評価対象論文リスト（要因：乳製品、アウトカム：フレイル・サルコペニア）
評価判定日：2024/7/26

（フレイル）

①既存の系統的レビュー・メタ解析・統合解析

1	Cuesta-Triana F, Verdejo-Bravo C, Fernández-Pérez C, Martín-Sánchez FJ. Effect of milk and other dairy products on the risk of frailty, sarcopenia, and cognitive performance decline in the elderly: a systematic review. Advances in Nutrition. 2019;10:S105-S119. doi:10.1093/advances/nmy105

②日本人集団の個別疫学研究

2	Hong YJ, Otsuka R, Song Z, et al. Association between milk consumption in middle age and frailty in later life: The Aichi Workers' cohort study. Geriatrics Gerontology Int. 2024;24(7):700-705. doi:10.1111/ggi.14916
3	Otsuka R, Tange C, Tomida M, et al. Dietary factors associated with the development of physical frailty in community-dwelling older adults. The Journal of nutrition, health and aging. 2019;23(1):89-95. doi:10.1007/s12603-018-1124-3
4	Otsuka R, Zhang S, Tange C, et al. Association of dietary intake with the transitions of frailty among japanese community-dwelling older adults. The Journal of Frailty & Aging. 2022;11(1):26-32. doi:10.14283/jfa.2021.42
5	Yamaguchi M, Yamada Y, Nanri H, et al. Association between the frequency of protein-rich food intakes and kihon-checklist frailty indices in older japanese adults: the kyoto-kameoka study. Nutrients. 2018;10(1):84. doi:10.3390/nu10010084
6	Shibasaki K, Kin SK, Yamada S, Akishita M, Ogawa S. Sex-related differences in the association between frailty and dietary consumption in Japanese older people: a cross-sectional study. BMC Geriatr. 2019;19(1):211. doi:10.1186/s12877-019-1229-5
7	Watanabe D, Kurotani K, Yoshida T, et al. Diet quality and physical or comprehensive frailty among older adults. Eur J Nutr. 2022;61(5):2451-2462. doi:10.1007/s00394-022-02819-w

（サルコペニア）

①既存の系統的レビュー・メタ解析・統合解析

1	Hanach NI, McCullough F, Avery A. The impact of dairy protein intake on muscle mass, muscle strength, and physical performance in middle-aged to older adults with or without existing sarcopenia: a systematic review and meta-analysis. Advances in Nutrition. 2019;10(1):59-69. doi:10.1093/advances/nmy065
2	Cuesta-Triana F, Verdejo-Bravo C, Fernández-Pérez C, Martín-Sánchez FJ. Effect of milk and other dairy products on the risk of frailty, sarcopenia, and cognitive performance decline in the elderly: a systematic review. Advances in Nutrition. 2019;10:S105-S119. doi:10.1093/advances/nmy105
3	Granic A, Dismore L, Hurst C, Robinson SM, Sayer AA. Myoprotective whole foods, muscle health and sarcopenia: a systematic review of observational and intervention studies in older adults. Nutrients. 2020;12(8):2257. doi:10.3390/nu12082257
4	Camargo LDR, Doneda D, Oliveira VR. Whey protein ingestion in elderly diet and the association with physical, performance and clinical outcomes. Experimental Gerontology. 2020;137:110936. doi:10.1016/j.exger.2020.110936
5	Li ML, Zhang F, Luo HY, et al. Improving sarcopenia in older adults: a systematic review and meta-analysis of randomized controlled trials of whey protein supplementation with or without resistance training. The Journal of nutrition, health and aging. 2024;28(4):100184. doi:10.1016/j.jnha.2024.100184

②日本人集団の個別疫学研究

6	川上浩, 朴眩泰, 朴晟鎭, 青柳幸利. 高齢者における牛乳摂取と身体活動に関する研究. 2014. doi:10.11465/milk.63.145

7	Mori H, Tokuda Y. De-training effects following leucine-enriched whey protein supplementation and resistance training in older adults with sarcopenia: a randomized controlled trial with 24 weeks of follow-up. The Journal of nutrition, health and aging. 2022;26(11):994-1002. doi:10.1007/s12603-022-1853-1

（フレイル）

■コホート研究（コホートのプール解析含む）

Reference			Study subjects						Category	Number among cases	Relative risk (95%CI or p)	P for trend	Confounding variables considered	**Magnitude of association**
Author	Title	Year	Study period	Number of subjects	Source of subjects	Event followed	Number of incident cases or	Participant's race						
Otsuka R, Tange C, Tomida M, Nishita Y, Kato Y, Yuki A, Ando F, Shimokata H, Arai H.	Dietary factors associated with the development of physical frailty in community-dwelling older adults	2019	2years 2008-2010 to 2010-2012	283	older participants (aged 65 -86)	Prefrail/frail	Robust n= 181 Prefrail/frail n=102	japanese			OR(95%CI)	p-value		
									Milk and dairy products	Mean(169.6g) 1SD (114.3g)	0.73 (0.55–0.96) 0.024	0.024	sex, baseline age, education, family income, smoking status, alcohol intake, BMI, and medical history	
											0.78 (0.59–1.03) 0.081	0.081	In addition to the above, enegy intake	
Otsuka R, Zhang S, Tange C, Nishita Y, Tomida M, Kinoshita K, Kato Y, Ando F, Shimokata H, Arai H.	Association of Dietary Intake with the Transitions of Frailty among JapaneseCommunity-Dwelling Older Adults	2022	2years 2008-2010 to 2010-2012	469	prefrail community dwellers aged 60–87	transitions of frailty		japanese	Transitions of frailty Milk and dairy products	n (g/day)				
									deterioration prefrailty →frailty	n=32 76.1 (28.9)	P-value(ANCOVA) <0.01	P-trend <0.01	sex, baseline age, years of education, annual family income, smoking status, and chronic disease history;total number of frailty criteria at baseline	
									Persistence prefrailty →Prefrailty	n=307 127.7 (20.0)				
									Reversal prefrailty → Robustness	n=130 161.5 (21.8)				
Hong YJ, Otsuka R, Song Z, Fukuda C, Tajima R, Lin J, Hibino M, Kobayashi M, He Y, Matsunaga M, Ota A, Nakano Y, Li Y, Tamakoshi K, Yatsuya H.	Association between milk consumption in middle age and frailty in later life: The Aichi Workers' cohort study	2024	15 years 2002-2018	265	civilservants aged 35–66 year	prefrailty/frailt	pefrailty/frailty was 37.7% in men and28.3% in women.	japanese	Man		OR(95%CI)		age, body mass index, smoking status, alcohol consumption, physical activity, histories of lifestyle-related diseases andheart diseases, stroke or cancer, protein, calcium and vitamin D	
									no consumption	33	Ref			
									Low consumption ～135.86 g/day	89	0.34 (0.14–0.84)	N/A		
									High consumption 135.86～ g/day	90	0.31 (0.10–0.95)	N/A		
									Women					
									Low consumption ～126.44 g/day	26	Ref			
									High consumption 126.44～ g/day	27	0.53 (0.11–2.65)	N/A		

(サルコペニア)

■メタ解析、系統的レビュー

Reference			Include study						Design	Category		Relative risk (95% CI or p)	Weight	**Magnitude of association**
Author	Title	Year	Ref No.	First author	Year	Study period	Study location	Event (*Definition)						
Granic A, Dismore L, Hurst C, Robinson SM, Sayer AA.	Myoprotective Whole Foods, Muscle Health and Sarcopenia: A Systematic Review of Observational and Intervention Studies in Older Adults	2020	32	kojima	2015	2008-2012	japan	decline of muscle strength (knee extension	cohort study	milk consumption		mean(SD)	p-value	
										once oer 2 days or less(N=204)		-22.31(2.78)		
										almost every day(N=311)		-19.26(2.13)	0.388	
Li ML, Zhang F, Luo HY, Quan ZW, Wang YF, Huang LT, Wang JH.	Improving sarcopenia in older adults: a systematic review and meta-analysis of randomized controlled trials of whey protein supplementation with or without resistance training	2024	47	Mori H	2022	24 week intervention	japan		RCT	Whey protein group vs. Isocaloric placebo/ Routine consultation group.	number of studies(n)	Standardized Mean Differences,(95%CI)		
			※10 RCT studies, including (japan:1study)							Appendicular skeletal muscle mass index (kg/m2)	3	0.47(0.23,0.71)	<0.0005	
										Appendicular skeletal muscle mass(kg)	4	0.28(0.11,0.45)	0.0002	
										Gait speed (m/s)	2	1.13(0.82,1.44)	<0.0005	
										Handgrip Strenght (Kg)	2	0.40(-0.28 ,1.07)	0.246	

■ランダム化比較試験

Author	Title	Year	Study subjects: Study Period	Type and source	Definition	Number of cases
Mori H, Tokuda Y.	De-Training Effects Following Leucine-Enriched Whey Protein Supplementation and Resistance Training in Older Adults with Sarcopenia: A Randomized Controlled Trial with 24 Weeks of Follow-Up	2022	24 week intervention	81 participants with sarcopenia	The PRO supplement beverage contained 160kcal of energy, 11.0g of protein, 2300mg of leucine per serving.	RT: n=23 PRO:n=24 RT＋PRO:n=23

Table 2 Primary and secondary outcomes at baseline, post-intervention, and 12 weeks and 24 weeks of de-training in older adults with sarcopenia in the RT, PRO, and RT +PRO groups

At baseline			
Outcome	RT (n=23)	PRO (n=24)	RT+PRO (n=23)
ASMI (kg/m²)	5.30±0.85	5.35±0.57	5.39±0.64
HGS (kg)	16.4±3.1	16.4±3.0	17.1±3.2
UWS (m/sec)	1.03±0.24	0.99±0.18	1.02±0.24
KES (kg)	14.1±5.8	14.1±3.3	13.9±2.8
At the end of intervention			
Outcome	RT (n=23)	PRO (n=24)	RT+PRO (n=23)
ASMI (kg/m²)	5.39±0.92^{TTT}	5.42±0.53^{TTT}	5.51±0.66^{TT}
HGS (kg)	16.8±3.0	16.3±3.0	17.6±3.4^{TT}
UWS (m/sec)	1.03±0.27	0.98±0.21	1.03±0.24
KES (kg)	14.6±5.9^{TT}	13.8±3.2^{TT}	14.6±3.0^{TTTT}
At 12 weeks of de-training			
Outcome	RT (n=23)	PRO (n=24)	RT+PRO (n=23)
ASMI (kg/m²)	5.32±0.88	5.39±0.54	5.47±0.66^{TT}
HGS (kg)	16.3±2.9	16.2±2.9	17.5±3.4^{TTTT}
UWS (m/sec)	1.02±0.23	0.98±0.19	1.01±0.23
KES (kg)	14.1±5.8	13.4±3.2^{TTTT}	14.3±2.9^{TT}
At 24 weeks of de-training			
Outcome	RT (n=23)	PRO (n=24)	RT+PRO (n=23)
ASMI (kg/m²)	5.25±0.85	5.32±0.53	5.44±0.65^{T}
HGS (kg)	16.2±2.8	15.9±2.9^{TT}	17.4±3.2^{TTTT}
UWS (m/sec)	1.02±0.24	0.98±0.19	1.01±0.24
KES (kg)	13.8±5.9^{T}	13.3±3.4^{TT}	14.1±2.9^{TT}

Average± standard deviation; ^{T}Group × Time interaction; two-way repeated analysis of variance. $^{T}p<0.05$, $^{TT}p<0.01$, $^{TTT}p<0.001$; paired one-way analysis of variance test. $^{T}p<0.05$ and $^{TT}p<0.01$ indicate changes from baseline were significantly different compared to the RT group. $^{T}p<0.05$ and $^{TT}p<0.01$ indicate changes from baseline were significantly different compared to the PRO group; a non-paired one-way analysis of variance test was performed. ASMI, appendicular skeletal muscle mass index; HGS, handgrip strength; KES, knee extension strength; PRO, whey protein group; RT, resistance training group; RT+PRO, resistance training and whey protein group; UWS, usual walking speed.

■横断研究

Reference			Study subjects		Variable	Low milk-intake group (<200 mL/day)	High milk-intake group (≥ 200 mL/day)	p-value
Author	Title	Year	Study period	Type and source				
川上 浩, 朴 眩泰, 朴 晟鎭, 青柳 幸利	高齢者における牛乳摂取と身体活動に関する研究(原著論文)	2014	cross-sectional	65歳以上の高齢者179名	Trunk muscle mass (kg)	20.3 ± 3.4	22.0 ± 3.9	<0.05
					Appendicular lean tissue index (kg/m²)	8.7 ± 1.5	9.1 ± 1.6	<0.05
					Body fat mass (kg)	15.6 ± 5.4	14.8 ± 4.3	NS
					Trunk fat mass (kg)	9.5 ± 3.2	9.2 ± 2.6	NS
					Lean body mass (kg)	38.0 ± 6.6	41.4 ± 7.6	NS
					Percent YAM of the calcaneus (%)	87.6 ± 9.9	91.3 ± 8.9	<0.05
					Serum albumin (g/dl)	4.29 ± 0.34	4.42 ± 0.18	<0.05