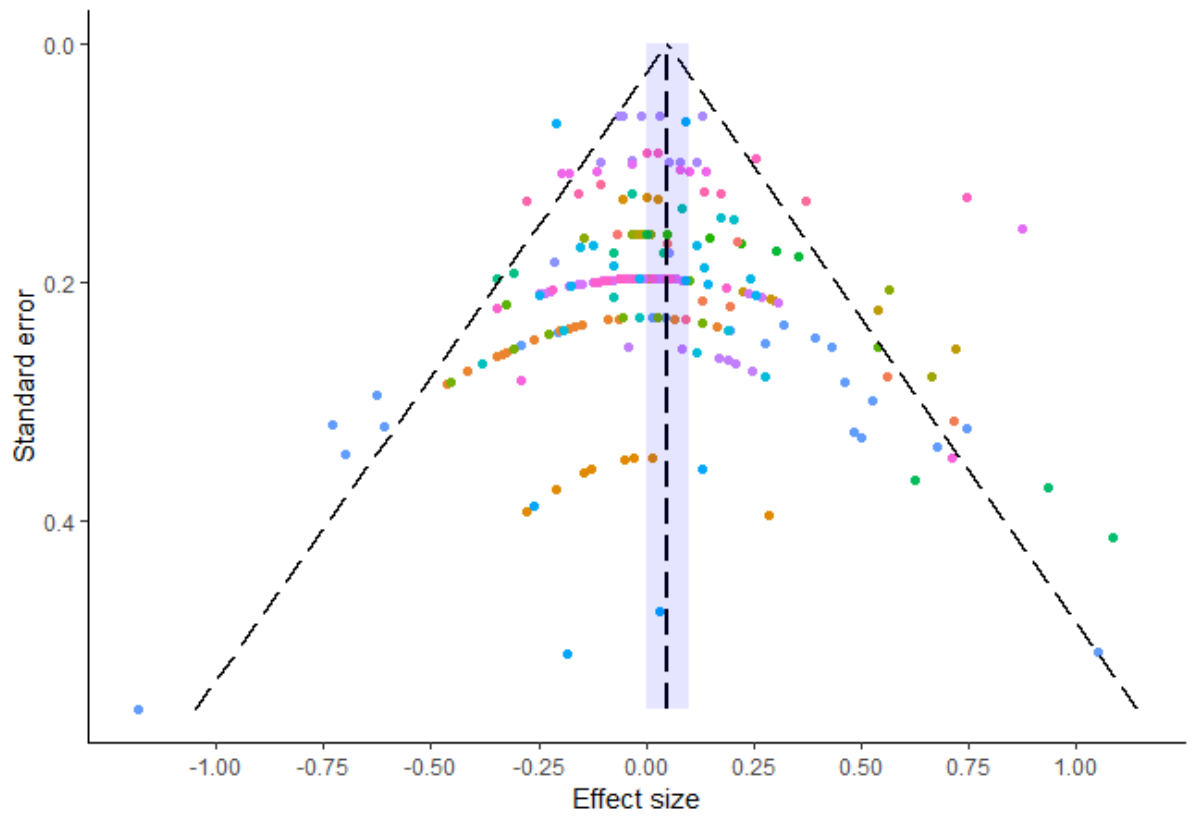
Egger Intercept$_{0.5}$ =-0.04 [95%CrI: -0.18 to 0.08].

PTH:
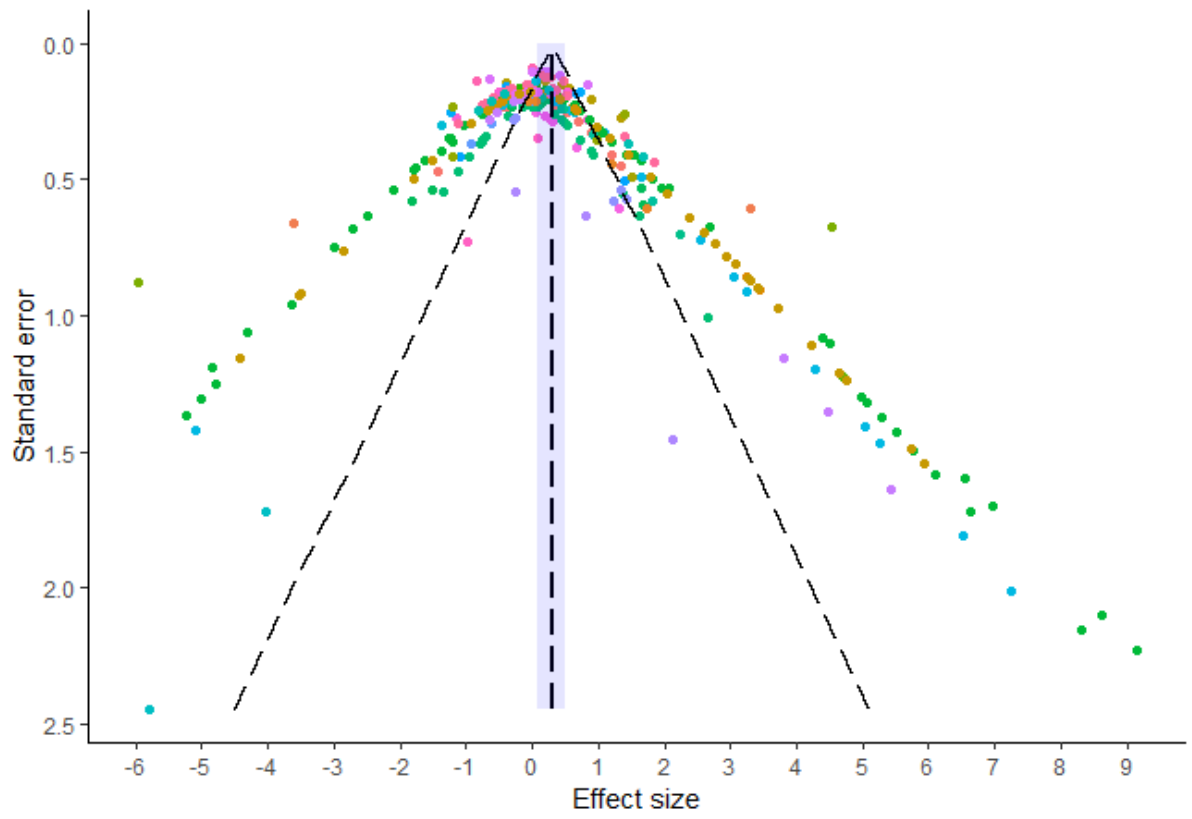
Egger Intercept$_{0.5}$ =-0.56 [95%CrI: -0.77 to -0.31].

The Bone Biomarker Response to an Acute Bout of Exercise:

A Systematic Review with Meta-Analysis

Supplementary File 7: Primary meta-analyses and moderator analyses for bone resorption

Dolan E[1]*, Dumas A[1], Keane KM[2], Bestetti G[1], Freitas LHM[1], Gualano B[1,3], Kohrt WM[4], Kelley GA[5], Pereira RMR[6], Sale C[7], Swinton PA[8]

[1] Applied Physiology & Nutrition Research Group; School of Physical Education and Sport; Rheumatology Division; Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[2] Department of Sport, Exercise and Nutrition, Galway Mayo Institute of Technology, Ireland.

[3] Food Research Centre, University of São Paulo, SP, BR.

[4] Department of Medicine, Division of Geriatric Medicine, University of Colorado Anschutz Medical Campus, USA.

[5] Department of Epidemiology and Biostatistics, West Virginia University, USA.

[6] Bone Metabolism Laboratory; Rheumatology Division, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[7] Musculoskeletal Physiology Research Group, Sport, Health and Performance Enhancement (SHAPE) Research Centre, School of Science and Technology, Nottingham Trent University, Nottingham, UK.

[8] School of Health Sciences, Robert Gordon University, Aberdeen, UK.

*Corresponding author:

Eimear Dolan:

Faculdade de Medicina FMUSP, Universidade de Sao Paulo – Av. Dr. Arnaldo, 455, 3º andar, ZIP code: 01246-903, Sao Paulo - SP, Brazil.

Phone: +55 11 2648-1337; Fax: +55 11 3061-7490; E-mail: eimeardol@gmail.com or eimeardolan@usp.br

	Summary of findings			Evidence Certainty				
Outcome (#/n)	Effect size Median [95% CrI]	Between study standard error (τ) Median [75% CrI]	ICC Median [75% CrI]	D1 Risk of Bias	D2 Directness	D3 Inconsistency	D4 Imprecision	D5 Small-study Effects
All biomarkers exercise 483 outcomes / 69 studies	0.10 [0.00 to 0.21]	0.41 [0.38 to 0.44]	0.11 [0.03 to 0.20]	High	Low	Very Low	Very Low	Very Low
CTX-1 276 outcomes / 44 studies	0.16 [-0.01 to 0.34]	0.53 [0.49 to 0.59]	0.14 [0.05 to 0.23]	High	Moderate	Low	Low	Very Low
TRAP5b 86 outcomes / 7 studies	-0.06 [-0.12 to -0.00]	0.03 [0.01 to 0.05]	0.33 [0.07 to 0.74]	High	High	High	High	Moderate
ICTP 51 outcomes / 14 studies	0.10 [-0.03 to 0.26]	0.17 [0.11 to 0.23]	0.39 [0.16 to 0.65]	Low	Very Low	Very Low	Very Low	Very Low
NTX 27 outcomes / 6 studies	0.06 [-0.20 to 0.36]	0.14 [0.07 to 0.24]	0.74 [0.38 to 0.93]	Moderate	Low	Very Low	Very Low	Very Low
OPG 24 outcomes / 6 studies	0.23 [-0.05 to 0.41]	0.11 [0.06 to 0.18]	0.46 [0.16 to 0.79]	Moderate	Low	Low	Very Low	Very Low
RANKL 19 outcomes / 5 studies	-0.14 [-0.51 to 0.18]	0.20 [0.10 to 0.34]	0.53 [0.19 to 0.85]	Moderate	Low	Very Low	Very Low	Very Low
All biomarkers Control	-0.11 [-0.34 to 0.08]	0.20 [0.11 to 0.30]	0.14 [0.03 to 0.47]	High	High	Moderate	Low	Very Low

36 outcomes / 9 studies
(CTX-1:20; ICTP:16)

Biomarkers control (CTX-1 only) 20 outcomes / 8 studies	-0.15 [-0.44 to 0.10]	0.19 [0.09 to 0.31]	0.49 [0.16 to 0.84]	High	High	Moderate	Low	Very Low
Moderator Analysis (CTX-1 Only)								
Timing								
(Immediately - 8 hours post) 199 outcomes / 41 studies	0.14 [-0.07 to 0.37]	0.61 [0.56 to 0.67]	0.15 [0.05 to 0.25]	Moderate	Low	Very Low	Very Low	Very Low
(Immediately - 15min post) 104 outcomes / 37 studies	0.15 [-0.05 to 0.36]	0.52 [0.46 to 0.58]	0.23 [0.09 to 0.34]	Moderate	Low	Very Low	Very Low	Very Low
(> 15 min, ≤ 2 hours post) 67 outcomes / 23 studies	0.40 [-0.13 to 0.97]	1.3 [1.1 to 1.4]	0.01 [0.00 to 0.02]	Moderate	Low	Very Low	Very Low	Very Low
(> 2 hours, ≤ 8 hours post) 28 outcomes / 9 studies	0.05 [-0.82 to 1.0]	1.2 [0.90 to 1.5]	0.04 [0.00 to 0.10]	Low	Very Low	Very Low	Very Low	Very Low
24 hours post 39 outcomes / 16 studies	0.00 [-0.17 to 0.18]	0.22 [0.15 to 0.29]	0.27 [0.09 to 0.56]	High	Moderate	Low	Low	Very Low
48 hours post 20 outcomes / 12 studies	0.08 [-0.11 to 0.30]	0.25 [0.17 to 0.34]	0.09 [0.02 to 0.31]	High	Moderate	Low	Very Low	Very Low
72 hour post 11 outcomes / 6 studies	0.23 [-0.05 to 0.53]	0.18 [0.09 to 0.29]	0.19 [0.04 to 0.57]	High	Moderate	Moderate	Low	Very Low
Exercise Type								
Aerobic 222 outcomes / 33 studies	0.25 [0.01 to 0.49]	0.63 [0.57 to 0.70]	0.13 [0.04 to 0.21]	High	Moderate	Low	Low	Very Low
Plyometric 28 outcomes / 6 studies	-0.04 [-0.29 to 0.20]	0.11 [0.05 to 0.20]	0.82 [0.47 to 0.96]	High	Moderate	Low	Very Low	Very Low

Resistance 17 outcomes / 12 studies	-0.14 [-0.32 to 0.10]	0.08 [0.03 to 0.16]	0.34 [0.07 to 0.78]	Moderate	Moderate	Moderate	Low	Very Low
Impact level								
Low impact/repetitive 92 outcomes / 13 studies	0.77 [0.23 to 1.3]	0.85 [0.71 to 1.0]	0.26 [0.10 to 0.40]	Moderate	Low	Very Low	Very Low	Very Low
Moderate impact/repetitive 130 outcomes / 22 studies	0.00 [-0.21 to 0.22]	0.46 [0.40 to 0.52]	0.05 [0.02 to 0.10]	High	Moderate	Low	Very Low	Very Low
Low impact / High load 24 outcomes / 8 studies	-0.15 [-0.32 to 0.00]	0.08 [0.04 to 0.15]	0.60 [0.19 to 0.90]	High	Moderate	Moderate	Moderate	Low
High impact / directional 30 outcomes / 6 studies	-0.03 [-0.24 to 0.20]	0.10 [0.05 to 0.18]	0.82 [0.48 to 0.96]	Moderate	Moderate	Low	Very Low	Very Low
Modality								
Running 103 outcomes / 15 studies	-0.04 [-0.25 to 0.17]	0.37 [0.31 to 0.43]	0.03 [0.01 to 0.08]	High	Moderate	Low	Very Low	Very Low
Cycling 90 outcomes / 12 studies	0.86 [0.31 to 1.4]	0.84 [0.73 to 0.97]	0.34 [0.14 to 0.49]	Moderate	Low	Very Low	Very Low	Very Low
Walking 27 outcomes / 8 studies	0.24 [-0.61 to 0.99]	0.89 [0.69 to 1.2]	0.19 [0.08 to 0.38]	Moderate	Low	Very Low	Very Low	Very Low
Exercise Characteristics								
Continuous 188 outcomes / 26 studies	0.36 [0.05 to 0.67]	0.70 [0.62 to 0.79]	0.14 [0.05 to 0.24]	Moderate	Low	Very Low	Very Low	Very Low
Intermittent 34 outcomes / 7 studies	-0.07 [-0.52 to 0.37]	0.47 [0.36 to 0.62]	0.04 [0.01 to 0.11]	High	Moderate	Low	Very Low	Very Low
Duration (Per 10 Mins) 225 outcomes / 33 studies	0.14 [0.09 to 0.19]	0.72 [0.65 to 0.80]	0.08 [0.02 to 0.14]	High	Moderate	Low	Low	Very Low
Intensity Low 153 outcomes / 20 studies	0.18 [-0.16 to 0.52]	0.69 [0.61 to 0.79]	0.13 [0.04 to 0.22]	High	Moderate	Low	Very Low	Very Low

Intensity High 51 outcomes / 8 studies	0.28 [-0.32 to 0.86]	0.71 [0.57 to 0.90]	0.09 [0.03 to 0.18]	High	Moderate	Low	Very Low	Very Low
Total work done (Per 1000 units) 208 outcomes / 23 studies	0.27 [0.21 to 0.34]	0.82 [0.73 to 0.92]	0.06 [0.02 to 0.11]	High	Moderate	Low	Low	Very Low
Participant Characteristics								
Male 182 outcomes / 26 studies	0.23 [-0.01 to 0.51]	0.61 [0.55 to 0.69]	0.09 [0.03 to 0.15]	High	Moderate	Low	Very Low	Very Low
Female 68 outcomes / 14 studies	0.15 [-0.22 to 0.50]	0.60 [0.51 to 0.70]	0.16 [0.06 to 0.26]	Moderate	Moderate	Low	Very Low	Very Low
Mixed: male/female 26 outcomes / 6 studies	0.29 [-0.68 to 1.3]	0.94 [0.72 to 1.2]	0.17 [0.05 to 0.32]	Moderate	Low	Very Low	Very Low	Very Low
Sedentary 31 outcomes / 5 studies	0.00 [-0.23 to 0.34]	0.17 [0.11 to 0.26]	0.15 [0.04 to 0.44]	High	Moderate	Low	Very Low	Very Low
Recreational 139 outcomes / 21 studies	-0.04 [-0.22 to 0.15]	0.39 [0.34 to 0.44]	0.07 [0.02 to 0.13]	High	Moderate	Low	Very Low	Very Low
Athlete 92 outcomes / 16 studies	0.63 [0.17 to 1.1]	0.85 [0.74 to 0.99]	0.26 [0.10 to 0.38]	Moderate	Moderate	Low	Very Low	Very Low

All variables with sufficient data to analyse are presented.

The Bone Biomarker Response to an Acute Bout of Exercise:

A Systematic Review with Meta-Analysis

Supplementary File 8: Primary meta-analyses and moderator analyses for bone formation

Dolan E[1]*, Dumas A[1], Keane KM[2], Bestetti G[1], Freitas LHM[1], Gualano B[1,3], Kohrt WM[4], Kelley GA[5], Pereira RMR[6], Sale C[7], Swinton PA[8]

[1] Applied Physiology & Nutrition Research Group; School of Physical Education and Sport; Rheumatology Division; Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[2] Department of Sport, Exercise and Nutrition, Galway Mayo Institute of Technology, Ireland.

[3] Food Research Centre, University of São Paulo, SP, BR.

[4] Department of Medicine, Division of Geriatric Medicine, University of Colorado Anschutz Medical Campus, USA.

[5] Department of Epidemiology and Biostatistics, West Virginia University, USA.

[6] Bone Metabolism Laboratory; Rheumatology Division, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[7] Musculoskeletal Physiology Research Group, Sport, Health and Performance Enhancement (SHAPE) Research Centre, School of Science and Technology, Nottingham Trent University, Nottingham, UK.

[8] School of Health Sciences, Robert Gordon University, Aberdeen, UK.

*Corresponding author:

Eimear Dolan:

Faculdade de Medicina FMUSP, Universidade de Sao Paulo – Av. Dr. Arnaldo, 455, 3º andar, ZIP code: 01246-903, Sao Paulo - SP, Brazil.

Phone: +55 11 2648-1337; Fax: +55 11 3061-7490; E-mail: eimeardol@gmail.com or eimeardolan@usp.br

Outcome (#/n)	Summary of findings			Evidence Certainty				
	Effect size Median [95% CrI]	Between study standard error (τ) Median [75% CrI]	ICC Median [75% CrI]	D1 Risk of Bias	D2 Directness	D3 Inconsistency	D4 Imprecision	D5 Small-study Effects
All biomarkers exercise 479 outcomes / 69 studies	0.06 [0.02 to 0.09]	0.11 [0.10 to 0.12]	0.33 [0.13 to 0.47]	High	Moderate	Low	Low	Low
P1NP 190 outcomes / 30 studies	0.08 [0.03 to 0.14]	0.12 [0.10 to 0.14]	0.07 [0.02 to 0.16]	High	Moderate	Low	Low	Low
β-ALP 151 outcomes / 27 studies	0.05 [-0.01 to 0.12]	0.03 [0.01 to 0.05]	0.01 [0.00 to 0.04]	High	Moderate	Moderate	Moderate	Moderate
Sclerostin 54 outcomes / 12 studies	0.13 [0.00 to 0.24]	0.09 [0.04 to 0.14]	0.75 [0.40 to 0.93]	High	Moderate	Moderate	Moderate	Moderate
PICP 52 outcomes / 14 studies	0.03 [-0.07 to 0.14]	0.13 [0.10 to 0.16]	0.33 [0.12 to 0.54]	Moderate	Low	Very Low	Very Low	Very Low
DKK 19 outcomes / 4 studies	0.22 [-0.50 to 0.64]	0.28 [0.18 to 0.44]	0.07 [0.01 to 0.24]	High	Moderate	Low	Very Low	Very Low
uOC 13 outcomes / 4 studies	0.09 [-0.10 to 0.29]	0.09 [0.04 to 0.17]	0.50 [0.13 to 0.86]	High	Moderate	Low	Very Low	Very Low
All biomarkers Control 64 outcomes / 16 studies (β-ALP:24; P1NP:14; Sclerostin: 10; PICP:10; DKK:4; uOC: 2)	-0.03 [-0.08 to 0.02]	0.03 [0.01 to 0.04]	0.43 [0.11 to 0.81]	High	Moderate	Low	Low	Low

Moderator Analyses (P1NP only)

Timing								
(Immediately - 8 hours post) 118 outcomes / 26 studies	0.12 [0.04 to 0.19]	0.16 [0.14 to 0.18]	0.05 [0.01 to 0.13]	High	Moderate	Low	Low	Low
(Immediately - 15min post) 49 outcomes / 22 studies	0.19 [0.10 to 0.28]	0.16 [0.13 to 0.19]	0.04 [0.01 to 0.12]	High	Moderate	Moderate	Moderate	Moderate
(> 15 min, ≤ 2 hours post) 40 outcomes / 17 studies	0.03 [-0.09 to 0.16]	0.19 [0.16 to 0.24]	0.03 [0.01 to 0.09]	High	Moderate	Low	Low	Low
(> 2 hours, ≤ 8 hours post) 29 outcomes / 9 studies	0.11 [-0.04 to 0.27]	0.12 [0.06 to 0.19]	0.24 [0.05 to 0.66]	High	Moderate	Low	Very Low	Very Low
24 hours post 37 outcomes / 16 studies	0.02 [-0.07 to 0.12]	0.08 [0.14 to 0.12]	0.30 [0.07 to 0.72]	High	Moderate	Low	Low	Low
48 hours post 18 outcomes / 11 studies	0.03 [-0.07 to 0.14]	0.06 [0.03 to 0.10]	0.36 [0.08 to 0.78]	High	Moderate	Low	Low	Low
Exercise Type								
Aerobic 156 outcomes / 22 studies	0.11 [0.07 to 0.17]	0.08 [0.06 to 0.10]	0.09 [0.02 to 0.25]	High	Moderate	Moderate	Moderate	Moderate
Plyometric 20 outcomes / 4 studies	-0.03 [-0.51 to 0.41]	0.31 [0.21 to 0.47]	0.03 [0.01 to 0.11]	Moderate	Moderate	Low	Very Low	Very Low
Impact level								
Low impact/repetitive 43 outcomes / 8 studies	0.09 [-0.02 to 0.20]	0.09 [0.05 to 0.13]	0.31 [0.08 to 0.65]	Low	Very Low	Very Low	Very Low	Very Low
Moderate impact/repetitive 115 outcomes / 17 studies	0.11 [0.05 to 0.18]	0.07 [0.05 to 0.10]	0.10 [0.02 to 0.33]	High	Moderate	Moderate	Moderate	Moderate
High impact / multi-directional 26 outcomes / 5 studies	-0.03 [-0.31 to 0.40]	0.24 [0.17 to 0.35]	0.07 [0.01 to 0.19]	Moderate	Moderate	Low	Very Low	Very Low
Modality								

Running 103 outcomes / 14 studies	0.10 [0.05 to 0.16]	0.05 [0.02 to 0.08]	0.23 [0.05 to 0.63]	High	Moderate	Moderate	Moderate	Moderate
Cycling 41 outcomes / 7 studies	0.10 [-0.02 to 0.23]	0.09 [0.06 to 0.14]	0.32 [0.09 to 0.66]	Low	Very Low	Very Low	Very Low	Very Low
Walking 12 outcomes / 3 studies	0.17 [-0.43 to 1.2]	0.33 [0.18 to 0.61]	0.03 [0.00 to 0.15]	Moderate	Low	Very Low	Very Low	Very Low
Exercise Characteristics								
Continuous 121 outcomes / 15 studies	0.12 [0.06 to 0.18]	0.06 [0.04 to 0.86]	0.14 [0.04 to 0.39]	High	Moderate	Moderate	Moderate	Moderate
Intermittent 37 outcomes / 8 studies	-0.07 [-0.52 to 0.37]	0.47 [0.36 to 0.62]	0.07 [0.02 to 0.23]	High	Moderate	Low	Very Low	Very Low
Duration (Per 10 Mins) 160 outcomes / 22 studies	0.05 [-0.02 to 0.02]	0.07 [0.05 to 0.10]	0.12 [0.03 to 0.33]	High	Moderate	Low	Low	Low
Intensity Low 113 outcomes / 15 studies	0.10 [0.03 to 0.17]	0.09 [0.07 to 0.12]	0.11 [0.03 to 0.30]	High	Moderate	Moderate	Moderate	Moderate
Intensity High 36 outcomes / 6 studies	0.13 [-0.05 to 0.37]	0.16 [0.11 to 0.25]	0.05 [0.01 to 0.17]	High	Moderate	Low	Very Low	Very Low
Total work done (Per 1000 units) 149 outcomes / 19 studies	0.02 [0.00 to 0.04]	0.07 [0.05 to 0.09]	0.14 [0.03 to 0.38]	High	Moderate	Low	Low	Low
Participant Characteristics								
Male 132 outcomes / 19 studies	0.10 [0.07 to 0.14]	0.02 [0.01 to 0.04]	0.46 [0.13 to 0.84]	High	Moderate	Moderate	Moderate	Moderate
Female 47 outcomes / 8 studies	0.03 [-0.16 to 0.24]	0.22 [0.18 to 0.29]	0.12 [0.04 to 0.25]	Moderate	Moderate	Low	Very Low	Very Low

Mixed: male/female 11 outcomes / 4 studies	0.01 [-0.47 to 0.39]	0.22 [0.11 to 0.39]	0.07 [0.00 to 0.32]	Moderate	Low	Very Low	Very Low	Very Low
Sedentary 32 outcomes / 5 studies	0.09 [-0.08 to 0.27]	0.08 [0.04 to 0.15]	0.59 [0.21 to 0.89]	Low	Moderate	Moderate	Low	Low
Recreational 107 outcomes / 12 studies	0.08 [0.03 to 0.13]	0.05 [0.03 to 0.07]	0.16 [0.04 to 0.46]	High	Moderate	Moderate	Moderate	Low
Athlete 37 outcomes / 11 studies	0.13 [-0.06 to 0.28]	0.13 [0.07 to 0.20]	0.43 [0.14 to 0.76]	High	Moderate	Low	Very Low	Very Low
Moderator Analyses (Sclerostin only)								
Timing								
(Immediately - 8 hours post) 28 outcomes / 9 studies	0.14 [-0.03 to 0.31]	0.11 [0.06 to 0.17]	0.73 [0.40 to 0.92]	High	Moderate	Moderate	Low	Low
(Immediately - 15min post) 14 outcomes / 8 studies	0.24 [-0.06 to 0.53]	0.16 [0.08 to 0.28]	0.64 [0.28 to 0.91]	High	Moderate	Moderate	Low	Low
(> 15 min, ≤ 2 hours post) 14 outcomes / 7 studies	0.05 [-0.16 to 0.27]	0.10 [0.05 to 0.18]	0.63 [0.25 to 0.90]	High	Moderate	Low	Very Low	Very Low
24 hours post 18 outcomes / 10 studies	0.16 [-0.07 to 0.38]	0.18 [0.10 to 0.27]	0.41 [0.12 to 0.79]	High	Moderate	Low	Very Low	Very Low
Exercise Type								
Aerobic 15 outcomes / 3 studies	0.24 [-0.37 to 0.72]	0.26 [0.11 to 0.55]	0.20 [0.04 to 0.67]	High	Moderate	Low	Very Low	Very Low
Plyometric 27 outcomes / 5 studies	0.14 [-0.11 to 0.40]	0.15 [0.08 to 0.25]	0.56 [0.21 to 0.85]	High	Moderate	Low	Very Low	Very Low
Resistance 10 outcomes / 3 studies	-0.06 [-0.86 to 0.68]	0.29 [0.12 to 0.61]	0.48 [0.13 to 0.86]	Moderate	Moderate	Low	Very Low	Very Low

Impact level								
Low impact / High load 16 outcomes / 6 studies	-0.03 [-0.28 to 0.24]	0.11 [0.05 to 0.20]	0.70 [0.31 to 0.93]	High	Moderate	Low	Very Low	Very Low
High impact / directional 23 outcomes / 4 studies	-0.18 [-0.14 to 0.49]	0.15 [0.07 to 0.26]	0.59 [0.21 to 0.89]	Moderate	Moderate	Moderate	Very Low	Very Low
Modality								
Intermittent 14 outcomes / 2 studies	0.20 [-0.80 to 0.76]	0.40 [0.13 to 1.3]	0.09 [0.01 to 0.53]	High	Moderate	Low	Very Low	Very Low
Duration (Per 10 Mins) 15 outcomes / 3 studies	0.16 [-0.40 to 2.3]	0.33 [0.11 to 0.92]	0.12 [0.01 to 0.60]	High	Moderate	Low	Very Low	Very Low
Intensity High 14 outcomes / 2 studies	0.20 [-0.80 to 0.76]	0.40 [0.13 to 1.3]	0.08 [0.01 to 0.53]	High	Moderate	Low	Very Low	Very Low
Total work done (Per 1000 units) 19 outcomes / 4 studies	0.03 [-0.94 to 0.68]	0.35 [0.15 to 0.65]	0.16 [0.04 to 0.54]	High	Moderate	Low	Very Low	Very Low
Participant Characteristics								
Male 20 outcomes / 5 studies	0.10 [-0.29 to 0.46]	0.27 [0.19 to 0.41]	0.13 [0.03 to 0.33]	High	Moderate	Low	Very Low	Very Low
Female 33 outcomes / 7 studies	0.13 [-0.06 to 0.31]	0.11 [0.05 to 0.18]	0.77 [0.43 to 0.95]	High	Moderate	Moderate	Very Low	Very Low
Recreational 37 outcomes / 7 studies	0.12 [-0.05 to 0.27]	0.10 [0.05 to 0.17]	0.71 [0.36 to 0.93]	High	Moderate	Moderate	Low	Low

All variables with sufficient data to analyse are presented.

The Bone Biomarker Response to an Acute Bout of Exercise:

A Systematic Review with Meta-Analysis

Supplementary File 9: Primary meta-analyses and moderator analyses for general bone metabolism

Dolan E[1]*, Dumas A[1], Keane KM[2], Bestetti G[1], Freitas LHM[1], Gualano B[1,3], Kohrt WM[4], Kelley GA[5], Pereira RMR[6], Sale C[7], Swinton PA[8]

[1] Applied Physiology & Nutrition Research Group; School of Physical Education and Sport; Rheumatology Division; Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[2] Department of Sport, Exercise and Nutrition, Galway Mayo Institute of Technology, Ireland.

[3] Food Research Centre, University of São Paulo, SP, BR.

[4] Department of Medicine, Division of Geriatric Medicine, University of Colorado Anschutz Medical Campus, USA.

[5] Department of Epidemiology and Biostatistics, West Virginia University, USA.

[6] Bone Metabolism Laboratory; Rheumatology Division, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[7] Musculoskeletal Physiology Research Group, Sport, Health and Performance Enhancement (SHAPE) Research Centre, School of Science and Technology, Nottingham Trent University, Nottingham, UK.

[8] School of Health Sciences, Robert Gordon University, Aberdeen, UK.

*Corresponding author:

Eimear Dolan:

Faculdade de Medicina FMUSP, Universidade de Sao Paulo – Av. Dr. Arnaldo, 455, 3º andar, ZIP code: 01246-903, Sao Paulo - SP, Brazil.

Phone: +55 11 2648-1337; Fax: +55 11 3061-7490; E-mail: eimeardol@gmail.com or eimeardolan@usp.br

Outcome (#/n)	Summary of findings			Evidence Certainty				
	Effect size Median [95% CrI]	Between study standard error (τ) Median [75% CrI]	ICC Median [75% CrI]	D1 Risk of Bias	D2 Directness	D3 Inconsistency	D4 Imprecision	D5 Small-study Effects
All biomarkers exercise (tOC: 218; Osteopontin: 2) 220 outcomes / 39 studies	0.05 [0.00 to 0.10]	0.09 [0.08 to 0.11]	0.29 [0.11 to 0.48]	High	Moderate	Low	Low	Low
tOC 218 outcomes / 39 studies	0.04 [0.00 to 0.09]	0.08 [0.07 to 0.10]	0.26 [0.09 to 0.44]	High	Moderate	Low	Low	Low
All biomarkers Control 35 outcomes / 10 studies (tOC:35)	-0.03 [-0.14 to 0.12]	0.11 [0.06 to 0.17]	0.20 [0.04 to 0.58]	High	High	Low	Low	Low
Moderator analysis tOC only								
Timing								
(Immediately - 8 hours post) 152 outcomes / 36 studies	0.06 [0.00 to 0.12]	0.10 [0.08 to 0.13]	0.278[0.11 to 0.50]	High	Moderate	Low	Low	Low
(Immediately - 15min post) 65 outcomes / 28 studies	0.08 [0.00 to 0.17]	0.17 [0.13 to 0.21]	0.07 [0.01 to 0.22]	High	Moderate	Low	Low	Low
(> 15 min, ≤ 2 hours post) 52 outcomes / 24 studies	0.06 [-0.01 to 0.16]	0.09 [0.06 to 0.13]	0.11 [0.02 to 0.36]	High	Very Low	Very Low	Very Low	Very Low
(> 2 hours, ≤ 8 hours post) 35 outcomes / 11 studies	-0.08 [-0.20 to 0.04]	0.08 [0.04 to 0.12]	0.55 [0.22 to 0.85]	High	Very Low	Very Low	Very Low	Very Low
24 hours post 36 outcomes / 16 studies	-0.02 [-0.11 to 0.06]	0.04 [0.02 to 0.07]	0.48 [0.14 to 0.83]	High	Very low	Very Low	Very Low	Very Low
48 hours post 13 outcomes / 8 studies	0.01 [-0.16 to 0.17]	0.09 [0.04 to 0.15]	0.34 [0.08 to 0.76]	High	Moderate	Low	Low	Low

72 hours post 12 outcomes / 8 studies	0.05 [-0.11 to 0.22]	0.07 [0.03 to 0.13]	0.41 [0.10 to 0.81]	High	Moderate	Low	Low	Low
Exercise Type								
Aerobic 163 outcomes / 32 studies	0.06 [0.00 to 0.13]	0.12 [0.09 to 0.14]	0.25 [0.09 to 0.44]	High	Moderate	Low	Low	Low
Plyometric 22 outcomes / 4 studies	-0.04 [-0.26 to 0.10]	0.06 [0.03 to 0.13]	0.35 [0.08 to 0.78]	High	High	Moderate	Moderate	Moderate
Resistance 11 outcomes / 4 studies	0.04 [-0.33 to 0.47]	0.16 [0.07 to 0.30]	0.22 [0.04 to 0.66]	High	High	Moderate	Low	Low
Impact level								
Low impact/repetitive 57 outcomes / 13 studies	0.07 [-0.03 to 0.18]	0.07 [0.03 to 0.12]	0.72 [0.37 to 0.93]	Low	Very Low	Very Low	Very Low	Very Low
Moderate impact/repetitive 107 outcomes / 20 studies	0.06 [-0.02 to 0.16]	0.15 [0.12 to 0.18]	0.08 [0.02 to 0.20]	High	Moderate	Low	Low	Low
Low impact/ high load 18 outcomes / 6 studies	0.04 [-0.13 to 0.18]	0.08 [0.04 to 0.14]	0.30 [0.06 to 0.70]	High	High	Moderate	Moderate	Moderate
High impact / directional 24 outcomes / 4 studies	-0.04 [-0.21 to 0.12]	0.06 [0.03 to 0.13]	0.39 [0.09 to 0.80]	High	Moderate	Low	Very Low	Very Low
Modality								
Running 90 outcomes / 15 studies	0.04 [-0.07 to 0.18]	0.17 [0.13 to 0.22]	0.02 [0.00 to 0.07]	High	Moderate	Low	Low	Low
Cycling 55 outcomes / 12 studies	0.05 [-0.05 to 0.14]	0.06 [0.03 to 0.09]	0.80 [0.49 to 0.95]	Low	Very Low	Very Low	Very Low	Very Low
Walking 17 outcomes / 6 studies	0.13 [-0.12 to 0.40]	0.15 [0.08 to 0.25]	0.52 [0.19 to 0.84]	Moderate	Low	Very Low	Very Low	Very Low
Exercise Characteristics								

Continuous 138 outcomes / 25 studies	0.07 [0.01 to 0.14]	0.10 [0.07 to 0.12]	0.24 [0.07 to 0.46]	High	Moderate	Low	Low	Low
Intermittent 26 outcomes / 8 studies	0.01 [-0.20 to 0.24]	0.20 [0.13 to 0.28]	0.24 [0.08 to 0.53]	High	High	Moderate	Low	Low
Duration (Per 10 Mins) 159 outcomes / 30 studies	0.01 [-0.01 to 0.04]	0.09 [0.07 to 0.12]	0.18 [0.05 to 0.38]	High	Moderate	Low	Low	Low
Intensity Low 106 outcomes / 18 studies	0.06 [-0.02 to 0.14]	0.09 [0.07 to 0.12]	0.28 [0.09 to 0.55]	High	Moderate	Low	Low	Low
Intensity High 24 outcomes / 8 studies	0.21 [-0.04 to 0.50]	0.24 [0.16 to 0.35]	0.18 [0.05 to 0.45]	Low	Very Low	Very Low	Very Low	Very Low
Total work done (Per 1000 units) 140 outcomes / 24 studies	0.03 [0.00 to 0.08]	0.08 [0.06 to 0.12]	0.21 [0.06 to 0.45]	High	Moderate	Low	Low	Low
Participant Characteristics								
Male 141 outcomes / 23 studies	0.04 [-0.02 to 0.13]	0.05 [0.02 to 0.08]	0.10 [0.03 to 0.24]	High	Moderate	Low	Low	Low
Female 61 outcomes / 13 studies	0.05 [-0.01 to 0.13]	0.05 [0.03 to 0.09]	0.58 [0.22 to 0.88]	Low	Very Low	Very Low	Very Low	Very Low
Mixed: male/female 16 outcomes / 6 studies	0.03 [-0.19 to 0.27]	0.13 [0.06 to 0.21]	0.51 [0.18 to 0.84]	Low	Very Low	Very Low	Very Low	Very Low
Sedentary 59 outcomes / 10 studies	0.06 [-0.05 to 0.20]	0.14 [0.10 to 0.18]	0.14 [0.03 to 0.34]	High	High	Moderate	Low	Low
Recreational 99 outcomes / 15 studies	0.00 [-0.05 to 0.06]	0.04 [0.02 to 0.06]	0.59 [0.26 to 0.88]	High	Moderate	Low	Low	Low
Athlete 51 outcomes / 12 studies	0.16 [0.01 to 0.36]	0.20 [0.14 to 0.28]	0.11 [0.03 to 0.28]	Low	Very Low	Very Low	Very Low	Very Low

All variables with sufficient data to analyse are presented.

The Bone Biomarker Response to an Acute Bout of Exercise:

A Systematic Review with Meta-Analysis

Supplementary File 10: Primary meta-analyses and moderator analyses for Ca Metabolism

Dolan E[1]*, Dumas A[1], Keane KM[2], Bestetti G[1], Freitas LHM[1], Gualano B[1,3], Kohrt WM[4], Kelley GA[5], Pereira RMR[6], Sale C[7], Swinton PA[8]

[1] Applied Physiology & Nutrition Research Group; School of Physical Education and Sport; Rheumatology Division; Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[2] Department of Sport, Exercise and Nutrition, Galway Mayo Institute of Technology, Ireland.

[3] Food Research Centre, University of São Paulo, SP, BR.

[4] Department of Medicine, Division of Geriatric Medicine, University of Colorado Anschutz Medical Campus, USA.

[5] Department of Epidemiology and Biostatistics, West Virginia University, USA.

[6] Bone Metabolism Laboratory; Rheumatology Division, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[7] Musculoskeletal Physiology Research Group, Sport, Health and Performance Enhancement (SHAPE) Research Centre, School of Science and Technology, Nottingham Trent University, Nottingham, UK.

[8] School of Health Sciences, Robert Gordon University, Aberdeen, UK.

*Corresponding author:

Eimear Dolan:

Faculdade de Medicina FMUSP, Universidade de Sao Paulo – Av. Dr. Arnaldo, 455, 3º andar, ZIP code: 01246-903, Sao Paulo - SP, Brazil.

Phone: +55 11 2648-1337; Fax: +55 11 3061-7490; E-mail: eimeardol@gmail.com or eimeardolan@usp.br

Outcome (#/n)	Summary of findings			Evidence Certainty				
	Effect size Median [95% CrI]	Between study standard error (τ) Median [75% CrI]	ICC Median [75% CrI]	D1 Risk of Bias	D2 Directness	D3 Inconsistency	D4 Imprecision	D5 Small-study Effects
PTH 187 outcomes / 36 studies	0.60 [0.27 to 0.93]	0.80 [0.71 to 0.90]	0.33 [0.11 to 0.50]	Moderate	Low	Very Low	Very Low	Very Low
ICA 102 outcomes / 18 studies	-0.43 [-1.2 to 0.20]	1.0 [0.82 to 1.3]	0.42 [0.18 to 0.62]	Moderate	Low	Very Low	Very Low	Very Low
ACA 32 outcomes / 9 studies	0.09 [-0.28 to 0.47]	0.37 [0.24 to 0.53]	0.36 [0.13 to 0.63]	Moderate	Low	Very Low	Very Low	Very Low
PTH Control 16 outcomes / 4 studies	0.04 [-0.51 to 0.68]	0.35 [0.21 to 0.58]	0.07 [0.01 to 0.25]	High	High	Moderate	Low	Very Low
Control 17 outcomes / 3 studies (ICA = 12; ACA: 5)	-0.39 [-1.9 to 1.2]	1.1 [0.74 to 1.6]	0.01 [0.00 to 0.04]	High	High	Moderate	Low	Very Low
Moderator analyses (PTH only)								
Timing								
(Immediately - 8 hours post) 167 outcomes / 35 studies	0.65 [0.30 to 1.0]	0.83 [0.72 to 0.94]	0.36 [0.14 to 0.52]	Moderate	Low	Very Low	Very Low	Very Low
(Immediately - 15min post) 83 outcomes / 32 studies	1.4 [0.80 to 1.9]	1.1 [0.96 to 1.3]	0.36 [0.14 to 0.53]	Moderate	Low	Low	Low	Very Low
(> 15 min, ≤ 2 hours post) 70 outcomes / 23 studies	0.05 [-0.33 to 0.41]	0.75 [0.66 to 0.87]	0.13 [0.04 to 0.22]	Moderate	Low	Very Low	Very Low	Very Low

(> 2 hours, ≤ 8 hours post) 14 outcomes / 8 studies	-0.09 [-0.43 to 0.24]	0.32 [0.22 to 0.43]	0.13 [0.03 to 0.38]	High	High	Moderate	Low	Very Low
24 hours post 14 outcomes / 9 studies	0.07 [-0.39 to 0.47]	0.37 [0.19 to 0.55]	0.33 [0.08 to 0.72]	High	High	Moderate	Low	Very Low
Exercise Type								
Aerobic 138 outcomes / 29 studies	0.91 [0.49 to 1.3]	0.80 [0.69 to 0.93]	0.50 [0.23 to 0.67]	Moderate	Low	Low	Very Low	Very Low
Resistance 26 outcomes / 5 studies	-0.28 [-0.58 to 0.40]	0.13 [0.06 to 0.25]	0.65 [0.25 to 0.91]	High	High	High	Moderate	Low
Plyometric 22 outcomes / 3 studies	-0.10 [-0.55 to 0.52]	0.17 [0.07 to 0.37]	0.70 [0.27 to 0.94]	High	High	Moderate	Low	Very Low
Impact level								
Low impact/repetitive 71 outcomes / 13 studies	0.95 [0.01 to 1.9]	1.1 [0.57 to 1.5]	0.37 [0.15 to 0.59]	Moderate	Low	Very Low	Very Low	Very Low
Moderate impact/repetitive 67 outcomes / 17 studies	0.82 [0.36 to 1.3]	0.61 [0.51 to 0.75]	0.48 [0.23 to 0.65]	Moderate	Low	Low	Very Low	Very Low
Low impact/ high load 31 outcomes / 7 studies	-0.26 [-0.50 to -0.04]	0.11 [0.05 to 0.19]	0.71 [0.33 to 0.93]	High	High	High	Moderate	Low
High impact / directional 18 outcomes / 2 studies	-0.13 [-1.3 to 0.89]	0.34 [0.15 to 0.91]	0.35 [0.07 to 0.80]	High	High	Moderate	Low	Very Low
Modality								
Running 34 outcomes / 11 studies	0.65 [0.25 to 1.1]	0.17 [0.08 to 0.32]	0.92 [0.72 to 0.99]	Moderate	Low	Low	Very Low	Very Low
Cycling 71 outcomes / 13 studies	0.95 [0.01 to 1.9]	1.3 [1.0 to 1.6]	0.37 [0.15 to 0.59]	Moderate	Low	Very Low	Very Low	Very Low
Walking 33 outcomes / 7 studies	1.0 [0.09 to 1.9]	0.93 [0.73 to 1.2]	0.29 [0.11 to 0.47]	Moderate	Low	Very Low	Very Low	Very Low

Exercise Characteristics								
Continuous 136 outcomes / 28 studies	0.89 [0.47 to 1.3]	0.82 [0.70 to 0.95]	0.46 [0.18 to 0.62]	Moderate	Low	Very Low	Very Low	Very Low
Duration (Per 10 Mins) 142 outcomes / 30 studies	0.08 [0.04 to 0.20]	0.86 [0.73 to 1.0]	0.44 [0.19 to 0.62]	Moderate	Low	Very Low	Very Low	Very Low
Intensity Low 96 outcomes / 16 studies	0.94 [0.30 to 1.6]	0.91 [0.76 to 1.1]	0.49 [0.23 to 0.66]	Moderate	Low	Very Low	Very Low	Very Low
Intensity High 20 outcomes / 4 studies	0.47 [-1.7 to 2.1]	1.6 [0.97 to 2.6]	0.22 [0.07 to 0.56]	Moderate	Low	Very Low	Very Low	Very Low
Total work done (Per 1000 units) 120 outcomes / 19 studies	0.11 [-0.08 to 0.32]	0.87 [0.74 to 1.0]	0.45 [0.20 to 0.61]	Moderate	Low	Very Low	Very Low	Very Low
Participant Characteristics								
Male 115 outcomes / 21 studies	0.53 [0.03 to 1.1]	0.95 [0.77 to 1.2]	0.23 [0.09 to 0.38]	High	Low	Very Low	Very Low	Very Low
Female 40 outcomes / 10 studies	0.71 [-0.07 to 1.5]	0.80 [0.61 to 1.0]	0.45 [0.18 to 0.65]	Moderate	Low	Very Low	Very Low	Very Low
Mixed: male/female 32 outcomes / 6 studies	1.1 [0.04 to 2.0]	0.95 [0.73 to 1.3]	0.22 [0.08 to 0.42]	Moderate	Low	Low	Very Low	Very Low
Sedentary 14 outcomes / 5 studies	0.66 [0.03 to 1.4]	0.38 [0.19 to 0.64]	0.53 [0.19 to 0.85]	Moderate	Low	Low	Very Low	Very Low
Recreational 88 outcomes / 15 studies	0.29 [-0.20 to 0.75]	0.81 [0.69 to 0.95]	0.17 [0.06 to 0.27]	High	Low	Very Low	Very Low	Very Low
Athlete 78 outcomes / 15 studies	1.1 [0.33 to 1.9]	0.97 [0.76 to 1.3]	0.61 [0.33 to 0.77]	Moderate	Low	Very Low	Very Low	Very Low

All variables with sufficient data to analyse are presented.