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Nature, Nurture, and Cancer Risks: Genetic and Nutritional Contributions to Cancer
Theodoratou et al.

Supplemental Box 1 Search strategies and MESH terms used to identify associations between the main cancer types and nutrition

Cancer type	Search strategy	Date	No. of hits
Lung cancer	(("lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields]) AND ("nutritional status"[All Fields] OR ("nutritional"[All Fields] AND "status"[All Fields]) OR "nutritional status"[All Fields] OR "nutrition"[All Fields] OR "nutritional sciences"[All Fields] OR ("nutritional"[All Fields] AND "sciences"[All Fields]) OR "nutritional sciences"[All Fields] OR ("diet"[MeSH Terms] OR "diet"[All Fields]) OR ("food"[MeSH Terms] OR "food"[All Fields]) OR ("food"[MeSH Terms] OR "food"[All Fields] OR "nutrients"[All Fields]))) AND ((Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Review[ptyp] OR systematic[sb]) AND "2005/09/07"[PDat] : "2016/06/01"[PDat] AND "humans"[MeSH Terms])	1/6/2016	677
Breast cancer	(("breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("nutritional status"[All Fields] OR ("nutritional"[All Fields] AND "status"[All Fields]) OR "nutritional status"[All Fields] OR "nutrition"[All Fields] OR "nutritional sciences"[All Fields] OR ("nutritional"[All Fields] AND "sciences"[All Fields]) OR "nutritional sciences"[All Fields] OR ("diet"[MeSH Terms] OR "diet"[All Fields]) OR ("food"[MeSH Terms] OR "food"[All Fields]) OR ("food"[MeSH Terms] OR "food"[All Fields] OR "nutrients"[All Fields]))) AND ((Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Review[ptyp] OR systematic[sb]) AND "2005/09/07"[PDat] : "2015/09/04"[PDat] AND "humans"[MeSH Terms])	4/9/2015	1,419
Prostate cancer	(("prostate neoplasms"[All Fields] OR “colorectal neoplasm” OR ("prostate"[All Fields] AND "neoplasms"[All Fields]) OR "prostate neoplasms"[All Fields] OR ("prostate"[All Fields] AND "cancer"[All Fields]) OR "prostate cancer"[All Fields]) AND ("nutritional status"[All Fields] OR ("nutritional"[All Fields] AND "status"[All Fields]) OR "nutritional status"[All Fields] OR "nutrition"[All Fields] OR "nutritional sciences"[All Fields] OR ("nutritional"[All Fields] AND "sciences"[All Fields]) OR "nutritional sciences"[All Fields] OR ("diet"[MeSH Terms] OR	4/9/2015	960

	"diet"[All Fields]) OR ("food"[MeSH Terms] OR "food"[All Fields]) OR ("food"[MeSH Terms] OR "food"[All Fields] OR "nutrients"[All Fields]))) AND ((Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Review[ptyp] OR systematic[sb]) AND "2005/09/07"[PDat] : "2015/09/04"[PDat] AND "humans"[MeSH Terms])		
Colorectal cancer	(("colon neoplasms"[All Fields] OR "rectal neoplasms"[All Fields] OR ("colon"[All Fields] AND "neoplasms"[All Fields]) OR ("rectal"[All Fields] AND "neoplasms"[All Fields]) OR "colon neoplasms"[All Fields] OR ("colon"[All Fields] AND "cancer"[All Fields]) OR ("rectal"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields] OR "rectal cancer"[All Fields] OR "colorectal cancer"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields])) AND ("nutritional status"[All Fields] OR ("nutritional"[All Fields] AND "status"[All Fields]) OR "nutritional status"[All Fields] OR "nutrition"[All Fields] OR "nutritional sciences"[All Fields] OR ("nutritional"[All Fields] AND "sciences"[All Fields]) OR "nutritional sciences"[All Fields] OR ("diet"[MeSH Terms] OR "diet"[All Fields]) OR ("food"[MeSH Terms] OR "food"[All Fields]) OR ("food"[MeSH Terms] OR "food"[All Fields] OR "nutrients"[All Fields]))) AND ((Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Review[ptyp] OR systematic[sb]) AND "2005/09/07"[PDat] : "2015/09/04"[PDat] AND "humans"[MeSH Terms])	4/9/2015	1,513
Stomach cancer	(("Stomach neoplasms"[All Fields] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("stomach"[All Fields] AND "cancer"[All Fields]) OR "stomach cancer"[All Fields] OR "gastric cancer"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields])) AND ("nutritional status"[All Fields] OR ("nutritional"[All Fields] AND "status"[All Fields]) OR "nutritional status"[All Fields] OR "nutrition"[All Fields] OR "nutritional sciences"[All Fields] OR ("nutritional"[All Fields] AND "sciences"[All Fields]) OR "nutritional sciences"[All Fields] OR ("diet"[MeSH Terms] OR "diet"[All Fields]) OR ("food"[MeSH Terms] OR "food"[All Fields]) OR ("food"[MeSH Terms] OR "food"[All Fields] OR "nutrients"[All Fields]))) AND ((Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Review[ptyp] OR systematic[sb]) AND "2005/09/07"[PDat] : "2015/09/04"[PDat] AND "humans"[MeSH Terms])	4/9/2015	634

Supplemental Box 2 Search strategies and MeSH terms used to identify gene--diet interactions for the main types of cancer

Nutrient	Search strategy	Date	No. of hits
Lung cancer			
β-cryptoxanthin	(("lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields]) AND (("beta cryptoxanthin"[All Fields]) OR ("cryptoxanthin"[All Fields])) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	0
Carotenoids	(("lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields]) AND (("carotenoids"[All Fields]) OR ("alpha carotene"[All Fields]) OR ("beta carotene"[All Fields])) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	1
Fruits	(("lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields]) AND (("fruit"[All Fields]) OR ("fruits"[All Fields])) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	0
Citrus fruits	(("lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields]) AND (("citrus fruit"[All Fields]) OR ("citrus"[All fields] AND "fruit"[All Fields]) OR ("citrus fruits"[All Fields]) OR ("citrus"[All fields] AND "fruits"[All Fields]) OR ("citrus"[All fields]) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide	08/25/2016	0

	Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))		
Breast cancer			
Alcohol	(("breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("alcohol"[All Fields] OR ("alcoholic"[All Fields] AND "drinks"[All Fields]) OR "alcoholic drinks"[All Fields] OR ("alcohol consumption"[All Fields]) OR ("alcohol"[All Fields] AND "consumption"[All Fields])) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	13
n-3 polyunsaturated fatty acids	(("breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND (("n-3 polyunsaturated fatty acids"[All Fields]) OR ("omega-3 polyunsaturated fatty acids"[All Fields]) OR ("n-3 PUFAs"[All Fields]) OR ("omega-3 PUFAS"[All Fields]) OR ("n 3 polyunsaturated fatty acids"[All Fields]) OR ("omega 3 polyunsaturated fatty acids"[All Fields]) OR ("n 3 PUFAs"[All Fields]) OR ("omega 3 PUFAS"[All Fields]) OR ("PUFAS" [All Fields]) OR ("fatty acids"[All Fields])) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	1
Vegetables	(("breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND (("vegetables"[All Fields])) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	1
α-carotene	(("breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND (("alpha carotene"[All Fields]) OR ("carotenoids"[All Fields])) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND	08/25/2016	2

	"variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))		
Prostate cancer			
Calcium	(("prostate neoplasms"[All Fields] OR ("prostate"[All Fields] AND "neoplasms"[All Fields]) OR "prostate neoplasms"[All Fields] OR ("prostate"[All Fields] AND "cancer"[All Fields]) OR "prostate cancer"[All Fields]) AND ("calcium"[All Fields]) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	3
Selenium	(("prostate neoplasms"[All Fields] OR ("prostate"[All Fields] AND "neoplasms"[All Fields]) OR "prostate neoplasms"[All Fields] OR ("prostate"[All Fields] AND "cancer"[All Fields]) OR "prostate cancer"[All Fields]) AND ("selenium"[All Fields]) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	0
Colorectal cancer			
Calcium	(("colon neoplasms"[All Fields] OR "rectal neoplasms"[All Fields] OR ("colon"[All Fields] AND "neoplasms"[All Fields]) OR ("rectal"[All Fields] AND "neoplasms"[All Fields]) OR ("colon"[All Fields] AND "cancer"[All Fields]) OR ("rectal"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields] OR "rectal cancer"[All Fields] OR "colorectal cancer"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields])) AND "calcium"[All Fields] AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	7
Fiber	(("colon neoplasms"[All Fields] OR "rectal neoplasms"[All Fields] OR ("colon"[All Fields] AND "neoplasms"[All Fields]) OR ("rectal"[All Fields] AND "neoplasms"[All Fields]) OR ("colon"[All Fields] AND "cancer"[All Fields]) OR ("rectal"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields] OR "rectal cancer"[All Fields] OR "colorectal cancer"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields])) AND ("fibre"[All Fields] OR "fiber"[All field]) AND ("gene" [All	08/25/2016	4

	fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))		
Alcohol	(("colon neoplasms"[All Fields] OR "rectal neoplasms"[All Fields] OR ("colon"[All Fields] AND "neoplasms"[All Fields]) OR ("rectal"[All Fields] AND "neoplasms"[All Fields]) OR ("colon"[All Fields] AND "cancer"[All Fields]) OR ("rectal"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields] OR "rectal cancer"[All Fields] OR "colorectal cancer"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields])) AND ("alcohol"[All Fields] OR ("alcoholic"[All Fields] AND "drinks"[All Fields]) OR "alcoholic drinks"[All Fields] OR ("alcohol consumption"[All Fields]) OR ("alcohol"[All Fields] AND "consumption"[All Fields])) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	9
Vegetables	(("colon neoplasms"[All Fields] OR "rectal neoplasms"[All Fields] OR ("colon"[All Fields] AND "neoplasms"[All Fields]) OR ("rectal"[All Fields] AND "neoplasms"[All Fields]) OR ("colon"[All Fields] AND "cancer"[All Fields]) OR ("rectal"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields] OR "rectal cancer"[All Fields] OR "colorectal cancer"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields])) AND "vegetables"[All Fields] AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	4
Dairy products	(("colon neoplasms"[All Fields] OR "rectal neoplasms"[All Fields] OR ("colon"[All Fields] AND "neoplasms"[All Fields]) OR ("rectal"[All Fields] AND "neoplasms"[All Fields]) OR ("colon"[All Fields] AND "cancer"[All Fields]) OR ("rectal"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields] OR "rectal cancer"[All Fields] OR "colorectal cancer"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields])) AND ("dairy"[All Fields] OR "dairy products"[All fields] OR ("dairy"[All fields] AND "products"[All fields])) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR	08/25/2016	1

	"Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))		
Nonfermented milk	(("colon neoplasms"[All Fields] OR "rectal neoplasms"[All Fields] OR ("colon"[All Fields] AND "neoplasms"[All Fields]) OR ("rectal"[All Fields] AND "neoplasms"[All Fields]) OR ("colon"[All Fields] AND "cancer"[All Fields]) OR ("rectal"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields] OR "rectal cancer"[All Fields] OR "colorectal cancer"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields])) AND ("milk"[All Fields]) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	1
Milk	(("colon neoplasms"[All Fields] OR "rectal neoplasms"[All Fields] OR ("colon"[All Fields] AND "neoplasms"[All Fields]) OR ("rectal"[All Fields] AND "neoplasms"[All Fields]) OR ("colon"[All Fields] AND "cancer"[All Fields]) OR ("rectal"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields] OR "rectal cancer"[All Fields] OR "colorectal cancer"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields])) AND ("milk"[All Fields]) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	1
Processed meat	(("colon neoplasms"[All Fields] OR "rectal neoplasms"[All Fields] OR ("colon"[All Fields] AND "neoplasms"[All Fields]) OR ("rectal"[All Fields] AND "neoplasms"[All Fields]) OR ("colon"[All Fields] AND "cancer"[All Fields]) OR ("rectal"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields] OR "rectal cancer"[All Fields] OR "colorectal cancer"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields])) AND ("processed meat"[All Fields] OR ("processed"[All fields] AND "meat"[All Fields])) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	2
Circulating vitamin D	(("colon neoplasms"[All Fields] OR "rectal neoplasms"[All Fields] OR ("colon"[All Fields] AND "neoplasms"[All Fields]) OR ("rectal"[All Fields] AND "neoplasms"[All Fields]) OR ("colon"[All Fields] AND "cancer"[All Fields]) OR ("rectal"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields] OR "rectal cancer"[All Fields] OR "colorectal cancer"[All	08/25/2016	10

	Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields])) AND ("vitamin D"[All Fields] OR "25OHD"[All Fields]) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))		
Whole grains	(("colon neoplasms"[All Fields] OR "rectal neoplasms"[All Fields] OR ("colon"[All Fields] AND "neoplasms"[All Fields]) OR ("rectal"[All Fields] AND "neoplasms"[All Fields]) OR ("colon"[All Fields] AND "cancer"[All Fields]) OR ("rectal"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields] OR "rectal cancer"[All Fields] OR "colorectal cancer"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields])) AND ("whole grains"[All Fields] OR "grains"[All Fields]) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms]))	08/25/2016	0
Stomach cancer			
Salt	(("stomach neoplasms"[All Fields] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("stomach"[All Fields] AND "cancer"[All Fields]) OR "stomach cancer"[All Fields] OR "gastric neoplasms"[All Fields] OR ("gastric"[All Fields] AND "neoplasms"[All Fields]) OR "gastric neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]) AND ("salt"[All Fields]) AND ("gene" [All fields] OR ("genetic variant" [All fields]) OR ("genetic"[All fields] AND "variant"[All Fields]) OR ("genetic variants" [All fields]) OR ("genetic"[All fields] AND "variants"[All Fields])) AND (Meta-Analysis[ptyp] OR "GWAS"[All fields] OR "Genome Wide Association Studies"[All fields] OR "Consortium"[All fields]) AND ("humans"[MeSH Terms])	08/25/2016	1

Supplemental Box 3 Criteria for inclusion in the GWAS Catalog and GWAS Central (adapted from the GWAS Catalog and GWAS Central)

GWAS Catalog is a manually curated database of all variant – trait associations with $P < 1.0 \times 10^{-5}$ identified through genome-wide association studies[1].

Eligibility criteria

Studies and associations are eligible for inclusion in the GWAS Catalog if they meet the following criteria:

- Include a primary GWAS analysis, defined as array-based genotyping and analysis of 100,000+ pre-QC SNPs selected to tag variation across the genome and without regard to gene content.
- GWAS data from published studies which are incorporated into new GWAS analyses are eligible, provided they meet the other criteria.
- Studies imputing sequencing data to genotyping arrays are eligible as long as the arrays include sufficient genome-wide coverage so that the post-imputation analysis meets the definition of a GWAS analysis, as described above.

Studies and associations are excluded if:

- The study was published in a language other than English.
- SNPs assayed or analyzed were limited to those in candidate genes.
- The study uses customized gene-based arrays without a clearly described GWAS backbone, including those selected to replicate published GWAS findings (e.g., Metabochip and Immunochip).
- Samples were assayed to measure somatic variation (e.g., in tumor samples).
- The study does not include any new GWAS data.

Individual SNP-trait associations identified in eligible studies are included in the Catalog if they meet the following criteria:

- Statistical significance (SNP-trait $P < 1.0 \times 10^{-5}$) in the overall (initial GWAS + replication) population.
- If a study does not report a combined *P* value, the *P* value and effect size from the largest sample size will be reported as long as the initial and replication samples each show an association of $P < 1.0 \times 10^{-5}$.
- If a study does not include a replication stage, significant SNPs from the discovery stage will be reported.
- SNP-trait associations that are described as previously known at the time of publication and are statistically significant in the GWAS sample, but are not attempted for replication, are reported.

The most significant SNP from each independent locus is extracted.

GWAS Central is an online database of summary level findings from genetic association studies, both large and small. Summary data are actively gathered from public domain projects and/or directly submitted by the researches, groups and consortia[2].

Eligibility criteria

- Case-control genome-wide and candidate association studies
-

Eligibility criteria for individual SNP-trait associations identified in eligible studies:

- No restrictions on *P* values are applied.
- Genetic variant should have valid dbSNP rs numbers and correct allele and strand information.
- No duplicated markers included

1 Welter, D. *et al.* The NHGRI GWAS Catalog, a curated resource of SNP-trait associations. *Nucleic Acids Res* **42**, D1001-1006, doi:10.1093/nar/gkt1229 (2014).
2 Beck, T., Hastings, R. K., Gollapudi, S., Free, R. C. & Brookes, A. J. GWAS Central: a comprehensive resource for the comparison and interrogation of genome-wide association studies. *Eur J Hum Genet* **22**, 949-952, doi:10.1038/ejhg.2013.274 (2014).

Supplemental Box 4 Search strategies and MeSH terms used to identify gene associations for the main types of cancer

Variant	Search strategy	Date	No. of hits
Breast cancer			
rs4880	("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND mnSOD[All Fields] OR rs4880[All Fields]	09/18/2016	235
rs17468277/rs1045485	("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("caspase 8"[MeSH Terms] OR "caspase 8"[All Fields] OR "casp8"[All Fields] OR rs17468277[All Fields] OR rs1045485[All Fields])	09/18/2016	668
rs2853826	("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ND3[All Fields] OR rs2853826[All Fields])	09/18/2016	14
rs698	("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancers"[All Fields]) OR "breast cancers"[All Fields]) AND ADH1C[All Fields] OR rs698[All Fields]	09/18/2016	45
rs2333227	("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancers"[All Fields]) OR "breast cancers"[All Fields]) AND MPO[All Fields] OR rs2333227[All Fields]	09/18/2016	52
Colorectal cancer			
rs1805087	("colonic neoplasms"[MeSH Terms] OR ("colonic"[All Fields] AND "neoplasms"[All Fields]) OR "colonic neoplasms"[All Fields] OR ("colon"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields]) AND ("colorectal neoplasms"[MeSH Terms] OR ("colorectal"[All Fields] AND "neoplasms"[All Fields]) OR "colorectal neoplasms"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields]) OR "colorectal cancer"[All Fields]) AND ("intestinal neoplasms"[MeSH Terms] OR ("intestinal"[All Fields] AND "neoplasms"[All Fields]) OR "intestinal neoplasms"[All Fields] OR ("bowel"[All Fields] AND "cancer"[All Fields]) OR "bowel cancer"[All Fields]) AND MTR[All Fields] OR rs1805087[All Fields]	09/18/2016	44

rs1042522	("colorectal neoplasms"[MeSH Terms] OR ("colorectal"[All Fields] AND "neoplasms"[All Fields]) OR "colorectal neoplasms"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields]) OR "colorectal cancer"[All Fields]) AND ("intestines"[MeSH Terms] OR "intestines"[All Fields] OR "bowel"[All Fields]) AND p53[All Fields] OR rs1042522[All Fields]	09/18/2016	718
rs16892766	("intestinal neoplasms"[MeSH Terms] OR ("intestinal"[All Fields] AND "neoplasms"[All Fields]) OR "intestinal neoplasms"[All Fields] OR ("bowel"[All Fields] AND "cancer"[All Fields]) OR "bowel cancer"[All Fields]) AND ("colonic neoplasms"[MeSH Terms] OR ("colonic"[All Fields] AND "neoplasms"[All Fields]) OR "colonic neoplasms"[All Fields] OR ("colon"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields]) AND ("colorectal neoplasms"[MeSH Terms] OR ("colorectal"[All Fields] AND "neoplasms"[All Fields]) OR "colorectal neoplasms"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields]) OR "colorectal cancer"[All Fields]) AND EIF3H[All Fields] OR rs16892766[All Fields]	09/18/2016	25
GSTM1 deletion	("intestinal neoplasms"[MeSH Terms] OR ("intestinal"[All Fields] AND "neoplasms"[All Fields]) OR "intestinal neoplasms"[All Fields] OR ("bowel"[All Fields] AND "cancer"[All Fields]) OR "bowel cancer"[All Fields]) AND ("colonic neoplasms"[MeSH Terms] OR ("colonic"[All Fields] AND "neoplasms"[All Fields]) OR "colonic neoplasms"[All Fields] OR ("colon"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields]) AND ("colorectal neoplasms"[MeSH Terms] OR ("colorectal"[All Fields] AND "neoplasms"[All Fields]) OR "colorectal neoplasms"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields]) OR "colorectal cancer"[All Fields]) AND GSTM1[All Fields]	08/25/2016	47
GSTT1 deletion	("intestinal neoplasms"[MeSH Terms] OR ("intestinal"[All Fields] AND "neoplasms"[All Fields]) OR "intestinal neoplasms"[All Fields] OR ("bowel"[All Fields] AND "cancer"[All Fields]) OR "bowel cancer"[All Fields]) AND ("colonic neoplasms"[MeSH Terms] OR ("colonic"[All Fields] AND "neoplasms"[All Fields]) OR "colonic neoplasms"[All Fields] OR ("colon"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields]) AND ("colorectal neoplasms"[MeSH Terms] OR ("colorectal"[All Fields] AND "neoplasms"[All Fields]) OR "colorectal neoplasms"[All Fields] OR ("colorectal"[All	08/25/2016	31

	Fields] AND "cancer"[All Fields]) OR "colorectal cancer"[All Fields]) AND GSTT1[All Fields]		
rs4143094	("intestinal neoplasms"[MeSH Terms] OR ("intestinal"[All Fields] AND "neoplasms"[All Fields]) OR "intestinal neoplasms"[All Fields] OR ("bowel"[All Fields] AND "cancer"[All Fields]) OR "bowel cancer"[All Fields]) AND ("colonic neoplasms"[MeSH Terms] OR ("colonic"[All Fields] AND "neoplasms"[All Fields]) OR "colonic neoplasms"[All Fields] OR ("colon"[All Fields] AND "cancer"[All Fields]) OR "colon cancer"[All Fields]) AND ("colorectal neoplasms"[MeSH Terms] OR ("colorectal"[All Fields] AND "neoplasms"[All Fields]) OR "colorectal neoplasms"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields]) OR "colorectal cancer"[All Fields]) AND GATA3[All Fields] OR rs4143094[All Fields]	08/25/2016	4

Supplemental Box 5 Score categories for an interaction between an environmental agent and a genetic variant based on the strength of evidence for a main effect of each of them (1 = strong, 2 = moderate, 3 = weak); Adapted from Boffetta et al. 2012

	Evidence for dietary main effect			
Evidence for genetic main effect	I (Strong)	II (Moderate)	III (Weak)	IV (Lack/evidence against)
Strong	1	2	2	3
Moderate	2	2	3	3
Weak	2	3	3	3
Lack/evidence against	3	3	3	3

Supplemental Box 6 Criteria for grading evidence in the Second Expert Review and Continuous Update Project from the WCRF (adapted from the Second Expert Review)

The grades that are used in the WCRF reports are the following: convincing, probable, limited — suggestive, limited — no conclusion, and substantial effect on risk unlikely.

Convincing

These criteria are for evidence strong enough to support a judgement of a convincing causal relationship, which justifies goals and recommendations designed to reduce the incidence of cancer. A convincing relationship should be robust enough to be highly unlikely to be modified in the foreseeable future as new evidence accumulates. All of the following were generally required:

• Evidence from more than one study type.

• Evidence from at least two independent cohort studies.

• No substantial unexplained heterogeneity within or between study types or in different populations relating to the presence or absence of an association, or direction of effect.

• Good quality studies to exclude with confidence the possibility that the observed association results from random or systematic error, including confounding, measurement error, and selection bias.

• Presence of a plausible biological gradient (dose response) in the association. Such a gradient need not be linear or even in the same direction across the different levels of exposure, so long as this can be explained plausibly.

• Strong and plausible experimental evidence, either from human studies or relevant animal models, that typical human exposures can lead to relevant cancer outcomes.

Probable

These criteria are for evidence strong enough to support a judgement of a probable causal relationship, which would generally justify goals and recommendations designed to reduce the incidence of cancer. All the following were generally required:

• Evidence from at least two independent cohort studies, or at least five case control studies.

• No substantial unexplained heterogeneity between or within study types in the presence or absence of an association, or direction of effect.

• Good quality studies to exclude with confidence the possibility that the observed association results from random or systematic error, including confounding, measurement error, and selection bias.

• Evidence for biological plausibility.

Limited — suggestive

These criteria are for evidence that is too limited to permit a probable or convincing causal judgement, but where there is evidence suggestive of a direction of effect. The evidence may have

methodological flaws, or be limited in amount, but shows a generally consistent direction of effect. This almost always does not justify recommendations designed to reduce the incidence of cancer. Any exceptions to this require special explicit justification. All the following were generally required:

• Evidence from at least two independent cohort studies or at least five case control studies.

• The direction of effect is generally consistent though some unexplained heterogeneity may be present.

• Evidence for biological plausibility.

Limited — no conclusion

Evidence is so limited that no firm conclusion can be made. This category represents an entry level, and is intended to allow any exposure for which there are sufficient data to warrant Panel consideration, but where insufficient evidence exists to permit a more definitive grading. This does not necessarily mean a limited quantity of evidence. A body of evidence for a particular exposure might be graded limited — no conclusion for a number of reasons. The evidence might be limited by the amount of evidence in terms of the number of studies available, by inconsistency of direction of effect, by poor quality of studies (for example, lack of adjustment for known confounders), or by any combination of these factors. When an exposure is graded limited — no conclusion, this does not necessarily indicate that the Panel has judged that there is evidence of no relationship. With further good quality research, any exposure graded in this way might in the future be shown to increase or decrease the risk of cancer. Where there is sufficient evidence to give confidence that an exposure is unlikely to have an effect on cancer risk, this exposure will be judged "substantial effect on risk unlikely." There are also many exposures for which there is such limited evidence that no judgement is possible.

Substantial effect on risk unlikely

Evidence is strong enough to support a judgement that a particular food, nutrition, or physical activity exposure is unlikely to have a substantial causal relation to a cancer outcome. The evidence should be robust enough to be unlikely to be modified in the foreseeable future as new evidence accumulates. All of the following were generally required:

• Evidence from more than one study type.

• Evidence from at least two independent cohort studies.

• Summary estimate of effect close to 1.0 for comparison of high versus low exposure categories.

• No substantial unexplained heterogeneity within or between study types or in different populations.

• Good quality studies to exclude, with confidence, the possibility that the absence of an observed association results from random or systematic error, including inadequate power, imprecision or error in exposure measurement, inadequate range of exposure, confounding, and selection bias.

• Absence of a demonstrable biological gradient (dose response).

• Absence of strong and plausible experimental evidence, either from human studies or from relevant animal models that typical human exposures lead to relevant cancer outcomes.

Factors that might misleadingly imply an absence of effect include imprecision of the exposure assessment, an insufficient range of exposure in the study population, and inadequate statistical power. Defects in these and other study design attributes might lead to a false conclusion of no effect.

The presence of a plausible, relevant biological mechanism does not necessarily rule out a judgement of "substantial effect on risk unlikely." But the presence of robust evidence from appropriate animal models or in humans that a specific mechanism exists, or that typical exposures can lead to cancer outcomes, argues against such a judgement.

Because of the uncertainty inherent in concluding that an exposure has no effect on risk, the criteria used to judge an exposure "substantial effect on risk unlikely" are roughly equivalent to the criteria used with at least a probable level of confidence. Conclusions of "'substantial effect on risk unlikely" with a lower confidence than this would not be helpful, and could overlap with judgements of limited — suggestive or limited — no conclusion.

Special upgrading factors

These are factors that form part of the assessment of the evidence that, when present, can upgrade the judgement reached. So an exposure that might be deemed a limited — suggestive causal factor in the absence, say, of a biological gradient, might be upgraded to probable in its presence. The application of these factors (listed below) requires judgement, and the ways in which these judgements affect the final conclusion in the matrix are stated.

• Presence of a plausible biological gradient (dose response) in the association. Such a gradient need not be linear or even in the same direction across the different levels of exposure, so long as this can be explained plausibly.

• A particularly large summary effect size (an odds ratio or relative risk of 2.0 or more, depending on the unit of exposure) after appropriate control for confounders.

• Evidence from randomized trials in humans.

• Evidence from appropriately controlled experiments demonstrating one or more plausible and specific mechanisms actually operating in humans.

• Robust and reproducible evidence from experimental studies in appropriate animal models showing that typical human exposures can lead to relevant cancer outcomes.