Supplementary Material

Non-Genetic Risk Factors for Parkinson's Disease: An Overview of 46 Systematic Reviews

Search strategy

EMBASE (3 June 2020)

1	exp Parkinson disease/cn, dm, dt, su, th [Congenital Disorder, Disease Management, Drug Therapy, Surgery, Therapy]	37739
2	systematic review.tw.	191823
3	meta-analysis.tw.	192694
4	2 or 3	306688
5	1 and 4	517
6	limit 5 to (human and yr="2011 -Current")	372

MEDLINE (3 June 2020)

1	exp Parkinson Disease/cn, dh, de, dt, mo, nu, pc, px, rt, rh, tu, th [Congenital, Diet Therapy, Drug Effects, Drug Therapy, Mortality, Nursing, Prevention & Control, Psychology, Radiotherapy, Rehabilitation, Therapeutic Use, Therapy]	29977
2	MEDLINE.tw.	96611
3	systematic review.tw.	118739
4	meta analysis.pt.	115325
5	2 or 3 or 4	230777
6	1 and 5	615
7	limit 6 to (humans and yr="2011 -Current")	409

PsycIFNO (3rd June, 2020)

1	exp Parkinson's Disease/	24713
2	meta-analysis.tw.	29989
3	search:.tw.	99948
4	2 or 3	121684
5	1 and 4	872
6	limit 5 to (human and yr="2011 -Current")	612

AMSTAR 2

1. Did the research questions and inclusion criteria for the review include the components of PICO?

For Yes:
- ☐ Population
- ☐ Intervention
- ☐ Comparator group
- ☐ Outcome

Optional (recommended)
- ☐ Timeframe for follow-up

- ☐ Yes
- ☐ No

2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

For Partial Yes:
The authors state that they had a written protocol or guide that included ALL the following:
- ☐ review question(s)
- ☐ a search strategy
- ☐ inclusion/exclusion criteria
- ☐ a risk of bias assessment

For Yes:
As for partial yes, plus the protocol should be registered and should also have specified:
- ☐ a meta-analysis/synthesis plan, if appropriate, *and*
- ☐ a plan for investigating causes of heterogeneity
- ☐ justification for any deviations from the protocol

- ☐ Yes
- ☐ Partial Yes
- ☐ No

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review should satisfy ONE of the following:
- ☐ *Explanation for* including only RCTs
- ☐ OR *Explanation for* including only NRSI
- ☐ OR *Explanation for* including both RCTs and NRSI

- ☐ Yes
- ☐ No

4. Did the review authors use a comprehensive literature search strategy?

For Partial Yes (all the following):
- ☐ searched at least 2 databases (relevant to research question)
- ☐ provided key word and/or search strategy
- ☐ justified publication restrictions (eg, language)

For Yes, should also have (all the following):
- ☐ searched the reference lists/bibliographies of included studies
- ☐ searched trial/study registries
- ☐ included/consulted content experts in the field
- ☐ where relevant, searched for grey literature
- ☐ conducted search within 24 months of completion of the review

- ☐ Yes
- ☐ Partial Yes
- ☐ No

5. Did the review authors perform study selection in duplicate?

For Yes, either ONE of the following:
- ☐ at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include
- ☐ OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 per cent), with the remainder selected by one reviewer

- ☐ Yes
- ☐ No

6. Did the review authors perform data extraction in duplicate?

For Yes, either ONE of the following:
- ☐ at least two reviewers achieved consensus on which data to extract

- ☐ Yes

from included studies

- ☐ OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 per cent), with the remainder extracted by one reviewer

☐ No

7. Did the review authors provide a list of excluded studies and justify the exclusions?

For Partial Yes:

- ☐ provided a list of all potentially relevant studies that were read in full text form but excluded from the review

For Yes, must also have:

- ☐ Justified the exclusion from the review of each potentially relevant study

☐ Yes
☐ Partial Yes
☐ No

8. Did the review authors describe the included studies in adequate detail?

For Partial Yes (ALL the following):

- ☐ described populations
- ☐ described interventions
- ☐ described comparators
- ☐ described outcomes
- ☐ described research designs

For Yes, should also have ALL the following:

- ☐ described population in detail
- ☐ described intervention and comparator in detail (including doses where relevant)
- ☐ described study's setting
- ☐ timeframe for follow-up

☐ Yes
☐ Partial Yes
☐ No

9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?

RCTs

For Partial Yes, must have assessed RoB from

- ☐ unconcealed allocation, *and*
- ☐ lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all cause mortality)

For Yes, must also have assessed RoB from:

- ☐ allocation sequence that was not truly random, *and*
- ☐ selection of the reported result from among multiple measurements or analyses of a specified outcome

☐ Yes
☐ Partial Yes
☐ No
☐ Includes only NRSI

NRSI

For Partial Yes, must have assessed RoB:

- ☐ from confounding, *and*
- ☐ from selection bias

For Yes, must also have assessed RoB:

- ☐ methods used to ascertain exposures and outcomes, *and*
- ☐ selection of the reported result from among multiple measurements or analyses of a specified outcome

☐ Yes
☐ Partial Yes
☐ No
☐ Includes only RCTs

10. Did the review authors report on the sources of funding for the studies included in the review?

For Yes

- ☐ Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies

☐ Yes
☐ No

11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?

RCTs

For Yes:

- ☐ The authors justified combining the data in a meta-analysis
  - ☐ AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present

☐ Yes
☐ No
☐ No meta-analysis

☐ AND investigated the causes of any heterogeneity	conducted
For NRSI For Yes: ☐ The authors justified combining the data in a meta-analysis ☐ AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present ☐ AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available ☐ AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review	☐ Yes ☐ No ☐ No meta-analysis conducted

12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

For Yes: ☐ included only low risk of bias RCTs ☐ OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect	☐ Yes ☐ No ☐ No meta-analysis conducted

13. Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?

For Yes: ☐ included only low risk of bias RCTs ☐ OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results	☐ Yes ☐ No

14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?

For Yes: ☐ There was no significant heterogeneity in the results ☐ OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review	☐ Yes ☐ No

15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?

For Yes: ☐ performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias	☐ Yes ☐ No ☐ No meta-analysis conducted

16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

For Yes: ☐ The authors reported no competing interests OR ☐ The authors described their funding sources and how they managed potential conflicts of interest	☐ Yes ☐ No

Supplementary Table 1. Summary results of included systematic reviews with meta-analysis which included not only prospective studies[a]

Author, year	Study design	Risk factor	No. of studies (No. of PD cases)	Pooled results (95% CI)	I^2 (%)	p (heterogeneity)
Habits						
Zhang et al. 2014 [40]	CC, Co	Alcohol intake (highest vs. lowest level)	32 (9994)	RR: 0.75 (0.66, 0.85)	52.3	NR
Noyce et al. 2012 [22]	CC, Co	Smoking (ever vs. never)	67 (17856)	RR: 0.64 (0.60, 0.69)	49.6	<0.01
Noyce et al. 2012 [22]	CC, Co	Smoking (current vs. never)	33 (13271)	RR: 0.44 (0.39, 0.50)	33.8	0.03
Noyce et al. 2012 [22]	CC, Co	Smoking (past vs. never)	31 (13405)	RR: 0.78 (0.71, 0.85)	52.9	<0.01
Noyce et al. 2012 [22]	CC, Co	Coffee (drinking vs. non-drinking)	19 (5801)	RR: 0.67 (0.58, 0.76)	42.9	0.03
Qi et al. 2014 [37]	CC , Co, NCC	Tea (highest vs. lowest category)	8 (1929)	RR: 0.63 (0.49, 0.81)	51.7	NR
Qi et al. 2014 [37]	CC, Co, NCC	Caffeine (highest vs. lowest category)	7 (2659)	RR: 0.55 (0.43, 0.71)	53.0	NR
Shen et al. 2015 [45]	CC	Outdoor work (with vs. without)	2 (4266)	OR: 0.72 (0.63, 0.81)	0.0	0.93

Environmental agents

Pezzoli et al. 2013 [32]	CC, Co	Pesticides (exposure vs. no exposure)	51 (NR)	OR: 1.76 (1.56, 2.04)	67.3	NR
Pezzoli et al. 2013 [32]	CC, Co	Herbicides (exposure vs. no exposure)	19 (NR)	OR: 1.33 (1.08, 1.65)	55.0	NR
Pezzoli et al. 2013 [32]	CC, Co	Insecticides (exposure vs. no exposure)	18 (NR)	OR: 1.53 (1.12, 2.08)	78.8	NR
Pezzoli et al. 2013 [32]	CC	Fungicides (exposure vs. no exposure)	12 (NR)	OR: 0.97 (0.69, 1.38)	35.4	NR
Pezzoli et al. 2013 [32]	CC	Rodenticides (exposure vs. no exposure)	4 (NR)	OR: 0.99 (0.53, 1.66)	0.0	NR
Pezzoli et al. 2013 [32]	CC, Co	Solvents (exposure vs. no exposure)	16 (NR)	OR: 1.35 (1.09, 1.67)	35.5	NR
Pezzoli et al. 2013 [32]	CC, Co	Organochlorines (exposure vs. no exposure)	5 (NR)	OR: 1.39 (0.77, 2.50)	60.6	NR
Pezzoli et al. 2013 [32]	CC, Co	Organophosphates (exposure vs. no exposure)	7 (NR)	OR: 1.27 (0.82, 1.98)	68.9	NR
Pezzoli et al. 2013 [32]	CC	Paraquat (exposure vs. no exposure)	7 (NR)	OR: 2.19 (1.48, 3.26)	51.1	NR
Pezzoli et al. 2013 [32]	CC	Maneb/mancozeb (exposure vs. no exposure)	4 (NR)	OR: 1.49 (0.85, 2.63)	13.8	NR

Pezzoli et al. 2013 [32]	CC	DDT (exposure vs. no exposure)	5 (NR)	OR: 1.03 (0.80, 1.34)	0.0	NR
Pezzoli et al. 2013 [32]	CC, Co	Farming (exposure vs. no exposure)	24 (NR)	OR: 1.30 (1.14, 1.49)	43.2	NR
Pezzoli et al. 2013 [32]	CC	Well water drinking (exposure vs. no exposure)	37 (NR)	OR: 1.34 (1.16, 1.55)	66.4	NR
Pezzoli et al. 2013 [32]	CC	Rural living (exposure vs. no exposure)	30 (NR)	OR: 1.32 (1.15, 1.51)	75.2	NR
Kasdagli et al. 2019 [14]	CC, Co	$PM_{2.5}$ (per 10 $\mu g/m^3$)	8 (205764)	RR: 1.06 (0.99, 1.14)	86.0	<0.01
Kasdagli et al. 2019 [14]	CC, Co	$PM_{2.5}$ (high vs. low exposure)	4 (3045)	RR: 1.05 (0.92, 1.21)	0.0	0.41
Kasdagli et al. 2019 [14]	CC, Co	PM_{10} (per 10 $\mu g/m^3$)	6 (27895)	RR: 0.99 (0.96, 1.01)	58.0	0.03
Kasdagli et al. 2019 [14]	CC, Co	PM_{10} (high vs. low exposure)	6 (15222)	RR: 1.00 (0.86, 1.18)	73.0	<0.01
Kasdagli et al. 2019 [14]	CC, Co	$PM_{2.5-10}$ (per 10 $\mu g/m^3$)	3 (14162)	RR: 0.97 (0.93, 1.01)	47.0	0.15
Kasdagli et al. 2019 [14]	CC, Co	$PM_{2.5-10}$ (high vs. low exposure)	3 (1494)	RR: 0.90 (0.74, 1.10)	0.0	0.96
Kasdagli et al. 2019 [14]	CC, Co	NO_2 (per 10 $\mu g/m^3$)	7 (68249)	RR: 1.06 (0.93, 1.20)	83.0	<0.01
Kasdagli et al. 2019 [14]	CC, Co	NO_2 (high vs. low exposure)	4 (4748)	RR: 1.06 (0.93, 1.20)	14.0	0.32

Kasdagli et al. 2019 [14]	CC, Co	NOx (per 10 μg/m^3)	4 (26977)	RR: 1.04 (0.98, 1.11)	81.0	<0.01
Kasdagli et al. 2019 [14]	CC, Co	NOx (high vs. low exposure)	3 (12613)	RR: 1.04 (0.98, 1.11)	0.0	0.55
Kasdagli et al. 2019 [14]	CC, Co	CO (per 1 mg/m^3)	3 (13873)	RR: 1.34 (0.85, 2.10)	82.0	<0.01
Kasdagli et al. 2019 [14]	CC, Co	CO (high vs. low exposure)	2 (12177)	RR: 1.04 (0.97, 1.11)	0.0	0.73
Kasdagli et al. 2019 [14]	CC, Co	O_3 (per 5 ppb)	5 (64026)	RR: 1.01 (1.00, 1.02)	0.0	0.69
Kasdagli et al. 2019 [14]	CC, Co	O_3 (high vs. low exposure)	2 (12177)	RR: 1.01 (0.81, 1.26)	77.0	0.04
Kasdagli et al. 2019 [14]	CC, Co	SO_2 (high vs. low exposure)	2 (12177)	RR: 0.98 (0.79, 1.21)	79..0	0.03
Huss et al. 2015 [42]	CC, Co	ELF-MF (higher vs. lowest exposure)	11 (63096)	RR: 1.05 (0.93, 1.13)	45.9	0.05
Huss et al. 2015 [42]	CC, Co	ELF-MF (highest-longest vs. lowest exposure)	9 (29257)	RR: 1.05 (0.92, 1.20)	14.8	0.31
Mortimer et al. 2012 [29]	CC, Co	Welding (exposure vs. no exposure)	9 (3001)	RR: 0.86 (0.80, 0.92)	0.0	0.82
Mortimer et al. 2012 [29]	CC, Co	Manganese (exposure vs. no exposure)	3 (1278)	RR: 0.76 (0.41, 1.42)	62.2	0.07
Palin et al. 2015 [44]	CC	Hydrocarbon (exposure vs. no exposure)	14 (4483)	OR: 1.36 (1.13, 1.63)	29.0	0.15

Zhou et al. 2019 [17]	CC	Sunlight (exposure vs. no exposure)	3 (295)	OR: 0.02 (0.00, 0.10)	78.8	<0.01
Dietary factors						
Takeda et al. 2014 [38]	CC, Co, CS	Vitamin A (retinol) intake (high vs. low level)	3 (624)	OR: 1.09 (0.84, 1.42)	0.0	0.42
Takeda et al. 2014 [38]	CC, Co, CS	α-carotene intake (high vs. low level)	3 (677)	OR: 0.78 (0.54, 1.14)	35.0	0.22
Takeda et al. 2014 [38]	CC, Co, CS	β-carotene intake (high vs. low level)	6 (1395)	OR: 0.91 (0.70, 1.20)	37.0	0.16
Takeda et al. 2014 [38]	CC, Co, CS	β-cryptoxanthin intake (high vs. low level)	3 (677)	OR: 0.96 (0.66, 1.40)	42.0	0.18
Takeda et al. 2014 [38]	CC, Co, CS	Lutein intake (high vs. low level)	4 (804)	OR: 1.49 (0.83, 2.68)	78.0	<0.01
Takeda et al. 2014 [38]	CC, Co, CS	Lycopene intake (high vs. low level)	3 (678)	OR: 1.03 (0.64, 1.65)	62.0	0.07
Cheng et al. 2015 [41]	CC, Co	Iron intake (moderate vs. low level)	NR (NR)	RR: 1.03 (0.83, 1.30)	49.6	0.11
Cheng et al. 2015 [41]	CC, Co	Iron intake (high vs. low level)	4 (2577)	RR: 1.08 (0.61, 1.93)	82.4	<0.01
Cheng et al. 2015 [41]	CC, Co	Zinc intake (moderate vs. low level)	NR (NR)	RR: 0.89 (0.36, 2.18)	92.2	<0.01

Cheng et al. 2015 [41]	CC, Co	Zinc intake (high vs. low level)	NR (NR)	RR: 0.69 (0.39, 1.23)	48.4	0.16
Cheng et al. 2015 [41]	CC, Co	Copper intake (moderate vs. low level)	NR (NR)	RR: 0.94 (0.47, 1.87)	86.9	<0.01
Cheng et al. 2015 [41]	CC, Co	Copper intake (high vs. low level)	NR (NR)	RR: 0.96 (0.65, 1.42)	0.0	0.32
Wang et al. 2015 [47]	CC, Co	Protein intake (highest vs. lowest level)	7 (1570)	RR: 1.13 (0.88, 1.44)	30.4	0.20
Wang et al. 2015 [47]	CC, Co	Carbohydrate intake (highest vs. lowest level)	8 (1482)	RR: 1.24 (1.05, 1.48)	0.0	0.45
Wang et al. 2015 [47]	CC, Co	Cholesterol intake (highest vs. lowest level)	7 (1713)	RR: 0.97 (0.75, 1.26)	62.4	0.01
Wang et al. 2015 [47]	CC, Co	Energy intake (highest vs. lowest level)	8 (1553)	RR: 1.39 (1.01, 1.92)	83.8	<0.01
Wang et al. 2015 [47]	CC, Co	Fat intake (highest vs. lowest level)	13 (2936)	RR: 0.88 (0.74, 1.06)	34.4	NR
Qu et al. 2019 [15]	CC, Co	Total fat intake (high vs. low level)	6 (4429)	OR: 1.07 (0.91, 1.25)	42.3	0.12
Medical history and comorbid diseases						
Jafari et al. 2013 [31]	CC, Co, NCC	Head trauma (with vs. without)	22 (18344)	OR: 1.57 (1.35, 1.83)	61.0	<0.01

Noyce et al. 2012 [22]	CC	Any relative have PD (with vs. without)	19 (3784)	RR: 4.45 (3.39, 5.83)	57.3	<0.01
Noyce et al. 2012 [22]	CC	Only first degree have PD (with vs. without)	26 (6321)	RR: 3.23 (2.65, 3.93)	52.2	<0.01
Noyce et al. 2012 [22]	CC	Family history of tremor (with vs. without)	10 (1756)	RR: 2.74 (2.10, 3.57)	0.0	0.74
Noyce et al. 2012 [22]	CC, Co	Prior mood disorder (with vs. without)	13 (16211)	RR: 1.86 (1.64, 2.11)	68.2	<0.01
Noyce et al. 2012 [22]	CC, Co	Diabetes (with vs. without)	13 (20025)	RR: 0.91 (0.72, 1.15)	70.9	<0.01
Lu et al. 2014 [21]	CC	Diabetes (with vs. without)	14 (21395)	OR: 0.75 (0.58, 0.98)	75.0	<0.01
Noyce et al. 2012 [22]	CC	Cancer (with vs. without)	7 (9693)	RR: 1.01 (0.94, 1.09)	50.4	0.06
Noyce et al. 2012 [22]	CC, Co	Hypertension (with vs. without)	12 (5993)	RR: 0.74 (0.61, 0.90)	76.5	<0.01
Noyce et al. 2012 [22]	CC	Gastric ulcer (with vs. without)	3 (406)	RR: 1.37 (0.36, 5.31)	81.0	0.05
Noyce et al. 2012 [22]	CC	General anaesthetic (with vs. without)	6 (1571)	RR: 1.10 (0.77, 1.58)	74.2	0.02

Noyce et al. 2012 [22]	CC, Co	Oophorectomy (with vs. without)	5 (775)	RR: 0.76 (0.52, 1.13)	58.8	0.05
Ungprasert et al. 2015 [46]	CC, Co	Gout (with vs. without)	5 (235299)	RR: 0.93 (0.79, 1.09)	87.0	<0.01
Adams et al. 2015 [49]	CC, Co	Premorbid constipation (with vs. without)	9 (11242)	OR: 2.27 (2.09, 2.46)	18.1	0.28
Adams et al. 2015 [49]	CC, Co	Constipation of duration ≥10 years (with vs. without)	4 (8567)	OR: 2.13 (1.27, 2.56)	0.0	0.76
Lv et al. 2017 [55]	CC, Co	Age at menarche (highest vs. lowest category)	7 (2134)	RR: 1.03 (0.84, 1.26)	25.5	0.23
Lv et al. 2017 [55]	CC, Co	Age at menopause (highest vs. lowest category)	8 (2206)	RR: 0.98 (0.75, 1.29)	49.8	0.05
Lv et al. 2017 [55]	CC, Co	Fertile lifespan (highest vs. lowest category)	5 (1379)	RR: 0.98 (0.77, 1.25)	8.0	0.36
Lv et al. 2017 [55]	CC, Co	Parity (highest vs. lowest category)	8 (2211)	RR: 0.99 (0.79, 1.25)	42.8	0.09
Lv et al. 2017 [55]	CC, Co	Type of menopause (surgical vs. natural)	7 (1857)	RR: 0.93 (0.68, 1.29)	74.8	<0.01
Milani et al. 2017 [56]	CC	Bullous pemphigoid (with vs. without)	10 (749)	OR: 3.06 (1.97, 4.77)	0.0	>0.45

Wang et al. 2018 [61]	CC, Co	Depression (with vs. without)	11 (NR)	OR: 2.20 (1.87, 2.58)	35.1	0.19
Zhou et al. 2019 [16]	CC, Co	Latent infection of T. gondii (with vs. without)	7 (448)	OR: 1.17 (0.86, 1.58)	40.5	0.11
Zhou et al. 2019 [16]	CC, Co	Acute infection of T. gondii (with vs. without)	3 (221)	OR: 1.13 (0.30, 4.35)	0.0	0.49
Faustino et al. 2020 [19]	Co, CS	Bipolar disorder (with vs. without)	6 (NR)	OR: 3.35 (2.00, 5.60)	92.0	<0.01
Wang et al. 2020 [20]	CC, Co	Infection of HP (with vs. without)	9 (NR)	OR: 1.65 (1.43, 1.92)	0.7	0.43
Wang et al. 2020 [20]	CC, Co	Infection of HCV (with vs. without)	7(NR)	OR: 1.20 (1.01, 1.41)	79.0	<0.01
Wang et al. 2020 [20]	CC, Co	Infection of malassezia (with vs. without)	2 (NR)	OR: 1.69 (1.37, 2.10)	0.0	0.88
Wang et al. 2020 [20]	CC, Co	Infection of pneumoniae (with vs. without)	2 (NR)	OR: 1.60 (1.02, 2.49)	17.5	0.27
Wang et al. 2020 [20]	CC, Co	Infection of measles (with vs. without)	3 (NR)	OR: 0.79 (0.53, 1.19)	60.2	0.08
Wang et al. 2020 [20]	CC, Co	Infection of influenza virus (with vs. without)	4 (NR)	OR: 1.95 (0.77, 4.94)	93.1	<0.01
Wang et al. 2020 [20]	CC, Co	Infection of herpes virus (with vs. without)	4 (NR)	OR: 1.52 (0.61, 3.78)	77.1	0.04

Wang et al. 2020 [20]	CC, Co	Infection of HBV (with vs. without)	6 (NR)	OR: 0.96 (0.72, 1.29)	90.5	<0.01
Wang et al. 2020 [20]	CC, Co	Infection of scarlet fever (with vs. without)	2 (NR)	OR: 2.08 (0.34, 12.91)	79.0	0.03
Wang et al. 2020 [20]	CC, Co	Infection of mumps virus (with vs. without)	3 (NR)	OR: 1.66 (0.57, 4.83)	94.6	<0.01
Wang et al. 2020 [20]	CC, Co	Infection of chicken pox (with vs. without)	3 (NR)	OR: 0.76 (0.61, 0.95)	0.0	0.99
Wang et al. 2020 [20]	CC, Co	Infection of pertussis (with vs. without)	2 (NR)	OR: 2.97 (0.19, 46.11)	85.1	0.01
Wang et al. 2020 [20]	CC, Co	Infection of German measles (with vs. without)	2 (NR)	OR: 1.31 (0.82, 2.12)	0.0	0.68
Drugs						
Lv et al. 2017 [55]	CC, Co	Oral contraceptives (ever vs. never use)	7 (1997)	RR: 1.00 (0.79, 1.28)	61.8	0.02
Lang et al. 2015 [43]	CC, Co	Calcium channel blocker (use vs. no use)	5 (6709)	RR: 0.76 (0.68, 0.84)	10.7	0.35
Wang et al. 2014 [39]	CC, Co	HRT (use vs. no use)	14 (2944)	RR: 1.00 (0.84, 1.20)	50.3	0.02
Noyce et al. 2012 [22]	CC, Co	NSAIDs (use vs. no use)	9 (9064)	RR: 0.83 (0.72, 0.95)	50.9	0.04

Noyce et al. 2012 [22]	CC, Co	Aspirin (use vs. no use)	6 (2781)	RR: 1.11 (0.93, 1.32)	55.1	0.05
Noyce et al. 2012 [22]	CC, Co	Acetaminophen/Paracetamol (use vs. no use)	2 (1671)	RR: 1.02 (0.76, 1.36)	74.5	0.05
Noyce et al. 2012 [22]	CC	Beta blocker (use vs. no use)	3 (5774)	RR: 1.28 (1.19, 1.39)	0.0	0.97
Bykov et al. 2017 [53]	CC, Co	Statin use[b] (use vs. no use)	6 (NR)	RR: 0.75 (0.60, 0.92)	92.0	<0.01
Bykov et al. 2017 [53]	CC, Co	Statin use[c] (use vs. no use)	4 (NR)	RR: 0.91 (0.68, 1.22)	75.0	<0.01
Bai et al. 2016 [50]	CC, Co	Statin use (use vs. no use)	11 (21011)	RR: 0.81 (0.71, 0.92)	64.5	<0.01
Bai et al. 2016 [50]	CC, Co	Long-term statin use[d] (yes vs. no)	4 (3711)	RR: 0.77 (0.56, 1.07)	64.2	0.04
Biomarkers						
Shen et al. 2015 [45]	CC, Co, CS	Serum vitamin D level (deficient and insufficient vs. normal level)	6 (966)	OR: 1.50 (1.31, 1.71)	55.9	0.05
Luo et al. 2018 [60]	CC, Co, CS	Serum vitamin D level[e] (PD patient vs. control)	11 (2346)	WMD: −3.96 (−5.00, −2.92)	82.6	<0.01

Luo et al. 2018 [60]	CC, Co, CS	Serum vitamin D level (insufficient vs. normal level)	6 (1613)	OR: 1.73 (1.48, 2.03)	31.0	0.20
Luo et al. 2018 [60]	CC, Co, CS	Serum vitamin D level (deficient vs. normal level)	10 (1879)	OR: 2.08 (1.35, 3.19)	84.7	<0.01
Gudala et al. 2013 [30]	CC, Co	Serum cholesterol (highest to lowest level)	8 (5488)	RR: 0.87 (0.67, 1.13)	70.3	<0.01
Shen et al. 2013 [34]	CC	Serum uric acid levels[e] (PD patient vs. control)	6 (1217)	SMD: -0.52 (-0.72, -0.31)	75.6	<0.01
Sheng et al. 2016 [52]	CC, Co	LDL-C level (high vs. normal baseline level)	3 (2336)	RR: 0.58 (0.31, 1.07)	71.0	<0.03
Mostile et al. 2017 [57]	CC	Serum iron level[e] (PD patient vs. control)	23 (1526)	SMD: -0.05 (-0.30, -0.20)	91.4	<0.01
Jin et al. 2018 [59]	CC	Serum Mg level[e] (PD patient vs. control)	12 (848)	SMD: 1.09 (0.52, 1.66)	95.6	<0.01
Jin et al. 2018 [59]	CC	Peripheral blood Mg level[e] (PD patient vs. control)	16 (1023)	SMD: 0.64 (0.10, 1.19)	96.2	<0.01
Jin et al. 2018 [59]	CC	CSF Mg level[e] (PD patient vs. control)	5 (180)	SMD: 0.55 (0.21, 0.88)	50.4	0.09
Jiang et al' 2019 [62]	CC	Serum BDNF level[e] (PD patient vs. control)	9 (838)	SMD: -1.03 (-1.83, -0.23)	97.5	<0.01
Qiu et al. 2019 [63]	CC	CRP in blood Level[e] (PD patient vs. control)	20 (2360)	SMD: 1.07 (0.72, 1.45)	96.2	<0.01

Qiu et al. 2019 [63]	CC	CRP in serum Level[e] (PD patient vs. control)	12 (1574)	SMD: 1.12 (0.62, 1.61)	96.7	<0.01
Qiu et al. 2019 [63]	CC	CRP in CSF Level[e] (PD patient vs. control)	4 (306)	SMD: 1.13 (0.13, 2.12)	95.2	<0.01

BDNF, brain-derived neurotrophic factor; CC, case-control study; CI, confidence interval; Co, cohort study; CRP, C-reactive protein; CS, cross-sectional study; CSF, central nervous system; DDT, dichloro-diphenyl-trichloroethane; ELF-MF, extremely-low frequency magnetic fields; HBV, hepatitis B virus; HCV, hepatitis C virus; HP, Helicobacter pylori; HRT, hormone replacement therapy; LDL-C, low-density lipoprotein cholesterol; MD, mean difference; NCC, nested case control; NR, not reported; NSAIDs, nonsteroidal anti-inflammatory drugs; OR, odds ratio; PD, Parkinson's disease; RR, relative risk; SMD, standardized mean difference; WMD, weighted mean difference.

[a] Prospective study including cohort study, nested case control study.

[b] Statin use c and PD in studies that did not adjust for cholesterol.

[c] Statin use d and PD in studies that adjusted for cholesterol

[d] The definitions of long-term statin use were at least 4 years, 5 years, or 6 years, respectively.

[e] Continuous variable.

Supplementary Table 2. Subgroup analyses of included systematic reviews with meta-analyses

Author, Year	Subgroup	Primary studies, n	Pooled results (95% CI)	I^2	p (heterogeneity)
Habits					
Zhang et al. 2014 [40]	**Alcohol intake (highest vs. lowest level)**				
	Study design				
	Prospective studies	8	RR: 0.86 (0.75, 1.00)	14.5	NR
	Matched case-control studies	17	RR: 0.72 (0.61, 0.86)	50.5	NR
	Unmatched case-control studies	7	RR: 0.67 (0.46, 1.01)	68.7	NR
	Quality of studies (NOS)				
	7 to 8 stars	NR	RR: 0.85 (0.76, 0.96)	0.6	NR
	6 stars	NR	RR: 0.73 (0.57, 0.93)	69.5	NR
	4 to 5 stars	NR	RR: 0.62 (0.49, 0.78)	44.2	NR
	Region				
	Europe	NR	RR: 0.60 (0.46, 0.77)	71.8	NR
	The United States	NR	RR: 0.86 (0.77, 0.96)	0.0	NR
	Asia	NR	RR: 0.89 (0.69, 1.16)	43.6	NR
Jiménez et al. 2019 [13]	**Alcohol intake (never vs. ever level)**				
	Study design				
	Case control studies	26	OR: 1.33 (1.20, 1.48)	NR	NR
	Cohort studies	5	OR: 1.04 (0.98, 1.22)	NR	NR
	Study design and gender				
	Man in case-control studies	6	OR: 1.36 (1.06, 1.75)	NR	NR
	Woman in case-control studies	6	OR: 1.21 (0.98, 1.49)	NR	NR
	Man in cohort studies	2	OR: 1.05 (0.68, 1.63)	NR	NR
	Woman in cohort studies	2	OR: 1.16 (0.96, 1.40)	NR	NR

Jiménez et al. 2019 [13]	**Alcohol intake (heavy + moderate vs. lack of exposure + light)**				
	Study design				
	Case-control studies	19	OR: 0.74 (0.64, 0.85)	NR	NR
	Cohort studies	4	OR: 1.00 (0.90, 1.10)	NR	NR
	Study design and gender				
	Man in case-control studies	4	OR: 0.44 (0.24, 0.80)	NR	NR
	Woman in case-control studies	3	OR: 0.69 (0.38, 1.26)	NR	NR
	Man in cohort studies	2	OR: 0.75 (0.62, 0.91)	NR	NR
	Woman in cohort studies	2	OR: 1.07 (0.83, 1.39)	NR	NR
Noyce et al. 2012 [22]	**Smoking (ever vs. never)**				
	Study design				
	Case-control	61	RR: 0.64 (0.60, 0.69)	48.4	<0.01
	Cohort	6	RR: 0.44 (0.39, 0.50)	63.8	0.02
Noyce et al. 2012 [22]	**Smoking (current vs. never)**				
	Study design				
	Case-control	26	RR: 0.46 (0.41, 0.50)	31.0	0.07
	Cohort	7	RR: 0.47 (0.40, 0.56)	49.8	0.06
Noyce et al. 2012 [22]	**Smoking (past vs. never)**				
	Study design				
	Case-control	26	RR: 0.80 (0.72, 0.89)	53.2	<0.01
	Cohort	5	RR: 0.75 (0.69, 0.81)	55.1	0.06
Noyce et al. 2012 [22]	**Coffee drinking (drinking vs. non-drinking)**				
	Study design				
	Case-control	13	RR: 0.68 (0.57, 0.82)	47.6	0.03

	Cohort	6	RR: 0.66 (0.57, 0.77)	29.0	0.03
Qi et al. 2014 [37]	**Tea drinking (highest vs. lowest consumption)**				
	Study design				
	Prospective study	4	RR: 0.64 (0.50, 0.82)	16.2	NR
	Case–control study	4	RR: 0.61 (0.38, 1.00)	72.5	NR
	Gender				
	Men	NR	RR: 0.64 (0.43, 0.95)	0.0	NR
	Women	NR	RR: 0.68 (0.44, 1.06)	29.7	NR
	Region				
	USA	4	RR: 0.85 (0.68, 1.07)	47.1	NR
	Asia	2	RR: 0.60 (0.45, 0.79)	38.1	NR
Qi et al. 2014 [37]	**Caffeine (highest vs. lowest consumption)**				
	Study design				
	Prospective study	4	RR: 0.54 (0.34, 0.84)	59.7	NR
	Case–control study	3	RR: 0.55 (0.44, 0.69)	27.2	NR
	Gender				
	Men	NR	RR: 0.57 (0.33, 0.98)	70.7	NR
	Women	NR	RR: 0.64 (0.46, 0.89)	0.0	NR
	Region				
	USA	3	RR: 0.45 (0.21, 0.96)	69.2	NR
	Asia	3	RR: 0.50 (0.40, 0.64)	0.0	NR
Fang et al. 2018 [58]	**Total physical activity (highest vs. lowest category)**				
	Gender				
	Male	5	RR: 0.68 (0.56, 0.82)	0.0	NR
	Female	4	RR: 0.91 (0.72, 1.14)	0.0	NR
	Location				
	US	6	RR: 0.82 (0.69, 0.98)	0.0	NR

	Europe	2	RR: 0.70 (0.52, 0.94)	0.0	NR
	Follow-up				
	>10 years	4	RR: 0.77 (0.59, 1.01)	26.3	NR
	≤ 10 years	3	RR: 0.82 (0.66, 1.01)	0.0	NR
	Participants				
	>50000	4	RR: 0.74 (0.61, 0.90)	0.0	NR
	≤50000	4	RR: 0.87 (0.68, 1.11)	0.0	NR
	Study quality(NOS)				
	Score>8	3	RR: 0.86 (0.61, 1.20)	31.1	NR
	Score≤8	5	RR: 0.77 (0.64, 0.92)	0.0	NR
Fang et al. 2018 [58]	**Physical activity (with vs. without)**				
	Type of physical activity				
	Light physical activity	3	RR: 0.86 (0.60, 1.23)	37.5	NR
	Moderate to vigorous physical activity	7	RR: 0.71 (0.58, 0.87)	30.7	NR
Exposure to toxic environmental agents					
Pezzoli et al. 2013 [32]	**Pesticides (exposure vs. no exposure)[a]**				
	NOS score				
	<7	33	OR: 1.88 (1.52, 2.32)	72.2	NR
	≥7	18	OR: 1.58 (1.34, 1.86)	45.1	NR
Pezzoli et al. 2013 [32]	**Herbicides (exposure vs. no exposure) [a]**				
	NOS score				
	<7	9	OR: 1.44 (0.90, 2.30)	68.0	NR
	≥7	10	OR: 1.36 (1.11, 1.66)	33.3	NR
Pezzoli et al. 2013 [32]	**Insecticides (exposure vs. no exposure) [a]**				
	NOS score				

	<7	8	OR: 2.03 (1.06, 3.89)	79.7	NR
	≥7	80	OR: 1.31 (0.92, 1.86)	79.2	NR
Pezzoli et al. 2013 [32]	**Fungicides (exposure vs. no exposure)** [a]				
	NOS score				
	<7	7	OR: 1.12 (0.56, 1.26)	0.0	NR
	≥7	5	OR: 0.94 (0.61, 1.43)	54.2	NR
Pezzoli et al. 2013 [32]	**Solvents (exposure vs. no exposure)** [a]				
	NOS score				
	<7	10	OR: 1.26 (0.92, 1.73)	44.9	NR
	≥7	6	OR: 1.58 (1.23, 2.04)	0.0	NR
Pezzoli et al. 2013 [32]	**Paraquat (exposure vs. no exposure)** [a]				
	NOS score				
	<7	2	OR: 3.22 (2.42, 4.30)	0	NR
	≥7	5	OR: 1.72 (1.28, 2.32)	0	NR
Pezzoli et al. 2013 [32]	**Farming (exposure vs. no exposure)** [a]				
	NOS score				
	<7	19	OR: 1.43 (1.18, 1.72)	42.7	NR
	≥7	15	OR: 1.18 (0.98, 1.43)	44.0	NR
Pezzoli et al. 2013 [32]	**Well water drinking (exposure vs. no exposure)** [a]				
	NOS score				
	<7	27	OR: 1.53 (1.27, 1.84)	67.5	NR
	≥7	10	OR: 1.00 (0.85, 1.17)	17.2	NR
Pezzoli et al. 2013 [32]	**Rural living (exposure vs. no exposure)** [a]				
	NOS score				

	<7	26	OR: 1.35 (1.16, 1.58)	76.7	NR
	≥7	4	OR: 1.14 (0.81, 1.62)	62.0	NR
Kasdagli et al. 2019 [14]	**$PM_{2.5}$ (per 10 µg/m^3)**				
	Study design				
	Cohort	6	RR: 1.06 (0.98, 1.15)	91.0	<0.01
	Case-control	3	RR: 1.19 (0.71, 1.97)	29.0	0.25
Kasdagli et al. 2019 [14]	**NO_2 (Per 10 µg/m^3)**				
	Study design				
	Cohort	3	RR: 1.00 (0.97, 1.03)	92.0	<0.01
	Case-control	5	RR: 1.07 (0.97, 1.08)	71.0	<0.01
Huss et al. 2015 [42]	**ELF-MF (higher to lowest exposure)**				
	The type of exposure assessment				
	Occupational records	4	RR: 1.07 (0.87, 1.33)	47.2	0.13
	Censuses	2	RR: 1.04 (0.99, 1.09)	0.0	0.33
	Interviews/questionnaires	2	RR: 0.98 (0.72, 1.32)	76.4	0.04
	Death certificates	3	RR: 1.06 (0.93, 1.20)	65.9	0.05
Huss et al. 2015 [42]	**ELF-MF (highest-longest to lowest exposure)**				
	The type of exposure assessment				
	Occupational records	4	RR: 1.07 (0.75, 1.52)	36.9	0.19
	Censuses	2	RR: 1.05 (0.92, 1.20)	0.0	0.94
	Interviews/questionnaires	2	RR: 0.91 (0.72, 1.16)	0.0	0.90
	Death certificates	1	RR: 1.50 (1.02, 2.20)	NA	NA
Mortimer et al. 2012 [29]	**Welding (exposure vs. no exposure)**				
	Study design				
	Cohort	2	RR: 0.91 (0.84, 0.99)	NR	NR

	Case-control	6	RR: 0.82 (0.67, 1.01)	NR	NR
	Mortality studies	1	RR: 0.87 (0.78, 0.97)	NA	NA
Dietary factors					
Takeda et al. 2014 [38]	**Vitamin A (high vs. low level of intake)**				
	Study design				
	Case-control studies	2	OR: 0.92 (0.53, 1.59)	17.0	0.27
	Cohort studies	1	RR: 1.16 (0.85, 1.58)	NA	NA
Takeda et al. 2014 [38]	**α-carotene (high vs. low level of intake)**				
	Study design				
	Case-control studies	1	OR: 0.61 (0.36, 1.03)	NA	NA
	Cohort studies	1	RR: 0.91 (0.64, 1.29)	NA	NA
Takeda et al. 2014 [38]	**β-carotene (high vs. low level of intake)**				
	Study design				
	Case-control studies	5	OR: 0.92 (0.64, 1.33)	50.0.	<0.01
	Cohort studies	1	RR: 0.90 (0.63, 1.29)	NA	NA
Takeda et al. 2014 [38]	**β-cryptoxanthin (high vs. low level of intake)**				
	Study design				
	Case-control studies	2	OR: 1.22 (0.80, 1.85)	0.0	0.72
	Cohort studies	1	RR: 0.74 (0.53, 1.03)	NA	NA
Takeda et al. 2014 [38]	**Lutein (high vs. low level of intake)**				
	Study design				
	Case-control studies	3	OR: 1.85 (1.19, 2.87)	27.0	0.26
	Cohort studies	1	RR: 0.78 (0.56, 1.09)	NA	NA
Takeda et al. 2014 [38]	**Lycopene (high vs. low level of intake)**				

	Study design				
	Case-control studies	2	OR: 1.13 (0.50, 2.55)	66.0	0.08
	Cohort studies	1	RR: 0.87 (0.63, 1.20)	NA	NA
Jiang et al. 2014 [36]	**Dairy food intake (highest vs. lowest category)**				
	Gender				
	Men	4	RR: 1.66 (1.29, 2.14)	0.0	0.60
	Women	3	RR: 1.15 (0.85, 1.56)	0.0	0.62
	Region				
	Europe	2	RR: 1.29 (1.07, 1.56)	0.0	NR
	USA	3	RR: 1.56 (1.19, 2.05)	27.4	NR
	Types of dairy food				
	Butter	2	RR: 0.76 (0.51, 1.13)	0.0	0.78
	Milk	5	RR: 1.45 (1.23, 1.73)	16.1	0.31
	Cheese	4	RR: 1.26 (0.99, 1.60)	29.2	0.23
	Yogurt	3	RR: 0.95 (0.76, 1.20)	14.6	0.31
Cheng et al. 2015 [41]	**Iron (moderate vs. low level of intake)**				
	Region				
	Western population	NR	RR: 1.10 (0.95, 1.28)	0.0	0.57
	Gender				
	Male	NR	RR: 1.07 (0.72, 1.59)	75.4	0.04
	Female	NR	RR: 1.16 (0.95, 1.41)	0.0	0.92
Cheng et al. 2015 [41]	**Iron (high vs. low level of intake)**				
	Region				
	Western population	NR	RR: 1.47 (1.17, 1.85)	0.0	0.46
	Gender				
	Male	NR	RR: 1.43 (1.01, 2.01)	37.4	0.21
	Female	NR	RR: 1.22 (0.89, 1.66)	0.0	0.77

Wang et al. 2015 [47]	**Protein intake (highest vs. lowest level of intake)**				
	Study design				
	Case-control	3	RR: 0.93 (0.51, 1.68)	16.0	NR
	Cohort	4	RR: 1.18 (0.89, 1.56)	44.9	NR
Wang et al. 2015 [47]	**Carbohydrate intake (highest vs. lowest level of intake)**				
	Study design				
	Case-control	4	RR: 1.62 (0.95, 2.76)	20.1	NR
	Cohort	4	RR: 1.19 (0.99, 1.43)	0.0	NR
Wang et al. 2015 [47]	**Energy intake (highest vs. lowest level of intake)**				
	Study design				
	Case-control	4	RR: 2.03 (0.81, 5.10)	89.8	NR
	Cohort	4	RR: 0.99 (0.92, 1.06)	3.8	NR
Wang et al. 2015 [47]	**Cholesterol intake (highest vs. lowest level of intake)**				
	Study design				
	Case-control	4	RR: 1.17 (0.61, 2.22)	78.8	NR
	Cohort	3	RR: 0.87 (0.74, 1.03)	0.0	NR
Wang et al. 2015 [47]	**Fat intake (highest vs. lowest level of intake)**				
	Study design				
	Case-control	7	RR: 1.06 (0.75, 1.52)	46.7	0.08
	Cohort	6	RR: 0.80 (0.68, 0.95)	3.0	0.40
Qu et al. 2019 [15]	**Fat intake (high vs. low level of intake)**				
	Fat subtypes				
	Saturated fatty acids	5	OR: 1.01 (0.87, 1.18)	0.0	0.62

	MUFA	5	OR: 1.06 (0.91, 1.23)	0.0	0.45
	PUFA	4	OR: 1.03 (0.88, 1.20)	73.5	0.01
	n-6 PUFA	3	OR: 1.15 (0.96, 1.36)	56.5	0.10
	Linoleic acid,	3	OR: 1.11 (0.94, 1.32)	65.9	0.06
	Arachidonic acid	2	OR: 1.15 (0.97, 1.37)	79.9	0.03
	n-3 PUFA	3	OR: 0.88 (0.73, 1.05)	62.2	0.07
	α-linolenic acid	3	OR: 0.86 (0.72, 1.02)	64.5	0.06
	n-3 to n-6 PUFA ratio	2	OR: 0.89 (0.75, 1.06)	0.0	0.46
	Cholesterol	3	OR: 1.09 (0.92, 1.29)	83.6	<0.01
Medical history and comorbid diseases					
Noyce et al. 2012 [22]	**Prior mood disorder (with vs. without)**				
	Study design				
	Case-control	11	RR: 1.90 (1.62, 2.22)	58.3	<0.01
	Cohort	2	RR: 1.79 (1.72, 1.87)	0.0	0.35
Noyce et al. 2012 [22]	**Diabetes (with vs. without)**				
	Study design				
	Case-control	9	RR: 0.72 (0.54, 0.97)	64.9	<0.01
	Cohort	4	RR: 1.31 (1.10, 1.57)	34.7	0.20
Lu et al. 2014 [21]	**Diabetes (with vs. without)**				
	Gender				
	Male	5	OR: 0.71 (0.40, 1.23)	74.0	<0.01
	Female	5	OR: 0.79 (0.41, 1.49)	68.0	0.01
	Geographic location				
	Europe	7	OR: 0.94 (0.69, 1.28)	77.0	<0.01
	North America (U.S.)	4	OR: 0.61 (0.45, 0.83)	0.0	0.85
	Asia	3	OR: 0.54 (0.23, 1.27)	68.0	0.04

	Source of the control				
	Hospital setting	7	OR: 0.88 (0.62, 1.25)	72.0	<0.01
	General population	7	OR: 0.63 (0.40, 0.99)	75.0	<0.01
	DM duration				
	<10 years	2	OR: 0.90 (0.63, 1.30)	0.0	0.34
	≥10 years	2	OR: 1.27 (0.79, 2.05)	0.0	0.59
	Antidiabetes drug				
	Insulin prescription	2	OR: 1.18 (0.74, 1.89)	0.0	0.93
	Smoking				
	Ever	2	OR: 0.67 (0.40, 1.13)	0.0	0.33
	Never	2	OR: 0.37 (0.21, 0.66)	0.0	0.97
	DM assessment				
	Medical record	6	OR: 0.92 (0.70, 1.21)	72.0	<0.01
	Questionnaire	7	OR: 0.57 (0.39, 0.85)	54.0	0.04
Noyce et al. 2012 [22]	**Hypertension (with vs. without)**				
	Study design				
	Case-control	10	RR: 0.69 (0.55, 0.87)	77.7	<0.01
	Cohort	2	RR: 0.98 (0.82, 1.17)	76.5	<0.01
Noyce et al. 2012 [22]	**Oophorectomy (with vs. without)**				
	Study design				
	Case-control	4	RR: 0.77 (0.42, 1.43)	69.1	0.02
	Cohort	1	RR: 0.75 (0.56, 1.00)	NA	NA
Ungprasert et al. 2015 [46]	**Gout (with vs. without)**				
	Study design				
	Cohort studies	2	RR: 0.89 (0.57, 1.39)	96.0	<0.01
	Case-control studies	3	RR: 0.97 (0.83, 1.13)	55.0	0.11
	Gender				

	Male	NR	RR: 0.89 (0.57, 1.39)	NR	NR
	Female	NR	RR: 0.95 (0.76, 1.19)	NR	NR
Lv et al. 2017 [55]	**Age at menarche (highest vs. lowest category)**				
	Study design				
	Case-control	5	RR: 1.05 (0.76, 1.45)	46.7	0.11
	Cohort	2	RR: 0.98 (0.75, 1.28)	0.0	0.55
	Adjusted for age				
	Yes	4	RR: 1.11 (0.79, 1.56)	46.8	0.13
	No	3	RR: 0.97 (0.75, 1.24)	1.7	0.36
	Adjusted for caffeine intake				
	Yes	3	RR: 1.05 (0.58, 1.87)	74.5	0.02
	No	4	RR: 1.02 (0.82, 1.28)	0.0	0.98
	Adjusted for smoking				
	Yes	6	RR: 1.03 (0.80, 1.33)	37.9	0.15
	No	1	RR: 1.02 (0.70, 1.48)	NA	NA
Lv et al. 2017 [55]	**Age at menopause (highest vs. lowest category)**	8	RR: 0.98 (0.75, 1.29)	49.8	0.05
	Study design				
	Case-control	6	RR: 1.00 (0.72, 1.40)	57.8	0.04
	Cohort	2	RR: 0.88 (0.48, 1.64)	48.0	0.17
	Adjusted for age				
	Yes	3	RR: 1.34 (0.92, 1.96)	34.2	0.22
	No	5	RR: 0.82 (0.60, 1.12)	37.5	0.17
	Adjusted for caffeine intake				
	Yes	3	RR: 0.93 (0.69, 1.27)	22.0	0.28
	No	5	RR: 1.01 (0.65, 1.57)	62.5	0.03
	Adjusted for smoking				
	Yes	6	RR: 1.02 (0.74, 1.40)	52.7	0.06
	No	2	RR: 0.80 (0.33, 1.92)	69.7	0.07

Lv et al. 2017 [55]	**Parity (highest vs. lowest category)**				
	Study design				
	Case-control	5	RR: 0.99 (0.69, 1.42)	62.2	0.03
	Cohort	3	RR: 1.02 (0.77, 1.35)	0.0	0.49
	Adjusted for age				
	Yes	4	RR: 0.84 (0.66, 1.06)	0.0	0.79
	No	4	RR: 1.22 (0.79, 1.87)	63.8	0.04
	Adjusted for caffeine intake				
	Yes	3	RR: 1.13 (0.67, 1.90)	75.1	0.02
	No	5	RR: 0.92 (0.73, 1.15)	0.0	0.44
	Adjusted for smoking				
	Yes	7	RR: 1.04 (0.79, 1.36)	46.2	0.08
	No	1	RR: 0.81 (0.56, 1.17)	NA	NA
Lv et al. 2017 [55]	**Type of menopause (surgical vs. natural)**	7	RR: 0.93 (0.68, 1.29)	74.8	<0.01
	Study design				
	Case-control	4	RR: 0.85 (0.45, 1.62)	81.0	<0.01
	Cohort	3	RR: 1.00 (0.69, 1.45)	73.6	0.02
	Adjusted for age				
	Yes	4	RR: 0.94 (0.67, 1.31)	67.5	0.03
	No	3	RR: 0.89 (0.34, 2.33)	86.3	<0.01
	Adjusted for caffeine intake				
	Yes	3	RR: 0.67 (0.45, 0.99)	58.6	0.09
	No	4	RR: 1.25 (0.78, 2.01)	77.2	<0.01
	Adjusted for smoking				
	Yes	5	RR: 0.77 (0.63, 0.94)	27.1	0.24
	No	2	RR: 1.91 (1.29, 2.83)	1.5	0.31
Wang et al. 2018 [61]	**Depression (with vs. without)**				

	Study design				
	Case-control	5	OR: 2.44 (1.97, 3.03)	50.6	0.09
	Cohort	6	OR: 1.92 (1.66, 2.22)	0.0	0.57
	Study location				
	USA	4	OR: 2.04 (1.70, 2.45)	0.0	0.78
	Europe	4	OR: 2.19 (1.79, 2.68)	15.3	0.32
	Others	3	OR: 2.04 (1.06, 3.95)	78.4	0.01
	Assessment of depress				
	Questionnaire	6	OR: 1.92 (1.65, 2.24)	0.0	0.53
	ICD, DSM, ICPC	5	OR: 2.55 (2.06, 3.15)	25.9	0.25
	Quality of studies (NOS)				
	High quality	7	OR: 2.38 (1.92, 2.95)	43.3	0.10
	Medium quality	4	OR: 1.92 (1.65, 2.24)	20.9	0.29
Faustino et al. 2020 [19]	**Bipolar disorder (with vs. without)**				
	Follow-up duration				
	>9 years	2	OR: 1.75 (1.36, 2.26)	0.0	0.49
	<9 years	4	OR: 5.20 (4.26, 6.35)	34.0	0.21
	Study design				
	Cohort studies	NR	OR: 3.12 (1.66, 5.88)	95.0	NR
	Cross-sectional studies	NR	OR: 3.61 (2.33, 5.60)	0.0	NR
Adams et al. 2015 [49]	**Premorbid constipation (with vs. without)**				
	Study design				
	Cohort studies	4	RR: 2.36 (2.00, 2.80)	NR	NR
	Case-control studies	5	OR: 2.24 (2.05, 2.46)	NR	NR
Drugs					
Lv et al. 2017 [55]	**OCs (ever vs. never use)**				
	Study design				

	Case-control	3	RR: 1.15 (0.67, 1.99)	79.2	<0.01
	Cohort	4	RR: 0.97 (0.73, 1.29)	48.9	0.12
	Adjusted for age				
	Yes	4	RR: 0.96 (0.63, 1.47)	75.0	<0.01
	No	3	RR: 1.09 (0.88, 1.35)	0.0	0.69
	Adjusted for caffeine intake				
	Yes	3	RR: 0.96 (0.52, 1.75)	79.0	<0.01
	No	4	RR: 1.09 (0.91, 1.31)	0.0	0.86
	Adjusted for smoking				
	Yes	6	RR: 1.00 (0.75, 1.32)	67.3	<0.01
	No	1	RR: 1.10 (0.69, 1.76)	NA	NA
Lang et al. 2015 [43]	**Calcium channel blocker use (use vs. no use)**				
	Study design				
	Prospective cohort studies	3	RR: 0.74 (0.64, 0.85)	42.6	0.16
	Case–control studies	2	RR: 0.78 (0.67, 0.91)	0.0	0.81
	Types of CCBs				
	Dihydropyridines CCB users	2	RR: 0.73 (0.64, 0.83)	0.0	0.51
	Nondihydropyridines CCB users	2	RR: 0.70 (0.53, 0.93)	0.0	0.55
Wang et al. 2014 [39]	**HRT (use vs. no use)**				
	Study design				
	Case–control studies	10	RR: 0.79 (0.62, 1.02)	27.8	0.19
	PBCC	5	RR: 0.89 (0.70, 1.13)	0.0	0.53
	HBCC	5	RR: 0.73 (0.45, 1.18)	54.7	0.07
	Cohort studies	4	RR: 1.24 (1.10, 1.41)	0.0	0.76
	Geographic region				
	North America	7	RR: 1.12 (0.92, 1.36)	14.6	0.07
	Europe	7	RR: 0.86 (0.63, 1.16)	34.8	0.16

	Study quality (NOS)				
	High	10	RR: 1.16 (1.02, 1.31)	14.6	0.31
	Low	4	RR: 0.58 (0.40, 0.82)	0.0	0.63
	Adjusted for age				
	Yes	10	RR: 1.05 (0.88, 1.26)	46.8	0.05
	No	4	RR: 0.87 (0.49, 1.53)	60.1	0.06
	Type of HRT				
	ERT	9	RR: 1.05 (0.79, 1.40)	54.1	0.02
	PRT	1	RR: 3.41 (1.23, 9.47)	NA	NA
Noyce et al. 2012 [22]	**NSAIDs use (use vs. no use)**				
	Study design				
	Case-control	5	RR: 0.86 (0.77, 0.96)	46.7	0.11
	Cohort	4	RR: 0.86 (0.66, 1.12)	65.8	0.03
Noyce et al. 2012 [22]	**Aspirin use (use vs. no use)**				
	Study design				
	Case-control	4	RR: 1.02 (0.74, 1.40)	69.0	0.02
	Cohort	2	RR: 1.20 (1.04, 1.39)	0.0	0.39
Noyce et al. 2012 [22]	**Acetaminophen/paracetamol use (use vs. no use)**				
	Study design				
	Case-control	1	RR: 1.16 (1.00, 1.35)	NA	NA
	Cohort	1	RR: 0.86 (0.67, 1.11)	NA	NA
Bai et al. 2016 [50]	**Statin use (use vs. no use)**				
	Study design				
	Case-control	5	RR: 0.77 (0.62, 0.97)	75.2	<0.01
	Cohort	6	RR: 0.82 (0.68, 0.99)	55.5	0.05
	Region				

	North America	6	RR: 0.76 (0.54, 1.08)	78.4	<0.01
	Europe	4	RR: 0.86 (0.80, 0.93)	0.0	0.49
	Asia	1	RR: 0.73 (0.60, 0.88)	NA	NA
	Adjusted for age				
	Yes	7	RR: 0.75 (0.60, 0.95)	74.1	<0.01
	No	4	RR: 0.86 (0.75, 0.99)	34.7	0.20
	Adjusted for gender				
	Yes	7	RR: 0.76 (0.59, 0.98)	77.7	<0.01
	No	4	RR: 0.85 (0.79, 0.92)	0.0	0.75
	Quality of studies (NOS)				
	High quality	7	RR: 0.71 (0.59, 0.87)	65.4	<0.01
	Medium quality	4	RR: 0.93 (0.78, 1.11)	61.4	0.05
	Individual statin use				
	Atorvastatin	4	RR: 0.83 (0.66, 1.05)	68.6	0.02
	Lovastatin	2	RR: 0.61 (0.16, 2.35)	82.6	0.02
	Sivastatin	4	RR: 0.68 (0.45, 1.01)	96.0	<0.01
	Pravastatin	3	RR: 1.35 (0.58, 3.10)	68.1	0.04
	Rosuvastatin				
Zhu et al. 2019 [18]	**TZDs (TZDs vs. non-TZD treatments)**				
	TZDs				
	Only pioglitazone	1	OR: 0.86 (0.67, 1.10)	NA	NA
	Any kind of TZDs	4	OR: 0.66 (0.44, 0.99)	89.0	<0.01
	Ethnicity				
	White	3	OR: 0.83 (0.72, 0.95)	39.0	0.19
	Asian	2	OR: 0.58 (0.26, 1.28)	94.0	<0.01
	Follow-up duration				
	<10 years	2	OR: 0.85 (0.68, 1.05)	0.0	0.81
	>10 years	3	OR: 0.63 (0.38, 1.03)	92.0	<0.01

Biomarkers					
Shen et al. 2013 [33]	**Serum urate (high vs. low level)**				
	Gender				
	Men	4	RR: 0.60 (0.40, 0.90)	50.6	0.12
	Women	3	RR: 0.99 (0.59, 1.67)	16.9	0.30
Shen et al. 2015 [45]	**Serum vitamin D level (deficient and insufficient vs. normal level)**				
	Deficient vitamin D levels (serum 25(OH)D level <50 nmol/L)	3	OR: 2.08 (1.63, 2.65)	0.0	0.91
	Insufficient vitamin D levels (serum 25(OH)D level <75 nmol/L)	3	OR: 1.29 (1.10, 1.51)	0.0	0.69
Wang et al. 2015 [48]	**BMI (per 5 kg/m2 increase)**				
	Region				
	USA	6	RR: 0.97 (0.88, 1.08)	47.3	0.09
	Europe	3	RR: 1.13 (0.89, 1.43)	68.6	0.04
	Gender				
	Men	6	RR: 1.03 (0.90, 1.18)	64.0	0.02
	Women	3	RR: 1.04 (0.83, 1.30)	68.6	0.02
	Both	5	RR: 1.07 (0.90, 1.28)	68.6	0.02
	Study duration				
	>15 years	5	RR: 1.06 (0.91, 1.24)	70.5	0.01
	<15 years	5	RR: 0.91 (0.75, 1.10)	60.6	0.04
	Age at baseline				
	>60 years	5	RR: 0.95 (0.79, 1.13)	60.7	0.04
	<60 years	5	RR: 1.03 (0.88, 1.22)	60.6	<0.01
	No. of cases				
	>200	5	RR: 1.05 (0.92, 1.20)	71.3	0.01
	<200	5	RR: 0.90 (0.72, 1.12)	58.0	0.05

	Statistical adjustment				
	Age				
	Yes	8	RR: 0.97 (0.83, 1.14)	71.7	<0.01
	No	2	RR: 1.01 (0.91, 1.14)	0.0	0.61
	Education				
	Yes	4	RR: 1.11 (0.95, 1.30)	63.9	0.04
	No	6	RR: 0.92 (0.79, 1.06)	58.0	0.28
	Energy intake				
	Yes	2	RR: 1.03 (0.93, 1.15)	0.0	0.33
	No	8	RR: 0.98 (0.84, 1.14)	71.3	0.28
	Smoking				
	Yes	7	RR: 1.00 (0.86, 1.16)	72.0	<0.01
	No	3	RR: 0.99 (0.84, 1.16)	36.7	0.21
	Alcohol consumption				
	Yes	4	RR: 1.13 (0.99, 1.29)	56.2	0.08
	No	6	RR: 0.90 (0.78, 1.04)	50.1	0.08
	Physical activity				
	Yes	5	RR: 1.03 (0.85, 1.25)	75.8	<0.01
	No	5	RR: 0.97 (0.87, 1.08)	21.4	0.28
	Coffee consumption				
	Yes	6	RR: 1.03 (0.88, 1.21)	70.7	<0.01
	No	4	RR: 0.95 (0.82, 1.10)	39.5	0.18
Chen et al. 2014 [35]	**BMI (BMI ≥ 30 vs. BMI < 25)**				
	Study design				
	Case-control	3	OR: 0.73 (0.33, 1.61)	87.0	<0.01
	Cohort	4	RR: 1.16 (0.67, 2.01)	92.0	<0.01
Chen et al. 2014 [35]	**BMI (25 ≤ BMI < 30 vs. BMI < 25)**				
	Study design				

	Case-control	3	OR: 0.91 (0.70, 1.17)	20.0	0.29
	Cohort	4	RR: 1.39 (1.04, 1.85)	90.0	<0.01
Chen et al. 2014 [35]	**BMI (BMI ≥ 30 vs. 25 ≤ BMI < 30)**				
	Study design				
	Case-control	3	OR: 0.81 (0.47, 1.41)	77.0	0.01
	Cohort	4	RR: 0.84 (0.61, 1.15)	76.0	<0.01
Luo et al. 2018 [60]	**Serum vitamin D levels (PD patient vs. control)**				
	Different latitude				
	Higher latitude area	9	WMD: −4.20 (−5.66, −2.75)	76.6	<0.01
	Lower latitude area	2	WMD: −3.45 (−5.75, −1.15)	93.4	<0.01
Gudala et al. 2013 [30]	**Serum cholesterol (highest to lowest level)**				
	Study design				
	Case-control	4	RR: 0.82 (0.59, 1.13)	54.9	<0.01
	Cohort	4	RR: 0.97 (0.62, 1.53)	84.7	<0.01
	Gender				
	Male	3	RR: 1.66 (1.12, 2.47)	46.6	0.15
	Female	3	RR: 0.75 (0.16, 3.58)	85.2	<0.01
	Quality of studies (NOS)				
	High quality	3	RR: 1.08 (0.64, 1.83)	85.2	<0.01
	Medium quality	1	RR: 0.79 (0.41, 1.31)	NA	NA
	Low quality	4	RR: 0.80 (0.60, 1.05)	36.0	0.19
Shen et al. 2013 [34]	**Serum uric acid levels (PD patient vs. control)**				
	Gender				
	Men	4	SMD: −0.62 (−0.94, −0.31)	84.2	<0.01
	Women	4	SMD: −0.56 (−0.72, −0.41)	27.0	0.25

Jin et al. 2018 [59]	**Serum Mg levels (PD patient vs. control)**				
	Location	5	SMD: 2.22 (0.82, 3.63)	97.6	<0.01
	Asia	5	SMD: 0.37 (−0.32, 1.06)	91.6	<0.01
	Europe	1	SMD: 0.08 (−0.33, 0.48)	NA	NA
	America	1	SMD: 1.18 (0.80, 1.55)	NA	NA
	Africa				
	Analysis method	8	SMD: 1.55 (0.54, 2.57)	97.0	<0.01
	ICP-MS/ICP-AES	3	SMD: 0.55 (−0.04, 1.14)	88.2	<0.01
	AAS	1	SMD: 0.08 (−0.33, 0.48)	NA	NA
	Colorimetry	5	SMD: 2.22 (0.82, 3.63)	97.6	<0.01
Jin et al. 2018 [59]	**Peripheral blood Mg levels (PD patient vs. control)**				
	Location				
	Asia	6	SMD: 1.78 (0.70, 2.86)	97.2	<0.01
	Europe	8	SMD: −0.14 (−0.89, 0.62)	94.9	<0.01
	America	1	SMD: 0.08 (−0.33, 0.48)	NA	NA
	Africa	1	SMD: 1.18 (0.80, 1.55)	NA	NA
	Analysis method				
	ICP-MS/ICP-AES	10	SMD: 1.13 (0.17, 2.09)	97.3	<0.01
	AAS	4	SMD: 0.41 (−0.06, 0.89)	86.6	<0.01
	Colorimetry	2	SMD: −0.08 (−2.79, 1.04)	95.6	<0.01
Jiang et al' 2019 [62]	**Serum BDNF level (PD patient vs. control)**				
	Region				
	Studies outside china	5	SMD: -0.43(-1.20, 0.34)	95.2	<0.01
	Studies inside china	4	SMD: -1.73 (-2.56, -0.91)	93.9	<0.01

AAS, atomic absorption spectrometry; BDNF, brain-derived neurotrophic factor; BMI, body mass index; CCB, calcium channel blocker; CI, confidence interval; DM, diabetes; DSM, diagnostic and statistical manual of mental disorders; ELF-MF, extremely-low frequency magnetic fields; ERT, estrogen replacement

therapy; HBCC, hospital-based case–control study; HRT, hormone replacement therapy; ICD, international classification of diseases; ICPC, international classification of primary care; ICP-AES, inductively coupled plasma-atomic emission spectrometer; ICP-MS, inductively coupled plasma-mass spectrometry; MUFA, monounsaturated fatty acid; NA, not applicable; NOS, Newcastle-Ottawa Scale; NR, not reported; NSAIDs, nonsteroidal anti-inflammatory drugs; OCs, oral contraceptives; OR, odds ratio; PBCC, population-based case–control study; PD, Parkinson's disease; PRT, progesterone replacement therapy; PUFA, polyunsaturated fatty acids; RR, relative risk; SMD, standardized mean difference; TZDs, thiazolidinediones; WMD, weighted mean difference.

[a] Subgroup analysis in case-control study

Supplementary Table 3. Detailed information of method for exposure assessment and adjusted factors

Author, year	Risk factor	Methods for exposure assessment
Habits		
Zhang et al. 2014 [40]	Alcohol intake (highest vs. lowest level)	Questionnaires
Noyce et al. 2012 [22]	Smoking (ever vs. never)	Questionnaire, interview
Noyce et al. 2012 [22]	Smoking (current vs. never)	Questionnaire, interview
Noyce et al. 2012 [22]	Smoking (past vs. never)	Questionnaire, interview
Noyce et al. 2012 [22]	Coffee (drinking vs. non-drinking)	Questionnaire, interview
Qi et al. 2014 [37]	Tea (highest vs. lowest category)	NR
Qi et al. 2014 [37]	Caffeine (highest vs. lowest category)	NR
Shen et al. 2015 [45]	Outdoor work (with vs. without)	NR
Fang et al. 2018 [58]	Total physical activity (highest vs. the lowest category)	Self-report;
Fang et al. 2018 [58]	Light physical activity (highest vs. the lowest category)	Self-report;
Fang et al. 2018 [58]	Moderate to vigorous physical activity (highest vs. the lowest category)	Self-report;
Exposure to toxic environmental agents		
Pezzoli et al. 2013 [32]	Pesticides (exposure vs. no exposure)	Questionnaires
Pezzoli et al. 2013 [32]	Herbicides (exposure vs. no exposure)	Questionnaires
Pezzoli et al. 2013 [32]	Insecticides (exposure vs. no exposure)	Questionnaires

Pezzoli et al. 2013 [32]	Fungicides (exposure vs. no exposure)	Questionnaires
Pezzoli et al. 2013 [32]	Rodenticides (exposure vs. no exposure)	Questionnaires
Pezzoli et al. 2013 [32]	Solvents (exposure vs. no exposure)	Questionnaires
Pezzoli et al. 2013 [32]	Organochlorines (exposure vs. no exposure)	Questionnaires
Pezzoli et al. 2013 [32]	Organophosphates (exposure vs. no exposure)	Questionnaires
Pezzoli et al. 2013 [32]	Paraquat (exposure vs. no exposure)	Questionnaires
Pezzoli et al. 2013 [32]	Maneb/mancozeb (exposure vs. no exposure)	Questionnaires
Pezzoli et al. 2013 [32]	DDT (exposure vs. no exposure)	Questionnaires
Pezzoli et al. 2013 [32]	Farming (exposure vs. no exposure)	Questionnaires
Pezzoli et al. 2013 [32]	Well water drinking (exposure vs. no exposure)	Questionnaires
Pezzoli et al. 2013 [32]	Rural living (exposure vs. no exposure)	Questionnaires
Kasdagli et al. 2019 [14]	$PM_{2.5}$ (per 10 μg/m^3)	NR
Kasdagli et al. 2019 [14]	$PM_{2.5}$ (high vs. low exposure)	NR
Kasdagli et al. 2019 [14]	PM_{10} (per 10 μg/m^3)	NR
Kasdagli et al. 2019 [14]	PM_{10} (high vs. low exposure)	NR
Kasdagli et al. 2019 [14]	$PM_{2.5-10}$ (per 10 μg/m^3)	NR
Kasdagli et al. 2019 [14]	$PM_{2.5-10}$ (high vs. low exposure)	NR
Kasdagli et al. 2019 [14]	NO_2 (per 10 μg/m^3)	NR
Kasdagli et al. 2019 [14]	NO_2 (high vs. low exposure)	NR

Kasdagli et al. 2019 [14]	NOx (per 10 μg/m^3)	NR
Kasdagli et al. 2019 [14]	NOx (high vs. low exposure)	NR
Kasdagli et al. 2019 [14]	CO (per 1 mg/m^3)	NR
Kasdagli et al. 2019 [14]	CO (high vs. low exposure)	NR
Kasdagli et al. 2019 [14]	O_3 (per 5 ppb)	NR
Kasdagli et al. 2019 [14]	O_3 (high vs. low exposure)	NR
Kasdagli et al. 2019 [14]	SO_2 (high vs. low exposure)	NR
Huss et al. 2015 [42]	ELF-MF (higher vs. lowest exposure)	Occupational records, censuses, questionnaires, death certificates
Huss et al. 2015 [42]	ELF-MF (highest-longest vs. lowest exposure)	Occupational records, censuses, questionnaires, death certificates
Mortimer et al. 2012 [29]	Welding (exposure vs. no exposure)	Self-reported, medical Record, questionnaire
Mortimer et al. 2012 [29]	Manganese (exposure vs. no exposure)	NR
Palin et al. 2015 [44]	Hydrocarbon (exposure vs. no exposure)	NR
Zhou et al. 2019 [17]	Sunlight (exposure vs. no exposure)	NR
Dietary factors		
Takeda et al. 2014 [38]	Vitamin A (retinol) (high vs. low intake)	Dietary estimate
Takeda et al. 2014 [38]	α-carotene intake (high vs. low intake)	Dietary estimate
Takeda et al. 2014 [38]	β-carotene intake (high vs. low intake)	Dietary estimate

Takeda et al. 2014 [38]	β-cryptoxanthin intake (high vs. low intake)	Dietary estimate
Takeda et al. 2014 [38]	Lutein intake (high vs. low intake)	Dietary estimate
Takeda et al. 2014 [38]	Lycopene intake (high vs. low intake)	Dietary estimate
Jiang et al. 2014 [36]	Dairy food intake (highest vs. lowest category)	NR
Cheng et al. 2015 [41]	Iron (moderate vs. low intake)	FFQ, DHQ
Cheng et al. 2015 [41]	Iron (high vs. low intake)	FFQ, DHQ
Cheng et al. 2015 [41]	Zinc (moderate vs. low intake)	FFQ, DHQ
Cheng et al. 2015 [41]	Zinc (high vs. low intake)	FFQ, DHQ
Cheng et al. 2015 [41]	Copper (moderate vs. low intake)	FFQ, DHQ
Cheng et al. 2015 [41]	Copper (high vs. low level of intake)	FFQ, DHQ
Hughes et al. 2017 [54]	Milk (highest vs. lowest level of intake)	Questionnaires
Wang et al. 2015 [47]	Protein (highest vs. lowest level of intake)	NR
Wang et al. 2015 [47]	Carbohydrate (highest vs. lowest level of intake)	NR
Wang et al. 2015 [47]	Cholesterol (highest vs. lowest level of intake)	NR
Wang et al. 2015 [47]	Energy (highest vs. lowest level of intake)	NR

Wang et al. 2015 [47]	Fat (highest vs. lowest level of intake)	NR
Qu et al. 2019 [15]	Total fat (high vs. low level of intake)	FFQ, DHQ, questionnaire

Medical history and comorbid diseases

Jafari et al. 2013 [31]	Head trauma (with vs. without)	NR
Noyce et al. 2012 [22]	Family history any relative (with vs. without)	Questionnaire, interview
Noyce et al. 2012 [22]	First degree relative (with vs. without)	Questionnaire, interview
Noyce et al. 2012 [22]	Family history of tremor (with vs. without)	Questionnaire, interview
Noyce et al. 2012 [22]	Prior mood disorder (with vs. without)	Questionnaire, interview
Noyce et al. 2012 [22]	Diabetes (with vs. without)	Questionnaire, interview, drug prescriptions in the database, medical record
Lu et al. 2014 [21]	Diabetes (with vs. without)	Physician-diagnosed diabetes , use of glucose- lowering medication, ICD codes , ATC codes, questionnaire, medical record, antidiabetes-drug use, diet recommendation in the medical record, interview
Noyce et al. 2012 [22]	Cancer (with vs. without)	Interview, medical record review, questionnaire, linked to Danish Cancer Registry
Noyce et al. 2012 [22]	Hypertension (with vs. without)	Questionnaire, interview, drug prescriptions in the database, medical record
Noyce et al. 2012 [22]	Gastric ulcer (with vs. without)	Questionnaire, interview
Noyce et al. 2012 [22]	General anaesthetic (with vs. without)	Questionnaire, interview

Noyce et al. 2012 [22]	Oophorectomy (with vs. without)	Questionnaire, interview
Ungprasert et al. 2015 [46]	Gout (with vs. without)	Diagnostic code of the database
Adams et al. 2015 [49]	Premorbid constipation (with vs. without)	Questionnaire, coded in patient medical records, medication used to treat
Adams et al. 2015 [49]	Constipation of duration ≥10 years (with vs. without)	Questionnaire, database review, general practice record review
Lv et al. 2017 [55]	Age at menarche (highest vs. lowest category)	NR
Lv et al. 2017 [55]	Age at menopause (highest vs. lowest category)	NR
Lv et al. 2017 [55]	Fertile lifespan (highest vs. lowest category)	NR
Lv et al. 2017 [55]	Parity (highest vs. lowest category)	NR
Lv et al. 2017 [55]	Type of menopause (surgical vs. natural)	NR
Milani et al. 2017 [56]	Bullous pemphigoid (with vs. without)	Electronic databases
Wang et al. 2018 [61]	Depression (with vs. without)	Self-report, questionnaire, ICD, DSM, ICPC, medical record
Zhou et al. 2019 [16]	Latent infection of T. gondii (with vs. without)	NR
Zhou et al. 2019 [16]	Acute infection of T. gondii (with vs. without)	NR
Faustino et al. 2020 [19]	Bipolar Disorder (with vs. without)	Medical records
Wang et al. 2020 [20]	Infection of HP (with vs. without)	NR

Wang et al. 2020 [20]	Infection of HCV (with vs. without)	NR
Wang et al. 2020 [20]	Infection of malassezia (with vs. without)	NR
Wang et al. 2020 [20]	Infection of pneumonia (with vs. without)	NR
Wang et al. 2020 [20]	Infection of measles (with vs. without)	NR
Wang et al. 2020 [20]	Infection of influenza virus (with vs. without)	NR
Wang et al. 2020 [20]	Infection of herpes virus (with vs. without)	NR
Wang et al. 2020 [20]	Infection of HBV (with vs. without)	NR
Wang et al. 2020 [20]	Infection of scarlet fever (with vs. without)	NR
Wang et al. 2020 [20]	Infection of mumps virus (with vs. without)	NR
Wang et al. 2020 [20]	Infection of chicken pox (with vs. without)	NR
Wang et al. 2020 [20]	Infection of pertussis (with vs. without)	NR
Wang et al. 2020 [20]	Infection of German measles (with vs. without)	NR
Drugs		
Lv et al. 2017 [55]	OCs (ever vs. never use)	NR
Lang et al. 2015 [43]	Calcium channel blocker (use vs. no use)	Self-reported, pharmacies record
Wang et al. 2014 [39]	HRT (use vs. no use)	Medical record, in-person interview, self-reported, telephone interview

Noyce et al. 2012 [22]	NSAIDs (use vs. no use)	Medical record review, questionnaire, British Columbia Linked Health Database
Gao et al. 2011 [28]	Ibuprofen (use vs. no use)	Questionnaire, review of prescription records, pharmacy records
Gao et al. 2011 [28]	Aspirin (use vs. no use)	Questionnaire, review of prescription records, pharmacy records, review of medical records
Noyce et al. 2012 [22]	Aspirin (use vs. no use)	Medical record review, computer record review, GHC pharmacy database, questionnaire
Gao et al. 2011 [28]	Other NSAIDs (use vs. no use)	Questionnaire, review of prescription records
Gao et al. 2011 [28]	Acetaminophen (use vs. no use)	Questionnaire, review of prescription records
Noyce et al. 2012 [22]	Acetaminophen/Paracetamol (use vs. no use)	Computer record review, questionnaire
Noyce et al. 2012 [22]	Beta blocker (use vs. no use)	GHC pharmacy database, drug prescriptions in the database, National prescriptions database for statin prescriptions
Zhu et al. 2019 [18]	TZDs use (TZDs vs. non-TZD treatments)	NR
Bykov et al. 2017 [53]	Statin use and PD in studies that did not adjust for cholesterol (use vs. no use)	NR
Bykov et al. 2017 [53]	Statin use and PD in studies that adjusted for cholesterol (use vs. no use)	NR
Bai et al. 2016 [50]	Statin use (use vs. no use)	Reviewing medical records, self-report
Bai et al. 2016 [50]	Long-term statin use (use vs. no use)	Reviewing medical records, self-report

Biomarkers

Shen et al. 2015 [45]	Serum vitamin D level (deficient and insufficient vs. normal level)	NR
Luo et al. 2018 [60]	Serum vitamin D level (PD patient vs. control)	NR
Luo et al. 2018 [60]	Serum vitamin D level (insufficient vs. normal level)	NR
Luo et al. 2018 [60]	Serum vitamin D level (deficient vs. normal level)	NR
Shen et al. 2013 [33]	Serum urate (high vs. low level)	NR
Gudala et al. 2013 [30]	Serum cholesterol (highest to lowest level)	Physician diagnosed, self- reported, usage of cholesterol lowering agents, medical records
Shen et al. 2013 [34]	Serum uric acid levels (PD patient vs. control)	NR
Wang et al. 2015 [48]	BMI (per 5 kg/m^2 increase)	NR
Gao et al. 2016 [51]	Plasma/serum urate level in man (highest vs. lowest quartiles)	Colorimetric enzyme assay
Gao et al. 2016 [51]	Plasma/serum urate level in woman (highest vs. lowest quartiles)	Colorimetric enzyme assay
Sheng et al. 2016 [52]	LDL-C level (high vs. normal baseline level)	Review of medical records, database
Mostile et al. 2017 [57]	Serum iron level (PD patient vs. control)	NR
Jin et al. 2018 [59]	Serum Mg level (PD patient vs. control)	Colorimetry, AAS, ICP-AES, ICP-MS
Jin et al. 2018 [59]	Peripheral blood Mg level (PD patient vs. control)	Colorimetry, AAS, ICP-AES;
Jin et al. 2018 [59]	CSF Mg level (PD patient vs. control)	AAS, ICP-AES, ICP-MS, ICP-OES

Jiang et al' 2019 [62]	Serum BDNF level (PD patient vs. control)	NR
Qiu et al. 2019 [63]	CRP in Blood level (PD patient vs. control)	NR
Qiu et al. 2019 [63]	CRP in Serum level (PD patient vs. control)	NR
Qiu et al. 2019 [63]	CRP in CSF level (PD patient vs. control)	NR

AAS, atomic absorption spectrometry; BDNF, brain-derived neurotrophic factor; BMI, body mass index; CRP, C-reactive protein; CSF, central nervous system; DDT, dichloro-diphenyl-trichloroethane; DHQ, diet history questionnaire; DSM, diagnostic and statistical manual of mental disorders; ELF-MF, extremely-low frequency magnetic fields; ELISA , enzyme-linked immunosorbent assay; FFQ, food frequency questionnaire; HBV, hepatitis B virus; HCV, hepatitis C virus; HP, helicobacter pylori; HRT, hormone replacement therapy; ICPC, international classification of primary care; ICD, international classification of diseases; ICP-AES, inductively coupled plasma-atomic emission spectrometer; ICP-MS, inductively coupled plasma-mass spectrometry; ICP-OES, inductively coupled plasma optical emission spectrometry; LDL-C, low-density lipoprotein cholesterol; LC–MS, liquid chromatography-tandem mass spectrometry; NR, not reported; NSAIDs, nonsteroidal anti-inflammatory drugs; OCs, oral contraceptives; PD, Parkinson's disease; RIA, radioimmunoassay; TZDs, thiazolidinediones.