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Pattern of Cardiovascular Comorbidity in COPD in a Country with Low-smoking Prevalence: Results from Two-population-based Cohorts from Sweden

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ABSTRACT
Cardiovascular diseases are the most common comorbidities in COPD, due to common risk factors such as smoking. The prevalence of current smokers in Sweden has decreased over four decades to around 10%. The aim of the present study was to investigate the prevalence, distribution, and associations of cardiovascular comorbidities in COPD by disease severity in two large areas of Sweden, both with low-smoking prevalence. Data from clinical examinations in 2009–2012, including spirometry and structured interview, from two large-scale population studies, the West Sweden Asthma Study (WSAS) and the OLIN Studies in Northern Sweden, were pooled. COPD was defined using post-bronchodilator spirometry according to the fixed ratio FEV\textsubscript{1}/FVC < 0.70 and the lower limit of normal (LLN\textsuperscript{5th percentile}) of the ratio of FEV\textsubscript{1}/FVC. Of the 1839 subjects included, 8.7% and 5.7% had COPD according to the fixed ratio and the LLN criterion. Medication for heart disease or hypertension among those with moderate-to-severe COPD was more common than among those without COPD (fixed ratio definition of COPD: 51% vs. 23%, p < 0.001; LLN definition: 42% vs. 24%, p = 0.002). After adjusting for known risk factors for COPD, including smoking, age, socio-economic status, and occupational exposure for gas, dust and fumes, only heart failure remained significantly, and independently, associated with COPD, irrespective of the definitions of COPD. Though a major decrease in smoking prevalence, the pattern of cardiovascular comorbidities in COPD still remains similar with previously performed studies in Sweden and in other Westernized countries as well.

Introduction
COPD is a major cause of morbidity and mortality worldwide (1, 2). COPD often causes chronic or recurrent symptoms such as cough, sputum production and wheeze, and, mainly in subjects with moderate and severe disease, dyspnoea and fatigue (1, 3, 4). Since COPD in most cases is caused by exposure from noxious gases and particles, with smoking being the principal exposure in Westernized countries (3), the prevalence of COPD is strongly dependent on smoking habits of the population (3).

COPD is associated with systemic manifestations and comorbidities including osteoporosis, coronary artery disease, heart failure, hypertension, cerebrovascular disease and diabetes (5–9). These diseases often share the same risk factors. Furthermore, the involvements on organs other than the lungs could also partly be a consequence of not fully identified common immunological, inflammatory and extra-cellular signalling pathways (8–13).

Cardiovascular diseases are the most common comorbid diseases in COPD (14). Previously performed analyses on the third cohort of the Obstructive Lung Disease in Northern Sweden (OLIN) Studies, reflecting the adult general population in Northern Sweden in 1994–1995, found heart diseases or hypertension in more than 50% of subjects with moderate and severe COPD (15). Over several decades, the prevalence of smoking has decreased substantially in Sweden from about 35% in 1980s to about 10% in recent years (16, 17), and similarly, the prevalence of particularly moderate and severe COPD has decreased (18).

These changes in smoking habits and prevalence of COPD may have resulted in change in the presence and distribution of COPD comorbidities. The aim of the present study was to investigate the prevalence, distribution and
associations of cardiovascular comorbidities in COPD by disease severity in two large areas of Sweden.

**Materials and Methods**

The present study is based on two population studies performed in Northern Sweden, the OLIN Studies, and in the southern part of West Sweden, the West Sweden Asthma Study (WSAS). The study was approved by the regional ethical review boards in Umeå and Gothenburg, and performed in accordance with the Declaration of Helsinki. All participating subjects signed informed consent.

**Study population**

**Study areas**

The OLIN Studies are in progress since 1985 in Norrbotten, the northernmost county of Sweden covering 25% of the area of Sweden with a population of about 250,000. The WSAS started in 2008 in the south-west located region of Sweden, West Gotha (Västra Götaland) with the second city of Sweden, Gothenburg, and a population of about 1.6 million inhabitants.

**Northern Sweden**

In 2006, a random sample of 7,997 subjects from the population of Norrbotten in ages 20–69 years was invited to participate in a postal questionnaire survey (17). Another randomly selected population sample in aged 30–79 years, which had participated in a similar questionnaire survey in 1996 (19), was also invited, n = 7,004. Overall, 12,055 subjects (80% of the invited) responded. After stratification by sex and age, thus aiming at reflecting the age and sex distribution of the population of the county, a random sample of 1,016 subjects was invited to clinical examinations in 2009 including structured interviews and pre- and post-bronchodilator spirometry. Interviews and spirometry, with acceptable technique, were performed by 726 subjects, or 71.5%, of the invited (18).

**West Sweden**

In 2008, a questionnaire was mailed to 30,000 randomly selected subjects aged 16–75 years in West Gotha. The response rate was 62% of those who received the questionnaire (20). A study of non-responders demonstrated high representativeness, for the population in the study region, of those who participated at the postal survey (21). From the responders to the postal questionnaire, 2,000 subjects were randomly selected and invited to clinical examinations including structured interview and spirometry, and in 2009–2012, 1,148 subjects (58%) participated with acceptable quality of spirometry (22).

These two cohorts were pooled and the present study is based on the overlapping ages, 21–78 years, which includes 1,839 subjects.

**Questionnaire**

The OLIN questionnaire was used in the two studies. It includes questions about respiratory symptoms and diseases, medication, family history of obstructive airway diseases and allergy, current and previous smoking habits, occupation, socio-economic status based on level of education and area of domicile in its short self-administrated version (16, 23), while its longer version for structured interview includes questions for screening of other diseases, and for potential risk factors for common non-communicable diseases updated in 2009 (24). The study is based on data from the structured interview, and, as for all the variables included in the present study, the only missing data are on smoking habits for only one subject. The questionnaires have been used in several national and international studies (17, 20, 23, 25, 26), and the short version has recently been externally validated against the Global Allergy and Asthma European Network (GA²LEN) questionnaire (27).

**Spirometry**

A pneumotachograph spirometer (Masterscope, Jaeger, JLABversion 5.21 software, CareFusion, Würzburg, Germany) was used in both studies and the calibration was controlled daily. After slow vital capacity (SVC) manoeuvres, forced vital capacity (FVC) measurements at least three and maximum six times were performed. The difference between the two best FVC and the two best forced expiratory volume in 1 second (FEV1) values, respectively, had to be <5% or <100 mL for values <2.0 litres. Both visual inspection and guideline-defined requirements were followed. In the OLIN cohort, bronchodilation (BD) was performed using 0.4 mg salbutamol via discus in all subjects. In the WSAS cohort, the BD test was performed using a combination of 0.4 mg salbutamol and 80 µg ipratropium bromide via spacer in all subjects. The OLIN reference values for spirometry were used (28, 29), and the FEV1/FVC ratio was based on post-bronchodilator values.

**Definitions**

COPD was defined by two criteria: The fixed ratio criterion of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) with FEV1/FVC <0.70 and the ERS Task Force recommendation with FEV1/FVC < LLN 5th percentile, the latter also suggested by the Global Lung Initiative (GLI) and discussed by ERS and ATS (1, 30–32). In the analyses with the fixed ratio criterion, COPD grades were defined according to GOLD guidelines with moderate-to-severe COPD as GOLD grade 2 and mild COPD as GOLD grade 1 (1). In the analyses with the LLN criterion, COPD of moderate-to-severe grade was defined as a FEV1 < LLN, and mild COPD as FEV1/FVC < LLN but FEV1 not below LLN. This is in line with previous publications by the NHANES and the OLIN studies (18, 33).

Smoking was categorized by current smoking status as smokers, ex-smokers and never smokers and by pack-year. Ex-smokers were defined as those who had smoked for at least one year but not during the last 12 months. Pack-years
were calculated among ever smokers, by number of cigarettes smoked per day/20 × number of years smoked. Diseases other than COPD were described by report at the structure interview. Ischaemic heart disease was defined as a history of myocardial infarction, coronary artery bypass graft (CABG) or angina pectoris. Any heart disease was defined as any report of angina pectoris, myocardial infarction, heart failure, arrhythmia, other heart disease and CABG. The classification of socio-economic status was based on educational level. Occupational exposure to gas, dust or fumes (GDF) at work was defined as ever heavy exposure to gas, dust and fumes at work. Height and weight was measured and BMI was calculated as weight in kilograms divided by the square of the height in meter according to the WHO definition (34) with one exception: underweight was defined as BMI <20 kg/m² which is commonly used in Scandinavia (15).

**Analyses**

In bivariate analyses, Fisher's exact test was used to test differences in proportions and the t-test for differences in
Risk of cardiovascular diseases in COPD

In unadjusted analyses, heart failure followed by intermittent claudication was the major comorbidity associated with COPD (Table 3). When all analyses were adjusted for age group, sex, pack-years, educational level and exposure to GDF at work, only heart failure was significantly associated with COPD yielding an OR of 4.52 (95% CI 1.61–12.7) when using the LLN criterion for COPD, while the fixed ratio criterion did not reach statistical significance. In the adjusted analyses, heart failure was strongly and significantly associated with moderate or severe COPD when using both the fixed ratio and the LLN criterion for COPD. Hypertension was significantly associated only with moderate-to-severe COPD defined by the fixed ratio criterion (Table 3).

The stratified analyses tend to support the main results, but the confidence intervals are wide due to few cases with COPD and heart disease in the stratified groups, particularly among never smokers. Significant results are found in the adjusted analysis only when the LLN criterion for COPD was applied, and statistical significance are found only for hypertension among never smokers with COPD, and for heart failure among ever smokers with COPD (On-line supplement Table 2).

Discussion

The present study is based on randomly selected samples of the general population from two large areas in Sweden, with low prevalence of current smoking and a relatively low COPD prevalence. We found a high prevalence of cardiovascular comorbidities in subjects with COPD, and among subjects with moderate-to-severe COPD about a half had heart disease or hypertension. The associations between cardiovascular diseases and COPD were strongly smoking dependent, and similar regardless of whether the fixed ratio or the LLN criteria for COPD were used.

The term comorbidity in COPD has in most epidemiological studies been used for all concomitant diseases. A review by Chatila et al (7) has listed cardiovascular diseases, hypertension, cerebrovascular diseases, lung cancer, pneumonia, musculoskeletal dysfunction, osteoporosis, gastroesophageal reflux, diabetes, dyslipidaemia, psychiatric diseases, pulmonary embolism, anaemia and arthritis as comorbidities in COPD. The number of comorbidities among 1,145 COPD patients was studied in the Netherlands (35), and 1–2 comorbidities was found among 50%, 16% had 3–4 and 7% of the patients had 5 or more comorbidities. From a recent study based on telephone interviews with self-reports of diagnoses, several chronic diseases were associated with COPD, and with smoking, such as coronary heart diseases, diabetes, hypertension and stroke (36). As we do not have data for all diseases, we cannot give a precise estimate of the
number of comorbidities in our study; however, more than 50% of those with COPD had at least one comorbid disease in our study, and as in line with others (14, 37) cardiovascular diseases and hypertension were the most common.

The association of COPD and heart diseases has been described in several studies and is well established. COPD and heart diseases, particularly ischaemic heart disease, share their probably most important modifiable risk factor in Westernized countries, smoking (15, 38). Studies that clearly document this association include the US Cardiovascular Health Study (CHS) and a large Italian registry study (14, 38), and our studies in Northern Sweden have also demonstrated that association (15, 39, 40). The US study found a correlation between COPD severity grades and cardiovascular diseases with higher ORs for increasing COPD severity grades (14). The Italian study based on records of general practitioners found a prevalence of ischemic heart disease, arrhythmia and heart failure 2 to 5 times higher in subjects with COPD compared to the whole population (38). A recent study from Germany based on subjects with a physician diagnosis of COPD and a control group identified a significantly higher prevalence of myocardial infarction in COPD with the highest prevalence in moderate and severe COPD (41). The association of COPD and heart failure has been shown, however only scarcely, in epidemiological studies (42).

Results on association between diabetes and COPD are conflicting. The US CHS study found a significant association between diabetes and moderate and severe COPD, but not with mild COPD in contrast to heart diseases (14). In contrast to the US study, the large Danish Copenhagen City Heart Study, with spirometry defined COPD, did not find an association between diabetes and COPD (43), results in line with ours with the analysis based on the LLN criterion for COPD. Another large Danish study, without information on spirometry, found diabetes to be associated with COPD, and as in our study an association with heart disease (44).

In an earlier study in the same area of Northern Sweden in 1994–1995 the prevalence of current smoking was 26.5% and the prevalence of COPD according to the fixed ratio criterion was 14.2% (15). In the present study, the prevalence of current smoking was 12.8% and the prevalence of COPD with the fixed ratio criterion 8.7%. The prevalence of current smoking was almost halved and the prevalence of

### Table 2a. Prevalence of comorbidities among subjects with and without COPD with the fixed ratio criterion.

<table>
<thead>
<tr>
<th></th>
<th>Non-COPD n = 1679</th>
<th>COPD fixed ratio n = 160</th>
<th>COPD GOLD &gt;=2 n = 72</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n  %</td>
<td>n  %</td>
<td>n  %</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>47  2.8%</td>
<td>8  5.0%</td>
<td>0.139</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>39  2.3%</td>
<td>7  4.4%</td>
<td>0.113</td>
</tr>
<tr>
<td>Coronary artery bypass graft</td>
<td>34  2.0%</td>
<td>5  3.1%</td>
<td>0.380</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>77  4.6%</td>
<td>13  8.1%</td>
<td>0.047</td>
</tr>
<tr>
<td>Heart failure</td>
<td>6  0.4%</td>
<td>4  2.5%</td>
<td>0.008</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>85  5.1%</td>
<td>9  5.6%</td>
<td>0.758</td>
</tr>
<tr>
<td>Any heart disease</td>
<td>198 11.8%</td>
<td>27 16.9%</td>
<td>0.061</td>
</tr>
<tr>
<td>Hypertension (or medicines)</td>
<td>409 24.4%</td>
<td>65 40.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medication for heart disease</td>
<td>275 16.4%</td>
<td>41 25.6%</td>
<td>0.003</td>
</tr>
<tr>
<td>Medication for heart disease or HT</td>
<td>391 23.3%</td>
<td>64 40.0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intermittent claudication</td>
<td>19  1.1%</td>
<td>6  3.8%</td>
<td>0.017</td>
</tr>
<tr>
<td>TI or stroke</td>
<td>57  3.4%</td>
<td>8  5.0%</td>
<td>0.293</td>
</tr>
<tr>
<td>Diabetes</td>
<td>70  4.2%</td>
<td>13  8.1%</td>
<td>0.021</td>
</tr>
</tbody>
</table>

HT = Hypertension.

p value = for comparisons against non-COPD. For comparisons of proportions across two groups, the Chi-square or Fisher’s exact tests were used, as appropriate. For comparisons of proportions across more than two groups, the Mantel–Haenzel test-for-trend was used. The t-test was used for comparisons of means.

### Table 2b. Prevalence of comorbidities among subjects with and without COPD with the LLN criterion.

<table>
<thead>
<tr>
<th></th>
<th>Non-COPD n = 1735</th>
<th>COPD LLN n = 104</th>
<th>COPD with FEV1&lt;LLN n = 57</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n   %</td>
<td>n   %</td>
<td>N   %</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>49  2.8%</td>
<td>6   5.8%</td>
<td>5   8.8%</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>42  2.4%</td>
<td>4   3.8%</td>
<td>3   5.3%</td>
</tr>
<tr>
<td>Coronary artery bypass graft</td>
<td>38  2.2%</td>
<td>1   1.0%</td>
<td>1   1.8%</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>82  4.7%</td>
<td>8   7.7%</td>
<td>6   10.5%</td>
</tr>
<tr>
<td>Heart failure</td>
<td>6   0.3%</td>
<td>4   3.8%</td>
<td>4   7.0%</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>88  5.1%</td>
<td>6   5.8%</td>
<td>3   5.3%</td>
</tr>
<tr>
<td>Any heart disease</td>
<td>207 11.9%</td>
<td>18  17.3%</td>
<td>11  19.3%</td>
</tr>
<tr>
<td>Hypertension (or medicines)</td>
<td>433 25.0%</td>
<td>41  39.4%</td>
<td>27  47.4%</td>
</tr>
<tr>
<td>Medication for heart disease</td>
<td>290 16.7%</td>
<td>26  25.0%</td>
<td>18  31.6%</td>
</tr>
<tr>
<td>Medication for heart disease or HT</td>
<td>419 24.1%</td>
<td>36  34.6%</td>
<td>24  42.1%</td>
</tr>
<tr>
<td>Intermittent claudication</td>
<td>21  1.2%</td>
<td>4   3.8%</td>
<td>3   5.3%</td>
</tr>
<tr>
<td>TI or stroke</td>
<td>60  3.5%</td>
<td>5   4.8%</td>
<td>5   8.8%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>81  4.7%</td>
<td>2   1.9%</td>
<td>1   1.8%</td>
</tr>
</tbody>
</table>

HT = Hypertension.

p value = for comparisons against non-COPD. For comparisons of proportions across two groups, the Chi-square or Fisher’s exact tests were used, as appropriate. For comparisons of proportions across more than two groups, the Mantel–Haenzel test-for-trend was used. The t-test was used for comparisons of means.
COPD was lower, particularly the prevalence of moderate and severe COPD (18). The high prevalence of comorbid heart disease, hypertension and medication seems to be unaltered despite the high impact of changed smoking habits on the prevalence of COPD (Figure 2). In the present study, we found a high and significant risk of reported heart failure among subjects with COPD versus without COPD, and the risk remained significant even after adjusting for confounders. Intermittent claudication disclosed high prevalence in COPD, but was not significant in the adjusted analyses. An association between COPD and intermittent claudication was not demonstrated in the referred study performed 15 years ago.

**Table 3. Comorbidities as unadjusted and adjusted relative risks for COPD.**

<table>
<thead>
<tr>
<th>Comorbidity (independent variable)</th>
<th>Fixed ratio criterion</th>
<th>Moderate-to-severe COPD</th>
<th>LLN criterion</th>
<th>Moderate-to-severe COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>1.72 (0.97–3.03)</td>
<td>2.43 (1.16–5.07)</td>
<td>1.62 (0.79–3.33)</td>
<td>2.29 (0.98–5.33)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>4.69 (1.74–12.7)</td>
<td>10.8 (3.92–29.5)</td>
<td>7.32 (2.69–19.9)</td>
<td>13.80 (5.00–38.1)</td>
</tr>
<tr>
<td>Any heart disease</td>
<td>1.46 (0.96–2.20)</td>
<td>1.73 (0.97–3.10)</td>
<td>1.50 (0.90–2.50)</td>
<td>1.72 (0.89–3.31)</td>
</tr>
<tr>
<td>Hypertension (HT)</td>
<td>1.97 (1.44–2.70)</td>
<td>3.60 (2.26–5.73)</td>
<td>1.87 (1.26–2.78)</td>
<td>2.59 (1.54–4.36)</td>
</tr>
<tr>
<td>Medication for heart disease or HT</td>
<td>2.03 (1.48–2.78)</td>
<td>3.22 (2.03–5.10)</td>
<td>1.61 (1.08–2.41)</td>
<td>2.21 (1.31–3.74)</td>
</tr>
<tr>
<td>Any heart disease. HT or medication</td>
<td>1.85 (1.36–2.53)</td>
<td>2.71 (1.70–4.32)</td>
<td>1.76 (1.19–2.58)</td>
<td>1.84 (1.10–3.10)</td>
</tr>
<tr>
<td>Intermittent claudication</td>
<td>2.83 (1.25–6.39)</td>
<td>6.60 (2.86–15.2)</td>
<td>2.90 (1.07–7.88)</td>
<td>4.03 (1.26–12.9)</td>
</tr>
<tr>
<td>TIA or stroke</td>
<td>1.44 (0.71–2.92)</td>
<td>2.94 (1.35–6.41)</td>
<td>1.38 (0.56–3.38)</td>
<td>2.62 (1.05–6.57)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.87 (1.06–3.30)</td>
<td>2.64 (1.27–5.52)</td>
<td>0.41 (0.10–1.68)</td>
<td>0.38 (0.05–2.73)</td>
</tr>
</tbody>
</table>

Unadjusted analyses

| Ischaemic heart disease           | 0.79 (0.44–1.43)       | 0.84 (0.39–1.82)        | 0.76 (0.36–1.62) | 0.84 (0.35–2.03)        |
| Heart failure                     | 2.08 (0.76–5.70)       | 4.47 (1.58–12.6)        | 4.52 (1.61–12.7) | 7.38 (2.55–21.4)        |
| Any heart disease                 | 0.82 (0.54–1.27)       | 0.80 (0.44–1.46)        | 0.92 (0.54–1.57) | 0.84 (0.42–1.66)        |
| Hypertension (HT)                | 1.17 (0.83–1.64)       | 1.95 (1.18–3.21)        | 1.32 (0.85–2.04) | 1.48 (0.85–2.59)        |
| Medication for heart disease or HT| 1.04 (0.74–1.47)       | 1.46 (0.87–2.44)        | 0.99 (0.62–1.59) | 1.06 (0.59–1.91)        |
| Any heart disease. HT or medication | 1.04 (0.74–1.46)     | 1.32 (0.80–2.20)        | 1.20 (0.77–1.86) | 0.94 (0.53–1.66)        |
| Intermittent claudication         | 1.21 (0.52–2.81)       | 2.03 (0.84–4.90)        | 1.17 (0.42–3.27) | 1.21 (0.36–4.01)        |
| TIA or stroke                     | 0.80 (0.39–1.64)       | 1.30 (0.56–2.90)        | 0.80 (0.32–2.02) | 1.24 (0.48–3.20)        |
| Diabetes                          | 1.13 (0.62–2.07)       | 1.39 (0.65–2.95)        | 0.27 (0.07–1.10) | 0.20 (0.03–1.44)        |

Adjusted analyses

*Analyses are adjusted for sex, age group, pack-years, educational level and exposure to gas, dust or fumes at work. Comorbidities are added one by one into the model. Grey shading indicates statistical significance.*
years earlier in Northern Sweden (15). There might be several reasons for the new findings regarding intermittent claudication and heart failure. There is a strong association of intermittent claudication and smoking (45), as well as of COPD and smoking (3). Identifying an independent association between intermittent claudication and COPD might be intricate and the high significant association of intermittent claudication in COPD did not remain in the adjusted analyses in our study. Heart failure, on the other hand, was significantly associated with COPD in the adjusted analyses. Since the last 20 years both diagnostics and treatment of heart failure have changed due to new blood analyses, such as various brain natriuretic peptides (BNP), more utilization of echocardiography, and more active treatments with ACE-inhibitors, beta-blockers and aldosterone inhibitors has been introduced. Both diagnosis and treatment for heart failure may thus have become clearer to the patient and increased the awareness contributing to improved quality of self-reporting.

The prevalence of current smoking in an area within the city of Gothenburg in 1990 was 44% in age 20–44 years (46) and decreased to 19% in 2008 (20). In another area of West Sweden, the smoking prevalence was 32% in 1994 (47). Thus, about 12% in our study demonstrate a further decrease in smoking in West Sweden. Similarly, the prevalence of current smokers decreased from more than 34% in 1985 (16) to 27% in 1994 (48), and then to 19% in 2009 in the Northern Sweden study area (18), while it in this study sample of the OLIN cohort was 15%. Another change in Northern Sweden is that current smokers smoked less in 2006 compared to 1996 (17) and that the prevalence of moderate-to-severe COPD has decreased (18). Thus, low-smoking prevalence, a low prevalence of COPD, and also a low prevalence of heart disease seem to covary. In the unadjusted analyses, we found high prevalence of heart comorbidities in COPD, but the strength of the association was not supported in the adjusted analyses, except for heart failure, when smoking habits were included in the statistical

Figure 2. Comparison between 1994 and 2009–2012 with respect to smoking habits, prevalence of COPD and cardiovascular diseases in COPD. Data from 1994 adapted from reference (15).
model. Neither could Danish studies verify an association beyond smoking (49, 50). Changes in smoking habits over decades have had an impact on COPD but not on the pattern of comorbidities.

Our study demonstrates strong associations between cardiovascular diseases and COPD, but does not reveal the mechanisms. Shared risk factors, viz. exposures predominantly for smoking (49), dominate, although several studies exhibit a significantly high prevalence of heart diseases among never smokers with COPD (51).

There were some differences between the West Sweden cohort and the Northern Sweden cohort. Particularly smoking was more common in the Northern Sweden cohort and paralleled with a somewhat higher COPD prevalence. Also, heart diseases and hypertension tended to be more common in the north, otherwise there were no major differences between the cohorts. These small differences between the study cohorts have probably had no influence on the magnitude of associations between the comorbid diseases and COPD in the merged study sample.

Regarding our study’s strengths, we consider the representativeness for two large areas of Sweden. Bias by non-response was not found in the study in West Sweden (21) and only limited bias in the studies in Northern Sweden, where participation rates have been high over decades (16–19, 52). Anthropometric values and spirometry data can be judged as valid and correctly measured by trained personnel. The prevalence of current smoking, heart diseases, hypertension and diabetes in our study is similar to the reported frequencies of these conditions in Sweden 2012–2013 according to Statistics Sweden (53). Concerning limitations, the data on comorbid conditions and smoking rely on self-reports from the structured interviews with risk of recall bias. Comorbidities and smoking are not validated by any objective measures. Self-reports on heart diseases have in previous studies been estimated reasonably fair for angina, and myocardial infarction but of lower accuracy for heart failure (54). Limitations are further that of cross-sectional studies and deductions beyond associations should be done with caution.

To summarize, in our study the prevalence of current smoking is low and lower than in previously performed studies in both West Sweden and Northern Sweden. The COPD prevalence is congruously low. The relative risk of concomitant heart disease is similar to a previous study in Northern Sweden. The greatest relative risk for having a comorbid cardiovascular disease in COPD was found to be heart failure followed by intermittent claudication, while heart diseases as a whole together with hypertension were the most common comorbid cardiovascular diseases among subjects with COPD in the present study. The issue of a causative association of COPD and heart disease, beyond smoking, cannot be answered by our study.

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