

Systematic review and meta-analysis of protein intake to support muscle mass and function in healthy adults

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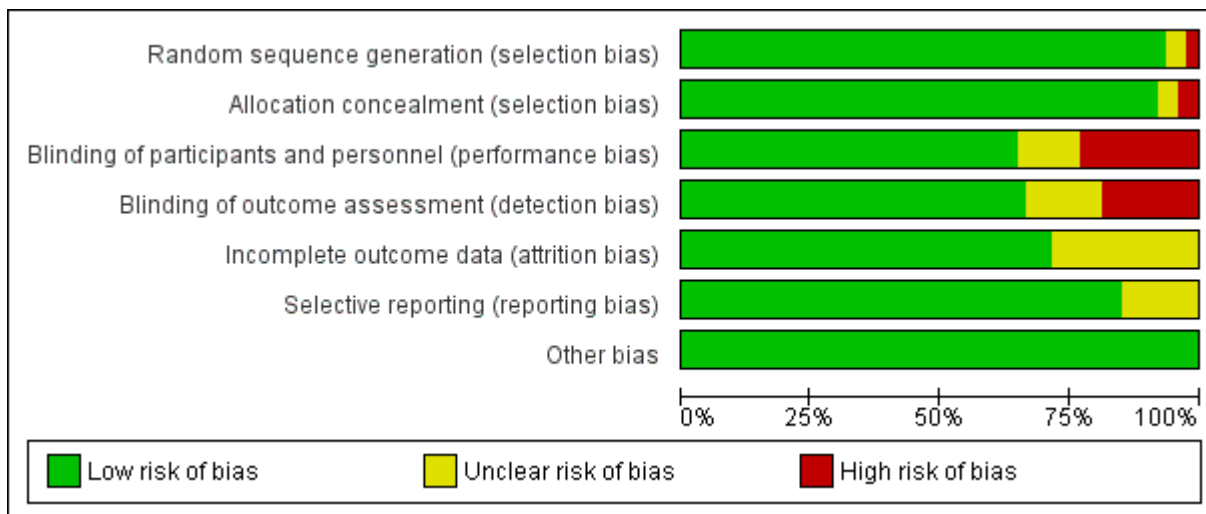
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	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Aas 2020	+	+	-	-	+	+	+
Aleman-Mateo 2014	+	+	-	-	+	+	+
Amasene 2019	+	+	-	-	+	+	+
Antonio 2014	?	-	-	-	+	+	+
Antonio 2015	?	-	-	-	+	+	+
Aristizabal 2015	+	+	+	+	+	+	+
Arnarson 2013	+	+	+	+	+	+	+
Babault 2014	+	+	+	+	+	+	+
Bartholomae 2019	+	-	?	?	+	+	+
Bridge 2019	+	?	?	?	+	+	+
Brown 2004	+	+	+	+	+	+	+
Burke 2001	+	+	+	+	+	+	+
Campbell 2018	?	?	?	?	+	+	+
Candow 2006	+	+	+	+	+	+	+
Candow 2006a	+	+	+	+	+	+	+
Chale 2013	+	+	+	+	+	+	+
Coburn 2006	+	+	+	+	+	+	+
Deibert 2011	+	-	-	?	+	+	+
Dillon 2009	+	+	+	+	+	+	+
Dulac 2020	+	+	+	+	+	+	+
Eliot 2008	+	+	+	+	+	+	+
Erskine 2012	+	+	+	+	+	+	+
Farup 2014	+	+	+	+	+	+	+
Gryson 2014	+	+	+	+	+	+	+
Hartman 2007	+	?	?	?	+	+	+
Haun 2018	+	+	+	+	+	+	+
Herda 2013	+	+	+	+	+	+	+
Hida 2012	+	+	+	+	+	+	+
Hoffman 2007	+	+	+	+	+	+	+
Hoffman 2009	+	?	?	?	+	+	+
Iglay 2009	+	-	-	?	+	+	+
Kerksick 2006	+	+	+	+	+	+	+
Kim 2014	+	+	+	+	+	+	+
Kim 2020	+	-	-	?	+	+	+
Kirmse 2019	+	+	+	+	+	+	+
Leenders 2013	+	+	+	+	+	+	+
Lockwood 2017	+	+	+	+	+	+	+
Maesta 2007	+	+	+	+	+	+	+
Mobley 2017	+	+	+	+	+	+	+
Mori 2018	?	?	-	?	+	+	+
Nabuco 2018	+	+	+	+	+	+	+
Nabuco 2019a	+	+	+	+	+	+	+
Nabuco 2019c	+	+	+	+	+	+	+
Naclerio 2017	+	+	+	+	+	+	+
Nacleno 2017a	+	+	+	+	+	+	+
Nahas 2019	+	?	?	?	+	+	+
Nakayama 2020	+	+	+	+	+	+	+
Negro 2014	+	-	-	?	?	+	+
Norton 2016	+	+	+	+	+	+	+
Oertzen-Hagemann 2019	+	+	+	+	+	+	+
Ormsbee 2018	+	?	?	?	?	+	+
Orsatti 2018	+	+	+	+	+	+	+
Ottestad 2017	+	+	+	+	+	+	+
Ozan 2020	-	?	-	?	?	+	+
Paoli 2015	+	-	-	?	?	?	+
Pihoker 2019	+	+	-	-	?	?	+
Planella-Farrugia 2019	+	-	-	?	?	+	+
Rankin 2004	-	-	-	?	?	+	+
Reidy 2016	+	+	+	+	+	+	+
Rossato 2017	+	?	?	?	?	+	+
Rozenek 2002	+	+	+	+	+	+	+
Sharp 2018	+	+	+	+	+	+	+
Snijders 2015	+	+	+	+	+	+	+
Spillane 2016	+	+	+	+	+	+	+
Taylor 2016	+	+	+	+	+	+	+
van Dongen 2020	+	-	-	?	?	+	+
Vangsoe 2018	+	?	?	?	?	+	+
Verdijk 2009	+	?	+	+	+	+	+
Votek 2013	+	+	+	+	+	+	+
Walker 2010	+	+	+	?	?	+	+
Watanabe 2018	+	+	+	+	+	+	+
Weisgarber 2012	+	+	+	+	+	+	+
Willoughby 2007	+	+	+	+	+	+	+
Zhu 2015	+	+	+	+	+	+	+

Supplementary Figure 1 – Risk of bias analysis of all studies included in the meta-analysis. (+) – Circles filled in green = Low risk of bias; (?) – Circles filled in yellow = Unclear risk of bias; (-) – Circles filled in red = High risk of bias.



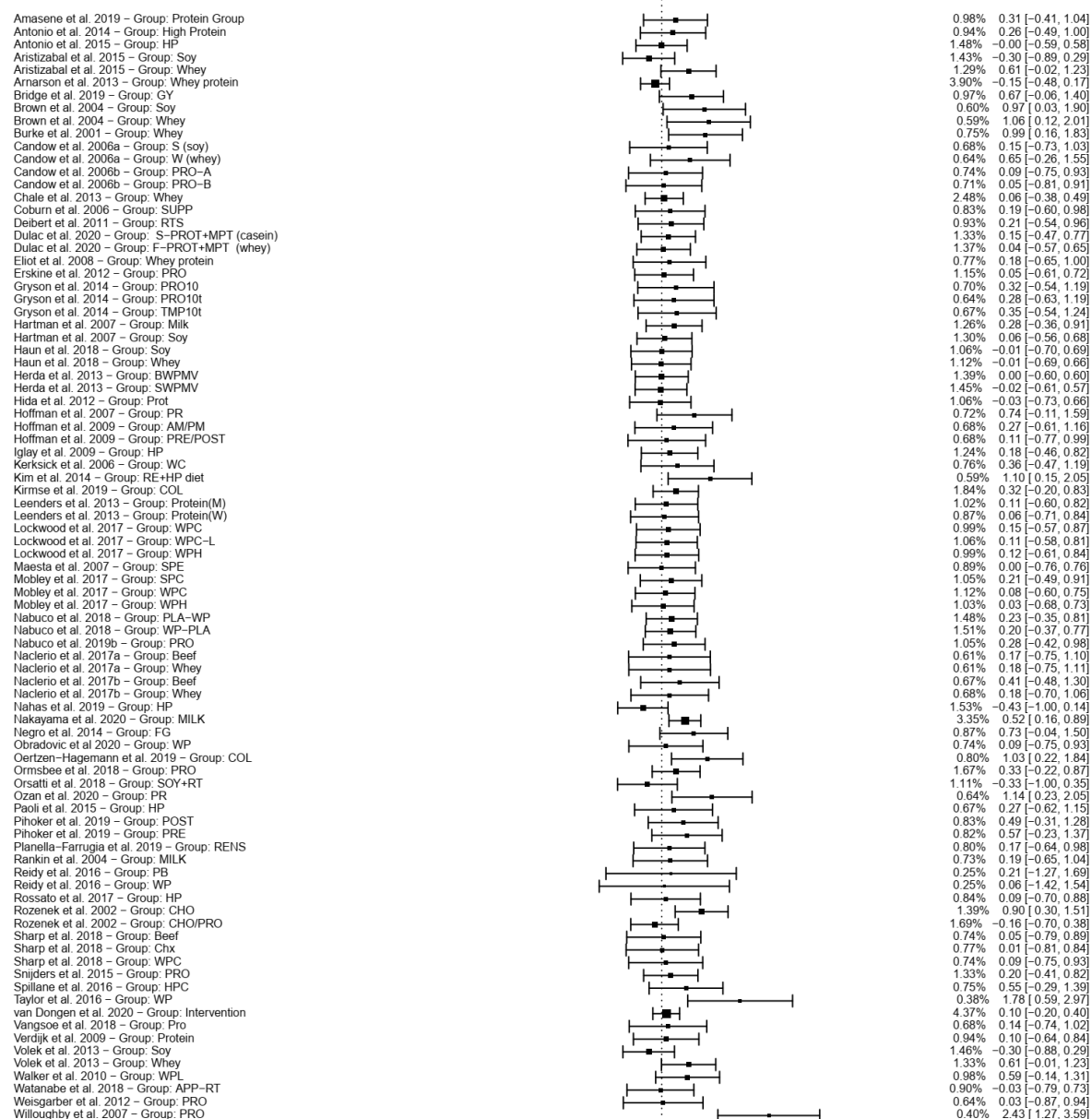
Supplementary Figure 2 – Summary of risk of bias analysis showing the percentage of studies with potential unclear or high risk of selection, performance, detection, attrition, reporting, or other bias.

Lean body mass gain with additional protein ingestion by resistance exercise enrolment

Study - Group

Weight SMD [95% CI]

RCT with Resistance Exercise

RE Multi-Level Model for Subgroup (Q = 88.77, df = 86, p = 0.398; I² = 6.24%)

0.22 [0.14, 0.30]

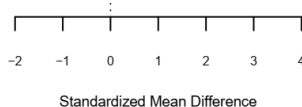
RCT without Resistance Exercise

RE Multi-Level Model for Subgroup (Q = 6.36, df = 6, p = 0.384; I² = 25.06%)

0.21 [-0.15, 0.58]

RE Multi-level model (Q = 94.69, df = 92, p = 0.403; Overall I² = 6.67%)

100.00% 0.22 [0.15, 0.30]

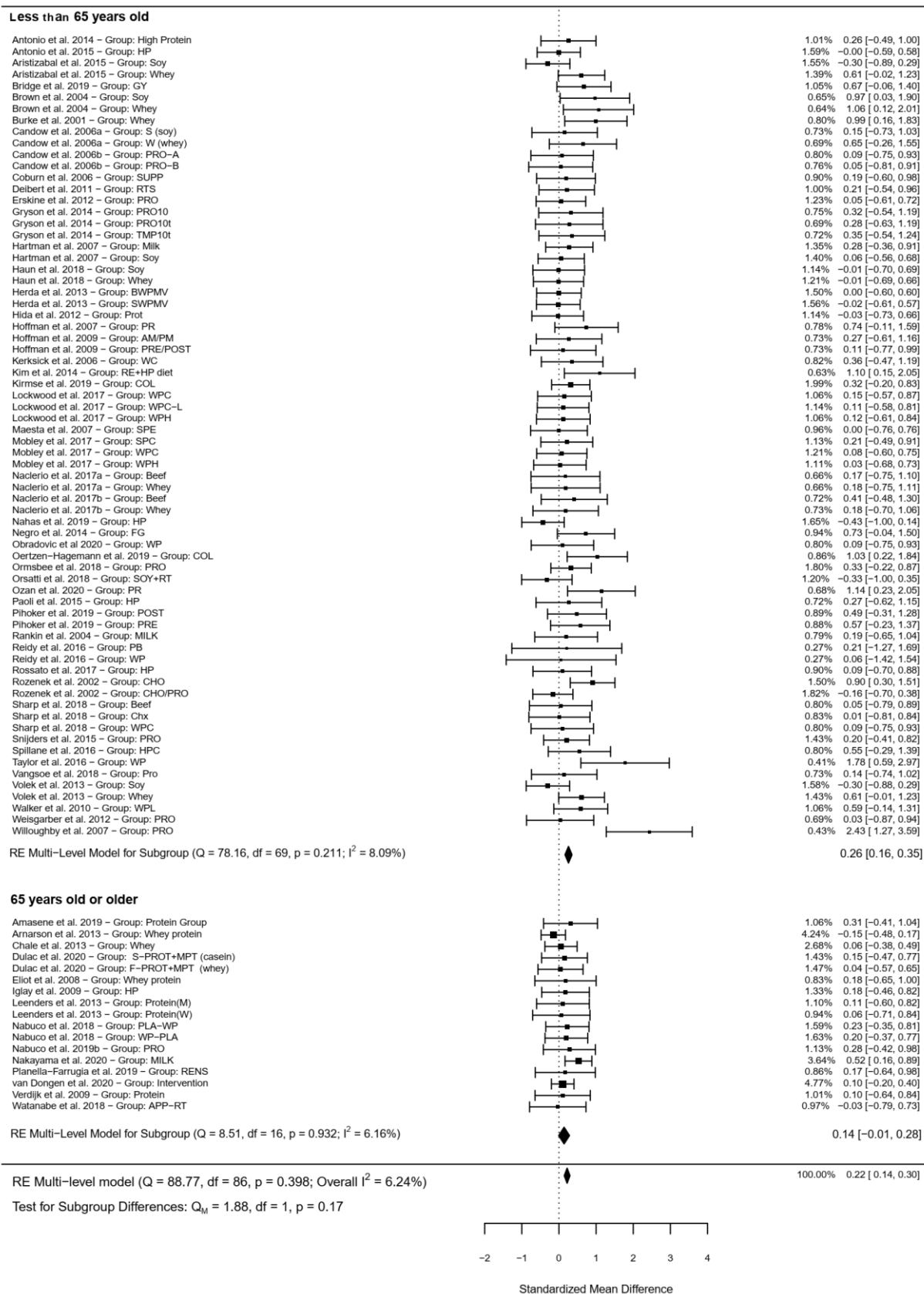
Test for Subgroup Differences: Q_M = 2.28, df = 1, p = 0.13

Supplementary Figure 3 – Forest plot showing results of the three-level random-effects meta-analysis of studies testing the effects of ingesting additional protein on adults' lean body or muscle mass, including or not a resistance exercise program.

Lean body mass gain with resistance exercise plus protein ingestion by Age

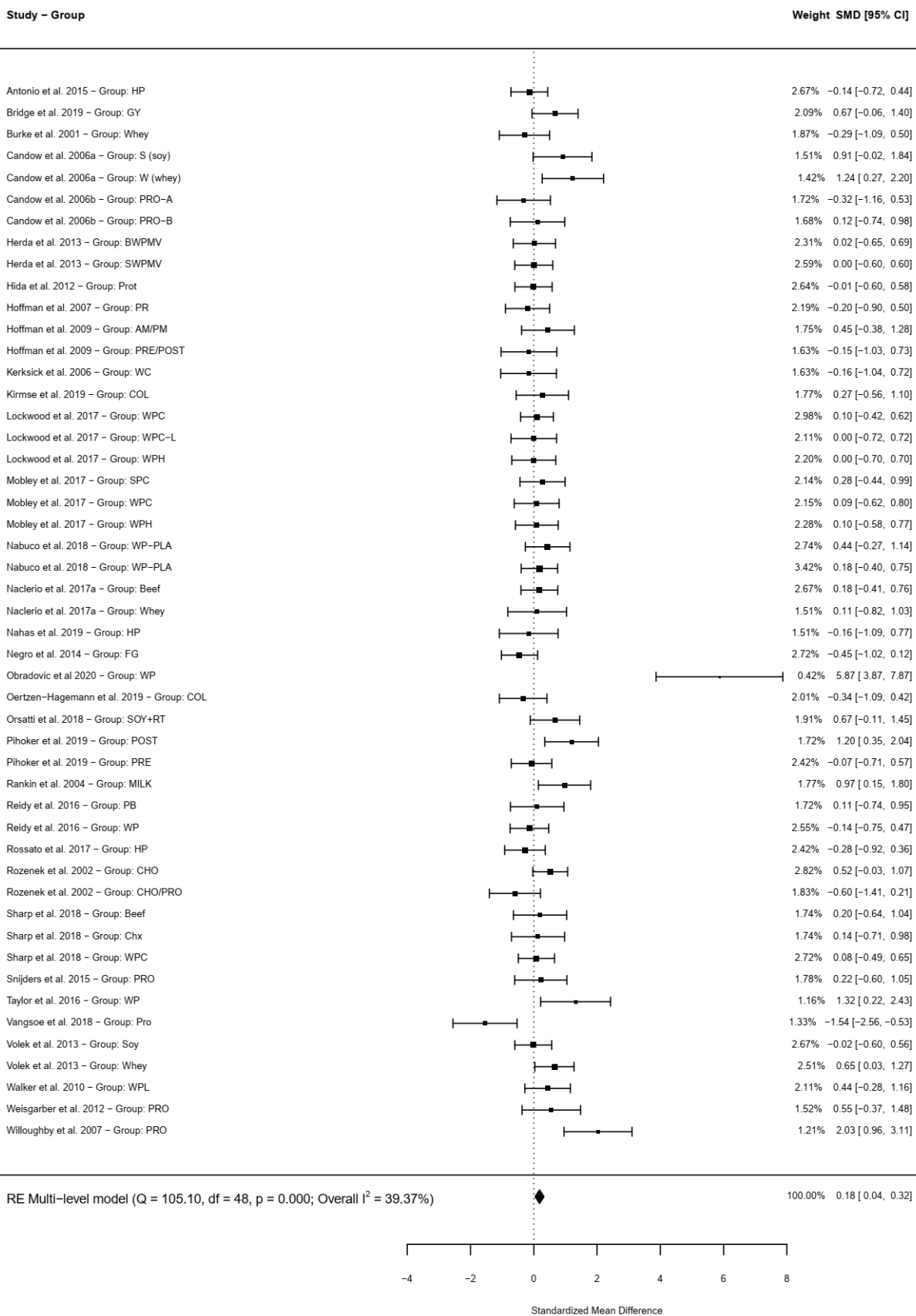
Study - Group

Weight SMD [95% CI]



Supplementary Figure 4 – Forest plot showing results of the three-level random-effects meta-analysis of studies testing the effects of ingesting additional protein on adults' lean body or muscle mass of subjects categorized by age < 65 or ≥ 65 years old in studies including a resistance exercise program.

Bench strength gain with resistance exercise and additional protein ingestion



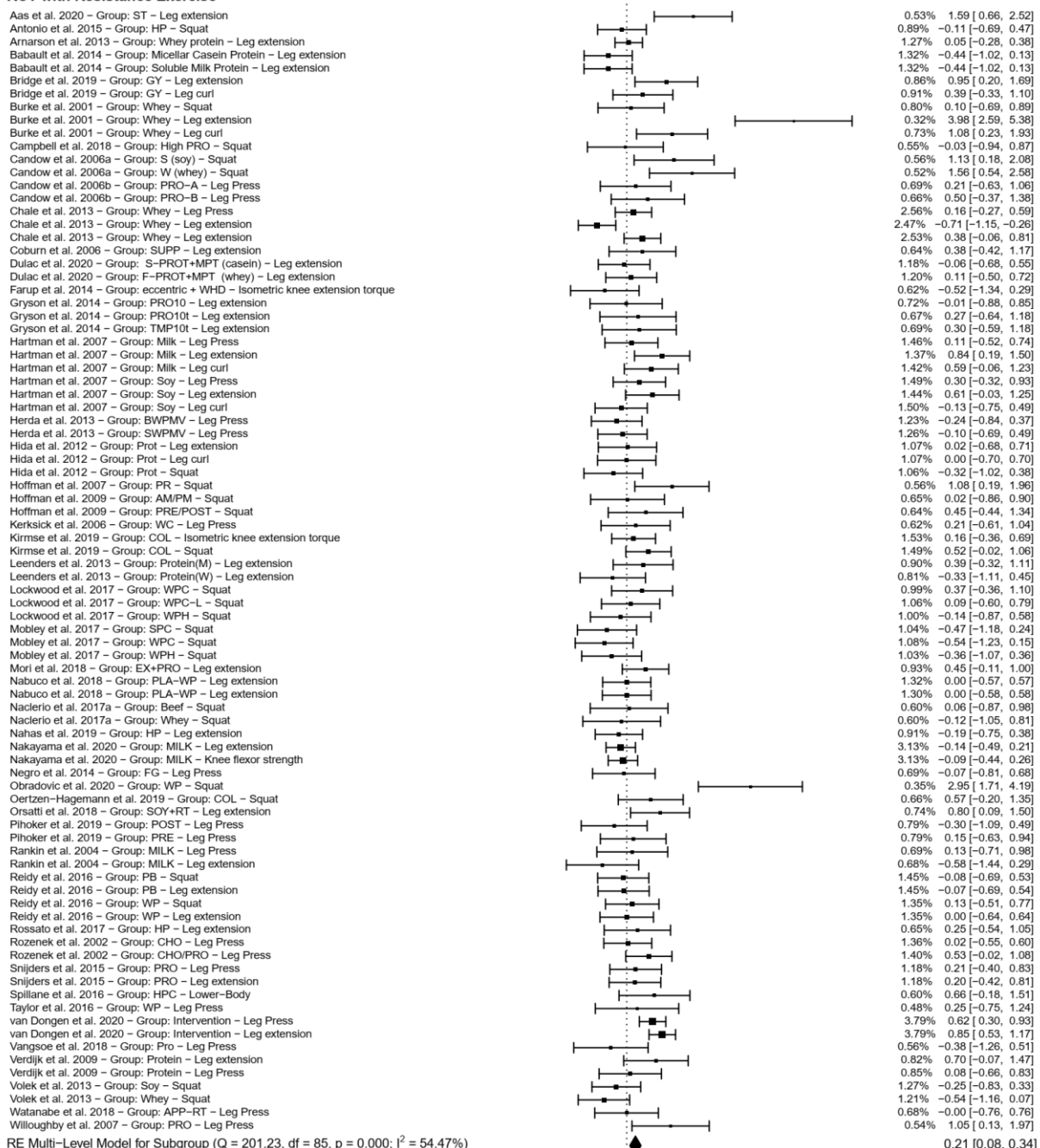
Supplementary Figure 5 – Forest plot showing results of the three-level random-effects meta-analysis of studies testing the effects of ingesting additional protein and resistance exercise on adults' bench press strength.

Lower body strength gain with additional protein ingestion by enrolment in resistance exercise training

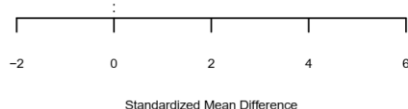
Study – Group

Weight SMD [95% CI]

RCT with Resistance Exercise



RCT without Resistance Exercise

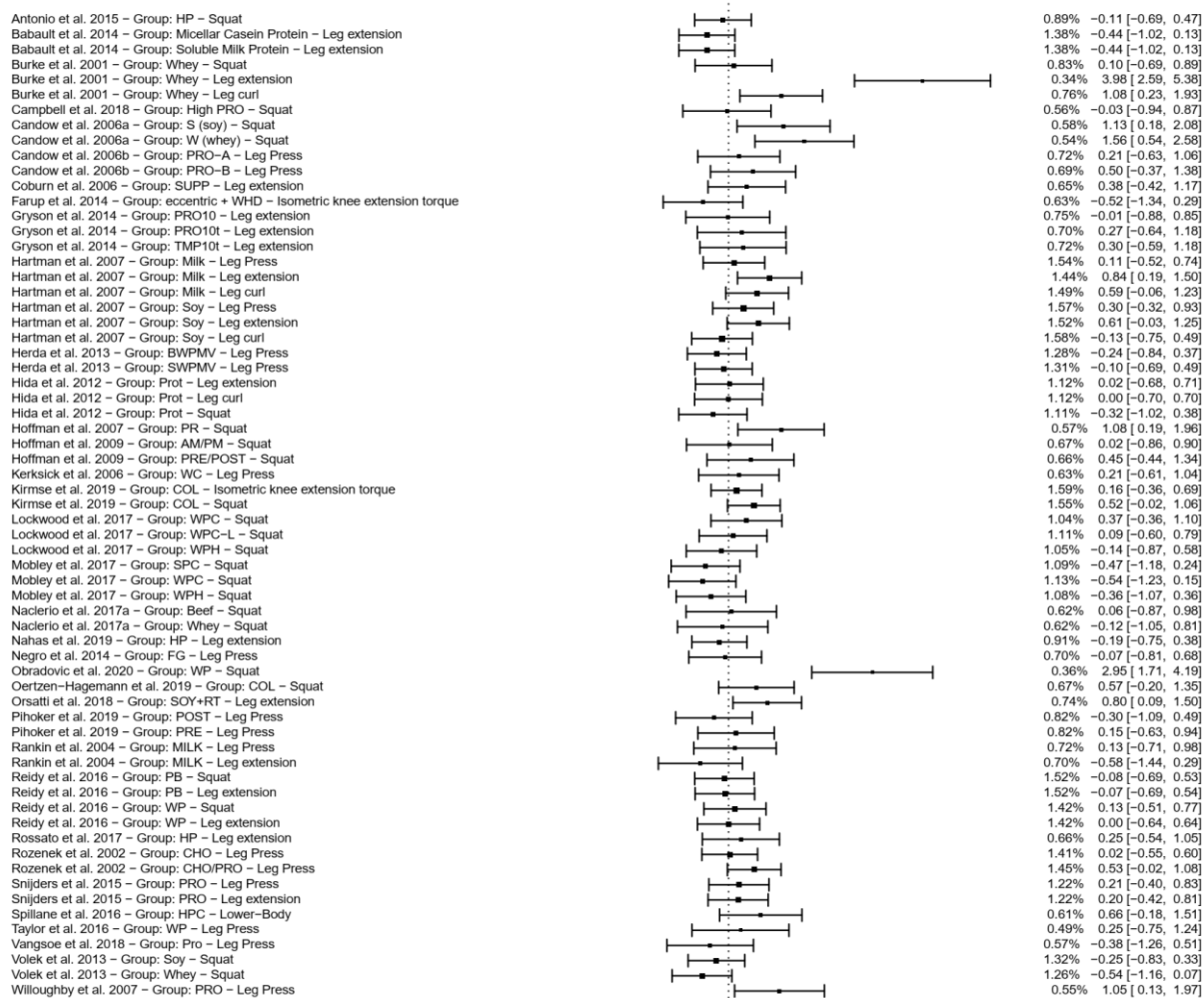
RE Multi-level model (Q = 204.23, df = 89, p = 0.000; Overall I² = 52.77%)Test for Subgroup Differences: Q_{tt} = 0.02, df = 1, p = 0.88

Supplementary Figure 6 – Forest plot showing results of the three-level random-effects meta-analysis of studies testing the effects of ingesting additional protein on adults' lower-body strength by the presence or not of resistance exercise training in a study research protocol.

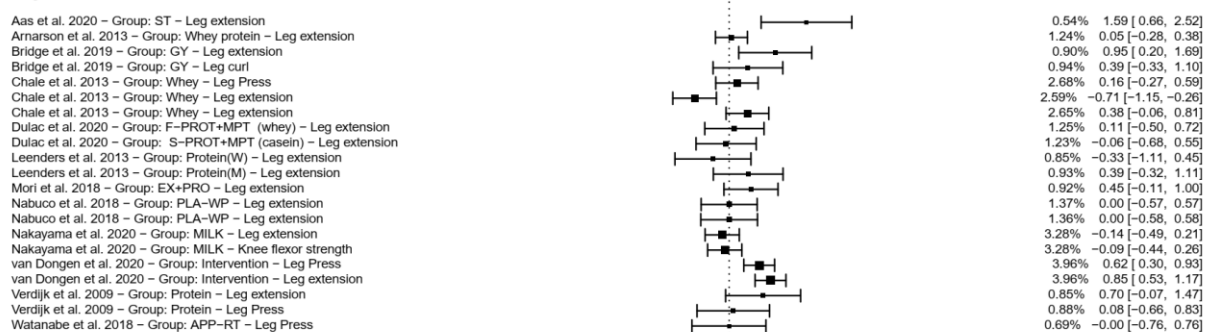
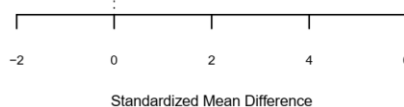
Lower body strength gain with resistance exercise plus protein ingestion by Age Study – Group

Weight SMD [95% CI]

Less than 65 years old

RE Multi-Level Model for Subgroup (Q = 134.22, df = 64, p = 0.000; I² = 52.78%)

65 years old or older

RE Multi-Level Model for Subgroup (Q = 65.44, df = 20, p = 0.000; I² = 60.57%)RE Multi-level model (Q = 201.23, df = 85, p = 0.000; Overall I² = 54.47%)Test for Subgroup Differences: Q_M = 0.20, df = 1, p = 0.66

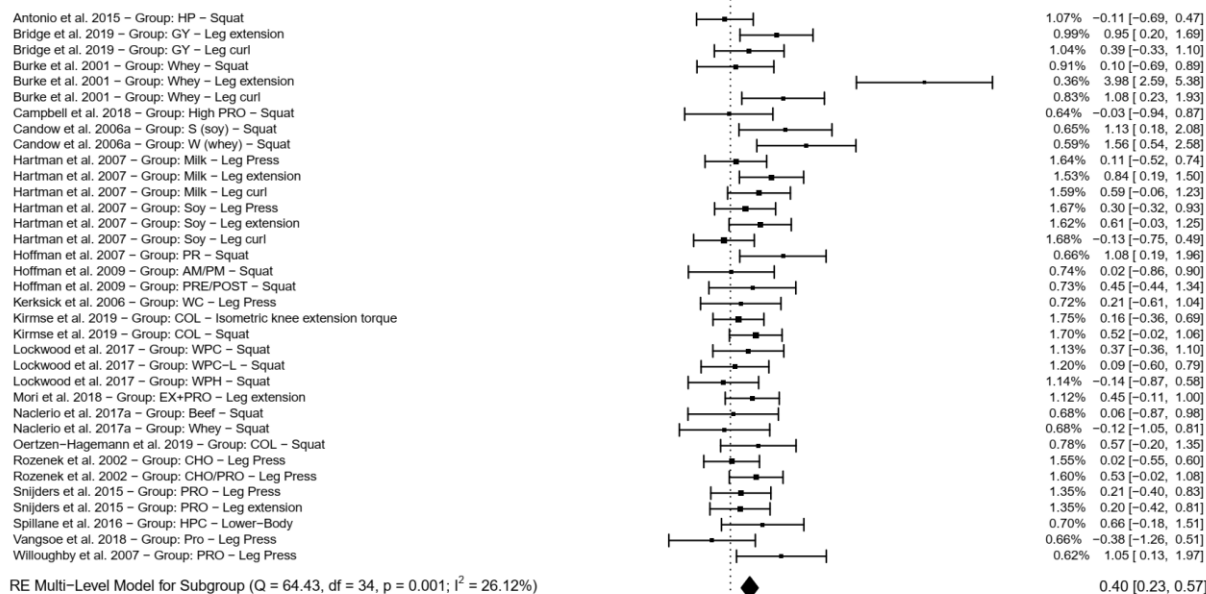
Supplementary Figure 7 – Forest plot showing results of the three-level random-effects meta-analysis of studies reporting daily protein ingestion and testing the effects of ingesting additional protein and resistance exercise on adults' lower body strength by age < 65 or ≥ 65 years old.

Lower body strength gain with resistance exercise plus protein ingestion by daily protein ingestion

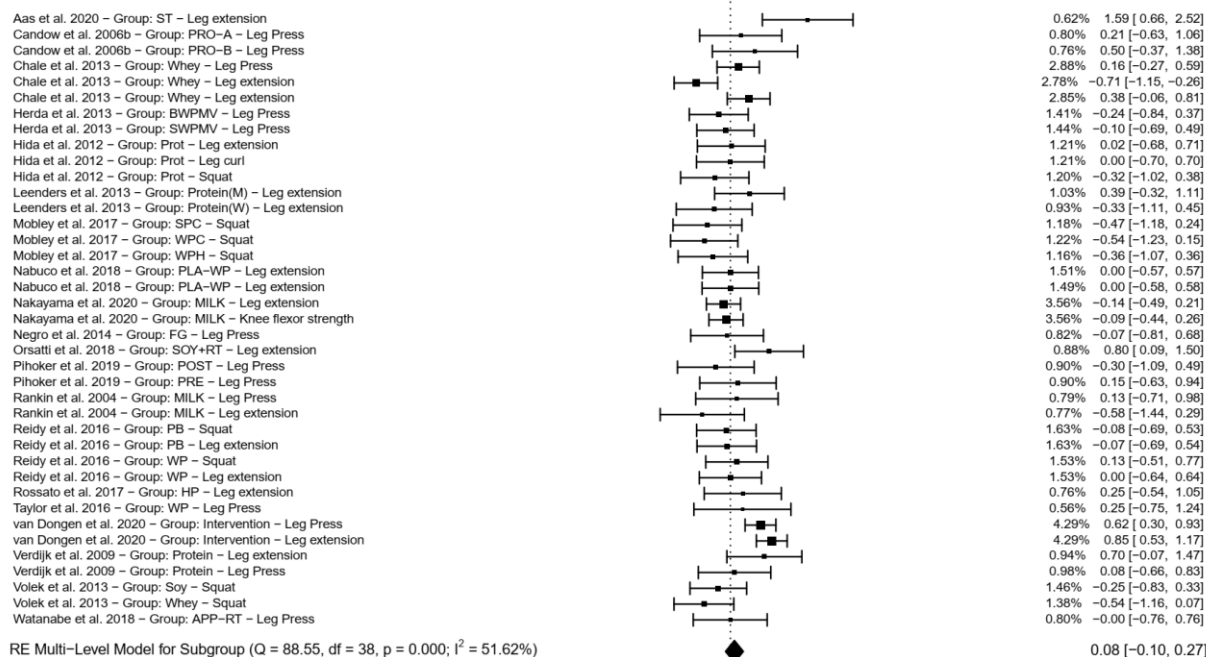
Study – Group

Weight SMD [95% CI]

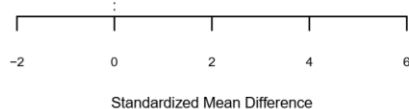
Higher or equal to 1.60 g/kg/day



Between 1.2 and 1.59 g/kg/day

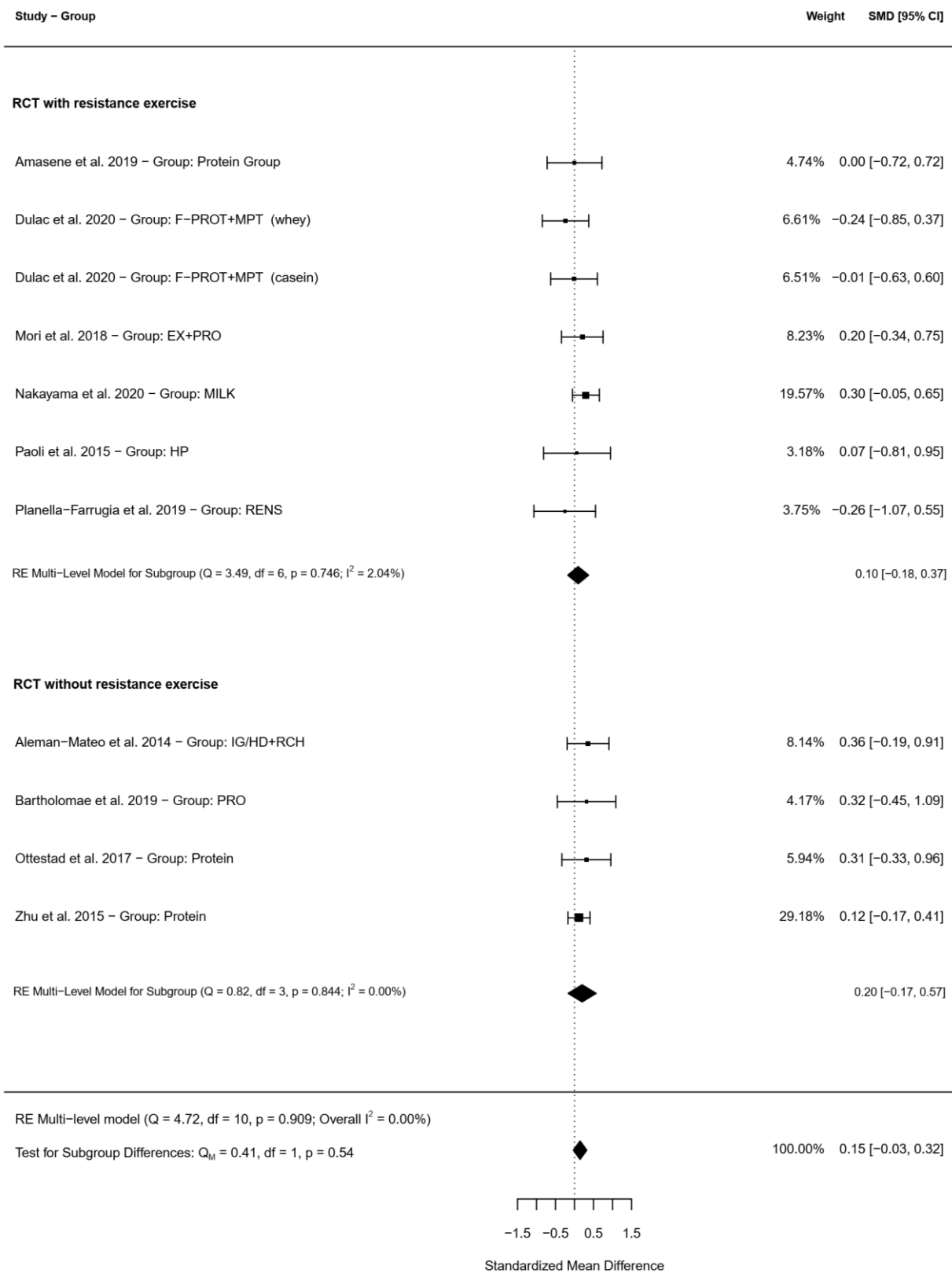


Less than 1.2 g/kg/day

RE Multi-level model (Q = 169.03, df = 75, p = 0.000; Overall I² = 49.49%)Test for Subgroup Differences: Q_M = 7.28, df = 1, p = 0.01

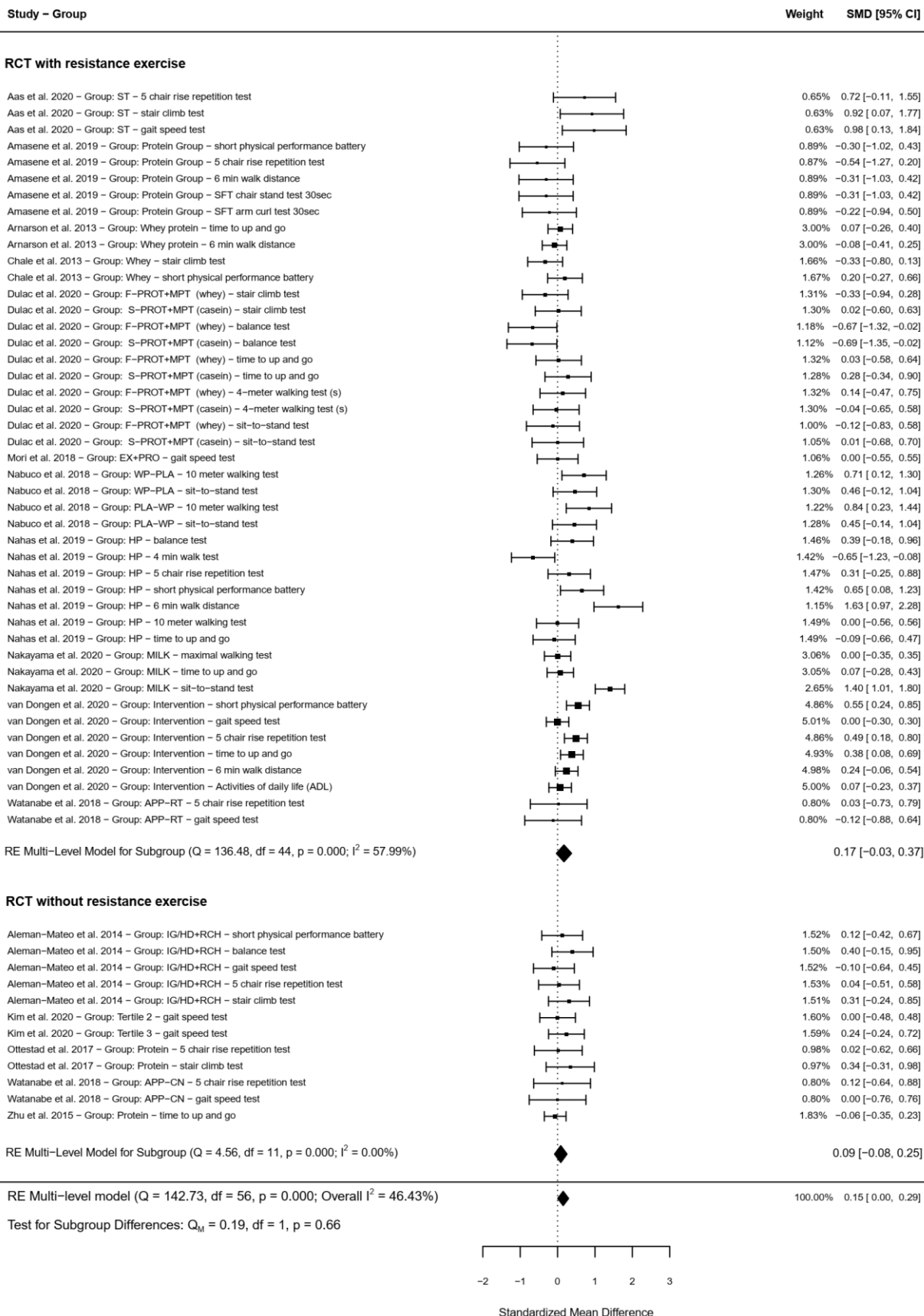
Supplementary Figure 8 – Forest plot showing results of the three-level random-effects meta-analysis of studies reporting daily protein ingestion and testing the effects of ingesting additional protein on adults' lower body strength by the level of protein ingestion.

Handgrip strength gains with protein supplementation by resistance exercise training

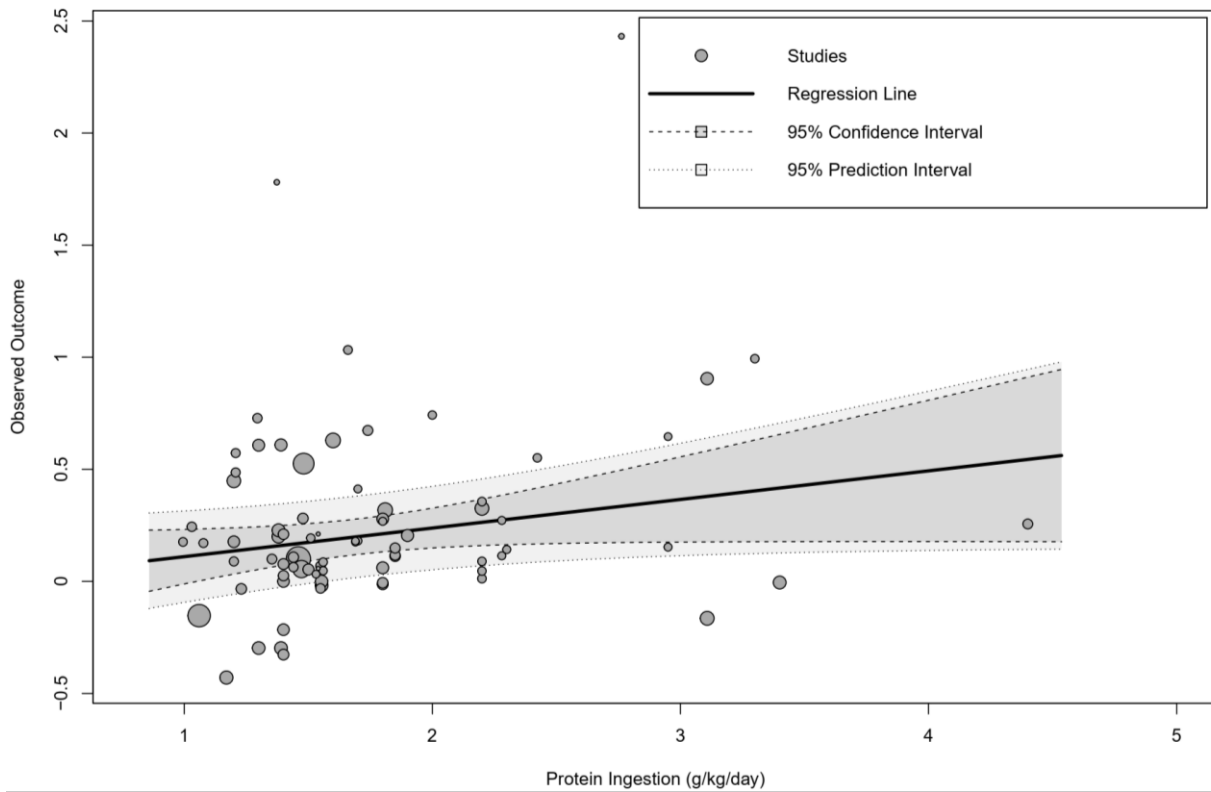


Supplementary Figure 9 – Forest plot showing results of the three-level random-effects meta-analysis of studies testing the effects of ingesting additional protein on adults' handgrip strength by the presence or not of resistance exercise training in a study research protocol.

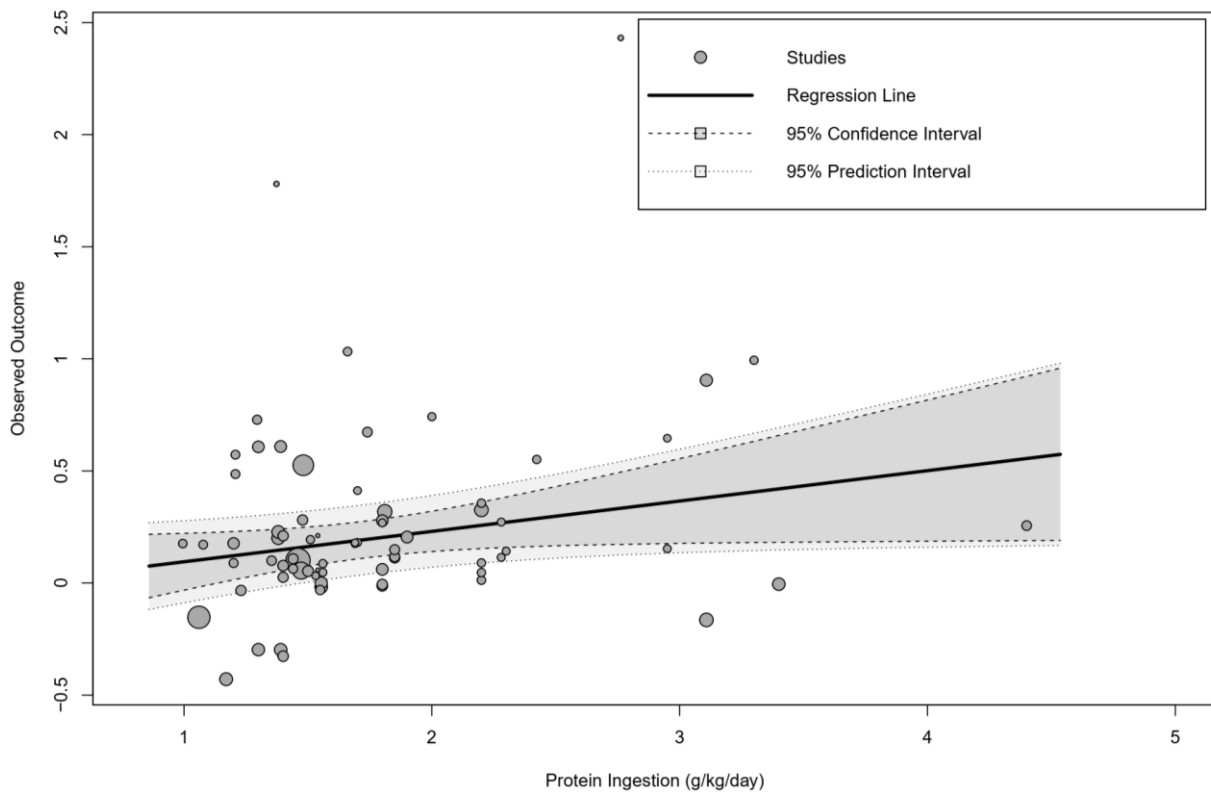
Physical function with protein supplementation by resistance exercise training



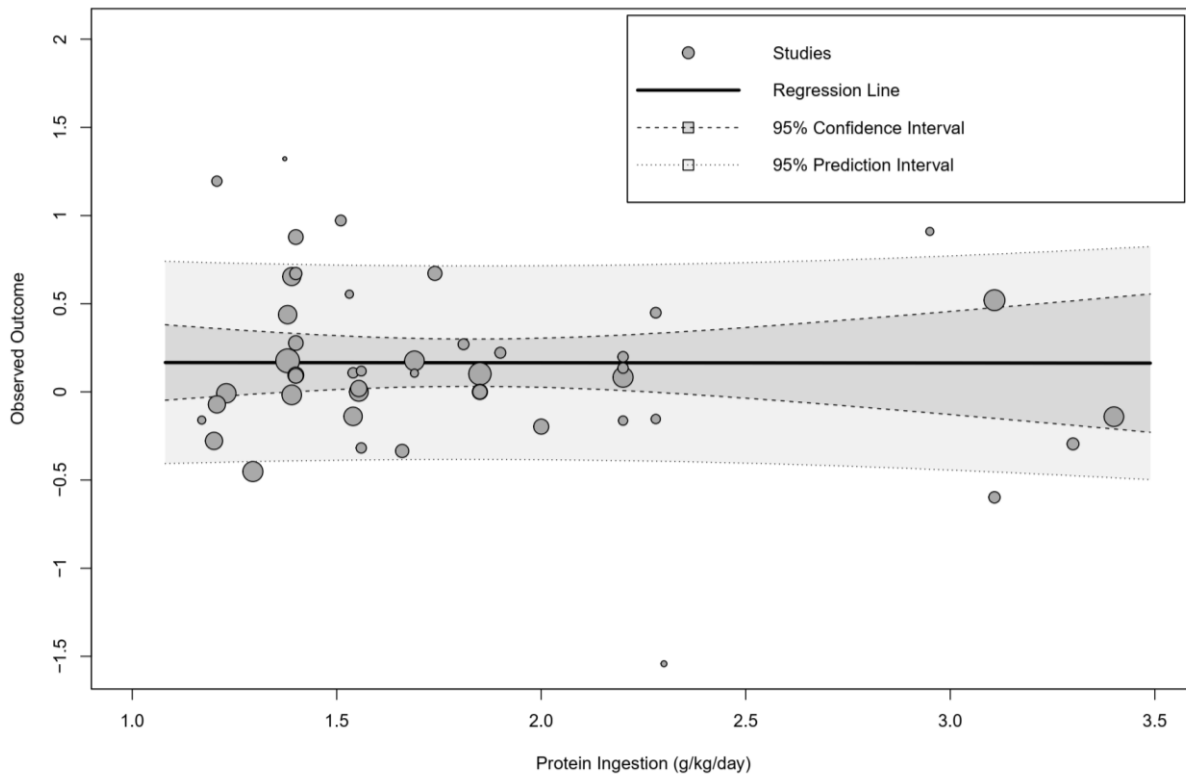
Supplementary Figure 10 – Forest plot showing results of the three-level random-effects meta-analysis of studies testing the effects of ingesting additional protein on adults' physical testing performance by the presence or not of resistance exercise training in a study research protocol.



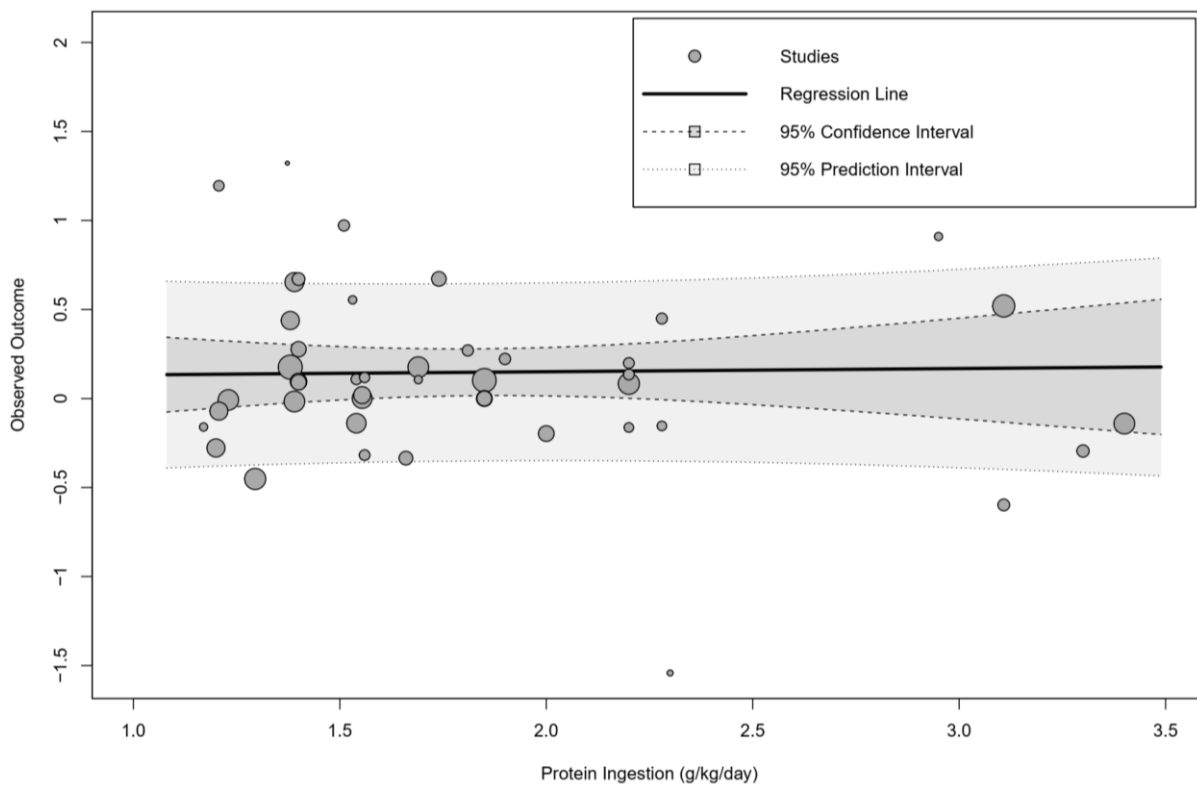
Supplementary Figure 11 – Bubble plot of three-level meta-regression analysis of the main effect on lean body mass vs. total daily protein ingestion (g/kg/day) in studies testing interventions to increase protein ingestion in all included RCT reporting protein ingestion.



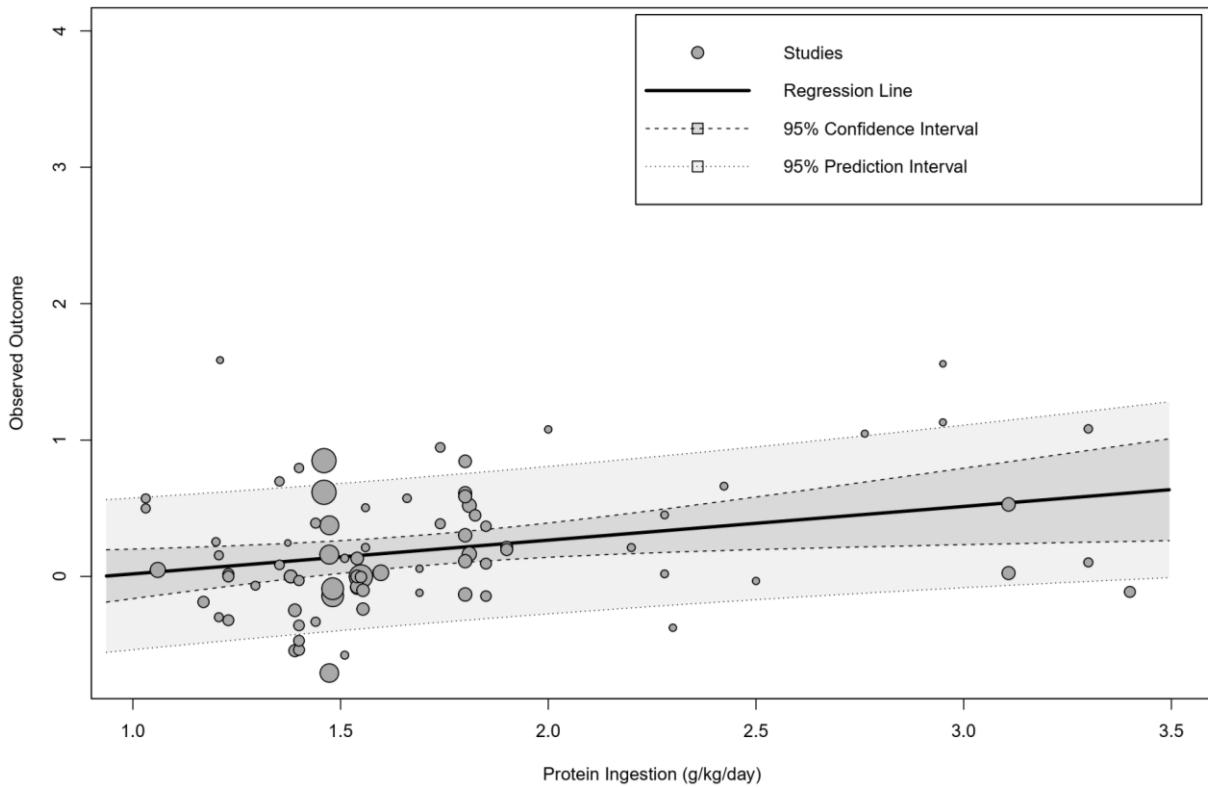
Supplementary Figure 12 – Bubble plot of three-level meta-regression analysis of the main effect on lean body mass vs. total daily protein ingestion (g/kg/day) in studies testing interventions to increase protein ingestion in all included RCT using resistance exercise training and reporting protein ingestion.



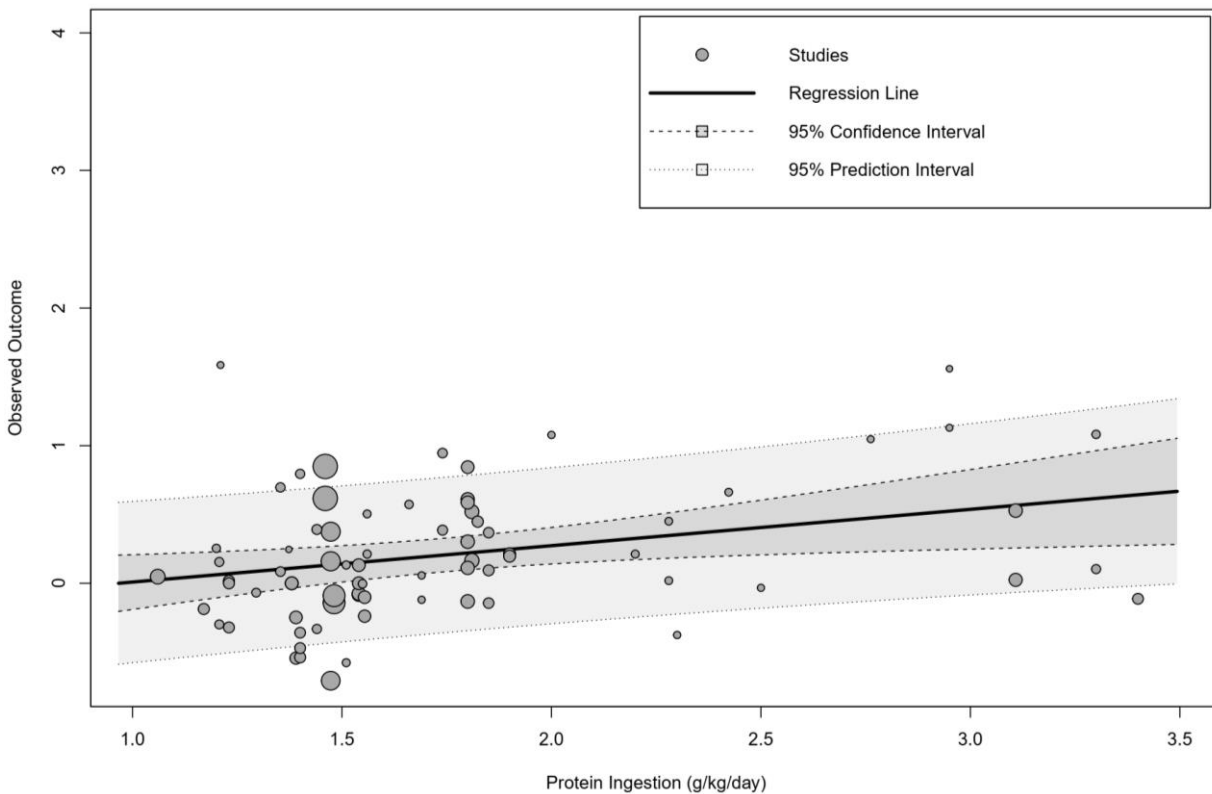
Supplementary Figure 13 – Bubble plot of three-level meta-regression analysis of the main effect on bench press strength vs. total daily protein ingestion (g/kg/day) in studies testing interventions to increase protein ingestion in all included RCT reporting protein ingestion.



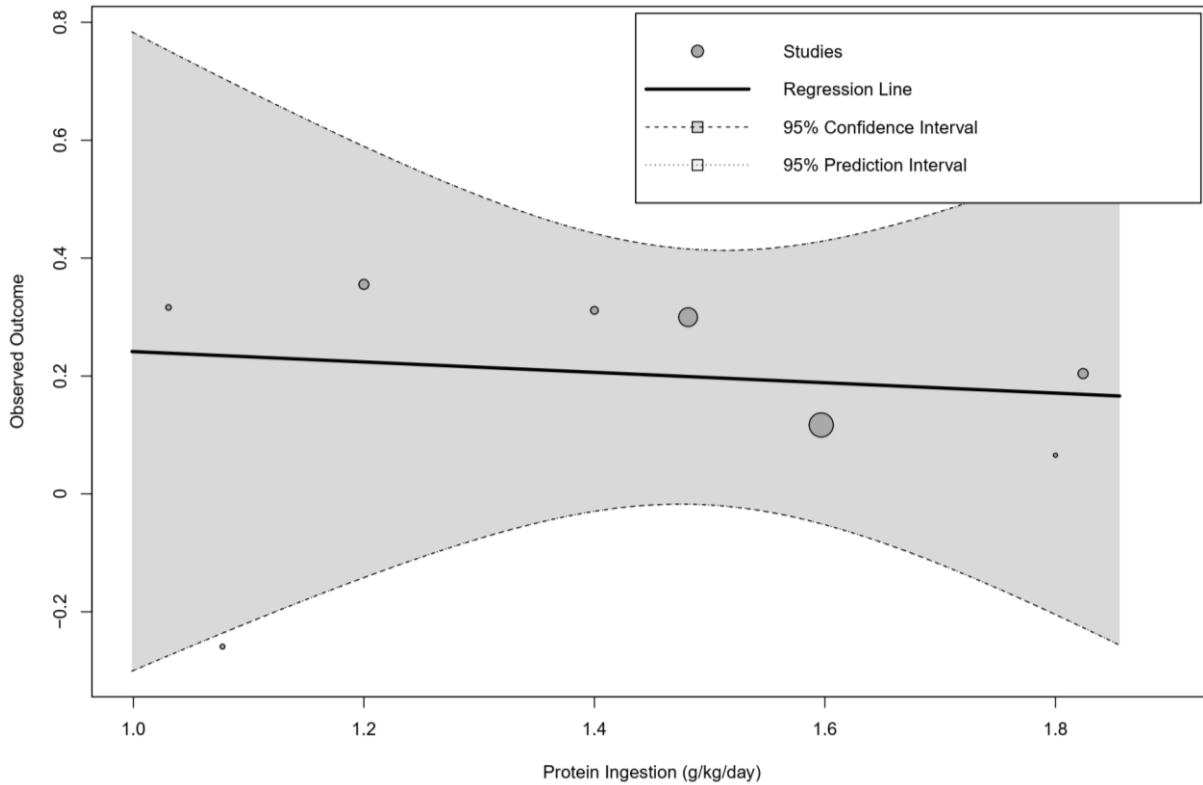
Supplementary Figure 14 – Bubble plot of three-level meta-regression analysis of the main effect on bench press strength vs. total daily protein ingestion (g/kg/day) in studies testing interventions to increase protein ingestion in all included RCT using resistance exercise training and reporting protein ingestion.



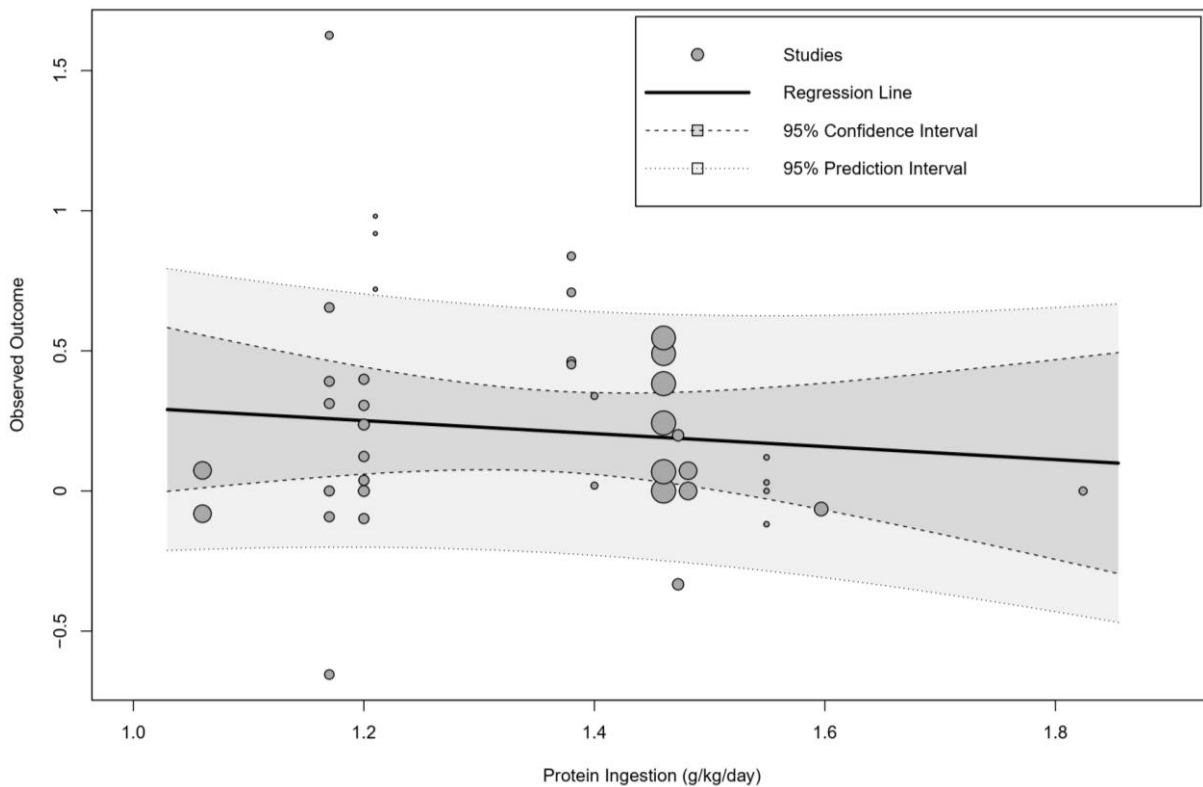
Supplementary Figure 15 – Bubble plot of three-level meta-regression analysis of the main effect on lower-body strength vs. total daily protein ingestion (g/kg/day) in studies testing interventions to increase protein ingestion in all included RCT reporting protein ingestion.



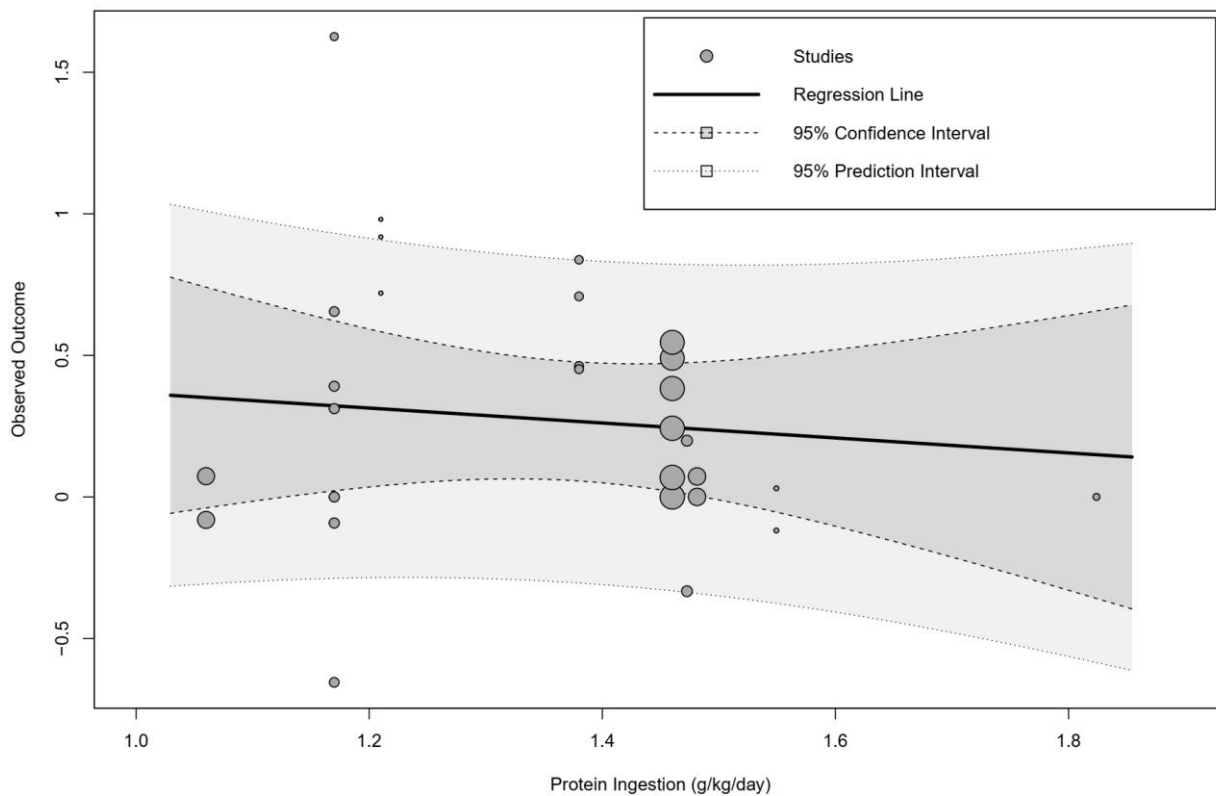
Supplementary Figure 16 – Bubble plot of three-level meta-regression analysis of the main effect on lower-body strength vs. total daily protein ingestion (g/kg/day) in studies testing interventions to increase protein ingestion in all included RCT using resistance exercise training and reporting protein ingestion.



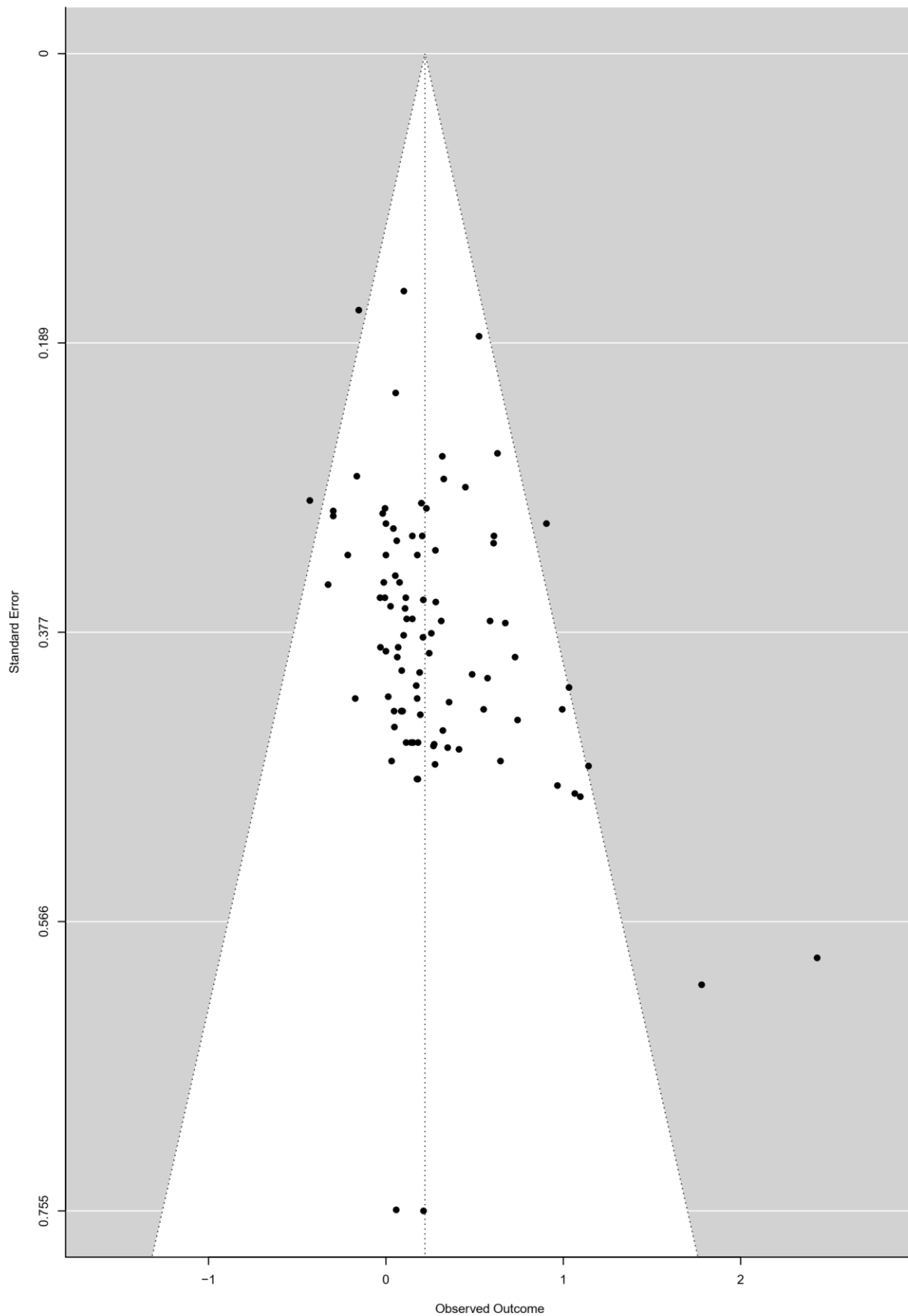
Supplementary Figure 17 – Bubble plot of three-level meta-regression analysis of the main effect on handgrip strength vs. total daily protein ingestion (g/kg/day) in studies testing interventions to increase protein ingestion in all included RCT reporting protein ingestion.



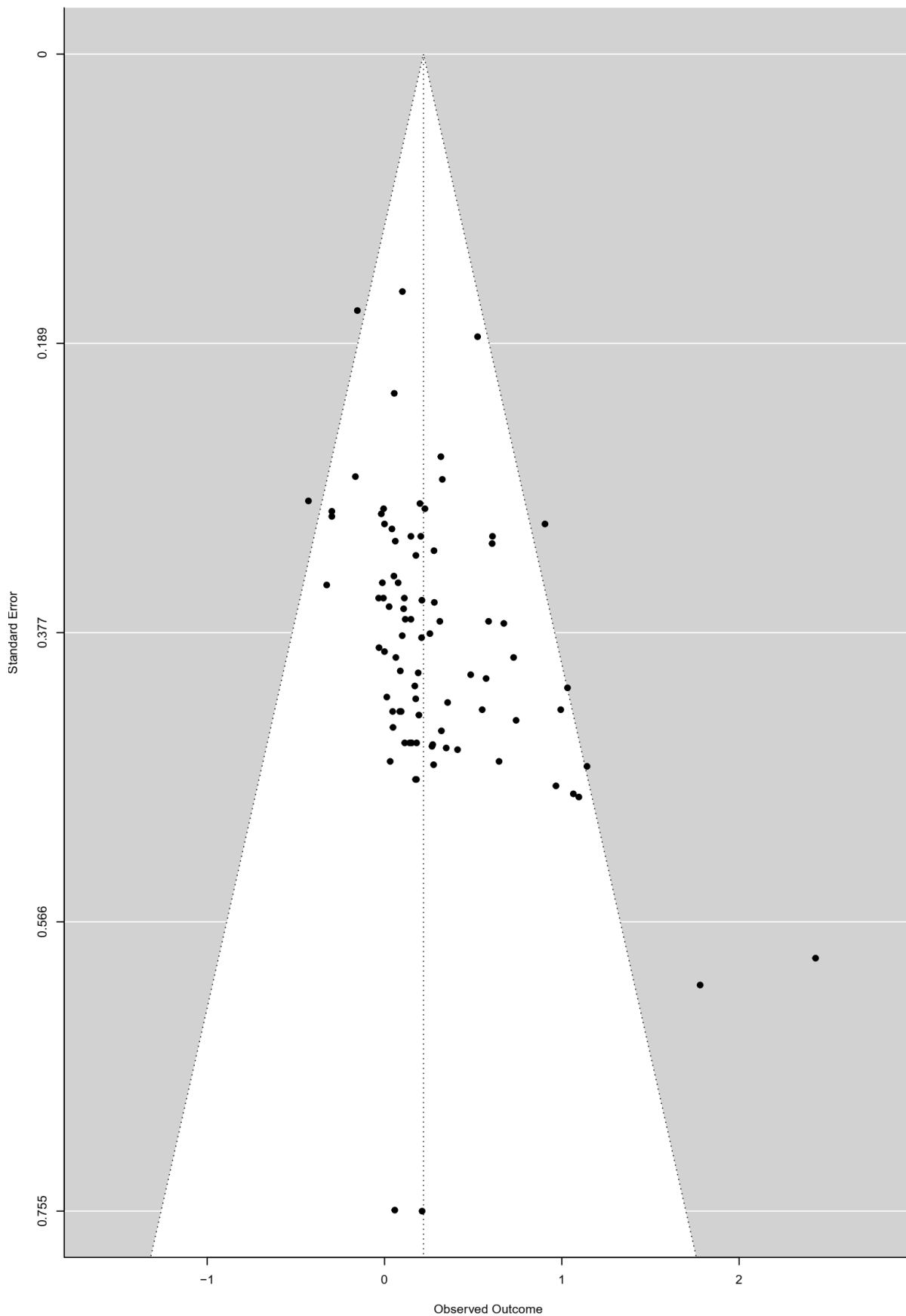
Supplementary Figure 18 – Bubble plot of three-level meta-regression analysis of the main effect on performance in physical and functional tests vs. total daily protein ingestion (g/kg/day) in studies testing interventions to increase protein ingestion in all included RCT reporting protein ingestion.



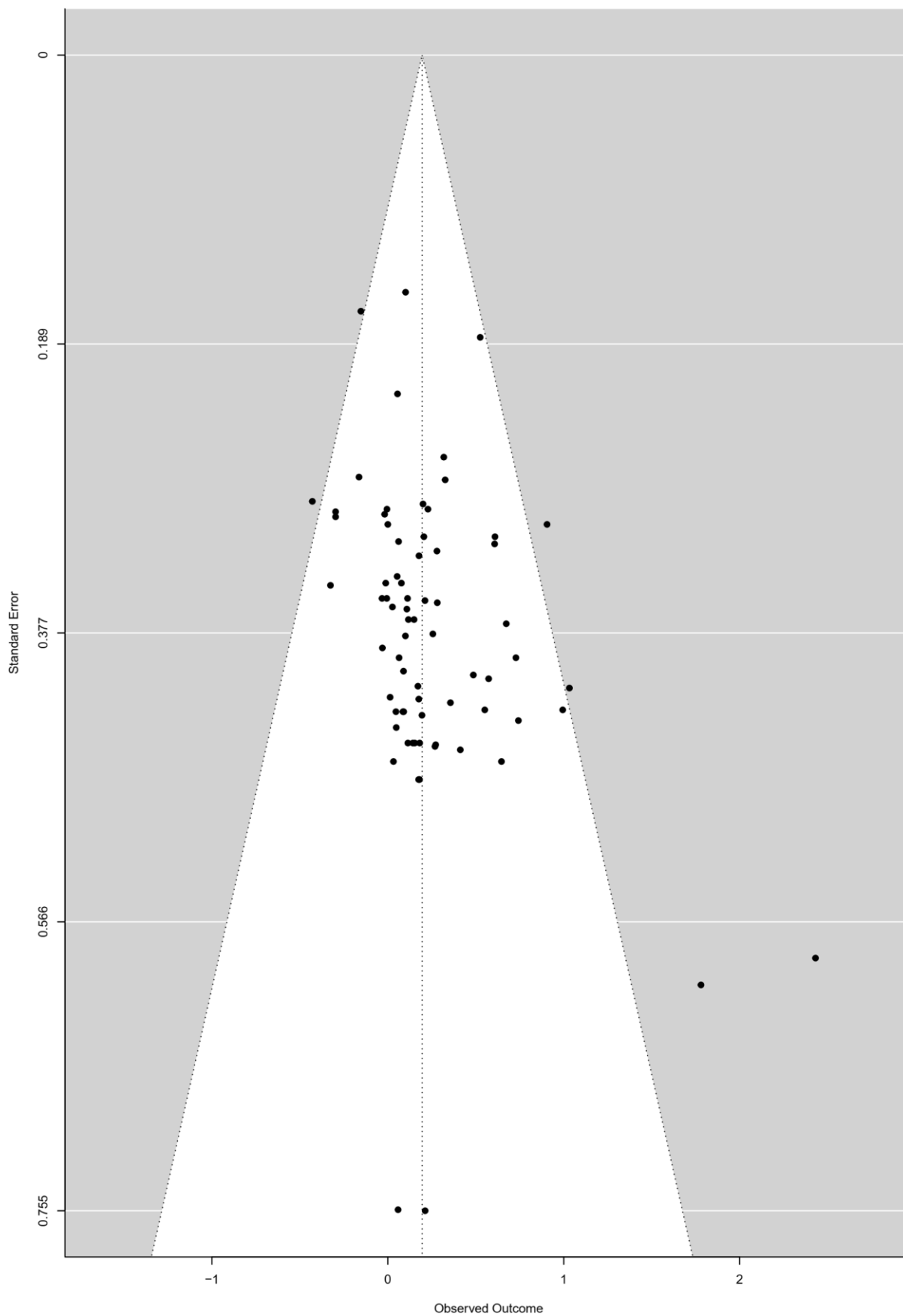
Supplementary Figure 19 – Bubble plot of three-level meta-regression analysis of the main effect on performance in physical and functional tests vs. total daily protein ingestion (g/kg/day) in studies testing interventions to increase protein ingestion in all included RCT using resistance exercise training and reporting protein ingestion.



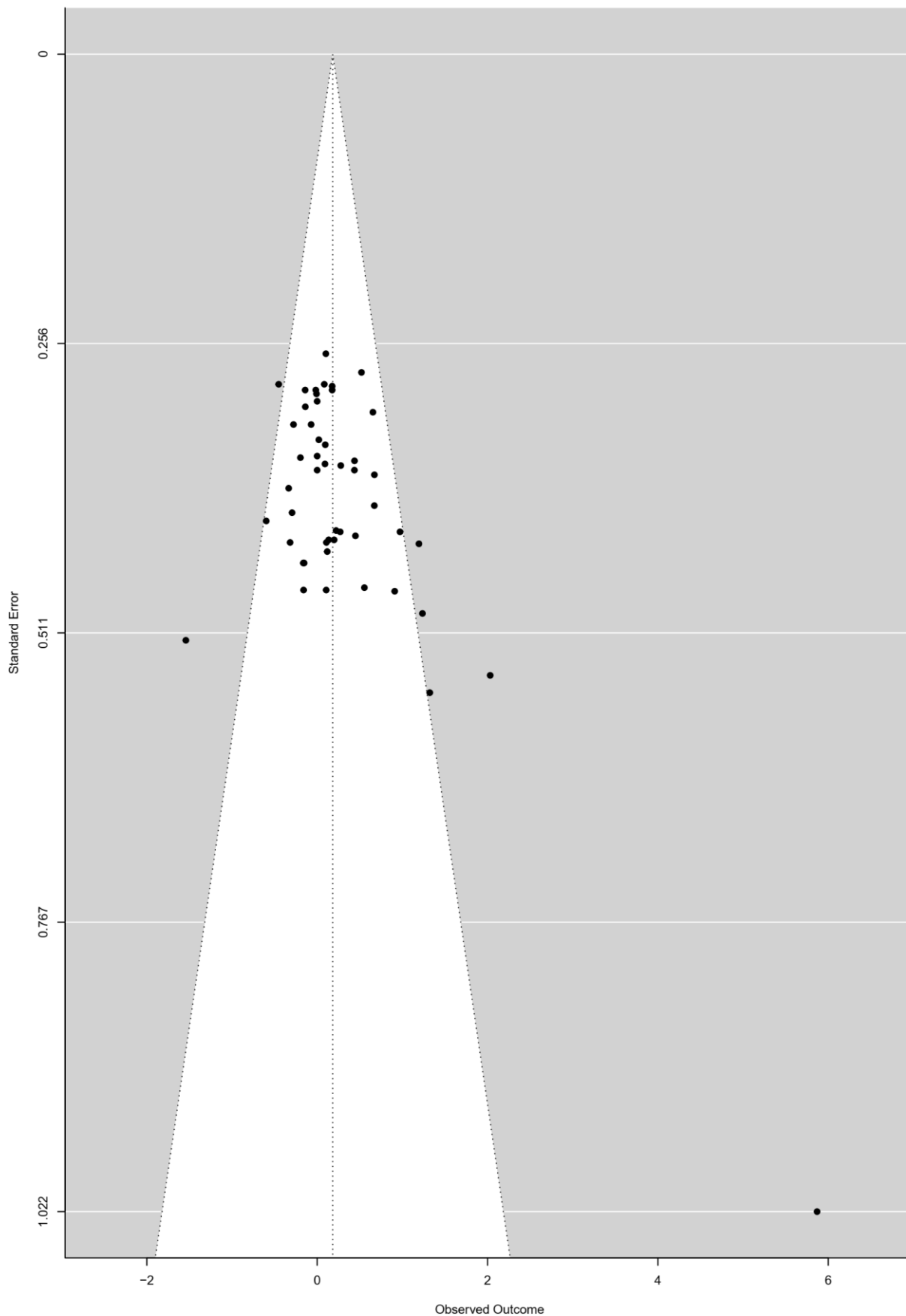
Supplementary Figure 20 – Funnel plot showing results studies testing the effects of ingesting additional protein on adults' lean body or muscle mass including or not a resistance exercise program.



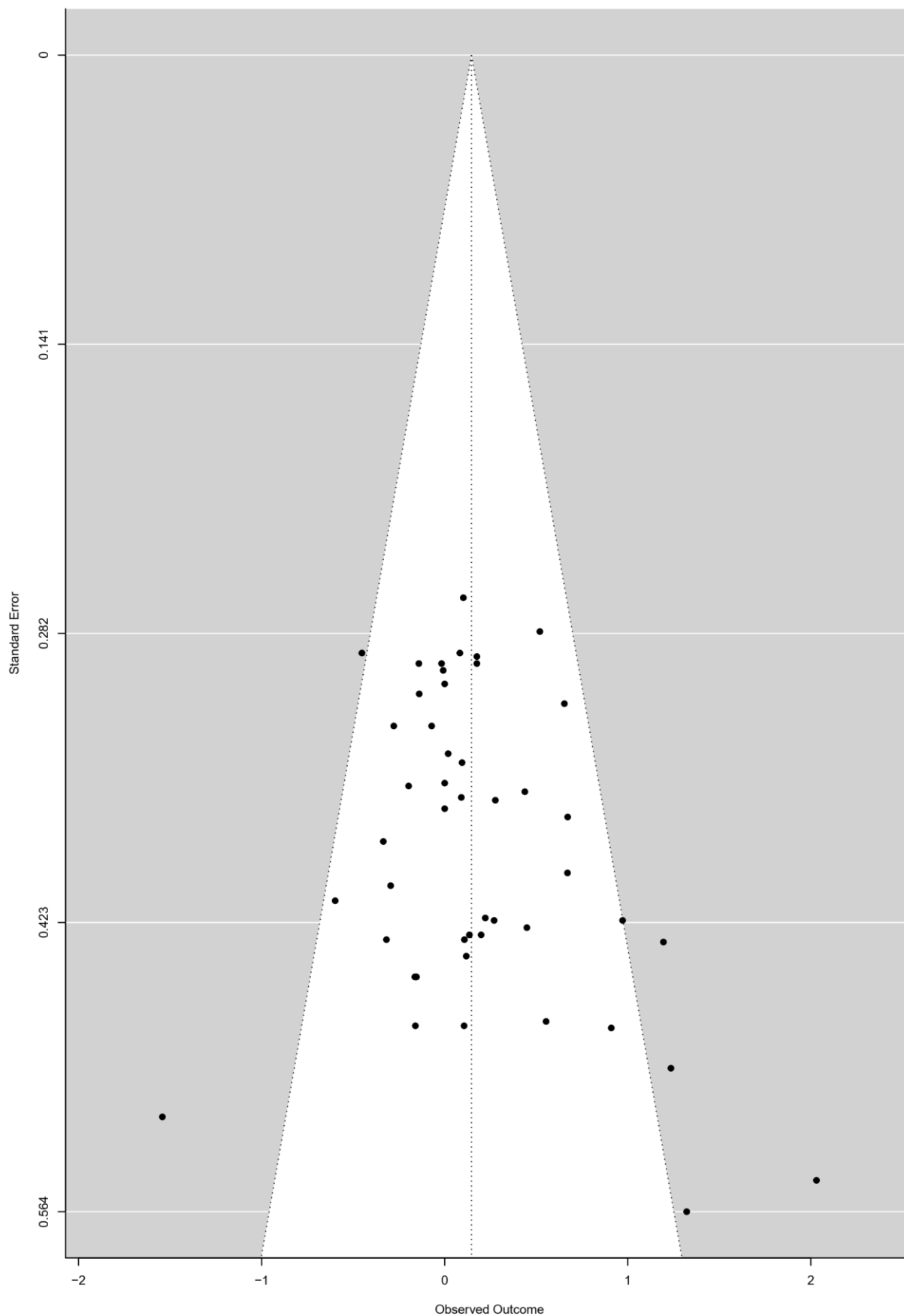
Supplementary Figure 21 – Funnel plot showing results studies testing the effects of ingesting additional protein on adults' lean body or muscle mass only in studies including a resistance exercise program.



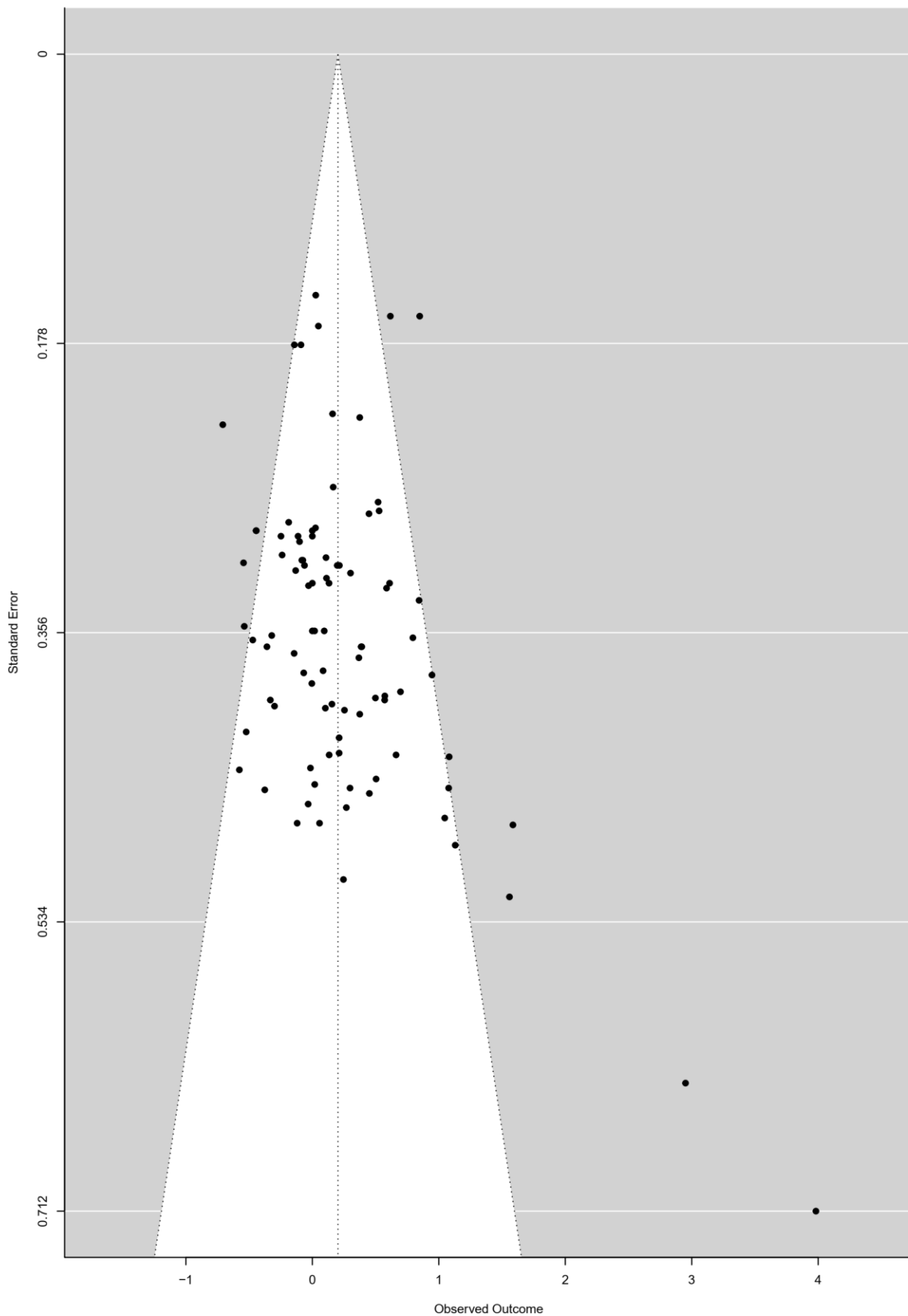
Supplementary Figure 22 – Funnel plot showing results studies testing the effects of ingesting additional protein on adults' lean body or muscle mass only in studies including a resistance exercise program reporting protein ingestion.



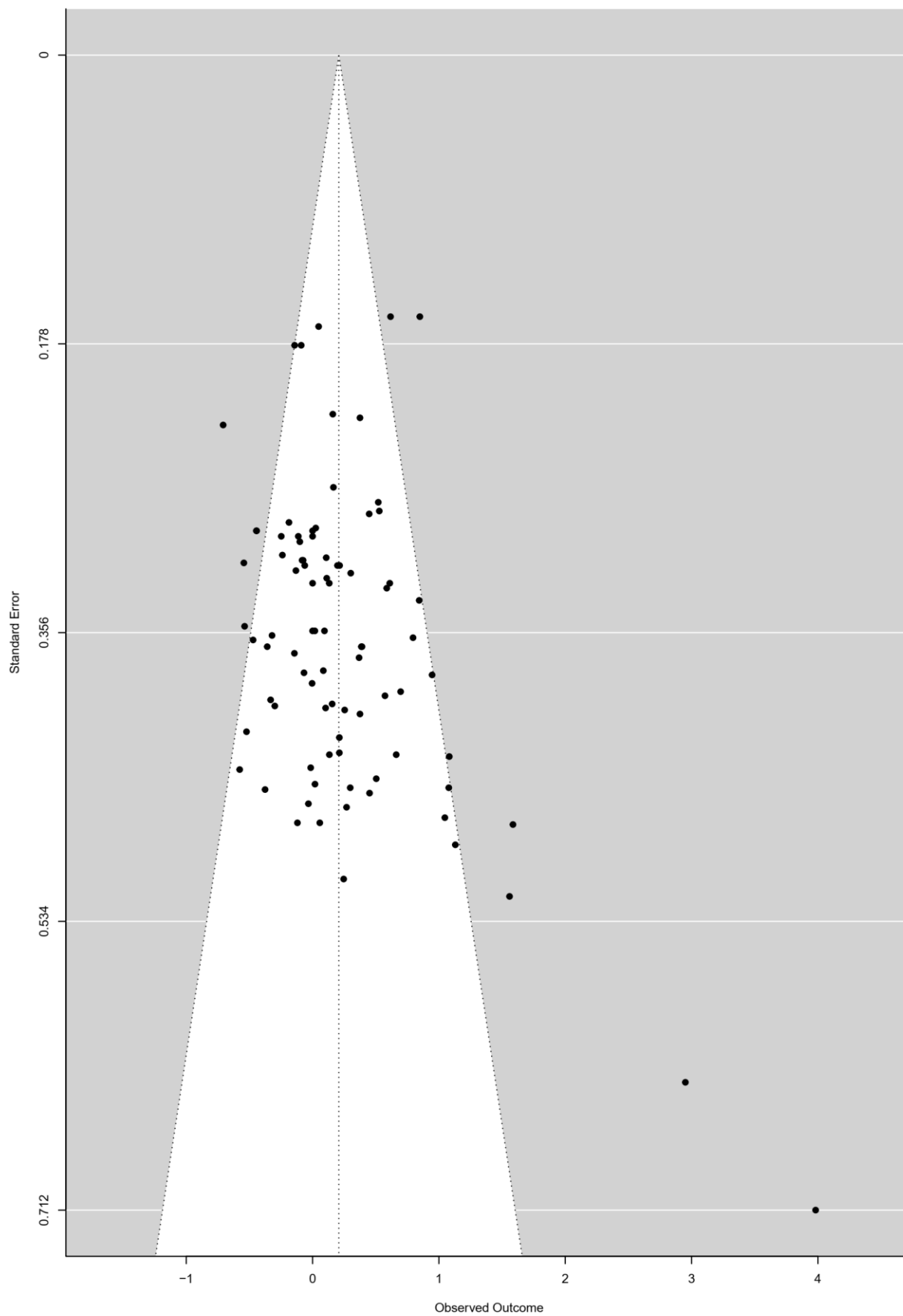
Supplementary Figure 23 – Funnel plot showing results studies testing the effects of ingesting additional protein on adults' bench press strength in studies including or not a resistance exercise program.



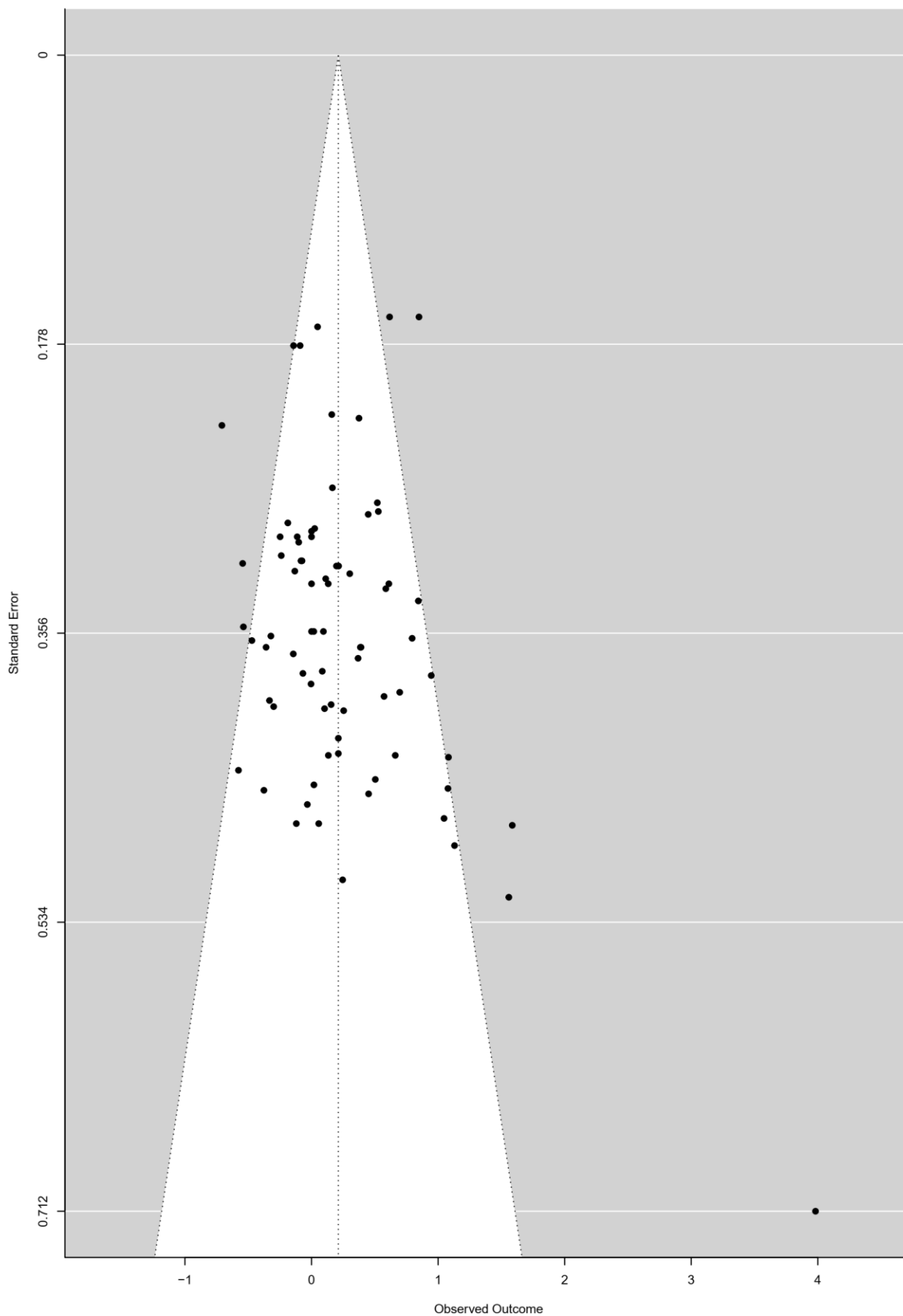
Supplementary Figure 24 – Funnel plot showing results studies testing the effects of ingesting additional protein on adults' bench press strength only in studies including a resistance exercise program reporting protein ingestion.



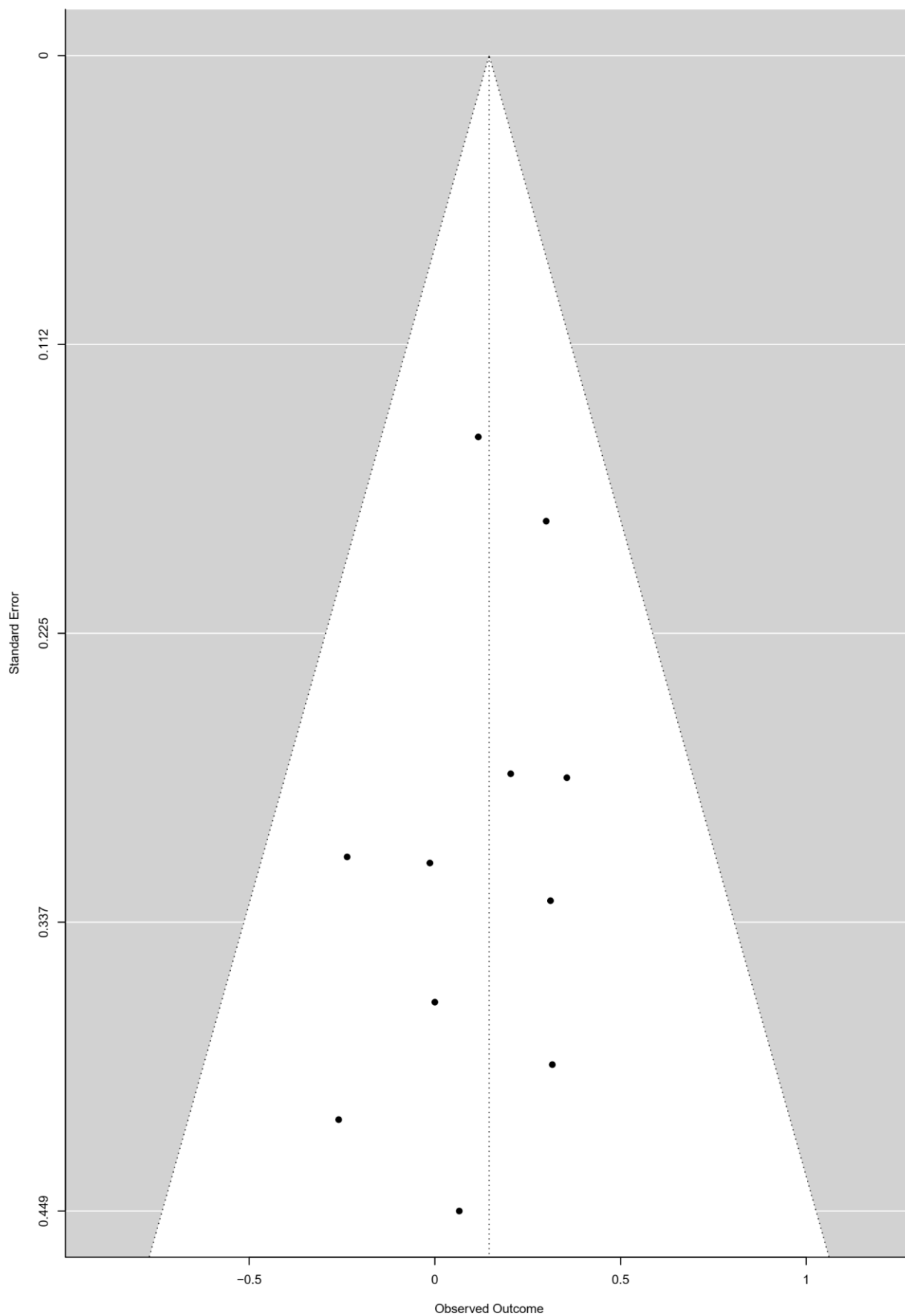
Supplementary Figure 25 – Funnel plot showing results studies testing the effects of ingesting additional protein on adults' lower-body strength in studies including or not a resistance exercise program.



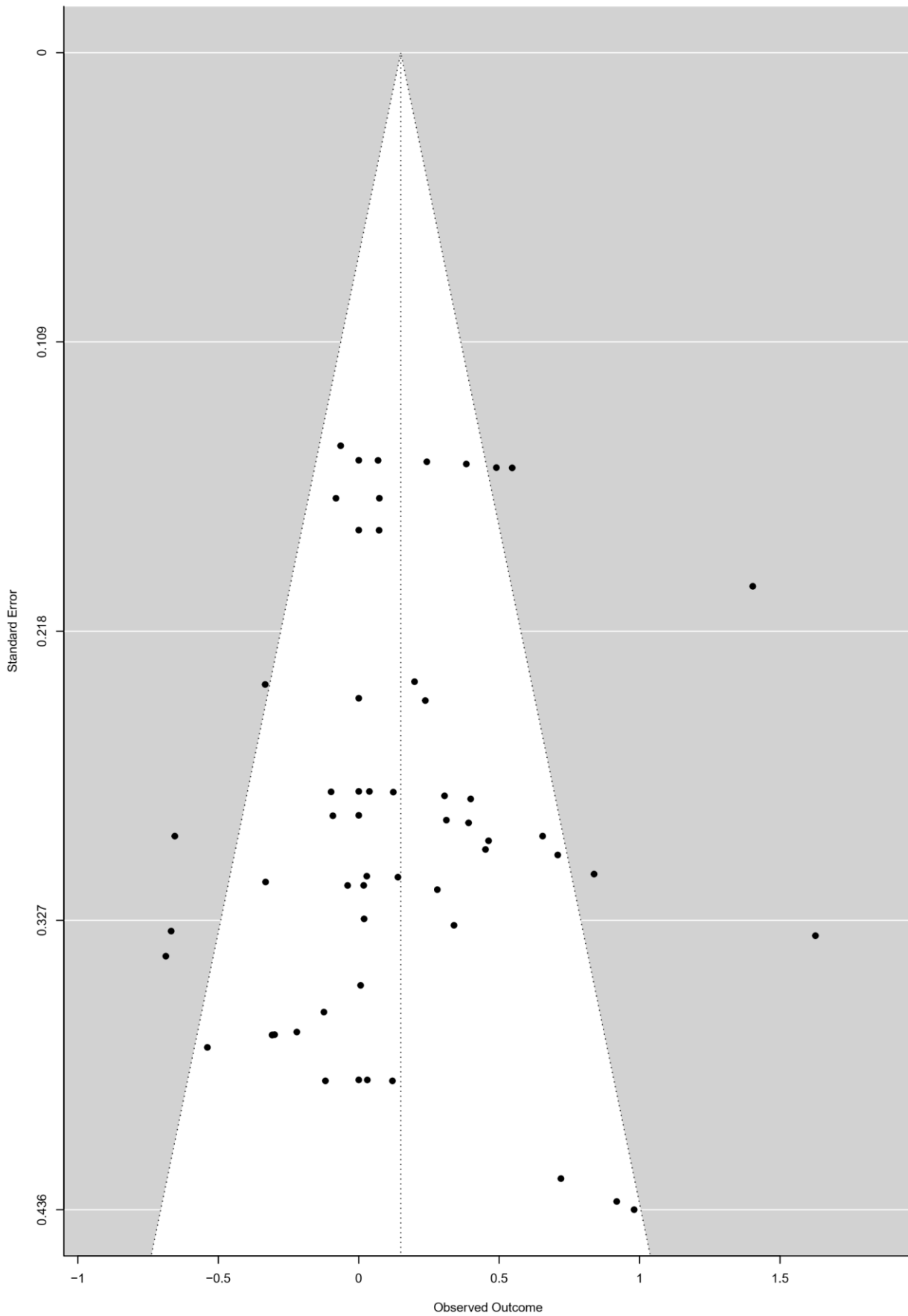
Supplementary Figure 26 – Funnel plot showing results studies testing the effects of ingesting additional protein on adults' lower-body strength only in studies including a resistance exercise program.



Supplementary Figure 27 – Funnel plot showing results studies testing the effects of ingesting additional protein on adults' lower-body strength only in studies including a resistance exercise program reporting protein ingestion.



Supplementary Figure 28 – Funnel plot showing results studies testing the effects of ingesting additional protein on adults' handgrip strength in studies including or not a resistance exercise program.



Supplementary Figure 29 – Funnel plot showing results studies testing the effects of ingesting additional protein on adults' performance in physical and functional tests in studies including or not a resistance exercise program.