Supplementary Online Content

Ospina-Romero M, Glymour MM, Hayes-Larson E, et al. Association between Alzheimer disease and cancer with evaluation of study biases: a systematic review and meta-analysis incorporating evaluation of study biases. *JAMA Netw Open*. 2020;3(11):e2025515. doi:10.1001/jamanetworkopen.2020.25515

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This supplementary material has been provided by the authors to give readers additional information about their work.
eFigure 1. PRISMA Flow Diagram of Screening and Inclusion Process. Studies considered ineligible cancer type were studies that investigated one type of cancer and this cancer was not breast, prostate, colorectal, or non-melanoma skin cancer.
| Method of ascertainment | Defined in the analysis as: | Study |
|-------------------------|----------------------------|-------|
| Self-reported cancer    | Three groups: prevalent, time-varying incident cancer, and no cancer during follow-up. | White 2013 |
|                         | Two groups: Cancer (prevalent and incident cases) and no cancer. Cancer variable was updated to include new cases during follow-up. | Driver 2012 |
|                         | Two groups: Prevalent cancer and no cancer at baseline | Roe 2005, Roe 2010 |
|                         | Two groups: history of cancer or no history of cancer at the time of AD diagnosis | Nudelman 2014, Realmuto 2012 |
| Linking data from cancer registries or surveillance research programs (e.g. Surveillance, Epidemiology, and End Result (SEER) program) | Three groups: prevalent cancer, time-varying incident cancer, and no cancer. Prevalent cancer cases assigned to incident cancer group if they had a new malignancy during follow-up. | Bowles 2017 |
|                         | Two groups: Cancer (prevalent and incident combined) and no cancer. Cancer variable was updated to include new cases during follow-up. | Driver 2012 |
|                         | Multiple approaches to define cancer groups. Authors aimed to demonstrate biases introduced by these analytical approaches. | Hanson 2017 |
|                         | Two groups: Incident cancer and random sample of cancer-free controls. | Musicco 2013 |
| Medical claims (hospitals, ambulatory centers, procedures) | New cancer diagnosis, recurrent primary or metastatic cancer (Roe 2010). | Frain 2017, Roe 2010, Chung 2016 |
| Pharmacy claims | First dispensed use of androgen deprivation therapy for prostate cancer vs no cancer controls. | Ng 2018 |
|-----------------|-----------------------------------------------------------------------------------------------|---------|
|                 |                                                                                              | Wu 2011 |
|                 |                                                                                              | Sun 2016|
|                 |                                                                                              | Smith 2018 |
**eTable 2. Cancer Types Reported in Studies in the Category “All Cancer Types”**

| Study               | Cancer types                                                                 |
|---------------------|------------------------------------------------------------------------------|
| Bowles et al. 2017  | Oral cavity/pharynx, colon and rectum, other digestive system, lungs and bronchus, soft tissue including heart, skin, breast, female genital system, prostate, urinary system, lymphoma. |
| Driver et al. 2012  | Head and neck, esophagus or stomach, colon, rectum, pancreas, lung, hematological, connective tissue, melanoma, breast, uterus and endometrium, cervix, ovary, prostate, kidney, brain lymph nodes, other. |
| Frain et al. 2017   | Prostate, lung, colorectal, breast, bladder, melanoma, lymphoma, leukemia, renal, myeloma, esophagus, pancreas, stomach, other |
| Freedman et al. 2016| Oral cavity, esophageal, stomach, small intestine, colon, rectum, pancreas, larynx, lung and bronchus, melanoma, breast, cervix, uterus, ovary, prostate, bladder, kidney/renal pelvis, thyroid, leukemia, |
| Hanson et al. 2017  | Non-malignant neoplasms and non-melanoma skin cancer were excluded.          |
| Musicco et al. 2013 | Breast, prostate, colon, lung, urinary bladder, gastric, metastases with/without unspecified primary tumor, rectal, liver, pancreas, kidney, lymphomas, uterine body, leukemias, multiple myeloma, brain, biliary system, larynx, ovary, other. |
| Nudelman et al. 2014| Breast, female other types, gastrointestinal, bladder, renal, oral cavity, glandular, leukemia, lymphoma, melanoma, non-melanoma skin cancer, prostate, male other types, other. |
| Ording et al 2020   | Bladder, brain, breast, colon, kidney, leukemia, lung, melanoma skin cancer, non-melanoma skin cancer, pancreatic, prostate, others. |
| Prinelli et al. 2018| Included cancer sites/types were not reported                                |
| Realmuto et al 2012 | Prostate, intestines, ovary, uterus, breast, skin, central nervous system, others |
| Roe et al. 2005     | Included cancer sites/types were not reported                                |
| Roe et al 2010      | Included cancer sites/types were not reported                                |
| Sun et al. 2020     | Oral cavity, salivary gland, esophageal, stomach, small intestine, colon, rectum, anus, liver, pancreas, nose, lung, breast, cervix, endometrium, ovary, other female genitals, prostate, testis, other male genitals, kidney, urinary bladder, melanoma, skin, eye, nervous system, thyroid gland, endocrine glands, connective tissue, non-Hodgkin lymphoma, Hodgkin lymphoma, myeloma, leukemia |
### eTable 3. Overview of Methodological Study Biases

| Types of Methodological Study Biases | Bias from handling of potential confounders | Diagnostic bias | Competing risks | Survival bias and related biases |
|-------------------------------------|---------------------------------------------|----------------|----------------|---------------------------------|
|                                     | Missing adjustment for age, sex, or education | Adjusted for factors influenced by cancer | Cognitively impaired individuals not excluded at baseline | Cancer status might influence AD diagnosis | Estimated cumulative risks (as opposed to incidence or hazard rates) | Prevalent cancers not separated from incident cancers | Cancer type that raises subsequent mortality risk | High % of missing data | Restrictive inclusion and exclusion criteria |
| **Meta-regressions**<sup>a</sup> |                               |               |                |                                 |                                 |                                 |                                 |                                 |                                 |
| Pooled lnHR (95% CI) in studies without the bias | -0.15 (-0.34, 0.04) | -0.15 (-0.28, -0.02) | -0.09 (-0.22, 0.03) | -0.32 (-0.54, -0.10) | -0.13 (-0.26, 0.00) | -0.09 (-0.20, 0.02) | -0.19 (-0.57, 0.20) | -0.10 (-0.22, 0.01) | -0.12 (-0.24, 0.00) |
| Difference in lnHR (95% CI) for studies with the bias | 0.04 (-0.20, 0.29) | 0.13 (-0.13, 0.39) | -0.14 (-0.45, 0.16) | 0.26 (0.01, 0.52) | 0.09 (-0.32, 0.50) | -0.34 (-0.71, 0.03) | 0.07 (-0.33, 0.48) | -0.46 (-1.13, 0.22) | -0.01 (-0.92, 0.90) |
| **R<sup>2</sup>** | 1.6% | 32.4% | 22.1% | 16.7% | 6.7% | 21.1% | 5.5% | 16.3% | 6.2% |

### Studies of all cancer types

| Studies of all cancer types | Bowles et al. 2017 | Driver et al. 2012 | Frain et al. 2017 | Freedman et al. 2016 | Hanson et al. 2017<sup>b</sup> | Musicco et al. 2013 | Nudelman et al. 2014 | Ording et al. 2020 | Prinelli et al. 2018 | Realmuto et al. 2012 | Roe et al. 2005 | Roe et al. 2010 | Sadahiro et al. 2019 | Sun et al. 2020 |
|----------------------------|-------------------|-------------------|-------------------|-----------------------|----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|----------------|----------------|-------------------|----------------|

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## Studies of prostate cancer

| Study                  | Effect Estimate | Meta-regression Adjusted for Study Design |
|------------------------|-----------------|-------------------------------------------|
| Chung et al. 2016      |                 |                                           |
| Ng et al. 2018         |                 |                                           |
| Robinson et al. 2018   |                 |                                           |
| Shahinian et al. 2006  |                 |                                           |
| Smith et al. 2018      |                 |                                           |

## Studies of nonmelanoma skin cancer

| Study                  | Effect Estimate | Meta-regression Adjusted for Study Design |
|------------------------|-----------------|-------------------------------------------|
| Schmidt et al. 2017    |                 |                                           |
| White et al. 2013      |                 |                                           |
| Wu et al. 2011         |                 |                                           |

## Studies of breast cancer

| Study                  | Effect Estimate | Meta-regression Adjusted for Study Design |
|------------------------|-----------------|-------------------------------------------|
| Sun et al. 2016        |                 |                                           |

*Meta-regressions additionally adjusted for study design (case-control vs cohort) as a covariate

*Studies not included in meta-regression because only age-stratified measures of association were reported

*Study not included in meta-regression to prevent double counting people from Denmark

*Case-control studies in which AD status might influence cancer ascertainment

**Estimated HR from Cox regression with Lunn-McNeil approach that incorporates competing risks

Abbreviations: AD, Alzheimer's disease; CI, Confidence interval
eFigure 2. Funnel Plot of Study Standard Error (a Function of Sample Size) by lnHR for Longitudinal Cohort Studies Estimating HRs for AD Risk ($k = 16$).