Supplementary Files updated: 15 June, 2021

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# 1 Supplementary Materials

## 1.1 Supplementary Material 1: Changes to protocol

Main changes include:

* Use of a time-varying treatment indicator, to correctly classify time-at-risk.
* Inclusion of additional covariates that are adjusted for in the main model.

# 2 Supplementary tables

## 2.1 Supplementary Table 1: Definition of exposures and covariates

Table 2.1: Definition of covariates

| **Covariate** | **How was the covariate defined?** |
| --- | --- |
| **Previous history of coronary arterial disease** | Presence of one or more relevant Read codes on record. |
| **Previous history of coronary bypass surgery** | Presence of one or more relevant Read codes on record. |
| **Previous history of cerebrovascular disease (including stroke)** | Presence of one or more relevant Read codes on record. |
| **Chronic illness, including cancer and arthritis** | Charlson index implemented using Read code lists. (4,5) Code lists based on those by Taylor et al. (6) |
| **Socioeconomic position** | 2010 English Index of Multiple Deprivation (IMD) at the ‘twentile’ level, where 1 represents the least deprived and 20 the most deprived. |
| **Consultation rate** | Calculated by dividing the total number of clinic visits by the length of the patient record prior to the index date to give an average annual rate. |
| **Alcohol status** | Recorded value (current, former or never). |
| **Smoking status** | Most recent of recorded value (current, former or never) or Read code indicating a recorded value. Code lists based on those by Wright et al. (7) |
| **BMI** | Recorded value if available, or a calculated value using the last recorded height and weight measurements. Measurements taken before the age of 25 were excluded to ensure adult measurements were used. |
| **Peripheral arterial disease** | Presence of one or more relevant Read codes on record. |
| **Hypertension** | Presence of one or more relevant Read codes on record. |
| **Baseline total cholesterol** | Continuous value recorded as test result (either by "enttype==163 & test\_data1==3" or by "enttype==177 & test\_data1==3") |
| **Chronic kidney disease** | Presence of one or more relevant Read codes on record. |
| **Type 1 Diabetes** | Presence of one or more relevant Read codes on record. |
| **Type 2 Diabetes** | Presence of one or more relevant Read codes on record. |

## 2.2 Supplementary Table 2: Adherence and switching by drug class

Table 2.2: cprdSSA

|  | **Whole Sample** | **Statins** | **Bile acid sequestrants** | **Ezetimibe** | **Ezetimibe & Statins** | **Fibrates** | **Nicotinic acid groups** | **Omega-3 Fatty Acid Groups** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Stopped** | 6.8% (115899) | 19.0% (111798) | 55.9% (3028) | 19.6% (150) | 12.6% (16) | 12.3% (478) | 44.0% (74) | 35.6% (355) |
| **Added** | 1.6% (27470) | 4.4% (26018) | 3.5% (192) | 18.9% (145) | 3.9% (5) | 21.6% (841) | 4.2% (7) | 26.3% (262) |
| **Switched** | 0.9% (14956) | 2.0% (12014) | 11.3% (614) | 34.5% (264) | 64.6% (82) | 44.0% (1714) | 44.6% (75) | 19.4% (193) |

## 2.3 Supplementary Table 3: STROBE Reporting Guidelines

**To be completed**

## 2.4 Supplementary Table 4: Statin type prescribing by year

Table 2.3: Statin prescription by year

| **Prescription Year Group** | **Hydrophilic** | **Lipophilic** | **Total** |
| --- | --- | --- | --- |
| **>=1996** | 7037 (18.2%) | 31531 (81.8%) | 38568 |
| **>=2001** | 21427 (10.3%) | 187018 (89.7%) | 208445 |
| **>=2006** | 3566 (1.6%) | 217726 (98.4%) | 221292 |
| **>=2011** | 1115 (0.9%) | 119035 (99.1%) | 120150 |

# 3 Supplementary figures

## 3.1 Supplementary Figure 1

knitr::include\_graphics(here::here("figures/cprd-analysis/decision\_tree.png"))

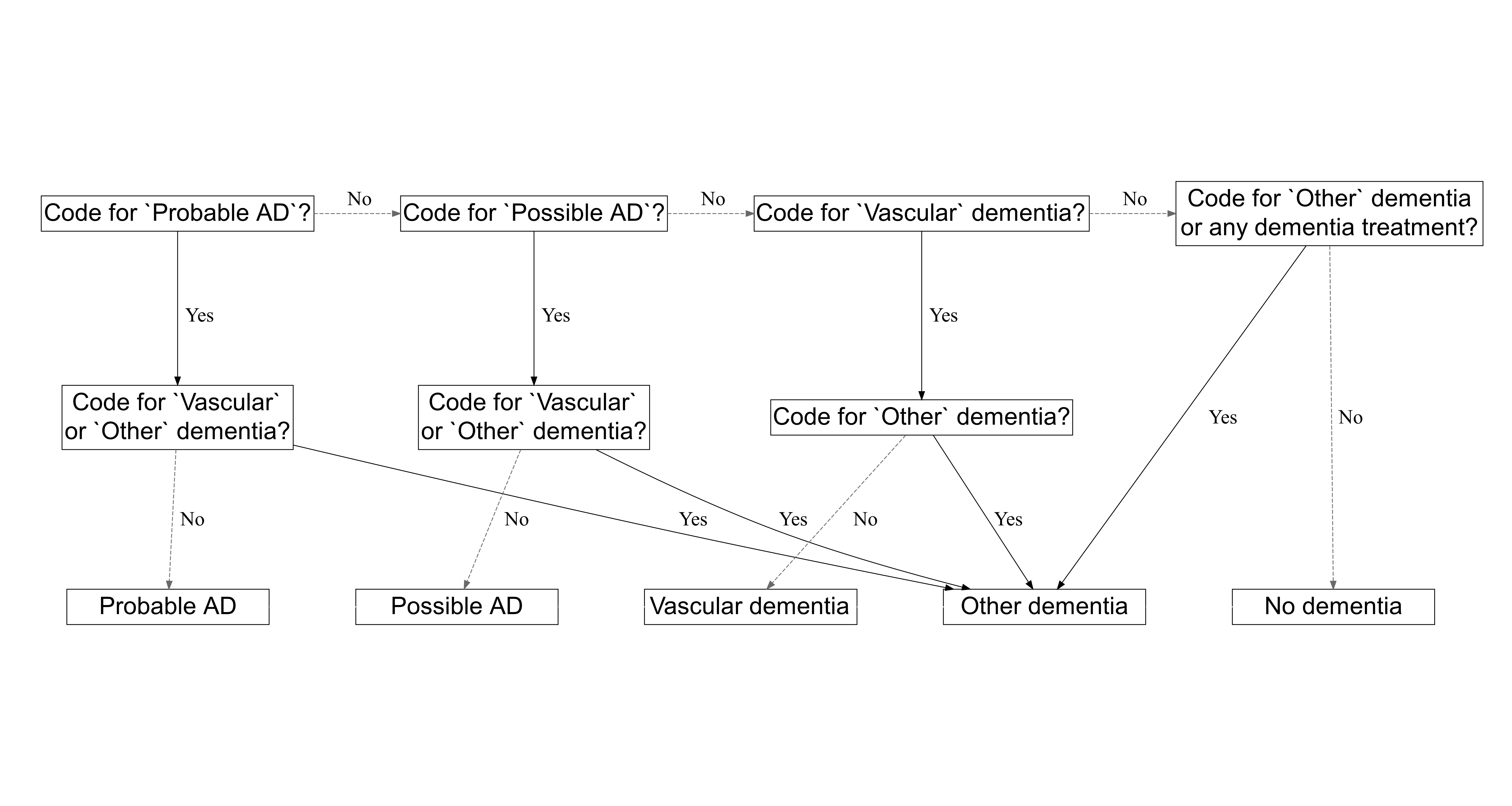


Figure 3.1: The algorithm used to choose between two diagnosis. This decision tree is adapted with permission from Walker *et al* (2019).(1)

## 3.2 Supplementary Figure 2

knitr::include\_graphics(here::here("figures/cprd-analysis/cohort\_attrition.png"))

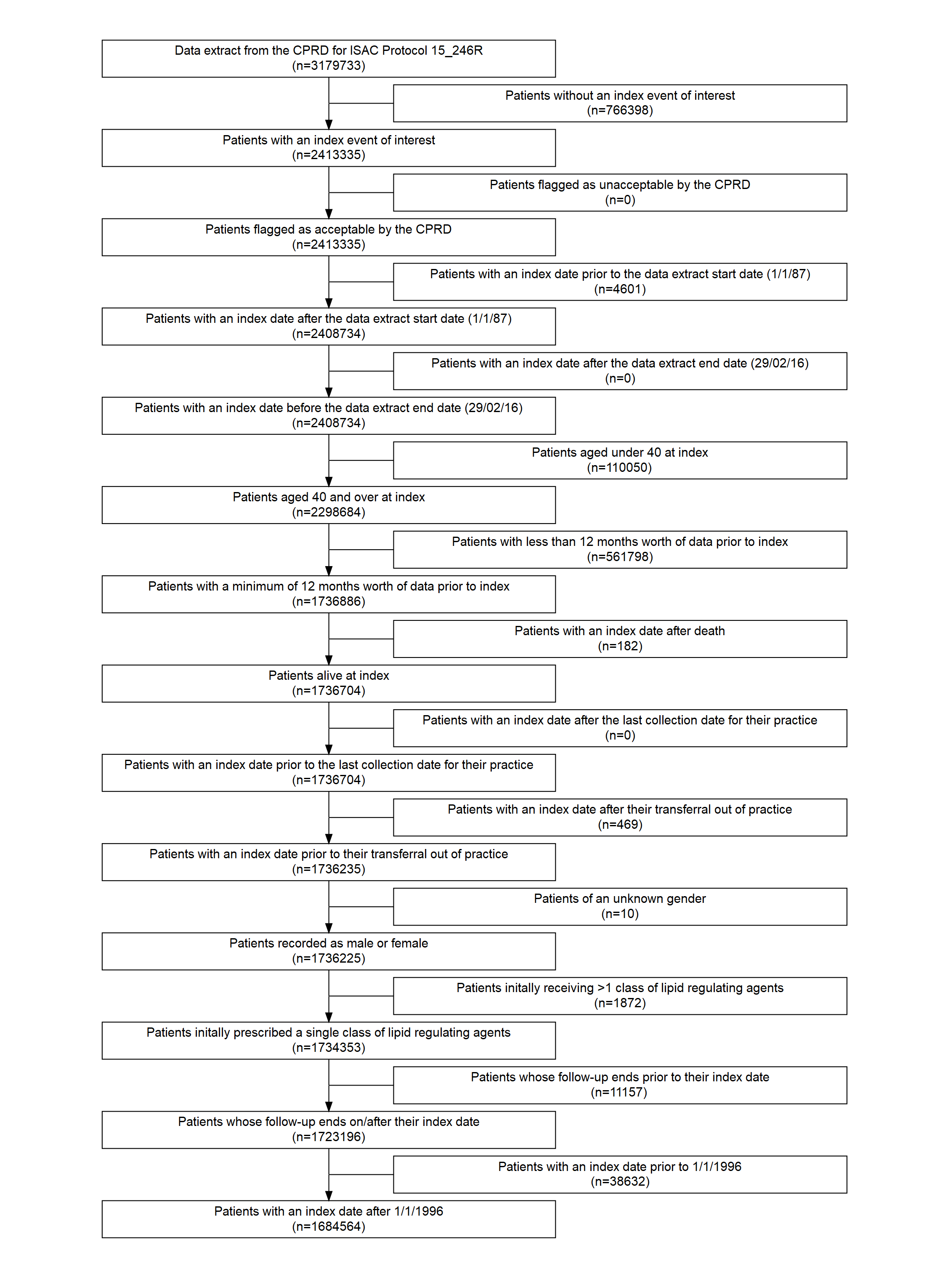


Figure 3.2: Attrition of participants as the eligibility criteria were applied.

## 3.3 Supplementary Figure 3

knitr::include\_graphics(here::here("figures/cprd-analysis/fp\_unadjusted.jpeg"))

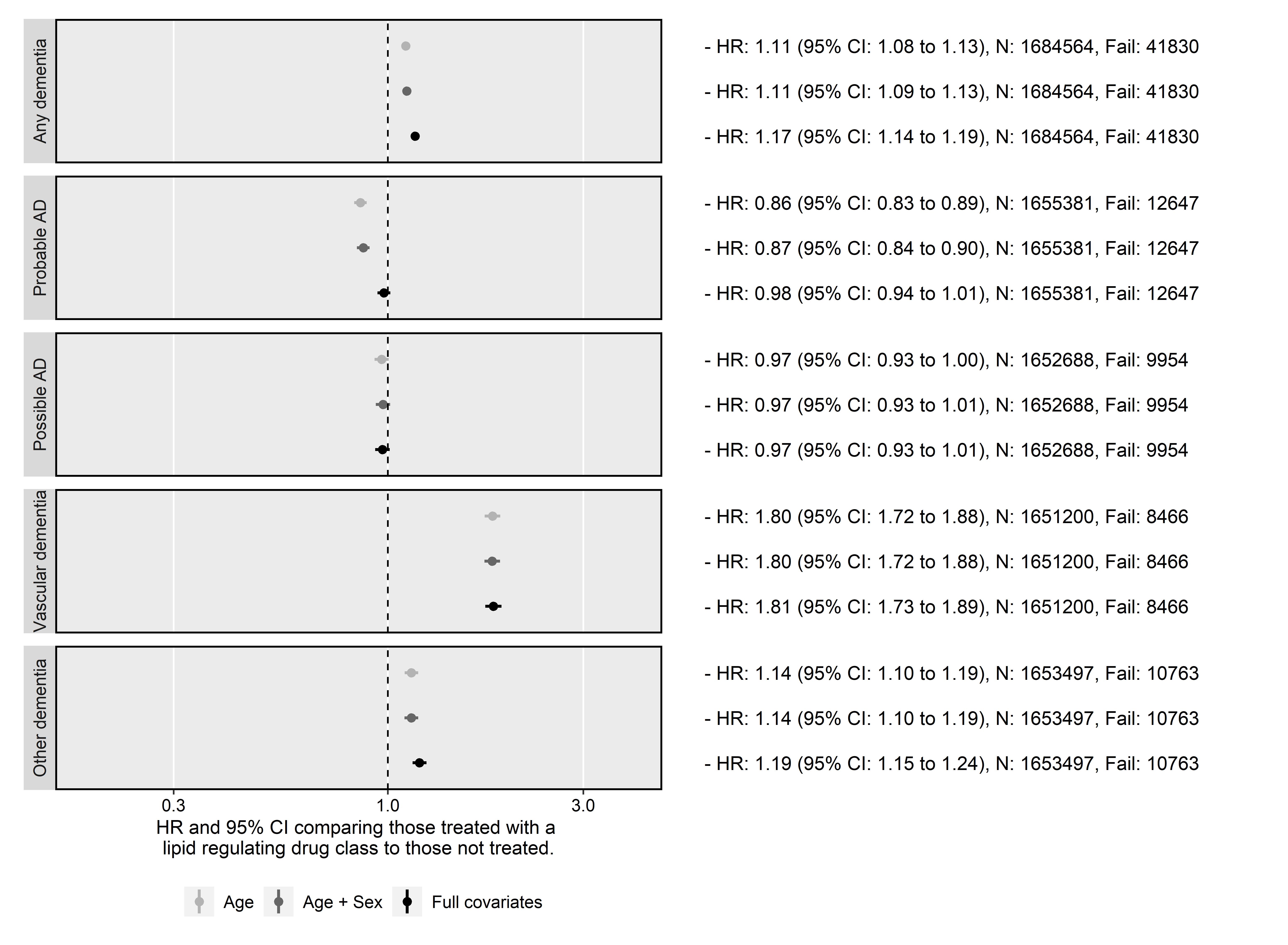


Figure 3.3: Association of any lipid regulating agent with a dementia or related outcome, adjusted only for age.

## 3.4 Supplementary Figure 4

knitr::include\_graphics(here::here("figures/cprd-analysis/fp\_cohort\_entry.jpeg"))

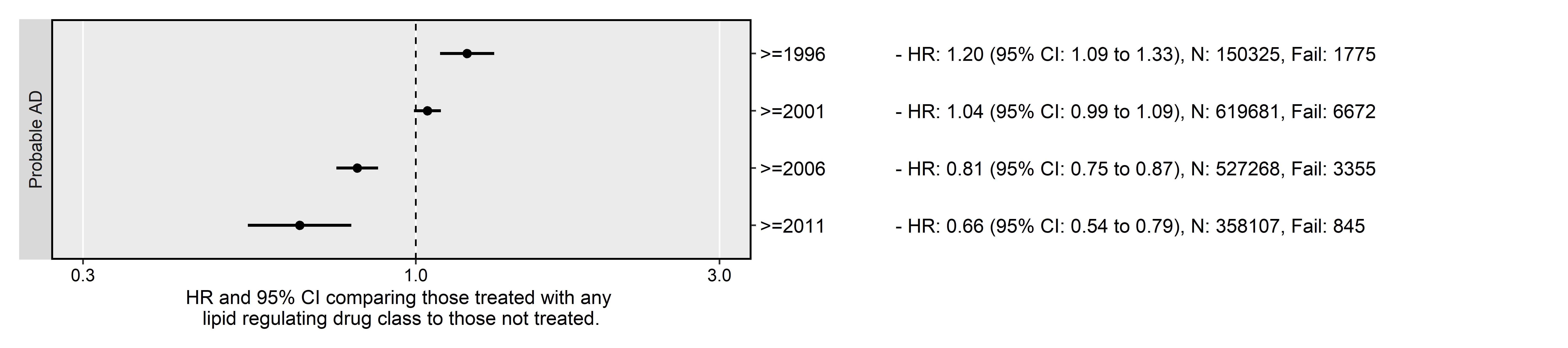


Figure 3.4: Association of any lipid regulating agent with a dementia or related outcome, stratified by year of entry into the cohort. {Note: Venexia reccomend including some info on average length of follow-up for each group beside the HR - will be done before submission.}

## 3.5 Supplementary Figure 5

knitr::include\_graphics(here::here("figures/cprd-analysis/fp\_pregnancy.jpeg"))

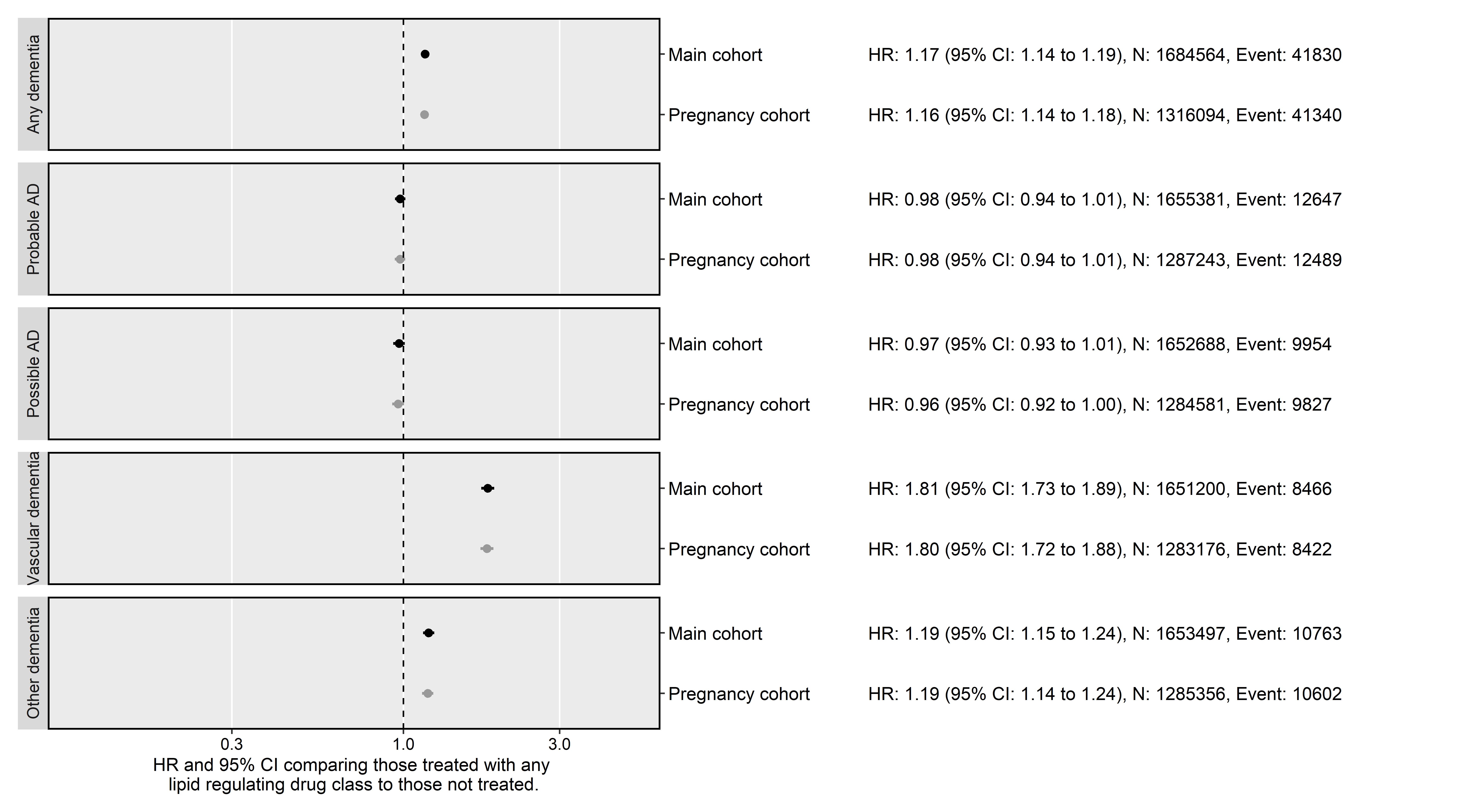


Figure 3.5: Association of any lipid regulating agent with a dementia or related outcome, removing women who were less than 55 years of age at index.

## 3.6 Supplementary Figure 6

knitr::include\_graphics(here::here("figures/cprd-analysis/fp\_sta\_type.jpeg"))

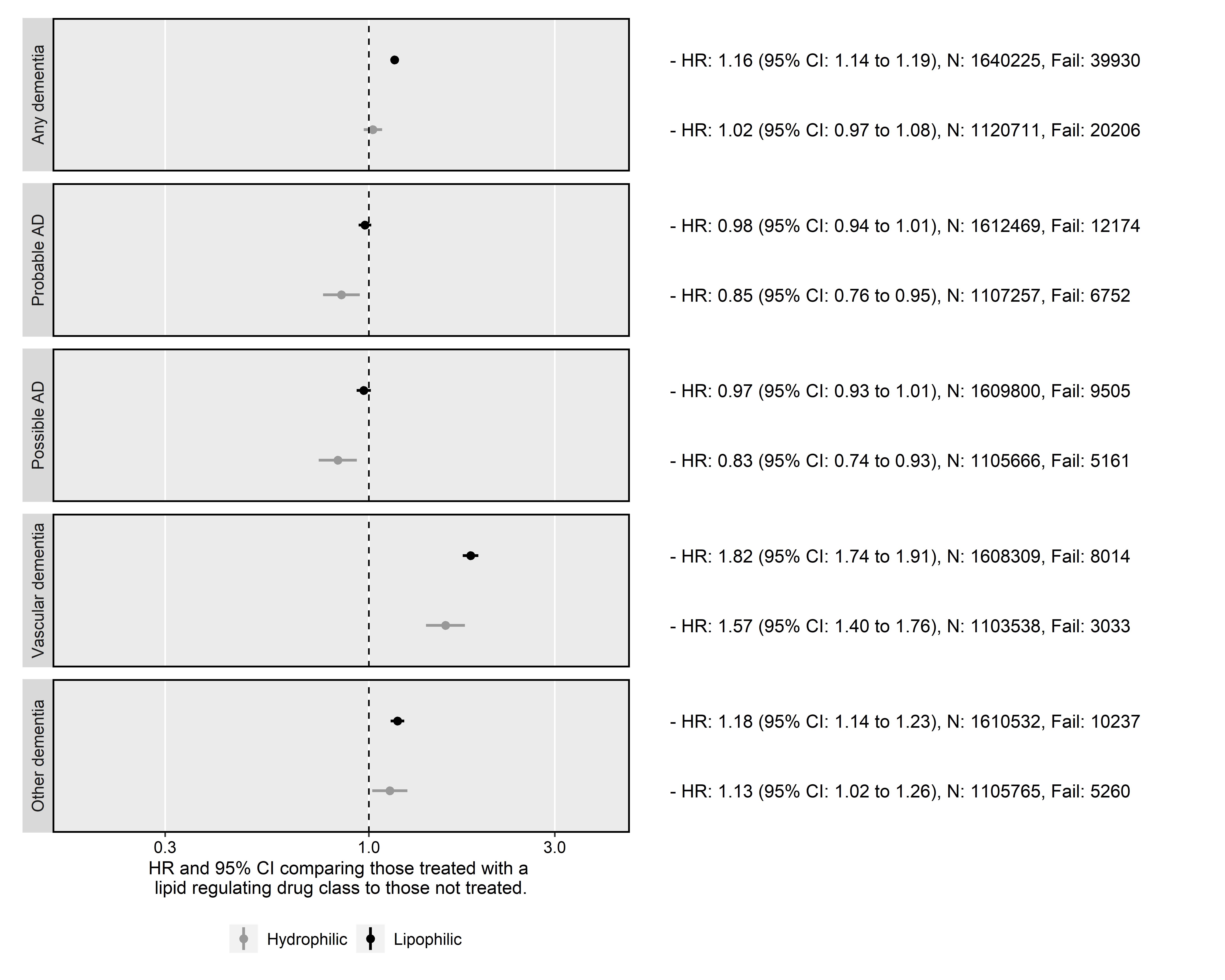


Figure 3.6: Association of statins with a dementia or related outcome, stratified by statin lipophilic/hydrophilic properties.

## 3.7 Supplementary Figure 7

knitr::include\_graphics(here::here("figures/cprd-analysis/fp\_control\_outcomes.jpeg"))

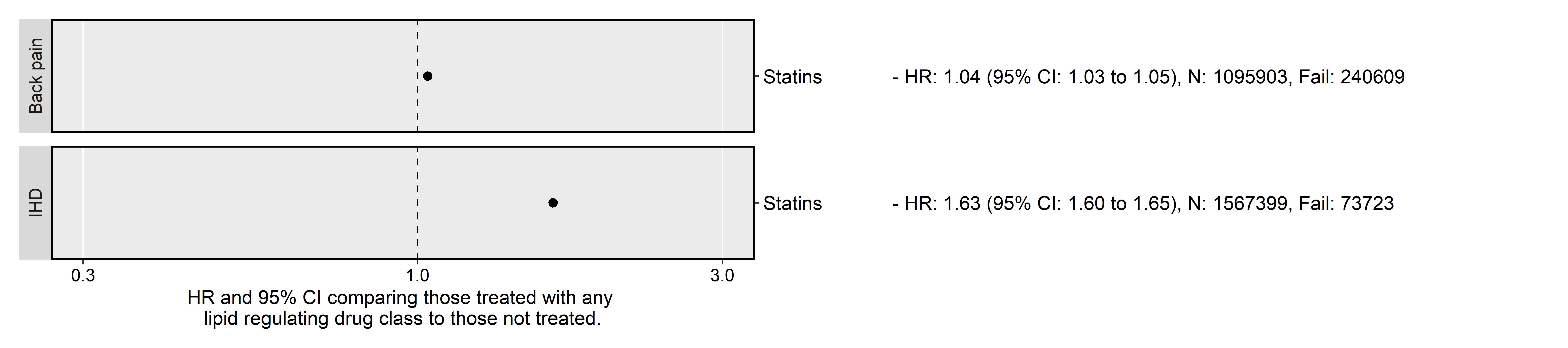


Figure 3.7: Association of any lipid regulating agent with backpain.

# References for supplementary materials

1. Walker VM, Davies NM, Martin RM, Kehoe PG. Comparison of antihypertensive drug classes for dementia prevention. bioRxiv. 2019 Jan;517482.