小児や妊婦も同様に外挿されている。

なお、文献の系統抽出後に乳がんに関するメタ解析論文が出され、21件のコホート研究(28編の論文)から、魚類やn-3系多価不飽和脂肪酸の摂取は乳がんの発症に予防的に働くことが示された(107)。

参考文献

1. Abeywardena MY, Patten GS. Role of omega3 long-chain polyunsaturated fatty acids in reducing cardio-metabolic risk factors. Endocr Metab Immune Disord Drug Targets. 2011;11(3):232-46.
2. Sasazuki S, Inoue M, Iwasaki M, Sawada N, Shimazu T, Yamaji T, et al. Intake of n-3 and n-6 polyunsaturated fatty acids and development of colorectal cancer by subsite: Japan Public Health Center-based prospective study. Int J Cancer. 2011;129(7):1718-29.
3. Sawada N, Inoue M, Iwasaki M, Sasazuki S, Shimazu T, Yamaji T, et al. Consumption of n-3 fatty acids and fish reduces risk of hepatocellular carcinoma. Gastroenterology. 2012;142(7):1468-75.
4. Nanri A, Mizoue T, Noda M, Takahashi Y, Matsushita Y, Poudel-Tandukar K, et al. Fish intake and type 2 diabetes in Japanese men and women: the Japan Public Health Center-based Prospective Study. Am J Clin Nutr. 2011;94(3):884-91.
5. Hamazaki K, Terashima Y, Itomura M, Sawazaki S, Inagaki H, Kuroda M, et al. Docosahexaenoic acid is an independent predictor of all-cause mortality in hemodialysis patients. Am J Nephrol. 2011;33(2):105-10.
6. Saito Y, Yokoyama M, Origasa H, Matsuzaki M, Matsuzawa Y, Ishikawa Y, et al. Effects of EPA on coronary artery disease in hypercholesterolemic patients with multiple risk factors: sub-analysis of primary prevention cases from the Japan EPA Lipid Intervention Study (JELIS). Atherosclerosis. 2008;200(1):135-40.
7. Oikawa S, Yokoyama M,

Origasa H, Matsuzaki M, Matsuzawa Y, Saito Y, et al. Suppressive effect of EPA on the incidence of coronary events in hypercholesterolemia with impaired glucose metabolism: Sub-analysis of the Japan EPA Lipid Intervention Study (JELIS). Atherosclerosis. 2009;206(2):535-9.

8. Ikeya Y, Fukuyama N, Kitajima W, Ogushi Y, Mori H. Comparison of eicosapentaenoic acid concentrations in plasma between patients with ischemic stroke and control subjects. Nutrition. 2013;29(1):127-31.

9. Chowdhury R, Stevens S, Gorman D, Pan A, Warnakula S, Chowdhury S, et al. Association between fish consumption, long chain omega 3 fatty acids, and risk of cerebrovascular disease: systematic review and meta-analysis. BMJ. 2012;345:e6698.

10. Mozaffarian D, Lemaitre RN, King IB, Song X, Huang H, Sacks FM, et al. Plasma phospholipid long-chain omega-3 fatty acids and total and cause-specific mortality in older adults: a cohort study. Ann Intern Med. 2013;158(7):515-25.

11. Kwak SM, Myung SK, Lee YJ, Seo HG. Efficacy of omega-3 fatty acid supplements (eicosapentaenoic acid and docosahexaenoic acid) in the secondary prevention of cardiovascular disease: a meta-analysis of randomized, double-blind, placebo-controlled trials. Arch Intern Med. 2012;172(9):686-94.

12. Vedtofte MS, Jakobsen MU, Lauritzen L, Heitmann BL. Dietary alpha-linolenic acid, linoleic acid, and n-3 long-chain PUFA and risk of ischemic heart disease. Am J Clin Nutr. 2011;94(4):1097-103.

13. Pan A, Chen M, Chowdhury R, Wu JH, Sun Q, Campos H, et al. alpha-Linolenic acid and risk of cardiovascular disease: a systematic review and meta-analysis. Am J Clin Nutr. 2012;96(6):1262-73.

14. Djousse L, Gaziano JM, Buring JE, Lee IM. Dietary omega-3 fatty acids and fish consumption and risk of type 2 diabetes. Am J Clin Nutr. 2011;93(1):143-50.
15. Kaushik M, Mozaffarian D, Spiegelman D, Manson JE, Willett WC, Hu FB. Long-chain omega-3 fatty acids, fish intake, and the risk of type 2 diabetes mellitus. Am J Clin Nutr. 2009;90(3):613-20.
16. Patel PS, Forouhi NG, Kuijsten A, Schulze MB, van Woudenbergh GJ, Ardanaz E, et al. The prospective association between total and type of fish intake and type 2 diabetes in 8 European countries: EPIC-InterAct Study. Am J Clin Nutr. 2012;95(6):1445-53.
17. Villegas R, Xiang YB, Elasy T, Li HL, Yang G, Cai H, et al. Fish, shellfish, and long-chain n-3 fatty acid consumption and risk of incident type 2 diabetes in middle-aged Chinese men and women. Am J Clin Nutr. 2011;94(2):543-51.
18. Brostow DP, Odegaard AO, Koh WP, Duval S, Gross MD, Yuan JM, et al. Omega-3 fatty acids and incident type 2 diabetes: the Singapore Chinese Health Study. Am J Clin Nutr. 2011;94(2):520-6.
19. Egert S, Fobker M, Andersen G, Somoza V, Erbersdobler HF, Wahrburg U. Effects of dietary alpha-linolenic acid, eicosapentaenoic acid or docosahexaenoic acid on parameters of glucose metabolism in healthy volunteers. Ann Nutr Metab. 2008;53(3-4):182-7.
20. Zheng JS, Huang T, Yang J, Fu YQ, Li D. Marine N-3 polyunsaturated fatty acids are inversely associated with risk of type 2 diabetes in Asians: a systematic review and meta-analysis. PLoS One. 2012;7(9):e44525.
21. Wallin A, Di Giuseppe D, Orsini N, Patel PS, Forouhi NG, Wolk A. Fish consumption, dietary long-chain n-3 fatty acids, and risk of type 2 diabetes: systematic review and meta-analysis of prospective

studies. Diabetes Care. 2012;35(4):918-29.

22. Xun P, He K. Fish Consumption and Incidence of Diabetes: meta-analysis of data from 438,000 individuals in 12 independent prospective cohorts with an average 11-year follow-up. Diabetes Care. 2012;35(4):930-8.

23. Belin RJ, Greenland P, Martin L, Oberman A, Tinker L, Robinson J, et al. Fish intake and the risk of incident heart failure: the Women's Health Initiative. Circ Heart Fail. 2011;4(4):404-13.

24. Muramatsu T, Yatsuya H, Toyoshima H, Sasaki S, Li Y, Otsuka R, et al. Higher dietary intake of alpha-linolenic acid is associated with lower insulin resistance in middle-aged Japanese. Prev Med. 2010;50(5-6):272-6.

25. Patterson RE, Flatt SW, Newman VA, Natarajan L, Rock CL, Thomson CA, et al. Marine fatty acid intake is associated with breast cancer prognosis. J Nutr. 2011;141(2):201-6.

26. Murff HJ, Shu XO, Li H, Yang G, Wu X, Cai H, et al. Dietary polyunsaturated fatty acids and breast cancer risk in Chinese women: a prospective cohort study. Int J Cancer. 2011;128(6):1434-41.

27. Sczaniecka AK, Brasky TM, Lampe JW, Patterson RE, White E. Dietary intake of specific fatty acids and breast cancer risk among postmenopausal women in the VITAL cohort. Nutr Cancer. 2012;64(8):1131-42.

28. Daniel CR, McCullough ML, Patel RC, Jacobs EJ, Flanders WD, Thun MJ, et al. Dietary intake of omega-6 and omega-3 fatty acids and risk of colorectal cancer in a prospective cohort of U.S. men and women. Cancer Epidemiol Biomarkers Prev. 2009;18(2):516-25.

29. Shen XJ, Zhou JD, Dong JY, Ding WQ, Wu JC. Dietary intake of n-3 fatty acids and colorectal cancer risk: a meta-analysis of data from 489 000 individuals. Br J Nutr. 2012;108(9):1550-6.

30. Carayol M, Grosclaude P,

Delpierre C. Prospective studies of dietary alpha-linolenic acid intake and prostate cancer risk: a meta-analysis. Cancer Causes Control. 2010;21(3):347-55.
31. Epstein MM, Kasperzyk JL, Mucci LA, Giovannucci E, Price A, Wolk A, et al. Dietary fatty acid intake and prostate cancer survival in Orebro County, Sweden. Am J Epidemiol. 2012;176(3):240-52.
32. Szymanski KM, Wheeler DC, Mucci LA. Fish consumption and prostate cancer risk: a review and meta-analysis. Am J Clin Nutr. 2010;92(5):1223-33.
33. Bosire C, Stampfer MJ, Subar AF, Park Y, Kirkpatrick SI, Chiuve SE, et al. Index-based dietary patterns and the risk of prostate cancer in the NIH-AARP diet and health study. Am J Epidemiol. 2013;177(6):504-13.
34. Wu S, Liang J, Zhang L, Zhu X, Liu X, Miao D. Fish consumption and the risk of gastric cancer: systematic review and meta-analysis. BMC Cancer. 2011;11:26.
35. van der Meij BS, Langius JA, Spreeuwenberg MD, Slootmaker SM, Paul MA, Smit EF, et al. Oral nutritional supplements containing n-3 polyunsaturated fatty acids affect quality of life and functional status in lung cancer patients during multimodality treatment: an RCT. Eur J Clin Nutr. 2012;66(3):399-404.
36. Ries A, Trottenberg P, Elsner F, Stiel S, Haugen D, Kaasa S, et al. A systematic review on the role of fish oil for the treatment of cachexia in advanced cancer: an EPCRC cachexia guidelines project. Palliat Med. 2012;26(4):294-304.
37. Mazzotta P, Jeney CM. Anorexia-cachexia syndrome: a systematic review of the role of dietary polyunsaturated Fatty acids in the management of symptoms, survival, and quality of life. J Pain Symptom Manage. 2009;37(6):1069-77.
38. Vargas ML, Almario RU, Buchan W, Kim K, Karakas

SE. Metabolic and endocrine effects of long-chain versus essential omega-3 polyunsaturated fatty acids in polycystic ovary syndrome. Metabolism. 2011;60(12):1711-8.

39. Turnbull T, Cullen-Drill M, Smaldone A. Efficacy of omega-3 fatty acid supplementation on improvement of bipolar symptoms: a systematic review. Arch Psychiatr Nurs. 2008;22(5):305-11.

40. Park Y, Kim M, Baek D, Kim SH. Erythrocyte n-3 polyunsaturated fatty acid and seafood intake decrease the risk of depression: case-control study in Korea. Ann Nutr Metab. 2012;61(1):25-31.

41. Oddy WH, Hickling S, Smith MA, O'Sullivan TA, Robinson M, de Klerk NH, et al. Dietary intake of omega-3 fatty acids and risk of depressive symptoms in adolescents. Depress Anxiety. 2011;28(7):582-8.

42. Lucas M, Mirzaei F, O'Reilly EJ, Pan A, Willett WC, Kawachi I, et al. Dietary intake of n-3 and n-6 fatty acids and the risk of clinical depression in women: a 10-y prospective follow-up study. Am J Clin Nutr. 2011;93(6):1337-43.

43. Lin PY, Huang SY, Su KP. A meta-analytic review of polyunsaturated fatty acid compositions in patients with depression. Biol Psychiatry. 2010;68(2):140-7.

44. Martins JG. EPA but not DHA appears to be responsible for the efficacy of omega-3 long chain polyunsaturated fatty acid supplementation in depression: evidence from a meta-analysis of randomized controlled trials. J Am Coll Nutr. 2009;28(5):525-42.

45. Murakami K, Miyake Y, Sasaki S, Tanaka K, Arakawa M. Fish and n-3 polyunsaturated fatty acid intake and depressive symptoms: Ryukyus Child Health Study. Pediatrics. 2010;126(3):e623-30.

46. Appleton KM, Rogers PJ, Ness AR. Updated systematic review and meta-analysis of

the effects of n-3 long-chain polyunsaturated fatty acids on depressed mood. Am J Clin Nutr. 2010;91(3):757-70.

47. Sarris J, Mischoulon D, Schweitzer I. Omega-3 for bipolar disorder: meta-analyses of use in mania and bipolar depression. J Clin Psychiatry. 2012;73(1):81-6.

48. Rondanelli M, Giacosa A, Opizzi A, Pelucchi C, La Vecchia C, Montorfano G, et al. Long chain omega 3 polyunsaturated fatty acids supplementation in the treatment of elderly depression: effects on depressive symptoms, on phospholipids fatty acids profile and on health-related quality of life. J Nutr Health Aging. 2011;15(1):37-44.

49. Rizzo AM, Corsetto PA, Montorfano G, Opizzi A, Faliva M, Giacosa A, et al. Comparison between the AA/EPA ratio in depressed and non depressed elderly females: omega-3 fatty acid supplementation correlates with improved symptoms but does not change immunological parameters. Nutr J. 2012;11:82.

50. Sydenham E, Dangour AD, Lim WS. Omega 3 fatty acid for the prevention of cognitive decline and dementia. Cochrane Database Syst Rev. 2012;6:CD005379.

51. Mazereeuw G, Lanctot KL, Chau SA, Swardfager W, Herrmann N. Effects of omega-3 fatty acids on cognitive performance: a meta-analysis. Neurobiol Aging. 2012;33(7):1482 e17-29.

52. Gao Q, Niti M, Feng L, Yap KB, Ng TP. Omega-3 polyunsaturated fatty acid supplements and cognitive decline: Singapore Longitudinal Aging Studies. J Nutr Health Aging. 2011;15(1):32-5.

53. Kesse-Guyot E, Peneau S, Ferry M, Jeandel C, Hercberg S, Galan P. Thirteen-year prospective study between fish consumption, long-chain n-3 fatty acids intakes and cognitive function. J Nutr Health Aging. 2011;15(2):115-20.

54. Quinn JF, Raman R, Thomas RG, Yurko-Mauro K, Nelson EB, Van Dyck C, et al. Docosahexaenoic acid supplementation and cognitive decline in Alzheimer disease: a randomized trial. JAMA. 2010;304(17):1903-11.
55. Cole GM, Ma QL, Frautschy SA. Omega-3 fatty acids and dementia. Prostaglandins Leukot Essent Fatty Acids. 2009;81(2-3):213-21.
56. Miyake Y, Sasaki S, Tanaka K, Fukushima W, Kiyohara C, Tsuboi Y, et al. Dietary fat intake and risk of Parkinson's disease: a case-control study in Japan. J Neurol Sci. 2010;288(1-2):117-22.
57. Gillies D, Sinn J, Lad SS, Leach MJ, Ross MJ. Polyunsaturated fatty acids (PUFA) for attention deficit hyperactivity disorder (ADHD) in children and adolescents. Cochrane Database Syst Rev. 2012;7:CD007986.
58. Raz R, Gabis L. Essential fatty acids and attention-deficit-hyperactivity disorder: a systematic review. Dev Med Child Neurol. 2009;51(8):580-92.
59. Cabre E, Manosa M, Gassull MA. Omega-3 fatty acids and inflammatory bowel diseases - a systematic review. Br J Nutr. 2012;107 Suppl 2:S240-52.
60. Hou JK, Abraham B, El-Serag H. Dietary intake and risk of developing inflammatory bowel disease: a systematic review of the literature. Am J Gastroenterol. 2011;106(4):563-73.
61. Kremmyda LS, Vlachava M, Noakes PS, Diaper ND, Miles EA, Calder PC. Atopy risk in infants and children in relation to early exposure to fish, oily fish, or long-chain omega-3 fatty acids: a systematic review. Clin Rev Allergy Immunol. 2011;41(1):36-66.
62. Batchelor JM, Grindlay DJ, Williams HC. What's new in atopic eczema? An analysis of systematic reviews published in 2008 and 2009. Clin Exp Dermatol. 2010;35(8):823-7; quiz 7-8.
63. Anandan C, Nurmatov U, Sheikh A. Omega 3 and 6 oils

for primary prevention of allergic disease: systematic review and meta-analysis. Allergy. 2009;64(6):840-8.

64. Lee YH, Bae SC, Song GG. Omega-3 polyunsaturated fatty acids and the treatment of rheumatoid arthritis: a meta-analysis. Arch Med Res. 2012;43(5):356-62.

65. Miller ER, 3rd, Juraschek SP, Appel LJ, Madala M, Anderson CA, Bleys J, et al. The effect of n-3 long-chain polyunsaturated fatty acid supplementation on urine protein excretion and kidney function: meta-analysis of clinical trials. Am J Clin Nutr. 2009;89(6):1937-45.

66. Merle B, Delyfer MN, Korobelnik JF, Rougier MB, Colin J, Malet F, et al. Dietary omega-3 fatty acids and the risk for age-related maculopathy: the Alienor Study. Invest Ophthalmol Vis Sci. 2011;52(8):6004-11.

67. Tan JS, Wang JJ, Flood V, Mitchell P. Dietary fatty acids and the 10-year incidence of age-related macular degeneration: the Blue Mountains Eye Study. Arch Ophthalmol. 2009;127(5):656-65.

68. Chong EW, Robman LD, Simpson JA, Hodge AM, Aung KZ, Dolphin TK, et al. Fat consumption and its association with age-related macular degeneration. Arch Ophthalmol. 2009;127(5):674-80.

69. Kabasawa S, Mori K, Horie-Inoue K, Gehlbach PL, Inoue S, Awata T, et al. Associations of cigarette smoking but not serum fatty acids with age-related macular degeneration in a Japanese population. Ophthalmology. 2011;118(6):1082-8.

70. Christen WG, Schaumberg DA, Glynn RJ, Buring JE. Dietary omega-3 fatty acid and fish intake and incident age-related macular degeneration in women. Arch Ophthalmol. 2011;129(7):921-9.

71. Sin HP, Liu DT, Lam DS. Lifestyle modification, nutritional and vitamins supplements for age-related

macular degeneration. Acta Ophthalmol. 2013;91(1):6-11.

72. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. JAMA. 2013;309(19):2005-15.

73. Merle BM, Delyfer MN, Korobelnik JF, Rougier MB, Malet F, Feart C, et al. High concentrations of plasma n3 fatty acids are associated with decreased risk for late age-related macular degeneration. J Nutr. 2013;143(4):505-11.

74. Gopinath B, Flood VM, Rochtchina E, McMahon CM, Mitchell P. Consumption of omega-3 fatty acids and fish and risk of age-related hearing loss. Am J Clin Nutr. 2010;92(2):416-21.

75. Virtanen JK, Mozaffarian D, Willett WC, Feskanich D. Dietary intake of polyunsaturated fatty acids and risk of hip fracture in men and women. Osteoporos Int. 2012;23(11):2615-24.

76. Farina EK, Kiel DP, Roubenoff R, Schaefer EJ, Cupples LA, Tucker KL. Dietary intakes of arachidonic acid and alpha-linolenic acid are associated with reduced risk of hip fracture in older adults. J Nutr. 2011;141(6):1146-53.

77. Moon HJ, Kim TH, Byun DW, Park Y. Positive correlation between erythrocyte levels of n-3 polyunsaturated fatty acids and bone mass in postmenopausal Korean women with osteoporosis. Ann Nutr Metab. 2012;60(2):146-53.

78. Jarvinen R, Tuppurainen M, Erkkila AT, Penttinen P, Karkkainen M, Salovaara K, et al. Associations of dietary polyunsaturated fatty acids with bone mineral density in elderly women. Eur J Clin Nutr. 2012;66(4):496-503.

79. Farina EK, Kiel DP, Roubenoff R, Schaefer EJ, Cupples LA, Tucker KL. Protective effects of fish intake and interactive effects of long-chain polyunsaturated fatty acid intakes on hip bone

mineral density in older adults: the Framingham Osteoporosis Study. Am J Clin Nutr. 2011;93(5):1142-51.

80. Iwasaki M, Taylor GW, Moynihan P, Yoshihara A, Muramatsu K, Watanabe R, et al. Dietary ratio of n-6 to n-3 polyunsaturated fatty acids and periodontal disease in community-based older Japanese: a 3-year follow-up study. Prostaglandins Leukot Essent Fatty Acids. 2011;85(2):107-12.

81. Simon JA, Chen YH, Bent S. The relation of alpha-linolenic acid to the risk of prostate cancer: a systematic review and meta-analysis. Am J Clin Nutr. 2009;89(5):1558S-64S.

82. Brouwer IA. Omega-3 PUFA: good or bad for prostate cancer? Prostaglandins Leukot Essent Fatty Acids. 2008;79(3-5):97-9.

83. Wennberg M, Stromberg U, Bergdahl IA, Jansson JH, Kauhanen J, Norberg M, et al. Myocardial infarction in relation to mercury and fatty acids from fish: a risk-benefit analysis based on pooled Finnish and Swedish data in men. Am J Clin Nutr. 2012;96(4):706-13.

84. Sioen I, De Henauw S, Verbeke W, Verdonck F, Willems JL, Van Camp J. Fish consumption is a safe solution to increase the intake of long-chain n-3 fatty acids. Public Health Nutr. 2008;11(11):1107-16.

85. Del Gobbo LC, Archbold JA, Vanderlinden LD, Eckley CS, Diamond ML, Robson M. Risks and benefits of fish consumption for childbearing women. Can J Diet Pract Res. 2010;71(1):41-5.

86. Sun Y, Vestergaard M, Christensen J, Olsen J, Olsen SF. Intake of marine n-3 fatty acids during pregnancy and risk for epilepsy in the offspring: a population-based cohort study. Epilepsy Res. 2010;91(2-3):267-72.

87. Mozaffarian D, Shi P, Morris JS, Spiegelman D, Grandjean P, Siscovick DS, et al. Mercury exposure and risk of cardiovascular disease in two U.S. cohorts. N Engl J Med.

2011;364(12):1116-25.

88. Boucher O, Burden MJ, Muckle G, Saint-Amour D, Ayotte P, Dewailly E, et al. Neurophysiologic and neurobehavioral evidence of beneficial effects of prenatal omega-3 fatty acid intake on memory function at school age. Am J Clin Nutr. 2011;93(5):1025-37.

89. Tsuji M, Ando T, Kitano T, Wakamiya J, Koriyama C, Akiba S. Relationship between RBC mercury levels and serum n3 polyunsaturated fatty acid concentrations among Japanese men and women. J Environ Public Health. 2012;2012:849305.

90. Kunitsugu I, Okuda M, Murakami N, Hashimoto M, Yamanishi R, Bando N, et al. Self-reported seafood intake and atopy in Japanese school-aged children. Pediatr Int. 2012;54(2):233-7.

91. Rosenfeld E, Beyerlein A, Hadders-Algra M, Kennedy K, Singhal A, Fewtrell M, et al. IPD meta-analysis shows no effect of LC-PUFA supplementation on infant growth at 18 months. Acta Paediatr. 2009;98(1):91-7.

92. Carlson SE, Colombo J, Gajewski BJ, Gustafson KM, Mundy D, Yeast J, et al. DHA supplementation and pregnancy outcomes. Am J Clin Nutr. 2013;97(4):808-15.

93. Gould JF, Smithers LG, Makrides M. The effect of maternal omega-3 (n-3) LCPUFA supplementation during pregnancy on early childhood cognitive and visual development: a systematic review and meta-analysis of randomized controlled trials. Am J Clin Nutr. 2013;97(3):531-44.

94. Drover JR, Hoffman DR, Castaneda YS, Morale SE, Garfield S, Wheaton DH, et al. Cognitive function in 18-month-old term infants of the DIAMOND study: a randomized, controlled clinical trial with multiple dietary levels of docosahexaenoic acid. Early Hum Dev. 2011;87(3):223-30.

95. Meldrum SJ, D'Vaz N, Simmer K, Dunstan JA, Hird K, Prescott SL. Effects of

high-dose fish oil supplementation during early infancy on neurodevelopment and language: a randomised controlled trial. Br J Nutr. 2012;108(8):1443-54.

96. Dziechciarz P, Horvath A, Szajewska H. Effects of n-3 long-chain polyunsaturated fatty acid supplementation during pregnancy and/or lactation on neurodevelopment and visual function in children: a systematic review of randomized controlled trials. J Am Coll Nutr. 2010;29(5):443-54.

97. Baumgartner J, Smuts CM, Malan L, Kvalsvig J, van Stuijvenberg ME, Hurrell RF, et al. Effects of iron and n-3 fatty acid supplementation, alone and in combination, on cognition in school children: a randomized, double-blind, placebo-controlled intervention in South Africa. Am J Clin Nutr. 2012;96(6):1327-38.

98. Skilton MR, Ayer JG, Harmer JA, Webb K, Leeder SR, Marks GB, et al. Impaired fetal growth and arterial wall thickening: a randomized trial of omega-3 supplementation. Pediatrics. 2012;129(3):e698-703.

99. Dotterud CK, Storro O, Simpson MR, Johnsen R, Oien T. The impact of pre- and postnatal exposures on allergy related diseases in childhood: a controlled multicentre intervention study in primary health care. BMC Public Health. 2013;13:123.

100. Harvey N, Dhanwal D, Robinson S, Kim M, Inskip H, Godfrey K, et al. Does maternal long chain polyunsaturated fatty acid status in pregnancy influence the bone health of children? The Southampton Women's Survey. Osteoporos Int. 2012;23(9):2359-67.

101. Nwaru BI, Erkkola M, Lumia M, Kronberg-Kippila C, Ahonen S, Kaila M, et al. Maternal intake of fatty acids during pregnancy and allergies in the offspring. Br J Nutr. 2012;108(4):720-32.

102. Kohlboeck G, Glaser C, Tiesler C, Demmelmair H,

Standl M, Romanos M, et al. Effect of fatty acid status in cord blood serum on children's behavioral difficulties at 10 y of age: results from the LISAplus Study. Am J Clin Nutr. 2011;94(6):1592-9.

103. Aranceta J, Perez-Rodrigo C. Recommended dietary reference intakes, nutritional goals and dietary guidelines for fat and fatty acids: a systematic review. Br J Nutr. 2012;107 Suppl 2:S8-22.

104. Harris WS, Kris-Etherton PM, Harris KA. Intakes of long-chain omega-3 fatty acid associated with reduced risk for death from coronary heart disease in healthy adults. Curr Atheroscler Rep. 2008;10(6):503-9.

105. Mozaffarian D, Wu JH. Omega-3 fatty acids and cardiovascular disease: effects on risk factors, molecular pathways, and clinical events. J Am Coll Cardiol. 2011;58(20):2047-67.

106. Kris-Etherton PM, Grieger JA, Etherton TD. Dietary reference intakes for DHA and EPA. Prostaglandins Leukot Essent Fatty Acids. 2009;81(2-3):99-104.

107. Zheng JS, Hu XJ, Zhao YM, Yang J, Li D. Intake of fish and marine n-3 polyunsaturated fatty acids and risk of breast cancer: meta-analysis of data from 21 independent prospective cohort studies. BMJ. 2013;346:f3706.

5. 一価不飽和脂肪酸

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1.血中代謝マーカーとの関連

高コレステロール患者に一価不飽和脂肪酸を 13en%から 26en% に増加させ(炭水化物は減少)させると、4週間でHDLコレステロール値は 12.5%増加することが認められている(1)。健常者の介入研究で、飽和脂肪酸に比較し、一価不飽和脂肪酸摂取群(20-22en%)は血中酸化 LDL が少なくなることも報告されている(2, 3)。

しかし、望ましくない効果も報告されている。飽和脂肪酸に比較して、動脈硬化のリスクになる食後の中性脂肪値(4)が高いことが多くの研究で示されている(5-7)。

2.心不全

動物実験でエルシン酸(エルカ酸)投与により、心筋障害を生じることが報告されていた(8)が、血中リン脂質中の脂肪酸組成を調べたコホート研究で、長鎖一価不飽和脂肪酸(22:1 erucic acid,24:1 nervonic acid)の多かった群で、心不全の増加が認められている(9)。20:1 はリスクになっていない。長鎖一価不飽和脂肪酸が、食事由来(魚、サラダ油、家禽類に多く含まれている)か体内で生成されたものか不明である。

3.肥満

主に肥満者を対象した 12 の RCT 介入研究を統合したメタ・アナリシスでは、高一価不飽和脂肪酸食(＞12en%)と低一価不飽和脂肪酸食(12en%以下)との間に体重の差は認められていないが、体脂肪を調べた 4 つの RCT を統合すると、高一価不飽和脂肪酸食群の方が低脂肪食群(高炭水化物食群)より、体脂肪量の減少を認めた(10)。遺伝的な背景(Apo A1、apoB、PPARs, WDTC1)の違いより、一価不飽和脂肪酸の肥満への影響が異なることを示す報告もある(11-14)。

安静時のエネルギー消費量に関して、飽和脂肪酸と比較し、一価不飽和脂肪酸が増加する報告(15)と差がないとする報告(16)があるが、食後のエネルギー消費量は増加することを示す報告がある(17)。

4.糖尿病

健康な人(過体重を含む)を対象にした介入研究では、高一価不飽和脂肪酸食はインスリン感受性や抵抗性を改善する報告もある(18, 19)が、影響を与えないことを示す報告も多くあり(20, 21)、結論は得られていない。耐糖能異常を示す患者を対象とした 9 つの介入研究のメタ・アナリシスでは、高一価不飽和脂肪酸食群は低一価不飽和脂肪酸食群に比べて、HbA1c減少効果(-0.21)が認められているが、空腹時血糖値には変化が見られていない(22)。

血中のパルミトオレイン酸が多いと、2 型糖尿病患者でインスリン感受性が良くなってい

るが、食事との関連は示されていない(23)。

5.炎症

炎症や内皮機能についても報告がある。高飽和脂肪酸との比較では、高一価不飽和脂肪酸食の方が食後の TNF-α(24)や sICAM-1 レベル(25)が低いが、低脂肪食との比較では、良い効果は認められていない(26, 27)。

6.血圧

9 の RCT 介入研究を統合したメタ・アナリシス(多くは肥満者を対象)では、高一価不飽和脂肪酸食群(＞12en%)の方が、低一価不飽和脂肪酸食群(12en%以下)より、収縮期圧は 2.26mmHg、拡張期圧は 1.15mmHg 低下した(10)。食後の血圧低下の程度も、飽和脂肪酸や n-3 脂肪酸に比べて、一価不飽和脂肪酸の方が少し強い(28)。

7.がん

ドイツでのコホート研究で、飽和脂肪酸、一価不飽和脂肪酸、n-3 系脂肪酸、n-6 系脂肪酸の多い食事パターンと乳がん罹患が正の関連を示した(29)。

8.認知能

4 年間の観察研究(Women's Health Study)で、一価不飽和脂肪酸摂取量の多い群で、認知能の改善が認められている(30)。

9.高齢者

420kcal/日の fat emulsion(60%は一価不飽和脂肪酸)を高齢者患者に投与すると、食欲が増加し(31)、透析患者に投与すると炎症反応が減少することが報告されている(32)。

10.AMD

一価不飽和脂肪酸が良いことを示す報告(33)と悪いことを示す報告がある(34)。

11.皮膚

横断研究で、皮膚の老化の程度とオリーブオイル摂取量は負の関連が認められる(35)。

12.女性に於いて、子供の時に飽和脂肪酸、一価不飽和脂肪酸、n-3 脂肪酸摂取量と成人の頸動脈内皮の肥厚に正の関連が認められている(36)。

参考文献

1. Jenkins DJ, Chiavaroli L, Wong JM, Kendall C, Lewis GF, Vidgen E, et al. Adding monounsaturated fatty acids to a dietary portfolio of cholesterol-lowering foods in hypercholesterolemia. CMAJ. 2010;182(18):1961-7.
2. Moreno JA, Lopez-Miranda J, Perez-Martinez P, Marin C, Moreno R, Gomez P, et al. A monounsaturated fatty acid-rich diet reduces macrophage uptake of plasma oxidised low-density

lipoprotein in healthy young men. Br J Nutr. 2008;100(3):569-75.

3. Egert S, Kratz M, Kannenberg F, Fobker M, Wahrburg U. Effects of high-fat and low-fat diets rich in monounsaturated fatty acids on serum lipids, LDL size and indices of lipid peroxidation in healthy non-obese men and women when consumed under controlled conditions. Eur J Nutr. 2011;50(1):71-9.

4. Iso H, Naito Y, Sato S, Kitamura A, Okamura T, Sankai T, et al. Serum triglycerides and risk of coronary heart disease among Japanese men and women. Am J Epidemiol. 2001;153(5):490-9.

5. Teng KT, Nagapan G, Cheng HM, Nesaretnam K. Palm olein and olive oil cause a higher increase in postprandial lipemia compared with lard but had no effect on plasma glucose, insulin and adipocytokines. Lipids. 2011;46(4):381-8.

6. Peairs AD, Rankin JW, Lee YW. Effects of acute ingestion of different fats on oxidative stress and inflammation in overweight and obese adults. Nutr J. 2011;10:122.

7. van Dijk SJ, Mensink M, Esser D, Feskens EJ, Muller M, Afman LA. Responses to high-fat challenges varying in fat type in subjects with different metabolic risk phenotypes: a randomized trial. PLoS One. 2012;7(7):e41388.

8. Bremer J, Norum KR. Metabolism of very long-chain monounsaturated fatty acids (22:1) and the adaptation to their presence in the diet. J Lipid Res. 1982;23(2):243-56.

9. Imamura F, Lemaitre RN, King IB, Song X, Steffen LM, Folsom AR, et al. Long-chain monounsaturated Fatty acids and incidence of congestive heart failure in 2 prospective cohorts. Circulation. 2013;127(14):1512-21, 21e1-18.

10. Schwingshackl L, Strasser B, Hoffmann G. Effects of monounsaturated fatty acids on cardiovascular risk factors: a systematic review and meta-analysis. Ann Nutr Metab. 2011;59(2-4):176-86.

11. Phillips CM, Goumidi L, Bertrais S, Field MR, McManus R, Hercberg S, et al. Gene-nutrient interactions and gender may modulate the association between ApoA1 and ApoB gene polymorphisms and metabolic syndrome risk. Atherosclerosis. 2011;214(2):408-14.

12. AlSaleh A, Sanders TA, O'Dell SD. Effect of interaction between PPARG,

PPARA and ADIPOQ gene variants and dietary fatty acids on plasma lipid profile and adiponectin concentration in a large intervention study. Proc Nutr Soc. 2012;71(1):141-53.

13. Garaulet M, Smith CE, Hernandez-Gonzalez T, Lee YC, Ordovas JM. PPARgamma Pro12Ala interacts with fat intake for obesity and weight loss in a behavioural treatment based on the Mediterranean diet. Mol Nutr Food Res. 2011;55(12):1771-9.
14. Lai CQ, Parnell LD, Arnett DK, Garcia-Bailo B, Tsai MY, Kabagambe EK, et al. WDTC1, the ortholog of Drosophila adipose gene, associates with human obesity, modulated by MUFA intake. Obesity (Silver Spring). 2009;17(3):593-600.
15. Kien CL, Bunn JY, Tompkins CL, Dumas JA, Crain KI, Ebenstein DB, et al. Substituting dietary monounsaturated fat for saturated fat is associated with increased daily physical activity and resting energy expenditure and with changes in mood. Am J Clin Nutr. 2013;97(4):689-97.
16. Cooper JA, Watras AC, Adams AK, Schoeller DA. Effects of dietary fatty acid composition on 24-h energy expenditure and chronic disease risk factors in men. Am J Clin Nutr. 2009;89(5):1350-6.
17. Casas-Agustench P, Lopez-Uriarte P, Bullo M, Ros E, Gomez-Flores A, Salas-Salvado J. Acute effects of three high-fat meals with different fat saturations on energy expenditure, substrate oxidation and satiety. Clin Nutr. 2009;28(1):39-45.
18. Kien CL, Bunn JY, Poynter ME, Stevens R, Bain J, Ikayeva O, et al. A lipidomics analysis of the relationship between dietary fatty acid composition and insulin sensitivity in young adults. Diabetes. 2013;62(4):1054-63.
19. Lopez S, Bermudez B, Ortega A, Varela LM, Pacheco YM, Villar J, et al. Effects of meals rich in either monounsaturated or saturated fat on lipid concentrations and on insulin secretion and action in subjects with high fasting triglyceride concentrations. Am J Clin Nutr. 2011;93(3):494-9.
20. Bos MB, de Vries JH, Feskens EJ, van Dijk SJ, Hoelen DW, Siebelink E, et al. Effect of a high monounsaturated fatty acids diet and a Mediterranean diet on serum lipids and insulin sensitivity in adults with mild abdominal obesity. Nutr Metab

Cardiovasc Dis. 2010;20(8):591-8.

21. Jebb SA, Lovegrove JA, Griffin BA, Frost GS, Moore CS, Chatfield MD, et al. Effect of changing the amount and type of fat and carbohydrate on insulin sensitivity and cardiovascular risk: the RISCK (Reading, Imperial, Surrey, Cambridge, and Kings) trial. Am J Clin Nutr. 2010;92(4):748-58.

22. Schwingshackl L, Strasser B, Hoffmann G. Effects of monounsaturated fatty acids on glycaemic control in patients with abnormal glucose metabolism: a systematic review and meta-analysis. Ann Nutr Metab. 2011;58(4):290-6.

23. Stefan N, Kantartzis K, Celebi N, Staiger H, Machann J, Schick F, et al. Circulating palmitoleate strongly and independently predicts insulin sensitivity in humans. Diabetes Care. 2010;33(2):405-7.

24. Cruz-Teno C, Perez-Martinez P, Delgado-Lista J, Yubero-Serrano EM, Garcia-Rios A, Marin C, et al. Dietary fat modifies the postprandial inflammatory state in subjects with metabolic syndrome: the LIPGENE study. Mol Nutr Food Res. 2012;56(6):854-65.

25. Perez-Martinez P, Moreno-Conde M, Cruz-Teno C, Ruano J, Fuentes F, Delgado-Lista J, et al. Dietary fat differentially influences regulatory endothelial function during the postprandial state in patients with metabolic syndrome: from the LIPGENE study. Atherosclerosis. 2010;209(2):533-8.

26. Bladbjerg EM, Larsen TM, Due A, Jespersen J, Stender S, Astrup A. Long-term effects on haemostatic variables of three ad libitum diets differing in type and amount of fat and carbohydrate: a 6-month randomised study in obese individuals. Br J Nutr. 2010;104(12):1824-30.

27. Bladbjerg EM, Larsen TM, Due A, Stender S, Astrup A, Jespersen J. Effects on markers of inflammation and endothelial cell function of three ad libitum diets differing in type and amount of fat and carbohydrate: a 6-month randomised study in obese individuals. Br J Nutr. 2011;106(1):123-9.

28. Esser D, van Dijk SJ, Oosterink E, Muller M, Afman LA. A high-fat SFA, MUFA, or n3 PUFA challenge affects the vascular response and initiates an activated state of cellular adherence in lean and obese middle-aged men. J Nutr. 2013;143(6):843-51.

29. Schulz M, Hoffmann K, Weikert C,

Nothlings U, Schulze MB, Boeing H. Identification of a dietary pattern characterized by high-fat food choices associated with increased risk of breast cancer: the European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam Study. Br J Nutr. 2008;100(5):942-6.

30. Okereke OI, Rosner BA, Kim DH, Kang JH, Cook NR, Manson JE, et al. Dietary fat types and 4-year cognitive change in community-dwelling older women. Ann Neurol. 2012;72(1):124-34.

31. Faxen-Irving G, Cederholm T. Energy dense oleic acid rich formula to newly admitted geriatric patients--feasibility and effects on energy intake. Clin Nutr. 2011;30(2):202-8.

32. Ewers B, Riserus U, Marckmann P. Effects of unsaturated fat dietary supplements on blood lipids, and on markers of malnutrition and inflammation in hemodialysis patients. J Ren Nutr. 2009;19(5):401-11.

33. Parekh N, Voland RP, Moeller SM, Blodi BA, Ritenbaugh C, Chappell RJ, et al. Association between dietary fat intake and age-related macular degeneration in the Carotenoids in Age-Related Eye Disease Study (CAREDS): an ancillary study of the Women's Health Initiative. Arch Ophthalmol. 2009;127(11):1483-93.

34. Reynolds R, Rosner B, Seddon JM. Dietary omega-3 fatty acids, other fat intake, genetic susceptibility, and progression to incident geographic atrophy. Ophthalmology. 2013;120(5):1020-8.

35. Latreille J, Kesse-Guyot E, Malvy D, Andreeva V, Galan P, Tschachler E, et al. Dietary monounsaturated fatty acids intake and risk of skin photoaging. PLoS One. 2012;7(9):e44490.

36. Kaikkonen JE, Jula A, Mikkila V, Juonala M, Viikari JS, Moilanen T, et al. Childhood serum fatty acid quality is associated with adult carotid artery intima media thickness in women but not in men. J Nutr. 2013;143(5):682-9.