Supplementary file

This supplementary file accompanies “What harm is there in exploration? How to distinguish pernicious ad hoc analyses from valuable scientific contributions” by Kim Luijken, Olaf Dekkers, Frits Rosendaal, and Rolf Groenwold. This file describes the count of analyses in the etiological studies published in the first issues of 2021 of four major epidemiological journals.

Aim

To count the number of primary analyses, sensitivity analyses, and additional analyses performed in original etiologic articles from the first issues of 2021 of four major epidemiological journals as an illustration that some recently published articles contained multiple analyses additional to the primary analysis of the study.

Methods

We identified all articles on original research in the first issue of 2021 in the following journals: American Journal of Epidemiology, Epidemiology, European Journal of Epidemiology and International Journal of Epidemiology. We excluded studies that did not address an etiologic research question, such as prediction studies, studies on therapeutic interventions, and randomized trials.

For each article, we counted the number of primary analyses, sensitivity analyses, and additional analyses that were performed. The unit of counting was the association estimator, where we only counted one association if they were reported on different scales (e.g., absolute and relative scales for binary endpoints).

The following analyses were counted as ***main analyses***:

- The primary analysis.
- Models addressing the same exposure and outcome as in the primary analysis but considering a different confounding structure.
- In studies that analyzed multiple outcomes, we could have distinguished outcomes that were strongly correlated to the outcome in the primary analysis from outcomes that were dissimilar. The former would be counted as primary and the latter as additional. We decided not to make this distinction, because it would require specific domain knowledge, and counted all different outcome-analyses as primary.

The following analyses were counted as ***sensitivity analyses***:

- Sensitivity analyses evaluating the primary analysis model.

The following analyses were counted as ***additional analyses***:

- Assessment of interaction effects not specified in the primary analysis.
- Subgroup analyses.
- Assessment of effects of exposure variables other than exposure of primary interest.
- Assessment of exposure effect on outcomes weakly correlated to the outcome in the primary analysis.
- Assessment of confounder-outcome effects.

The following analyses were ***not included*** in the count:

- Statistical tests in the baseline table, bivariate correlations or other preliminary analyses of variables that were included in the primary analysis.
- Absolute risks and model intercepts.
- Crude effect estimates of both main and exploratory models.
- Cross-sectional analyses.
- P for trend.
- Explained variance.

For all additional analyses we quoted explicit reporting of pre-specification or exploration.

Finally, we recorded the study sample size (number of participants); whether correction for multiple testing was performed (yes/no); and whether a public protocol of the analyses was referenced (yes/no).

Results

The first issues of 2021 of the American Journal of Epidemiology, Epidemiology, European Journal of Epidemiology and International Journal of Epidemiology contained 43 original articles in total, 25 of which were etiologic observational studies. On average 33 (range 1 – 120) main analyses, on average 30 (range 0 – 336) sensitivity analyses, and on average 163 (range 0 – 1467) additional analyses were performed per article. The median sample size was 16,243 (range 510 – 3,666,657). Two studies performed multiple testing corrections (with a sample size of 131,430 and 6,483, and a total number of 804 and 210 analyses, respectively). A detailed clarification of the count in each study is given on the next pages.

Clarification per study

James H Buszkiewicz, Heather D Hill, Jennifer J Otten, "Association of State Minimum Wage Rates and Health in Working-Age Adults Using the National Health Interview Survey", *American Journal of Epidemiology*, Volume 190, Issue 1, January 2021, Pages 21–30, https://doi.org/10.1093/aje/kwaa018

- Sample size: 131,430
- Correction for multiple testing: yes, Benjamini-Hochberg false discovery rate.
- Protocol referenced: no.

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 4	Primary model in full sample for six different outcomes.	Primary	12
	Sensitivity analyses in restricted sample and with different operationalization of exposure, each for six different outcomes.	Sensitivity	48
Table 5	Separate full-interaction models by sex, race/ethnicity, age, and employment status for the primary analysis under two operationalizations of exposure.	Additional	96
Supplementary material			
Table 2	Fully interacted with third difference (state level), overall and full-interaction models by sex, race/ethnicity, age, and employment status.	Additional	108
Table 3	Sensitivity analysis: further adjustment for state unemployment.	Sensitivity	108
Table 4	Sensitivity analysis: restricted sample to those currently employed.	Sensitivity	72
Table 5	Restricted definition of comparator group.	Sensitivity	108
Table 6	All covariate-outcome associations	Additional	252

Jun Ren, Yue Chen, Fenfen Li, Cheng Xue, Xiaoya Yin, Juanjuan Peng, Ji Liang, Qiming Feng, Shumei Wang, "Road Injuries Associated With Cellular Phone Use While Walking or Riding a Bicycle or an Electric Bicycle: A Case-Crossover Study", *American Journal of Epidemiology*, Volume 190, Issue 1, January 2021, Pages 37–43, https://doi.org/10.1093/aje/kwaa164

- Sample size: 643
- Correction for multiple testing: no.
- Protocol referenced: yes, but we did not find a publicly available version ("The protocol was reviewed and approved by the Ethics Committee of Fudan University (International registration number: IRB00002408 & FWA00002399)").

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Primary model in full sample using different control periods	Primary	10
Figure 1	Primary model in full sample using different hazard intervals	Sensitivity	4
Figure 2	Subgroup analyses.	Additional	13
Supplementary material			
Table 1	Unclear how these analyses differ or relate to analyses in main text. Description appears to be the same, yet numeric values differ.		
Table 2	Unclear how these analyses differ or relate to analyses in main text. Description appears to be the same, yet numeric values differ.		

Hongjie Chen, Lusine Yaghjyan, Christopher Li, Ulrike Peters, Bernard Rosner, Sara Lindström, Rulla M Tamimi, "Association of Interactions Between Mammographic Density Phenotypes and Established Risk Factors With Breast Cancer Risk, by Tumor Subtype and Menopausal Status", *American Journal of Epidemiology*, Volume 190, Issue 1, January 2021, Pages 44–58, https://doi.org/10.1093/aje/kwaa131

- Sample size: 6,483.
- Correction for multiple testing: yes, Bonferroni (although "Nominally significant results with P value < 0.05 are still reported and discussed").
- Protocol referenced: no.

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 1	Significant interactions mammographic density measures and breast cancer risk factors on risk of invasive breast cancer.	Additional	Counted in supplementary materials
Table 2	Significant interactions mammographic density measures and breast cancer risk factors on risk of premenopausal breast cancer.	Additional	Counted in supplementary materials
Table 3	Significant interactions mammographic density measures and breast cancer risk factors on risk of postmenopausal breast cancer.	Additional	Counted in supplementary materials
Table 4	Significant interactions mammographic density measures and breast cancer risk factors on risk of estrogen receptor–positive breast cancer.	Additional	Counted in supplementary materials
Table 5	Significant interactions mammographic density measures and breast cancer risk factors on risk of estrogen receptor–negative breast cancer.	Additional	Counted in supplementary materials
Supplementary file			
Table 2	Main exposure-outcome association of interest for three correlated outcomes.	Primary	27
	Sensitivity analysis modelling mammographic density measures continuously.	Sensitivity	9
Table 3	Interactions between mammographic density measures and breast cancer risk factors on risk of invasive breast cancer.	Additional	261
Table 4	Interactions between mammographic density measures and breast cancer risk factors on risk of premenopausal breast cancer.	Additional	261
Table 5	Interactions between mammographic density measures and breast cancer risk factors on risk of postmenopausal breast cancer.	Additional	315
Table 6	Interactions between mammographic density measures and breast cancer risk factors on risk of estrogen receptor–positive breast cancer.	Additional	315
Table 7	Interactions between mammographic density measures and breast cancer risk factors on risk of estrogen receptor–negative breast cancer.	Additional	315

Markus Eidemüller, Erik Holmberg, Marie Lundell, Per Karlsson, "Evidence for Increased Susceptibility to Breast Cancer From Exposure to Ionizing Radiation Due to a Familial History of Breast Cancer: Results From the Swedish Hemangioma Cohort", *American Journal of Epidemiology*, Volume 190, Issue 1, January 2021, Pages 76–84, https://doi.org/10.1093/aje/kwaa163

- Sample size: 17,200.
- Correction for multiple testing: no.
- Protocol referenced: no.

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Excess relative risk and excess absolute risk of breast cancer in subset of cohort without information on familial history of breast cancer.	Primary	5
Table 3	Effect measure of main interest (radiation-induced breast cancer risk) for full cohort.	Primary	1
	Effect measure of main interest (radiation-induced breast cancer risk) for three subgroups.	Additional	3
In text	Familial history of breast cancer where cancer was experienced in subgroup < 45 years old.	Additional	2
Supplementary file			
Table 2	Effect measure of main interest (spontaneous breast cancer risk) for full cohort.	Primary	1
	Effect measure of main interest (spontaneous breast cancer risk) for three subgroups.	Additional	3
Table 3	Sensitivity analysis for effect measure of main interest (radiation-induced breast cancer risk) for full cohort.	Sensitivity	1
	Sensitivity analysis for effect measure of main interest (radiation-induced breast cancer risk) for three subgroups.	Additional	3

John S Kim, Brian T Steffen, Anna J Podolanczuk, Steven M Kawut, Imre Noth, Ganesh Raghu, Erin D Michos, Eric A Hoffman, Gisli Thor Axelsson, Gunnar Gudmundsson, Vilmundur Gudnason, Elias F Gudmundsson, Rachel A Murphy, Josée Dupuis, Hanfei Xu, Ramachandran S Vasan, George T O'Connor, William S Harris, Gary M Hunninghake, R Graham Barr, Michael Y Tsai, David J Lederer, "Associations of **ω**-3 Fatty Acids With Interstitial Lung Disease and Lung Imaging Abnormalities Among Adults", *American Journal of Epidemiology*, Volume 190, Issue 1, January 2021, Pages 95–108, https://doi.org/10.1093/aje/kwaa168

- Sample size: 6,573.
- Correction for multiple testing: no
- Protocol referenced: no.

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 3	Effect of baseline plasma phospholipid ω-3 and ω-6 polyunsaturated fatty acid levels with interstitial lung disease hospitalization and mortality, adjusted for propensity score 2.	Primary	6
	Effect of baseline plasma phospholipid ω-3 and ω-6 polyunsaturated fatty acid levels with main outcomes stratified by fatty acid subtypes, adjusted for propensity score 2.	Additional	18
Table 5	Effect of baseline plasma phospholipid ω-3 polyunsaturated fatty acid levels with interstitial lung disease hospitalization and mortality by smoking status, adjusted for propensity score 3.	Additional	24
Supplementary file			
Table 5	Effect of baseline plasma phospholipid polyunsaturated fatty acids with interstitial lung disease hospitalization and mortality stratified by race/ethnicity	Additional	96
Table 6	Effect of baseline plasma phospholipid ω-3 and ω-6 polyunsaturated fatty acid levels with interstitial lung disease hospitalization and mortality, adjusted for propensity score 1.	Primary	6
	Effect of baseline plasma phospholipid ω-3 and ω-6 polyunsaturated fatty acid levels with main outcomes stratified by fatty acid subtypes, adjusted for propensity score 1.	Additional	18
Table 7	Effect of baseline plasma phospholipid ω-6 polyunsaturated fatty acid levels with interstitial lung disease hospitalization and mortality by smoking status, adjusted for propensity score 3.	Additional	24
Table 8	Effect of baseline plasma phospholipid ω-6 polyunsaturated fatty acid levels with interstitial lung disease hospitalization and mortality by smoking status (different operationalization), adjusted for propensity score 3.	Additional	96

Priyanka deSouza, Danielle Braun, Robbie M. Parks, Joel Schwartz, Francesca Dominici, Marianthi-Anna Kioumourtzoglou, "Nationwide Study of Short-term Exposure to Fine Particulate Matter and Cardiovascular Hospitalizations Among Medicaid Enrollees", *Epidemiology*, Volume 32, Issue 1, January 2021, Pages 6-13, doi: 10.1097/EDE.0000000000001265

- Sample size: 3,666,657 case days and 12,452,125 control days (not indicated how many participants).
- Correction for multiple testing: no
- Protocol referenced: yes, but we did not find a publicly available version ("This study was approved by the Institutional Review Board at the Harvard T.H. Chan School of Public Health").

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Percent change in CVD hospitalization rates per 10 μg/m3 increase in fine particulate matter.	Primary	1
	Sensitivity analyses for exposure operationalization.	Sensitivity	2
	Percent change in CVD hospitalization rates per 10 μg/m3 increase in fine particulate matter for subgroups.	Additional	16
Supplementary file			
Table 1	Sensitivity analyses of percent change in CVD hospitalization rates per 10 μg/m3 increase in fine particulate matter when using different degrees of freedom to account for air temperature and dew-point confounding, as well as by including estimates of ozone.	Sensitivity	4

Dana E. Goin, Monika A. Izano, Stephanie M. Eick, Amy M. Padula, Erin DeMicco, Tracey J. Woodruff, Rachel Morello-Frosch, "Maternal experience of multiple hardships and fetal growth: Extending environmental mixtures methodology to social exposures." *Epidemiology*, Volume 32, Issue 1, January 2021, Pages 18-26, doi: 10.1097/EDE.0000000000001272

- Sample size: 510 (different models included 168 – 507 participants based on propensity common support).
- Correction for multiple testing: no.
- Protocol referenced: yes, but we did not find a publicly available version ("The Institutional Review Boards of the University of California, San Francisco and Berkeley approved this study (Protocol # 13-12160))".

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Figure 1	Differences in birthweight for gestational age z-scores associated with eight self-reported hardships before and during pregnancy, analyzed individually and mutually adjusted for other hardships.	Primary	16
Figure 2	Differences in birthweight for gestational age z-scores and 95% CI associated with pairwise combinations of reported hardships before and during pregnancy (28 hardship pairs).	Primary	28
Supplementary file			
Figure 3	Differences in birthweight associated with eight self-reported hardships before and during pregnancy, analyzed individually and mutually adjusted for other hardships.	Primary	16
Figure 4	Differences in birthweight and 95% CI associated with pairwise combinations of reported hardships before and during pregnancy (28 hardship pairs).	Primary	28
Table 4	Same as Figure 1 and Figure 3.		
Table 5	Same as Figure 2 and Figure 4.		

Christopher N. Morrison, Elinore J. Kaufman, David K. Humphreys, Douglas J. Wiebe, "Firearm Homicide Incidence, Within-state Firearm Laws, and Interstate Firearm Laws in US Counties". *Epidemiology*, Volume 32, Issue 1, January 2021, Pages 36-45, doi: 10.1097/EDE.0000000000001262.

- Sample size: 3,107 counties.
- Correction for multiple testing: no.
- Protocol referenced: no.

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Effect of within-state and interstate fire-arm laws on homicide incidence rate, model 1.	Primary	2
	Confounder effects on homicide incidence rate across covariate strata, model 1.	Additional	14
	Effect of within-state and interstate fire-arm laws on homicide incidence rate, model including within-state laws × interstate laws interaction.	Primary	3
	Confounder effects on homicide incidence rate across covariate strata, model 2.	Additional	14
	Effect of within-state and interstate fire-arm laws on homicide incidence rate stratified by type of law, model 3.	Primary	18
	Confounder effects on homicide incidence rate across covariate strata, model 3.	Additional	14
In text	Sensitivity analyses model 3: two Spearman correlations and a global Moran's I.	Sensitivity	3
Supplementary file			
Table 3	Sensitivity analyses model 3, with social policy variables removed and lagged laws.	Additional	36

Adina Zeki Al Hazzouri, Lanyu Zhang, Audrey R. Murchland, Leslie Grasset, Jacqueline M. Torres, Richard N. Jones, Rebeca Wong, Maria M. Glymour, "Quantifying Lifecourse Drivers of International Migration: A Cross-national Analysis of Mexico and the United States", *Epidemiology*, Volume 32, Issue 1, January 2021, Pages 50-60. doi: 10.1097/EDE.0000000000001266.

- Sample size: 19,433
- Correction for multiple testing: no.
- Protocol referenced: no.

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 3	Effect of migration on all-cause mortality for different confounding adjustment sets/ procedures.	Primary	4
	Effect of migration on all-cause mortality for different confounding adjustment sets/ procedures by sex.	Additional	8
Supplementary file			
Table 1	Sensitivity analysis, restricted inclusion: effect of migration on all-cause mortality for different confounding adjustment sets/ procedures.	Sensitivity	4
	Sensitivity analysis, restricted inclusion: effect of migration on all-cause mortality for different confounding adjustment sets/ procedures by sex.	Additional	8
Table 2	Effect of age-specific migration on all-cause mortality for different confounding adjustment sets/ procedures.	Additional	12
Table 3	Effect of age-specific migration on all-cause mortality for different confounding adjustment sets/ procedures by sex.	Additional	24

Liliana Paloma Rojas-Saunero, Saima Hilal, Eleanor J. Murray, Roger W. Logan, Mohammad Arfan Ikram, Sonja A. Swanson. "Hypothetical blood-pressure-lowering interventions and risk of stroke and dementia." *European journal of epidemiology*, Volume 36, Issue 1, January 2021, Pages 69-79, https://doi.org/10.1007/s10654-020-00694-5

- Sample size: 4,930
- Correction for multiple testing: no
- Protocol referenced: no.

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Primary analysis in full sample for outcome 'stroke' (counted one of two effect measures)	Primary	9
Table 3	Primary analysis in full sample for outcome 'dementia' (counted one of two effect measures)	Primary	9
Table 4	Subgroup analyses in full sample for outcomes 'stroke' and 'dementia' (counted one of two effect measures)	Additional	Counted in supplementary materials
Supplementary material			
Table 4	Sensitivity analysis (death as censored) for outcome 'stroke'.	Sensitivity	9
Table 5	Sensitivity analysis (composite outcome) for outcome 'stroke'.	Sensitivity	9
Table 6	Subgroup analysis (age under 65 years) for outcome 'stroke'.	Additional	9
Table 7	Subgroup analysis (age above 65 years, under 80 years) for outcome 'stroke'.	Additional	9
Table 8	Subgroup analysis (women) for outcome 'stroke'.	Additional	9
Table 9	Subgroup analysis (men) for outcome 'stroke'.	Additional	9
Table 10	Subgroup analysis (without hypertension medication at baseline) for outcome 'stroke'.	Additional	9
Table 11	Subgroup analysis (no history of heart disease at baseline) for outcome 'stroke'.	Additional	9
Table 12	Sensitivity analysis (death as censored) for outcome 'dementia'.	Sensitivity	9
Table 13	Sensitivity analysis (composite outcome) for outcome 'dementia'.	Sensitivity	9
Table 14	Subgroup analysis (age under 65 years) for outcome 'dementia'.	Additional	9
Table 15	Subgroup analysis (age above 65 years, under 80 years) for outcome 'dementia'.	Additional	9
Table 16	Subgroup analysis (women) for outcome 'dementia'.	Additional	9
Table 17	Subgroup analysis (men) for outcome 'dementia'.	Additional	9
Table 18	Subgroup analysis (without hypertension medication at baseline) for outcome 'dementia'.	Additional	9
Table 19	Subgroup analysis (free of heart disease at baseline) for outcome 'dementia'.	Additional	9

Christoph Mueller, Christeena John, Gayan Perera, Dag Aarsland, Clive Ballard, Robert Stewart, "Antipsychotic use in dementia: the relationship between neuropsychiatric symptom profiles and adverse outcomes", *European journal of epidemiology*, Volume 36, Issue 1, January 2021, Pages 89-101, https://doi.org/10.1007/s10654-020-00643-2

- Sample size: 10,106
- Correction for multiple testing: no ("We elected to increase the error rate from 5% to 10% and considered interactions with $p < 0.1$ as true interactions.")
- Protocol referenced: no, only for data platform ("has received ethical approval as an anonymized data resource (Oxford Research Ethics Committee C, reference 08/H0606/71+5)").

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Main effect measure for interaction exposure group on four outcomes, using three different confounder specification in full sample.	Primary	48
Table 3	Subgroup effects of antipsychotic use on the four outcomes in strata of dementia types.	Additional	48
Table 4	Subgroup effects of antipsychotic use on the four outcomes in strata of antipsychotic drug types.	Additional	36
Supplementary file			
Table 1	Subgroup effects of antipsychotic use on the four outcomes in strata of antipsychotic drug types for two different confounder specifications.	Additional	72
Table 2	Effect measure for interaction exposure group on four outcomes interacted with symptom profile.	Additional	32
Table 3	Effect measure for dementia subtype on four outcomes interacted with diagnosis presence.	Additional	32

Sara Hallum, Marianne Antonius Jakobsen, Thomas Alexander Gerds, Anja Pinborg, Anne Tjønneland, Mads Kamper-Jørgensen, Male origin microchimerism and ovarian cancer, *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 87–94, https://doi.org/10.1093/ije/dyaa019

- Sample size: 700.
- Correction for multiple testing: no.
- Protocol referenced: yes, but we did not find a publicly available version ("The study was approved by the Danish Committee on Health Research Ethics (H-16021411) and the Danish Data Protection Agency through the joint notification of the Faculty of Health and Medical Sciences at University of Copenhagen").

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Main effect measure for male origin microchimerism detection on ovarian cancer incidence.	Primary	1
	Sensitivity analyses with different modelling of exposure (4 levels of exposure).	Sensitivity	3
Table 3	Interaction of male origin microchimerism detection and hormonal exposure status on ovarian cancer incidence.	Additional*	3
Supplementary file			
Table 2	Period-specific hazard rate of male origin microchimerism detection on ovarian cancer incidence.	Sensitivity	3
Table 3	Interaction of male origin microchimerism detection and age on ovarian cancer incidence.	Additional	3

* Quote: "we explored possible effect modification by hormonal exposure on the association between male origin microchimerism and ovarian cancer risk"

Ann Von Holle, Katie M O'Brien, Dale P Sandler, Clarice R Weinberg, "Evidence for familial clustering in breast cancer age of onset", *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 97–104, https://doi.org/10.1093/ije/dyaa201

- Sample size: 23,087.
- Correction for multiple testing: no.
- Protocol referenced: yes, but we did not find a publicly available version ("This study was reviewed and overseen by the institutional review boards of the National Institute of Environmental Health Sciences and the Copernicus Group").

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Main effect measure for proximity of a participant's time-dependent age to her proband sister's age at breast cancer diagnosis on breast cancer.	Primary	10
	Main effect measure for proximity of a participant's time-dependent age to her proband sister's age at breast cancer diagnosis on breast cancer, adjusted for confounding (described as sensitivity analysis).	Primary	10
Intext	Sensitivity analysis, included a covariate indicating whether the participant's current age was within 2 years of the proband's age at diagnosis	Sensitivity	1
	Sensitivity analysis in restricted sample of main effect measure for proximity of a participant's time-dependent age to her proband sister's age at breast cancer diagnosis on breast cancer.	Sensitivity	1
Supplementary file			
Table 1	Sensitivity analysis, Cochran-Armitage trend tests to evaluate there was earlier detection when participant age at diagnosis was closer to the proband age at diagnosis.	Sensitivity analysis (p for trend; not counted)	
Table 2	Sensitivity analysis, Cochran-Armitage trend tests to evaluate there was earlier detection when participant age at diagnosis was closer to the proband age at diagnosis.	Sensitivity analysis (p for trend; not counted)	

Pierre-Antoine Dugué, Allison M Hodge, Ee Ming Wong, JiHoon E Joo, Chol-Hee Jung, John L Hopper, Dallas R English, Graham G Giles, Roger L Milne, Melissa C Southey, "Methylation marks of prenatal exposure to maternal smoking and risk of cancer in adulthood", *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 105–115, https://doi.org/10.1093/ije/dyaa210

- Sample size: 7,258.
- Correction for multiple testing: no.
- Protocol referenced: no.

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Figure 1	Main effect measure maternal smoking methylation scores with risk of 9 types of cancer, confounding structure of model 2.	Primary	45
Figure 2	Main effect measure maternal smoking methylation scores with risk of urothelial cancer, 5 different confounding structures (model 2 counted for figure 1 only).	Primary	20
Figure 3	Main effect measure maternal smoking methylation scores with risk of lung cancer (negative control), 5 different confounding structures (model 2 counted for figure 1 only). (First mentioning of lung cancer as negative outcome control is in the results section).	Primary	20
Table 3	Effect of personal smoking methylation scores on risk of lung cancer and urothelial cancer, 2 different confounding structures. (First mentioning of personal smoking as positive exposure control is in the results section).	Additional	12
Supplementary file			
Table 2	Main effect measure maternal smoking methylation scores with risk of 9 types of cancer, confounding structure of model 2.	Identical to Figure 1.	
Table 3	Main effect measure maternal smoking methylation scores with risk of urothelial cancer, 5 different confounding structures.	Identical to Figure 2.	
Table 4	Main effect measure maternal smoking methylation scores with risk of lung cancer (negative control), 5 different confounding structures.	Identical to Figure 3.	
Table 5	Sensitivity analysis, main effect measure maternal smoking methylation scores with risk of urothelial cancer, stratified by exposure sample type.	Sensitivity analysis	15
Table 6	Sensitivity analysis, main effect measure maternal smoking methylation scores with risk of urothelial cancer, stratified by sample collection period.	Sensitivity analysis	10
Table 6	Sensitivity analysis, main effect measure maternal smoking methylation scores with risk of urothelial cancer, in restricted sample.	Sensitivity analysis	5

Matthew T Keys, Miquel Serra-Burriel, Natalia Martínez-Lizaga, Maria Pellisé, Francesc Balaguer, Ariadna Sánchez, Enrique Bernal-Delgado, Antoni Castells, Population-based organized screening by faecal immunochemical testing and colorectal cancer mortality: a natural experiment, *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 143–155, https://doi.org/10.1093/ije/dyaa166

- Sample size: 47 provinces (= unit of analysis).
- Correction for multiple testing: no.
- Protocol referenced: yes.
    - Quote: "This study was registered with International Standard Randomised Controlled Trial Number 1768442".
      Available from: https://doi.org/10.1186/ISRCTN11768442

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Figure 2	Difference-in-difference estimates of population-based screening program on colorectal cancer incidence, for two correlated outcomes.	Primary	Counted in supplementary materials
Figure 3	Synthetic control estimates of population-based screening program on colorectal cancer incidence, for two correlated outcomes.	Primary	Counted in supplementary materials
Table 2	Difference-in-differences and synthetic control models overall and stratified by gender	Primary and additional*	Counted in supplementary materials
Figure 4	Synthetic control estimates of population-based screening program on colorectal cancer incidence, for two correlated outcomes, in different age-band than primary analysis.	Sensitivity	Counted in supplementary materials
Figure 5	Synthetic control estimates of population-based screening program on 10 other outcomes, negative controls.	Sensitivity	Counted in supplementary materials
Supplementary file			
Table S3.1.1.	Difference-in-difference estimates of population-based screening program on colorectal cancer incidence, for two correlated outcomes.	Primary	26
Table S3.1.2.	Difference-in-difference estimates of population-based screening program on colorectal cancer incidence, for two correlated outcomes, in men.	Additional*	26
Table S3.1.3.	Difference-in-difference estimates of population-based screening program on colorectal cancer incidence, for two correlated outcomes, in women.	Additional*	26
Table S3.1.4.	Synthetic control estimates of population-based screening program on colorectal cancer incidence, for two correlated outcomes.	Primary	14
Table S3.1.5.	Synthetic control estimates of population-based screening program on colorectal cancer	Additional*	14

	incidence, for two correlated outcomes, in men.		
Table S3.1.6.	Synthetic control estimates of population-based screening program on colorectal cancer incidence, for two correlated outcomes, in women.	Additional*	14
Table S3.1.7.	Synthetic control estimates of population-based screening program on colorectal cancer incidence, for two correlated outcomes, in different age-band than primary analysis.	Sensitivity	14
Table S3.1.8.	Synthetic control estimates of population-based screening program on colorectal cancer incidence, for two correlated outcomes, in different age-band than primary analysis.	Sensitivity	14
Table S3.1.9.	Synthetic control estimates of population-based screening program on 10 other outcomes, negative controls.	Sensitivity	60

* Prespecified hypothesis in ISRCTN: "Has the implementation of colorectal cancer screening in Spanish provinces had a differential effect by gender?"

Yoshihito Goto, Marie Mandai, Takeo Nakayama, Shin Yamazaki, Shoji F Nakayama, Tomohiko Isobe, Tosiya Sato, Hiroshi Nitta, "Association of prenatal maternal blood lead levels with birth outcomes in the Japan Environment and Children's Study (JECS): a nationwide birth cohort study", *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 156–164, https://doi.org/10.1093/ije/dyaa162

- Sample size: 16,243.
- Correction for multiple testing: no.
- Protocol referenced: no.

	Description	Analysis type (primary/ sensitivity/ additional)	Number of analyses
Main text			
Table 3	Main effect measure between maternal prenatal blood lead levels and seven correlated infant birth outcomes.	Primary	7
	Main effect measure between maternal prenatal blood lead levels and seven correlated infant birth outcomes, with different exposure operationalization.	Sensitivity	14
In text	Quadratic spline operationalization of exposure mentioned but not presented.		
Supplementary file			
Table 2	Sex-specific effect of maternal prenatal blood lead levels on birthweight.	Additional*	6
	Association of all confounders with birthweight, for three operationalizations of exposure.	Additional	36
Table 3	Sex-specific effect of maternal prenatal blood lead levels on small for gestational age births.	Additional*	6
	Association of all confounders with small for gestational age births, for three operationalizations of exposure.	Additional	36
Table 4	Sex-specific effect of maternal prenatal blood lead levels on low birthweight.	Additional*	6
	Association of all confounders with low birthweight, for three operationalizations of exposure.	Additional	36
Table 5	Sex-specific effect of maternal prenatal blood lead levels on head circumference.	Additional*	6
	Association of all confounders with head circumference, for three operationalizations of exposure.	Additional	36
Table 6	Sex-specific effect of maternal prenatal blood lead levels on birth length.	Additional*	6
	Association of all confounders with birth length, for three operationalizations of exposure.	Additional	36
Table 7	Sex-specific effect of maternal prenatal blood lead levels on pregnancy duration.	Additional*	6
	Association of all confounders with pregnancy duration, for three operationalizations of exposure.	Additional	36

Table 8	Sex-specific effect of maternal prenatal blood lead levels on preterm delivery.	Additional*	6
	Association of all confounders with preterm delivery, for three operationalizations of exposure.	Additional	36
Table 9	Sensitivity analysis with less restricted exclusion criteria, main effect measure between maternal prenatal blood lead levels and seven correlated infant birth outcomes, for three exposure operationalizations.	Sensitivity	21
Table 10	Sensitivity analysis, main effect measure between maternal prenatal blood lead levels and age- and sex-standardized birthweight, for three exposure operationalizations.	Sensitivity	3
Table 11	Further confounding adjustment for maternal prenatal blood lead levels and infant birthweight.	Primary	3
	Association of all confounders with birthweight, for three operationalizations of exposure.	Additional	39
Table 12	Sensitivity analysis with more restricted exclusion criteria for maternal prenatal blood lead levels and infant birthweight.	Sensitivity	3
	Association of all confounders with birthweight, for three operationalizations of exposure.	Additional	39
Table 13	Further confounding adjustment for maternal prenatal blood lead levels and infant birthweight.	Primary	3
	Association of all confounders with birthweight, for three operationalizations of exposure.	Additional	39

* Quote: “Adding to the original statistical analysis plan, we assessed the effect modification by infant sex for all birth outcomes, using stratification and modelling of interaction terms.”

Samrawit F Yisahak, Stefanie N Hinkle, Sunni L Mumford, Mengying Li, Victoria C Andriessen, Katherine L Grantz, Cuilin Zhang, Jagteshwar Grewal, "Vegetarian diets during pregnancy, and maternal and neonatal outcomes", *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 165–178, https://doi.org/10.1093/ije/dyaa200

- Sample size: 1,633 (1,596 for some analyses).
- Correction for multiple testing: no.
- Protocol referenced: no.
    - Protocol available for entire cohort, accessible at https://clinicaltrials.gov/ct2/show/NCT00912132, but this does not contain information on the design of this specific study.

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Main effect measure for maternal vegetarianism during pregnancy on 16 correlated neonatal outcomes.	Primary	16
	Main effect measure for maternal vegetarianism during pregnancy on 16 correlated neonatal outcomes, stratified by type of vegetarianism.	Additional	48
Table 3	Main effect measure for maternal vegetarianism during pregnancy on 11 correlated maternal outcomes.	Primary	11
	Main effect measure for maternal vegetarianism during pregnancy on 11 correlated maternal outcomes, stratified by type of vegetarianism.	Additional	33
In text	Sensitivity analyses for sustained effects.	Sensitivity	2

Claire E Margerison, Amber L Pearson, Zihan Lin, Jonnell Sanciangco, "Changes in residential greenness between pregnancies and birth outcomes: longitudinal evidence from Michigan births 1990—2012", *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 190–198, https://doi.org/10.1093/ije/dyaa158

- Sample size: 1,633 (1,596 for some analyses).
- Correction for multiple testing: no.
- Protocol referenced: yes, but we did not find a publicly available version ("Health data for this study were approved by Michigan State University's Institutional Review Board and the Michigan Department of Health and Human Services (MDHHS) (#201505-08-XA)").

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Main effect of greenness on pre-term birth, for four different confounding adjustment sets.	Primary	4
	Confounder-outcome associations.	Additional	26
Table 3	Main effect of greenness on birth weight, for four different confounding adjustment sets.	Primary	4
	Confounder-outcome associations.	Additional	26
Table 4	Within-mother between greenness on pre-term firth and birthweight in mothers with 2 or 3 births in the dataset	Primary	4
Supplementary file			
Table 1	Robustness checks for preterm birth.	Sensititivy	4
Table 2	Robustness checks for birthweight.	Sensititivy	4
Table 3	Sensitivity analyses extra exclusion criterion for both outcomes.	Sensitivity	8

Wing Ching Chan, Iona Y Millwood, Christiana Kartsonaki, Huaidong Du, Yu Guo, Yiping Chen, Zheng Bian, Robin G Walters, Jun Lv, Pan He, Chen Hu, Liming Li, Ling Yang, Zhengming Chen, for the China Kadoorie Biobank (CKB) Collaborative Group, "Spicy food consumption and risk of gastrointestinal-tract cancers: findings from the China Kadoorie Biobank", *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 199–211, https://doi.org/10.1093/ije/dyaa275

- Sample size: 510,101.
- Correction for multiple testing: no.
- Protocol referenced: no.

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Main effect of spicy food consumption frequency on four correlated gastrointestinal cancers, adjusted for three different confounding adjustment sets.	Primary	48
Figure 1	Main effect of spicy food consumption frequency on three correlated gastrointestinal cancers, stratified by smoking status.	Additional	18
Figure 2	Main effect of spicy food consumption frequency on three correlated gastrointestinal cancers, stratified by drinking status.	Additional	18
Figure 3	Main effect of spicy food consumption frequency on three correlated gastrointestinal cancers, in participants who never smoked or drank regularly.	Sensitivity	9
Figure 4	Effects of 20 different subgroups of type of spicy food consumption on three correlated gastrointestinal cancers, in regular consumers of spicy food.	Additional	60
Supplementary file			
Table 4	Main effect of spicy food consumption frequency on subtypes of the outcome.	Primary*	15
Table 5	Main effect of spicy food consumption frequency on mortality of the primary outcome GI cancers.	Primary	12
Table 6	Main effect of spicy food consumption frequency on three correlated gastrointestinal cancers, stratified by region.	Additional	6
Table 7	Main effect of spicy food consumption frequency on four correlated gastrointestinal cancers, with additional confounding adjustment.	Primary	36
Table 8	Main effect of spicy food consumption frequency on four correlated gastrointestinal cancers, with additional confounding adjustment.	Primary	9
Figure 2	Main effect of spicy food consumption frequency on three correlated gastrointestinal cancers, stratified by sex and smoking status.	Additional	27
Figure 3	Main effect of spicy food consumption frequency on three correlated gastrointestinal cancers, stratified by sex and drinking status.	Additional	27

Figure 4	Main effect of spicy food consumption frequency on three correlated gastrointestinal cancers, excluding two regions.	Sensitivity	9
Figure 5	Main effect of spicy food consumption frequency on three correlated gastrointestinal cancers, excluding prior GI diseases.	Sensitivity	18

* Quote: "We also separately explored associations with cancer subtypes and sub-sites, using the preliminary data from event adjudication."

Aurora Perez-Cornago, Francesca L Crowe, Paul N Appleby, Kathryn E Bradbury, Angela M Wood, Marianne Uhre Jakobsen, Laura Johnson, Carlotta Sacerdote, Marinka Steur, Elisabete Weiderpass, Anne Mette L Würtz, Tilman Kühn, Verena Katzke, Antonia Trichopoulou, Anna Karakatsani, Carlo La Vecchia, Giovanna Masala, Rosario Tumino, Salvatore Panico, Ivonne Sluijs, Guri Skeie, Liher Imaz, Dafina Petrova, J Ramón Quirós, Sandra Milena Colorado Yohar, Paula Jakszyn, Olle Melander, Emily Sonestedt, Jonas Andersson, Maria Wennberg, Dagfinn Aune, Elio Riboli, Matthias B Schulze, Emanuele di Angelantonio, Nicholas J Wareham, John Danesh, Nita G Forouhi, Adam S Butterworth, Timothy J Key, "Plant foods, dietary fibre and risk of ischaemic heart disease in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort", *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 212–222, https://doi.org/10.1093/ije/dyaa155

- Sample size: 490,311 (16,425 for exploratory biomarker analyses).
- Correction for multiple testing: no.
- Protocol referenced: yes, but we did not find a publicly available version ("All participants gave written informed consent and the study protocol was approved by ethical review boards of all institutions where participants were recruited").

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Main effect of portions per day of fruit and vegetables on first fatal IHD or non-fatal MI.	Primary	10
Figure 1	Main effect of increment in statistically calibrated intake of plant foods and dietary fibre on first fatal IHD or non-fatal MI.	Primary	18
Supplementary file			
Table 2	Main effect of portions per day of fruit and vegetables on first fatal IHD or non-fatal MI by overall fifths and non-calibrated increments of observed intake (different operationalization of exposure).	Sensitivity	90
Table 3	Main effect of increment in statistically calibrated intake of plant foods and dietary fibre on first fatal IHD or non-fatal MI, with further confounding adjustment.	Primary	36
Table 4	Main effect of increment in statistically calibrated intake of plant foods and dietary fibre on first fatal IHD or non-fatal MI, with exclusion first 4 years of follow-up.	Sensitivity	18
Table 5	Effect of increment in statistically calibrated intake of plant foods and dietary fibre on first fatal IHD or non-fatal MI, by smoking status.	Additional	54
Table 6	Effect of increment in statistically calibrated intake of plant foods and dietary fibre on first fatal IHD or non-fatal MI, by age at recruitment.	Additional	54
Table 7	Effect of increment in statistically calibrated intake of plant foods and dietary fibre on first fatal IHD or non-fatal MI, by sex.	Additional	36
Table 8	Effect of increment in statistically calibrated intake of plant foods and dietary fibre on first fatal IHD or non-fatal MI, by BMI status.	Additional	54

Table 9	Effect of increment in statistically calibrated intake of plant foods and dietary fibre on first fatal IHD or non-fatal MI, by European region.	Additional	54
Table 10	Effect of increment in statistically calibrated intake of plant foods and dietary fibre on first fatal IHD or non-fatal MI, by prior disease status.	Additional	36
Table 11	Exploration of mediation by biomarkers in non-cases.	Additional*	205

* Quote: "To explore whether the intakes of these exposures are associated with major established physiological IHD risk factors at baseline, we examined the associations of food intakes with BMI, systolic and diastolic blood pressure, total cholesterol, high-density lipoprotein (HDL) cholesterol, non-HDL cholesterol and glycated haemoglobin (HbA1c) (restricted to participants with these measurements in the sub-cohort), calculating mean levels of these biomarkers in each fifth of dietary intake of the exposure of interest, with adjustment for age, sex and EPIC centre."

Victor W Zhong, Norrina B Allen, Philip Greenland, Mercedes R Carnethon, Hongyan Ning, John T Wilkins, Donald M Lloyd-Jones, Linda Van Horn, "Protein foods from animal sources, incident cardiovascular disease and all-cause mortality: a substitution analysis", *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 223–233, https://doi.org/10.1093/ije/dyaa205

- Sample size: 29,682.
- Correction for multiple testing: no.
- Protocol referenced: no.

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Main effects of substituting one animal protein food with another protein food on incident cardiovascular disease and all-cause mortality, under two different operationalizations of exposure.	Primary	100
Table 3	Same analyses, but different effect measure.		
Table 4	Effects of simultaneously substituting two or more animal protein foods with other protein foods, selective examples.	Additional*	18

*Quote: "Several examples selected based on the available scientific evidence and individual-food substitution results of this study were presented to evaluate the hypothesis that substituting two or more unfavourable foods with favourable foods was associated with lower risks of CVD and all-cause mortality compared with substituting one unfavourable food with one favourable food."

Adam Mitchell, Tove Fall, Håkan Melhus, Alicja Wolk, Karl Michaëlsson, Liisa Byberg, "Is the effect of Mediterranean diet on hip fracture mediated through type 2 diabetes mellitus and body mass index?", *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 234–244, https://doi.org/10.1093/ije/dyaa239

- Sample size: 50,755.
- Correction for multiple testing: no.
- Protocol referenced: yes, but we did not find a publicly available version ("The research was performed in accordance with the Declaration of Helsinki and was approved by the regional ethics review boards at Uppsala University, Uppsala, Sweden, and Karolinska Institutet, Stockholm, Sweden").

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 3	Direct effects of Mediterranean diet on hip fracture with respect to T2DM as a mediator, in 4 models for two exposure categories.	Primary	8
Table 4	Component effects from the natural effects model (direct and indirect effects), for two exposure categories.	Primary	6
Supplementary file			
Table 1	Numerical values are different from main text but are described as the same analysis as Table 3.		
Table 2	Interaction terms for auxiliary variables in natural effect model.	Additional	8

Angelo Campanella, Giovanni Misciagna, Antonella Mirizzi, Maria Gabriella Caruso, Caterina Bonfiglio, Laura R Aballay, Liciana Vas de Arruda Silveira, Antonella Bianco, Isabella Franco, Paolo Sorino, Claudia Buongiorno, Anna Maria Cisternino, Maria Notarnicola, Vito M B Guerra, Alberto R Osella, "The effect of the Mediterranean Diet on lifespan: a treatment-effect survival analysis of a population-based prospective cohort study in Southern Italy", *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 245–255, https://doi.org/10.1093/ije/dyaa222

- Sample size: 4,896.
- Correction for multiple testing: no.
- Protocol referenced: a protocol is mentioned, but it is unclear whether it applies to the conduct of this study specifically, and we could not find a publicly available version ("All procedures performed were in accordance with the ethical standards of the institutional research committee [IRCCS Saverio de Bellis Research and Ethical Committee approval for the MICOL Study (DDG-CE-347/1984; DDG-CE-453/1991; DDG-CE-589/2004; DDG-CE 782/2013)]; and the NUTRIHEP Study in 2005 and 2014 (DDG-CE-502/2005; DDG-CE-792/2014) and with the 1964 Helsinki declaration.")

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 3	Effect of adherence to Mediterranean diet on lifespan, for two levels of adherence.	Primary	2
Supplementary file			
Table 4	13 Different propensity score models for two exposure levels. Note: unclear which model is used in main text, so not accounted for in count.	Primary	26
Table 5	Outcome model effects for the 13 different propensity score models for two exposure levels.	Primary	26

Caroline dos Santos Costa, Maria Cecília Formoso Assunção, Christian Loret de Mola, Juliane de Souza Cardoso, Alicia Matijasevich, Aluísio J D Barros, Iná S Santos, "Role of ultra-processed food in fat mass index between 6 and 11 years of age: a cohort study", *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 256–265, https://doi.org/10.1093/ije/dyaa141

- Sample size: 4,231.
- Correction for multiple testing: no.
- Protocol referenced: a protocol is mentioned, but it is unclear whether it applies to the conduct of this study specifically, and we could not find a publicly available version ("The Ethics Committee of the Faculty of Medicine of the Federal University of Pelotas approved the perinatal study and the 6- and 11-year follow-ups (of. 4.06.01.116, of. 35/10 and of. 889.753, respectively").

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 4	Effect of consumption of ultra-processed foods on fat mass index.	Primary	3
	Effect of consumption of ultra-processed foods on fat mass index, by sex.	Additional*	6
Figure 1	Direct and indirect effect of ultra-processed food consumption on change in fat mass index.	Primary	2
	Direct and indirect effect of ultra-processed food consumption on change in fat mass index, by sex.	Additional*	4
Intext	Interaction between consumption of ultra-processed foods and sex, age at menarche (for girls) and level of physical activity was tested but not presented.		
Supplementary file			
Table 2	Effect of consumption of ultra-processed foods on body mass index (correlated outcome), for various exposure definitions.	Primary	8
	Effect of consumption of ultra-processed foods on body mass index (correlated outcome), for various exposure definitions, by sex.	Additional*	16
Table 3	Effect of consumption of ultra-processed foods on fat mass index, for different exposure definitions.	Sensitivity	6
	Effect of consumption of ultra-processed foods on fat mass index, for different exposure definitions, by sex.	Additional*	12

* Quote: "For theoretical reasons (differences between boys and girls during childhood and adolescence related to body composition),[34] all the analyses were stratified by sex."

Mahdi Nalini, Masoud Khoshnia, Farin Kamangar, Maryam Sharafkhah, Hossein Poustchi, Akram Pourshams, Gholamreza Roshandel, Samad Gharavi, Mahdi Zahedi, Alireza Norouzi, Masoud Sotoudeh, Arash Nikmanesh, Paul Brennan, Paolo Boffetta, Sanford M Dawsey, Christian C Abnet, Reza Malekzadeh, Arash Etemadi, "Joint effect of diabetes and opiate use on all-cause and cause-specific mortality: the Golestan cohort study", *International Journal of Epidemiology*, Volume 50, Issue 1, February 2021, Pages 314–324, https://doi.org/10.1093/ije/dyaa126

Correction: funding source was omitted from original version.

- Sample size: 50,045.
- Correction for multiple testing: no.
- Protocol referenced: a protocol is mentioned, but it is unclear whether it applies to the conduct of this study specifically, and we could not find a publicly available version ("The Golestan Cohort Study protocol was approved by the ethical review committees of the Digestive Disease Research Institute of Tehran University of Medical Sciences, the US National Cancer Institute and the International Agency for Research on Cancer").

	Description	**Analysis type (primary/ sensitivity/ additional)**	**Number of analyses**
Main text			
Table 2	Joint effect of diabetes and opiate use on all-cause mortality and cardiovascular/ cancer/ other mortality.	Primary	12
Table 3	Sensitivity analyses with stricter exclusion criteria, stratified for diabetes status.	Sensitivity	10
	Subgroup analyses for the effect of opiate use on mortality, stratified for diabetes status.	Additional	30
Intext	Effect of opiate use before diabetes diagnosis on mortality, in full cohort and diabetic subgroup. (not clear from the text how these cohorts differ)	Additional	2

* For one subgroup, an explanation was given: "To restrict the confounding effects of cigarette smoking, we studied the associations stratified by the history of tobacco use." (additional to confounding adjustment)