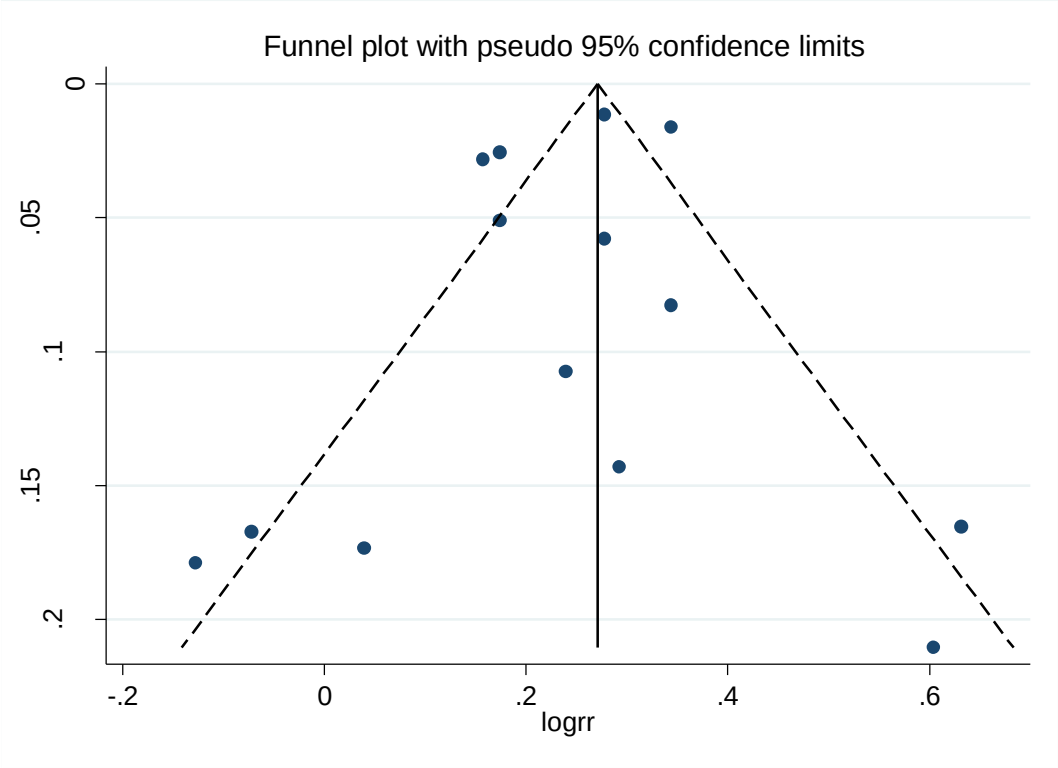
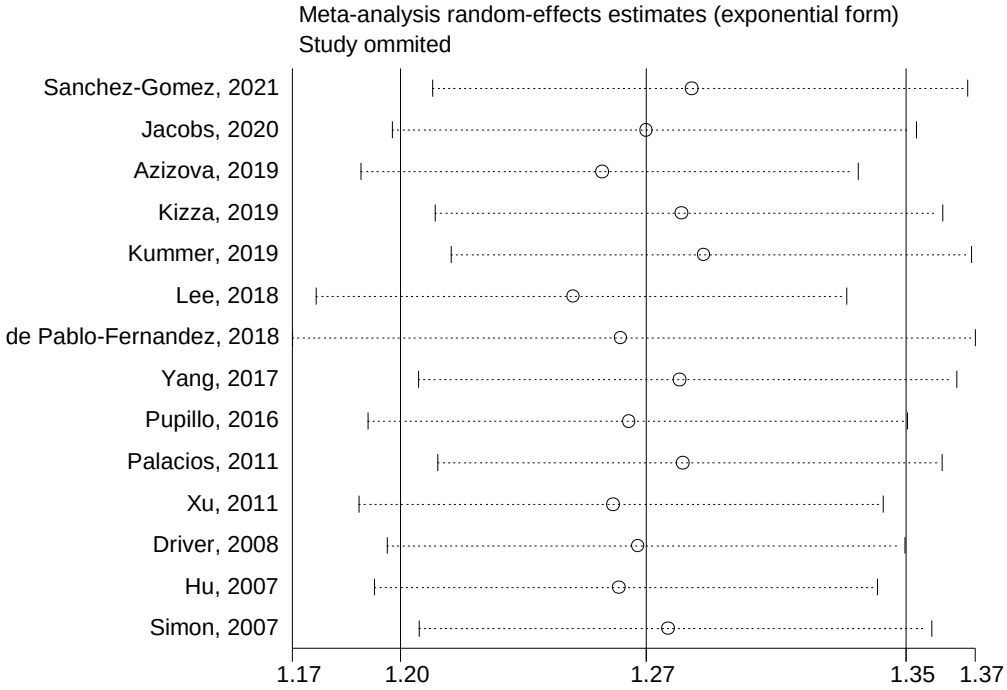
Supplement for:

Aune D, Schlesinger S, Mahamat-Saleh Y, Zheng B, Udeh-Momoh CT, Middleton LT. Diabetes mellitus, pre-diabetes and the risk of Parkinson's disease: a systematic review and meta-analysis of 15 cohort studies with 29.9 million participants and 86,345 cases. European Journal of Epidemiology https://doi.org/10.1007/s10654-023-00970-0

Supplementary Figure 1. Funnel plot of diabetes mellitus and Parkinson's disease

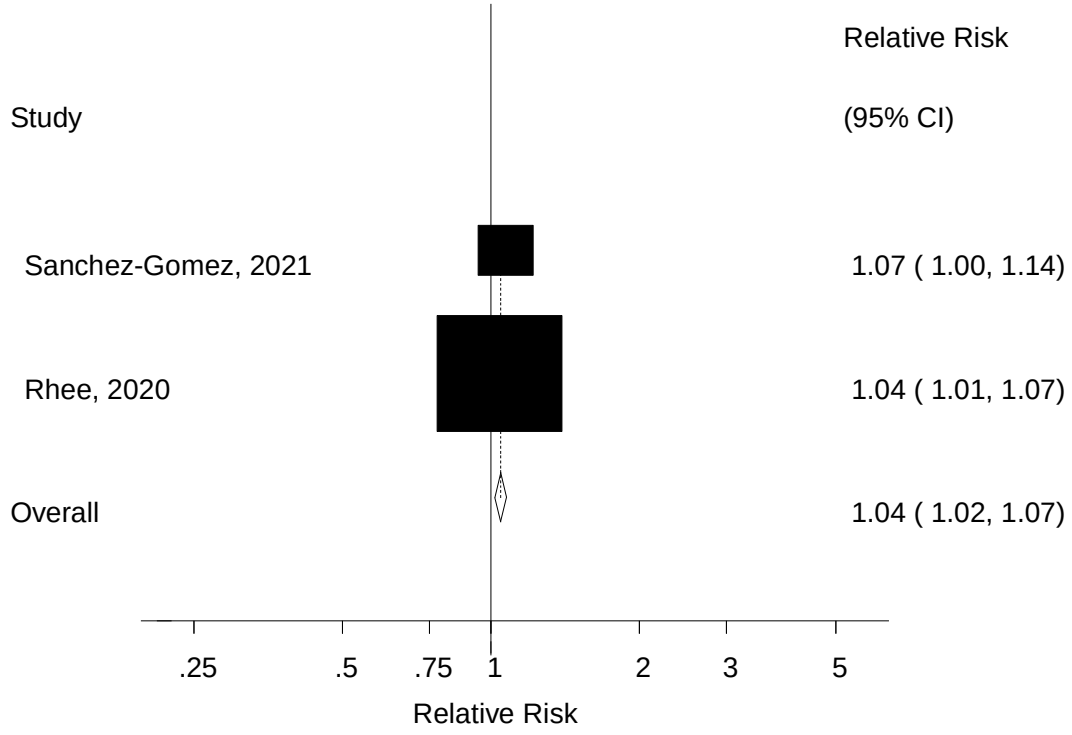


Supplementary Figure 2. Influence analysis of diabetes mellitus and risk of Parkinson's disease



Study omitted	e^coef.	[95% Conf.	Interval]
Sanchez-Gomez, 2021	1.286213	1.2110984	1.3659863
Jacobs, 2020	1.2729714	1.1993399	1.3511233
Azizova, 2019	1.2602396	1.1903292	1.3342559
Kizza, 2019	1.2831489	1.211754	1.3587502
Kummer, 2019	1.289562	1.2163094	1.3672262
Lee, 2018	1.2517939	1.1773205	1.330978
de Pablo-Fernandez, 2018	1.2654898	1.1704093	1.3682944
Yang, 2017	1.2825159	1.2068717	1.3629012
Pupillo, 2016	1.2680068	1.1922166	1.3486149
Palacios, 2011	1.2835622	1.2125785	1.3587011
Xu, 2011	1.2633793	1.1897087	1.3416119
Driver, 2008	1.2705973	1.197821	1.3477954
Hu, 2007	1.2649577	1.1941773	1.3399332
Simon, 2007	1.2791802	1.2070223	1.3556517
Combined	1.2728658	1.2016861	1.3482618

Supplementary Figure 3. Prediabetes and Parkinson's disease



Supplementary text

PubMed search terms

(diabetes OR diabetes[MeSH] OR "blood glucose" OR blood glucose[MeSH] OR "plasma glucose" OR plasma glucose[MeSH] OR "serum glucose" OR serum glucose[MeSH] OR "medical history" OR medical history[MeSH])

AND

("Parkinson’s" OR Parkinson’s[MeSH] OR "Parkinson")

AND

("case-control" OR cohort OR prospective OR longitudinal OR retrospective OR "follow-up" OR "cross-sectional" OR "hazard ratio" OR "hazard ratios" OR "relative risk" OR "relative risks" OR "incidence rate ratio" OR "incidence rate ratios" OR "odds ratio" OR odds ratios OR incidence)

Embase search terms

((diabetes or blood glucose or serum glucose or plasma glucose or medical history).ab,ti.

OR diabetes/ or blood glucose/ or serum glucose/ or plasma glucose/ or medical history/)

AND

((Parkinson's or Parkinson).ab,ti. OR (Parkinson's/ or Parkinson/))

AND

(case-control or cohort or prospective or longitudinal or retrospective or follow-up or cross-sectional or hazard ratio or hazard ratios or relative risk or relative risks or incidence rate ratio or incidence rate ratios or odds ratio or odds ratios or incidence).af.

Supplementary Table 1. List of excluded studies and exclusion reasons

Exclusion reason	Reference number
Abstract	(1-30)
Case-control study	(31-55)
Case only study	(56-59)
Comment, editorial, letter	(60-74)
Cross-sectional study	(75-84)
Duplicate	(85-91)
Genetic study	(92)
Meta-analysis	(93-101)
No risk estimates	(102-104)
Not relevant data	(105-114)
Not relevant exposure	(115-167)
Not relevant outcome	(168-173)
Not retrieved	(174)
Patient population	(175-177)
Progression of Parkinson's disease	(178-184)
Review	(185-201)

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Supplementary Table 2. World Cancer Research Fund grading criteria

Grading	Criteria
Convincing	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 are 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 in the association. Such a gradient need not be linear or even in the same direction across 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 outcomes
Probable	All of the following are generally required: - Evidence from at least two independent cohort studies, or at least five case-control 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 - Evidence for biological plausibility
Limited - suggestive	All of the following are 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, but this does not mean that there is evidence of no relationship. The evidence might be graded "limited - no conclusion" for several reasons: - limited number of studies - inconsistency of direction of effect - poor quality of studies (e.g. lack of adjustment for known confounders) - or any combination of these factors
Substantial effect on risk unlikely	All of the following are 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 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 relevant animal models, that typical human exposures lead to relevant outcomes

Specific upgrading factors:
1) 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.
2) 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.
3) Evidence from randomised trials in humans.
4) Evidence from appropriately controlled experiments demonstrating one or more plausible and specific mechanisms actually operating in humans.
5) Robust and reproducible evidence from experimental studies in appropriate animal models showing that typical human exposures can lead to relevant health outcomes.

Supplementary Table 3. Modified Newcastle Ottawa Scale score for the individual studies

Author, year	Selection			Comparability	Outcome assessment			Total
	Selection of non-exposed cohort	Exposure ascertainment	Demonstration of outcome not present at start	0.25 points for each adjustment	Outcome assessment	Long enough follow-up	Adequacy of follow-up	
Simon, 2007	1	1	1	0.75	1	1	0	5.75
Hu, 2007	1	1	1	2	1	1	0	7
Driver, 2008	1	0	1	1.75	1	1	0	5.75
Xu, 2011	1	0	1	2	1	1	0	6
Palacios, 2011	1	0	1	2	1	1	0	6
Pupillo, 2016	1	1	1	2	0.5	0	0	5.5
Yang, 2017	1	1	1	2	0.5	1	1	7.5
Lee, 2018	1	1	1	2	0.5	1	0	6.5
De Pablo-Fernandez, 2018	1	1	1	1.25	0.5	1	0	5.75
Kummer, 2019	1	1	1	1	0.5	1	0	5.5
Kizza, 2019	1	0	0	2	0.5	1	0	4.5
Azizova, 2019	1	1	0	0.5	0.5	1	1	5
Jacobs, 2020	1	1	1	1	0.5	1	0	5.5

Sanchez-Gomez, 2021	1	1	1	1.25	1	1	0	6.25