

IBS feature:

Claire Barnes:

- 1 Kennedy PJ, Cryan JF, Dinan TG, Clarke G. Irritable bowel syndrome: A microbiome-gut-brain axis disorder? *World J. Gastroenterol.* 2014; 20: 14105–25.
- 2 Introduction | Irritable bowel syndrome in adults: diagnosis and management | Guidance | NICE. <https://www.nice.org.uk/guidance/cg61/chapter/Introduction> (accessed Sept 30, 2022).
- 3 Patel N, Shackelford KS. Irritable Bowel Syndrome. *StatPearls* 2022; published online July 4. <https://www.ncbi.nlm.nih.gov/books/NBK534810/> (accessed Sept 30, 2022).
- 4 Oka P, Parr H, Barberio B, Black CJ, Savarino EV, Ford AC. Global prevalence of irritable bowel syndrome according to Rome III or IV criteria: a systematic review and meta-analysis. *lancet Gastroenterol Hepatol* 2020; 5: 908–17.
- 5 Palsson OS, Whitehead W, Törnblom H, Sperber AD, Simren M. Prevalence of Rome IV Functional Bowel Disorders Among Adults in the United States, Canada, and the United Kingdom. *Gastroenterology* 2020; 158: 1262-1273.e3.
- 6 Lacy B, Patel N. Rome Criteria and a Diagnostic Approach to Irritable Bowel Syndrome. *J Clin Med* 2017; 6: 99.
- 7 Quigley E. The Gut-Brain Axis and the Microbiome: Clues to Pathophysiology and Opportunities for Novel Management Strategies in Irritable Bowel Syndrome (IBS). *J Clin Med* 2018; 7: 6.
- 8 Poon D, Law GR, Major G, Andreyev HJN. A systematic review and meta-analysis on the prevalence of non-malignant, organic gastrointestinal disorders misdiagnosed as irritable bowel syndrome. *Sci Rep* 2022; 12. DOI:10.1038/S41598-022-05933-1.
- 9 Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology* 2006; 130: 1480–91.
- 10 Fadgyas-Stanculete M, Buga A-M, Popa-Wagner A, Dumitrascu DL. The relationship between irritable bowel syndrome and psychiatric disorders: from molecular changes to clinical manifestations. *J Mol Psychiatry* 2014; 2: 4.
- 11 Portincasa P, Bonfrate L, de Bari O, Lembo A, Ballou S. Irritable bowel syndrome and diet. *Gastroenterol Rep* 2017; 5: 11–9.
- 12 Torres MJ, Sabate JM, Bouchoucha M, Buscail C, Hercberg S, Julia C. Food consumption and dietary intakes in 36,448 adults and their association with irritable bowel syndrome: Nutrinet-Santé study. *Therap Adv Gastroenterol* 2018; 11. DOI:10.1177/1756283X17746625.
- 13 Rodiño-Janeiro BK, Vicario M, Alonso-Cotoner C, Pascua-García R, Santos J. A Review of Microbiota and Irritable Bowel Syndrome: Future in Therapies. *Adv. Ther.* 2018; 35: 289–310.
- 14 Ishaque SM, Khosruzzaman SM, Ahmed DS, Sah MP. A randomized placebo-controlled clinical trial of a multi-strain probiotic formulation (Bio-Kult®) in the management of diarrhea-predominant irritable bowel syndrome. *BMC Gastroenterol* 2018; 18: 71.

Hania Opienski:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5467063/>
<https://pubmed.ncbi.nlm.nih.gov/31103370/>
<https://pubmed.ncbi.nlm.nih.gov/27725652/>
<https://pubmed.ncbi.nlm.nih.gov/31029650/>
<https://www.tandfonline.com/doi/full/10.1080/21501201003735556>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6579922/>
<https://www.drbrianlum.com/post/functional-medicine-relief-for-ibs-with-patient-examples>
<https://pubmed.ncbi.nlm.nih.gov/32872510/>
https://www.researchgate.net/figure/Amino-Acid-Profile-and-GABA-Content-of-Dry-Hericium-erinaceus-and-FHJ_tbl2_324253170
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6982118/>
<https://pubmed.ncbi.nlm.nih.gov/26244378/>

Sue McGarrigle:

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health and social care directorate Quality standards and indicators Briefing paper Quality standard topic: Irritable bowel syndrome 2015
J Clin Med. 2017 Nov; 6(11): 99. Published online 2017 Oct 26. doi: 10.3390/jcm6110099 PMCID: PMC5704116 PMID: 29072609 Rome Criteria and a Diagnostic Approach to Irritable Bowel Syndrome Brian E. Lacy and Nihal K. Patel*
JGH Open. 2020 Aug; 4(4): 656–662. Published online 2020 Feb 12. doi: 10.1002/jgh3.12311 PMCID: PMC7411643 PMID: 32782953
Nutritional status in irritable bowel syndrome: A North American population-based study Isabel A Hujoel corresponding author 1

Ben Makeham:

Öhman L, Törnblom H, Simrén M. Crosstalk at the mucosal border: importance of the gut microenvironment in IBS. *Nat Rev Gastroenterol Hepatol.* 2015 Jan;12(1):36-49.
<https://theromefoundation.org/rome-iv/rome-iv-criteria/>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5358086/>

Vitamin D feature:

Rachel Bartholemew:

1. Grober U, Holick M. Live longer with vitamin D? *Nutrients*. 2015 Mar; 7(3): 1871-1880. Published online 2015 Mar 12. doi: 10.3390/nu7031871
2. Garland C.F., Kim J.J., et al. Meta-analysis of all-cause mortality according to serum 25-hydroxyvitamin D. *Am. J. Public Health*. 2014; 104:e43–e50. doi: 10.2105/ AJPH.2014.302034.
3. Schöttker B., Jorde R., et al. Consortium on Health and Ageing: Network of Cohorts in Europe and the United States: Vitamin D and mortality: Meta-analysis of individual participant data from a large consortium of cohort studies from Europe and the United States. *BMJ*. 2014; 34: g3656. doi: 10.1136/bmj.g3656.
4. Lindqvist PG. The winding path towards an inverse relationship between sun exposure and all-cause mortality. *Anticancer Res* 2018 Feb; 38(2): 1173-1178
5. National Diet and Nutrition Survey. Results from Years 5-6 (combined) of the Rolling Programme (2012/13-2013/14) A Survey carried out on behalf of Public Health England and Food Standards Agency.
6. Munns CF, Shaw N et al. Global consensus recommendations on prevention and management of nutritional rickets. *J Clin Endocrinol Metab*. 2016; 101 (2): 394-41
7. Vitamin D & Health Report. Scientific advisory committee on nutrition (SACN) 2016. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/537616/SACN_Vitamin_D_and_Health_report.pdf

Dr Marilyn Glenville:

<https://www.frontiersin.org/articles/10.3389/fimmu.2022.790444/full#h13>

Hania Opienski:

<https://www.ncbi.nlm.nih.gov/books/NBK532266/>
<https://pubmed.ncbi.nlm.nih.gov/32857334/>
<https://pubmed.ncbi.nlm.nih.gov/28815282/>
<https://pubmed.ncbi.nlm.nih.gov/30529281/>
<https://pubmed.ncbi.nlm.nih.gov/24494050/>
<https://pubmed.ncbi.nlm.nih.gov/21540874/>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5440113/>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2851242/>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7385774/>
<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0268396>
<https://my.clevelandclinic.org/health/diseases/15050-vitamin-d-vitamin-d-deficiency>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7513835/>
<https://www.contagionlive.com/view/vitamin-d-deficiency-increases-risk-of-severe-or-fatal-covid-19>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8509048/>

Amy Rushton:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3356951/#:~:text=Vitamin%20D%20is%20known%20to,muscle%20strength%2C%20thereby%20preventing%20falls.>
<https://www.nutrition.org.uk/news/2021/british-nutrition-foundation-survey-reveals-49-adults-unaware-of-uk-government-guidelines-for-vitamin-d/#:~:text=The%20National%20Diet%20and%20Nutrition,vitamin%20D%20in%20their%20blood.>
<https://pubmed.ncbi.nlm.nih.gov/21918215/>
<https://pubmed.ncbi.nlm.nih.gov/31418463/>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3782116/#:~:text=Aging%20reduces%20vitamin%20D%20production,the%20formation%20of%20previtamin%20D3.>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4399494/>

Heart health feature:

1. British Heart Foundation, 2022a. Global Heart and Circulatory Diseases Factsheet. [pdf] British Heart Foundation. Available at: <<https://www.bhf.org.uk/-/media/files/research/heart-statistics/bhf-cvd-statistics-global-factsheet.pdf?rev=1ec126bd94344f8cade4d86df6f0598c&hash=7E7D15FC4B59B6544C92A19DCF8F4B9E>> [Accessed 13 October 2022].
2. World Health Organisation, 2021a. Noncommunicable diseases. [online] Available at: <<https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases#:~:text=Cardiovascular%20diseases%20account%20for%20most,of%20all%20premature%20NCD%20deaths>> [Accessed 13 October 2022].
3. British Heart Foundation, 2022b. UK Factsheet. [pdf] British Heart Foundation. Available at: <<https://www.bhf.org.uk/-/media/files/research/heart-statistics/bhf-cvd-statistics-uk-factsheet.pdf?rev=4b0be2cd03eb412f8f2703b63a3b4ebb&hash=E6965279D61DEA4CBD0C97E176CAA671>> [Accessed 13 October 2022].
4. British Heart Foundation, 2021. How a healthy heart works. [online] Available at: <<https://www.bhf.org.uk/informationsupport/how-a-healthy-heart-works>> [Accessed 13 October 2022].
5. NHS Inform, 2020. How your heart works. [online] Available at: <<https://www.nhsinform.scot/illnesses-and-conditions/heart-and-blood-vessels/about-the-heart/understanding-how-your-heart-functions>> [Accessed 13 October 2022].
6. Wikipedia, 2022. Endothelium. [online] Available at: <<https://en.wikipedia.org/wiki/Endothelium>> [Accessed 13 October 2022].

7. Park, K. and Park, W., 2015. Endothelial dysfunction: clinical implications in cardiovascular disease and therapeutic approaches. *Journal of Korean Medical Science*, [e-journal] 30(9), pp.1213-1225. <https://doi.org/10.3346/jkms.2015.30.9.1213>.
8. Botts, S., Fish, J. and Howe, K., 2021. Dysfunctional vascular endothelium as a driver of atherosclerosis: emerging insights into pathogenesis and treatment. *Frontiers in Pharmacology*, [e-journal] 12. <https://doi.org/10.3389/fphar.2021.787541>.
9. Vallance, P. and Chan, N., 2001. Endothelial function and nitric oxide: clinical relevance. *Heart*, [e-journal] 85(3), pp.342-350. <https://doi.org/10.1136/heart.85.3.342>.
10. British Heart Foundation, 2022c. Facts and figures. [online] Available at: <<https://www.bhf.org.uk/what-we-do/news-from-the-bhf/contact-the-press-office/facts-and-figures#:~:text=There%20are%20around%207.6%20million,common%20type%20of%20heart%20disease>> [Accessed 13 October 2022].
11. NIH National Heart, Lung and Blood Institute, 2022. Coronary Heart Disease – What is Coronary Heart Disease? [online] Available at: <<https://www.nhlbi.nih.gov/health/coronary-heart-disease>> [Accessed 13 October 2022].
12. Bots, S., Peters, S. and Woodward, M., 2017. Sex differences in coronary heart disease and stroke mortality: a global assessment of the effect of ageing between 1980 and 2010. *BMJ Global Health*, [e-journal] 2(2), pp.1-8. <https://doi.org/10.1136/bmjgh-2017-000298>.
13. Newby, D., Grubb, N. and Bradbury, A. n.d. Cardiovascular Disease. In: Walker, B., Colledge, N., Ralston, S. and Penman, I., ed. 2014. *Davidson's Principles and Practices of Medicine*. Churchill Livingstone: Elsevier. Ch.18.
14. John Hopkins Medicine, n.d. Heart Attack. [online] Available at: <<https://www.hopkinsmedicine.org/health/conditions-and-diseases/heart-attack>> [Accessed 13 October 2022].
15. British Heart Foundation, 2022d. Heart failure. [online] Available at: <<https://www.bhf.org.uk/informationsupport/conditions/heart-failure>> [Accessed 13 October 2022].
16. World Health Organisation, 2021b. Hypertension. [online] Available at: <<https://www.who.int/news-room/fact-sheets/detail/hypertension>> [Accessed 13 October 2022].
17. Millett, E., Peters, S. and Woodward, M., 2018. Sex differences in risk factors for myocardial infarction: cohort study of UK Biobank participants. *BMJ*, 363. <https://doi.org/10.1136/bmj.k4247>.
18. Newson, L., 2018. Menopause and cardiovascular disease. *Post Reproductive Health*, [e-journal] 24(1), pp.44-49. <https://doi.org/10.1177/2053369117749675>.
19. Appelman, Y., van Rijn, B., Monique, E., Boersma, E. and Peters, S., 2015. Sex differences in cardiovascular risk factors and disease prevention. *Atherosclerosis*, [e-journal] 241(1), pp.211-218. <https://doi.org/10.1016/j.atherosclerosis.2015.01.027>.
20. Barbaresko, J., Rienks, J. and Nöthlings, U., 2018. Lifestyle indices and cardiovascular disease risk: a meta-analysis. *American Journal of Preventive Medicine*, [e-journal] 55(4), pp.555-564. <https://doi.org/10.1016/j.amepre.2018.04.046>.
21. British Heart Foundation, 2022e. Reducing daily salt intake could save lives and costs in coming years. [online] Available at: <<https://www.bhf.org.uk/what-we-do/news-from-the-bhf/news-archive/2022/june/bhf-salt-report>> [Accessed 13 October 2022].
22. World Health Organisation, n.d. Salt intake. [online] Available at: <<https://www.who.int/data/gho/indicator-metadata-registry/imr-details/3082>> [Accessed 13 October 2022].
23. Gaudal, N., Jürgens, G., Baslund, B. and Alderman, M., 2014. Compared with usual sodium intake, low-and excessive-sodium diets are associated with increased mortality: a meta-analysis. *American Journal of Hypertension*, [e-journal] 27(9), pp.1129-1137. <https://doi.org/10.1093/ajh/hpu028>.
24. Kendall, C., Esfahani, A., and Jenkins, D., 2010. The link between dietary fibre and human health. *Food Hydrocolloids*, [e-journal] 24(1), pp. 42-48. <https://doi.org/10.1016/j.foodhyd.2009.08.002>.
25. Temple, N., 2018. Fat, sugar, whole grains and heart disease: 50 years of confusion. *Nutrients*, [e-journal] 10(1). <https://doi.org/10.3390/nu10010039>.
26. Threapleton, D., Greenwood, D., Evans, C., Cleghorn, C., Nykjaer, C., Woodhead, C., Cade, J., Gale, C. and Burley, V., 2013. Dietary fibre intake and risk of cardiovascular disease: systematic review and meta-analysis. *BMJ*, [e-journal] 347. <https://doi.org/10.1136/bmj.f6879>.
27. Aune, D., 2019. Plant foods, antioxidant biomarkers, and the risk of cardiovascular disease, cancer, and mortality: a review of the evidence. *Advances in Nutrition*, [e-journal] 10(Supplement 4), pp. S404-S421. <https://doi.org/10.1093/advances/nmz042>.
28. Moser, M. and Chun, O., 2016. Vitamin C and heart health: a review based on findings from epidemiologic studies. *International Journal of Molecular Sciences*, [e-journal] 17(8), p.1328. <https://doi.org/10.3390/ijms17081328>.
29. Getz, G. and Reardon, C., 2017. Nutrition and cardiovascular disease. In: C. Geissler and H. Powers, eds. 2017. *Human Nutrition*. 13th ed. New York: Oxford University Press. Ch.19.
30. Wang, D., Li, Y., Chiuve, S., Stampfer, M., Manson, J., Rimm, E., Willett, W. and Hu, F., 2016. Association of specific dietary fats with total and cause-specific mortality. *JAMA Internal Medicine*, [e-journal] 176(8), pp.1134-1145. <https://doi.org/10.1001/jamainternmed.2016.2417>.
31. Siri-Tarino, P., Sun, Q., Hu, F. and Krauss, R., 2010. Saturated fat, carbohydrate, and cardiovascular disease. *The American Journal of Clinical Nutrition*, [e-journal] 91(3), pp.502-509. <https://doi.org/10.3945/ajcn.2008.26285>.
32. Clifton, P. and Keogh, J., 2017. A systematic review of the effect of dietary saturated and polyunsaturated fat on heart disease. *Nutrition, Metabolism and Cardiovascular Diseases*, [e-journal] 27(12), pp.1060-1080. <https://doi.org/10.1016/j.numecd.2017.10.010>.
33. Li, Y., Hruby, A., Bernstein, A., Ley, S., Wang, D., Chiuve, S., Sampson, L., Rexrode, K., Rimm, E., Willett, W. and Hu, F., 2015. Saturated fats compared with unsaturated fats and sources of carbohydrates in relation to risk of coronary heart disease: a prospective cohort study. *Journal of the American College of Cardiology*, [e-journal] 66(14), pp.1538-1548. <https://doi.org/10.1016/j.jacc.2015.07.055>.
34. Doughty, K., Del Pilar, N., Audette, A. and Katz, D., 2017. Lifestyle medicine and the management of cardiovascular disease. *Current Cardiology Reports*, [e-journal] 19(11), pp.1-10. <https://doi.org/10.1007/s11886-017-0925-z>.
35. Paula, T., Viana, L., Neto, A., Leitao, C., Gross, J. and Azevedo, M., 2015. Effects of the DASH diet and walking on blood pressure in patients with type 2 diabetes and uncontrolled hypertension: a randomized controlled trial. *The Journal of Clinical Hypertension*, [e-journal] 17(11), pp.895-901. <https://doi.org/10.1111/jch.12597>.
36. Nystoriak, M.A. and Bhatnagar, A., 2018. Cardiovascular effects and benefits of exercise. *Frontiers in Cardiovascular Medicine*, [e-journal] 5. p.135. <https://doi.org/10.3389/fcvm.2018.00135>.

37. British Heart Foundation, n.d. Physical inactivity. [online] Available at: <<https://www.bhf.org.uk/informationsupport/risk-factors/physical-inactivity>> [Accessed 13 October 2022].
38. Tian, D. and Meng, J., 2019. Exercise for prevention and relief of cardiovascular disease: prognoses, mechanisms, and approaches. *Oxidative Medicine and Cellular Longevity*, [e-journal] 2019. <https://doi.org/10.1155/2019/3756750>.
39. Brown, J., Gerhardt, T. and Kwon, E., 2022. Risk Factors for Coronary Artery Disease. [e-book] Treasure Island (FL): StatPearls Publishing. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK554410/#_NBK554410_pubdet_> [Accessed 13 October 2022].
40. Kraus, W., Houmard, J., Duscha, B., Knetzger, K., Wharton, M., McCartney, J., Bales, C., Henes, S., Samsa, G., Otvos, J. and Kulkarni, K., 2002. Effects of the amount and intensity of exercise on plasma lipoproteins. *New England Journal of Medicine*, [e-journal] 347(19), pp.1483-1492. <https://doi.org/10.1056/NEJMoa020194>.
41. Wang, Y., Wang, J., Chen, S., Li, J., Lu, Q., Vitiello, M., Wang, F., Tang, X., Shi, J., Lu, L. and Wu, S., 2020. Association of longitudinal patterns of habitual sleep duration with risk of cardiovascular events and all-cause mortality. *JAMA Network Open*, [e-journal] 3(5), pp.1-15. <https://doi.org/10.1001/jamanetworkopen.2020.5246>.
42. Spiegel, K., Leproult, R. and Van Cauter, E., 1999. Impact of sleep debt on metabolic and endocrine function. *The Lancet*, [e-journal] 354(9188), pp.1435-1439. [https://doi.org/10.1016/S0140-6736\(99\)01376-8](https://doi.org/10.1016/S0140-6736(99)01376-8).
43. Frank, S., Gonzalez, K., Lee-Ang, L., Young, M., Tamez, M. and Mattei, J., 2017. Diet and sleep physiology: public health and clinical implications. *Frontiers in Neurology*, [e-journal] 8(AUG), pp.1-9. <https://doi.org/10.3389/fneur.2017.00393>.
44. Steptoe, A. and Kivimäki, M., 2013. Stress and cardiovascular disease: an update on current knowledge. *Annual Review of Public Health*, [e-journal] 34, pp.337-354. <https://doi.org/10.1146/annurev-publhealth-031912-114452>.
45. Rosengren, A., Hawken, S., Ōunpuu, S., Sliwa, K., Zubaid, M., Almahmeed, W.A., Blackett, K., Sitthi-Amorn, C., Sato, H., Yusuf, S. and INTERHEART investigators, 2004. Association of psychosocial risk factors with risk of acute myocardial infarction in 11 119 cases and 13 648 controls from 52 countries (the INTERHEART study): case-control study. *The Lancet*, [e-journal] 364(9438), pp.953-962. [https://doi.org/10.1016/S0140-6736\(04\)17019-0](https://doi.org/10.1016/S0140-6736(04)17019-0).
46. Varvogli, L. and Darviri, C., 2011. Stress management techniques: Evidence-based procedures that reduce stress and promote health. *Health Science Journal*, [online] Available at: <<https://www.itmedicalteam.pl/articles/stress-management-techniques-evidencebased-procedures-that-reduce-stress-and-promote-health-105632.html>> [Accessed 14 October 2022].
47. Hopper, S.I., Murray, S.L., Ferrara, L.R. and Singleton, J.K., 2019. Effectiveness of diaphragmatic breathing for reducing physiological and psychological stress in adults: a quantitative systematic review. *JBISIR*, [e-journal] 17(9), pp.1855-1876. <https://doi.org/10.11124/JBISIR-2017-003848>.
48. Zhang, F., Barr, S., McNulty, H., Li, D. and Blumberg, J., 2020. Health effects of vitamin and mineral supplements. *BMJ*, [e-journal] 369. <https://doi.org/10.1136/bmj.m2511>.
49. Jain, A., Aggarwal, K. and Zhang, P., 2015. Omega-3 fatty acids and cardiovascular disease. *Eur Rev Med Pharmacol Sci*, [online] Available at: <<https://www.europeanreview.org/article/8446>> [Accessed 14 October 2022].
50. Bernasconi, A., Wiest, M., Lavie, C., Milani, R. and Laukkanen, J., 2021. Effect of omega-3 dosage on cardiovascular outcomes: an updated meta-analysis and meta-regression of interventional trials. *Mayo Clinic Proceedings*, [e-journal] 96(2), pp. 304-313. <https://doi.org/10.1016/j.mayocp.2020.08.034>.
51. Elagizi, A., Lavie, C., O'Keefe, E., Marshall, K., O'Keefe, J. and Milani, R., 2021. An update on omega-3 polyunsaturated fatty acids and cardiovascular health. *Nutrients*, [e-journal] 13(1), p.1-12. <https://doi.org/10.3390/nu13010204>.
52. Geleijnse, J., Vermeer, C., Grobbee, D., Schurgers, L., Knapen, M., Van Der Meer, I., Hofman, A. and Witteman, J., 2004. Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. *The Journal of Nutrition*, [e-journal] 134(11), pp.3100-3105. <https://doi.org/10.1093/jn/134.11.3100>.
53. Hariri, E., Kassis, N., Iskandar, J., Schurgers, L., Saad, A., Abdelfattah, O., Bansal, A., Isogai, T., Harb, S. and Kapadia, S., 2021. Vitamin K2—a neglected player in cardiovascular health: a narrative review. *Open Heart*, [e-journal] 8(2), p.e001715. <https://doi.org/10.1136/openhrt-2021-001715>.
54. Choi, S., Liu, X. and Pan, Z., 2018. Zinc deficiency and cellular oxidative stress: prognostic implications in cardiovascular diseases. *Acta Pharmacologica Sinica*, [e-journal] 39(7), pp.1120-1132. <https://doi.org/10.1038/aps.2018.25>.
55. Martelli, A., Testai, L., Colletti, A. and Cicero, A., 2020. Coenzyme Q10: Clinical applications in cardiovascular diseases. *Antioxidants*, [e-journal] 9(4), p.341. <https://doi.org/10.3390/antiox9040341>.
56. Gao, L., Mao, Q., Cao, J., Wang, Y., Zhou, X. and Fan, L., 2012. Effects of coenzyme Q10 on vascular endothelial function in humans: a meta-analysis of randomized controlled trials. *Atherosclerosis*, [e-journal] 221(2), pp.311-316. <https://doi.org/10.1016/j.atherosclerosis.2011.10.027>.
57. Kunadian, V., Ford, G., Bawamia, B., Qiu, W. and Manson, J., 2014. Vitamin D deficiency and coronary artery disease: a review of the evidence. *American Heart Journal*, [e-journal] 167(3), pp.283-291. <https://doi.org/10.1016/j.ahj.2013.11.012>.
58. Skaaby, T., Husemoen, L., Pisinger, C., Jørgensen, T., Thuesen, B., Fenger, M. and Linneberg, A., 2012. Vitamin D status and changes in cardiovascular risk factors: a prospective study of a general population. *Cardiology*, [e-journal] 123(1), pp.62-70. <https://doi.org/10.1159/000341277>.
59. Wang, Z., Liu, Y., Liu, G., Lu, H. and Mao, C., 2018. L-Carnitine and heart disease. *Life Sciences*, [e-journal] 194, pp.88-97. <https://doi.org/10.1016/j.lfs.2017.12.015>.
60. Mingorance, C., Rodriguez-Rodriguez, R., Justo, M., Herrera, M. and de Sotomayor, M., 2011. Pharmacological effects and clinical applications of propionyl-L-carnitine. *Nutrition Reviews*, [e-journal] 69(5), pp.279-290. <https://doi.org/10.1111/j.1753-4887.2011.00387.x>.
61. Cheng, H., Koutsidis, G., Lodge, J., Ashor, A., Siervo, M. and Lara, J., 2017. Tomato and lycopene supplementation and cardiovascular risk factors: A systematic review and meta-analysis. *Atherosclerosis*, [e-journal] 257, pp.100-108. <https://doi.org/10.1016/j.atherosclerosis.2017.01.009>.
62. Mozos, I., Stoian, D., Caraba, A., Malainer, C., Horbańczuk, J. and Atanasov, A., 2018. Lycopene and vascular health. *Frontiers in Pharmacology*, [e-journal] 9, p.521. <https://doi.org/10.3389/fphar.2018.00521>.

63. Trautwein, E. and McKay, S., 2020. The role of specific components of a plant-based diet in management of dyslipidemia and the impact on cardiovascular risk. *Nutrients*, [e-journal] 12(9), p.2671. <https://doi.org/10.3390/nu12092671>.
64. Ras, R., Geleijnse, J. and Trautwein, E., 2014. LDL-cholesterol-lowering effect of plant sterols and stanols across different dose ranges: a meta-analysis of randomised controlled studies. *British Journal of Nutrition*, [e-journal] 112(2), pp.214-219. <https://doi.org/10.1017/S0007122614000000>

Ingredient spotlight:

- Ambati, R. R., Phang, S. M., Ravi, S., & Aswathanarayana, R. G. (2014). Astaxanthin: sources, extraction, stability, biological activities and its commercial applications—a review. *Marine drugs*, 12(1), 128–152. <https://doi.org/10.3390/md12010128>
- Capelli, B., Bagchi, D., and Cysewski, G.R. (2013). Synthetic astaxanthin is significantly inferior to algal-based astaxanthin as an antioxidant and may not be suitable as a human nutraceutical supplement. *Nutrafoods*, 12:145-152.
- Davinelli, S., Nielsen, M. E., & Scapagnini, G. (2018). Astaxanthin in Skin Health, Repair, and Disease: A Comprehensive Review. *Nutrients*, 10(4), 522. <https://doi.org/10.3390/nu10040522>
- Fassett, R. G., & Coombes, J. S. (2011). Astaxanthin: a potential therapeutic agent in cardiovascular disease. *Marine drugs*, 9(3), 447–465. <https://doi.org/10.3390/md9030447>
- Giannaccare, G., Pellegrini, M., Senni, C., Bernabei, F., Scoria, V., & Cicero, A. (2020). Clinical Applications of Astaxanthin in the Treatment of Ocular Diseases: Emerging Insights. *Marine drugs*, 18(5), 239. <https://doi.org/10.3390/md18050239>
- Higuera-Ciapara, I., Félix-Valenzuela, L., & Goycoolea, F. M. (2006). Astaxanthin: a review of its chemistry and applications. *Critical reviews in food science and nutrition*, 46(2), 185–196. <https://doi.org/10.1080/10408690590957188>
- Katagiri, M., Satoh, A., Tsuji, S., & Shirasawa, T. (2012). Effects of astaxanthin-rich *Haematococcus pluvialis* extract on cognitive function: a randomised, double-blind, placebo-controlled study. *Journal of clinical biochemistry and nutrition*, 51(2), 102–107. <https://doi.org/10.3164/jcbn.D-11-00017>
- Li, X., Wang, X., Duan, C., Yi, S., Gao, Z., Xiao, C., Agathos, S. N., Wang, G., & Li, J. (2020). Biotechnological production of astaxanthin from the microalga *Haematococcus pluvialis*. *Biotechnology advances*, 43, 107602. <https://doi.org/10.1016/j.biotechadv.2020.107602>
- Park, J. S., Chyun, J. H., Kim, Y. K., Line, L. L., & Chew, B. P. (2010). Astaxanthin decreased oxidative stress and inflammation and enhanced immune response in humans. *Nutrition & metabolism*, 7, 18. <https://doi.org/10.1186/1743-7075-7-18>
- Park, J. S., Mathison, B. D., Hayek, M. G., Massimino, S., Reinhart, G. A., & Chew, B. P. (2011). Astaxanthin stimulates cell-mediated and humoral immune responses in cats. *Veterinary immunology and immunopathology*, 144(3-4), 455–461. <https://doi.org/10.1016/j.vetimm.2011.08.019>
- Piermarocchi, S., Saviano, S., Parisi, V., Tedeschi, M., Panozzo, G., Scarpa, G., Boschi, G., Lo Giudice, G., & Carmis Study Group (2012). Carotenoids in Age-related Maculopathy Italian Study (CARMIS): two-year results of a randomized study. *European journal of ophthalmology*, 22(2), 216–225. <https://doi.org/10.5301/ejo.5000069>
- Shah, M. M., Liang, Y., Cheng, J. J., & Daroch, M. (2016). Astaxanthin-Producing Green Microalga *Haematococcus pluvialis*: From Single Cell to High Value Commercial Products. *Frontiers in plant science*, 7, 531. <https://doi.org/10.3389/fpls.2016.00531>
- Su, F., Yu, W., and Liu, J. (2020). Comparison of effect of dietary supplementation with *Haematococcus pluvialis* powder and synthetic astaxanthin on carotenoid composition, concentration, esterification degree and astaxanthin isomers in ovaries, hepatopancreas, carapace, epithelium of adult female Chinese mitten crab (*Eriocheir sinensis*). *Aquaculture*, 523. doi: 10.1016/j.aquaculture.2017.03.010
- Sztretye, M., Dienes, B., Gönczi, M., Cziráj, T., Csernoch, L., Dux, L., Szentesi, P., & Keller-Pintér, A. (2019). Astaxanthin: A Potential Mitochondrial-Targeted Antioxidant Treatment in Diseases and with Aging. *Oxidative medicine and cellular longevity*, 2019, 3849692. <https://doi.org/10.1155/2019/3849692>
- Tominaga, K., Hongo, N., Fujishita, M., Takahashi, Y., & Adachi, Y. (2017). Protective effects of astaxanthin on skin deterioration. *Journal of clinical biochemistry and nutrition*, 61(1), 33–39. <https://doi.org/10.3164/jcbn.17-35>
- Uttara, B., Singh, A. V., Zamboni, P., & Mahajan, R. T. (2009). Oxidative stress and neurodegenerative diseases: a review of upstream and downstream antioxidant therapeutic options. *Current neuropharmacology*, 7(1), 65–74. <https://doi.org/10.2174/157015909787602823>
- Young, A. J., & Lowe, G. L. (2018). Carotenoids-Antioxidant Properties. *Antioxidants (Basel, Switzerland)*, 7(2), 28. <https://doi.org/10.3390/antiox7020028>
- Yuan, J. P., Peng, J., Yin, K., & Wang, J. H. (2011). Potential health-promoting effects of astaxanthin: a high-value carotenoid mostly from microalgae. *Molecular nutrition & food research*, 55(1), 150–165. <https://doi.org/10.1002/mnfr.201000414>

Ask the experts:

Lorena Carboni:

1. Ulrich CM, Potter JD. Folate supplementation: too much of a good thing? *Cancer Epidemiol Biomarkers Prev*. 2006 Feb;15(2):189-93.
2. Wald DS, Law M, Morris JK. Homocysteine and cardiovascular disease: evidence on causality from a meta-analysis. *BMJ (Clinical Research ed.)*. 2002 Nov;325(7374):1202. DOI: 10.1136/bmj.325.7374.1202. PMID: 12446535; PMCID: PMC135491.
3. Tinelli C, Di Pino A, Ficulle E, et al., "Hyperhomocysteinemia as a Risk Factor and Potential Nutraceutical Target for Certain Pathologies," *Frontiers in Nutrition*, vol. 6, p. 49, 2019.
4. Henderson AM, Aleliunas RE, Loh SP, Khor GL, Harvey-Leeson S, Glier MB, et al. L-5-methyltetrahydrofolate supplementation increases blood folate concentrations to a greater extent than folic acid supplementation in Malaysian women. *J Nutr*. 2018;148:855–90.
5. Lamers Y, Prinz-langenohl R, Bramswig S, Pietrzik K. Red blood cell folate concentrations increase more after supplementation with [6S]-5-methyltetrahydrofolate than with folic acid in women of childbearing age. *Am J Clin Nutr*. 2006;84:156–61.
6. Venn BJ, Green T, Moser R, Mann JI. Comparison of low-dose supplementation with L-5-methyltetrahydrofolate or folic acid on plasma homocysteine: a randomized placebo controlled study. *Am J Clin Nutr*. 2003;77:658–62.
7. Lamers Y, Prinz-Langenohl R, Moser R, Pietrzik K. Supplementation with [6S]-5-methyltetrahydrofolate or folic acid equally reduces plasma total homocysteine concentrations in healthy women. *Am J Clin Nutr*. 2004;79:473–8.
8. Huo Y, Li J, Qin X, Huang Y, Wang X, Gottesman RF, Tang G, Wang B, Chen D, He M, Fu J, Cai Y, Shi X, Zhang Y, Cui Y, Sun N, Li X, Cheng X,

- Wang J, Yang X, Yang T, Xiao C, Zhao G, Dong Q, Zhu D, Wang X, Ge J, Zhao L, Hu D, Liu L, Hou FF; CSPPT Investigators. Efficacy of folic acid therapy in primary prevention of stroke among adults with hypertension in China: the CSPPT randomized clinical trial. *JAMA*. 2015 Apr 7;313(13):1325-35. doi: 10.1001/jama.2015.2274. PMID: 25771069.
9. Mazza A, Cicero AF, Ramazzina E, et al., "Nutraceutical approaches to homocysteine lowering in hypertensive subjects at low cardiovascular risk: a multicenter, randomized clinical trial," *Journal of biological regulators and homeostatic agents*, vol. 30, no. 3, pp. 921–927, 2016.

Sarah Oboh:

1. NICE (2014). Available at <https://www.nice.org.uk/guidance/qs73/documents/fertility-problems-briefing-paper2#:~:text=It%20is%20estimated%20that%20infertility,heterosexual%20couples%20in%20the%20UK>
2. Perez-Carrasco V et al. *Front Cell Infect Microbiol* 2021;11:617002
3. Amabebe E et al. *Frontiers in Medicine* 2018;5:181
4. Chen X et al. *Frontiers in Cellular and Infection Microbiology* 2021;11:631972
5. Rosati D et al. *Microorganisms* 2020;8:144
6. Köhler GA et al. *Infectious Diseases in Obstetrics and Gynecology* 2012;2012:636474
7. van de Wijgert J et al. *British Journal of Obstetrics and Gynaecology* 2020;127:287-299
8. Ravel J et al. *American Journal of Obstetrics and Gynecology* 2021;224:251-257
9. World Health Organisation. Guidelines for the Evaluation of Probiotics in Food. Available at https://www.who.int/foodsafety/fs_management/en/probiotic_guidelines.pdf
10. Morelli L et al. *Journal of Clinical Gastroenterology* 2004;38:S107-10
11. Reid G et al. *FEMS Immunology and Medical Microbiology* 2001;30:49-52
12. Anukam K et al. *Microbes and Infection* 2006;8:1450-4
13. Anukam KC et al. *Microbial Ecology in Health and Disease* 2009;21:72-77
14. Koradia P et al. *Expert Review of Anti-infective Therapy* 2019;17:733-740