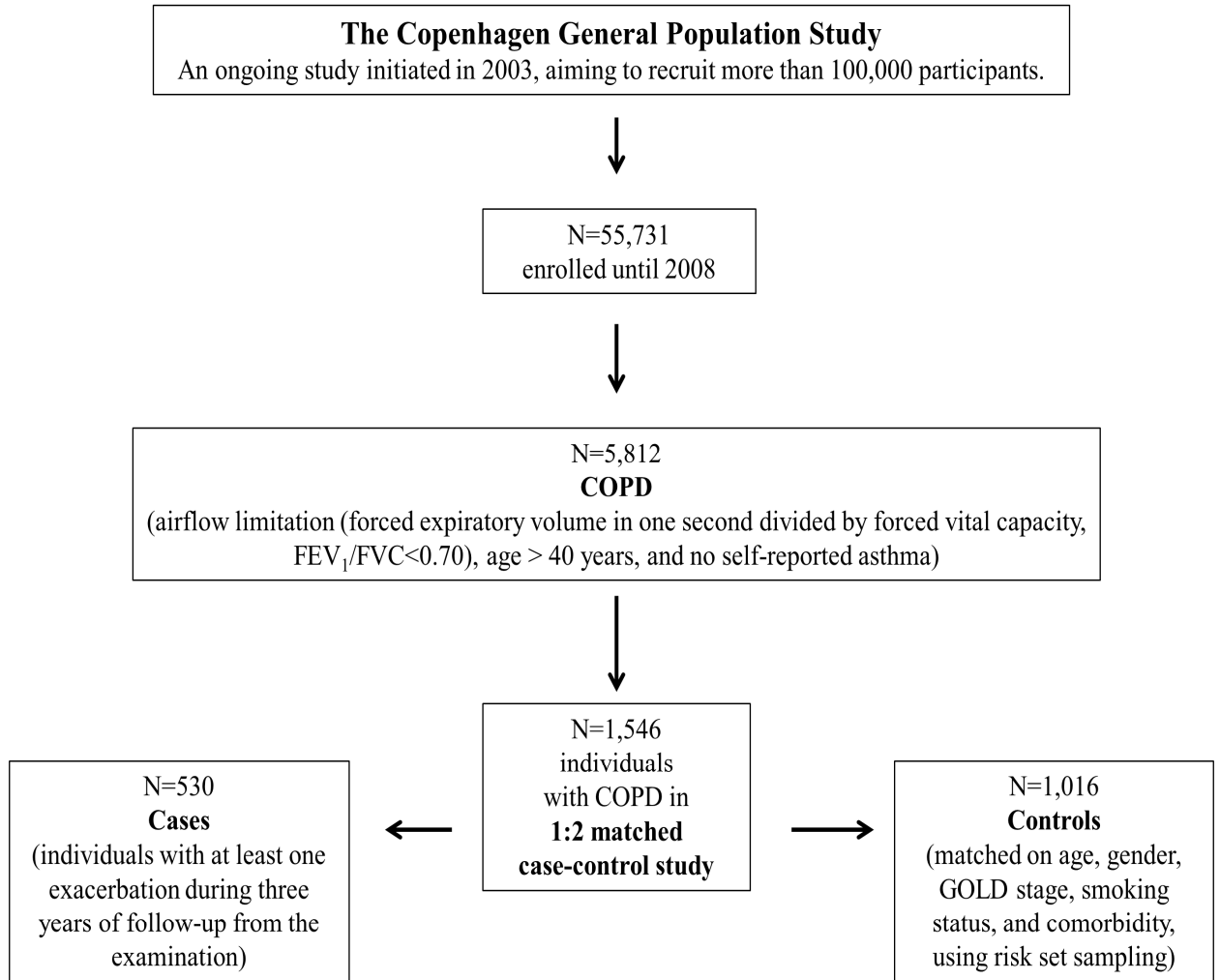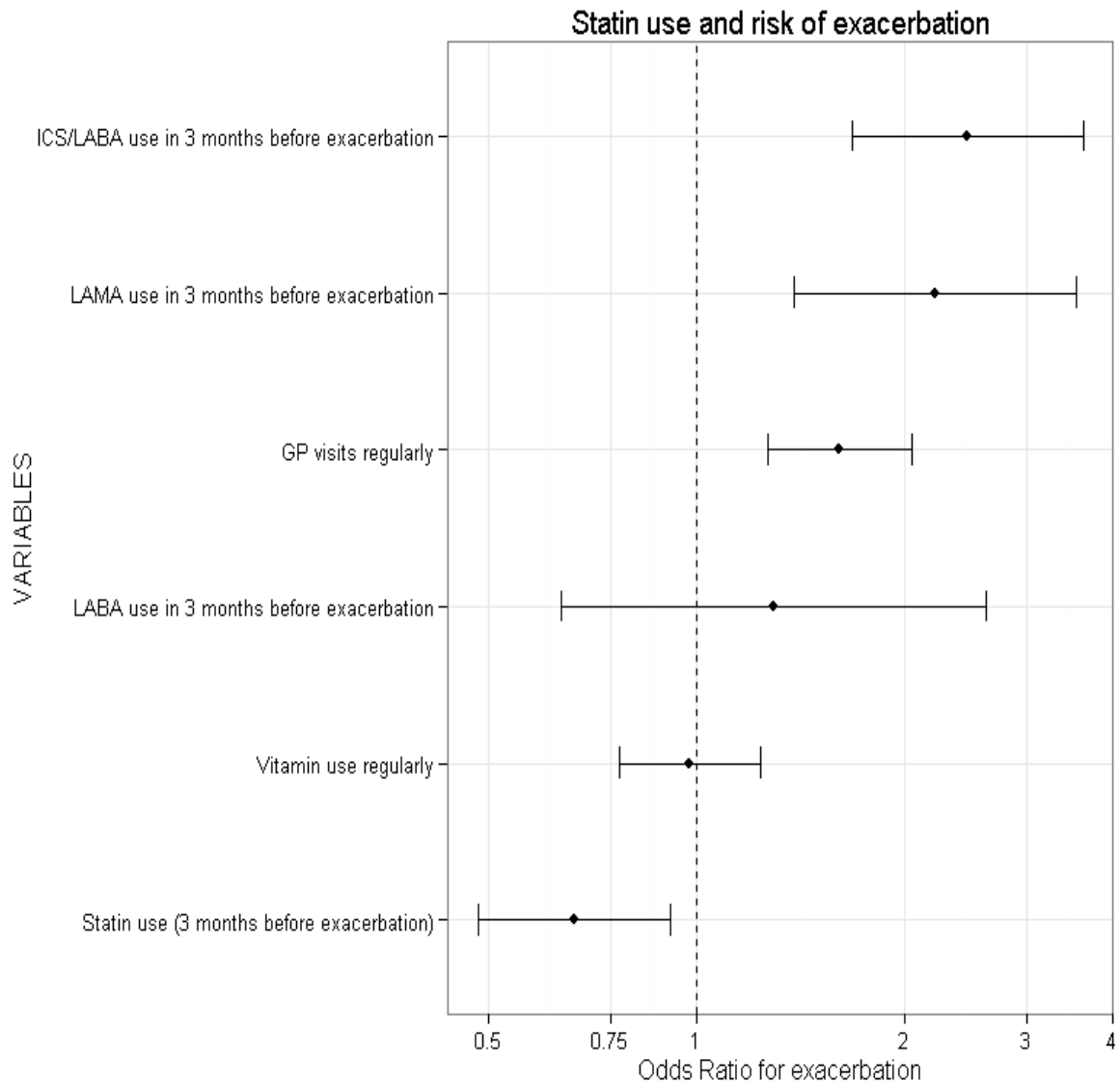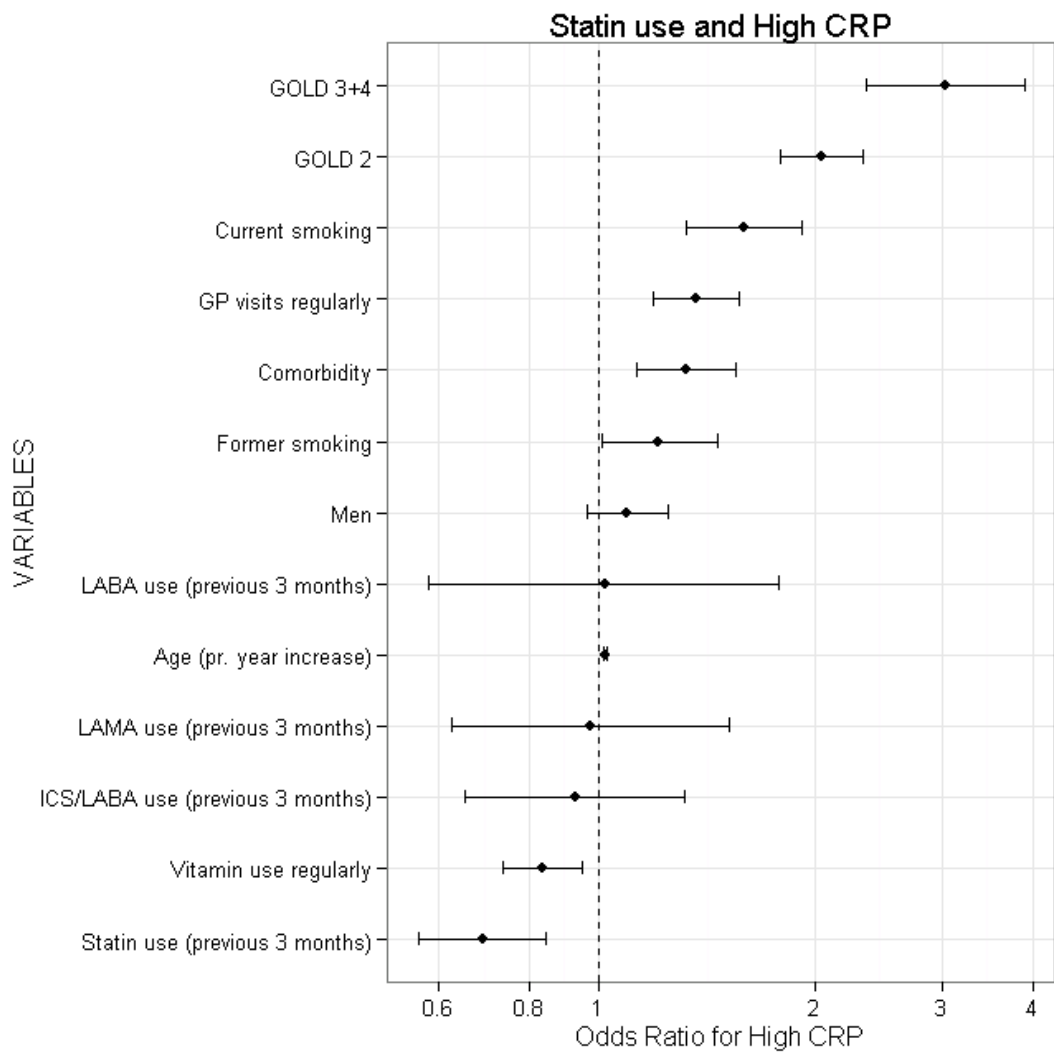Supplementary Figures

Suppl Figure 1: FLOW-DIAGRAM. Flow-diagram of the selection of cases and controls among individuals with COPD in the Copenhagen General Population Study.

| **The Copenhagen General Population Study** |
| An ongoing study initiated in 2003, aiming to recruit more than 100,000 participants. |

↓

N=55,731
enrolled until 2008

↓

N=5,812
COPD
(airflow limitation (forced expiratory volume in one second divided by forced vital capacity, FEV_1/FVC<0.70), age > 40 years, and no self-reported asthma)

↓

N=1,546
individuals
with COPD in
**1:2 matched
case-control study**

← N=530
Cases
(individuals with at least one exacerbation during three years of follow-up from the examination)

→ N=1,016
Controls
(matched on age, gender, GOLD stage, smoking status, and comorbidity, using risk set sampling)

Suppl Figure 2: STATINS AND EXACERBATIONS. Variables included as possible confounders in the multivariable conditional logistic regression analysis in the case-control study, and their associated odds of exacerbations. Abbreviations: GP=general practitioner; ICS/LABA= fixed-dose combinations of inhaled corticosteroids with long-acting beta2-agonists; LABA=long-acting beta2-agonists; LAMA=long-acting anti-cholinergics.

Suppl Figure 3: STATINS AND CRP. Variables included as possible confounders in the multivariable logistic regression analysis, and their associated odds of having a high CRP. Abbreviations: GOLD=Global initiative of Obstructive Lung Disease; GP=general practitioner; ICS/LABA= fixeddose combinations of inhaled corticosteroids with long-acting beta2-agonists; LABA=long-acting beta2-agonists; LAMA=long-acting anti-cholinergics.

Suppl Figure 4: POTENTIAL CONFOUNDERS. Potential measured and unmeasured confounders that could affect the association between statin use and exacerbation.

Measured potential confounders

- Age
- Gender
- Pulmonary function
- Smoking
- Comorbidity (cardiovascular)
- Pulmonary medications
- Health behaviour (visits to the general practitioner (GP) and regular use of vitamins)
- CRP (C-reactive protein)
- Socio-economic status (school education and household income)
- Frailty: markers of psychological distress
- Alcohol consumption categories
- Exacerbations: admissions and treatment with systemic corticosteroids

Unmeasured potential confounders

- Lipid levels
- Medications (others than statins and pulmonary)
- Comorbidity (non cardiovascular)
- Markers of systemic inflammation (not CRP)
- Health behaviour: (not GP visits and vitamin use)
- Frailty: not markers of psychological distress
- Others

STATIN USE → **EXACERBATION**