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Society inhaled

Social Epidemiology of COPD

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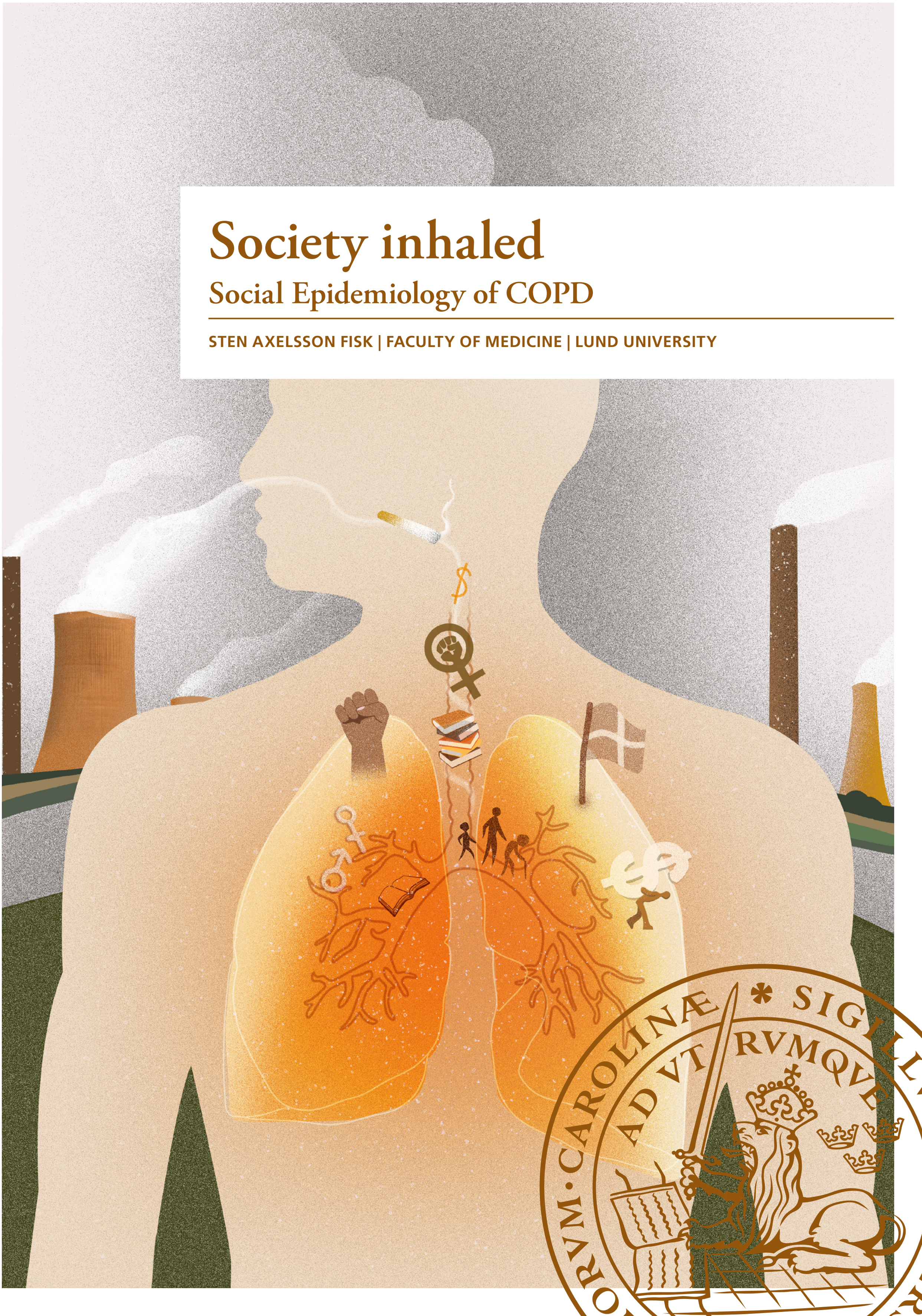

Sten Axelsson Fisk (SAF) is a medical doctor that studied medicine at Lund University in Malmö and is presently doing his residency in Gynecology and Obstetrics at Ystad Hospital. SAF has been engaged in public debate advocating equity in health and in political movements defending public health care for a decade.

Society inhaled – is a thesis that describes the social epidemiology of COPD in Sweden and inquires how the socially patterned risk of COPD emerges. Explicitly incorporating different social theories regarding the genesis of health inequalities, this thesis uses novel statistical methods to study incidence of COPD, discontinuation to maintenance medication among COPD patients and risk of smoking. By directing attention not only to average differences between socioeconomic groups but also to the discriminatory accuracy of socioeconomic models, the thesis constitutes an argument that social epidemiological studies should report measures of discriminatory accuracy and individual heterogeneity to better inform public health interventions. The thesis supports the adoption of an intersectional perspective to improve understanding of how society is inhaled and calls for increased attention to socioeconomic factors in the management of COPD patients.

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Society Inhaled

Social Epidemiology of COPD

Sten Axelsson Fisk

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Abstract

Chronic Obstructive Pulmonary Disease (COPD) is a common disease that in its advanced stages is a life-limiting condition and a leading cause of death globally. This thesis aims at increasing the understanding of the socioeconomic disparities that exist both for COPD and its major risk factor, tobacco smoking. A related aim is to advance the theory and epidemiological methods used to evaluate equity in health and health care. In concrete terms, the thesis discusses absolute versus relative measures of income and applies Analysis of Individual Heterogeneity and Discriminatory Accuracy (AIHDA) within an intersectional framework.

In three prospective national studies, register data including socioeconomic information, hospital diagnoses (I–III) and prescriptions (III) was used. Investigating incident COPD, study I evaluates absolute versus relative income and study II adopts an intersectional Multilevel AIHDA (MAIHDA). Study III is a MAIHDA which disentangles the effect of geographical (i.e. counties) and sociodemographic contexts on discontinuation to maintenance therapy among COPD patients. Study IV is a cross-sectional intersectional AIHDA, analysing smoking risk in the Swedish National Health Surveys. Discriminatory Accuracy (DA) is assessed through Area Under the ROC Curve (AUC) in study I, III and IV and the Variance Partition Coefficient (VPC) in study II and III.

Absolute income had a higher DA than relative income and seems more relevant for predicting incident COPD. Intersectional information on age, gender, education, income, civil status and country of birth had a good DA, as 20% of total variance in propensity to develop COPD was found between intersectional strata. The stratum with older native females with low income and low education who live alone presented 49 times higher COPD risk than the stratum defined by young, native males with high income and high education who cohabit (0.98% versus 0.02%). Sociodemographic differences were more relevant than geographic (i.e. counties) differences for explaining patient variance in discontinuation to maintenance therapy (VPC 5.0% versus 0.4%). Intersectional information provided a moderate DA (AUC=0.66) for predicting smoking status.

Although complex to disentangle from one another, our results suggest that material conditions matter more than psychosocial status for incidence of COPD. The intersectional MAIHDA and AIHDA approaches improve our understanding of heterogeneities in risk of COPD and smoking in the population. This approach can also disentangle geographical from sociodemographic contextual effects and provides an innovative instrument for planning interventions according to the idea of *proportionate universalism*.

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“There is no exception to the rule, that, in every district which has a large indoor industry, the increased mortality of the workpeople is such as to colour the death-return of the whole district with a marked excess of lung disease.”

Dr John Simon, quoted in Capital, Volume III (1894), Karl Marx

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Abbreviations

AATD	Alpha-1-antitrypsin deficiency
ACE	Average Causal Effect
AUC	Area Under the ROC Curve
COPD	Chronic Obstructive Pulmonary Disease
DA	Discriminatory Accuracy
FEV_1	Forced Expiratory Volume in 1 Second
FVC	Forced Vital Capacity
GOLD	Global Initiative for Obstructive Lung Disease
HR	Hazard Ratio
ICC	Intraclass Correlation Coefficient
ICD	International Statistical Classification of Diseases and Related Health Problems
ICE	Individual Causal Effect
OR	Odds Ratio
PCV	Proportional Change of the Variance
PHC	Primary Healthcare Centre
PR	Prevalence Ratio
ROC	Receiver Operator Characteristic Curve
RR	Relative Risk
SDH	Social Determinants of Health
SEP	Socioeconomic Position
SES	Socioeconomic Status
SNAR	Swedish National Airway Register
SPDR	Swedish Prescribed Drug Register
TPR	The Total Population Register
VPC	Variance Partition Coefficient
WHO	World Health Organization

List of papers

Paper I: "Absolute rather than relative income is a better socioeconomic predictor of chronic obstructive pulmonary disease in Swedish adults" by **Axelsson Fisk, S.**, & Merlo, J. (2017). *Int J Equity Health, 16*(1), 70. doi:10.1186/s12939-017-0566-2. Published with kind permission from BioMed Central, licensed under CC BY 4.0

Paper II: "Chronic Obstructive Pulmonary Disease in Sweden: an intersectional multilevel analysis of individual heterogeneity and discriminatory accuracy" by **Axelsson Fisk, S.**, Mulinari, S., Wemrell, M., Leckie, G., Perez-Vicente, R., & Merlo, J. (2018). *SSM-Population Health, 4, 334-346*. doi:10.1016/j.ssmph.2018.03.005. Published with kind permission from Elsevier, licensed under CC BY-NC-ND 4.0

Paper III: "Geographical and sociodemographic differences in discontinuation of medication for Chronic Obstructive Pulmonary Disease - A Cross-Classified Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (MAIHDA)" by Khalaf, K*., **Axelsson Fisk, S***., Ekberg-Jansson, A., Leckie, G., Perez-Vicente, R., & Merlo, J. (2020). *Clin Epidemiol, 12*, 783-796. doi:10.2147/clep.s247368. Published with permission from DovePress, licensed under CC BY-NC 3.0.

Paper IV: "Understanding the complexity of socioeconomic disparities in smoking prevalence in Sweden: a cross-sectional study applying intersectionality theory" by **Axelsson Fisk, S.**, Lindstrom, M., Perez-Vicente, R., & Merlo, J. (2021) *BMJ open, 11*(2), e042323. doi:10.1136/bmjopen-2020-042323. Published with kind permission from British Medical Journal under CC BY 4.0.

*Both authors contributed equally to the manuscript.

Abstract

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also disentangle geographical from sociodemographic contextual effects and provides an innovative instrument for planning interventions according to the idea of *proportionate universalism*.

Introduction

Reviews of publications on inequities in risk of Chronic Obstructive Pulmonary Disease (COPD) have confirmed the existence of socioeconomic disparities (Adeloye et al., 2015, Gershon et al., 2012). However, most of those studies are based on unidimensional socioeconomic, demographic or geographical dimensions without considering that the distribution of power and resources that condition the risk of COPD is complex and intersectional. Further, those previous studies are mostly focused on measures of association like odds ratios and relative risks without considering the discriminatory accuracy (DA) of their findings (Merlo, 2014, Merlo, 2018). However, during the last few years a small but growing number of studies focusing on different outcomes (Hernández-Yumar et al., 2018, Evans et al., 2018, Persmark et al., 2019, Wemrell et al., 2017a) are filling those knowledge gaps, and this thesis has a pioneer role in that initiative.

In a review of the association between socioeconomic position (SEP) and COPD, relative risks for negative COPD outcomes were at least two-fold for the most deprived compared to the most privileged groups in most studies (Gershon et al., 2012). No other organ system shows such strong socioeconomic inequities as the respiratory system (Schraufnagel et al., 2013, Pleasants et al., 2016, Black et al., 1980). This thesis investigates the airways as the anatomic site of *embodiment* of socioeconomic inequities (Krieger, 2005). I adopt a multilevel perspective in which socioeconomic factors are considered not as individual characteristics but rather as a relational concept that restrains chances of healthy airways for some individuals and protects others from individual-level risk factors that mediate the association between SEP and COPD morbidity.

The aim is to apply novel methods that develop the understanding of the societal factors driving inequities in COPD morbidity and that aid the evaluation of equity in COPD health care. In this way, the final aim is to provide and improve the knowledge basis for better treatment and prevention of COPD in the population.

Background

Chronic Obstructive Pulmonary Disease

Although emphysema and chronic bronchitis are medical conditions that have been known for at least 200 years, COPD as a disease entity is a rather young condition (Swedish Medical Products Agency, 2015). It was in 1987 and the 8th version of the International Statistical Classification of Diseases and Related Health Problems (ICD) that it was first merited with its own code (Socialstyrelsen, 2017). COPD is defined as airflow limitation determined by spirometry in combination with symptoms including dyspnea, cough and/or sputum production (GOLD, 2020). Diagnosis of COPD is based on the ratio of air exhaled during the first second of a forced expiration (FEV_1) over the forced total volume that is exhaled (FVC). A FEV_1/FVC ratio under 0.7 is diagnostic of COPD (Kasper et al., 2015). COPD is an insidious disease where narrowing of peripheral airways alone or in combination with destruction of pulmonary parenchyma are characteristic structural changes. The pathogenesis is complex and involves several contributing processes, including oxidative stress, altered inflammatory response of the airways, imbalance between proteases and interstitial fibrosis (GOLD, 2020). While the disease was previously viewed as a strictly pulmonary disease, it is now understood as a systematic disease where an inflammatory process (Rabe and Watz, 2017) may lead to a negative spiral with aggravated inflammation of airways, leading to more mucus production and destruction of pulmonary tissue, reducing elasticity of the lungs, both leading to airway obstruction (Larsson, 2007).

COPD should be considered whenever an adult patient presents with dyspnea and/or prolonged cough in combination with exposure to risk factors for COPD (described in a following section). Whereas dynamic spirometry is necessary to establish diagnosis, devices assessing FEV_1/FEV_6 can be used for screening (Labor et al., 2016). According to Swedish guidelines, once COPD diagnosis is established, further assessment of symptoms, exacerbation history, physical capacity assessed through a 6 minutes walking test, BMI, and comorbidities should be performed (Swedish Medical Products Agency, 2015). Based on the lung-function, degree of dyspnea and history of exacerbation, COPD is classified into stage A–D. Non-pharmacological treatments include adequate nutrition, physiotherapy and COPD education. For patients at any stage who are active smokers, active smoking cessation care is the most important therapeutic intervention, since it increases survival (Anthonisen et al., 2005). For patients with mild symptoms, less than two exacerbations during the previous 12 months and an FEV_1 >50% expected value, short-acting agents to relieve symptoms is the only bronchodilating medication recommended. Patients with GOLD stage B, C and D are recommended long-acting β-2 agonists (LABA) or long-acting muscarinic antagonists (LAMA), or a combination of both. Patients who suffer frequent exacerbations and have COPD stage C–D should also be prescribed inhaled corticosteroids (ICS) in combination with LABA or, if necessary, triple therapy with LAMA, LABA and ICS. Patients must be properly educated in how to use the inhalation devices, since misuse is a common problem with negative health implications (Gregoriano et al., 2018, GOLD, 2020). Additional therapies should be considered in patients with advanced disease and hypoxemia (long-term oxygen therapy) or increased mucus production (roflumilast) (Swedish Medical Products Agency, 2015).

The global prevalence of COPD is uncertain since both under- and over-diagnosis remain problems globally (Ho et al., 2019, Gershon et al., 2018) and in Sweden (Axelsson et al., 2020). The World Health Organization (WHO) estimates that chronic respiratory disease is the third leading cause of death among non-communicable diseases (Alwan, 2011). By 2014, Swedish authorities estimated that around 500,000 individuals suffered from the disease, but only a fifth had an established diagnosis (Socialstyrelsen, 2014), and hence the opportunity for correct treatment. A recent prevalence study based on data between 2009–2012 from northern Sweden found a COPD prevalence of 7% among people aged 21–78 years, and a 23% decrease in prevalence from 1994 to 2009, presumably due to falling smoking rates. Prevalence of moderate to severe disease had halved during the same period (Backman et al., 2020). In a research project where COPD burden was compared between twelve countries, Sweden had the fourth lowest prevalence with 16.2% (Danielsson et al., 2012). In a study based on telephone interviews with 244 patients, the total cost of COPD in Sweden in 2010 was estimated to be 13.9 billion SEK, including both direct and indirect costs. Patients with severe disease had 29 times higher mean total cost compared to patients with mild disease, primarily due to more hospitalisations (Jansson et al., 2013). Another publication found that most of the costs for COPD patients proved to be attributable to hospital nights unrelated to COPD, underscoring the necessity of managing comorbidities among COPD patients properly (Lisspers et al., 2018).

Socioeconomic disparities and COPD

The association between low SEP and COPD has been studied in many previous publications (Gershon et al., 2012, Marmot et al., 1991). In prevalence studies from northern Sweden, occupational class was not associated with prevalence of COPD among non-smokers (Hagstad et al., 2012). However, in a study from western Sweden, Axelsson et al. (2016) found that compared to non-smoking individuals with university education, having a low education implied a similar increase in odds of chronic bronchitis as being a current smoker. Danielsson et al. (2012) published a study reporting decreased prevalence of COPD with increasing years of education, in a model adjusted for age, gender, previous tuberculosis and pack-years of smoking. In a recent publication by Borné et al. (2019), an income gradient was observed for incident COPD with a two-fold risk of COPD for individuals with incomes below the median. When adjusting for smoking status and FEV_1 by baseline, both income and occupational class remained significant risk factors for incident COPD, although hazard ratios decreased after this adjustment.

Furthermore, COPD patients with low socioeconomic position have worse prognosis than those with high SEP, regarding both risk of hospitalisation and mortality. In a longitudinal Canadian study by Gershon et al. (2014), mortality among COPD patients in all socioeconomic strata decreased between 1996/7 and 2011/12. Since mortality decreased less among the poorest income quintile compared to the richer quintiles, income disparities in mortality widened. In Denmark, COPD patients with lower education have higher risks of exacerbation and hospital admission and have higher mortality compared to individuals with university education. While partly explained by disparities in mediators between low SEP and COPD, such as smoking status, FEV_1 and history of exacerbations, the educational gradient remained after adjustment for these factors (Lange et al., 2014).

This thesis focuses on COPD and smoking in Sweden, a high-income country with a universal health care system. It should be kept in mind that low- and middle-income countries carry the largest global burden of COPD morbidity and mortality (Halpin et al., 2019).

Factors mediating socioeconomic gradient for COPD

Smoking

In high-income countries, smoking is the most important individual-level risk factor for COPD (Soriano et al., 2017). In Sweden, the epidemic of tobacco smoking has passed over its initial steps during which tobacco consumption was more common among the higher social classes compared to manual occupations (Vågerö and Norell, 1989), and today people with low SEP smoke more frequently than people with high SEP (Giskes et al., 2005, Eek et al., 2010). The higher prevalence of smoking among people with low SEP results both from higher rates of initiation (Joffer et al., 2014) and less successful smoking cessation (Gilman et al., 2008). Among women, life course factors such as early motherhood and non-cohabitation both increase odds of smoking and reduce chances of being a former smoker (Graham et al., 2006). Findings are diverging regarding the influence of childhood socioeconomic position on smoking, but it seems to have a stronger influence on women's smoking patterns than men's (Jefferis et al., 2004, Power et al., 2005). Recent evidence further indicate that offspring to women that smoke during most of their pregnancy have increased risk of respiratory disease in adult life (Johansson et al., 2020).

The factors hypothesised to mediate the association between low SEP and smoking depend on the level in the eco-social framework in which the analysis is performed (Krieger, 2005). Individual-level factors such as sleep disturbance and psychological stress, together with financial strain, did mediate the association between low SEP and increased risk of smoking, according to one study (Martinez et al., 2018). Other factors higher up in the social causal pathway that influence risk of smoking include work place and neighbourhood norms (Ahern et al., 2009) and family smoking habits (Jackson and Henriksen, 1997). Tobacco marketing that is more oriented towards people with low SEP may also contribute to SEP disparities in smoking, according to studies on tobacco marketing strategies in the USA (Barbeau et al., 2004, Barbeau et al., 2005).

One focus of this thesis is directed to the theories of how low SEP translates into different health behaviours, including smoking. In the Black Report, published in the UK in 1982, three major explanation models for how health inequities are generated were presented (Black et al., 1980), not counting the artefact theory. First, the natural and social selection model views social class as a consequence of health rather than the opposite, i.e. people that smoke will develop poor health and thus be prevented from reaching high SEP. Second, the materialist explanation model (presented in detail below) stresses that different material life circumstances of people with different SEP offer different possibilities to choose a healthy life (Roos and Prättälä, 2012). Last, the cultural/behavioural explanation model focuses on how class-dependent cultures and norms regarding smoking and other health behaviours are central to the understanding of SEP disparities in smoking. This explanation model aligns with Bourdieu's view of how tastes, preferences and cultural practices are shaped by the social conditions in which we grow up and live (Bottero, 2005). The process through which class-differentiated practices reproduce the social order define what Bourdieu terms habitus. According to this concept, it is more in congruence with common expectations that a working class person smokes than it is for people of higher social classes. These expectations affect decisions on whether to take up and quit smoking (Katainen, 2010).

The strong causal association between smoking and COPD has contributed to a conception of the disease as a pure *cigarettosis*, despite its multifactorial causes (Larsson, 2007). Such a simplistic view is erroneous, since approximately 20-25% of Swedish COPD patients have never smoked (Skold, 2017, Hagstad et al., 2012).

Other risk factors for COPD

As smoking prevalence decreases in Sweden, the etiologic fraction attributable to other risk factors increases. Occupational exposure to dusts, mineral dusts, fumes and asbestos is calculated to cause between 15% (Blanc and Toren, 2007) and 37% (Torén et al., 2017) of COPD morbidity. Among never-smokers, the population attributable fraction of occupational exposures to COPD is 31% (95% CI 18-43%) (Blanc et al., 2019). Individuals with low SEP run a higher risk of being exposed both to occupational exposures and living near major roads, increasing the risk of COPD (Schikowski et al., 2008). In low- and middle-income countries, combustion of biofuels constitutes an important risk factor for COPD among women (Po et al., 2011), and with increasing migration this may contribute to COPD burden in Sweden as well, although this has still not been studied. Several environmental exposures in-utero and early life also condition risk of COPD (Savran and Ulrik, 2018) Pre-term delivery and factors causing intra-uterine growth restriction of the lungs, correlated to low birth weight, also predispose people with low SEP to COPD (Brostrom et al., 2013) due to decreased pulmonary reserve capacity. Infections in early life increases risk of asthma and chronic respiratory conditions, and such infections are more common among people with low SEP (Dowd et al., 2009). Living near a major road during adulthood is associated with increased odds of COPD (Lindgren et al., 2009) and air pollution exposure in early life is associated with decreased FEV_1 during adolescence, which in turn predisposes individuals to COPD (Schultz et al., 2016). Air pollutions are more common in socioeconomically deprived areas (Chaix et al., 2006). Interest is also emerging regarding a potential harmful effect on lung function of Western diet contrasted by a reduced risk among people consuming a balanced diet rich in anti-oxidants, but conclusive evidence is lacking (Scoditti et al., 2019). The problem of residual confounding by unmeasured aspects of social class is a concern that should be highlighted when studying individual life style factors mediating the association between SEP and COPD (Oakes and Andrade, 2017).

Alpha-1-antitrypsin deficiency (AATD) is a genetic disorder that through different pathophysiologic mechanisms predisposes affected individuals to early onset COPD. The deficiency of alpha-1-antitrypsin protein causes an imbalance between protease and antiprotease activity, primarily due to excess neutrophil elastase activity. This, in turn, may lead to a destruction of pulmonary parenchyma characteristic of emphysema, a process which is accelerated in the presence of tobacco smoke or pulmonary infection, both of which increase the elastase burden in the lungs (Stoller and Aboussouan, 2012). Epigenetic alterations including DNA-methylation have been suggested as one mechanism contributing to socioeconomic inequalities in health, and low education was associated with accelerated epigenetic ageing in a study comprising 17 independent cohorts, even after adjustment for smoking, BMI, alcohol and physical activity (Fiorito et al., 2019). Recently, conflicting results have been reported regarding the association between epigenetic indicators of accelerated ageing and COPD. One study found very weak or non-existent associations between epigenetic markers of accelerated ageing and COPD (Breen et al., 2020) while another found stronger associations (Hillary et al., 2020). In addition to this, hypotheses exist about other gene-environment interactions, for example related to genetic predispositions to addiction which increase risk of exposure to smoking (Molfino and Coyle, 2008).

Theories of the genesis of socioeconomic health inequities

Social epidemiology is distinguished from classic epidemiology through its treating of social factors as explanatory variables of interest rather than as a source of bias (Oakes and Kaufman, 2017). WHO defines health inequities as

> avoidable inequalities in health between groups of people within countries and between countries. These inequities arise from inequalities within and between societies. Social and economic conditions and their effects on people's lives determine their risk of illness and the actions taken to prevent them becoming ill or treat illness when it occurs (WHO, 2020).

Some health disparities depend on natural biomedical factors that are not readily amenable through policy interventions, for example some biological differences between men and women. Such disparities do not imply the same moral imperative as avoidable inequalities in health (Alonge and Peters, 2015) and accordingly are not defined as health inequities. In the case of COPD, it is not yet possible to alter the genetic predisposition arising from alpha-1-antitrypsin deficiency, in the same way that the frequency of low income and low educational achievement or discrimination on the basis of gender or ethnicity can be modified. The width and strength of the association between low SEP and ill health has led to the formulation of the fundamental cause theory. In this theory, Phelan and Link claim that the robust association between high SEP and better health is attributable to the concentration of a large set of resources such as money, education, prestige, power and beneficial social connections among individuals higher up in the social hierarchy. Through multiple pathways, people with higher SEP will find ways of attaining resources that are beneficial for their health (Link and Phelan, 2010).

Critique has been directed at both the fundamental cause theory (Oversveen et al., 2017) and social epidemiology as a discipline, targeting the relative lack of explicit social theory (Krieger, 1994, Ng and Muntaner, 2014, Wemrell et al., 2016). As a response to this critique, one aim of this thesis is to contribute to the development of methods to evaluate the relevance of different social theories for the understanding of the social distribution of COPD. When explicitly stating which social theories are being hypothesised to explain socioeconomic disparities in COPD, one can approach knowledge about mechanisms that generate these inequities (Oversveen et al., 2017). In contrast, if associations between different socioeconomic categories and health hazards are presented without a proper theory-grounded explanation, this may perpetuate conceptions of social health gradients as constant and unchangeable phenomena.

Embodiment and eco-social theory

Embodiment is a core concept in the eco-social theory (Krieger, 2005) and refers to the process through which people, as all living creatures, incorporate their surroundings into their bodies. Therefore, by studying the states of our bodies we can reach insights about the distribution of power and resources in any given society. The eco-social theory also stresses that health conditions are affected by biological and social factors acting upon us at several different levels, from molecular levels to macroeconomics. The scientific questions that are being asked and the research that is performed in a society is influenced by dominant social beliefs. Epidemiologists, as do other scientists, have a responsibility to acknowledge at which levels they seek causes of diseases (Krieger, 2001). Although neither the embodiment concept nor the eco-social theory are addressed directly in any of the papers, the ideas have influenced the work within this thesis.

Measuring socioeconomic position

Despite being one of the most studied and influential determinants of health, there is no universal agreement on how to define or denominate SEP. On the contrary, the choice of SEP measurement is influenced by available data, a priori hypotheses on causal mechanisms between SEP and the studied outcome as well as political ideology. Neither is there a consensual terminology. Socioeconomic position, socioeconomic status and social class are to some extent exchangeable synonyms, but express different nuances in how the socioeconomic variable is hypothesised to influence health (Oakes and Andrade, 2017). Social class is a term with a Marxist origin, and in its original form it separates individuals dichotomously into an owning capitalist class and a working class, depending on whether people own their means of production (and pay others to work for them) or sell their labour in exchange for a salary. This dichotomous class definition has been further developed by Marxist scholar Olin Wright, who presented a class matrix including several dimensions: the relation to the means of production, number of employees, authority at the work place and possession of scarce skills (Wright, 2000). Other class definitions stem from a Weberian tradition and focus on the character of the employment relationships that are either service relationships or labour contracts. Service relationships are typically present for high status occupations and are characterised by a higher degree of freedom. Labour contracts, on the contrary, dominate among occupations requiring less skill and imply a stricter control over employees. These ideas have inspired the construction of the Swedish Socioeconomic Index (SEI), the Eriksson-Goldthorpe-Portocarero (EGP) and the more recent European Socio-economic Classification (ESeC) (Bihagen and Nermo, 2018). Social class is usually operationalised using occupational status, and the association between working class occupations and increased odds of COPD have been shown in Sweden (Montnemery et al., 2001, Borné et al., 2019), although another study only found insignificant trends of manual workers having higher odds of COPD (Lindberg et al., 2005). Socioeconomic status, perhaps the most commonly used term within both social and traditional epidemiology, is implicitly linked to the subjective experiences of being more or less deprived. Status is a concept that also has a Weberian origin and was first defined in direct opposition to the concept of class, since class, according to Weber, was defined by mere economic interests and situation in the labour market whereas status is determined by honour and social lifestyle (Weber, 2010). The term socioeconomic status thus directs attention to the subjective aspects of deprivation (Humber, 2019). Socioeconomic position (SEP), thirdly, is a term that avoids connotations of prestige and is therefore often preferred by researchers who are interested in both material and prestige aspects of social stratification (Krieger, 2001). It is the term used in this thesis when not specifically referring to the psychosocial pathway as outlined below.

The measurement of SEP can be broadly categorised into composite measurements and proxy measurements. The prior category are aggregate measurements taking into account several aspects of SEP, such as earnings, wealth, education, occupation and prestige. The advantage of this is that such measurements better capture the full aspects of SEP compared to proxy measurements, a downside is that combined measurements are more complicated to transform into policy change. It is hard to launch campaigns directed at individuals with a specific score on a composite SEP measurement, compared to targeting individuals with low education or low income. Proxy variables take advantage of the fact that possession of desirable resources tend to correlate; an individual with high SEP has a good chance to have a high income, high education, high-prestige occupation and live in a wealthy neighbourhood. Measuring any of these aspects thus captures important aspects of SEP, although not as exhaustively as the composite measurements (Oakes and Andrade, 2017).

In study I, absolute and relative income are compared as predictors of incident COPD. In study II we included both education and income in the intersectional matrix as two separate dimensions. This choice was based on the hypothesis that across categories of gender and migration status, education would perform differently as a proxy for SEP; we therefore chose to include income as well. In the study focused on discontinuation with maintenance therapy, we chose income as the proxy for SEP since we hypothesised that financial strain could be one reason that

COPD patients discontinued their medication. When studying the intersectional pattern of smoking prevalence, we chose to include education rather than income in the main analysis, although we performed a sensitivity analysis using income instead. This choice was based on the purpose of providing an alternative way of mapping health disparities for authorities, and education is a frequently used proxy for SEP in evaluations of health disparities in Sweden (Socialstyrelsen, 2015). It should be noted that the lack of a consensual terminology may confuse readers of research in this field. For example, relative income as defined in study I is not synonymous to the concept of living beneath the "relative poverty line", which is usually defined as having an income below 50% or 60% of the median income (Betson and Warlick, 2017) or having an income below a poverty line defined as the minimum cost of living (Lee et al., 2019). This concept of relative poverty rather resembles our absolute income definition and its effect on health may be mediated through both materialistic and psychosocial pathways, as explained below.

Theories linking low SEP to poor health

Psychosocial model

While it is evident that poor people will have worse health outcomes when poverty leads to a deprivation of basic material resources such as clean water, food and shelter, it has been scientifically debated how persistent socioeconomic disparities in high-income countries should be explained. Two explanation models that can be distinguished are the *psychosocial* and the *materialistic* theories of the genesis of socioeconomic health gradients.

The psychosocial explanation model recognises the existence of a continuous socioeconomic health gradient. That is, socioeconomic status does not only matter among the most deprived individuals in society but are also important for longevity of affluent individuals. For example, Redelmeier and Singh (2001) found that actors who were only nominated for an Oscars award had higher mortality compared to the actors who actually won the awards. The presence of a socioeconomic gradient from the bottom to the top among civil servants at Whitehall has been interpreted as evidence that the status in the hierarchy rather than the material aspects linked to higher positions are most important for health (Marmot et al., 1991, Marmot, 2007). This is supported by the absence of a beneficial health impact of GDP growth, above a threshold level where material deprivation ceases to have serious health impact, claim psychosocial proponents (Wilkinson, 1999). Explanations of how socioeconomic status influences health includes both different health behaviours and neuroendocrinologic pathways engaging the hypothalamus-pituitary gland-adrenal gland axis, which has proved to be triggered by threatened social position among monkeys (Shively and Clarkson, 1994).

Rather than the materialistic aspects of health, it is the psychosocial comparison that is placed at the focus of interest. Once basic material needs are satisfied, the reason why higher income improves our health is that it can buy us cars, houses, clothes or experiences that increase our status. Income is related to health because it functions as a score counter for socioeconomic status. The degree to which these items increase an individual's status is then dependent on what people who surround the person can purchase. Therefore, it is the relative income rather than the absolute income that matters most. Since the psychosocial comparison exists across all socioeconomic strata, relative income will be important across the whole socioeconomic gradient (Marmot, 2007).

Materialist model

The materialist model emphasises the importance of health promoting resources as key determinants of health, even in rich societies. The material goods an individual possesses will determine the availability of healthy housing, leisure time activities, health care including medications, transportation and education. While the poorest strata are excluded from some of the studies of psychosocial researchers, materialist researchers tend to direct comparatively more focus to the poorest proportion of the population (Lynch et al., 2000a).

A related debate with its peak intensity at the advent of this century concerns the interpretation of the association between income inequality and health. Wilkinson and Pickett (2009) presented data showing that above a certain level of GDP, rather than increased wealth it is the degree of economic equality that is most important for how healthy a population is. While Wilkinson et al. claimed this association was due to negative subjective experiences of inferiority related to low relative income (Marmot and Wilkinson, 2001), Lynch et al. (2000b) questioned the robustness of this finding and shifted focus to the political and economic processes that determine the degree of income inequality. A materialistic interpretation of this observation is that the same historical and cultural processes that result in income inequalities will affect important determinants of public infrastructure available to an individual. They also underscore the unintended risk that psychosocial explanation models locating the cause of health disparities in subjective processes may result in victim blaming and hamper structural change. Humber (2019) highlights the correlation in time between increased union membership and increased life expectancy in the UK. In the materialist framework, absolute income as a proxy for available material assets of an individual is more important for health than the relative income compared to other individuals as a proxy for psychosocial strain. The materialist model is also related to the Social Determinants of Health (SDH) approach that is summarised in the rainbow model (see Figure 1) (Dahlgren and Whitehead, 1991). This model conceptualises the different layers at which social factors act upon health. The outermost layer 1 represents macro-level factors such as the economic system, social policies and environmental factors that tend to be stressed by materialistic researchers. In layer 2 we find the socioeconomic factors most frequently analysed within social epidemiology, such as education, work environment and health care services, which are equally stressed by psychosocial and materialistic researchers. Moving closer to the individual, in layer 3, social factors located in the communities such as social support and participation in society are located. These are more related to psychosocial theories of social cohesion as a key determinant of health. In layer 4, finally, we find the individual level determinants of health which include health behaviours and other factors that constitute the major interest for general epidemiology. Individual coping mechanisms can also be located in this layer.

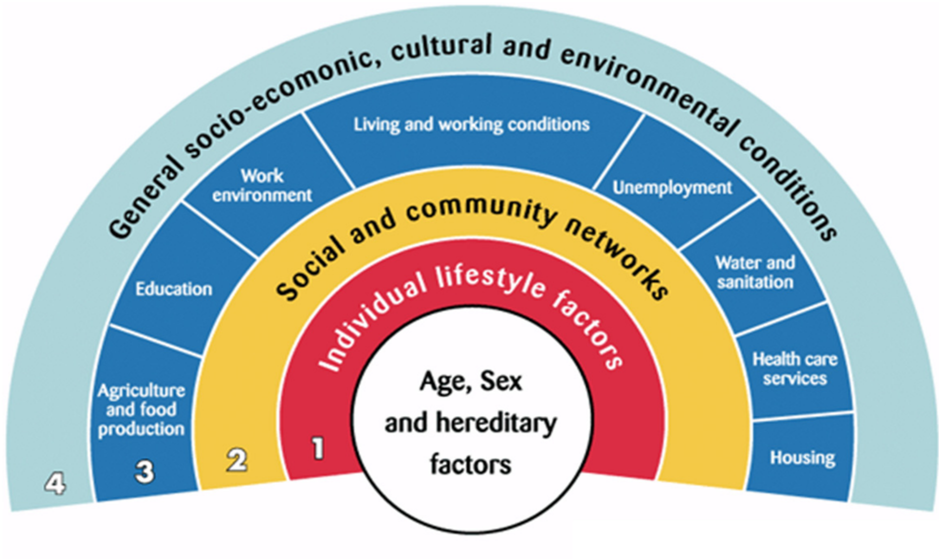


Figure 1. Rainbow model of the Social Determinants of Health
Rainbow model of four layers of the Social Determinants of Health, originally presented by Dahlgren and Whitehead (Dahlgren, 1995).

Gender

While biological sex is determined by characteristics such as chromosomal constitution, gonads or secondary sex characteristics, the concept of gender refers to characteristics of women and men that are socially constructed and due to conventions and norms regarding behaviours, gender roles and the relationship among and between women and men (Krieger, 2001). Both sex and gender can be of relevance to the diagnosis, prevention and treatment of disease (Mauvais-Jarvis et al., 2020). Sex disparities that may be relevant for the distribution of COPD exist, for example average airway size which is smaller for women than men with the same lung size (Merkus et al., 1996). Several downstream risk factors for COPD are differently distributed among men and women due to gender roles. For example, smoking prevalence in Sweden has in the past shifted from being more common among men to being more common among women (Ali et al., 2009), but now prevalence is similar for men and women. Findings regarding the vulnerability to tobacco smoke for incident COPD are diverging. Haghani et al. (2020) found that risk of developing COPD as a consequence of smoking was higher among men than women, but other researchers have found smoking women to be more susceptible to COPD compared to smoking men (Prescott et al., 1997, Sorheim et al., 2010). Occupational exposures hazardous for airways are most common among men (Blanc et al., 2009) whereas exposure to biomass fuels appears to be a more important risk factor for COPD among women in low- and middle-income countries (Liu et al., 2007).

Country of birth

Ethnicity and "race" are sensitive concepts and a tension exists between the need to utilise categories in order to unveil health inequalities and the risk of contributing to stigmatising stereotypes of socially constructed categories by utilising such labels. The concept of "nation" is also a socially constructed entity that contains ideas of homogeneity regarding culture, language and solidarity between inhabitants of any given country (Karlsen and Nazroo, 2017). Ethnicity or race is a commonly used concept in Anglo-Saxon research whereas in Sweden register studies more frequently utilise country of birth, since ethnicity or race is not registered.

Immigrants have higher mortality (Albin et al., 2005) and worse self-rated health compared to people born in Sweden (Rostila, 2010). However, these associations differ depending on the group of migrants and the studied health outcome (Rostila and Hjern, 2018). Among men, immigrants have higher smoking rates compared to people born in Sweden, but that association is less clear for women (Landberg et al., 2018). Existing evidence does not show a clear association between migration status and COPD risk (Eisner et al., 2010, Borné et al., 2019, Hu et al., 2016).

Ethnicity and country of birth are relevant in the social epidemiological study of COPD for several reasons. First, the probability of belonging to a higher SEP is lower for immigrants compared to people born in Sweden (Katz and Österberg, 2013). Second, the effect of having a given SEP, defined through income, education or another proxy or composite measurements may differ according to whether you belong to an ethnic minority or not. Kaufman, Cooper and McGee (1997) showed that ethnic minority groups in the USA are more likely to live in neighbourhoods where expenses are higher, and therefore similar incomes do not lend similar access to material resources. *Status incongruence* refers to the fact that immigrants not only face higher thresholds to enter the labour market, but that immigrants who get a job tend to have lower salaries, lower status occupations and occupations that do not match their educational achievements (Rostila and Hjern, 2018). Third, smoking habits of immigrants' country of origin may influence their risk of smoking, over and above the risk or protective effect conveyed by their SEP (Lindstrom and Sundquist, 2002). Fourth, being exposed to racism increases risk of smoking as an unhealthy coping mechanism (Shariff-Marco et al., 2010) and racism within Swedish health care is an under-investigated issue that contributes to health inequities (Bradby et al., 2019). While the specific study of the association between ethnic group and COPD is not the focus of this thesis, I consider country of birth in the intersectional studies (II and IV). This is a crude variable that conflates individuals from different country groups and does not necessarily consider experienced racism, but we nonetheless consider it an important dimension in an intersectional matrix.

Civil status

Civil status was included in study II and IV since it is a variable that captures aspects of normativity central to intersectional research. Evidence exists that living alone constitutes a risk factor for poorer quality of life (Henoch et al., 2016b) and inadequate medical treatment (Tottenborg et al., 2016) among COPD patients. People in Sweden who live alone, especially unmarried and divorced individuals, have higher risks of smoking compared to married or cohabiting individuals. These risks are attenuated but remain when adjusting for economic conditions (Lindström, 2010). The effect of civil status on a composite health outcome termed frailty was different between men and women in a cohort of elderly individuals in Sweden. While being partnered protected men against frailty, older women who lost their partner displayed lower odds of frailty compared to women who remained partnered (Trevisan et al., 2020).

Age, embodiment and life course epidemiology

While older age implies an increased risk of COPD and ageing lungs show pathological and immunological similarities with lungs of COPD patients (MacNee, 2016), it is unclear whether a healthy ageing process implies increased risk of COPD or if it is the accumulation of exposure to risk factors for COPD across the life course that make elderly individuals more vulnerable to COPD (GOLD, 2020). Although ageing may be shallowly grasped as a strictly biological phenomenon, the mode in which we age is a highly social process. With increasing age, experiences of material deprivation or prosperity, discrimination, or privilege leaves its marks on our bodies (Krieger, 2005). Therefore, socioeconomic inequities in health are best understood from a life course perspective where specific vulnerable periods exist. The SEP of a child's parents influence the risk of low birthweight (Diderichsen et al., 2012), which in turn is associated to low pulmonary reserve capacity and increased susceptibility to COPD (Brostrom et al., 2013). Furthermore, the socioeconomic circumstances of the family, interplaying with societal institutions such as preschools and schools, influence the course of an individual through the educational system with long-lasting effects on individual SEP and adult health (Diderichsen et al., 2012). The association between age and health can be mediated through the ageing process, period effects that account for time-varying levels of exposures across calendar years and cohort effects if specific cohorts are exposed to increased risk of COPD (Cerdá and Keyes, 2017). In social epidemiologic studies of COPD, age constitutes a challenging confounder. Age is positively associated to both incident COPD and increasing income levels until the age of retirement, which is around 65 years in Sweden. Average length of education has increased for successively later cohorts. Exposure to immediate risk factors for COPD such as smoking and occupational exposures have diminished during the last decades, while socioeconomic gradients in exposures to risk factors remain (Pleasants et al., 2016).

Intersectionality

While intersectionality is accepted as the most valid concept of social stratification in modern sociology (Green et al., 2017, Bauer, 2014, Merlo, 2018), it has been sparsely applied in the context of social epidemiology. Stratification and adjustment for several social factors is common, but an explicit intersectional approach that simultaneously considers several power dimensions has never been applied in the study of COPD epidemiology. The intersectionality scholar Hancock (2007) distinguishes between “multiple approaches” and “intersectional approaches”, and claims that while both consider several social categorisations at the time, the former implies a static view of categorisations and a presumption that members of a single category can be regarded to be uniform, whereas the intersectional approach has a more dynamic stance on social categorisations and acknowledges heterogeneity within such categories. In other words, it is not possible to isolate the effect of class by adjusting for ethnicity, since ethnicity may be one way that social class is experienced. One cornerstone of intersectionality theory is the notion that the socioeconomic situation, or the position of relative privilege or advantage in society, of an individual is impossible to properly assess by simply summing the effects of the different categories that define their social location. This is expressed by Bowleg in the title of a seminal paper: “When Black plus Lesbian plus Woman not equal Black Lesbian Woman”. The reason for the inappropriateness of summing Black plus Lesbian plus Woman is that intersectional interaction occurs between the different social dimensions of race, sexual orientation and gender (Bowleg, 2008). Intersectionality research is not a homogenous research field and McCall distinguishes between inter-categorical, intra-categorical (not further discussed here) and anti-categorical intersectionality. The anti-categorical approach emerged simultaneously from feminist, poststructuralist and antiracist theories, resulting in the coining of the term *intersectionality* by the legal scholar and feminist Crenshaw in 1989 (Crenshaw, 1989, Bauer, 2014). These three research fields formulated a critique of the validity of analytical categories that were being used (McCall, 2005). In anti-categorical intersectionality, social life and its multiple and fluid subjects and structures are considered too complex for fixed categories to be anything but simplifying social fictions. Furthermore, the application of those simplified categorisations by authorities and the research community can contribute to the production or essentialization of differences between groups. Some researchers, claims McCall, argue that the language creates the categorical reality more than the reality produces the categories (McCall, 2005). In conclusion, the anti-categorical approach refutes the use of the common social categorisations that constitute the foundation of quantitative social epidemiology.

Inter-categorical intersectionality, henceforth simply called categorical intersectionality, acknowledges that there are observable relations of inequality between already defined categories, although these categories are imperfect and changing. The complexity that arises when performing comparative multi-group analyses has to do with the exponentially increasing number of unique social locations that appear when simultaneously considering even simple categorisations of SEP (high, middle, low), gender (male, female) and migration status (native, immigrant) (McCall, 2005). Bauer argues that public health research may be much enriched by the intersectionality framework which can both provide an improved mapping of health disparities and constitute a theoretical foundation to increase the understanding of heterogeneity within unidimensional categories (Bauer, 2014). To contribute to the application of intersectionality approaches in quantitative research Bauer identifies seven challenges that need to be dealt with, among others the problems arising when interpreting intersectional interactions on the logistic scale. This is problematic since it is the additive scale that is most consistent with both social and biological causation. Bauer also notes that multilevel analysis is a promising statistical approach to bridging the gap between intersectionality theory and public health (Bauer, 2014).

Intersectionality is not only a research approach but also a platform for political activism aiming for social change. While one advantage of including an intersectionality perspective into population health research is that it adds specificity, and thereby improves the understanding of the individual heterogeneity within unidimensional categories, cautions must be made against presumptive intersectional approaches that simply add more social categories to increase the discriminatory accuracy (DA) of a model (Wemrell, 2017). The intersectional character of research is defined by the questions that are being asked and the critical stance towards the social categorisations adopted, and not by the applied methodology.

Individual heterogeneity in modern epidemiology

One of the main tasks for modern epidemiology is to identify risk factors for different health outcomes that can ideally guide interventions to improve population health (Galea, 2013). Risk factors are frequently evaluated by reporting measures of average differences such as odds ratios (OR), absolute risk difference (ARD) and relative risks (RR). In several publications during the last two decades, Merlo et al. have directed critique at this exclusive focus on average differences between categorisations that can be defined by biological, geographical and socioeconomic criteria (Merlo et al., 2017, Merlo and Mulinari, 2015, Merlo, 2014, Merlo et al., 2013, Merlo et al., Merlo et al., 2005b, Merlo, 2003, Lynch et al., 2010, Merlo et al., 2012). A higher average risk pertaining to a certain group is often interpreted as entailing increased risk for *all* individuals belonging to that category, which has been denominated as the *tyranny of the averages* in risk factor epidemiology (Merlo et al., 2017). Nevertheless, it is known that even average differences that are generally considered as large, such as an OR of 10, can be found in the presence of a very poor ability of the risk factor to discriminate individuals that develop the outcome from those that do not (Pepe et al., 2004). This is because the same difference between two groups in average propensity to develop an outcome may exist regardless of whether the overlap in distribution of individuals' propensities is large or small. This concept corresponds with assessment of the so-called area under the receiving operator characteristic (ROC) curve or AUC (Royston and Altman, 2010), which is a measure of DA.

Analogously, when comparing health outcomes between categories of exposure such as intersectional strata or counties, it is highly relevant to quantify not only average differences in outcome between groups but also how much of the total individual variance in the health outcome that is located between the categories' averages. This notion corresponds with measurement of the variance partition coefficient (VPC). To explain this key idea, I use a modified example published elsewhere (Merlo, 2019, Merlo et al., 2019).

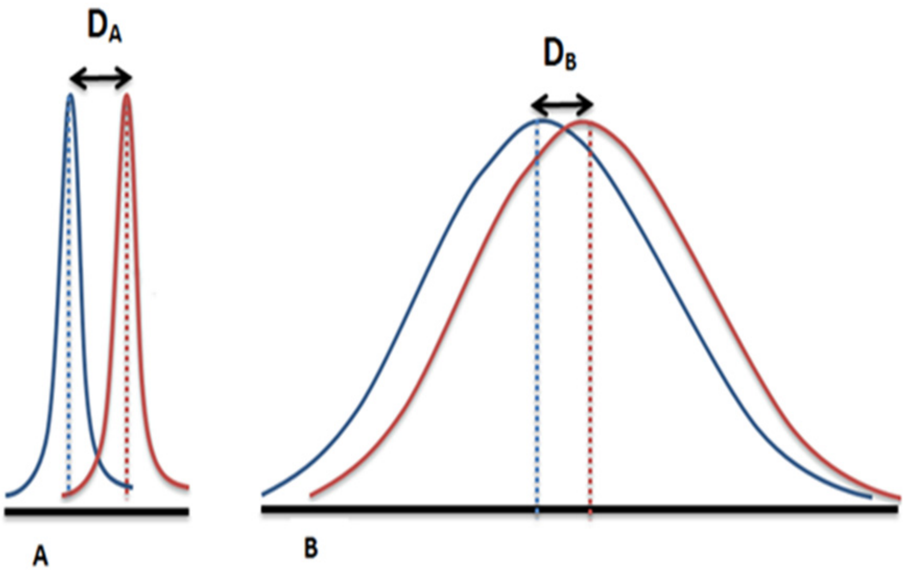


Figure 2a–b. Same average difference in the presence of small versus large intra-group individual heterogeneity around the averages
The figure represents the individual distributions of a continuous variable, for instance Forced Expiratory Volume in 1 second (FEV_1), in two hypothetical income groups.

Figure 2a–b presents the distribution of FEV_1 in two hypothetical income groups. The difference in average individual FEV_1 between the two income groups in scenario A (D_A) is as large as that presented in scenario B (D_B), but the individual variation around the average values is much smaller in scenario A than in scenario B. Clearly, the same difference in the average value between the two income groups is possible with very different degrees of individual variation within those groups.

In the first scenario, 2a, the individual variation in FEV_1 around the average values is very small in relation to the difference between the income groups' average values. Since there is almost no overlap between the two groups' individual distributions, we can say that a large share of the total variation in individual lung function operates at the income group-level. Thus, when the overlap is very small (i.e., a high VPC), we can initially say that the relevance of the income groups in relation to the outcome is strong.

In contrast, in the second scenario, 2b, the variation in individual outcomes around the income groups' averages is very large in relation to the difference between the average values. In this scenario, there is substantial overlap across the two distributions (i.e. a low VPC) and, therefore, the relevance of the two income groups in relation to the outcome is more questionable.

In the former case, it makes sense to intervene on individuals in the high-risk group with preventive, diagnostic or therapeutic interventions. In the second case, on the other hand, exclusively targeting individuals in one group would both lead to many cases being missed and to unmotivated interventions.

Evaluating discriminatory accuracy

Both the AUC and the VPC are measures of DA with rather similar interpretation. The choice of one versus another mainly depends on technical reasons. While scarcely applied in social epidemiology, the notion that average differences need to be accompanied by measures of discriminatory accuracy is recognised in clinical research evaluating prognostic abilities of risk factors and risk scores (Pepe et al., 2004). The ROC curve plots the True Positive Fraction (TPF) (number of exposed individuals that have the outcome / number of individuals that have the outcome) against the False Positive Fraction (FPF) (number of exposed individuals that do not have the outcome / number of individuals that do not have the outcome). This can equivalently be expressed as sensitivity / 1-specificity. The TPF will be higher if you accept a larger FPF. By plotting the TPF against the FPF for all different FPF values (0–1) a line is drawn that creates a curve. The area under that curve can take a value between 1 and 0.5 and constitutes the AUC which is a numerical representation of the DA of a model. A value of 1 implies that a model perfectly discriminates between individuals with and without the outcome whereas a value 0.5 means that the model is as informative as flipping an unbiased coin.

The concept of VPC identified above is also a measure of the discriminatory accuracy of a model and has been mostly used in multilevel regression analysis. The VPC corresponds with the Intraclass Correlation Coefficient (ICC) (Rasbash and Goldstein, 1994, Merlo et al., 2005a) when the structure of the data is hierarchical. In this case the VPC is the ICC, as it corresponds with the correlation in the outcome between two individuals randomly selected from the same cluster (i.e. county, intersectional stratum).

In multilevel analyses the total variance is partitioned between different levels of analyses. The relevance of a specific context can then be evaluated by assessing what proportion of the total variance that is attributable to the context of interest. The share of the total variance that exists between groups is compared with the total variance and expressed as ICC or VPC. Contexts with high relevance for an outcome will thus express a large ICC, whereas a low ICC indicates a heterogeneous distribution of the outcome within the different groups.

When the groups or strata have a similar size the correlation between AUC and VPC is high, as it has been calculated by Merlo and Leckie using simulated data and is presented in Figure 3 (Merlo et al., 2019). However, if the strata have very different sizes the AUC and the VPC may differ, and in that situation they provide complementary information (Merlo et al., 2016).

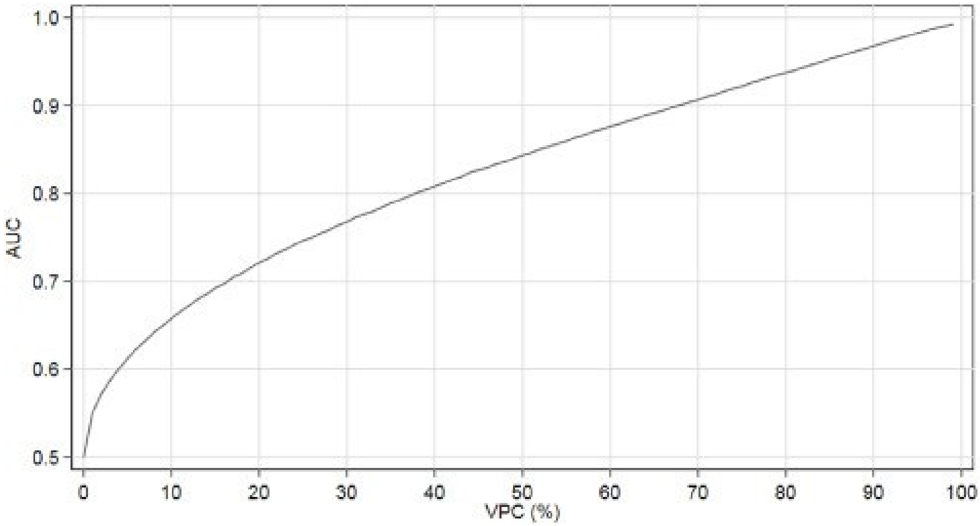


Figure 3. Correlation between AUC and VPC
This figure was published by Merlo and Leckie (2019) and illustrates the relationship between the variance partition coefficient (VPC) and the area under receiver operating characteristics curve (AUC) for a binary individual health outcome. The figures are based on simulated data. Specifically, balanced two-level datasets (100 areas with 100 individuals per area) where the population average prevalence is 50% and where VPC varies from 0 to 100% in increments of 1. For each simulated dataset, the AUC was calculated based on the individual predicted probabilities. Simulations were repeated 1,000 times to average away the simulation variability.

The above referenced literature on the associations between COPD on one hand and SEP, gender, ethnicity, civil status and geographical contexts on the other, are focused on average differences, without assessment of DA. Revisiting well documented health disparities with a DA perspective may provide novel insights on the appropriateness of interventions targeting groups with higher average risk of negative health outcomes (Mulinari et al., 2015). Therefore, the quantification of DA throughout this thesis provides novel and complementary information that is necessary to appropriately assess the socioeconomic disparities in COPD morbidity and plan public health interventions.

Causation in (social) epidemiology

Much methodological development in both general and social epidemiology aims at approaching causal conclusions despite lack of experimental data. To infer causality of an exposure, such as low SEP, on an outcome, such as COPD, requires a comparison between the risk for incident COPD if an individual were exposed to low SEP with the risk if the same individual were not exposed to low SEP. Since an individual cannot simultaneously be both exposed and un-exposed to low SEP, researchers aiming at assessing causality need to speculate about the counterfactual situation in which an individual actually exposed to low income were unexposed, or vice versa. The problem of causal inference is thus a problem of missing data (Rosenbaum and Rubin, 1983). That is, the fundamental problem is that individual causal effect (ICA) cannot be estimated because the potential outcome in the counterfactual situation can never be observed. However, we can calculate the average causal effect (ACE) if by randomisation or other techniques we can ensure that the assignation of the exposure is not associated with the outcome when we compare groups with different exposure. A randomised clinical trial (RCT) is one way of estimating ACE. If people at random are assigned to a life with or without low SEP and the risk for incident COPD is analysed, that would constitute a (hypothetical) study design that estimates the ACE of SEP on incident COPD (Bind and Rubin, 2019, Rubin, 1974). The randomisation in an RCT ensures that the probability of being exposed to a given treatment is random, regarding all observed and unobserved baseline variables. The comparison groups are balanced with regard to all observed and unobserved variables that can condition the probability of both the exposure and the outcome and that could therefore be confounders. Exposure is thus the only thing that differs between the two groups. The ACE is as close as we can theoretically get to the counterfactual world in which an exposed individual is simultaneously unexposed (Austin, 2011).

In New York, an RCT studied the effect on mental health of moving from public housing in poor neighbourhoods to private housing or non-poor neighbourhoods among 512 children (Leventhal and Brooks-Gunn, 2003). In Sweden, a small experiment has been performed that provided individuals with severe mental disorders an extra monthly income of USD 72 and studied the effect on self-rated health. (Topor and Ljungqvist, 2017). It is unfeasible for both economical and practical reasons to perform randomised experimental studies on a large scale to investigate a causal effect of low SEP on the incidence of COPD. A conceptually interesting alternative to estimate ACE of low income on health using observational data is the propensity score analysis (Elstad and Pedersen, 2012, Austin, 2011). Here, one first calculates the propensity of the exposure (e.g. low income) based on observed information and then calculates the risk difference in individuals with a similar propensity but differential exposure (e.g. we identify people with low income and people with high income who have the same propensity of being in the low income category and calculate the difference in COPD risk between the low and the high income categories).

During the work with this thesis, one research project evaluating a propensity score model to investigate an eventual causal relationship between low income and incident COPD was initiated. However, despite good access to socioeconomic and demographic as well as clinical variables, it was not possible to obtain a propensity score model that created groups that were balanced. That is, the distribution of the propensity for low income badly overlapped between the groups with low and with high income. Therefore, since we could not find enough individuals with similar propensity scores but different income the analysis was abandoned.

Whereas the lack of a methodological focus on the causal relationship between social factors and COPD can be considered a weakness, the focus on approaching causal conclusions in current epidemiology has been criticised, since this etiologic focus comes at the expense of research guided by a consequentialist principle, i.e. research that can result in health improvement (Galea, 2013).

Proportionate universalism

The evident socioeconomic gradient in COPD prevalence, morbidity and mortality has led researchers to conclude that "a standardized method must be created to include socioeconomic status in the prognostic calculations of disease" (Sahni et al., 2017). As pointed out above, if interventions should be directed differently to individuals according to their SEP, it does not suffice to design such interventions based on average differences between individuals with different SEP. It is imperative to assess the individual heterogeneity around those averages. Therefore, the large literature showing increased average morbidity among COPD patients with low socioeconomic position (Gershon et al., 2012) needs to be complemented with studies that assess the DA of those socioeconomic factors.

If social epidemiologists should convince policy makers and public health professionals that social and economic risk factors merit clinical consideration, we must evaluate such risk factors rigorously and acknowledge likely side effects of proposed interventions. If an intervention is planned based on categorisations with low DA, the risk of detrimental side effects must be minimised to align with the principle of not doing harm (Merlo et al., 2017).

These ideas pair well with the concept of proportionate universalism, proposed by Marmot and Bell (Marmot and Bell, 2012), as one strategy to reduce socioeconomic disparities in health. Universalism and targeting have been considered as opposing principles to guide interventions aiming at increased equality, i.e. an intervention can either be universal and directed at the whole population or targeted when directed only at specific groups with enhanced needs (Korpi and Palme, 1998). According to proportionate universalism, that distinction is not necessary. When universalism is instead coupled with targeting, interventions directed at the whole population can be more intense among people with increased needs. There is no consensual definition of interventions that align with this principle and rather few studies exist that evaluate interventions guided by proportionate universalism, according to a recent review (Francis-Oliviero et al., 2020). According to proportionate universalism, a response to a finding of an increased average COPD risk for people with low SEP in combination with low DA would thus be universal interventions such as increasing tobacco taxation, ensuring education, and healthy living and working conditions for all. When the DA is high, on the other hand, a proportionately higher degree of targeting of interventions to the exposed group(s) can be motivated.

Health care (e)quality

An overarching programmatic aim of Swedish health care is to provide equitable care that is distributed according to needs (Kommissionen för Jämlik Hälsa, 2017). In addition to moral arguments for an equitable health care system that may or may not be shared by political and public health leadership (Berwick, 2020), there is an efficacy argument that is of strategic importance. The greatest return from health investments can be achieved when directing health care resources to population groups that have worse health (Dahlgren and Whitehead, 1991). The efficacy gained through equitable health care was also stressed in a report on equitable health care where a conceptual framework viewing equality, availability, knowledge-base, patient focus, safe health care and prevention as indispensable dimensions of an efficient health care was presented. It was also stressed that the continuous evaluation of quality of health care, along all these dimensions, is per se its own dimension of health care quality (Merlo et al., 2008).

Equity in health care can be divided into horizontal equity referring to equal access to health care for people with similar needs, and vertical equity meaning that health care is most available for people with more health care needs (von dem Knesebeck, 2015). The determinants of health care utilisation are complex and include health status, perceptions of care need and cultural factors as well as geographically and economically accessible health care supply (Burström, 2009). However, according to the Inverse Care Law presented by Tudor Hart (1971), health care tends to be more available for groups with lesser needs, especially when health care systems are exposed to market mechanisms. The need for monitoring of health care equity is therefore increasing, since Swedish health care reforms over the last decades have increased exposure to market mechanisms. Although evidence of the effect of these market-orientations of the Swedish health care sector is limited, studies from northern Sweden have shown pro-rich inequalities in the use of Primary Healthcare Centre (PHC) physicians but horizontal equity in the use of specialists (San Sebastián et al., 2017). A review of the effects of privatisation of health care indicated that access has increased most in more affluent areas with lesser needs (Burstrom et al., 2017).

The equitability of the health care system should not only be evaluated along socioeconomic and intersectional dimensions. Geographical inequalities must also be assessed and county disparities have become a focus of Swedish health care evaluation (Socialstyrelsen, 2015). Investigating socioeconomic and county disparities in cancer care, the Swedish Agency for Health and Care Services Analysis acknowledges difficulties in comparing the relevance of counties and sociodemographic contexts (author's translation):

> even though it is not very simple to objectively decide whether a difference is large or small, and there are problems comparing socioeconomic and demographic disparities with regional disparities, we consider that regional disparities are generally more evident for the interventions that we have analysed. While the spread between counties for multidisciplinary conference and treatments are around 10, 20 or 30 percentage units, disparities across educational groups are generally a few percent, maximum 8 percent units, when they exist. (Vårdanalys, 2019)

The study on discontinuation (paper III) includes a framework for evaluation of the (e)quality of health care systems that presents a solution to the problem of comparing the relevance of sociodemographic versus geographical contexts.

General aims

The principal aim of this thesis is to deepen the understanding of socioeconomic inequities in COPD morbidity. Further aims are to contribute to the inclusion of social theory in the social epidemiologic study of COPD and to the development of epidemiological methods to assess disparities in incidence of COPD, in health care provided to COPD patients and in the prevalence of smoking, a major mediator of the detrimental effects of low SEP on COPD risk.

Questions

1. To what extent do absolute income and relative income influence the risk of incident COPD, over and above age?
    a. What is the DA of models including absolute income and relative income, respectively?

2. What is the intersectional pattern of smoking prevalence and of incident COPD?
    a. To what extent is the risk of smoking and the risk of COPD attributable to main effects of variables included in an intersectional model versus interaction effects between these variables?

3. How does discontinuation to inhalatory maintenance medication among patients with a hospital COPD diagnosis and previous maintenance medication in Sweden vary across sociodemographic categories and counties?
    a. What proportion of the variance in discontinuation is attributable to sociodemographic factors and to counties? That is, which information has the highest DA?

Methods

Study population

Swedish registers with national coverage

This thesis is based on data from several registers with national coverage as well as data from the Swedish National Health Survey (NHS). In Sweden, there is a long tradition of epidemiologic register studies. Conditions are favourable considering the existence of a unique personal identity number and high quality registers containing both medical and socioeconomic information (Ludvigsson et al., 2009).

The Total Population Register (TPR) is administered by Statistics Sweden and contains data for the whole Swedish population on birth, death, immigration, emigration and internal migration as well as data on the family structure. This register is updated on a daily basis with data from the Swedish Tax Agency and provides background data for other national registries as well as functioning as a coordination register. In this thesis, the TPR provided information on age, gender, civil status and migration status. Statistics Sweden also administers longitudinal integrated databases for health insurance and labour market studies (LISA), which comprise detailed data covering demographics, educational achievement, income, employment and social insurance, which is registered at the end of each calendar year (Statistics Sweden 2016). In this thesis, LISA provided information on income and education.

The National Board of Health and Welfare runs three registers that were used for the construction of the databases utilised in this thesis. First, the Swedish cause of death register is a national register that provides data on the cause of death of all fatalities in Sweden. Data is based on medical death certificates that are submitted by physicians to the National Board of Health and Welfare within three weeks of the date of death (Brooke et al., 2017). Mortality data was used to exclude individuals from the study populations. Second, the National Patient Register (NPR) includes medical information including ICD codes from both outpatient external visits as well as inpatient discharges. Primary health care visits are not recorded. Last, information on prescribed drugs were retrieved from the Swedish Prescribed Drug Register (SPDR) which has, since 2005, recorded all medications dispensed by Swedish pharmacies, excluding storage in hospitals and nursing homes (Wettermark et al., 2007).

Study I–III are based on a database constructed from all the above mentioned registers. The database includes all individuals who resided in Sweden by the 31st of December 2010. The National Board of Health and Welfare linked data on ICD codes from in- and outpatient specialist care, mortality data from the National Mortality Register as well as information on all dispensed drugs at pharmacies requiring a prescription. Statistics Sweden linked detailed socioeconomic information to the database. The inclusion and exclusion criteria as well as the final study samples of study I-IV are summarised in Table 1.

Table 1. List of papers and selection criteria for the study populations
This table presents study questions, populations, selection criteria and final study samples for paper I–IV. ICD=International Classification of Diagnosis; NHS=Swedish National Health Surveys; MAIHDA=Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy; AIHDA=Analysis of Individual Heterogeneity and Discriminatory Accuracy.

Paper	Inclusion criteria	Exclusion criteria	Study sample
Paper I. Importance of absolute income and relative income for predicting incident COPD.	All individuals residing in Sweden on 31st December 2010 aged 55–60 years (N=688 650)	Registered as dead before 2011 (N=77) Emigrated during 2011 (N=4 369) Moved to Sweden in 2006 or later (N=10 482) Previous COPD diagnosis (N=6 628)	N=667 094
Paper II. Intersectional MAIHDA studying incident COPD in strata defined by age, sex, income, education, civil status and country of birth.	All individuals residing in Sweden on 31st December 2010 aged 45–65 years (N=2 536 789)	Dead during 2010–2011 (N=11 722) Moved to Sweden in 2006 or later (N=54 161) Emigrated during 2011 (N=3 643) Previous COPD (N=21 762)	N=2 445 501
Paper III. Relevance of geographical and sociodemographic contexts for risk of discontinuation to maintenance medication for COPD.	Individuals aged 45–80 years residing in Sweden on 31st December 2010 with COPD diagnosis ICD J43–J44 and previous maintenance medication. (N=69 391)	No previous medication (N=16 402) Died during 2011 (N=3 640) Moved to Sweden 2006 or later (N=330)	N=49 019
Paper IV. Intersectional AIHDA mapping smoking prevalence in strata defined by age, gender, education, household composition and country of birth.	NHS respondents between 2004–2016 and 2018 (N=136 301)	People aged <30 years (N=20 566) Missing values on education (N=4 840) Missing values on cohabiting status (N=1) Missing values on smoking (N=850)	N=110 044

Study I

All 688,650 individuals aged 55–60 years as of the 31st of December 2010 and residing in Sweden were included. The narrow age span was chosen to minimise the confounding effect of age on the association between income and incident COPD. We excluded individuals who died before 2011 (N=77), who emigrated during 2011 (N=4,369) or moved to Sweden after 2006 (N=10,482). Finally, we excluded individuals with a registered COPD diagnosis during the previous five years to study incident COPD. A total of 667,094 individuals remained and were included in the analyses.

Study II

In the second study, due to the intersectional approach with 96 strata, we widened the age span and included all individuals aged 45–65. The upper age limit of 65 was chosen to avoid the confounding effect of retirement, generally at age 65, on income. We started with the total Swedish population of 2,536,789 individuals aged 45–65 years as of the 31st of December 2010. We then excluded individuals who died during 2011 (N=11,722), who moved to Sweden during 2006 or later (N=54,161), who emigrated during 2011 (N=3,643) and who had previous hospital diagnosis of COPD (N=21,762). We ended up with a final sample of 2,445,501 individuals.

Study III

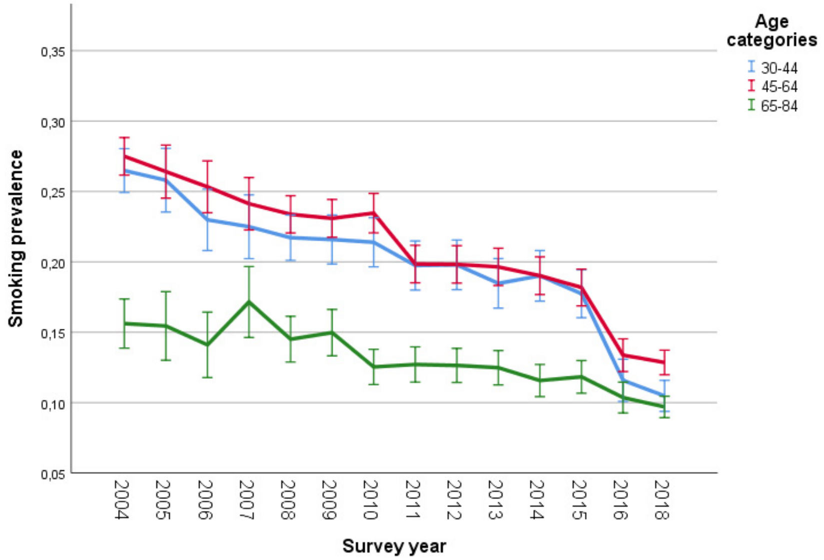
In the third study, we started with 69,391 individuals with a previous diagnosis of emphysema or other COPD (ICD J43 or J44), whereafter we excluded individuals without previous inhalatory maintenance medication (N=16,402) (see below for definition). We then excluded individuals who died during 2011 (N=3,640) or who had lived in Sweden for less than five years (N=330). The final study population consisted of 49,019 COPD patients with previous maintenance medication who had lived in Sweden for at least five years.

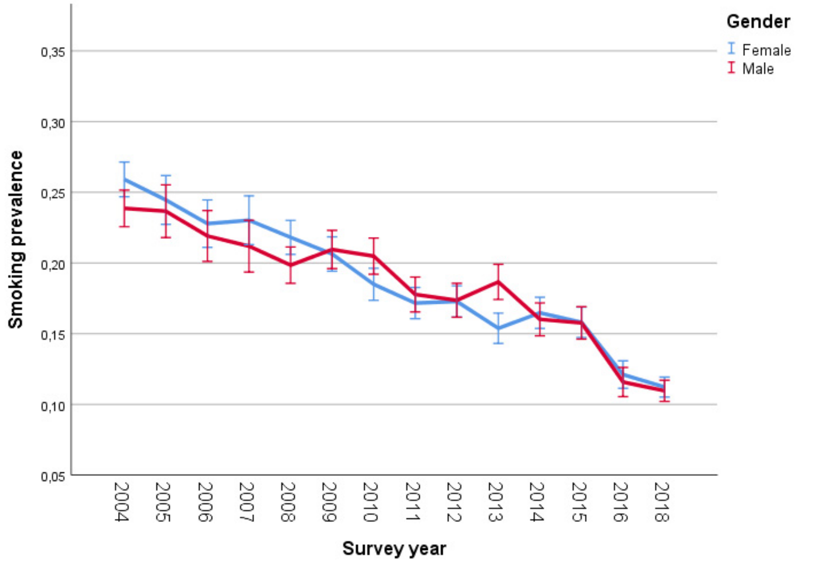
Study IV

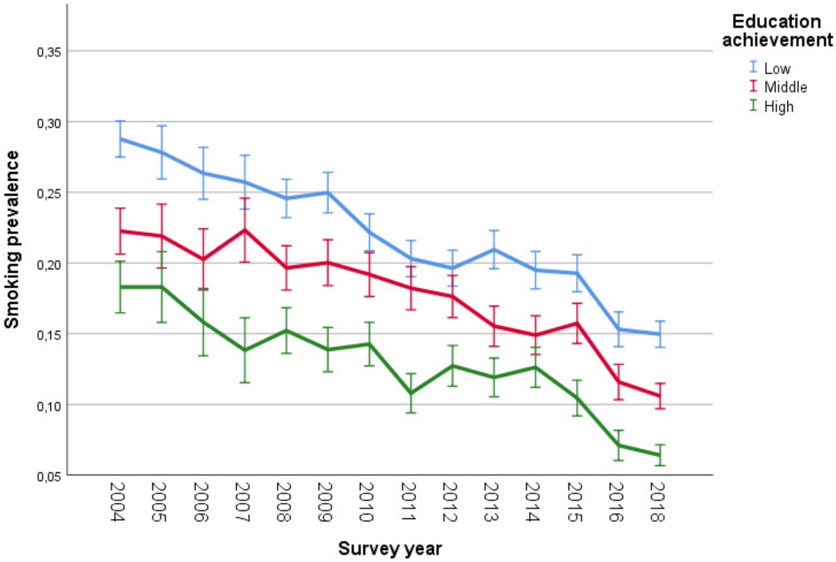
In the fourth study, we used data from the Swedish National Health Survey (NHS). The NHS is administered by the Authority for Public Health and entails 63 questions that are largely identical from year to year. Questionnaires were sent to 10,000 individuals in 2005–2007, 20,000 individuals in 2004 and 2008–2016 and to 40,000 individuals in 2018. No survey was performed during 2017. Response rates have been declining and spans from 60.8% in 2004 to 42.1% in 2018. Respondents answer questions regarding health and social circumstances. Information from Statistics Sweden on income, country of birth, highest educational attainment, civil status and gender was subsequently added to the dataset using the unique personal identity number of all residents in Sweden.

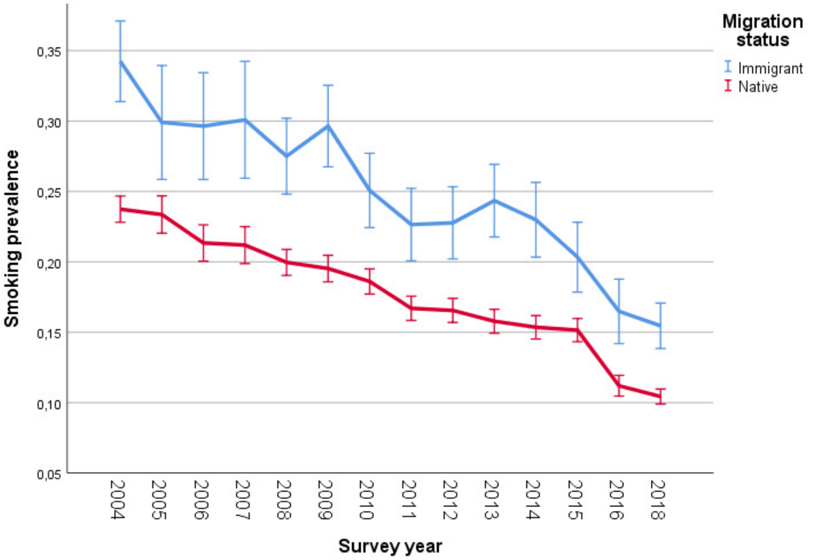
It is known that smoking prevalence in Sweden is decreasing, therefore we expected a cohort effect of the calendar year during which an individual responded to the NHS on the probability of smoking. To assess whether survey year influenced the association between the included sociodemographic variables and prevalence of smoking we started our analysis by investigating the temporal fluctuations in these associations, as shown in Figure 4. While sex differences were small throughout the period and the sex category with highest smoking prevalence changed, we observed consistent differences between groups defined by age, country of birth, educational achievement and household composition. In absolute terms, the gaps between subgroups were static, except for differences between age categories that narrowed in later years.

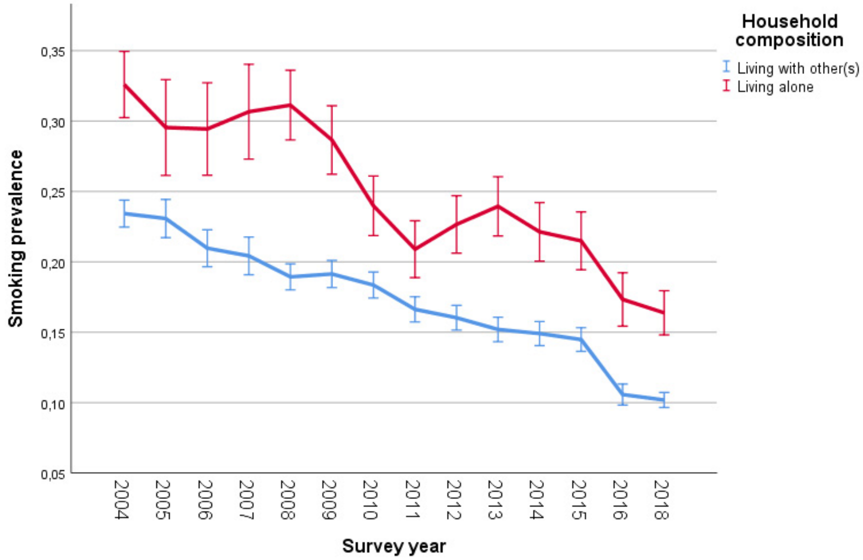
Figures 4a–f. Trends in smoking prevalence in the National Health Surveys for Sweden between 2004 and 2018. Categories of age, gender, educational achievement, migration status and household composition are shown with different lines in the respective graphs, including 95% confidence intervals. The last graph shows the trend of overall prevalence of smoking in the Swedish population aged 30–84 years between 2004 and 2018.



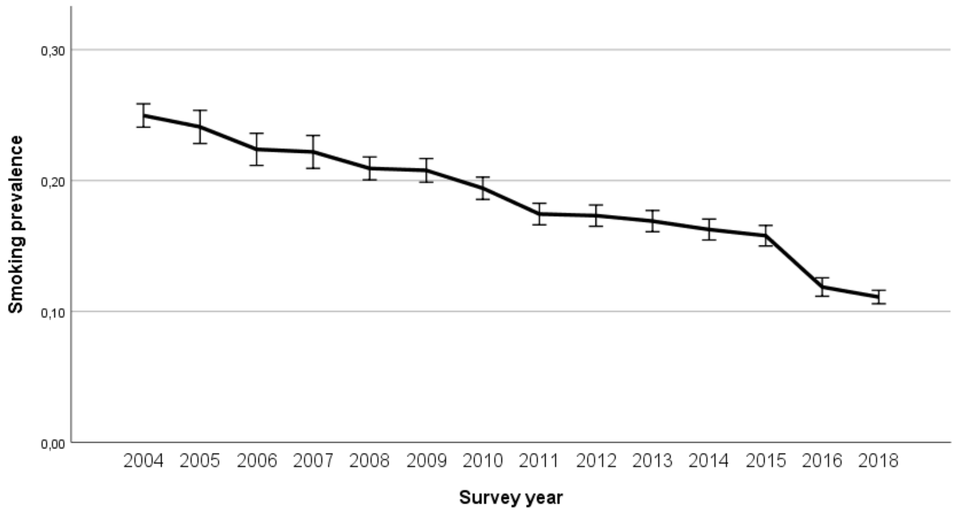



Education achievement
Low
Middle
High
Smoking prevalence
0,35
0,30
0,25
0,20
0,15
0,10
0,05
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2018
Survey year


Migration status
Immigrant
Native
Smoking prevalence
0,35
0,30
0,25
0,20
0,15
0,10
0,05
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2018
Survey year



Household composition
Living with other(s)
Living alone
Smoking prevalence
0,35
0,30
0,25
0,20
0,15
0,10
0,05
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2018
Survey year



Smoking prevalence
0,30
0,20
0,10
0,00
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2018
Survey year

Assessment of variables

Income

Throughout the thesis, all income variables used are individualised disposable family income calculated by Statistics Sweden. This income variable divides the total family income by the number of individuals in the family, taking into account the different consumption weights of different members of the household. For example, an adult who lives alone has a higher consumption weight than each adult in a cohabiting couple. Children have different consumption weights that increase with age. This income variable is the most frequently used for research purposes and reflects the available assets after taxes and different subsidies (Statistics Sweden 2016).

In study 1 the absolute income variable was defined by dividing the whole Swedish population aged 35–80 into five equally sized groups by quintiles based on the income during 2010. The absolute income variable was hypothesised to act through the materialistic pathway. There is no consensus on how to define relative income. We calculated relative income by creating new quintiles of income within the absolute income quintiles. Thereby, individuals with similar materialistic assets (i.e. disposable income) were categorised into different relative income groups and eventual disparities in propensity of COPD across these relative income groups would, according to our hypothesis, be attributable to psychosocial comparison. We then pooled all individuals belonging to the same relative income quintile from the five absolute income groups together to create our final relative income variable.

In study II, the income categorization was limited to tertiles of income during 2010 in order to limit the number of intersectional strata. In study III, we also used tertiles of income but instead computed a cumulative income variable. We used information on individualised disposable family income for the years 2000, 2005 and 2010 to compute a cumulative measurement of absolute income. For each of the three years, income was categorised in 25 groups (1 to 25) by quantiles using the complete Swedish population. The quantiles from the three years were then summed up so a patient could have a value between 3 (always in the lowest income group) and 75 (always in the highest income group). Thereafter, we categorised the cumulative income in three groups by tertiles. Individuals with missing values for income during 2000 or 2005 (N=1,002) were assigned the tertile values of the year 2010; no individuals had missing income information for 2010. In study IV, we performed a sensitivity analysis using tertiles of household disposable income.

Other sociodemographic variables

In study II, education was binary defined as high if the individual had any further education after high school, otherwise as low. In study IV, the education variable was coded into three categories by Statistics Sweden. Educational achievement was categorised as low if the respondent had not completed three years of high school education; as middle if they had high school education but less than three years of education after high school; and high if the respondent had at least three years of education after high school. In study II and IV, migration status was defined as immigrant if the individual was born outside Sweden, otherwise as innate. In study III, the geographical context of interest were the counties. COPD patients were categorised into 21 different counties depending on where they resided as of the 31st of December 2010. Gender was always binary defined as legal male or female. In studies I-III, age was defined according to the age as of the 31st of December 2010. People below the age of 35 were excluded from all analyses since AATD is more common among young COPD patients (Köhnlein and Welte, 2008) and the social epidemiology of COPD in a younger cohort may therefore be different. Sixty-five years is the official age of retirement in Sweden and in all studies we wanted to account for the effect on both income and health from retirement (Merlo et al., 2003), either by excluding individuals above this age or by analysing individuals older than 65 separately. In study I, we had a narrow age span (55–60 years) and adjusted for age. In study II, we categorised age into two categories (45–54 and 55–65). In study III, where we studied COPD-patients, we needed to expand the age span to include all individuals aged 35–80 years but created age categories of 35–49, 50–64 and 65–80 years. In study IV, where smoking is the outcome, the age groups were 30–44, 45–64 and 65–84. We chose 30 years as the lower age limit in study IV since we used educational achievement as the indicator of SEP. Around three quarters of people in Sweden who will eventually complete a three year tertiary education will have achieved that educational status when they are 30 years old (OECD, 2010). In study II, cohabitation status was defined as cohabiting if the individual lived with a married partner, registered partner or lived together with a partner with a common child, otherwise as living alone. In study IV, household composition was defined by Statistics Sweden as living with other(s) if the individual lived with a married partner or with a registered partner, otherwise as living alone.

COPD

In both studies where we studied incidence (study I and II), one of the following ICD codes were used to define COPD: J40 (bronchitis, not specified as acute or chronic); J41 (simple and mucopurulent chronic bronchitis); J42 (unspecified chronic bronchitis); J43 (emphysema); or J44 (other chronic obstructive pulmonary disease). We identified new cases of COPD from January 1st, 2011 to December 31st, 2011. In study III, where we wanted to isolate a COPD population with indication for maintenance therapy (i.e. COPD stage II–IV (Swedish Medical Products Agency, 2015) or B–D in the new classification (GOLD, 2020)), we defined COPD more narrowly using only ICD codes J43 and J44, in addition to the presence of retrieval of any maintenance medication during the previous five years. COPD diagnoses from Swedish hospitals have been validated and less than 10% of diagnoses were uncertain or misclassified, therefore they are considered to be of acceptable validity for epidemiologic studies (Inghammar et al., 2012).

Maintenance medication

In study III, we used the SPDR to get information on both previous maintenance medication and discontinuation. Retrieval of any prescription during 2006–2010 in combination with hospital COPD diagnosis was sufficient to classify an individual as a COPD patient with indication for maintenance medication. Absolute absence of retrieval of any prescription of maintenance medication from January 1st to December 31st of 2011 was defined as discontinuation. All prescriptions with the indication maintenance treatment of COPD available and recommended during the study period were included in the definition and consisted of LABA (salmeterol, formoterol and indacaterol), LAMA (tiotropium bromide) and combinations of LABA with ICS (formeterol and budenoside, salmeterol and fluticasone, and formeterol and beclomethasone).

Smoking

Smoking status was based on self-reported smoking in the NHS. The exact questions have undergone minor changes between 2004 and 2018, but in each survey people were asked the question “Do you smoke?” and if the answer was “yes, sometimes” or “yes” they were considered as smokers. If the response was “no” they were considered as non-smokers. Previous smoking was not assessed in the study.

Statistical methods

Discriminatory accuracy

In study I we performed gender-stratified logistic regression analyses with COPD as the dependent variable. In model 1, we analysed the AUC of a model with only age as a reference value. Model 2 included age and absolute income. Model 3 included age and relative income. Model 4, finally, included age, absolute income and relative income. In all models we presented ORs that were interpreted as relative risks, since the incidence was low. We compared the increment in AUC in models 2–4 to the AUC of model 1.

Intersectional MAIHDA

As described in the introduction, intersectionality theory stresses the necessity of considering several social dimensions at the same time. This creates a number of questions when translating intersectionality from its traditionally qualitative scholarly field into quantitative social epidemiology. The anti-categorical questioning of the social categorisations adopted in epidemiologic research stresses the need to appropriately judge the relevance of social categories. Practical problems come with the numerous intersectional strata that emerge even when using rather simple intersectional matrices.

Intersectionality scholars like Bauer and Green have called for the use of intersectional multilevel models to improve quantitative intersectionality research (Green et al., 2017, Bauer, 2014). Intersectional Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (MAIHDA) is a term that was first proposed by Merlo in 2018 (Evans and Erickson, 2019) and has gained recognition as the new "gold-standard" for investigating health inequalities because it solves many practical issues and brings methods into closer alignment with theory (Merlo, 2018). The conceptual underpinnings and advantages of intersectional MAIHDA are discussed in detail both in the pioneering work by Evans et al. (2018) and in a commentary on that article by Merlo (2018).

Summarising, intersectional MAIHDA provides a detailed mapping of health disparities while treating the social location of an individual, formed by interlocking social dimensions, as a higher-level context rather than as individual characteristics. Thereby, the multilevel approach harmonises with the view of health inequities arising through unequal distribution of power and resources rather than through a combination of risky identities (Merlo, 2018). The calculation of the ICC constitutes a quantification of the relevance of a context for a specific outcome, which for public health purposes can help in the judgement of whether a categorical or anti-categorical perspective is most adequate. Intersectional MAIHDA also enables feasible assessment of multiple interactions, which is valuable since the number of intersectional strata and possible interaction is large in most intersectional models. The multilevel approach also presents precision-weighted estimates of the strata specific risk (i.e. shrunken residuals). This is advantageous when the number of individuals in some strata is small.

In study II, we investigated incident COPD by applying intersectional MAIHDA. In the first step, we constructed an intersectional matrix consisting of all possible combinations of age, gender, income, education, country of birth and cohabitation status (2x2x3x2x2x2=96 strata). The choice of these social dimensions was informed by previous intersectional research and by what is known about associations between different social dimensions and the mediators of COPD, but was also restricted by available data. We then performed a multilevel analysis with the intersectional strata at the second level of analysis and individuals at the first level of analysis. We modelled incident COPD in three successive models.

Model 1, the *simple intersectional model,* is an unadjusted random intercepts model that served two purposes. First, we performed an analysis of components of variance to calculate the ICC. This model conflates the additive effects of the social dimensions used to construct the intersectional matrix and eventual intersectional interaction, and the ICC thus expresses the ceiling explanatory power of our intersectional matrix on incident COPD. Since the outcome was binary, we calculated the ICC using the latent response formulation of the model, which is the most widely used version of the ICC:

$$\mathrm{ICC} = \frac{\sigma_u^2}{\sigma_u^2 + 3.29}$$

Formula 1

where σ_u^2 denotes the between-stratum variance in the propensity to receive a new COPD diagnosis and 3.29 denotes the within-stratum-between-individual variance constrained equal to the variance of the standard logistic distribution (Goldstein et al., 2002, Merlo et al., 2005a). There is no official grading scale for evaluating the ICC of a socioeconomic modelling of incident disease. In the ideal scenario, the ICC of a socioeconomic risk factor should be 0, since that implies no socioeconomic disparities at all. Aligning with the questioning of social categorisations, and in order to avoid perpetuations of socially constructed categorisations that do not represent a relevant context for public health purposes, we want an intersectional model to have a high discriminatory accuracy to consider it relevant. In line with the terminology suggested for evaluation of psychometric test reliability (Cicchetti, 1994), and similar to the grading subsequently proposed by Merlo et al. (2019), we therefore consider that a reasonable grading for social epidemiologic purposes could be (ICC as %): non-existent (0–1), poor (>1–≤5), fair (>5–≤10), good (>10–≤20), very good (>20–≤30), excellent (>30). The second purpose of the model was to calculate predicted incidence and 95% CIs for every stratum. In order to use an additive scale, we transformed the predicted logit (log-odds) of receiving a new COPD diagnosis from the multilevel analyses into probabilities. The probability of receiving a COPD diagnosis in stratum j was calculated according to the formula:

$$\pi_j = \mathrm{logit}^{-1}(\beta_0 + u_j)$$

Formula 2

where π_j is the probability of receiving a COPD diagnosis, β_0 is the intercept and u_j is the random effect for stratum j.

In model 2, the *partly adjusted intersectional model*, we adjusted for one of the dimensions at a time and calculated the ICC in the models that were adjusted for one variable. By doing so, we could quantify how much each of the dimensions contributed to the between-stratum variance seen in model 1. We also calculated the proportional change in between-stratum variance (PCV):

$$\text{PCV} = \frac{\sigma^2_{u(1)} - \sigma^2_{u(2)}}{\sigma^2_{u(1)}}$$

Formula 3

where $\sigma^2_{u(1)}$ and $\sigma^2_{u(2)}$ denote the between-stratum variance from models 1 and 2, respectively. PCVs are typically multiplied by 100 and reported as percentages.

Last, in model 3, the *intersectional interaction model*, we expanded model 1 by including as fixed main effects all the variables that were used to construct the intersectional strata. If all between-stratum variance of model 1 was attributable to the main effects, all 96 random effects in model 3 would equal 0. If intersectional interaction is present, this will be expressed as the between-stratum variance that remains unexplained by the additive effects. The ICC of model 3 thus represents the part of the original model 1 stratum variance that is due to intersectional interaction effects, at least in relation to the set of variables included. Model 3 also served to calculate *total predicted incidences* and *predicted incidences based on the main effects only.* By subtracting the incidence attributable to the main effects from the total incidence, we isolated the incidence attributable to intersectional interaction in each stratum. A positive interaction effect indicates that people in that intersectional stratum have higher incidences than expected based on the simple addition of the risks conveyed by the categories that constitute the intersectional stratum, while a negative interaction means a lower incidence than expected. Model 3 was also used to calculate mutually adjusted unidimensional ORs and 95% CIs for the main effects of age, gender, income, education, civil status and migration status.

Cross-classified MAIHDA in health care evaluation

In study III we focused on quality of COPD maintenance medication and analysed the risk of discontinuation. We used a simple sociodemographic categorisation consisting of 18 strata based on age (35–49, 50–64 and 65–80), gender (male/female) and income tertiles (low, medium and high). The geographical context we investigated were the 21 counties, since counties are the administrative units responsible for health care in Sweden. We used cross-classified multilevel logistic regression models with COPD patients simultaneously nested within the 18 sociodemographic contexts, and within the 21 counties. Underneath these two higher levels of analysis were 372 strata (18x21=378; six strata were empty).

In order to not give higher weight to strata with large numbers of patients, as in the case of traditional single-level analysis, we calculated the average proportion of discontinuation across the geographic and sociodemographic categories. The reliability and precision of the strata information is considered in multilevel models since they are based on reliability-weighted strata residuals (i.e. shrunken residuals) and average proportions (Jones et al., 2016). In addition to this, county differences may be confounded by disparities in the sociodemographic composition of the county populations. Similarly, sociodemographic categories could be confounded by a contextual effect of the county of residence, e.g. an effect of different health care policies of the counties. In the two-way cross-classified MAIHDA, the estimates of the effects on discontinuation of the two contexts are mutually adjusted. We performed a two-way cross-classified multilevel model that decomposes the higher-level variance into county and sociodemographic components. Let y_i denote the number of patients who discontinue in stratum i ($i = 1, \dots, 372$). The model is written as:

$$y_i \sim \text{Binomial}(n_i, \pi_i)$$

$$\text{logit}(\pi_i) \equiv \log\left(\frac{\pi_i}{1-\pi_i}\right) = \beta_0 + v_k + u_j$$

$$v_k \sim N(0, \sigma_v^2)$$

$$u_j \sim N(0, \sigma_u^2)$$

Formula 4

where n_i denotes the total number of patients in that stratum, π_i denotes the probability of discontinuation, β_0 denotes the intercept, u_j denotes the random effect for sociodemographic context j ($j = 1, \dots, 18$) and v_k denotes the random effect for county of residence k ($k = 1, \dots, 21$). The random effects are assumed to be normally distributed with mean 0 and variances σ_v^2 (between-counties) and σ_u^2 (between sociodemographic contexts). The intercept, β_0, is the average proportion (on the log-odds scale) of discontinuation (i.e. grand mean) across all counties and sociodemographic categories, defined as the 372 strata.

This model had three purposes.

1. Mapping county and sociodemographic differences in discontinuation risk

First, we wanted to obtain a mapping of how the individual risk of discontinuation was distributed across counties and sociodemographic strata. Using the intercept and predicted random effects (i.e. shrunken residuals) from the multilevel regression we calculated the absolute risk of discontinuation and its 95% credible interval for each county and sociodemographic stratum. We did this by transforming the predicted logit of discontinuation into predicted proportions. The following formula was used to calculate the absolute risk (AR_C) of the different counties:

$$\mathrm{AR}_C \equiv \pi_k = \mathrm{logit}^{-1}(\beta_0 + v_k) \equiv \frac{\exp(\beta_0 + v_k)}{1 + \exp(\beta_0 + v_k)}$$

Formula 5

Similarly, the following formula was used to calculate the absolute risk of discontinuation of the sociodemographic contexts:

$$\mathrm{AR}_{SD} \equiv \pi_j = \mathrm{logit}^{-1}\left(\beta_0 + u_j\right) \equiv \frac{\exp\left(\beta_0 + u_j\right)}{1 + \exp\left(\beta_0 + u_j\right)}$$

Formula 6

In these formulas the predictions isolate the effects of counties and sociodemographic strata respectively, by holding the effect of the other context constant. The values are thus mutually adjusted. However, the absolute risk predictions represent average values that should be accompanied by measures of county, sociodemographic context and individual patient components of variance and DA.

2. Evaluating the components of variance: the variance partition coefficient (VPC)

In order to consider individual heterogeneities around the averages obtained through formula 2 and 3, we calculated the VPC for counties and sociodemographic strata. The VPC expresses the share of the total variance in latent propensity of discontinuation that is attributable to the contexts of counties and sociodemographic strata. The higher VPC for the county level (VPC_C), the more relevant the county context is for understanding individual variation in the latent risk for discontinuation. The outcome was binary, so we used the latent response formulation and calculated the VPC_C as:

$$VPC_C = \frac{\sigma_v^2}{\sigma_v^2 + \sigma_u^2 + \frac{\pi^2}{3}}$$

Formula 7

where π denotes the mathematical constant 3.1416, and $\frac{\pi^2}{3} = 3.29$ is the variance of the standard logistic distribution. We then multiply the VPC_C by 100 and interpret it as a percentage. Analogously, the VPC for the sociodemographic level ($\mathrm{VPC_{SD}}$) can be calculated as:

$$VPC_{SD} = \frac{\sigma_u^2}{\sigma_v^2 + \sigma_u^2 + \frac{\pi^2}{3}}$$

Formula 8

3. Evaluating DA of the information on counties and sociodemographic contexts

As explained in previous sections, AUC is a well-known measure of DA. The AUC values for the contexts of counties and sociodemographic strata computed from formula 5 and 6 respectively provides complementary information to the VPC_C and VPC_{SD}.

Auditing sociodemographic and geographical differences in discontinuation

The framework of health care evaluation we propose is a reaction to the exclusive focus on average differences between geographical and sociodemographic contexts, which is common (Socialstyrelsen, 2015). The same concept has been presented elsewhere (Merlo et al., 2019) and is outlined in Table 2. By combining the achievement in relation to the benchmark value with information on the VPC, 15 different scenarios emerge which guide the interpretation of the results.

In the first step, a predetermined benchmark value for acceptable achievement should be established. For discontinuation of COPD medication, no such benchmark exists in Sweden. In Denmark, adherence above 90% is considered standard for COPD outpatients with dyspnea (Lange et al., 2016, Regionernes Kliniske Kvalitetsudviklingsprogram, 2019). We proposed that a prevalence of discontinuation below 10% should be considered as full achievement, between 10–15% close to full achievement and above 15% insufficient achievement. While this is a reasonable proposal based on findings of prevalence of non-adherence of 5% among patients treated at a specialist pulmonary clinic in Denmark (Tottenborg et al., 2016), we underscore the need for establishment of a proper benchmark for Swedish circumstances. Both the crude prevalence, i.e. the number of patients that discontinue treatment divided by the number of patients in the study population, and the grand mean are relevant figures to compare with the predetermined benchmark. In this multilevel analysis we use a precision-weighted grand mean.

In the second step, we looked at the geographical or sociodemographic differences between the groups. In addition to a visual presentation of the adjusted average differences between counties and sociodemographic groups, we paid special attention to the measurements of the DA. The primary focus lies at the VPC, but as a complementary measurement we also present the AUC values, which is a measurement that is known to most readers. Although significant average differences may exist, if the VPC is absent or very low (0–1%), variance between individuals is not explained by the investigated context and interventions that exclusively target groups with higher average rates of discontinuation are not recommended. If the VPC is very large (>20%), on the other hand, the evaluated context explains a large proportion of the total variance, which means that it is highly relevant and interventions should indeed target the more vulnerable groups. In Table 2, a framework for how to interpret results from a cross-classified MAIHDA is presented. Noteworthy, this framework is suitable to guide interventions according to the principle of proportionate universalism.

Table 2. Framework for evaluating continuity of maintenance medication among COPD patients (III).
The table outlines a two-dimensional evaluation of continuity with maintenance medication. First, we locate the overall achievement in relation to a pre-defined benchmark value. Second, we quantify the size of county- and sociodemographic differences expressed as variance partition coefficients (VPC) and area under receiver operating characteristics curve (AUC). Combining this information, we obtain 15 different scenarios (A to O) useful for the evaluation.

			Benchmark value achievement		
Size of the county/sociodemographic differences					
	VPC (%)	AUC	Full <10%	Close 10%–15%	Insufficient > 15%
Absent / Very small	0 to 1	0.50 to 0.55	A	B	C
Small	1 to 5	0.55 to 0.61	D	E	F
Moderate	5 to 10	0.61 to 0.66	G	H	I
Large	10 to 20	0.66 to 0.72	J	K	L
Very large	>20	>0.72	M	N	O

AIHDA

In the fourth study we present an intersectional approach that can be easily adopted for different health outcomes in different contexts (Wemrell et al., 2017b, Wemrell et al., 2019). To maintain a feasible intersectional matrix, we restricted the included variables to age, gender, education status, household composition and migration status. In a stepwise procedure we successively included age, gender, education status, household composition and migrations status in Cox regression analyses with fixed follow-up time set to 1 in order to calculate adjusted prevalence ratios (PR) in smoking prevalence. A quantification of the addition to the DA was obtained by evaluating the increase in AUC. Lastly, we analysed smoking prevalence performing a Cox regression analysis in which we included the same variables in an intersectional matrix, which allows for detection of eventual intersectional interaction effects if they exist.

Ethics

The Regional Ethics Review Board in southern Sweden (# 2012/ 637) as well as the data safety committees from the National Board of Health and Welfare and from Statistics Sweden approved the construction of the database used in study I-III. Study IV was approved by the Swedish Ethical Review Authority (Dnr: 2019–01793) and the data safety committee at the Public Health Agency of Sweden.

Results

Study I

In total 1,754 of 667,094 individuals (0.26%, erroneously stated to be 0.31% in the published article) suffered a new hospital COPD event during 2011. The absolute risk differences between the highest and lowest absolute income quintiles were 3.1 per 1,000 among both men and women. For women, the highest incidence was found among individuals with medium-low income (quintile 4) who had an absolute risk that exceeded the high-income quintile by 3.9 events per 1,000 individuals. Both absolute income and relative income were associated with incident COPD, but whereas absolute income presented a clear gradient, no gradient was observed for relative income. In model 2, relative risks for COPD was 3.44 and 3.71 times higher in the medium-low absolute income quintile for men and women respectively, compared to the highest income quintile. For relative income, absolute risk differences between the highest quintile and the quintile with the highest incidence were 0.7 per 1,000 individuals for both men and women. The highest incidence was found in the medium income group for men and the medium-low income group for women. Compared to the highest quintile in model 3, relative risks for all other relative income groups ranged between 1.32–1.37 among men and 1.09–1.27 among women. Results are presented in Table 3 and 4.

The AUC of the model including only age was 0.54 for men and 0.53 for women. Inclusion of the relative income increased the AUC compared to the model with age only by 0.01 units in both genders. AUC increased with 0.11 and 0.10 units after inclusion of absolute income among men and women and reached values of 0.65 and 0.63 respectively.

In a sensitivity analysis, the relative income gradient was analysed separately in the different absolute income strata, but relative income did not show a consistent socioeconomic gradient with incident COPD in that analysis either.

Table 3. Age and crude incidence of COPD in study population (I)
Age and incidence of Chronic Obstructive Pulmonary Disease by absolute and relative income groups in the 333,952 men and 333,142 women aged 55–60 years that resided in Sweden in 2011. The absolute income is categorised by quintiles of all 4,994,921 people aged 35–80 years registered as residents in Sweden on December 31st 2010. The relative income categories are defined by quintile groups within absolute income quintiles. These were pooled so that all people that belong to the poorest quintile within their absolute income group constitute the low relative income category.

	MEN				WOMEN			
	Age (mean)	Number of cases	Number of people	Incidence (per 1000 individuals)	Age (mean)	Number of cases	Number of people	Incidence (per 1000 individuals)
Absolute income								
Low	57.4	167	38 125	4.4	57.4	140	30 567	4.6
Medium low	57.4	175	39 481	4.4	57.5	208	38 624	5.4
Medium	57.4	138	50 760	2.7	57.5	182	52 913	3.4
Medium high	57.5	161	856 77	1.9	57.5	256	95 865	2.7
High	57.6	158	119 909	1.3	57.6	169	115 173	1.5
Relative income								
Low	57.5	150	59 477	2.5	57.5	161	58 513	2.8
Medium low	57.5	157	62 965	2.5	57.5	203	63 045	3.2
Medium	57.5	173	67 131	2.6	57.5	186	67 881	2.7
Medium high	57.5	179	70 374	2.5	57.5	221	71 018	3.1
High	57.5	140	74 005	1.9	57.5	184	72 685	2.5

Table 4. ORs and AUC for incident COPD of absolute and relative income, gender stratified (I)
Association between absolute and relative income and risk of Chronic Obstructive Pulmonary Disease in the 333,952 men and 333,142 women aged 55–60 years and residing in Sweden in 2011. Values are OR, 95% CI and AUC. The absolute income is categorised by quintiles of all 4,994,921 people aged 35–80 years registered as residents in Sweden on December 31st 2010. The relative income categories are defined by quintile groups within absolute income quintiles. These were pooled so that all people that belong to the poorest quintile within their absolute income group constitute the low relative income category.

	Model 1 (Age)	**Model 2** (Age and absolute income)	**Model 3** (Age and relative income)	**Model 4** (Age and absolute and relative income)
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
MEN				
Age (1 year)	1.09 (1.05–1.14)	1.05 (1.06–1.15)	1.09 (1.05–1.14)	1.11 (1.06–1.15)
Absolute income*				
High		REF		REF
Medium high		1.43 (1.15–1.78)		1.44 (1.16–1.80)
Medium		2.10 (1.67–2.64)		2.11 (1.68–2.65)
Medium low		3.44 (2.77–4.27)		3.44 (2.77–4.27)
Low		3.40 (2.73–4.23)		3.39 (2.73–4.22)
Relative income **				
High			REF	REF
Medium high			1.35 (1.08–1.68)	1.34 (1.08–1.68)
Medium			1.37 (1.09–1.71)	1.36 (1.08–1.69)
Medium low			1.32 (1.05–1.66)	1.31 (1.04–1.64)
Low			1.34 (1.06–1.69)	1.31 (1.04–1.64)
AUC (95% CI)	0.54 (0.52–0.56)	0.65 (0.63–0.66)	0.55 (0.53–0.57)	0.65 (0.63–0.67)
WOMEN				
Age (1 year)	1.05 (1.01–1.09)	1.06 (1.02–1.10)	1.05 (1.01–1.09)	1.06 (1.02–1.10)
Absolute income				
High		REF		REF
Medium high		1.83 (1.51–2.22)		1.84 (1.52–2.24)
Medium		2.36 (1.92–2.91)		2.39 (1.94–2.95)
Medium low		3.71 (3.03–4.55)		3.73 (3.05–4.58)
Low		3.17 (2.54–3.97)		3.20 (2.56–4.01)
Relative income				
High			REF	REF
Medium high			1.23 (1.01–1.50)	1.25 (1.03–1.52)
Medium			1.08 (0.88–1.33)	1.11 (0.91–1.36)
Medium low			1.27 (1.04–1.56)	1.34 (1.10–1.64)
Low			1.09 (0.88–1.35)	1.15 (0.93–1.42)
AUC (95% CI)	0.53 (0.51–0.54)	0.63 (0.62–0.65)	0.54 (0.52–0.55)	0.64 (0.62–0.65)

Study II

In this study the incidence of COPD during 2011 was 0.22%. The lower incidence in this cohort compared to the incidence in study I is presumably due to the lower average age of the cohort. From model 3, adjusted ORs (95% CI) for the different unidimensional variables used to construct the intersectional matrix were obtained and are presented in Table 5. In short, the risk of COPD was higher for people who were older, women, people with lower income and lower education as well as people living alone and people who had immigrated.

Table 6 and Figure 5 show the results from intersectional model 1, which revealed substantial heterogeneities between strata when including both additive and interactive effects in the calculated predicted incidence of COPD. The smallest stratum had 1,236 individuals. The stratum with the highest incidence comprised older native females with low income and low education who lived alone (0.98%, 95% CI: 0.89%–1.08%). It was followed by the strata including older immigrant females with low income and low education who lived alone (0.87%, 95% CI: 0.72%–1.05%) and older immigrant males with low income and low education who lived alone (0.82%, 95% CI: 0.66%–1.00%). The three strata with the lowest predicted incidence all included younger cohabiting men with high education with low (0.02%, 95% CI: 0.01%–0.04%), medium (0.03% 95% CI:0. 02%–0.04%) and high income (0.03%, 95% CI: 0.02%–0.05%). The ICC of model 1 was 20.0%, which means that a substantial share of the total individual differences in COPD incidence was found at the intersectional strata level.

Table 5. Number of COPD cases, unidimensional ORs and variance of the different MAIHDA-models (II)

Results from the intersectional multilevel analysis of individual heterogeneity in Chronic Obstructive Pulmonary Disease (COPD) risk, for people aged 45–65 residing in Sweden in 2010, according to demographic and socioeconomic groupings used to construct intersectional strata. Model 1 (simple intersectional) is a random intercepts model with individuals nested in intersectional strata. Model 2 (age adjusted) is partially adjusted and model 3 (intersectional interaction) is adjusted for all the main variables used to define the intersectional strata. In this table we only present measures of variance and of association (ORs and 95% CIs) between the main individual variables and COPD risk. The incidences for specific intersectional strata are hidden in this table but we present them in Figure 5 and in Table 6. The green boxes indicate the actual category. For each category, we show the total number of individuals and the absolute incidence of COPD. Low age: 45–54; high age: 55–65; Hi: high; Me: medium; Lo: Low.

High age		Female gender		Income			Low education		Living alone		Immigrant		Number (% COPD)	Model 1	Model 2	Model 3
No	Yes	No	Yes	Hi	Me	Lo	No	Yes	No	Yes	No	Yes			OR (95% CI)	OR (95% CI)
													1 180 420 (0.10)		Ref.	Ref.
													1 265 081 (0.33)		3.79 (2.90–4.91)	3.62 (3.22–4.08)
													1 228 715 (0.20)			Ref.
													1 216 786 (0.24)			1.21 (1.08–1.36)
													831 992 (0.14)			Ref.
													829 423 (0.21)			1.52 (1.31–1.76)
													784 086 (0.32)			2.25 (1.96–2.59)
													1 070 164 (0.11)			Ref.
													1 375 337 (0.30)			1.97 (1.76–2.21)
													1 665 239 (0.16)			Ref.
													780 262 (0.36)			1.88 (1.69–2.10)
													2 080 162 (0.21)			Ref.
													365 339 (0.26)			1.15 (1.01–1.29)
Variance between strata (Standard Error)														0.83 (0.14)	0.40 (0.07)	0.04 (0.01)
Intra-class Correlation (95% Credible Interval)														20.0 (15.6–25.6)	10.8 (8.1–14.1)	1.1 (0.6–2.1)
Bayesian diagnostic information criterion (DIC)														661.87	650.21	628.31

Table 6. Total predicted incidence of COPD of intersectional strata (II)

Total number of individuals, number of cases of Chronic Obstructive Pulmonary Disease and predicted incidence in 2011 for people aged 45–65 residing in Sweden on December 31st 2010, by intersectional strata. Predictions are based on model 1 multilevel regression analysis with individuals at the first level and intersectional strata at the second level. Main effects and interactive effects are conflated. Intersectional strata were calculated by categories of age, gender, income based on tertiles in the whole population aged 45–65 years, education, civil status and country of birth. Intersectional strata are ordered according to predicted incidence of COPD, with increasing incidence in decreasing rows.

Age		Gender		Income			Education		Living alone		Immigrant		Model 1			
													Number of individuals	*Number of cases*	*Incidence*	*95% Credible interval*
45–54	55–65	Male	Female	High	Medium	Low	High	Low	No	Yes	Yes	No				
✓		✓		✓			✓		✓			✓	50 798	9	0.02	(0.01–0.04)
✓		✓			✓		✓		✓			✓	72 164	19	0.03	(0.02–0.04)
✓		✓				✓	✓		✓			✓	54 482	16	0.03	(0.02–0.05)
✓			✓		✓		✓		✓			✓	74 237	26	0.04	(0.03–0.05)
✓			✓	✓			✓		✓		✓		6 991	1	0.04	(0.01–0.09)
✓			✓	✓			✓		✓			✓	56 851	25	0.05	(0.03–0.07)
✓		✓		✓				✓		✓	✓		5 473	1	0.05	(0.01–0.11)
✓		✓			✓		✓			✓		✓	6 685	2	0.05	(0.02–0.11)
✓		✓		✓			✓			✓		✓	27 451	14	0.06	(0.03–0.08)
✓		✓			✓			✓	✓			✓	58 098	31	0.06	(0.04–0.08)
✓			✓			✓	✓		✓			✓	55 705	30	0.06	(0.04–0.08)
✓		✓		✓				✓	✓			✓	25 075	14	0.06	(0.04–0.09)
✓			✓	✓			✓			✓		✓	22 160	14	0.07	(0.04–0.10)
✓			✓		✓			✓	✓		✓		9 021	5	0.07	(0.03–0.13)
✓		✓				✓	✓		✓		✓		20 321	13	0.07	(0.04–0.11)
✓			✓			✓	✓			✓		✓	13 516	8	0.07	(0.03–0.12)
✓			✓	✓				✓	✓			✓	31 143	21	0.07	(0.05–0.10)
✓		✓			✓		✓		✓		✓		9 481	6	0.08	(0.03–0.14)
✓		✓			✓			✓	✓		✓		6 549	4	0.08	(0.03–0.15)
✓			✓		✓		✓		✓		✓		11 853	8	0.08	(0.04–0.14)

✓		✓		✓				✓		✓		✓	57 497	45	0.08	(0.06–0.10)
✓		✓				✓		✓	✓			✓	68 586	58	0.09	(0.07–0.11)
✓			✓			✓	✓		✓		✓		19 625	16	0.09	(0.05–0.13)
✓		✓				✓	✓			✓		✓	7 809	6	0.09	(0.04–0.16)
✓			✓	✓				✓	✓		✓		3 076	2	0.09	(0.03–0.20)
✓		✓		✓				✓	✓		✓		1 993	1	0.09	(0.02–0.22)
✓			✓	✓				✓		✓		✓	20 237	19	0.10	(0.06–0.14)
✓			✓		✓		✓			✓		✓	11 206	10	0.10	(0.05–0.16)
✓			✓		✓		✓			✓	✓		1 943	1	0.10	(0.02–0.23)
✓		✓		✓			✓		✓		✓		4 613	4	0.10	(0.04–0.20)
✓			✓		✓			✓		✓	✓		4 351	4	0.11	(0.04–0.20)
✓		✓		✓			✓			✓	✓		3 334	3	0.11	(0.04–0.23)
	✓		✓	✓			✓		✓			✓	98 120	113	0.12	(0.10–0.14)
	✓	✓		✓			✓		✓			✓	101 692	120	0.12	(0.10–0.14)
✓			✓		✓			✓	✓			✓	62 902	76	0.12	(0.10–0.15)
✓			✓	✓			✓			✓	✓		2 926	3	0.12	(0.04–0.24)
✓		✓			✓			✓		✓		✓	32 367	40	0.13	(0.09–0.17)
✓			✓	✓				✓		✓	✓		2 450	3	0.14	(0.04–0.30)
✓		✓			✓			✓		✓	✓		4 795	7	0.15	(0.07–0.28)
✓			✓			✓	✓			✓	✓		4 099	6	0.15	(0.06–0.28)
✓			✓			✓		✓	✓			✓	71 224	111	0.16	(0.13–0.19)
	✓	✓		✓			✓			✓	✓		2 606	4	0.16	(0.06–0.32)
	✓	✓		✓			✓		✓		✓		6 786	11	0.16	(0.09–0.27)
	✓		✓			✓	✓		✓		✓		9 085	15	0.17	(0.09–0.25)
	✓	✓			✓		✓		✓			✓	57 439	98	0.17	(0.14–0.21)
	✓	✓		✓				✓	✓		✓		4 071	7	0.17	(0.08–0.32)
✓		✓				✓		✓	✓		✓		21 782	38	0.18	(0.12–0.23)
	✓	✓				✓	✓		✓			✓	25 095	44	0.18	(0.13–0.23)

	✓	✓		✓				✓	✓			✓	59 437	105	0.18	(0.15–0.21)
✓		✓			✓		✓			✓	✓		1 626	3	0.19	(0.06–0.40)
	✓		✓		✓		✓		✓			✓	54 766	104	0.19	(0.16–0.23)
	✓	✓		✓			✓			✓		✓	28 371	54	0.19	(0.14–0.25)
	✓		✓		✓		✓		✓		✓		8 181	16	0.20	(0.11–0.29)
	✓		✓	✓			✓		✓		✓		8 567	17	0.20	(0.12–0.30)
	✓	✓			✓		✓		✓		✓		7 825	16	0.20	(0.11–0.31)
✓		✓				✓	✓			✓	✓		3 886	8	0.20	(0.09–0.35)
	✓		✓			✓	✓		✓			✓	21 579	47	0.22	(0.16–0.28)
✓			✓			✓		✓	✓		✓		22 559	49	0.22	(0.16–0.29)
	✓		✓	✓			✓			✓		✓	36 219	87	0.24	(0.19–0.30)
	✓		✓	✓				✓	✓			✓	57 118	148	0.26	(0.22–0.30)
✓			✓		✓			✓		✓		✓	28 024	73	0.26	(0.21–0.32)
	✓	✓			✓		✓			✓	✓		1 236	4	0.27	(0.09–0.57)
	✓		✓	✓			✓			✓	✓		4 219	12	0.27	(0.15–0.43)
	✓		✓	✓				✓	✓		✓		4 986	14	0.27	(0.15–0.42)
	✓	✓		✓				✓		✓		✓	54 576	153	0.28	(0.24–0.33)
	✓	✓				✓	✓		✓		✓		11 252	33	0.29	(0.20–0.40)
	✓	✓		✓				✓		✓	✓		4 864	15	0.29	(0.17–0.45)
	✓	✓			✓		✓			✓		✓	6 858	21	0.30	(0.19–0.43)
	✓	✓			✓			✓	✓			✓	82 655	247	0.30	(0.26–0.34)
	✓		✓		✓		✓			✓	✓		2 049	7	0.31	(0.14–0.56)
✓		✓				✓		✓		✓		✓	41 080	130	0.32	(0.26–0.37)
	✓		✓	✓				✓		✓	✓		4 275	15	0.33	(0.18–0.52)
	✓	✓				✓	✓			✓		✓	7 596	26	0.33	(0.22–0.49)
	✓		✓		✓			✓	✓			✓	85 879	285	0.33	(0.29–0.37)
	✓		✓		✓			✓	✓		✓		11 217	38	0.33	(0.24–0.45)
✓		✓				✓		✓		✓	✓		11 402	40	0.34	(0.24–0.46)

✓			✓			✓		✓		✓	✓		10 107	36	0.35	(0.24–0.47)
	✓		✓	✓				✓		✓		✓	34 017	125	0.37	(0.30–0.43)
	✓		✓		✓		✓			✓		✓	12 088	48	0.39	(0.29–0.50)
	✓	✓				✓		✓	✓			✓	43 509	177	0.40	(0.35–0.47)
	✓		✓			✓		✓	✓		✓		15 257	63	0.41	(0.32–0.51)
✓			✓			✓		✓		✓		✓	36 867	155	0.42	(0.35–0.49)
	✓	✓			✓			✓	✓		✓		9 411	42	0.44	(0.32–0.59)
	✓		✓			✓	✓			✓	✓		3 106	15	0.45	(0.25–0.70)
	✓	✓				✓		✓	✓		✓		13 963	64	0.45	(0.34–0.58)
	✓		✓			✓	✓			✓		✓	8 710	43	0.48	(0.35–0.62)
	✓		✓			✓		✓	✓			✓	48 220	236	0.49	(0.43–0.55)
	✓	✓			✓			✓		✓		✓	38 031	187	0.49	(0.43–0.56)
	✓		✓		✓			✓		✓	✓		7 166	37	0.50	(0.35–0.68)
	✓	✓			✓			✓		✓	✓		4 749	29	0.58	(0.39–0.81)
	✓		✓		✓			✓		✓		✓	44 571	264	0.59	(0.52–0.66)
	✓	✓				✓	✓			✓	✓		2 957	19	0.59	(0.36–0.90)
	✓	✓				✓		✓		✓		✓	45 939	370	0.80	(0.72–0.88)
	✓	✓				✓		✓		✓	✓		10 450	88	0.82	(0.66–1.00)
	✓		✓			✓		✓		✓	✓		12 805	113	0.87	(0.72–1.05)
	✓		✓			✓		✓		✓		✓	41 513	409	0.98	(0.89–1.08)

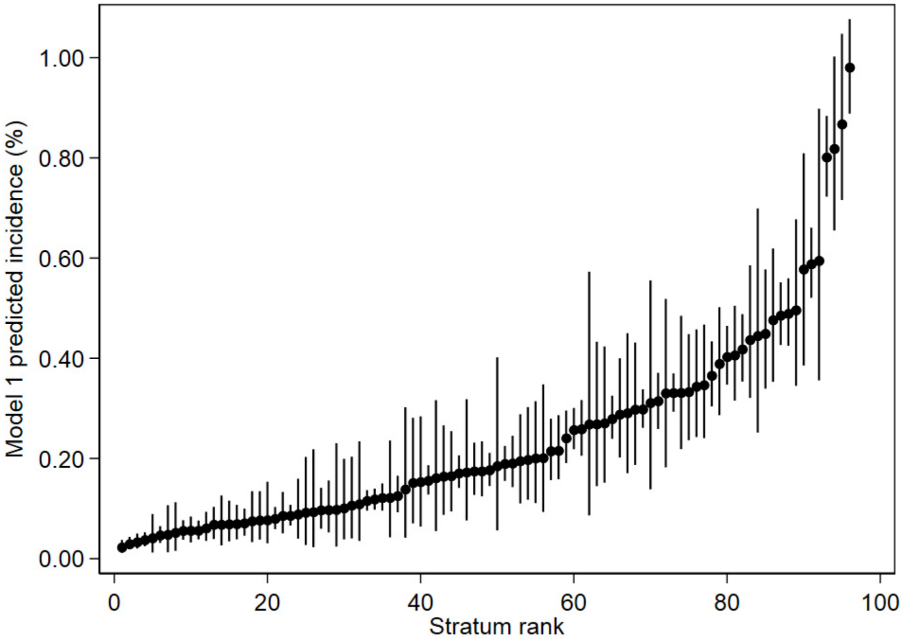


Figure 5. Total predicted incidence of COPD by intersectional strata (II)
Predicted incidence of Chronic Obstructive Pulmonary Disease in 2011 for people aged 45–65 residing in Sweden on December 31st 2010, by intersectional strata. Predictions are based on model 1 multilevel regression analysis with individuals at the first level and intersectional strata at the second level. Main effects and interactive effects are conflated. Intersectional strata were calculated by categories of age, gender, income based on tertiles in the whole population aged 45–65 years, education, civil status and country of birth. Intersectional strata are ordered according to their rank; strata with lowest rank to the left. For identification of the different intersectional strata, see Table 6.

In model 2, the ICC fell to 10.8% when adjusting for age, implying that more than half of the intersectional clustering was attributable to age. For the other variables, the changes were smaller; ICC fell to 17.7% when adjusting for civil status, to 17.8% when adjusting for education, to 18.2% when adjusting for income, remained 20.0% when adjusting for migration status and was 20.4% when adjusting for gender.

In model 3, the intersectional interaction model, ICC was 1.1%, which suggests that additive rather than interactive effects explain most of the differences in incident COPD between intersectional strata. Figure 6 shows the predicted incidences when accounting for both additive and interaction effects alongside predicted incidences when isolating additive effects, visualising the small changes attributable to intersectional interaction. Of the 96 strata, only three had interaction effects with confidence intervals excluding 0: young native women with low income and low education who cohabited (interaction effect 0.13 95% CI 0.07–0.20), young native males with low income and low education who lived alone (interaction effect 0.08 95% CI 0.03–0.13) and young native women with medium income and low education who lived alone (interaction effect 0.06 95% CI 0.01–0.11).

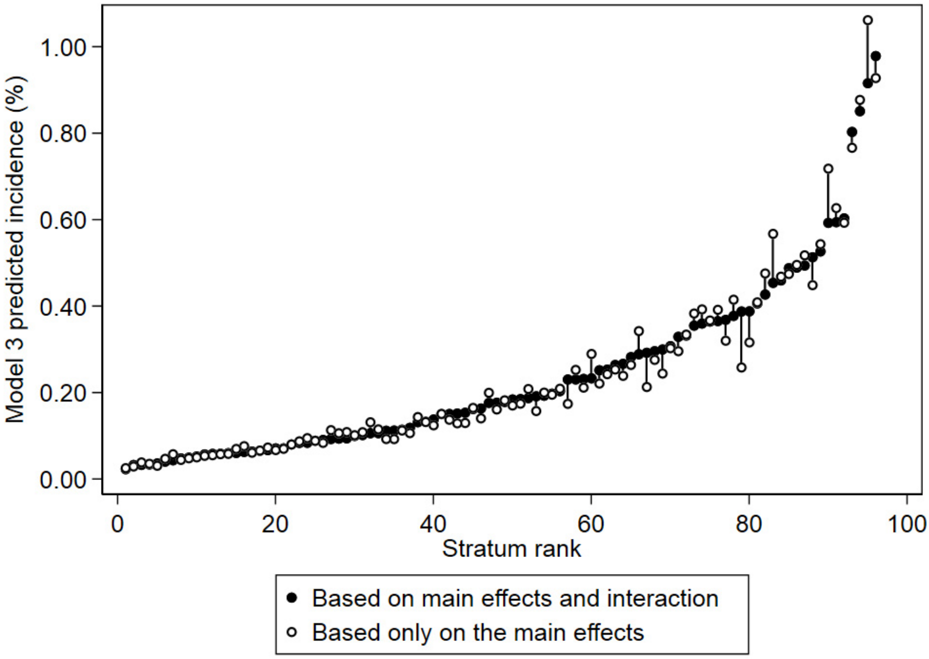


Figure 6. Predicted incidence of COPD by intersectional strata, additive and interactive effect separated (II)
Incidence of Chronic Obstructive Pulmonary Disease during 2011 for people aged 45–65 residing in Sweden on December 31st 2010, by intersectional strata. Point estimates of predicted incidences based on model 3. Black circles indicate the incidence according to predictions based on the total effect (intersectional effects and main effects) while white circles indicate the incidence according to predictions based on main effects only. The differences between black and white circles depict the interaction effects. Intersectional strata were calculated by categories of age, gender, income based on tertiles in the whole population aged 45–65 years, education, living alone and immigration status. To identify the different intersectional strata, see Table 6.

Study III

Mean age of COPD patients in the study was 68 years. Women were slightly over-represented in the study population and people with low income constituted the most common income tertile in all counties except Stockholm. Among 49,019 COPD patients with previous maintenance medication, 18.4% (8,998 individuals) discontinued their medication. The distribution of patients across counties and the absolute risks of discontinuation across counties is presented in Table 7. Absolute risks of discontinuation among sociodemographic strata are presented in Table 8. The crude county prevalence of discontinuation ranged from 14% in Värmland to 21% in Stockholm. For sociodemographic strata, differences in crude prevalence were larger: women aged 65–80 years with high income had the lowest prevalence of 15%, while the highest prevalence of 37% was found among men aged 35–49 years with low income.

Table 7. Characteristics of discontinuation among COPD-patients in Sweden by county (III)
Characteristics of the 49,019 COPD patients by county of residence and sociodemographic factors as well as absolute risk of discontinuation (AR-D) to inhaled maintenance medication in 2011. Values are percentages if not otherwise indicated.

Counties	Number of patients	AR-D Crude %	AR-D adjusted %	Female, %	Mean age (years)	Income groups, %		
						High	Middle	Low
Stockholms län	10 028	21.01	25.80	57.14	67.50	31.46	36.35	32.19
Uppsala län	1 699	16.48	20.77	54.97	67.25	22.66	37.08	40.26
Södermanlands län	1 604	16.77	21.21	56.80	67.76	21.32	37.66	41.02
Östergötlands län	2 264	15.28	19.73	55.30	67.72	20.32	36.75	42.93
Jönköpings län	1 759	15.86	20.31	53.21	67.96	18.65	38.26	43.09
Kronobergs län	909	16.17	20.93	53.91	68.07	19.47	40.26	40.26
Kalmar län	1 330	17.74	21.94	53.83	67.88	17.74	36.54	45.71
Gotlands län	331	20.24	22.74	50.45	67.35	13.90	34.44	51.66
Blekinge län	850	18.12	22.09	53.06	67.76	17.06	41.06	41.88
Skåne län	8 034	17.70	21.84	56.97	67.28	21.55	35.69	42.77
Hallands län	1 523	16.41	21.17	55.88	68.31	24.43	37.16	38.41
Västra Götalands län	7 567	19.65	24.21	57.31	68.11	19.41	36.91	43.68
Värmlands län	1 161	13.87	19.15	53.66	68.57	15.93	33.76	50.30
Örebro län	1 597	17.41	21.36	54.16	67.17	16.91	35.82	47.28
Västmanlands län	1 324	18.88	22.67	56.34	67.19	18.96	38.44	42.60
Dalarnas län	1 394	17.29	21.60	55.24	67.97	16.43	39.38	44.19
Gävleborgs län	1 358	17.82	22.12	57.73	68.22	17.45	36.16	46.39
Västernorrlands län	1 083	16.99	21.35	56.14	67.85	19.85	34.44	45.71
Jämtlands län	602	18.44	22.54	58.80	68.26	16.94	37.38	45.68
Västerbottens län	1 150	18.00	22.39	57.83	68.70	17.48	39.91	42.61
Norrbottens län	1 452	19.28	23.54	55.65	68.44	19.70	41.18	39.12
Sweden	49 019	18.36	21.86	56.25	67.75	22.08	36.91	41.01

a) Estimated from the cross-classified MAIHDA

Table 8. Discontinuation to COPD medication by sociodemographic groups (III)
Number of patients by sociodemographic group as well as crude and county-adjusted absolute risk of discontinuation (AR-D) to inhaled maintenance medication in 2011. Values are percentages if not otherwise indicated. Adjusted values are estimated from the cross-classified MAIHDA.

Sociodemographic groups	Number of patients (N)	AR-D Crude	AR-D Adjusted (%)
65–80 male high	3 530	17.65	16.71
65–80 male middle	5 913	17.74	17.07
65–80 male low	5 731	18.79	18.22
50–64 male high	1 528	21.53	20.59
50–64 male middle	1 831	24.30	23.39
50–64 male low	2 288	26.79	25.61
35–49 male high	115	29.57	26.54
35–49 male middle	161	34.78	31.58
35–49 male low	347	36.60	34.05
65–80 female high	3 555	14.74	13.81
65–80 female middle	7 070	15.30	14.56
65–80 female low	7 813	15.33	14.85
50–64 female high	2 026	15.20	14.55
50–64 female middle	2 904	17.84	17.24
50–64 female low	3 091	21.51	20.72
35–49 female high	68	23.53	21.79
35–49 female middle	214	32.24	29.58
35–49 female low	834	31.77	30.46
Total	49 019	18.36	21.86

In addition to the crude prevalence, we pay special attention to the results from the cross-classified MAIHDA that are presented in Table 9. The average prevalence of discontinuation across geographical and sociodemographic contexts was 21.9% (95% CI 19.1%–25.0%). The evaluation of the VPC and AUC showed that county differences were very small since the VPC is 0.4% and the AUC is 0.53. The relevance of the sociodemographic contexts was larger, but differences were still small with a VPC of 5.0% and an AUC of 0.57. From the coefficients obtained in the MAIHDA, we calculated average risk for discontinuation for counties and sociodemographic strata; these are mutually adjusted so county risks are adjusted for sociodemographic composition and vice versa. Results for counties are presented in Table 7 and Figure 7. Results for sociodemographic strata are found in Table 8 and Figure 8. Värmland remained the county with the lowest risk of discontinuation with 19%, and Stockholm had the highest risk with 26%. Again, sociodemographic disparities were larger. Men aged 35–49 years with low income had an average risk of discontinuation of 34% and women aged 65–80 years with high income had the lowest risk with 14%.

Table 9. Variance, VPC and AUC for counties and sociodemographic contexts from cross-classified MAIHDA, analysing discontinuation with COPD medication (III)

Results (95% confidence intervals) from the multilevel cross-classified analysis of counties and sociodemographic contexts in relation to discontinuation with inhaled maintenance medication in 2011, among 49,019 patients with COPD. VPC: Variance partition coefficient; AUC: area under the receiver operating characteristic curve

Variance	
County level	0.012 (0.005–0.026)
Sociodemographic categories	0.174 (0.082–0.352)
VPC (%)	
County level	0.35 (0.15–0.75)
Sociodemographic contexts	4.98 (2.42–9.63)
AUC	
County level (AUC_v)	0.54 (0.53–0.54)
Sociodemographic contexts (AUC_u)	0.57 (0.56–0.57)

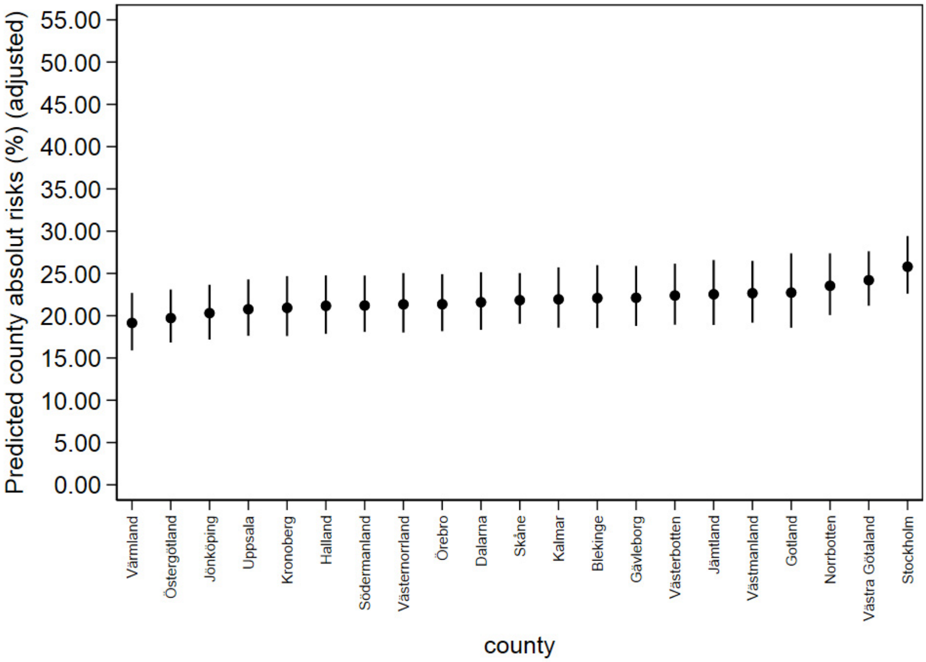


Figure 7. Risk of discontinuation to maintenance medication among COPD patients, by county

Risk differences between the 21 counties in discontinuation with inhaled maintenance medication among 49,019 COPD patients according to the cross-classified MAIHDA, adjusted for sociodemographic characteristics.

Risk of discontinuation decreased with age, but we did not find clear income gradients, except among women aged 50–64 years. Discontinuation rates were similar for men and women, but among patients aged 50–64 and 65–80 years men had slightly higher rates of discontinuation.

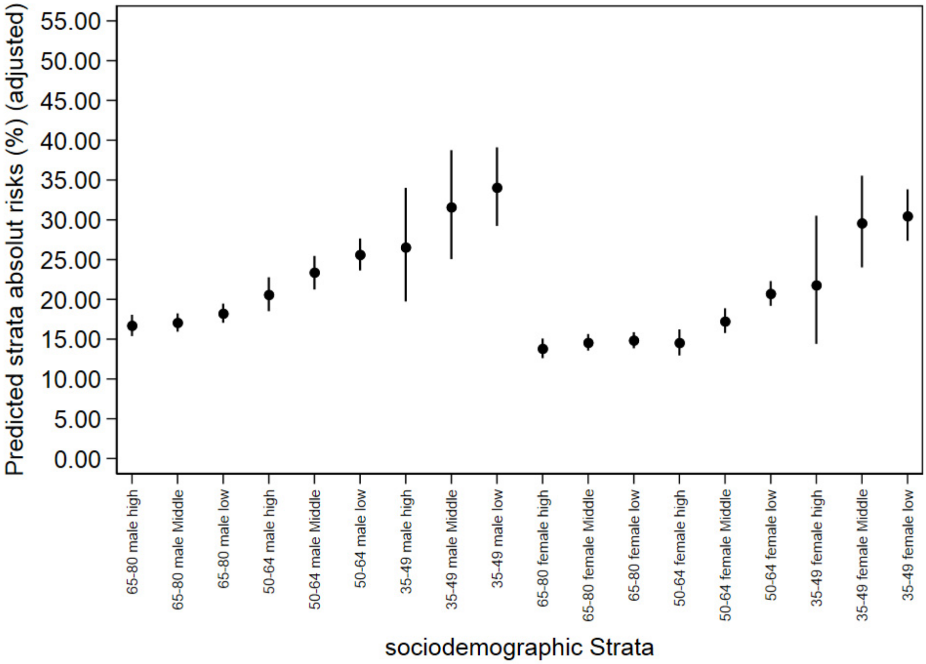


Figure 8. Risk of discontinuation to maintenance medication among COPD patients, by sociodemographic strata
Adjusted absolute risk differences between the 18 sociodemographic categories in discontinuation with inhaled maintenance medication among 49,019 COPD patients according to the cross-classified multilevel model.

Sociodemographic context influences risk of discontinuation more than county of residence, but the discriminatory accuracy of both these contexts is low. According to the framework presented in Table 2, county disparities can be placed in scenario C and sociodemographic disparities in scenario F.

Study IV

The proportion of smokers across all survey years was 18%, and decreased from 25% in 2004 to 11% in 2018. While gender differences were small throughout the period and the gender category with highest smoking prevalence changed, we observed consistent differences between groups defined by age, country of birth, educational achievement and household composition. In absolute terms, the gaps between subgroups were static, except for differences between age categories that narrowed in later years. Time trends in smoking prevalence for the different dimensions included in the intersectional matrix as well as overall prevalence in the survey populations of the different years are shown in Figure 4a–f. Table 10 shows that 20.6% of people aged 45–64 years smoked, compared to 19.8% and 12.4% for younger and older individuals respectively. Men and women had similar smoking rates (17.9% and 17.8%), but there was an educational gradient where people with low, middle and high education had smoking rates of 21.7%, 17.0% and 11.9% respectively. Smoking was more common among immigrants (23.9%) than among natives (17.0%) and the smoking rate was 24.1% among people living alone, compared to 16.5% for people living with other(s). Table 11 shows smoking prevalence across four regions of birth stratified by gender. Except for women born outside Europe, all other groups had higher smoking rates than people born in Sweden. The results from the intersectional analysis in Figure 9 shows that the absolute risk of smoking was 9 times higher in the stratum with highest prevalence (young immigrant men with low education who lived alone) than in the stratum with the lowest prevalence (older native women with high education who lived with other(s)). Corresponding PRs compared to the reference stratum of young native men with high education living with other(s) was 0.55 for older native women with high education who lived with other(s), and 4.45 for young immigrant men with low educational achievement who lived alone. PRs for all 72 strata are shown in Table 12.

Table 10. Descriptive statistics of smokers and non-smokers in Sweden (IV)
Distribution (prevalence) of smokers across categories of age, gender, education, migration status and household composition in the 110,044 participants in the Swedish National Health Surveys (2004–2018). Values are number (and percentage) of individuals.

	Non smokers	Smokers
30–44	22 799 (80.23%)	5 618 (19.77%)
45–64	38 024 (79.41%)	9 862 (20.59%)
65–84	29 575 (87.65%)	4 166 (12.35%)
Female	48 782 (82.08%)	10.653 (17.92%)
Male	41 616 (82.23%)	8 993 (17.77%)
Low	38 791 (78.32%)	10 738 (21.68%)
Middle	27 716 (83.02%)	5 670 (16.98)
High	23 891 (88.06%)	3 238 (11.94%)
Immigrant	10 410 (76.07%)	3 274 (23.93%)
Native	79 988 (83.01%)	16 372 (16.99%)
Cohabiting	75 625 (83.48%)	14 964 (16.52%)
Living Alone	14 773 (75.93%)	4 682 (24.07%)
2004	6 803 (75.03%)	2 264 (24.97%)
2005	3 339 (75.90%)	1 060 (24.10%)
2006	3 450 (77.62%)	995 (22.38%)
2007	3 272 (77.81%)	933 (22.19%)
2008	6 525 (79.07%)	1 727 (20.93%)
2009	6 123 (79.22%)	1 606 (20.78%)
2010	6 718 (80.59%)	1 618 (19.41%)
2011	6 760 (82.56%)	1 428 (17.44%)
2012	6 893 (82.68%)	1 444 (17.32%)
2013	6 770 (83.10%)	1 377 (16.90%)
2014	6 845 (83.74%)	1 329 (16.26%)
2015	6 978 (84.21%)	1 308 (15.79%)
2016	7 086 (88.13%)	954 (11.87%)
2018	12 836 (88.90%)	1 603 (11.10%)

Table 11. Smoking prevalence across region of birth (IV)
Smoking prevalence across regions of birth among 110,044 individuals responding to National Health Surveys during 2004–2016 and 2018. Both everyday smokers and sometimes smokers are included in the proportions presented.

Region of birth	Women	Men
Sweden	17.5%	16.4%
Nordic countries	21.7%	23.0%
Europe	24.0%	27.1%
Outside Europe	16.3%	32.5%

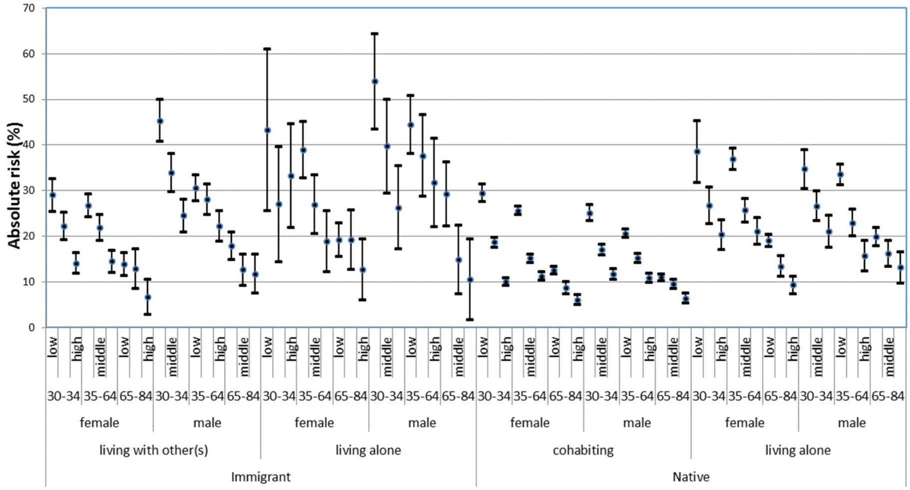


Figure 9. Absolute risks of smoking by intersectional strata
Absolute risk (i.e. prevalence) and 95% confidence intervals of smoking in different intersectional strata according to the National Health Survey in Sweden between 2004 and 2018.

The PR of smoking decreased with increasing age in the fully adjusted Cox regression analysis, being lowest in the oldest age group. This contrasts with the crude prevalence which are unadjusted for survey year. Relative risk of smoking was increased for people with lower education, for immigrants and for people living alone, but no age-adjusted gender differences were detectable. Results are shown in Table 13.

The AUC of the model including only survey year was 0.58 and increased to 0.60 when including age, and remained so after the inclusion of gender in model 3. The inclusion of education increased the AUC with 0.04 units. AUC did not change when we included migration in model 5. After inclusion of household composition in model 6, AUC increased by 0.01 units to 0.65. The AUC was 0.66 in the intersectional interaction model 7, but the confidence interval overlapped with AUC of model 6. This indicates that the difference in smoking prevalence between the strata was due to the main effects of the variables used to construct the intersectional matrix and that no conclusive intersectional interaction between the included variables was found.

In a sensitivity analysis, we used income tertiles instead of educational achievement in the intersectional matrix. Results largely remained stable and are presented in Table 14 (model 1–6) and Table 15 (intersectional model 7).

Table 12. Relative risks of smoking according to intersectional AIHDA model 7 (IV)
Results from the intersectional model 7 indicating the prevalence ratios (PR) with 95% confidence intervals (CI) of smoking across intersectional strata in the Swedish population using the stratum of young native men with high education who were living with other(s) (LWO) as reference in the comparisons.

Age	Gender	Educational achievement	Migration status	Household composition	PR (95% CI)
30–44	Female	Low	Immigrant	LWO	2.35 (1.96–2.82)
30–44	Female	Low	Immigrant	Living alone	3.41 (1.96–5.94)
30–44	Female	Low	Native	LWO	2.24 (1.96–2.56)
30–44	Female	Low	Native	Living alone	2.95 (2.29–3.78)
30–44	Female	Middle	Immigrant	LWO	1.83 (1.51–2.21)
30–44	Female	Middle	Immigrant	Living alone	2.33 (1.34–4.05)
30–44	Female	Middle	Native	LWO	1.53 (1.35–1.73)
30–44	Female	Middle	Native	Living alone	2.2 (1.8–2.7)
30–44	Female	High	Immigrant	LWO	1.22 (0.99–1.49)
30–44	Female	High	Immigrant	Living alone	2.87 (1.86–4.42)
30–44	Female	High	Native	LWO	0.86 (0.74–0.98)
30–44	Female	High	Native	Living alone	1.72 (1.39–2.12)
30–44	Male	Low	Immigrant	LWO	3.66 (3.07–4.35)
30–44	Male	Low	Immigrant	Living alone	4.45 (3.29–6.03)
30–44	Male	Low	Native	LWO	1.92 (1.68–2.2)
30–44	Male	Low	Native	Living alone	2.67 (2.21–3.21)
30–44	Male	Middle	Immigrant	LWO	2.84 (2.36–3.43)
30–44	Male	Middle	Immigrant	Living alone	3.33 (2.35–4.71)
30–44	Male	Middle	Native	LWO	1.43 (1.25–1.63)
30–44	Male	Middle	Native	Living alone	2.21 (1.85–2.64)
30–44	Male	High	Immigrant	LWO	2.13 (1.74–2.6)
30–44	Male	High	Immigrant	Living alone	2.32 (1.53–3.5)

30–44	Male	High	Native	LWO	Reference
30–44	Male	High	Native	Living alone	1.75 (1.41–2.18)
45–64	Female	Low	Immigrant	LWO	2.19 (1.88–2.55)
45–64	Female	Low	Immigrant	Living alone	3.22 (2.56–4.06)
45–64	Female	Low	Native	LWO	2.08 (1.85–2.34)
45–64	Female	Low	Native	Living alone	2.99 (2.61–3.41)
45–64	Female	Middle	Immigrant	LWO	1.87 (1.56–2.23)
45–64	Female	Middle	Immigrant	Living alone	2.23 (1.66–3.01)
45–64	Female	Middle	Native	LWO	1.29 (1.14–1.46)
45–64	Female	Middle	Native	Living alone	2.16 (1.84–2.53)
45–64	Female	High	Immigrant	LWO	1.27 (1.03–1.57)
45–64	Female	High	Immigrant	Living alone	1.63 (1.08–2.45)
45–64	Female	High	Native	LWO	0.97 (0.84–1.11)
45–64	Female	High	Native	Living alone	1.76 (1.46–2.13)
45–64	Male	Low	Immigrant	LWO	2.55 (2.18–2.98)
45–64	Male	Low	Immigrant	Living alone	3.61 (2.9–4.5)
45–64	Male	Low	Native	LWO	1.71 (1.52–1.93)
45–64	Male	Low	Native	Living alone	2.77 (2.42–3.17)
45–64	Male	Middle	Immigrant	LWO	2.39 (2.01–2.86)
45–64	Male	Middle	Immigrant	Living alone	3.1 (2.26–4.26)
45–64	Male	Middle	Native	LWO	1.28 (1.12–1.45)
45–64	Male	Middle	Native	Living alone	1.92 (1.61–2.31)
45–64	Male	High	Immigrant	LWO	1.91 (1.56–2.35)
45–64	Male	High	Immigrant	Living alone	2.7 (1.84–3.98)
45–64	Male	High	Native	LWO	0.92 (0.8–1.07)
45–64	Male	High	Native	Living alone	1.35 (1.04–1.75)

65–84	Female	Low	Immigrant	LWO	1.23 (0.98–1.54)
65–84	Female	Low	Immigrant	Living alone	1.62 (1.28–2.05)
65–84	Female	Low	Native	LWO	1.1 (0.97–1.25)
65–84	Female	Low	Native	Living alone	1.62 (1.42–1.86)
65–84	Female	Middle	Immigrant	LWO	1.18 (0.81–1.71)
65–84	Female	Middle	Immigrant	Living alone	1.66 (1.12–2.46)
65–84	Female	Middle	Native	LWO	0.8 (0.66–0.96)
65–84	Female	Middle	Native	Living alone	1.2 (0.97–1.48)
65–84	Female	High	Immigrant	LWO	0.61 (0.33–1.11)
65–84	Female	High	Immigrant	Living alone	1.16 (0.65–2.07)
65–84	Female	High	Native	LWO	0.55 (0.45–0.69)
65–84	Female	High	Native	Living alone	0.83 (0.64–1.06)
65–84	Male	Low	Immigrant	LWO	1.57 (1.27–1.95)
65–84	Male	Low	Immigrant	Living alone	2.49 (1.84–3.37)
65–84	Male	Low	Native	LWO	0.96 (0.84–1.1)
65–84	Male	Low	Native	Living alone	1.71 (1.47–2)
65–84	Male	Middle	Immigrant	LWO	1.12 (0.82–1.51)
65–84	Male	Middle	Immigrant	Living alone	1.29 (0.74–2.24)
65–84	Male	Middle	Native	LWO	0.85 (0.73–0.99)
65–84	Male	Middle	Native	Living alone	1.47 (1.18–1.83)
65–84	Male	High	Immigrant	LWO	1.06 (0.72–1.57)
65–84	Male	High	Immigrant	Living alone	0.91 (0.38–2.21)
65–84	Male	High	Native	LWO	0.58 (0.48–0.71)
65–84	Male	High	Native	Living alone	1.19 (0.88–1.6)

Table 13. Discriminatory accuracy and unidimensional ORs of smoking from intersectional AIHDA model 1–6 (IV)
Prevalence ratios (PR) and 95% confidence intervals (CI) of smoking among people aged 30–84 included in the National Health Surveys between 2004 and 2018 in relation to survey year, age, gender, education, migration status and household composition. AUC values with 95% CI representing the discriminatory accuracy and ΔAUC values of the models are also presented. PRs and AUC of model 7 are presented in Table 12.

		Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Year							
	2004	2.25 (2.11–2.40)	2.07 (1.95–2.21)	2.08 (1.95–2.21)	1.85 (1.74–1.98)	1.88 (1.76–2.00)	1.84 (1.73–1.97)
	2005	2.17 (2.01–2.35)	2.01 (1.86–2.17)	2.01 (1.86.2.17)	1.83 (1.69.1.98)	1.85 (1.71–2.00)	1.83 (1.69–1.98)
	2006	2.02 (1.86–2.18)	1.87 (1.72–2.02)	1.87 (1.72–2.02)	1.70 (1.57–1.84)	1.71 (1.58–1.85)	1.68 (1.55–1.82)
	2007	2.00 (1.84 –2.17)	1.86 (1.71–2.01)	1.86 (1.71–2.01)	1.71 (1.57–1.85)	1.65 (1.54–1.77)	1.70 (1.56–1.84)
	2008	1.89 (1.76–2.02)	1.76 (1.64–1.88)	1.76 (1.64–1.88)	1.64 (1.53–1.75)	1.66 (1.55–1.78)	1.63 (1,52–1.74)
	2009	1.87 (1.75–2.01)	1.75 (1.64–1.89)	1.76 (1.64–1.88)	1.65 (1.54–1.77)	1.62 (1.51–1.73)	1.63 (1.52–1.75)
	2010	1.75 (1.63–1.87)	1.70 (1.58–1.82)	1.70 (1.58–1.82)	1.61 (1.50–1.72)	1.46 (1.36–1.57)	1.59 (1.48–1.70)
	2011	1.57 (1.46–1.69)	1.53 (1.43–1.64)	1.53 (1.43–1.64)	1.45 (1.35–1.56)	1.47 (1.37–1.58)	1.43 (1.33–1.54)
	2012	1.56 (1.45–1.68)	1.53 (1.42–1.64)	1.53 (1.42–1.64)	1.47 (1.37–1.57)	1.45 (1.35–1.56)	1.44 (1.34–1.55)
	2013	1.52 (1–42–1.64)	1.49 (1.39–1.60)	1.49 (1.39–1.60)	1.45 (1.35–1.55)	1.45 (1.35–1.56)	1.42 (1.32–1.52)
	2014	1.47 (1.36–1.75)	1.45 (1.35–1.56)	1.45 (1.35–1.56)	1.41 (1.31–1.52)	1.42 (1.32–1.53)	1.39 (1.30–1.50)
	2015	1.42 (1.32–1.53)	1.40 (1.30–1.51)	1.40 (1.30–1.51)	1.37 (1.27–1.47)	1.38 (1.28–1.48)	1.35 (1.26–1.46)
	2016	1.07 (0.99–1.16)	1.06 (0.97–1.14)	1.06 (0.97–1.14)	1.04 (0.96–1.13)	1.05 (0.97–1.13)	1. 03 (0.95–1.11)
	2018	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.

Age						
	30–44	Ref.	Ref.	Ref.	Ref.	Ref.
	45–64	1.06 (1.0.3–1.10)	1.06 (1.03–1.10)	0.94 (0.91–0.97)	0.94 (0.91–0.98)	0.93 (0.90–0.96)
	65–84	0.68 (0.65–0.71)	0.68 (0.65–0.71)	0.56 (0.54–0.58)	0.57 (0.55–0.59)	0.53 (0.51–0.56)
Gender						
	Male		Ref.	Ref.	Ref.	Ref.
	Female		1.00 (0.97–1.02)	1.02 (0.99–1.05)	1.02 (0.99–1.05)	1.01 (0.98–1.04)
Education						
	Low			1.96 (1.88–2.04)	1.96 (1.88–2.04)	1.93 (1.86–2.01)
	Middle			1.42 (1.36–1.48)	1.43 (1.37–1.49)	1.42 (1.36–1.49)
	High			Ref.	Ref.	Ref.
Born in Sweden						
	Native				Ref.	Ref.
	Immigrant				1.39 (1.34–1.45)	1.39 (1.24–1.44)
Living alone						
	Living alone					1.53 (1.48–1.58)
	Living with other(s)					Ref.
AUC		0.60 (0.60–0.61)	0.60 (0.60–0.61)	0.64 (0.63–0.64)	0.64 (0.64–0.65)	0.65 (0.65–0.66)
ΔAUC		0.02	0.00	0.04	0.00	0.01

Table 14. Sensitivity analysis where income tertiles replace educational achievement in model 1–6 (IV)

Prevalence ratios (PR) and 95% confidence intervals (CI), of smoking among people aged 30–84 included in the National Health Surveys between 2004 and 2018 in relation to survey year, age, gender, income, migration status and household composition. Model 7 includes the same variables as model 6 but as a multi-categorical variable. AUC values with 95% CI representing the discriminatory accuracy and ΔAUC values of the models are also presented. The PRs for model 7 are presented in Table 15.

		Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Year							
	2004	2.25 (2.11-2.40)	2.08 (1.95-2.21)	2.08 (1.95-2.21)	2.07 (1.94-2.21)	2.09 (1.96-2.23)	2.06)1-94-2.20)
	2005	2.17 (2.01-2.35)	2.01 (1.86.1.17)	2.01 (1.95-2.21)	2.01 (1.86-2.17)	2.03 (1.88-2.19)	2.01 (1.86-2.18)
	2006	2.02 (1.86-2.18)	1.87 (1.72-2.02)	1.87 (1.72-2.02)	1.86 (1.72-2.01)	1.87 (1.72-2.02)	1.85 (1.71-2.00)
	2007	2.00 (1.84-2.17)	1.86 (1.71-2.01)	1.86 (1.71-2.01)	1.86 (1.71-2.01)	1.87 (1.73-2.03)	1.85 (1.70-2.00)
	2008	1.89 (1.76-2.02)	1.76 (1.64-1.88)	1.76 (1.64-1.88)	1.76 (1.64-1.88)	1.76 (1.65-1.89)	1.75 (1.63-1.87)
	2009	1.87 (1.75-2.01)	1.75 (1.64.1.88)	1.76 (1.64-1.88)	1.75 (1.63-1.88)	1.76 (1.65-1.89)	1.74 (1.62-1.87)
	2010	1.75 (1.63-1.87)	1.70 (1.58-1.82)	1.70 (1.58-1.82)	1.68 (1.57-1.80)	1.69 (1.57-1.81)	1.67 (1.56-1.79)
	2011	1.57 (1.46-1.69)	1.53 (1.43-1.64)	1.53 (1.43-1.64)	1.52 (1.41-1.63)	1.52 (1.42-1.64)	1.51 (1.40-1.62)
	2012	1.56 (1.45-1.68)	1.53 (1.42-1.64)	1.53 (1.42-1.64)	1.48 (1.37-1.59)	1.53 (1.42-1.64)	1.51 (1.41-1,62)
	2013	1.52 (1.42-1.64)	1.49 (1.39-1.60)	1.49 (1.39-1.60)	1.45 (1.34-1.55)	1.48 (1.38-1.59)	1.46 (1.36-1.57)
	2014	1.46 (1.36-1.57)	1.45 (1.35-1.56)	1.45 (1.35-1.56)	1.40 (1.30-1.50)	1.45 (1.35-1.56)	1.44 (1.33-1.54)
	2015	1.42 (1.32-1.53)	1.40 (1.30-1.51)	1.40 (1.30-1.51)	1.40 (1.30-1.50)	1.40 (1.30-1.51)	1.39 (1.29-1.50)
	2016	1.07 (0.99-1.16)	1.06 (0.97-1.14)	1.06 (0.97-1.14)	1.05 (0.97-1.14)	1.06 (0.97-1.14)	1.04 (0.96-1.13)
	2018	Reference	Reference	Reference	Reference	Reference	Reference

Age							
	30–44		Reference	Reference	Reference	Reference	Reference
	45–64		1.06 (1.03-1.10)	1.06 (1.03-1.10)	1.11 (1.07-1.15)	1.11 (1.08-1.15)	1.09 (1.06-1.13)
	65–84		0.68 (0.65-0.71)	0.68 (1.86-0.71)	0.61 (0.58-0.63)	0.62 (0.59-0.64)	0.61 (0.58-0.63)
Gender							
	Male			Reference	Reference	Reference	Reference
	Female			1.00 (0.97-1.02)	0.98 (0.95-1.00)	0.98 (0.95-1.00)	0.98 (0.95-1.00)
Income							
	Low				1.93 (1.86-2.00)	1.88 (1.82-1.95)	1.72 (1.65-1.78)
	Middle				1.34 (1.29-1.39)	1.32 (1.28-1.33)	1.30 (1.25-1.34)
	High				Reference	Reference	Reference
Born in Sweden							
	Native					Reference	Reference
	Immigrant					1.28 (1.23-1.33)	1.30 (1.25-1.35)
Household composition							
	Living alone						1.26 (1.21-1.31)
	Living with other(s)						Reference
AUC		0.58 (0.58-0.59)	0.60 (0.60-0.61)	0.60 (0.60-0.61)	0.64 (0.63-0.64)	0.64 (0.64-0.65)	0.64 (0.64-0.65)
ΔAUC		-	0.02	0.00	0.04	0.00	0.01

Table 15. Sensitivity analysis where income tertiles replace educational achievement in intersectional model 7 (IV)

Results from the intersectional model 7 indicating the strata with the 10 highest and the 10 lowest prevalence ratio (PR) with 95% confidence intervals (CI) of smoking across intersectional strata in the Swedish population using the stratum of young native men with high income who were living with other(s) (LWO) as reference in the comparisons.

Age	Gender	Income	Migration status	Civil status	RR (95% CI)
65–84	Male	High	Immigrant	LWO	0.51 (0.07–3.61)
65–84	Female	High	Immigrant	Living alone	0.64 (0.37–1.08)
65–84	Male	High	Native	Living alone	0.64 (0.55–0.74)
65–84	Female	High	Native	Living alone	0.66 (0.56–0.78)
65–84	Female	High	Native	LWO	0.71 (0.45–1.12)
65–84	Male	Middle	Native	Living alone	0.74 (0.65–0.83)
65–84	Female	Middle	Native	Living alone	0.76 (0.67–0.86)
65–84	Male	High	Immigrant	Living alone	0.77 (0.51–1.15)
65–84	Male	Low	Native	Living alone	0.87 (0.76–0.99)
65–84	Male	High	Native	LWO	0.91 (0.57–1.46)
30–44	**Male**	**High**	**Native**	**LWO**	**Reference**
30–44	Male	High	Immigrant	Living alone	2.37 (0.98–5.73)
45–64	Male	Low	Immigrant	LWO	2.53 (2.14–2.98)
65–84	Female	High	Immigrant	Living alone	2.58 (0.96–6.89)
30–44	Female	High	Immigrant	Living alone	2.62 (0.98–7.02)
45–64	Male	Middle	Immigrant	Living alone	2.63 (1.86–3.7)
30–44	Female	Low	Immigrant	Living alone	2.64 (1.89–3.68)
30–44	Male	Middle	Immigrant	Living alone	2.66 (1.74–4.08)
30–44	Male	Low	Immigrant	LWO	2.73 (2.32–3.2)
30–44	Male	Low	Immigrant	Living alone	2.94 (2.31–3.74)
45–64	Male	Low	Immigrant	Living alone	2.96 (2.45–3.58)
AUC					0.65
ΔAUC compared with model 6					0.01

Conclusions

Study I

There is a clear socioeconomic gradient in incident COPD in Sweden; people with low absolute income have a threefold relative risk of COPD compared to high income individuals. No such gradient exists for relative income. Although it is impossible to isolate psychosocial from material effects with the applied methodology, the lack of a relative income gradient in COPD incidence and the low DA of the relative income model compared to the absolute income model supports the materialistic explanation model rather than the psychosocial model for the genesis of income disparities in COPD incidence. The AUC of 0.63 for women and 0.65 for men imply that income alone does not explain a large share of the disparities in COPD incidence in Sweden.

Study II

Intersectional analysis of COPD incidence provides an improved mapping of socioeconomic disparities in COPD compared to unidimensional studies. The intersectional analysis showed that socioeconomic risk factors like low income may not imply a high risk of COPD in the presence of protecting factors, and conversely, individuals at specific intersectional locations may possess a protective factor like high education and still be at high risk of COPD. As expected, age was the most important dimension in the intersectional matrix and explained half the variance found in the null model. More surprisingly, second to age the adjustment for civil status lead to the largest drop in ICC. The DA of the intersectional model was good with an ICC of 20%. Additive rather than interactive effects explain intersectional disparities. MAIHDA is a suitable tool to perform quantitative intersectional research.

Study III

The overall average prevalence of discontinuation to COPD maintenance medication across geographical and sociodemographic contexts is high. Sociodemographic context (age, gender and education) influences risk of discontinuation more than county of residence. Sociodemographic disparities in discontinuation are small and geographical disparities between counties are very small. Cross-classified MAIHDA is a useful method to evaluate health care inequalities and to compare the relevance of different contexts. The results from this study supports interventions targeted to the whole population rather than specific sociodemographic groups or counties.

Study IV

The intersectional pattern of smoking prevalence in Sweden is complex. Immigrant men aged 30–44 years with low education who lived alone, immigrant men aged 30–44 years with low education who lived with other(s) and immigrant men aged 45–64 years with low education who lived alone occupied the three strata with highest crude smoking prevalence. Young immigrant women living alone had a rather high PR of smoking despite their high educational achievement. The DA of the intersectional model was moderate and had a confidence interval that overlapped with the previous model, which indicates that additive effects rather than interactive effects explained the intersectional disparities in smoking prevalence. AIHDA constitutes a good complement to MAIHDA that is easy to apply and that provides specific information of value for public health policy.

Discussion

This thesis confirms that the risk of smoking and the risk of COPD in the population are conditioned by socioeconomic and demographic factors, and so is the probability of continuous maintenance medication among COPD patients. Among the socioeconomic factors, absolute income and materialistic mechanisms seem more relevant than relative income and psychosocial mechanisms for understanding the risk of COPD in the population. However, both kinds of income mechanisms may act together, and they are difficult to disentangle. Studies based on the analysis of separated socioeconomic, demographic or geographical dimensions seem insufficient for investigating inequities in health and healthcare quality. Much previous research on the social epidemiology of COPD lack an explicit social theoretical framework and focus only on differences between group averages. On the contrary, intersectional MAIHDA/AIHDA use social theory to analyse an array of intersectional contexts (i.e. intersectional strata) that better reflect the distribution of power and resources in the population and may condition individual health and health care utilisation. When doing so, MAIHDA/AIHDA focus not only on differences between strata averages but also on their DA. In this way intersectional MAIHDA/AIHDA may avoid stigmatisation, allow for a more complete picture of the distribution of ill health and lead to more effective guidance of clinical and public health interventions according to the idea of proportionate universalism.

When it comes to understanding adherence to COPD treatment, we observed that contexts defined by socioeconomic and demographic dimensions were more relevant than those defined by the geographical boundaries of the Swedish counties. However, neither of those contexts displayed a high DA.

Overall, this thesis suggests that interventions to eliminate socioeconomic disparities in smoking, COPD risk and COPD care are needed. Such interventions should primarily be universal and focus on equitable distribution of SDH. Since substantial heterogeneity within the intersectional strata exists, interventions exclusively focused on intersectional strata with a higher risk are unlikely to be efficient.

Relation to previous research

Study I

For study I, the gradient with a threefold relative risk of incident COPD for people with medium-low and low absolute income compared to the high-income quintile confirms previous findings of a socioeconomic income gradient for COPD. Borné et al. (2019) reported hazard ratios of incident COPD of 2.23 (95% CI: 1.97–2.53) for people with low annual income. In a review of the association between different measures of SEP and COPD, Gershon et al. (2012) conclude that most studies report at least twofold risks for poor outcomes for the lowest socioeconomic strata. Although studies exist that assess DA by calculating AUC of models with clinical data to predict the course of COPD (Amalakuhan et al., 2012, Sundh and Ekstrom, 2017), I have not found any study assessing the DA of socioeconomic risk factors for incident nor prevalent COPD.

To my knowledge, there is no previous studies that explicitly compare the importance of materialistic and psychosocial explanation models for incident COPD. Cho et al. (2016) investigated the association between individual household income and mortality among 9,275 COPD patients in South Korea, and whether that association changed if people lived in advantaged compared to disadvantaged neighbourhoods. They found that low individual household income was associated with increased mortality regardless of deprivation status of the neighbourhood, but that mortality was higher among low-income individuals living in disadvantaged (HR=1.43; 95% CI, 1.17–1.74 vs. HR), compared to advantaged neighbourhoods (HR=1.36; 95% CI, 1.11–1.66). While the difference between neighbourhoods is not conclusive, this finding is hypothesised to be explained by increased psychosocial stress and relative deprivation experienced by people with low income living in a disadvantaged area. This interpretation of the effect of living in a deprived area contrasts with other publications. Gerdtham and Johannesson (2004) explored the effect of individual income, community income inequality and mean community income on mortality among adults in Sweden. According to these authors, the relative income hypothesis posits that mean municipality income should be positively associated with mortality rates, holding individual-level income constant. However, this relative income hypothesis was not supported. The income variable that can be hypothesised to act mostly through the materialistic pathway, low individual-level income, was the only variable that was associated with increased mortality. Hillemeier et al. (2003) found that poverty by national standards rather than US state relative poverty was more related to infant mortality. This suggests that capacity to afford the basic needs is more important than the relative position in a state hierarchy for infant mortality. When accounting for the effect of area level economic deprivation, Zhang et al. (2013) found higher prevalence of long-term illness and self-reported “not good health” in areas that had more affluent neighbouring areas. This hypothesised psychosocial effect was strongest in the least deprived areas, suggesting that psychosocial effect becomes more important when material deprivation is absent. Overall, the inherent difficulties in disentangling materialistic and psychosocial mediators between low SEP and COPD is partly attributable to the fact that both pathways act through health behaviours (Mackenbach, 2006) that are decisive for incident COPD.

Study II

Intersectionality research on respiratory diseases is a novel research field. Fuller-Thomson et al. (2016) studied self-reported COPD among 129,535 non-Hispanic black and white never-smokers in the USA and found that both black and white women had higher odds of COPD compared to men, but that gender and ethnic disparities were modified when adjusting for SEP. The odds of COPD decreased for black women but was slightly increased for white women after SEP adjustment. While there were no differences between black and white men prior to SEP adjustment, the odds of COPD became significantly higher for white compared to black men after this adjustment. This study did not assess interactions between nor individual heterogeneity within the different social dimensions, but the slightly increased odds of COPD among women and immigrants are consistent with our findings. The unidimensional ORs obtained in model 3 confirm previous findings of increased risk of COPD for people with higher age but contradict the estimation of higher prevalence of COPD among men by Raherison and Girodet (2009). Other studies have found similar odds of prevalent (Lindberg et al., 2006a) and incident (Lindberg et al., 2006b) COPD between men and women. The income and educational disparities in COPD morbidity are, as already noted, in line with existing evidence (Gershon et al., 2012). Borné et al. (2019) did not find any effect of country of birth on incidence of COPD in a Swedish sample. Whereas the OR for incident COPD among immigrants was conclusive but only 1.15 (95% CI 1.01–1.29), the ICC in our study did not change after adjustment for migration status, indicating a small or non-existent contribution by migration status to the overall DA. Our findings regarding migration status thus resembles those presented by Borné et al. Second to age category, civil status was the dimension that contributed most to the ICC according to the analysis in model 2. Yet civil status has been scarcely investigated in relation to incident COPD. Borné et al. report that compared to married individuals, hazard ratios for incident COPD was 1.61 (95% CI 1.46–1.78) for divorced people and 1.30 (95% CI 1.16–1.46) for widowed individuals (Borné et al., 2019). Remarriage after divorce or bereavement diminishes risk of incident COPD among women but not men, according to a study from the USA including 2,676 individuals (Noda et al., 2009). In a Danish study focused on prognosis among COPD patients, people living alone had lower hospitalisation rates due to exacerbation, but worse adherence to maintenance therapy and higher mortality rates (Tottenborg et al., 2016).

The MAIHDA approach has not been applied for respiratory outcomes before or after publication of study II, yet the same methodology has been applied for other outcomes. When studying BMI among US adults, Evans et al. (2018) found an ICC=5.0% for the null model, and 35% of this between-strata variance was due to intersectional interaction. In a study utilising Spanish data to study BMI from an intersectional perspective (Hernández-Yumar et al., 2018), the ICC dropped from 12.9% (additive effects and interaction effects conflated) to 1.9% when isolating interaction effects. In a study from 2020, Kern et al. (2020) found modest ICCs for null models (3.1–6.4%) when investigating life dissatisfaction and psychosomatic complaints in a study adopting a MAIHDA approach with three dimensions: native/immigrant, high/middle/low SES and boys/girls. A total of 98–99% of the between-strata variance was explained by main effects, thus intersectional interaction was absent or contributed very little. This study comprised data from 33 different countries and included a comparison of how the intersectional strata influenced outcomes in countries with high versus low income inequality. They found that in more equal countries the most advantaged groups performed worse, whereas the multiply disadvantaged strata had better health compared to countries with higher income inequalities. Persmark et al. (2019) studied opioid prescriptions and found a modest VPC of 13.2% for the null model, and the VPC of the interaction model was only 0.42%. Other studies have applied MAIHDA to study rheumatological diseases (Kiadaliri and Englund, 2020, Kiadaliri et al., 2020) and biomarkers for common chronic diseases (Holman et al., 2020) and found ICCs for the null model much lower than 20%, as well as very small intersectional interaction effects.

In comparison to these studies, the intersectional MAIHDA seems especially relevant for the study of COPD since the VPC of the null model was 20.0%. The modest contribution of intersectional interaction in our study has mostly been replicated in the mentioned studies. Different health outcomes in different contexts should be revisited utilising this intersectional approach.

Study III

The prevalence of discontinuation found in study III is close to those reported from other Swedish studies on adherence to maintenance medication among COPD patients. In a study including both COPD and asthma patients with prescriptions of inhalatory medication, including short-acting beta2-agonists, 24% retrieved their medication only once during a five year period (Haupt et al., 2008). Another study comparing pharmacological treatment among patients in 2004 and 2014 showed a decrease in the proportion of patients without maintenance therapy from 36% in 2004 to 31% in 2014, including patients from both primary and secondary care. In secondary care, the prevalence of no maintenance therapy in 2014 was 22% (Sundh et al., 2017). In the annual report from the Swedish National Airway Register

(SNAR) 2019 (Hesselmar et al., 2019), a lower prevalence of absence of maintenance medication is noted among patients reported from specialist care. Patients with COPD stadium 2 have a prevalence of about 8% and for patients with COPD stage 3 and 4 the prevalence of no maintenance medication is below 5%. Possible explanations to the difference in this report compared to our results include better compliance to guidelines among clinics that report to SNAR, inclusion of some patients with COPD stage 1 in our cohort and improved adherence to guidelines in 2019 compared to 2011. As noted above, there is a lack of an established way of comparing regional and sociodemographic disparities in health care.

Study IV

The unidimensional relationships between smoking on one hand and age, educational attainment, civil status and migration status on the other, largely confirm previous research on socioeconomic patterns of smoking in Sweden. For example, Landberg et al. investigated cigarette addiction, rather than self-reported smoking as in our study, and found increased odds of cigarette addiction among people with low education and low income. Immigrant men had higher odds of smoking compared to natives but the same pattern was not as clear for women, where people born in other Nordic countries had higher prevalence of smoking but women born outside the Nordic countries had lower odds of smoking (Landberg et al., 2018). The same pattern was found in our study, where women born outside Europe was the only group with lower smoking prevalence than people born in Sweden, according to Table 11. In a working paper, Spika et al. (2018) have found that an increase in the proportion of the population with more than 12 years of education can explain part of the decreasing prevalence of smoking in Sweden between 1994 and 2018. While overall prevalence of smoking decreased, both income- and education-related inequalities increased for daily smoking as well as for smoking related hospitalisations and death.

In contrast to COPD, explicit intersectional research exists for smoking, although intersectional matrices and outcomes are different. Potter et al. (2020) investigated successful smoking cessation and found no significant intersectional interaction. In a study on temporal development of light and intermittent smoking among men and women of different ethnic groups in California, Pulvers et al. (2015) found gender differences to be maintained only among non-Hispanic whites, whereas gender differences disappeared for blacks and Hispanics.

Qualitative intersectional studies have provided important insights into how the stigma associated with smoking may interact with other identities such as being low class, a bad mother, country of birth and norms of femininity. The strengthened stigma experienced by smokers as a result of anti-smoking campaigns can either be an incentive to stop smoking or a side effect constituting an extra health burden

(Triandafilidis et al., 2016). The stigma associated with smoking may be differently experienced for people with different SEP, and according to Graham (2011) this may contribute to widening disparities in smoking rates between social classes. While stigma is not assessed in this paper, it should be considered when strategies to eliminate smoking in the population are designed.

Strengths and limitations of individual studies

Study I

One challenge when studying relative income is to find the appropriate reference group. This translates into the question of whether individuals compare themselves with neighbours and colleagues, with the richest people in their country or with people in other countries and continents. Our methodology is based on the hypothesis that people compare themselves with others sharing similar economic circumstances, i.e. people who belong to the same absolute income quintile. Kawachi et al. (2002) claim that people most likely compare themselves in several directions, and hence the effect we observed for absolute income on COPD incidence could contain both materialistic and psychosocial components. A key point made by proponents of the psychosocial model of health inequalities is that its effect exists across the whole socioeconomic gradient (Wilkinson and Pickett, 2009). Therefore, we would have expected a relative income gradient for incident COPD if psychosocial stress was the major pathway causing the socioeconomic disparities in COPD. Additionally, we performed a sensitivity analysis in which we analysed the relationship between relative income and COPD separately in the different absolute income quintiles, but saw no consistent gradient and very small increments in AUC compared to a model including only age.

We did not have information on COPD from primary health care where mild cases of COPD patients are treated. Although this is a limitation, it is not a serious concern since the purpose of the study was to compare absolute and relative income as predictors of incident COPD, rather than establishing the precise incidence in the population. The income data we used covers income from wages, subsidies, retirements, insurances, profits from capital and other sources, which is a strength. However, since 2007, wealth statistics are not monitored in Sweden after abolition of capital taxes (Statistics Sweden, 2021), so we did not consider wealth in this study nor in any of the other studies included in this thesis. This can be considered a weakness since in Sweden wealth inequalities are larger than income inequalities. For example, the ten percent with the highest income earn close to 30% of the total annual income in Sweden, but the ten percent with largest capital own nearly 60% of the total capital in the country (Piketty, 2015). Our results may therefore underestimate socioeconomic differences in COPD incidence, since the wealth or absence of savings of an individual also condition access to material resources. It can be considered a weakness that we only measured income data at one point in time, the year prior to measuring incident COPD, since COPD may influence the possibilities for an individual to participate in work life. The fact that we excluded individuals with previous COPD reduces the problem of reverse causality.

The application of AUC is a strength of this study. The AUC is a feasible way of evaluating the relevance of absolute versus relative income models for predicting incident COPD. In the case of this study, the clear socioeconomic gradient with threefold relative risks for COPD among people in the middle-low and low income quintiles among both genders could lead to the conclusion that income and age explain a large share of an individuals' propensity to develop COPD. The DA of the absolute income models indicates a large remaining heterogeneity within income quintiles and that other factors must be explored to increase the understanding of the social mechanisms behind disparities in COPD incidence.

Study II

A main strength of this study is that it is the first study to describe the particularities of intersectional MAIHDA when modelling a binary outcome in logistic regression and thus contributes to the application of intersectionality theory in a quantitative framework. However, while intersectional MAIHDA is becoming one of the standard tools to perform quantitative intersectional research, a methodological criticism has been directed at the MAIHDA analyses, including conclusions drawn in paper II (Lizotte et al., 2019). This critique represents a classical debate on the suitability of multilevel analyses based on cluster-specific information versus single-level traditional studies based on population averages. In a publication by Evans, Leckie and Merlo (2019) the differences between MAIHDA and the traditional single-level approach are discussed. In analogy with the analyses of multiple measurements within individuals, MAIHDA considers individuals within intersectional strata. The "context" in the case of multiple measurements is the individual, while in the intersectional case the "context" is the stratum. In both cases, multilevel regression is appropriate for both statistical and substantive reasons. Statistically, if the "context" matters, the multiple measurements will be correlated within individuals and, analogously, the individuals will be correlated within strata. This correlation is taken into account by the multilevel regression. For instance, if we were investigating the FEV_1 of 100 patients and had 2 measurements for 80 patients, 4 measurements for 15 patients and 16 measurements for 5 patients the number of measurements would be 300. However, the effective sample size would not be 300 but rather close to 100 because the measurements within the patients are highly correlated. For this reason, when calculating the average FEV_1 of the patient populations we firstly calculate the average FEV_1 in each patient and then we calculate the mean of the patient values (that is the mean of the patients' means). Otherwise, the 5 patients with 16 measurements each would be overrepresented, and the population average would be biased.

Analogously, if we were investigating intersectional strata, our interest would be to obtain information on the average FEV_1 of each stratum, and we would use this information to calculate the average in the population (i.e. mean of the strata's means). Otherwise, strata with many patients would be overrepresented. This situation is especially relevant in social epidemiology and intersectionality where we are especially interested in the health of minorities. In addition, the multilevel approach gives reliability-weighted estimations of the strata values which prevents excess influence of extreme values due to a very small number of individuals in some strata.

Quantifying the correlation of the information within the context provides knowledge on the relevance of that context for the outcome under investigation (Merlo et al., 2005a). In the example of analyses of multiple measurements within individuals, the "individual body" is obviously very relevant, so the intra-individual correlation between measurement can be close to 100% (Merlo et al., 2009). However, in the case of intersectional strata, it is not given that the intra-strata correlation between individuals is high. It could be low, indicating that the intersectional strata were not relevant.

In the traditional population average estimations defended by (Lizotte et al., 2019), neither the intra-strata correlation nor the size of the strata is considered and the population average represents the average of the individuals' values, not the grand mean of the strata means. Besides, when calculating the interactions in the MAIHDA, the results are the same whatever the reference category used for the estimation of the main effects (Evans et al., 2019). Both methodological approaches are correct but because of the way they conceptualise the information may give different results.

This study is based on a large database that covers the whole population of Sweden and the socioeconomic and demographic information is of high quality (Statistics Sweden, 2019). Noteworthy, the stratum with the least number of individuals still had 1,236 individuals, which increases the precision of the estimates.

Our intersectional matrix has some limitations. For example, important axes of oppression such as sexual orientation and functionality were not included. This was partly due to a lack of information, but also stems from a wish to present a parsimonious intersectional model. The assessment of some of the social dimensions that were included can also be questioned. A limitation shared by all studies in this thesis is the binary assessment of gender. Due to a lack of more nuanced data, individuals were categorised as either male or female depending on their legal gender (study I–III) or self-reported data (study IV). Lamentably, this thesis thereby perpetuates the discrimination of trans-sexual and transgender individuals by ignoring the existence of more than two sexual identities. We did not have information on ethnicity but included country of birth as a proxy variable that captures experiences of migration. As a consequence, we could not assess racism, but on the other hand avoid contributing to the idea of cultural differences based on ethnicity (Karlsen and Nazroo, 2017). As for study I, we did not have information on COPD patients from primary health care.

Study III

The principal weakness of this study is that we did not have information on the COPD stage of the patients, due to a lack of data on FEV_1, symptoms of dyspnea and number of exacerbations during the previous 12 months. While our double criteria for the definition of the COPD cohort, requiring both previous maintenance medication and a hospital COPD diagnosis, makes it probable that patients who were included had an indication for maintenance therapy, it would have been valuable to stratify for disease stage. It is known that patients with more severe disease have better adherence (Humenberger et al., 2018) and that people with low SEP have more severe COPD (Lange et al., 2014). Thus, it is possible that a more pronounced sociodemographic gradient in adherence to maintenance medication is counterweighted by more advanced disease among more deprived sociodemographic strata. Similarly, older individuals have more severe disease so the differences between age categories may be underestimated. With access to COPD stage, this hypothesis could have been explored. A total of 3,636 patients died during 2011 and were excluded from the study. This raises the question of whether any selection bias was introduced. These patients accounted for 6.6% of the study population, and in a sensitivity analysis where we maintained people who died during 2011 in the analysis results remained stable.

MAIHDA has previously been used to simultaneously study average differences between geographical contexts and the individual variance around those averages (Merlo et al., 2016), but this is the first study to compare geographical and sociodemographic disparities adopting a cross-classified MAIHDA approach. I see three principal advantages of the framework we propose to evaluate equity in health care. First, our method offers a clear way of comparing the proportion of variance in patients' propensity to discontinue their medication that is attributable to a geographic versus a sociodemographic context. This means that with our method, health care policies can be designed that target the context with most relevance for the studied outcome. If such decisions are based only on comparisons between the average disparities between counties on the one hand and sociodemographic groups on the other, they can be very imprecise since the degree of heterogeneity within the categories is not known. Second, current epidemiology has been criticised for its lack of a consequentialist focus, since it is not always clear how results from epidemiologic research should be translated into a more equitable health distribution in society (Galea, 2013). The coupling of our methodology with the concept of proportionate universalism thus answers the call for a more consequentialist epidemiology since we a priori define how results shall translate into different strategies depending on the overall prevalence of discontinuation on one hand, and on the VPC and AUC on the other. When the VPC is high, interventions should be targeted to specific vulnerable strata, but when the VPC is low they should be more universal. Thirdly, rather than focusing on the crude prevalence of discontinuation in counties and sociodemographic groups, we present precision-weighted absolute risks calculated from the multilevel model. The grand mean is the prevalence of discontinuation that would be found if all combinations of geographical and sociodemographic contexts were of the same size (Evans et al., 2019). While the crude prevalence of discontinuation is relevant to evaluate the discontinuation rate in the whole country, the adjusted precision-weighted absolute risks are more informative when the focus of research is the contextual effect of counties and sociodemographic strata on maintenance medication.

The cross-classified MAIHDA makes it easy to detect interaction between two contexts at the second level. As a supplementary analysis we investigated whether any interaction occurred between county of residence and sociodemographic strata for risk of discontinuation. While this was not the case, it should be investigated in future studies in other contexts or with other outcomes. An interaction between sociodemographic strata and counties could imply that county-level policies affect the sociodemographic gradient, i.e. that counties perform better or worse in terms of equitable health care. Additionally, characteristics of the counties such as urban versus rural dwellings, political majority or number of PHCs per inhabitant could be included as explanatory variables at the second level to evaluate specific contextual effect. However, when the VPC is very low, it does not make sense to evaluate the specific contextual effect of a very weak general contextual effect.

Study IV

One limitation of this study is that participation rates in the NHS were rather low and diminished from 60.8% in 2004 to 42.1% in 2018. According to an analysis of non-participants performed by Statistics Sweden, people with low education, immigrants and people living alone were more likely to be non-responders. If people who did not respond had higher smoking rates compared to responders, it is possible that we have underestimated the socioeconomic disparities in smoking prevalence. Statistics Sweden provides a weighted data-set that calibrates the bias introduced by non-participation (Franzén, 2018); the variables used for the calculation of the calibrated weights were age, gender, education status, migration status, civil status and urban versus rural dwelling. We performed a sensitivity analysis where the weighted data was used and the results were very similar. We consider it a strength that socioeconomic and demographic data was obtained from registers, but smoking status was self-reported and enabled the inclusion of both sometimes smokers and daily smokers in the definition of the outcome. However, we did not have information on the amount of tobacco consumed by the participants, which could have rendered a more nuanced mapping of the smoking habits in the population. This would have been valuable in order to analyse light and intermittent smoking rates in Sweden since previous intersectional research report light and intermittent smoking to be increasing among ethnic minorities but decreasing among whites (Pulvers et al., 2015). We did perform a sensitivity analysis where the outcome was restricted to daily smokers; as expected, smoking prevalence was lower, at 11% compared to 18%. Socioeconomic disparities were more pronounced since the intersectional context had a DA of 0.70 compared to 0.66 in the main analysis. The prevalence of everyday smoking was only 1.6% for the stratum presumed to occupy greatest structural privilege, compared to 11.8% when sometimes smokers were included. Our main results combined with the results from this sensitivity analysis reflect the existence of socioeconomic disparities not only in prevalence but also in intensity of smoking (Bobak et al., 2000). Our results may therefore underestimate the intersectional disparities in health hazards attributable to smoking.

The advantages of an intersectional approach when studying inequalities in health have already been discussed under the section on strength and limitations for study II. Inherent to the intersectional approach is a view of social and demographic categories as socially constructed that are relevant only insofar as they capture axes of oppression. Therefore, the adoption of an intersectional approach to the study of smoking directs focus away from individual factors, such as moral character and self-discipline, towards the social mechanisms that cause the complex pattern of socioeconomic differences in smoking rates. This is especially important in the context of COPD and smoking. COPD patients frequently suffer from feelings of guilt due to ideas of having a self-inflicted disease (Strang et al., 2014). If health care workers and people in general had better understanding of the social factors that influence the risks of smoking, problems of self-accusation could be alleviated.

The intersectional AIHDA presented here should not be viewed as a substitution of MAIHDA. Rather, the two approaches provide different information and serve complementary functions. AIHDA and MAIHDA share three crucial advantages. First, the intersectional mapping is superior to unidimensional, albeit multiple, analyses when it comes to identifying vulnerable population groups towards which interventions should be directed. Second, the assessment of the DA, analogous to the ICC, informs on the heterogeneity within the intersectional strata and thus the relevance of that intersectional matrix for the specific outcome under study. Third, in both the AIHDA and the MAIHDA, the intersectional strata are conceptualised as contexts rather than as individual characteristics.

While MAIHDA may seem inconvenient for researchers not familiar with multilevel models, intersectional AIHDA can be readily performed by researchers familiar with single-level regression models and still provide worthy and correct information. Some differences between the two approaches should be noted. AIHDA uses a specific stratum as reference in the comparisons while MAIHDA uses the grand mean (or the mean of the strata means) as reference. Whereas MAIHDA allows for a more detailed analysis of the specific strata where intersectional interaction is taking place, AIHDA only informs on the increase in AUC when the intersectional interaction effects are accounted for. In our case, there was no conclusive intersectional interaction taking place and therefore this attribute of the MAIHDA would not have increased our understanding of smoking patterns in Sweden. When the study population is small in comparison to the number of intersectional strata, the problem of empty or small strata may arise. In such situations, the MAIHDA approach is advantageous due to the use of shrunken residuals, as explained in the methodology section.

Implications and future research

Materialistic and psychosocial approaches

Without claiming that study I should be interpreted as definitive evidence that the materialistic perspective is the only relevant theory when it comes to understanding COPD risk, our results indicate that it merits more attention than the psychosocial approach. I will therefore shortly outline the different implications of the two approaches, both for COPD specifically and for the general strive for equity in health. It is important to underscore that regardless of whether socioeconomic health disparities are mediated through psychosocial or materialistic pathways, both approaches concord in the view that more equitable resource distribution is necessary to reduce socioeconomic health disparities. Contrary to this, there are widening income and wealth disparities in Sweden. The gap in disposable annual income between people at the 5th and 95th percentiles increased by 82,000 SEK between 2011 and 2017 (Folkhälsomyndigheten, 2020a). The wealth gap also increases in Sweden (Piketty, 2015).

The concept of status originates in Weberian research and was further developed by Giddens. It is based on a subjective perception of an individual's location in society rather than an objective one (Humber, 2019). Hence, if the causes of health inequalities are subjective it will be attractive to find solutions that alter this subjective perception of inequalities. Research to find healthy responses to financial strain constitutes one such example (Perzow et al., 2018). Although most proponents of the psychosocial explanation model do not propose subjective solutions, the risk of such conclusions is inherent to the psychosocial theory of the genesis of health inequities itself. As a contrast to this, an SDH approach directs attention to the material and objective roots of health disparities. This approach was first proposed in the Black Report on inequalities in health in the U.K. (that found the steepest class gradients in mortality among respiratory diseases) (Black et al., 1980), and was then developed by Dahlgren and Whitehead (1991) in the rainbow model explained above (see Figure 1). This model presents four layers into which SDH can be divided. Each layer requires different levels of interventions. In the original report, Dahlgren and Whitehead exemplify how the goal of reducing over-all smoking rates can be achieved through simultaneous interventions at level 1 (structural changes such as increased tobacco taxes), level 2 (bans on cigarette advertisement, smoke-free spaces), level 3 (communities joining together to avoid sales of tobacco to children in local shops) and level 4 (education to the general public of the dangers of smoking). While many of these interventions have been performed in Sweden and have contributed to a continuous reduction in smoking prevalence (Sohlberg, 2019), inequities in smoking remain, as seen in study IV. A recent review conclude that there is evidence that financial incentives for smoking cessation is effective even at prolonged follow-up (Notley et al., 2019). While such incentives can be presumed to be stronger among people with low SEP and the intervention aligns with the materialistic approach, the review did not evaluate the effect on socioeconomic disparities in smoking of campaigns with financial incentives.

In Sweden, the Public Health Agency has listed eight areas of strategic priority to reach the goal of closing the gap in preventable disease in one generation. These align with the SDH approach and include early life circumstances, education and competence, work life, income, housing, lifestyle factors, control and participation, and equitable and health promoting health care (Folkhälsomyndigheten, 2020b). Although the direction set forth through these prioritised areas of intervention has the potential to reduce socioeconomic health inequalities, the development of many of them are unsatisfying. As mentioned above, income and wealth disparities are widening. Unfortunate trends of increasing inequalities rather than gaps being closed are also occurring for lifestyle factors (as exemplified in study IV), housing conditions and housing segregation (Lilja and Pemer, 2010) and long-term unemployment (Folkhälsomyndigheten, 2020c), whereas for educational achievement social inequalities are stable (Bjorklund et al., 2003).

Building on Wright's operationalisation of social class, McCartney et al. (2019) have recently presented an integrated model for deepening the understanding of how different class processes contribute to health inequalities. Urging researchers to include theoretical hypotheses of how social class conditions health, the model includes both individual attributes aligning with Bourdieus' class concepts, a phenomenon denominated 'opportunity hoarding' that resembles Weberian ideas of class definition based on similar opportunities, and relational processes of exploitation and domination most closely related to Marxism. The model further includes an intersectional perspective since it considers the interaction with discrimination based on gender, race and sexual identity and other social dimensions, as well as the specific importance of early life experiences. The role of health behaviours is also included in the model. The authors admit that datasets seldom allow assessment of all class processes that contribute to health inequalities. This model puts focus on processes of domination and is a promising tool that can help researchers identifying and contextualising which specific process that is being investigated and could be useful for future social epidemiologic studies of COPD.

Implications of moderate DA for income

Although individual income conditions the risk of developing COPD, no recommendations have been formulated for how the health care system should tackle this risk factor. Screening interventions in socioeconomically deprived areas have been proposed (Dirven et al., 2013, Pleasants et al., 2016) and constitute a logical response to the disparities in COPD incidence. However, since the DA for the absolute income model in our study was only 0.63 for women and 0.65 for men, clinical interventions exclusively directed to specific income strata are not justified by our data. Rather, as outlined above, preventive and universal measures aiming to improve equal distribution of the SDH should be the focus, since this may benefit other aspects of population health as well. The finding of a moderate DA in this unidimensional analysis motivated exploration of the intersectional approaches adopted in study II and IV.

Health policies guided by intersectional research

Although the ICC of 20% in study II shows that substantial heterogeneity remains unexplained, the DA of the intersectional model is sufficiently large to support the categorical standpoint that health care interventions aiming at reducing disparities in COPD incidence should be guided by the intersectional mapping presented in study II. If a similar ICC would have been found for any unidimensional model (i.e. based on gender, age, SEP, civil status or migration status alone), interventions targeting vulnerable groups according to a unidimensional analysis would be more feasible, since it is easier to design interventions in groups defined by a single social axis.

Important insights emerge from the intersectional modelling of smoking and COPD. For example, high level of education is known to be a protective factor when it comes to both COPD and smoking. Yet, older immigrant men with low income who lived alone had the fifth highest risk of COPD of the 96 strata despite their high education. For smoking, high education failed to protect young immigrant women who lived alone from smoking, since they displayed the tenth highest smoking rates of the 72 strata. One potential explanation is that education status constitutes a poorer indicator of SEP among some immigrant groups due to discrimination in the labour market (Carlsson and Rooth, 2007). This finding can also reflect maintained smoking patterns from countries of birth (Lindstrom and Sundquist, 2002). Findings from study I and other unidimensional studies indicate that low income is a risk factor for COPD. Despite this, young men with high education who were born in Sweden and cohabited belonged to the three strata with lowest predicted incidence regardless of whether their income was high (predicted incidence =0.02%, 95% CI 0.01%–0.04%), medium (predicted incidence =0.03% 95% CI 0.02%–0.04%) or low (predicted incidence =0.03%, 95% CI: 0.02%–0.05%). This indicates that with sufficient protecting factors, exposure to low income is not as hazardous as it is for individuals lacking those protective factors. In addition to this, our results from study II and IV indicate that civil status/household composition is a variable that merits more attention since it is an important part of the intersectional matrix when studying both risk of COPD and smoking.

Several questions remain unanswered regarding how to perform health care interventions informed by studies applying intersectional MAIHDA or AIHDA. First, multi-categorical approaches including socioeconomic, demographic and individual-level risk factors as well as clinical variables should be explored to further increase our understanding of groups with increased risk of smoking/COPD where targeted interventions could be motivated. Older individuals with low income who live alone comprised most of the strata with the highest COPD risk, with similar prevalence pertaining to both genders and immigrants as well as natives. For smoking, all three strata with the highest risk of smoking included immigrant men younger than 65 years with low education. The immediate risk factors that drive increased risk of COPD and smoking in these strata should be further explored.

Second, there is poor evidence that currently adopted approaches to reduce socioeconomic disparities in individual level determinants of health are efficient (Vilhelmsson and Ostergren, 2018). Qualitative methods could be utilised to identify and develop interventions with support from members of groups with a high risk of COPD and smoking according to quantitative intersectional analyses. One aim should be to further the understanding of how the different dimensions of power operate, including exploration of the specific causal mechanisms that cause intersectional disparities in COPD and smoking. Such studies should preferably involve members of those groups and have a clear focus on generating knowledge that can guide implementations, such as the community-based participatory research approach (Andrews et al., 2012).

Third, quantitative intersectional research should be further developed to present a solution to the question of which strata should be considered at risk for the studied outcome, i.e. in which strata could the interventions be recommended. Such discernment could be based on pre-defined cut-off values for average risk in the presence of sufficient DA, but other methods including likelihood-ratios (Rodriguez-Lopez et al., 2017) could also be explored.

The intersectional approach should not be conceptualised as a study of the intensity of the oppression at the different social axes. Rather, it is a way to let theories of social dynamics guide the study of which social factors that have an implication for the incidence of COPD and the prevalence of smoking.

Maintenance medication for COPD patients

According to the framework presented in study III, Table 2, there is a need to improve continuity in maintenance medication among COPD patients, as the country average was 18.4% – which is above the proposed threshold level of 10% as an acceptable level of discontinuation. In one study, primary health care staff reported that COPD patients constitute a low priority patient group. Compared to other common chronic diseases such as diabetes, it is less frequent, with specific teams responsible for COPD health care at PHC (Lundell et al., 2017). This may contribute to the high over-all prevalence of discontinuation and constitutes an argument for a standardised and cohesive care for COPD patients, as discussed below.

While county of residence has no or very small influence on discontinuation rates, sociodemographic categorisations based on age, income and gender is more relevant for assessing risk of discontinuation but still explain only a small proportion of the variance in propensity to discontinue COPD medication. Thus, universal interventions that are proportionately more intense among the sociodemographic strata with highest prevalence should be implemented. The introduction of a standardised care process for COPD patients that was initiated in 2019 is supported by the findings in study III. The aim of this standardised process is to identify COPD patients earlier, improve equity in health care and improve adherence. The process should be initiated when a patient has symptoms of COPD or if a patient has been exposed to risk factors for COPD. Through rapid investigation and establishment of a written treatment plan for both pharmacological and non-pharmacological therapies as well as a contract describing the divided responsibility between the patient and the health care provider, all patients should be ensured care according to national and international guidelines (Nationellt system för kunskapsstyrning, 2020). While there is a plan to follow-up several health care quality indicators, including both outcome and process indicators, no cut-off for the proportion of patients that should be on maintenance medication is proposed. It has been stressed that one of the main reasons for the standardised and cohesive care is to “ensure accessible and equitable care for all patients, regardless of where in the country they reside” (Nationellt system för kunskapsstyrning, 2020). However, socioeconomic equity is not explicitly mentioned and there is no plan for how an evaluation of how socioeconomic equity in COPD care should be performed, since SEP is not registered in the SNAR, which will serve as the principal tool for evaluation. Our data implies that more focus should be dedicated to equity between sociodemographic groups rather than between counties, since the VPC for the sociodemographic groups was much higher than for counties when it comes to discontinuation to maintenance medication.

The cross-classified MAIHDA is a suitable tool when it comes to evaluating equity in health care, and makes it easy to compare the relevance of different contexts. Future studies should explore equity in non-pharmacological treatment and prognosis and compare patients with similar COPD stage.

Swedish National Airway Register

In 2009, the first version of the SNAR was launched. The target population of SNAR corresponds to all patients with either a diagnosis of COPD, asthma or of asthma-COPD overlap syndrome. In 2019, 80,372 unique patients with COPD were included in the register (Stridsman et al., 2020). Based on prevalence studies, it is estimated that 85% of individuals with moderate to severe COPD are present in the register (Hesselmar et al., 2019). Until 2013, all data in the register was reported manually by health care professionals and administrators. A key factor for the rapid increase in the number of patients in the register is the implementation of automatic transfer of data from medical journals to the register. In recent years, several papers using data from SNAR (Henoch et al., 2019, Henoch et al., 2016b, Henoch et al., 2016a, Sundh and Ekstrom, 2017, Henoch et al., 2018), have provided insight into the quality and equity of Swedish health care for airway diseases.

The register has several purposes, including monitoring health care quality, facilitating evidence-based and equitable health care and to provide data for research. One way of contributing to an improved care is by facilitating the reporting units' quality development and offering a possibility to identify groups of patients with needs for special interventions (Stridsman et al., 2020). From now on, SNAR will also be used for follow-up of the standardised cohesive care for COPD patients.

Initially, the plan for this thesis was to incorporate a study focusing on socioeconomic disparities in treatment and prognosis among COPD patients utilising data from SNAR. A database to perform such studies was constructed, including data from SNAR, socioeconomic and demographic data from Statistics Sweden and information on prescriptions and medical conditions from the National Board of Health and Welfare. Since the quality of some of the variables from SNAR that should be included in that study was not guaranteed, I participated in a pilot study evaluating the validity of some key variables in SNAR through comparison of register data with data from the medical records, this project is still ongoing (Axelsson Fisk et al., 2021a).

Together with other researchers, I argue that socioeconomic variables should be included in SNAR and other patient quality registers in order to enable continuous surveillance of equity in health care (Axelsson Fisk et al., 2021b). Today, there is no way for a clinic or region to detect how well they manage to deliver equitable

COPD care. If socioeconomic variables, for example educational achievement, civil status and country of birth, were included in the registers, health care staff could easily realise if they fail to deliver care according to guidelines for specific socioeconomic strata. In that way, efficacy of health care can also be improved. The question of registering socioeconomic variables in patient quality registers was discussed at a meeting arranged by the Network for Law and National Quality Registers which I attended. It was concluded that no legal obstacles exist as long as the registered variables have a relevance for the quality of care (Nymark, 2020).

For asthma patients in Sweden gender disparities in treatment have been detected through SNAR (Stridsman et al., 2020). The further benefits of incorporating socioeconomic variables in a patient quality register are exemplified by studies based on data from the National Quality Register for better management of patients with osteoarthritis. This register includes information on educational achievement, country of birth and status in the labour market. Utilising this register, Unevik et al. (2020) showed that several outcomes among rheumatoid patients are better for native people with higher educational status.

SNAR is a powerful tool that has the potential to offer new insights into the socioeconomic inequities in COPD health care. Studies on socioeconomic disparities in prognosis could motivate or rule out the efficacy of different follow-up for different socioeconomic strata. The cross-classified MAIHDA focused on discontinuation could be repeated with stratification for disease stage. Further, non-pharmacological treatments and diagnostic interventions could be investigated.

Towards pulmonary health equity

Limited research exists on which interventions are efficient when it comes to reducing socioeconomic disparities in COPD morbidity. In an article titled "Defining and targeting health disparities in COPD", Pleasants et al. (2016) discuss strategies to reduce COPD health disparities. They list three broad principles that should be adopted: 1) include all stakeholders in development and implementation; 2) adapt interventions to unique barriers and facilitators of different groups; and 3) target all levels in the socioecological framework, from individual, interpersonal to organizational, community and public policy. Subsequently, the authors turn their focus to individual-level interventions and interventions in the local setting. The suggestions they offer are screening of high-risk populations; educational efforts in high-risk populations regarding hazardous effects of biomass smoke and tobacco; providing alternatives to indoor biomass cooking; identifying cost-effective health strategies in vulnerable populations; and identifying strategies to reduce costs of medication. Other researchers have called for governing bodies to create a standardised method to include SEP in the prognostic calculations of people with respiratory diseases and to account for SEP in the clinical management of patients with respiratory diseases (Sahni et al., 2017).

The principal strategies to promote equitable airway health emanating from this PhD project can be summarised into three categories.

Future research

In my view, the two principal research challenges that should be prioritised to advance towards equitable COPD health care are the designation of efficient preventive interventions informed by AIHDA/MAIHDA, and studies on socioeconomic disparities in clinical management and prognosis of COPD patients accounting for disease stage of the patient. In addition to this, future research on social epidemiology of COPD should report DA of different socioeconomic categorisations to better inform any health policy decisions and intersectional models should be considered, due to the heterogeneity within unidimensional socioeconomic categories regarding risk of both COPD and smoking.

Targeting social determinants of health at all levels

Whereas continuous education about risk factors for COPD and general health information is necessary, the current trend with disproportionate focus on individual interventions (level 4 in Dahlgren and Whiteheads' scheme) is insufficient if intersectional disparities in COPD should be eliminated. First, policy changes targeting economic and environmental conditions in order to increase economic equality and healthy living environments for all are needed (level 1). Second, education systems, housing conditions and working conditions should develop in a direction favouring equal health. Specifically, such interventions should involve people with low SEP, people living alone and people born outside Sweden. Availability of health care must be prioritised for disadvantaged population strata instead of the current trend of rapid access to health care for people with private health care insurance (level 2). Third, political institutions in conjunction with members of communities should engage in raising awareness of risk factors for COPD and early signs of the disease in order to reduce both the prevalence and the problem of underdiagnosis (level 3).

Standardised care as an intervention aligning with proportionate universalism

The standardised and cohesive care for COPD patients that is already taking place is a universal intervention that also has the potential to reduce and even eliminate socioeconomic disparities in COPD health care (Tottenborg et al., 2017). As indicated in study III, inequities between sociodemographic groups should be given more attention than county disparities. In order to achieve and document this, the inclusion of socioeconomic disparities as one quality indicator of care should be adopted both for health care units and as a way of evaluating quality of COPD health care nationally. The low VPC found for both counties and sociodemographic strata suggests that other areas than pharmacological maintenance medication should be prioritised to reduce socioeconomic inequities.

Sammanfattning på svenska

Kroniskt Obstruktiv Lungsjukdom (KOL) är en folksjukdom som upp till en halv miljon människor i Sverige beräknas lida av. Sjukdomar som drabbar lungor och luftvägar följer det generella mönstret att personer med låg socioekonomisk position har en högre risk att insjukna än människor med högre socioekonomisk position, men dessa skillnader är särskilt uttalade för KOL. Medan många studier har genomförts som har visat på dessa sociala skillnader i KOL-sjuklighet har förhållandevis lite forskning ägnats åt att utvärdera relevansen av olika förklaringsmodeller för uppkomsten av den ojämlika KOL-sjukligheten. Ett av syftena med denna avhandling är att inkludera sociala teorier i studiet av hur KOL-sjukligheten fördelas i befolkningen.

Ett annat fokus för denna avhandling är att tillämpa statistiska metoder som inte enbart fokuserar på genomsnittliga skillnader mellan socioekonomiska grupper. Detta är viktigt eftersom de genomsnittliga skillnader mellan grupper som oftast rapporteras när ojämlikhet i hälsa studeras inte säger någonting om hur storleken på skillnaderna *mellan* grupperna förhåller sig till storleken på skillnaderna *inom* grupperna. Anta att en grupp med låg social position har tre gånger så hög risk för KOL som en grupp med hög social position. I ett scenario kan alla personer med låg social position ha en hög risk för KOL och alla personer med hög social position ha en låg risk för KOL, då är skillnaden mellan grupperna större än skillnaderna inom grupperna och social position har hög prediktiv träffsäkerhet (engelska: *discriminatory accuracy, DA*). I ett annat scenario kan risken för KOL istället vara mycket varierande inom grupperna med låg och hög social position, och överlappningen i risk mellan grupperna därmed bli stor. Då är DA låg. I denna avhandling används svenska registerdata och data från folkhälsoenkäten för att genom beräkning av DA utvärdera olika sociala kontexters betydelse för insjuknande i KOL, risk för avbruten underhållsbehandling samt förekomsten av rökning i samhället.

I studie I användes en ny metod för att jämföra betydelsen för KOL-risk av psykosociala respektive materiella aspekter av att ha en låg inkomst. Absolut inkomst antas påverka risken för KOL genom att den avgör tillgången till materiella resurser som har betydelse för hälsan, exempelvis bostad, utbildning, hälsosamma fritidsaktiviteter och sjukvård. Relativ inkomst, det vill säga hur mycket man tjänar jämfört med personer som lever under likartade materiella förutsättningar, antas verka genom psykosocial jämförelse med personer i omgivningen. Vi fann att KOL-risken var drygt tre gånger högre för personer med låg absolut inkomst jämfört med höginkomsttagare men att relativ inkomst saknade betydelse. DA var låg för relativ inkomst och medelhög för absolut inkomst, vilket tyder på att andra saker än inkomst också behöver beaktas för att förstå KOL-sjuklighetens spridning.

Studie II är en intersektionell analys av risken för insjuknande i KOL som tillämpar en innovativ flernivåmetod. Utifrån ett intersektionellt perspektiv hänger olika sociala kategorier samman på ett komplext sätt, vilket gör att man inte kan isolera effekterna av till exempel kön, klass, ursprungsland eller civilstånd från varandra eftersom de interagerar. Denna intersektionella interaktion är komplicerad att ta hänsyn till statistiskt när flera sociala dimensioner samtidigt beaktas men den metod som här används visar lovande resultat. Vi fann att 20% av KOL-sjukligheten förklarades av en intersektionell modell bestående av grupperingar baserade på ålder, kön, inkomst, utbildning, civilstånd och härkomst. Skillnaden i risk kunde tillskrivas den adderade effekten på KOL-risk av de enskilda kategorierna som definierade den intersektionella modellen. Intersektionell interaktion mellan de olika sociala dimensionerna bidrog i liten utsträckning till skillnader i risk.

I studie III studeras jämlikhet i sjukvård genom att undersöka förekomsten av avbruten underhållsbehandling bland KOL-patienter. Genom en flernivåmetod undersöktes betydelsen av geografisk kontext (vilket landsting en patient är skriven i) och en sociodemografisk gruppering baserad på ålder, kön och inkomst för att beräkna risken för en patient att inte använda underhållsmedicinering under ett helt år. Studien presenterar också en modell för hur folkhälsointerventioner kan designas utifrån resultat från denna flernivåanalys. Vi fann att var femte KOL-patient avbröt sin underhållsbehandling, vilket är klart högre än önskvärt. Vilket landsting en patient bor i saknar betydelse, den sociodemografiska grupperingen är mycket mer relevant men har ändå en liten betydelse för risken att avbryta behandling. Sammantaget finns en problematiskt hög förekomst av avbruten underhållsbehandling men såväl geografiska som sociodemografiska ojämlikheter är små.

Studie IV är en intersektionell analys av förekomsten av rökning bland personer som är 35 till 80 år gamla och bor i Sverige. En lättillgänglig statistisk metod användes som delar flera fördelar med flernivåmetoden i studie II. Lägst risk för rökning fann vi bland äldre kvinnor med hög utbildning som bodde med någon annan vuxen och var födda i Sverige. Vi fann högst risk för rökning bland unga män med låg utbildning som var ensamstående och var födda utanför Sverige, risken i denna grupp var nio gånger högre än i gruppen med lägst risk. Den intersektionella modellen hade en medelhög DA.

Även om metoden i studie I inte styrker någon definitiv slutsats antyder resultaten att materiella aspekter är viktigare än psykosociala för risken att insjukna i KOL. Kunskap om enbart inkomst är otillräckligt för att förutsäga risken för KOL hos en individ. De sociala skillnaderna i KOL-sjuklighet och rökning framträder tydligare med ett intersektionellt perspektiv. Sociodemografisk information och landstingstillhörighet förklarar endast en liten respektive mycket liten del av en enskild KOL-patients risk att avbryta underhållsbehandling. Den sociodemografiska grupptillhörigheten är klart mer relevant än information om vilket landsting en patient bor i.

Denna avhandling inkluderar sociala teorier i studiet av hur förekomsten av KOL är fördelad i samhället. Avhandlingen bidrar till utveckling av nya metoder för utvärdering av (o)jämlikhet i KOL-sjuklighet, avbruten underhållsbehandling och rökning. När genomsnittliga socioekonomiska skillnader existerar men DA är låg är insatser riktade till hela befolkningen som syftar till att förbättra hälsans sociala bestämningsfaktorer motiverade. Ju högre DA är, desto mer motiverat är det att kombinera de universella insatserna med interventioner som är mer intensiva bland grupper med förhöjd risk för rökning, KOL eller avbruten behandling. Vidare forskning krävs för att ta fram effektiva åtgärder för att minska intersektionella skillnader i KOL-sjuklighet.

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Paper I

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Absolute rather than relative income is a better socioeconomic predictor of chronic obstructive pulmonary disease in Swedish adults

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Abstract

Background: While psychosocial theory claims that socioeconomic status (SES), acting through social comparisons, has an important influence on susceptibility to disease, materialistic theory says that socioeconomic position (SEP) and related access to material resources matter more. However, the relative role of SEP versus SES in chronic obstructive pulmonary disease (COPD) risk has still not been examined.

Method: We investigated the association between SES/SEP and COPD risk among 667 094 older adults, aged 55 to 60, residing in Sweden between 2006 and 2011. Absolute income in five groups by population quintiles depicted SEP and relative income expressed as quintile groups *within* each absolute income group represented SES. We performed sex-stratified logistic regression models to estimate odds ratios and the area under the receiver operator curve (AUC) to compare the discriminatory accuracy of SES and SEP in relation to COPD.

Results: Even though both absolute (SEP) and relative income (SES) were associated with COPD risk, only absolute income (SEP) presented a clear gradient, so the poorest had a three-fold higher COPD risk than the richest individuals. While the AUC for a model including only age was 0.54 and 0.55 when including relative income (SES), it increased to 0.65 when accounting for absolute income (SEP). SEP rather than SES demonstrated a consistent association with COPD.

Conclusions: Our study supports the materialistic theory. Access to material resources seems more relevant to COPD risk than the consequences of low relative income.

Keywords: Health inequality - absolute income - relative income, Chronic obstructive pulmonary disease, Materialistic theory, Psychosocial theory, Health equity

Background

By 2020, chronic obstructive pulmonary disease (COPD) is predicted to become the fifth largest disease burden and the third cause of death globally [1, 2]. The Swedish National board of Health and Welfare estimates that about 500 000 people in Sweden suffer from COPD, but only approximately 100 000 of them have established diagnoses [3].

Smoking is the major risk factor for developing COPD [4] and is more frequent among people with socioeconomic disadvantage, which is consistent with the higher prevalence of COPD in that group [5–7]. Socioeconomic differences in COPD risk remains when controlling for smoking [6], so other independent mechanisms could explain those differences [8–12]. An open discussion in social epidemiology concerns the relative importance of material versus psychosocial factors in the genesis of socioeconomic differences in health [13–15].

Socioeconomic position (SEP) is often operationalized by using information on absolute income. Materialistic theory assumes that an individual's health depends on their own (and only their own) level of income, rather than that of those around them. It is a person's SEP and

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the related access to material resources and power that matters most [9, 16]. Although this approach to social class has been criticized by Marxist health researchers for transforming a societal process into an individual characteristic, it can be considered a pragmatic class definition [17]. For instance, deprivation in low household SEP might impair intra-uterine and childhood environments [18], increasing the risk of growth restriction and of repeated viral infections. In turn, decreased pulmonary reserve capacity might then predispose an individual to COPD later in life [19]. Sociological mechanisms in adulthood may promote smoking habits [20], low physical activity, and inappropriate nutrition [21] in people with low SEP. These factors alone or in combination with harmful occupational exposures [22], air pollution [23, 24], and reduced access to appropriate health care and medication may also increase risk of developing COPD in people with low SEP [2].

In contrast, the psychosocial theory focuses on characteristics such as low social cohesion, income inequalities and the experience of relative poverty in the understanding of mechanisms behind the social health gradient. In this study we investigate whether low income compared to people in the same strata of society is related to incidence of COPD. One key question is the individual's socioeconomic status (SES), which can be operationalized by using information on relative income, in relation to the reference socioeconomic group. In this view, those with relatively lower income within a high SEP group will show a higher COPD risk even if access to material resources is high for the entire reference group. The harmful effect is hypothesized to act by mechanisms precipitated by psychosocial harm (e.g., shame, loss of self-respect) from social comparisons [16, 25] directly related to the individual's SES [16]. The psychosocial model emphasizes that relative income inequalities are relevant not only to the poor, but also to the middle and even upper strata [25–27]. Low SES is assumed to cause stress that activates neuroendocrine systems, especially the sympathetic response and the hypothalamus-pituitary-adrenal-axis (HPA-axis). Chronic psychological stress increases cortisol levels via the HPA-axis [28], which has harmful effects when the stress response is prolonged [29, 30]. Low relative income could cause COPD through lowered immunity due to increased cortisol levels and predisposition to infections. Chronic stress is also detrimental through promoting inappropriate coping behaviours, such as excessive alcohol consumption, smoking, and unhealthy eating [31]. So far, the role of psychosocial stress in COPD seems not to have been as thoroughly studied as it has in cardiovascular diseases.

It is difficult, not to say impossible, to isolate the relative and the absolute income hypotheses, especially when it comes to identifying the appropriate reference groups for social comparison [9]. There is also an underlying political tension. One criticism of psychosocial explanation models is their propensity to "blame the victim". If psychosocial stress is due to low status and lack of supportive relationships in deprived neighbourhoods, could we not simply teach the poor to be less stressed? [16]. Some authors [13], but not others [26], claim that exaggerated focus on material conditions might misdirect policies.

Only a few investigations [32–34] have examined the socioeconomic differences in COPD in Sweden and, as far we know, no one in the global literature has assessed the relative relevance of SEP versus SES to incidence of COPD. Therefore, we aimed to analyse those questions using a nationwide cohort of adults aged 55 to 60 and residing in Sweden in 2011.

Methods

Study population

The National Board of Health and Welfare, in coordination with Statistics Sweden, linked the register of the Total Swedish Population to other national databases such as the National Inpatient Register, the National Mortality Register, and the Income and Asset Register. This record linkage was performed by the Swedish authorities using a unique personal identification number given to each person residing in Sweden. In the data we analysed, the identification numbers were replaced with arbitrary numbers to safeguard the anonymity of the subjects.

The process of selection of individuals included in the study database is visualized in Fig. 1. From the initial 688 650 individuals aged 55 to 60 years and residing in Sweden by the baseline date of December 31st, 2010, we excluded 77 who died before 2011 and were erroneously registered in the population file. Since age is associated to both income level and COPD risk, we restricted our study by selecting a narrow age span (i.e., 55-60) in order to reduce the confounding influence of age. To ensure information on incident COPD during 2011 we excluded 4 369 individuals who emigrated during 2011. 10 482 individuals residing in Sweden less than four years were also excluded to make sure that information on prevalence of COPD was available. Finally, we excluded individuals with a COPD diagnosis within the four years before baseline, which rendered a final study sample of 667 094 individuals.

Assessment of variables

The variable COPD was defined as a hospital discharge or visit to a hospital clinic diagnosis with one of the following International Statistical Classification of Diseases and related Health Problems 10th revision [35] (ICD-10) codes: J40 (bronchitis, not specified as acute or chronic), J41 (simple and mucopurulent chronic bronchitis), J42

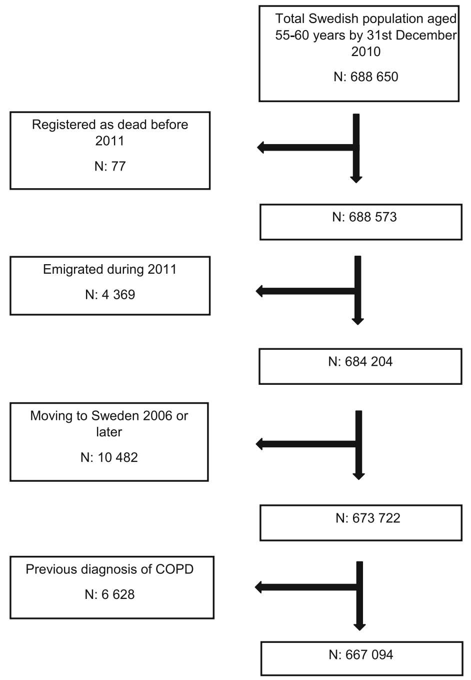

Fig. 1 Study sample

(unspecified chronic bronchitis), J43 (emphysema), or J44 (other chronic obstructive pulmonary disease). We identified new cases of COPD from January 1st, 2011 to December 31st, 2011.

We calculated household individualized disposable income by dividing the total disposable income of a family by the number of family members, taking into account the different consumption weight of adults and children according to Statistics Sweden. We operationalized SEP by categorizing the income into quintiles of the whole Swedish population between 35 and 80 years old. That is, we created five groups of *absolute income* as the groups were created using the whole population. The five groups were named *high income*, *medium high income*, *medium income*, *medium low income*, and *low income*. To operationalize SES we calculated a relative income variable by making new quintiles within each quintile of absolute income. E.g. all people that belonged to the poorest quintile within their absolute income quintiles were pooled together to compose the *low relative income group.* We used the same category labels as those used for absolute income and the *high income* category as reference in the analyses.

We defined *age* as age in 2010 and *sex* as binary: legally male or female.

Statistical and epidemiologic methods

We performed sex-stratified logistic regression models to examine the association between COPD risk and age, SEP (absolute income) and SES (relative income). Model A included only the continuous age variable; model B included age and absolute income; model C included age and relative income; and model D included age and both absolute and relative income. We expressed associations by means of ORs and 95% confidence intervals (CI). Since COPD incidence was low, ORs correspond well to relative risks.

We paid special attention to calculating the discriminatory accuracy of the models, as commented in more detail elsewhere [36, 37]. For this purpose, we calculated the area under the receiver-operating characteristic curve (AUC). The AUC measured the ability of the model to correctly classify those with and without COPD assuming a value between 1 and 0.5, where 1 is perfect discrimination and 0.5 is as informative as flipping an unbiased coin. Even though our cohort only included people between 55 and 60 years of age, the incidence of COPD increases with age. Therefore, we calculated the AUC of model A to estimate how much absolute and relative income added in discriminatory accuracy (DA) compared to models using age only.

We used SPSS version 21 (SPSS Inc., Chicago, IL, USA) to perform the statistical analyses.

Results

Overall, 3.1 per 1000 individuals (1754/667 094) in the study sample suffered a COPD event during 2011. Table 1 shows a clear gradient in the incidence of COPD for absolute income groups, with an absolute risk difference between the *low* and *high income* groups of 3.1 per thousand in both men and women. For relative income groups this risk difference is rather inconsistent in both genders. As expected, the average age was about 57 years in all income groups.

Table 2, models 2, 3, and 4 show that both absolute and relative income are associated with COPD risk. In both men and women there is a clear gradient for absolute income groups with increasing COPD risk as the absolute income decreases. However, there is no such gradient for relative income that also shows much smaller ORs.

As expected, because of the short age range (55 to 60 years), the AUC for age in model 1 was close to 0.5 in both men and women. Inclusion of absolute income in model 2 increased the AUC to 0.65 in men and to 0.63 in women. Relative income in model 3, on the other hand, did not add much to model 1 (age only), as the AUC was 0.55 in both men and women.

Table 1 Age and incidence of chronic obstructive pulmonary disease by absolute and relative income groups in the 333 952 men and 333 142 women aged 55 to 60 years and residing in Sweden in 2011

	MEN				WOMEN			
	Age (mean)	Number of cases	Number of people	Incidence (per 1000 individuals)	Age (mean)	Number of cases	Number of people	Incidence (per 1000 individuals)
Absolute income[a]								
Low	57.4	167	38125	4.4	57.4	140	30567	4.6
Medium low	57.4	175	39481	4.4	57.5	208	38624	5.4
Medium	57.4	138	50760	2.7	57.5	182	52913	3.4
Medium high	57.5	161	85677	1.9	57.5	256	95865	2.7
High	57.6	158	119909	1.3	57.6	169	115173	1.5
Relative income[b]								
Low	57.5	150	59477	2.5	57.5	161	58513	2.8
Medium low	57.5	157	62965	2.5	57.5	203	63045	3.2
Medium	57.5	173	67131	2.6	57.5	186	67881	2.7
Medium high	57.5	179	70374	2.5	57.5	221	71018	3.1
High	57.5	140	74005	1.9	57.5	184	72685	2.5

[a]The absolute income is categorized by quintiles of all 4 994 921 people aged 35 to 80 years registered as residents in Sweden by December 31st, 2010. [b]The relative income categories are defined by quintile groups within absolute income categories

Discussion

In this large, population-based study both SEP (measured as absolute income) and SES (assessed as relative income) were associated with COPD risk. However, while the association between relative income groups and COPD was rather inconsistent, we found a clear socioeconomic gradient for absolute income groups, which confirms previous findings [5, 6, 38]. COPD risk increased with decreasing absolute income, so ORs for COPD were around three times higher for the poorest than for the richest individuals. Even if the AUC value was rather low for both absolute and relative income, the AUC for absolute income was clearly higher than for relative income. Therefore, our study suggests that the materialistic absolute income model is more relevant than the psychosocial relative income model for understanding socioeconomic disparities in COPD risk. It seems that limited material resources per se (i.e., low SEP) are more relevant to COPD risk than the psychosocial consequences of having relatively less resources than the others with a similar income (i.e., low SES). Similar conclusions have previously been drawn for other health outcomes [14, 39].

By including a measure of DA like the AUC, our study adds a new tool for evaluating the relevance of (socioeconomic) categorizations in public health as recently discussed [37].

Material or psychosocial mechanisms

Relative income is a complex concept. A fundamental aspect is the difficulty of identifying appropriate reference groups for social comparison. It could be questioned whether individuals compare themselves with people below or above them, or if they compare themselves with others like them or to celebrities and moguls portrayed in the mass media. Kawachi et al. (2002) concluded that most likely people compare themselves simultaneously in several directions.

Our aim was to contribute to the question of whether material or psychosocial mechanisms best explain income-related inequalities in COPD risk. It could be argued that OR and DA for absolute income reflect the effects of psychosocial stress and not of material deprivation. The impaired health observed in the poorest groups could be because poor people compare themselves with the rich people, which leads to chronic stress, higher cortisol levels, and increased general susceptibility to diseases, including COPD. Wilkinson and Picket (2006), for example, argue that it is relative socioeconomic differences between broader groups, such as nations, rather than between neighbourhoods that cause psychosocial stress. Since the psychosocial stress is presumably present across all societal strata, we would have expected a difference in incidence between people with similar absolute incomes but different relative incomes if the incidence of COPD would have depended on the psychosocial comparison. As an alternative to our main analysis including absolute and relative income in the same model, we performed analyses of the association of SES and COPD in separate models within the five strata of absolute income quintiles. However, relative income did not show a consistent gradient within any of the absolute income quintiles.

Strengths and weaknesses of the study

Our results are derived from a large hospital database comprising the whole Swedish population but we did

Table 2 Association between absolute and relative income and risk of chronic obstructive pulmonary disease in the 333 952 men and 333 142 women aged 55 to 60 years and residing in Sweden in 2011. Values are OR, 95% CI, and AUC

	Model 1 (Age)	Model 2 (Age and absolute income)	Model 3 (Age and relative income)	Model 4 (Age and absolute and relative income)
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
MEN				
Age (1 year)	1.09 (1.05–1.14)	1.05 (1.06–1.15)	1.09 (1.05–1.14)	1.11 (1.06–1.15)
Absolute income[a]				
High		REF		REF
Medium high		1.43 (1.15–1.78)		1.44 (1.16–1.80)
Medium		2.10 (1.67–2.64)		2.11 (1.68–2.65)
Medium low		3.44 (2.77–4.27)		3.44 (2.77–4.27)
Low		3.40 (2.73–4.23)		3.39 (2.73–4.22)
Relative income[b]				
High			REF	REF
Medium high			1.35 (1.08–1.68)	1.34 (1.08–1.68)
Medium			1.37 (1.09–1.71)	1.36 (1.08–1.69)
Medium low			1.32 (1.05–1.66)	1.31 (1.04–1.64)
Low			1.34 (1.06–1.69)	1.31 (1.04–1.64)
AUC (95% CI)	0.54 (0.52–0.56)	0.65 (0.63–0.66)	0.55 (0.53–0.57)	0.65 (0.63–0.67)
WOMEN				
Age (1 year)	1.05 (1.01–1.09)	1.06 (1.02–1.10)	1.05 (1.01–1.09)	1.06 (1.02–1.10)
Absolute income				
High		REF		REF
Medium high		1.83 (1.51–2.22)		1.84 (1.52–2.24)
Medium		2.36 (1.92–2.91)		2.39 (1.94–2.95)
Medium low		3.71 (3.03–4.55)		3.73 (3.05–4.58)
Low		3.17 (2.54–3.97)		3.20 (2.56–4.01)
Relative income				
High			REF	REF
Medium high			1.23 (1.01–1.50)	1.25 (1.03–1.52)
Medium			1.08 (0.88–1.33)	1.11 (0.91–1.36)
Medium low			1.27 (1.04–1.56)	1.34 (1.10–1.64)
Low			1.09 (0.88–1.35)	1.15 (0.93–1.42)
AUC (95% CI)	0.53 (0.51–0.54)	0.63 (0.62–0.65)	0.54 (0.52–0.55)	0.64 (0.62–0.65)

[a]The absolute income is categorized by quintiles of all 4,994,921 people aged 35 to 80 years registered as residents in Sweden by December 31st, 2010. [b]The relative income categories are defined by quintile groups within absolute income categories

not have information on COPD diagnoses from primary health care. Hence, we only identified cases treated at the hospital (hospitalizations or visits to an external clinic at the hospital), which may underestimate the incidence of COPD in the population. We do not think this situation had a major influence on our study as our aim was to investigate the contributions of absolute and relative income rather than the exact incidences of COPD in the population. Also, we used ICD codes recorded in routine care rather than in clinical examinations focused on identifying COPD cases in a prospective cohort study. However, hospital ICD codes of COPD from the Swedish Inpatient Registry have been considered to have acceptable validity for epidemiological research in a previous study [40]. If the people that were excluded because of emigration or recent immigration belong to lower SEP-groups and also have a higher risk for COPD our results may underestimate the socioeconomic gradients. We do not believe this affects the conclusions of our study since only 0.7% of the individuals emigrated and 1.6% resided in Sweden less than four years (see section on study population).

The quality of income data is high, including income from wages, subsidies, retirement, insurance, profits on capital, and other sources, according to Statistics Sweden. Lynch and Kaplan [41] suggest that repeated measures of income and assessment of wealth should be included to better reflect life course effects of SEP and total material resources available for an individual. The fact that we only measured income on one occasion can be considered a weakness. For instance, suffering from COPD may lead to a reduced income rather than the opposite. We excluded individuals with previous COPD, which reduces the problem of reverse causality.

When planning the analyses, we considered the existence of common causes of both income and COPD that could confound the association between those variables. Education and occupation are alternative indicators of SEP. If we were to adjust for them, we would underestimate the association between low SEP and COPD. Since prevalence of COPD increases with age [4] and income normally increases with age until retirement, age was the only variable that we adjusted for in addition to choosing a study population with individuals of similar age (i.e., 55 to 60 tears). Different smoking patterns among men and women motivated the sex-stratified analyses [42].

Smoking is the most important risk factor for COPD [4, 23, 43]. It is known to be more prevalent among people with low SEP [44, 45]. Since it is low income that causes smoking rather than smoking that causes low income, adjusting for smoking would underestimate the association between income and COPD.

Psychosocial versus materialistic interventions

The dichotomous description of psychosocial versus materialistic theories used hitherto is pedagogic but not entirely true. Psychosocial researchers agree that material deprivation exists even in high-income countries and materialistic epidemiologists admit the presence of a psychosocial pathway. Although followers of the materialist theory and those of the psychosocial one disagree on to what extent specific mechanisms explain socioeconomic health gradients, they harmonize about the political direction needed. Effective smoking prevention programmes among low income people would probably reduce the slope of the socioeconomic gradient observed in this study. Solving health problems by teaching the poor to live healthily conveys a risk of blaming the victim if the health problems are the result of the political and cultural system [25]. Therefore, interventions should be directed at upstream societal causes of those health problems. An equalitarian distribution of resources in the society will lead to better health whether the underlying mechanisms are materialistic, psychosocial, or both. To ameliorate the effects of materialistic inequalities in COPD incidence, investments in public primary health care with greater availability of spirometry could be effective. Subsidized medications, improved housing for children to prevent respiratory infections in early life, and strict regulation of working conditions and air pollution are other materialistic interventions to reduce the social gradient for incidence of COPD. The trend of privatization in primary health care in Sweden has benefited high income groups more than low income groups [46, 47] and therefore may exacerbate the social gradient for COPD incidence.

The psychosocial model of how relative poverty causes bad health is a significant advance over purely behavioural explanations that blame poor people for their unhealthy life styles. Thanks to this, struggles for equality in health have earned broad scientific support. Although suggestions to ameliorate income and class division are presented by psychosocial researchers [25], little attention is directed at the capitalist structure of production as an upstream causes of economic and health gaps in society.

Future research and conclusion

Our study is innovative as we calculated and interpreted not only measures of association such as the OR but also measures of DA such as the AUC as recently proposed in public health research [37]. By doing so we pioneer a new *imaginative* approach in social epidemiology [48] that goes beyond probabilities to explain heterogeneity around averages [36, 37, 49]. Our study indicates that neither SEP nor SES sufficiently increases the AUC of a model including only age for discriminating patients with, from those without COPD. Therefore, interventions exclusively directed at people with low income might convey the risk of stigmatizing people who already bear a high load of psychosocial stress and impaired material resources. Based on our results, prevention of COPD should not exclusively be understood as a fundamental socioeconomic issue. However, we have used rather simple categorizations of income that may not properly capture the social and economic heterogeneity in the distribution of COPD risk. For instance, the materialistic approach hypothesizes health depends on what resources a person possesses.

This study is based on the assumption that income captures purchasing power. Nevertheless, the same amount of money might be less efficient in "buying health" if, for example, you are a female immigrant and have a low SEP compared to a rich man born in Sweden. We also discussed this in previous studies from the analogous perspective of multilevel analysis of individual heterogeneity [36]. The key idea is to understand social heterogeneity by identifying categories that better discriminate between who suffers from COPD and who not. Future research should include intersectional analyses as a model for identifying socially defined groups that are more vulnerable to poor health outcomes

[50]. Given the higher precision when including more variables, it is possible to identify smaller groups suffering from the consequences of structural inequalities and at high risk for COPD and where interventions are more easily affordable than for the whole population. Combining intersectionality theory with measures of discriminatory accuracy may be a useful tool in modern social epidemiology as recently indicated [36, 37].

Conclusions

In conclusion, it seems that limited material resources per se are more relevant than the psychosocial consequences of having a relatively lower status than others with a similar income. Our results, therefore, suggest that the materialistic explanatory model is more relevant than the psychosocial relative income model for understanding socioeconomic disparities in COPD risk. However, the rather low DA of both SEP and SES suggest that public health interventions should target the structural factors in the whole society, rather than target specific income groups.

Abbreviations

AUC: Area under receiver-operating characteristic curve; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; DA: Discriminatory accuracy; OR: Odds ratio; SEP: Socioeconomic position; SES: Socioeconomic status

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Availability of data and material

The database we analyzed is not publicly available for ethical and data safety reasons according to the Swedish National Board of Health and Welfare. However, the same dataset can be constructed by request to the Swedish National Board of Health and Welfare after approval of the research project by an Ethical Committee and by the data safety committee at the Swedish National Board of Health and Welfare.

Authors' contribution

Both authors made substantial contributions to conception and design of the study. JM acquired the data. SAF performed the analysis and both authors revised and interpreted the data. SAF wrote the first draft of the manuscript and JM revised it. Both authors have approved the final version and take public responsibility for the content.

Competing interests

Both authors declare they have no competing interests.

Consent for publication

Not applicable.

Ethics approval

The Regional Ethics Review Board in southern Sweden (# 2012/637) as well as the data safety committees from the National Board of Health and Welfare and from Statistics Sweden approved the construction of the database used in this study.

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Paper II

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Article

Chronic Obstructive Pulmonary Disease in Sweden: An intersectional multilevel analysis of individual heterogeneity and discriminatory accuracy

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ABSTRACT

Socioeconomic, ethnic and gender disparities in Chronic Obstructive Pulmonary Disease (COPD) risk are well established but no studies have applied multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA) within an intersectional framework to study this outcome. We study individuals at the first level of analysis and combinations of multiple social and demographic categorizations (i.e., intersectional strata) at the second level of analysis. Here we used MAIHDA to assess to what extent individual differences in the propensity of developing COPD are at the intersectional strata level. We also used MAIHDA to determine the degree of similarity in COPD incidence of individuals in the same intersectional stratum. This leads to an improved understanding of risk heterogeneity and of the social dynamics driving socioeconomic and demographic disparities in COPD incidence. Using data from 2,445,501 residents in Sweden aged 45–65, we constructed 96 intersectional strata combining categories of age, gender, income, education, civil- and migration status. The incidences of COPD ranged from 0.02% for young, native males with high income and high education who cohabited to 0.98% for older native females with low income and low education who lived alone. We calculated the intra-class correlation coefficient (ICC) that informs on the discriminatory accuracy of the categorizations. In a model that conflated additive and interaction effects, the ICC was good (20.0%). In contrast, in a model that measured only interaction effects, the ICC was poor (1.1%) suggesting that most of the observed differences in COPD incidence across strata are due to the main effects of the categories used to construct the intersectional matrix while only a minor share of the differences are attributable to intersectional interactions. We found conclusive interaction effects. The intersectional MAIHDA approach offers improved information to guide public health policies in COPD prevention, and such policies should adopt an intersectional perspective.

Introduction

Social epidemiological studies have long been criticized for the relative absence of explicit sociological theory (Krieger, 1994; Ng & Muntaner, 2014), and further integration of, and dialogue between, epidemiology and social theory has been advocated (Wemrell, Merlo, Mulinari & Hornborg, 2016). From this perspective, and following similar initiatives in the social sciences, several authors have argued for an integration of intersectionality theory within epidemiology and public health (Bauer, 2014; Bowleg, 2008; Evans, Williams, Onnela & Subramanian, 2017; Merlo, 2017; Merlo & Mulinari, 2015; Mulinari, Wemrell, Rönnerstrand, Subramanian & Merlo, 2017; Wemrell, Mulinari & Merlo, 2017b). The advantage of incorporating an intersectional framework in social epidemiology is that it goes beyond the unidimensional study of socioeconomic and demographic categorizations by considering the effect of belonging to specific strata simultaneously defined by multiple social, economic and demographic dimensions. Intersectionality theory stresses the possible existence of an interaction effect over and above the additive influence of the isolated dimensions (Bauer, 2014; Bowleg, 2008; Evans et al., 2017). In this study, we aim to apply an innovative methodological approach combining *multilevel analysis of individual heterogeneity and discriminatory accuracy* (MAIHDA) (Merlo, 2014, 2017) with an intersectional framework (Evans et al., 2017; Green, Evans & Subramanian, 2017;

Abbreviations: MAIHDA, Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy; CI, Credible Interval; DA, Discriminatory Accuracy; ICC, Intra Class Correlation

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Wemrell, Mulinari & Merlo, 2017a). This approach may improve our understanding of both the heterogeneous distribution of risk in the population and the social dynamics driving socioeconomic and demographic disparities in health.

Chronic Obstructive Pulmonary Disease (COPD) constitutes a growing but underestimated population health challenge (GOLD, 2017) that by 2020 is predicted to become the third leading cause of death globally (Murray & Lopez, 1997). Smoking is considered the most important risk factor for COPD (GOLD, 2017). From a causal perspective, many individual level risk factors for COPD can be understood as downstream mediators of upstream social and economic determinants of health (Kaplan, 1999). While global initiatives are underway to investigate risk factors for COPD many, including smoking (Hiscock, Bauld, Amos, Fidler & Munafò, 2012), low birthweight (Brostrom, Akre, Katz-Salamon, Jaraj & Kaijser, 2013), exposure to biofuels (Po, FitzGerald & Carlsten, 2011) and hazardous particles in working environment (Boschetto et al., 2006) are differently distributed among social strata (GOLD, 2017). Whereas policy-documents may mention equity in health as an overarching aim (Schraufnagel et al., 2013; Socialstyrelsen, 2015b) the focus of clinical guidelines (GOLD, 2017) and public health strategies (Socialstyrelsen, 2015a) tend to downplay upstream interventions and little research is done on the social processes that drive disparities in COPD morbidity. Altogether, this may contribute to the image of COPD as a self-inflicted smoking related disease and increase feelings of guilt among COPD-patients (Lindqvist & Hallberg, 2010; Strang et al., 2014).

There is strong evidence that social and economic factors influence the risk of COPD (Gershon, Dolmage, Stephenson & Jackson, 2012; Schraufnagel et al., 2013; Stringhini *et al.* 2017). Most epidemiological studies consider one social categorization at a time (gender, class, civil- or migration status etc.) while the others are adjusted for. A limitation in the literature on socioeconomic disparities in health in general and on COPD risk in particular is the disregard for heterogeneity within socioeconomic categories (Gershon et al., 2012; Kanervisto et al., 2011; Miravitlles, Naberan, Cantoni & Azpeitia, 2011). Typically, studies on socioeconomic disparities in COPD-morbidity report odds ratios (ORs) (Chen, Breithaupt & Muhajarine, 2000; Marmot, Shipley, Brunner & Hemingway, 2001; Montnemery et al., 2001) or differences in prevalence (Eachus et al., 1996; Kainu et al., 2013), or other measurements of average risk differences, between social strata based on one factor at a time (e.g., income, education and occupation). This may inadvertently strengthen the belief in the effectiveness of selective interventions based on unidimensional categorizations. Indeed, some researchers suggest selective screening of COPD among people with low socioeconomic status (Dirven et al., 2013; Pleasants, Riley & Mannino, 2016). Yet it is known that measurements of average risk differences are insufficient to inform on the ability of an exposure category to discriminate individuals with an outcome from those without it. For instance, an OR that is usually considered high, for example OR = 10, can be associated with a low discriminatory accuracy (DA), due to heterogeneity within categories and overlap between categories (Merlo, Mulinari, Wemrell, Subramanian & Hedblad, 2017; Pepe, Janes, Longton, Leisenring & Newcomb, 2004). We have previously suggested that when reporting and interpreting risk factors, measures of average associations should be accompanied by analyses of heterogeneity using measures of DA, such as the area under the ROC curve or the intra-class correlation coefficient (ICC) obtained in multilevel regression modeling (Merlo, 2003, 2014, 2017; Merlo & Mulinari, 2015; Merlo, Chaix, Yang, Lynch & Råstam, 2005; Merlo et al., 2017).

As a further development of this line of research we (Merlo, 2014, 2017; Wemrell et al., 2017a) and other scholars (Evans et al., 2017; Jones, Johnston & Manley, 2016) have recently suggested the use of multilevel analysis of variance within an intersectional matrix framework. From the perspective of social epidemiology (Merlo, 2017), the intersectional MAIHDA approach can be used to evaluate the strength of intersectional strata for disease prediction. Among several conceptual and technical advantages (Evans et al., 2017; Jones et al., 2016; Merlo, 2017) the intersectional MAIHDA approach provides a feasible way of measuring multiple interactions and analysing groups of small size. By considering the social context (i.e., intersectional strata) as a higher level in the multilevel analysis, this approach also avoids the treatment of societal factors as individual level characteristics.

In the present study we apply MAIHDA to investigate an intersectional matrix that simultaneously considers different social power dimensions and therefore may improve our understanding of the socioeconomic, gendered and ethnically patterned distribution of COPD in society. Our investigation had three specific aims. First, we aimed to provide a detailed intersectional map of COPD risk in the population in order to evaluate to what extent intersectional categorizations help predict COPD at the individual level. Second, we sought to investigate whether potential differences in average incidence for COPD between intersectional strata depend on intersectional interaction or if the average risk differences are explained by the additive effects of the dimensions used to construct the intersectional matrix. Our third aim was to contribute to methodological development by applying intersectional MAIHDA in social epidemiology in general and the study of socioeconomic disparities in COPD incidence in particular.

Population and methods

Study population

The National Board of Health and Welfare, in coordination with Statistics Sweden, linked the register of the Total Swedish Population to other national databases such as the National Inpatient Register, the National Mortality Register, and the Longitudinal Integration Database for Health Insurance and Labor Market Studies (LISA), using the unique personal identification number given to each person residing in Sweden. In the data we analysed, the identification numbers were replaced with arbitrary numbers to safeguard the anonymity of the subjects. The Regional Ethics Review Board in southern Sweden as well as the data safety committees from the National Board of Health and Welfare and from Statistics Sweden approved the construction of the database used in this study.

In Fig. 1 we have visualized the selection of individuals included in the database. We restricted the population to individuals aged 45 years and older since COPD is a rare condition below that age (GOLD, 2017). To avoid the confounding effect of retirement we did not include individuals older than 65 years, which is the official age of retirement in Sweden. From 2,536,789 individuals aged 45 to 65 years and residing in Sweden at the baseline date of December, 31st 2010, we excluded 11,722 individuals who died during 2010 or 2011. We also excluded 54,161 individuals who had spent less than 5 years in Sweden to assure that the information on previous diagnosis of COPD was reliable. We also excluded 3643 individuals that emigrated during 2011 to make sure we could obtain information on incident COPD. Finally, since our study was concerned with incidence (i.e., new cases) of COPD, we excluded 21,762 individuals who received a COPD-diagnosis between 2006 and 2010. This rendered a final study sample of 2,445,501 individuals or 96% of the Swedish population in that age span.

Assessment of variables

The outcome variable was the presence or absence of a new diagnosis of COPD between January 1st, 2011 and December 31st, 2011. We defined COPD based on hospital diagnosis (visit to a hospital clinic or hospital discharge) using one of the following International Statistical Classification of Diseases and related Health Problems 10th revision (WHO, 2016) (ICD-10) codes: J40 (bronchitis, not specified as acute or chronic), J41 (simple and mucopurulent chronic bronchitis), J42 (unspecified chronic bronchitis), J43 (emphysema), or J44 (other chronic obstructive pulmonary disease).

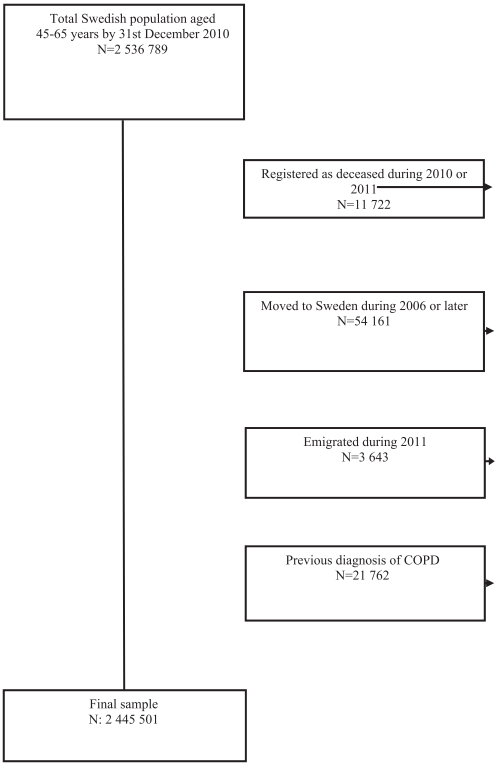

Fig. 1. Flow diagram showing the selection of the study population.

We categorized age into two categories (45–54 and 55–65). Gender was dichotomized as male or female according to legal status. We calculated household individualized disposable income by dividing the total disposable income of a family by the number of family members, taking into account the different consumption weights of adults and children, according to Statistics Sweden. Using the tertile values of the income distribution we divided the study population into three groups, termed high, medium and low income. We constructed two education categories based on whether individuals had any further education after high school or not, and these categories were also termed high and low. We computed a cohabitation variable by categorizing people that lived together as a married couple, in a registered partnership or with a common child as cohabiting and grouping all others into another category termed living alone. Finally, migration status was defined using information on country of birth from Statistics Sweden. We categorized people born outside Sweden as immigrants and individuals born in Sweden as natives.

Intersectional multilevel analysis of individual heterogeneity

We created a matrix with 96 intersectional strata based on combinations of age, gender, income, education, country of birth and cohabitation ($96 = 2 \times 2 \times 3 \times 3 \times 2 \times 2 \times 2$). The choice of these intersectional locations was restricted by the available information but it was to the largest degree possible informed by previous intersectional research (Bauer, 2014; Collins, 2002; Veenstra, 2013) and by what is known about associations between different social dimensions and mediators for COPD risk. Using this matrix, we performed an intersectional MAIHDA (Evans et al., 2017; Green et al., 2017; Merlo, 2017; Wemrell et al., 2017a) with individuals at the first level and the intersectional strata at the second level. We modelled COPD risk through three successive multilevel logistic regression models and estimated the predicted incidences and 95% credible intervals (CIs). To make the article as accessible as possible, we restrict the technical details of these models to Supplemental materials.

Model 1: Simple intersectional model

The first model is an *unadjusted,* random intercepts model (i.e., a variance components model) with individuals nested within intersectional strata. The purpose of this model was two-fold. First, we performed simple analysis of components of variance in order to calculate the ICC. This measure expresses the share of the total individual variance in the propensity for developing COPD that is at the intersectional stratum level. The higher the ICC, the greater the degree of similarity in COPD incidence within the strata and the greater the difference in incidence between the strata. Models with higher ICCs are therefore better at discriminating individuals that developed COPD from those that did not, compared to models with lower ICCs. In summary, the ICC evaluates the relevance of the intersectional strata for understanding individual risk heterogeneity. The ICC also informs on the DA of the intersectional categorization for distinguishing individuals with COPD from those without.

To calculate the ICC, we used the most popular version of the ICC derived from the latent response formulation of the model. This ICC was computed as:

$$\text{ICC} = \frac{\sigma_u^2}{\sigma_u^2 + 3.29} \tag{1}$$

where σ_u^2 denotes the between-stratum variance in the propensity to receive a new COPD diagnosis and 3.29 denotes the within-stratum-between-individual variance constrined equal to the variance of the standard logistic distribution (Goldstein, Browne & Rasbash, 2002; Merlo et al., 2005). There is currently no official grading scale for interpreting the magnitude of the ICC within social epidemiology. However, in line with the terminology suggested for evaluation of psychometric test reliability (Cicchetti, 1994) we consider that a reasonable grading for social epidemiologic purposes could be (ICC as %): non-existent (0–1), poor (> 1 to ≤ 5), fair (> 5 to ≤ 10), good (> 10 to ≤ 20), very good (> 20 to ≤ 30), excellent (> 30).

The second purpose of this model was to calculate predicted incidence and the 95% CIs for every intersectional stratum. For doing so, and in order to use an additive scale, we transformed the predicted logit (log-odds) of receiving a new COPD diagnosis in stratum j obtained in the multilevel logistic regression into the probability of receiving a new COPD diagnosis in stratum j according the formula

$$\pi_j = \text{logit}^{-1}(\beta_0 + u_j) \tag{2}$$

Model 2: Partially-adjusted intersectional model

The purpose of the *partially adjusted* model 2 was to quantify to what degree the different dimensions used to construct the intersectional strata contributed to the between stratum variance seen in the previous model. In six different versions we expanded model 1 by adjusting for one of these dimensions at a time (i.e., a different model for each dimension). Thereafter we calculated the Proportional Change in the between-stratum Variance (PCVs):

$$\text{PCV} = \frac{\sigma^2_{u(1)} - \sigma^2_{u(2)}}{\sigma^2_{u(1)}} \tag{3}$$

where $\sigma^2_{u(1)}$ and $\sigma^2_{u(2)}$ denote the between-stratum variance from models 1 and 2 respectively. PCVs are typically multiplied by 100 and reported as percentages.

Model 3: Intersectional interaction model

The ICC of model 1 represents the ceiling of the explanatory power of the intersectional strata and encompasses both additive and potential interactive effects of the variables that define the strata. Model 3 expands model 1 by simultaneously including as fixed main effects all the variables used to construct the intersectional strata. In the absence of stratum specific interactions, the inclusion of the main effects would completely explain between stratum variance and all 96 stratum random effects would equal zero. If this is not the case, the stratum residuals represent the excess risk due to interaction and the stratum variance and corresponding ICC of model 3 represents that part of the original model 1 stratum variance that is due to intersectional interaction effects, at least in relation to the set of variables included. This model also yields mutually adjusted unidimensional ORs representing the main effects of age, gender, income, education, civil status and migration status, respectively.

Model 3 was used to calculate *total predicted incidences* (main effects and interactive effects) and *predicted incidences based on the main effects* only. By subtracting the incidence attributable to main effects from the total incidence we isolated the incidence attributable to interaction in each intersectional stratum. We also calculated their 95% CIs. A positive interaction effect means that individuals in that intersectional stratum have a *higher* incidence than expected based on the simple addition of the risks conveyed by the categories that constitute the intersectional stratum, while a negative interaction means a *lower* incidence than expected. For further details, see the *statistical details*.

Software

The models were fitted using Markov chain Monte Carlo (MCMC) methods as implemented in MLwiN version 3.01 (Browne, 2017; Charlton, Rasbash, Browne, Healy & Cameron, 2017). We called MLwiN from within Stata version 14.1 using the runmlwin command (Leckie & Charlton, 2013).

Results

Overall, 0.22% (5419/2,445,501) of the study population developed COPD in 2011. As expected, we observed (Table 1, model 3) that, compared to men, women had a higher incidence of COPD. The same was true for high compared to low age, low and medium compared to high income, low compared to high education, as well as for people living alone and immigrants compared to people cohabiting and natives, respectively.

Table 2 (for full version see Table A1 Appendix) presents the number of individuals, number of new cases of COPD, and the model 1 total predicted incidences (main effects and interaction effects). The stratum with the highest predicted incidence of COPD comprised older native females with low income and low education who lived alone (0.98%, 95%CI: 0.89%–1.08%). It was followed by the strata including older immigrant females, with low income and low education who lived alone (0.87%, 95%CI: 0.72%–1.05%) and older immigrant males with low income and low education who lived alone (0.82%, 95%CI: 0.66%–1.00%).

At the other side of the spectrum, the strata with lowest predicted incidences included young native males with high income and high education who cohabited (0.02%, 95%CI: 0.01%–0.04%). It was followed by young native males with medium income and high education who cohabited (0.03% 95%CI:0.02%–0.04%) and by young native males with low income and high education who cohabited (0.03%, 95%CI: 0.02%–0.05%).

The ICC of model 1 (see Table 1) was good (i.e., 20.0%), which means that a substantial share of the total individual differences in the propensity of suffering from COPD was at the intersectional strata level. In the age-adjusted model (model 2) the ICC fell to 10.8%, which demonstrates that half of the clustering of COPD incidence observed in model 1 was attributable to the age of the individuals. In similar analyses with adjustment for one dimension at a time (not shown in tables) the ICC changed to 17.7%, 17.8%, 18.2%, 20.0 and 20.4% when we adjusted for civil status, education, income, migration status and gender respectively. Thus, age was by far the most important single factor in explaining variation in the propensity of developing COPD between strata. In the intersectional interaction model (model 3) the ICC dropped to 1.1%, which suggests that additive rather than interactive effects of age, gender, income, education, civil status and country of birth, explain most of the differences in COPD incidence across intersectional strata.

Fig. 2 demonstrates the heterogeneity between intersectional strata in predicted COPD incidence based on model 1 and thus conflating main and interaction effects of the six social dimensions. Fig. 3 demonstrates the small changes in predicted incidence in model 3 when comparing predictions based on the total effects with predictions based on main effects only. The difference between these predictions represent the interaction effects. The isolated interaction effects are visualized in Fig. 4. Most strata have interaction effects that cannot be statistically distinguished from 0. Three strata, however, have positive interactions and 95% CIs excluding 0: young native women with low income and low education who cohabited (interaction effect 0.13 95%CI 0.07–0.20), young native males with low income, low education who lived alone (interaction effect 0.08 95%CI 0.03–0.13) and young native women with medium income and low education who lived alone (interaction effect 0.06 95%CI 0.01–0.11). This finding is consistent with the poor ICC observed in model 3 and illustrates that the interaction effects are small.

Discussion

Our study advances social epidemiological research by incorporating MAIHDA (Merlo, 2014) within an intersectionality framework (Merlo, 2017). By doing so, we go beyond unidimensional measures of socioeconomic position to improve our understanding of risk heterogeneity and social dynamics driving disparities in COPD incidence in the society. While MAIHDA has mainly been applied for investigating geographical (Merlo, 2003; Merlo, Wagner, Ghith & Leckie, 2016) and institutional effects (Ghith, Wagner, Frolich & Merlo, 2016; Ohlsson, Librero, Sundquist, Sundquist & Merlo, 2011) on individual outcomes, pioneers scholars (Evans et al., 2017; Green et al., 2017) have applied this methodology for analysing an intersectional matrix of interlocking social dimensions. This innovative approach represents, we think, a major step forward in the study of socioeconomic and demographic disparities in health in general, including COPD incidence.

Socioeconomic distribution of COPD incidence and intersectional interaction

We found that intersectional strata defined by combinations of age, gender, income, education, civil status and country of birth provided good information for classifying individuals according to their COPD incidence in Sweden, with an ICC of 20.0%. The intersectional strata effect was mostly additive, and half of it due to the age differences between the strata. About 1.1% of the individual differences in COPD risk were due to the interaction effect between the variables defining the intersectional strata.

The intersectional multilevel approach allowed us to map socioeconomic differences in health in the population and, thereby, identify specific strata with an overtly increased COPD incidence (e.g., older native females with low income and low education who lived alone).

Table 1

Results from the intersectional multilevel analysis of individual heterogeneity in Chronic Obstructive Pulmonary Disease (COPD) risk, for people aged 45–65 residing in Sweden 2010, according to demographic and socioeconomic groupings used to construct intersectional strata. Model 1 (simple intersectional) is a random intercepts model with individuals nested in intersectional strata. Model 2 (age adjusted) is partially adjusted for and model 3 (intersectional interaction) is adjusted for all the main variables used to define the intersectional strata. In this table we present only measures of variance and of association (ORs and 95% CIs) between the main individual variables and COPD risk. The incidences for specific intersectional strata are hidden in this table but we present them in Fig. 2 and in Table 2 and Table A1 (Appendix). The green boxes indicate the actual category. For each category, we show the total number of individuals and the absolute incidence of COPD.

High age		Female gender		Income			Low education		Living alone		Immi-grant		Number (% COPD)	Model 1	Model 2	Model 3
No	Yes	No	Yes	Hi	Me	Lo	No	Yes	No	Yes	No	Yes			OR (95% CI)	OR (95%CI)
■													1180420 (0.10)		Ref.	Ref.
	■												1265081 (0.33)		3.79(2.90–4.91)	3.62 (3.22–4.08)
		■											1228715 (0.20)			Ref.
			■										1216786 (0.24)			1.21 (1.08–1.36)
				■									831992 (0.14)			Ref.
					■								829423 (0.21)			1.52 (1.31–1.76)
						■							784086 (0.32)			2.25 (1.96–2.59)
							■						1070164 (0.11)			Ref.
								■					1375337 (0.30)			1.97 (1.76–2.21)
									■				1665239 (0.16)			Ref.
										■			780262 (0.36)			1.88 (1.69–2.10)
											■		2080162 (0.21)			Ref.
												■	365339 (0.26)			1.15 (1.01–1.29)
Variance between strata (SE)														0.83 (0.14)	0.40 (0.07)	0.04 (0.01)
Intra Class Correlation (95% Credible Interval)														20.0 (15.6–25.6)	10.8 (8.1–14.1)	1.1 (0.6–2.1)
Bayesian diagnostic information criterion (DIC)														661.87	650.21	628.31

Table 2

Total number of individuals, number of cases of Chronic Obstructive Pulmonary Disease (COPD) and predicted incidence in 2011 for people aged 45-65 residing in Sweden on Dec 31st 2010, by intersectional strata. Predictions are based on model 1 multilevel regression analysis with individuals at the first level and intersectional strata at the second level. Main effects and interactive effects are conflated. Intersectional strata were calculated by categories of age, gender, income based on tertiles in the whole population aged 45–65 years, education, civil status and country of birth. Intersectional strata are ordered according to predicted incidence of COPD, with increasing incidence in descending rows. For a full table with data for all 96 intersectional strata, see Appendix Table A1.

Age		Gender		Income			Education		Living alone		Immigrant				Model 1	
45-54	55-65	Male	Female	High	Medium	Low	High	Low	No	Yes	Yes	No	*Number of individuals*	*Number of cases*	*Incidence*	*95% Credible interval*
The five strata with lowest incidence of Chronic Obstructive Pulmonary Disease in 2011																
✓		✓		✓			✓		✓			✓	50798	9	0.02	(0.01 – 0.04)
✓		✓			✓		✓		✓			✓	72164	19	0.03	(0.02 – 0.04)
✓		✓				✓	✓		✓			✓	54482	16	0.03	(0.02 – 0.05)
✓			✓		✓		✓		✓			✓	74237	26	0.04	(0.03 – 0.05)
✓			✓	✓			✓		✓		✓		6991	1	0.04	(0.01 – 0.09)
The five strata with highest incidence of Chronic Obstructive Pulmonary Disease in 2011																
	✓	✓				✓	✓			✓	✓		2957	19	0.59	(0.36 – 0.90)
	✓	✓				✓		✓		✓		✓	45939	370	0.80	(0.72 – 0.88)
	✓	✓				✓		✓		✓	✓		10450	88	0.82	(0.66 – 1.00)
	✓		✓			✓		✓		✓	✓		12805	113	0.87	(0.72 – 1.05)
	✓		✓			✓		✓		✓		✓	41513	409	0.98	(0.89 – 1.08)

Table 3

Incidence of Chronic Obstructive Pulmonary Disease during 2011 for people aged 45-65 residing in Sweden on Dec 31st 2010, by intersectional strata. Predicted incidences and their 95% CIs based on the total effect (intersectional effects and main effects) and main effects only, in model 3. Interaction effects calculated as total effect minus main effect. Intersectional strata were calculated by categories of age, gender, income based on tertiles in the whole population aged 45-65 years, education, living alone and immigration status. In this table only the five strata with the most negative (protective) and the most positive (hazardous) interaction effects are shown. Intersectional strata are ordered according to their interaction effects with the lowest first and increased interaction effects in descending rows. Strata with 95% CIs excluding 0 are bold. For a full table showing data for all 96 intersectional strata, see Table A2 in Appendix and Figs. 3 and 4.

Age		Gender		Income			Education		Living alone		Immigrant		Model 3					
													Total		*Main effects*		*Total - main effects*	
45-54	55-65	Male	Female	High	Medium	Low	High	Low	No	Yes	Yes	No	*Incidence*	*95% CI*	*Incidence*	*95% CI*	*Interaction*	*95% CI*
The five intersectional strata with the most negative (protective) interaction effect																		
	✓		✓			✓		✓		✓	✓		0.92	0.77 – 1.07	1.06	0.92 – 1.23	-0.15	-0.35 – 0.06
	✓		✓		✓			✓		✓	✓		0.59	0.46 – 0.75	0.72	0.61 – 0.84	-0.13	-0.28 – 0.04
	✓		✓			✓		✓	✓		✓		0.45	0.36 – 0.55	0.57	0.49 – 0.65	-0.11	-0.23 – 0.00
	✓		✓			✓	✓		✓		✓		0.23	0.17 – 0.31	0.29	0.25 – 0.34	-0.06	-0.12 – 0.02
	✓	✓		✓				✓		✓		✓	0.29	0.25 – 0.33	0.34	0.29 – 0.40	-0.05	-0.12 – 0.01
The five intersectional strata with the most positive (hazardous) interaction effect																		
✓			✓		✓			✓		✓		✓	0.23	0.18 – 0.28	0.17	0.15 – 0.20	**0.06**	**0.01 – 0.11**
	✓	✓				✓	✓			✓	✓		0.51	0.37 – 0.72	0.45	0.38 – 0.53	0.06	-0.08 – 0.25
	✓	✓			✓			✓	✓		✓		0.39	0.29 – 0.50	0.32	0.27 – 0.37	0.07	-0.02 – 0.18
✓		✓				✓		✓		✓		✓	0.29	0.25 – 0.35	0.21	0.18 – 0.25	**0.08**	**0.03 – 0.13**
✓			✓			✓		✓		✓		✓	0.39	0.33 – 0.45	0.26	0.22 – 0.30	**0.13**	**0.07 – 0.20**

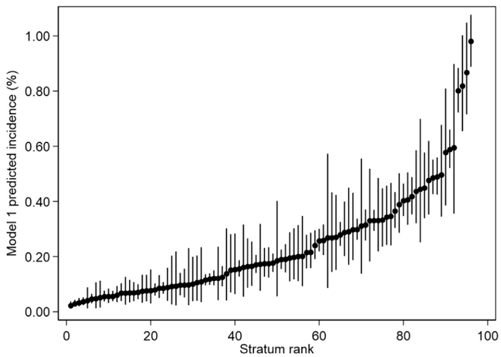

Fig. 2. Predicted incidence of Chronic Obstructive Pulmonary Disease in 2011 for people aged 45–65 residing in Sweden on Dec 31st 2010, by intersectional strata. Predictions are based on model 1 multilevel regression analysis with individuals at the first level and intersectional strata at the second level. Main effects and interactive effects are conflated. Intersectional strata were calculated by categories of age, gender, income based on tertiles in the whole population aged 45–65 years, education, civil status and country of birth. Intersectional strata are ordered according to their rank, strata with lowest rank to the left. For identification of the different intersectional strata, see Table 2 and Table A1.

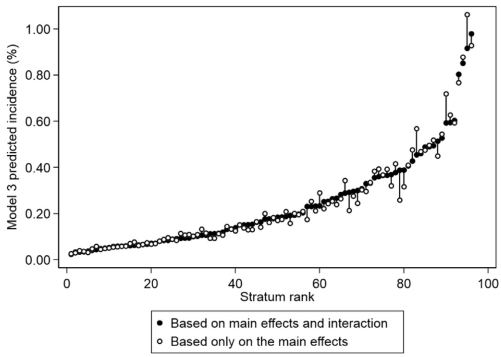

Fig. 3. Incidence of Chronic Obstructive Pulmonary Disease during 2011 for people aged 45–65 residing in Sweden on Dec 31st 2010, by intersectional strata. Point estimates of predicted incidences based on model 3. Black circles indicate the incidence according to predictions based on the total effect (intersectional effects and main effects) while white circles indicate the incidence according to predictions based on main effects only. The differences between black and white circle depict the interaction effects. Intersectional strata were calculated by categories of age, gender, income based on tertiles in the whole population aged 45–65 years, education, living alone and immigration status. To identify the different intersectional strata, see Table 3 and Table A2 (Appendix).

The same was true for identifying groups with a lower COPD incidence (e.g., young native males with high income and high education who cohabited). The incidence in the most vulnerable stratum was 49 times higher than the incidence in the most protected stratum. Compared to studies focused on unidimensional demographic and socioeconomic measures, this approach allows for a better understanding of the distribution of COPD incidence in the population. For example, both low income and low education are considered to be socioeconomic predictors of COPD (Gershon et al., 2012). Nevertheless, young men with high education that cohabited with another adult and were born in Sweden always belong to the strata with the lowest predicted incidence regardless of whether their income was high (predicted incidence =0.02%, 95%CI 0.01–0.04%), medium (predicted incidence =0.03% 95%CI 0.02–0.04%) or low (predicted incidence = 0.03%, 95%CI: 0.02–0.05%). This indicates that with sufficient protecting factors, exposure to low income is not as hazardous as it is for individuals lacking those protective factors. On the other hand, older men with low income who were cohabiting and had immigrated had a clear COPD risk despite high education (predicted incidence = 0.60 95%CI 0.36–0.90). These results show that a protective factor like high education cannot counterbalance increased COPD-risk caused by additive hazardous effects of other social exposures. Intersectional MAIHDA, thus, provides worthy quantitative information on how societal factors that condition COPD risk intersect and overlap.

Though the ICC of model 3 that isolated interaction effects was poor

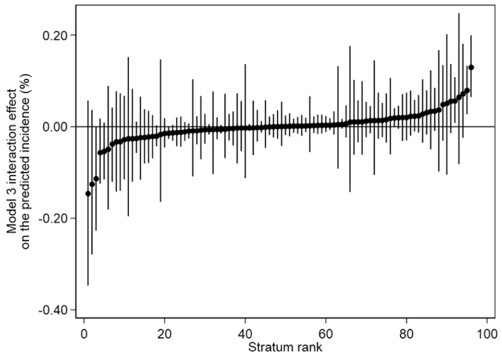

Fig. 4. Intersectional interaction effects on incidence of Chronic Obstructive Pulmonary Disease during 2011 for people aged 45–65 residing in Sweden on Dec 31st 2010, by intersectional strata. Point estimates of the incidences attributable to intersectional interaction and their 95% CIs based on model 3. Interaction effects are calculated as the incidence according to the total effect (intersectional effects and main effects) minus incidence according to main effect only, for each intersectional stratum. Intersectional strata were calculated by categories of age, gender, income based on tertiles in the whole population aged 45–65 years, education, living alone and immigration status. Intersectional strata are ordered according to their intersectional interaction effect. To identify the different intersectional strata, see Table 3 and Table A2 (Appendix).

and only three of the 96 strata had interaction effects with 95% CIs excluding 0, which is about what would be expected by chance, the directions of the interactions are interesting. For example, among young women with low education and low income that lived alone, intersectional interaction may explain why natives had higher incidence of COPD than immigrants. A previous study using a fixed effects approach found interactions between gender and race in the USA (Fuller-Thomson, Chisholm & Brennenstuhl, 2016). Also, a study of lung cancer mortality in the USA with an explicit intersectional approach comprising gender, race, income and education found that black men had a higher mortality risk than white men but black women had markedly lower mortality risk than white women (Williams et al., 2012). Intersectional interaction has been shown for obesity in the USA using multilevel analyses (Evans et al., 2017), but not for ischemic heart disease in Sweden applying a traditional logistic regression analyses and measures of DA (Wemrell et al., 2017b). Altogether, this suggests that whether or not intersectional interaction takes place depends on both the context and the studied outcome, which underscores the importance of replicating intersectional findings in different contexts and for distinct health outcomes.

Implications of MAIHDA for social epidemiology of COPD incidence

From a public health perspective, it is less important however whether observed differences between intersectional strata are due to additive or interaction effects. The analysis of ICC, on the other hand, is relevant for public health researchers and policy-makers. The ICC provides analogous information to that delivered by measures of DA, which is a standard measure for evaluating biomarkers and diagnostic tests (Pepe et al., 2004). While measures of DA are used for the evaluation of predictive risk models among COPD-patients (Garcia-Rivero et al., 2016; Sundh & Ekström, 2017), the DA approach is also being applied for questioning the role of traditional risk factors (Merlo et al., 2017), and other categorizations in public health (Merlo & Mulinari, 2015). Socioeconomic and demographic categorizations are cornerstone concepts in (social) epidemiology that provide fundamental information for policy makers and clinicians. However, the relevance of such categorizations must be properly assessed.

While intersectional categories from the "normative" vantage point adopted in much qualitative intersectional research represent social locations whose relevance cannot be tested or refuted statistically (Hancock, 2013), from a public health perspective intersectionality generates empirically testable research questions that can guide quantitative social epidemiological research. More specifically, MAIHDA and the decomposition of the variance to within-group and between-group components is a suitable tool for the evaluation of the relevance of an intersectional categorization in quantitative public health research (Merlo, 2017).

A related and key question for public health is if selective interventions can be justified in specific strata on the basis of knowledge on the size of the difference between strata averages (e.g., differences in incidences between intersectional strata). The answer we propose to this question is influenced by the three perspectives or "complexities" within intersectionality that McCall recognizes (McCall, 2005): the *intercategorical*, the *anticategorical* and the *intracategorical*. According to this author, the *anticategorical approach* is based on the insight that social life is too complex for simple categorization and that unproblematized use of social categories runs the risk of essentialization and perpetuation of existing power structures of which such categorizations form part. Those social categories should be deconstructed since society is too complex to be reduced to simple categories and deconstructing categorizations is a way of deconstructing inequality itself. The *intercategorical approach,* accepts the provisional adoption of categories with the purpose of documenting inequalities between categories. Finally, the *intracategorical approach* tends to "focus on particular social groups at neglected points of intersection…in order to reveal the complexity of lived experiences within such groups" (McCall, 2005) (p.1774). The intracategorical approach is reasonable within a qualitative framework. However, from a quantitative perspective, the intracategorical approach cannot be distinguished from the intercategorical approach but it just suggests the need for a more detailed classification. Consequently, the intercategorical and anticategorical perspectives appear most relevant for addressing the question of whether selective intervention can be justified in specific intersectional strata on the basis of knowledge of the size of the difference between strata averages (Merlo, 2017; Mulinari et al., 2017; Wemrell et al., 2017a).

Specifically we argue, from an anti-categorical point of view, should the ICC be poor, an intervention in specific intersectional strata guided by difference between strata averages should be considered inappropriate since the overlap in individual risk heterogeneity between strata is very high. Even a good ICC of 20.0%, as found in our study, points towards substantial remaining heterogeneity regarding COPD-incidence within intersectional strata. From a public health perspective, the increased incidence of COPD identified for some strata together with a good ICC supports intercategorical intersectionality and the idea of identifying societal factors that condition COPD risk in those specific strata. Besides, from a clinical perspective, a high DA also supports targeted interventions (for instance voluntary spirometry screening) in specific intersectional strata. In this case, the intersectional approach ensures a much higher accuracy than customary unidimensional analyses based on income, education or occupation gradients.

Strengths and weaknesses

Our study is based on a large database that covers the whole population of Sweden and the socioeconomic and demographic information is of high quality (Statistics Sweden, 2012). Noteworthy, the smallest stratum had 1236 individuals which increases the reliability of the stratum specific estimations and render unnecessary the use of shrunken residuals. Also, ICD-codes for COPD in Sweden have been validated and are sufficiently valid for epidemiological studies

(Inghammar, Engstrom, Lofdahl & Egesten, 2012). In this study, we analysed incidence rather than prevalence of COPD. This may generate more conservative results since more individuals were excluded due to prior COPD-diagnosis in strata with high incidence of COPD than in more privileged strata with a low incidence. We chose to study incidence to avoid reverse causality between income and COPD (i.e., existence of COPD leads to low income rather than the opposite).

In intersectionality theory, focus is directed towards power dynamics and social processes that position individuals along interwoven axes of socio-economic differentiation in society. In register studies, these processes (e.g., capitalist exploitation, sexism, racism) are not accessible for direct investigation but are measured through proxies (e.g., individual income, education, sex, country of birth). Whereas this flaw is inherent to intersectional register studies, we have designed our matrix using variables that are as close to the power dynamics of interest as possible. Due to lack of further information about gender, this variable was subject to binary definition as male or female, although this excludes recognition of people of trans- or non-binary gender. We did not have information on sexual orientation, which limits the accuracy of our intersectional stratification since homo- and transphobia are important components in intersectionality research (Collins, 2002) and since some risk factors for COPD are more prevalent among Lesbian-Gay-Bisexual-Transgender individuals (Jannat-Khah, Dill, Reynolds & Joseph, 2017). By using information on country of birth rather than on ethnicity, we avoid endorsing hypotheses of cultural differences, but on the other hand, we fail to assess racism and racialization directly. Similarly, our lack of data on class relations impeded a proper class analysis. Income is a measure of purchasing power that theoretically affects health by determining what material assets are available for an individual (Lynch, Smith, Kaplan & House, 2000). Education is a Weberian-originated variable that corresponds to life-chances (Galobardes, Shaw, Lawlor & Lynch, 2006). Neither of these evaluate the influence of social class as a multidimensional parameter reflecting ownership, skill and authority (Wright, 1997).

As discussed in a previous paper (Axelsson Fisk & Merlo, 2017), smoking is considered a mediator rather than a confounder for socio-economic disparities in respiratory health. Adjustment for smoking would lead to underestimation of differences across intersectional strata. The lack of information on tobacco use can still be considered a limitation of this study, since it would be valuable to discern how much of the differences between intersectional strata observed that are due to tobacco use.

We only had information on COPD-diagnoses retrieved from hospitals, although most COPD-patients visit primary health care. This situation may reduce the absolute incidence values. We cannot exclude, however, that individuals with COPD belonging to socially advantaged strata are well controlled at the primary health care and have less frequent hospital visits, which could underestimate the incidence of COPD among privileged strata. On the other hand, if privileged strata are referred to specialists more readily than patients in disadvantaged strata (Bongers, van der Meer, van den Bos & Mackenbach, 1997), this could counterbalance this effect. In the future, socioeconomic studies should be performed on Swedish databases comprising diagnoses from both hospitals and primary health care.

Since an intersectional life-course approach (Warner & Brown, 2011) was, unfortunately, beyond the scope of our study we wanted to include age-categories in our intersectional matrix. We included only two age categories but evaluated the contribution of age to ICC in model 2. Use of finer age-stratifications would have decreased the number of individuals in the intersectional strata and reduced the interpretability of the results.

Conclusions and recommendations

Although no causal conclusions can be drawn from this observational study, policies that enhance equality between genders, social classes, people from different countries and people living in different family situations are needed to reduce socially determined disparities in COPD incidence. Research has shown that social disparities are best addressed by broad policies that may be beneficial not only for preventing COPD incidence but for decreasing health disparities for many other diseases and for all social strata (Wilkinson & Pickett, 2009). A systematic quality improvement initiative in Denmark eliminated socioeconomic differences in COPD care during four years (Tottenborg, Lange, Thomsen, Nielsen & Johnsen, 2017). In contrast, the privatizations of primary health care that have taken place in Sweden allocate health resources to affluent individuals (Burstrom *et al.* 2017) with lower risk and may therefore exacerbate such disparities.

Intersectional MAIHDA provides a better theoretical and analytical framework for the evaluation of socioeconomic and demographic disparities in respiratory health and health care utilisation than unidimensional analyses of gradients in health. The relevance of intersectionality for COPD risk calls on researchers and policy makers to simultaneously consider combinations of demographic, social and economic dimensions when investigating and targeting inequalities in COPD morbidity.

Ethics

The Regional Ethics Review Board in southern Sweden (# 2012/637) as well as the data safety committees from the National Board of Health and Welfare and from Statistics Sweden approved the construction of the database used in this study.

Acknowledgements

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Appendix

See Appendix Tables A1 and A2.

Table A1

Total number of individuals, number of cases of Chronic Obstructive Pulmonary Disease and predicted incidence in 2011 for people aged 45–65 residing in Sweden on Dec 31st 2010, by intersectional strata. Predictions are based on model 1 multilevel regression analysis with individuals at the first level and intersectional strata at the second level. Main effects and interactive effects are conflated. Intersectional strata were calculated by categories of age, gender, income based on tertiles in the whole population aged 45–65 years, education, civil status and country of birth. Intersectional strata are ordered according to predicted incidence of COPD, with increasing incidence in decreasing rows.

Age		Gender		Income			Education		Living alone		Immigrant				*Model 1*	
45-54	55-65	Male	Female	High	Medium	Low	High	Low	No	Yes	Yes	No	*Number of individuals*	*Number of cases*	*Incidence*	*95% Credible interval*
✓		✓		✓			✓		✓			✓	50798	9	0.02	(0.01 – 0.04)
✓		✓			✓		✓		✓			✓	72164	19	0.03	(0.02 – 0.04)
✓		✓				✓	✓		✓			✓	54482	16	0.03	(0.02 – 0.05)
✓			✓		✓		✓		✓			✓	74237	26	0.04	(0.03 – 0.05)
✓			✓	✓			✓		✓		✓		6991	1	0.04	(0.01 – 0.09)
✓			✓	✓			✓		✓			✓	56851	25	0.05	(0.03 – 0.07)
✓		✓		✓				✓		✓	✓		5473	1	0.05	(0.01 – 0.11)
✓		✓			✓		✓			✓		✓	6685	2	0.05	(0.02 – 0.11)
✓		✓		✓			✓			✓		✓	27451	14	0.06	(0.03 – 0.08)
✓		✓			✓			✓	✓			✓	58098	31	0.06	(0.04 – 0.08)
✓			✓			✓	✓		✓			✓	55705	30	0.06	(0.04 – 0.08)
✓		✓		✓				✓	✓			✓	25075	14	0.06	(0.04 – 0.09)
✓			✓	✓			✓			✓		✓	22160	14	0.07	(0.04 – 0.10)
✓			✓		✓			✓	✓		✓		9021	5	0.07	(0.03 – 0.13)
✓		✓				✓	✓		✓		✓		20321	13	0.07	(0.04 – 0.11)
✓			✓			✓	✓			✓		✓	13516	8	0.07	(0.03 – 0.12)
✓			✓	✓				✓	✓			✓	31143	21	0.07	(0.05 – 0.10)
✓		✓			✓		✓		✓		✓		9481	6	0.08	(0.03 – 0.14)
✓		✓			✓			✓	✓		✓		6549	4	0.08	(0.03 – 0.15)
✓			✓		✓		✓		✓		✓		11853	8	0.08	(0.04 – 0.14)
✓		✓		✓				✓		✓		✓	57497	45	0.08	(0.06 – 0.10)
✓		✓				✓		✓	✓			✓	68586	58	0.09	(0.07 – 0.11)
✓			✓			✓	✓		✓		✓		19625	16	0.09	(0.05 – 0.13)
✓		✓				✓	✓			✓		✓	7809	6	0.09	(0.04 – 0.16)
✓			✓	✓				✓	✓		✓		3076	2	0.09	(0.03 – 0.20)
✓		✓		✓				✓	✓		✓		1993	1	0.09	(0.02 – 0.22)
✓			✓	✓				✓		✓		✓	20237	19	0.10	(0.06 – 0.14)
✓			✓		✓		✓			✓		✓	11206	10	0.10	(0.05 – 0.16)
✓			✓		✓		✓			✓	✓		1943	1	0.10	(0.02 – 0.23)
✓		✓		✓			✓		✓		✓		4613	4	0.10	(0.04 – 0.20)
✓			✓		✓			✓		✓	✓		4351	4	0.11	(0.04 – 0.20)
✓		✓		✓			✓			✓	✓		3334	3	0.11	(0.04 – 0.23)
	✓		✓	✓			✓		✓			✓	98120	113	0.12	(0.10 – 0.14)
	✓	✓		✓			✓		✓			✓	101692	120	0.12	(0.10 – 0.14)
✓			✓		✓			✓	✓			✓	62902	76	0.12	(0.10 – 0.15)
✓			✓	✓			✓			✓	✓		2926	3	0.12	(0.04 – 0.24)
✓		✓			✓			✓		✓		✓	32367	40	0.13	(0.09 – 0.17)
✓			✓	✓				✓		✓	✓		2450	3	0.14	(0.04 – 0.30)
✓		✓			✓			✓		✓	✓		4795	7	0.15	(0.07 – 0.28)
✓			✓			✓	✓			✓	✓		4099	6	0.15	(0.06 – 0.28)
✓			✓			✓		✓	✓			✓	71224	111	0.16	(0.13 – 0.19)
	✓	✓		✓			✓			✓	✓		2606	4	0.16	(0.06 – 0.32)
	✓	✓		✓			✓		✓		✓		6786	11	0.16	(0.09 – 0.27)
	✓		✓			✓	✓		✓		✓		9085	15	0.17	(0.09 – 0.25)
	✓	✓			✓		✓		✓			✓	57439	98	0.17	(0.14 – 0.21)
	✓	✓		✓				✓	✓		✓		4071	7	0.17	(0.08 – 0.32)

(*continued on next page*)

Table A1 (*continued*)

✓		✓				✓		✓	✓		✓		21782	38	0.18	(0.12 – 0.23)
	✓	✓				✓	✓		✓			✓	25095	44	0.18	(0.13 – 0.23)
	✓	✓		✓				✓	✓			✓	59437	105	0.18	(0.15 – 0.21)
✓		✓			✓		✓			✓	✓		1626	3	0.19	(0.06 – 0.40)
	✓		✓		✓		✓		✓			✓	54766	104	0.19	(0.16 – 0.23)
	✓	✓		✓			✓			✓		✓	28371	54	0.19	(0.14 – 0.25)
	✓		✓		✓		✓		✓		✓		8181	16	0.20	(0.11 – 0.29)
	✓		✓	✓			✓		✓		✓		8567	17	0.20	(0.12 – 0.30)
	✓	✓			✓		✓		✓		✓		7825	16	0.20	(0.11 – 0.31)
✓		✓				✓	✓			✓	✓		3886	8	0.20	(0.09 – 0.35)
	✓		✓			✓	✓		✓			✓	21579	47	0.22	(0.16 – 0.28)
✓			✓			✓		✓	✓		✓		22559	49	0.22	(0.16 – 0.29)
	✓		✓	✓			✓			✓		✓	36219	87	0.24	(0.19 – 0.30)
	✓		✓	✓				✓	✓			✓	57118	148	0.26	(0.22 – 0.30)
✓			✓		✓			✓		✓		✓	28024	73	0.26	(0.21 – 0.32)
	✓	✓			✓		✓			✓	✓		1236	4	0.27	(0.09 – 0.57)
	✓		✓	✓			✓			✓	✓		4219	12	0.27	(0.15 – 0.43)
	✓		✓	✓				✓	✓		✓		4986	14	0.27	(0.15 – 0.42)
	✓	✓		✓				✓		✓		✓	54576	153	0.28	(0.24 – 0.33)
	✓	✓				✓	✓		✓		✓		11252	33	0.29	(0.20 – 0.40)
	✓	✓		✓				✓		✓	✓		4864	15	0.29	(0.17 – 0.45)
	✓	✓			✓		✓			✓		✓	6858	21	0.30	(0.19 – 0.43)
	✓	✓			✓			✓	✓			✓	82655	247	0.30	(0.26 – 0.34)
	✓		✓		✓		✓			✓	✓		2049	7	0.31	(0.14 – 0.56)
✓		✓				✓		✓		✓		✓	41080	130	0.32	(0.26 – 0.37)
	✓		✓	✓				✓		✓	✓		4275	15	0.33	(0.18 – 0.52)
	✓	✓				✓	✓			✓		✓	7596	26	0.33	(0.22 – 0.49)
	✓		✓		✓			✓	✓			✓	85879	285	0.33	(0.29 – 0.37)
	✓		✓		✓			✓	✓		✓		11217	38	0.33	(0.24 – 0.45)
✓		✓				✓		✓		✓	✓		11402	40	0.34	(0.24 – 0.46)
✓			✓			✓		✓		✓	✓		10107	36	0.35	(0.24 – 0.47)
	✓		✓	✓				✓		✓		✓	34017	125	0.37	(0.30 – 0.43)
	✓		✓		✓		✓			✓		✓	12088	48	0.39	(0.29 – 0.50)
	✓	✓				✓		✓	✓			✓	43509	177	0.40	(0.35 – 0.47)
	✓		✓			✓		✓	✓		✓		15257	63	0.41	(0.32 – 0.51)
✓			✓			✓		✓		✓		✓	36867	155	0.42	(0.35 – 0.49)
	✓	✓			✓			✓	✓		✓		9411	42	0.44	(0.32 – 0.59)
	✓		✓			✓	✓			✓	✓		3106	15	0.45	(0.25 – 0.70)
	✓	✓				✓		✓	✓		✓		13963	64	0.45	(0.34 – 0.58)
	✓		✓			✓	✓			✓		✓	8710	43	0.48	(0.35 – 0.62)
	✓		✓			✓		✓	✓			✓	48220	236	0.49	(0.43 – 0.55)
	✓	✓			✓			✓		✓		✓	38031	187	0.49	(0.43 – 0.56)
	✓		✓		✓			✓		✓	✓		7166	37	0.50	(0.35 – 0.68)
	✓	✓			✓			✓		✓	✓		4749	29	0.58	(0.39 – 0.81)
	✓		✓		✓			✓		✓		✓	44571	264	0.59	(0.52 – 0.66)
	✓	✓				✓	✓			✓	✓		2957	19	0.59	(0.36 – 0.90)
	✓	✓				✓		✓		✓		✓	45939	370	0.80	(0.72 – 0.88)
	✓	✓				✓		✓		✓	✓		10450	88	0.82	(0.66 – 1.00)
	✓		✓			✓		✓		✓	✓		12805	113	0.87	(0.72 – 1.05)
	✓		✓			✓		✓		✓		✓	41513	409	0.98	(0.89 – 1.08)

Table A2

Incidence of Chronic Obstructive Pulmonary Disease for people aged 45-65 residing in Sweden on Dec 31st 2010, by intersectional strata. Predicted incidences and their 95% CIs based on total effect (intersectional effects and main effects) and main effects only. Interaction effects calculated as total effect minus main effect. Intersectional strata were calculated by categories of age, gender, income based on tertiles in the whole population aged 45-65 years, education, living alone and immigration status. Intersectional strata are ordered according to their interaction effects with the lowest first and increased interaction effects in descending rows. Strata with 95% CIs excluding 0 are bold.

Age		Gender		Income			Education		Living alone		Immigrant		Model 3					
													Total		*Main effects*		*Total - main effects*	
45-54	55-65	Male	Female	High	Medium	Low	High	Low	No	Yes	Yes	No	*Incidence*	*95% CI*	*Incidence*	*95% CI*	*Interaction*	*95% CI*
	✓		✓			✓		✓		✓	✓		0.92	0.77 – 1.07	1.06	0.92 – 1.23	-0.15	-0.35 – 0.06
	✓		✓		✓			✓		✓	✓		0.59	0.46 – 0.75	0.72	0.61 – 0.84	-0.13	-0.28 – 0.04
	✓		✓			✓		✓	✓		✓		0.45	0.36 – 0.55	0.57	0.49 – 0.65	-0.11	-0.23 – 0.00
	✓		✓			✓	✓		✓		✓		0.23	0.17 – 0.31	0.29	0.25 – 0.34	-0.06	-0.12 – 0.02
	✓	✓		✓				✓		✓		✓	0.29	0.25 – 0.33	0.34	0.29 – 0.40	-0.05	-0.12 – 0.01
	✓		✓	✓				✓		✓	✓		0.43	0.31 – 0.58	0.48	0.40 – 0.57	-0.05	-0.18 – 0.09
	✓		✓	✓				✓		✓		✓	0.38	0.32 – 0.44	0.42	0.36 – 0.48	-0.04	-0.12 – 0.04
	✓	✓		✓				✓		✓	✓		0.36	0.26 – 0.48	0.39	0.33 – 0.46	-0.03	-0.14 – 0.08
	✓		✓		✓			✓		✓		✓	0.60	0.53 – 0.67	0.63	0.54 – 0.72	-0.03	-0.14 – 0.07
	✓		✓		✓			✓	✓		✓		0.36	0.28 – 0.45	0.38	0.33 – 0.45	-0.03	-0.12 – 0.07
	✓	✓				✓	✓			✓		✓	0.37	0.27 – 0.47	0.39	0.33 – 0.46	-0.03	-0.12 – 0.08
	✓	✓				✓		✓		✓	✓		0.85	0.71 – 1.01	0.88	0.76 – 1.02	-0.03	-0.20 – 0.15
✓			✓			✓	✓			✓		✓	0.11	0.07 – 0.15	0.13	0.11 – 0.16	-0.03	-0.06 – 0.01
	✓	✓			✓			✓		✓		✓	0.49	0.43 – 0.56	0.52	0.45 – 0.60	-0.02	-0.12 – 0.07
✓			✓		✓			✓		✓	✓		0.18	0.12 – 0.24	0.20	0.17 – 0.24	-0.02	-0.08 – 0.04
	✓		✓			✓	✓		✓			✓	0.23	0.18 – 0.29	0.25	0.22 – 0.29	-0.02	-0.08 – 0.03
✓		✓				✓		✓	✓			✓	0.09	0.07 – 0.11	0.11	0.10 – 0.13	-0.02	-0.04 – 0.00
	✓	✓				✓	✓		✓			✓	0.19	0.15 – 0.23	0.21	0.18 – 0.24	-0.02	-0.07 – 0.03
	✓		✓			✓	✓			✓	✓		0.53	0.38 – 0.71	0.54	0.46 – 0.64	-0.02	-0.16 – 0.15
✓		✓		✓				✓		✓	✓		0.10	0.06 – 0.13	0.11	0.09 – 0.13	-0.02	-0.05 – 0.02
✓		✓				✓	✓		✓			✓	0.04	0.03 – 0.06	0.06	0.05 – 0.07	-0.01	-0.03 – 0.00
✓		✓			✓			✓	✓			✓	0.06	0.05 – 0.08	0.08	0.06 – 0.09	-0.01	-0.03 – 0.00
✓			✓		✓			✓	✓		✓		0.09	0.06 – 0.13	0.11	0.09 – 0.13	-0.01	-0.04 – 0.02
✓		✓			✓			✓		✓		✓	0.13	0.10 – 0.17	0.14	0.12 – 0.17	-0.01	-0.04 – 0.02
✓		✓		✓				✓		✓		✓	0.08	0.07 – 0.10	0.10	0.08 – 0.11	-0.01	-0.03 – 0.01
✓			✓	✓				✓		✓		✓	0.11	0.08 – 0.14	0.12	0.10 – 0.14	-0.01	-0.04 – 0.02
✓			✓			✓	✓		✓			✓	0.06	0.05 – 0.08	0.07	0.06 – 0.08	-0.01	-0.03 – 0.01
	✓	✓				✓		✓	✓		✓		0.46	0.37 – 0.56	0.47	0.40 – 0.54	-0.01	-0.11 – 0.10
✓		✓				✓	✓			✓		✓	0.10	0.07 – 0.14	0.11	0.09 – 0.13	-0.01	-0.04 – 0.03
	✓	✓		✓			✓			✓	✓		0.19	0.13 – 0.28	0.20	0.17 – 0.24	-0.01	-0.07 – 0.07
✓		✓			✓		✓		✓			✓	0.03	0.02 – 0.04	0.04	0.03 – 0.05	-0.01	-0.02 – 0.00
✓		✓			✓		✓			✓		✓	0.07	0.05 – 0.10	0.07	0.06 – 0.09	-0.01	-0.03 – 0.02
✓			✓		✓		✓		✓			✓	0.04	0.03 – 0.05	0.05	0.04 – 0.06	-0.01	-0.02 – 0.01
	✓	✓		✓				✓	✓		✓		0.20	0.14 – 0.28	0.21	0.17 – 0.24	-0.01	-0.07 – 0.07
	✓		✓			✓		✓	✓			✓	0.49	0.43 – 0.55	0.50	0.43 – 0.57	-0.01	-0.10 – 0.08
✓		✓			✓			✓	✓		✓		0.08	0.06 – 0.12	0.09	0.07 – 0.10	0.00	-0.03 – 0.03
	✓	✓		✓				✓	✓			✓	0.18	0.15 – 0.21	0.18	0.16 – 0.21	0.00	-0.04 – 0.03
✓		✓			✓			✓		✓	✓		0.16	0.11 – 0.22	0.17	0.14 – 0.20	0.00	-0.05 – 0.06
	✓	✓				✓		✓	✓			✓	0.41	0.36 – 0.46	0.41	0.35 – 0.47	0.00	-0.08 – 0.07
	✓		✓		✓		✓			✓	✓		0.37	0.25 – 0.52	0.37	0.31 – 0.44	0.00	-0.11 – 0.14
✓		✓		✓			✓		✓			✓	0.02	0.02 – 0.03	0.03	0.02 – 0.03	0.00	-0.01 – 0.01
✓			✓	✓			✓		✓		✓		0.03	0.02 – 0.05	0.04	0.03 – 0.04	0.00	-0.01 – 0.01
✓			✓		✓		✓			✓	✓		0.10	0.07 – 0.15	0.10	0.08 – 0.12	0.00	-0.03 – 0.04
	✓		✓		✓			✓	✓			✓	0.33	0.29 – 0.37	0.34	0.29 – 0.39	0.00	-0.06 – 0.06
✓			✓			✓	✓			✓	✓		0.15	0.10 – 0.21	0.15	0.13 – 0.18	0.00	-0.05 – 0.06
✓		✓				✓	✓		✓		✓		0.07	0.05 – 0.09	0.07	0.06 – 0.08	0.00	-0.02 – 0.02
✓			✓		✓		✓			✓		✓	0.09	0.06 – 0.13	0.09	0.07 – 0.11	0.00	-0.03 – 0.04
✓			✓			✓	✓		✓		✓		0.08	0.06 – 0.11	0.08	0.07 – 0.09	0.00	-0.02 – 0.03
✓		✓		✓				✓	✓		✓		0.06	0.04 – 0.09	0.06	0.05 – 0.07	0.00	-0.02 – 0.02
✓			✓	✓				✓	✓		✓		0.07	0.05 – 0.10	0.07	0.06 – 0.09	0.00	-0.02 – 0.03
✓			✓	✓				✓		✓	✓		0.13	0.09 – 0.19	0.13	0.11 – 0.16	0.00	-0.04 – 0.05
✓		✓		✓			✓			✓		✓	0.05	0.04 – 0.07	0.05	0.04 – 0.06	0.00	-0.01 – 0.02
✓		✓		✓				✓	✓			✓	0.05	0.04 – 0.07	0.05	0.04 – 0.06	0.00	-0.01 – 0.02
✓			✓	✓			✓			✓		✓	0.06	0.04 – 0.08	0.06	0.05 – 0.07	0.00	-0.02 – 0.02

(*continued on next page*)

Table A2 (*continued*)

	✓		✓	✓			✓		✓			✓	0.12	0.10 – 0.14	0.11	0.10 – 0.13	0.00	-0.02 – 0.03
	✓		✓		✓		✓		✓		✓		0.20	0.14 – 0.26	0.20	0.17 – 0.23	0.00	-0.06 – 0.07
✓		✓		✓			✓		✓		✓		0.03	0.02 – 0.05	0.03	0.02 – 0.04	0.00	-0.01 – 0.02
✓		✓		✓			✓			✓	✓		0.06	0.04 – 0.09	0.06	0.05 – 0.07	0.00	-0.02 – 0.03
✓		✓			✓		✓		✓		✓		0.05	0.03 – 0.07	0.05	0.04 – 0.05	0.00	-0.01 – 0.02
✓			✓	✓				✓	✓			✓	0.06	0.05 – 0.09	0.06	0.05 – 0.07	0.00	-0.01 – 0.02
✓			✓		✓		✓		✓		✓		0.06	0.04 – 0.08	0.05	0.05 – 0.07	0.00	-0.02 – 0.03
✓			✓	✓			✓			✓	✓		0.07	0.05 – 0.10	0.07	0.06 – 0.08	0.00	-0.02 – 0.03
✓			✓	✓			✓		✓			✓	0.04	0.03 – 0.05	0.03	0.03 – 0.04	0.01	-0.00 – 0.02
	✓	✓			✓		✓			✓	✓		0.31	0.21 – 0.44	0.30	0.25 – 0.36	0.01	-0.09 – 0.13
✓		✓			✓		✓			✓	✓		0.09	0.06 – 0.14	0.08	0.07 – 0.10	0.01	-0.02 – 0.05
	✓	✓			✓			✓		✓	✓		0.60	0.46 – 0.77	0.59	0.50 – 0.70	0.01	-0.14 – 0.18
	✓		✓	✓				✓	✓		✓		0.26	0.19 – 0.36	0.25	0.21 – 0.30	0.01	-0.06 – 0.10
	✓	✓		✓			✓			✓		✓	0.19	0.15 – 0.23	0.18	0.15 – 0.20	0.01	-0.03 – 0.06
	✓		✓	✓			✓			✓	✓		0.25	0.18 – 0.35	0.24	0.20 – 0.29	0.01	-0.06 – 0.10
	✓	✓		✓			✓		✓		✓		0.12	0.08 – 0.17	0.11	0.09 – 0.13	0.01	-0.02 – 0.05
✓			✓			✓		✓	✓			✓	0.15	0.13 – 0.18	0.14	0.12 – 0.16	0.01	-0.02 – 0.05
	✓		✓			✓	✓			✓		✓	0.49	0.38 – 0.62	0.48	0.40 – 0.55	0.01	-0.11 – 0.14
✓		✓				✓	✓			✓	✓		0.14	0.09 – 0.20	0.13	0.10 – 0.15	0.01	-0.03 – 0.07
	✓		✓		✓		✓		✓			✓	0.19	0.15 – 0.22	0.17	0.15 – 0.20	0.01	-0.02 – 0.05
	✓	✓			✓		✓		✓		✓		0.18	0.13 – 0.24	0.16	0.14 – 0.19	0.02	-0.04 – 0.07
	✓	✓			✓		✓			✓		✓	0.28	0.20 – 0.37	0.27	0.22 – 0.31	0.02	-0.06 – 0.11
	✓	✓		✓			✓		✓			✓	0.11	0.09 – 0.13	0.09	0.08 – 0.11	0.02	0.00 – 0.04
✓			✓		✓			✓	✓			✓	0.11	0.09 – 0.14	0.09	0.08 – 0.11	0.02	-0.01 – 0.05
	✓	✓			✓			✓	✓			✓	0.30	0.26 – 0.33	0.28	0.24 – 0.32	0.02	-0.03 – 0.07
	✓		✓	✓			✓			✓		✓	0.23	0.19 – 0.28	0.21	0.18 – 0.25	0.02	-0.03 – 0.07
	✓	✓			✓		✓		✓			✓	0.16	0.14 – 0.20	0.14	0.12 – 0.16	0.02	-0.01 – 0.06
	✓		✓	✓			✓		✓		✓		0.15	0.11 – 0.21	0.13	0.11 – 0.16	0.02	-0.02 – 0.08
✓		✓				✓		✓	✓		✓		0.15	0.12 – 0.20	0.13	0.11 – 0.15	0.02	-0.01 – 0.07
	✓	✓				✓	✓		✓		✓		0.27	0.20 – 0.35	0.24	0.20 – 0.28	0.03	-0.04 – 0.10
	✓		✓	✓				✓	✓			✓	0.25	0.22 – 0.29	0.22	0.19 – 0.26	0.03	-0.02 – 0.08
✓			✓			✓		✓		✓	✓		0.33	0.25 – 0.42	0.30	0.25 – 0.35	0.03	-0.05 – 0.12
✓			✓			✓		✓	✓		✓		0.19	0.15 – 0.24	0.16	0.13 – 0.18	0.03	-0.01 – 0.08
	✓	✓				✓		✓		✓		✓	0.80	0.72 – 0.89	0.77	0.66 – 0.88	0.04	-0.10 – 0.17
	✓		✓		✓		✓			✓		✓	0.37	0.29 – 0.46	0.32	0.27 – 0.37	0.05	-0.03 – 0.13
	✓		✓			✓		✓		✓		✓	0.98	0.89 – 1.07	0.93	0.80 – 1.07	0.05	-0.11 – 0.20
✓		✓				✓		✓		✓	✓		0.30	0.23 – 0.38	0.24	0.21 – 0.29	0.06	-0.01 – 0.14
✓			✓		✓			✓		✓		✓	0.23	0.18 – 0.28	0.17	0.15 – 0.20	**0.06**	**0.01 – 0.11**
	✓	✓				✓	✓			✓	✓		0.51	0.37 – 0.72	0.45	0.38 – 0.53	0.06	-0.08 – 0.25
	✓	✓			✓			✓	✓		✓		0.39	0.29 – 0.50	0.32	0.27 – 0.37	0.07	-0.02 – 0.18
✓		✓				✓		✓		✓		✓	0.29	0.25 – 0.35	0.21	0.18 – 0.25	**0.08**	**0.03 – 0.13**
✓			✓			✓		✓		✓		✓	0.39	0.33 – 0.45	0.26	0.22 – 0.30	**0.13**	**0.07 – 0.20**

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.ssmph.2018.03.005.

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Paper III

Clinical Epidemiology

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ORIGINAL RESEARCH

Geographical and sociodemographic differences in discontinuation of medication for Chronic Obstructive Pulmonary Disease – A Cross-Classified Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (MAIHDA)

This article was published in the following Dove Press journal:
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Background: While discontinuation of COPD maintenance medication is a known problem, the proportion of patients with discontinuation and its geographical and sociodemographic distribution are so far unknown in Sweden. Therefore, we analyse this question by applying an innovative approach called multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA).

Patients and Methods: We analysed 49,019 patients categorized into 18 sociodemographic contexts and 21 counties of residence. All patients had a hospital COPD diagnosis and had been on inhaled maintenance medication during the 5 years before the study baseline in 2010. We defined "discontinuation" as the absolute lack of retrieval from a pharmacy of any inhaled maintenance medication during 2011. We performed a cross-classified MAIHDA and obtained the average proportion of discontinuation, as well as county and sociodemographic absolute risks, and compared them with a proposed benchmark value of 10%. We calculated the variance partition coefficient (VPC) and the area under the receiver operating characteristics curve (AUC) to quantify county and sociodemographic differences. To summarize the results, we used a framework with 15 scenarios defined by the size of the differences and the level of achievement in relation to the benchmark value.

Results: Around 18% of COPD patients in Sweden discontinued maintenance medication, so the benchmark value was not achieved. There were very small county differences (VPC=0.35%, AUC=0.54). The sociodemographic differences were small (VPC=4.98%, AUC=0.57).

Conclusion: Continuity of maintenance medication among COPD patients in Sweden could be improved by reducing the unjustifiably high prevalence of discontinuation. The very small county and small sociodemographic differences should motivate universal interventions across all counties and sociodemographic groups. Geographical analyses should be combined with sociodemographic analyses, and the cross-classified MAIHDA is an appropriate tool to assess health-care quality.

Keywords: COPD, socioeconomic inequity, multilevel analysis, equity in health care, health care quality, compliance, discriminatory accuracy

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive and irreversible disorder that impairs quality of life,[1] increases the risk of premature mortality and

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conveys considerable costs for both the individual and society.[2] While smoking cessation reduces mortality among COPD patients,[3] life-long inhaled maintenance medication of COPD reduces symptoms and exacerbations, increases activity tolerance and improves health-related quality of life.[4–6] Life-long inhaled maintenance medication is recommended in both international[5] and the national Swedish guidelines for COPD management, except for the mildest stage.[7] Because COPD is a chronic condition, once a patient has initiated inhaled maintenance medication, it should not be discontinued, unless the initial diagnosis was incorrect or the patient suffers intolerable side effects from the medication, which is not a frequent problem.[5,8]

The evidence is divergent regarding the influence of socioeconomic factors on adherence with inhaled maintenance medication among COPD patients. Low socioeconomic position was associated with more moderate adherence in the USA,[9] while in Denmark one study found an association with lower,[10] and another with higher adherence.[11] In a Swedish study, adherence was equal across age and gender categories but socioeconomic factors were not analysed.[12] In Sweden, health-care management is a county council responsibility and geographical differences between counties in health-care quality are regularly monitored by the Swedish authorities.[13] However, it is still unknown whether there are geographical and sociodemographic differences in discontinuation of inhaled maintenance medication (henceforth "discontinuation"). Therefore, the aim of our study was to evaluate such possible differences. We analysed 49,019 patients from 18 different sociodemographic contexts and residing in the 21 Swedish counties in 2010.

For the purpose of our investigation, we apply an innovative methodological approach called multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA).[14–17] MAIHDA is not a new methodology per se, but it may be viewed as a reorganization of existing multilevel modelling concepts. The MAIHDA approach proposed here stresses the relevance of performing a systematic analysis that simultaneously considers county and sociodemographic differences in the average risk of discontinuation and the extent of individual variation around such averages. This methodology allows the disentangling of geographical from sociodemographic inequalities. It also maps and quantifies the sizes of such inequalities and provides information on the discriminatory accuracy of the sociodemographic and geographical information when predicting discontinuation in COPD patients. Compared with traditional analysis based on differences between group averages, the MAIHDA methodology provides an improved tool for auditing geographical and sociodemographic inequalities in quality of health care.

Patients and Methods

Databases and Study Population

We analysed a database constructed by record linkage between several Swedish registers with national coverage: the Swedish Population Register[19] and the Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA), administrated at Statistics Sweden; as well as data from the National Patient Register (NPR),[20] the Swedish Prescribed Drug Register (SPDR)[21] and the Cause of Death Register,[22] administrated by the National Board of Health and Welfare. We linked the registers by means of the anonymized personal identification number provided by the Swedish authorities.

Initially, we selected all 4,994,992 individuals aged 35–80 years who resided in Sweden on 31st December 2010. We then restricted this to 69,391 patients with a COPD diagnosis defined according to the International Classification of Diseases, 10th edition (codes at any position) as emphysema (J43) or other chronic obstructive pulmonary disease (J44). The NPR includes information from all Swedish hospitals on both outpatient external visits and inpatient discharges. However, it does not cover information on diagnoses in primary health care. Next, we excluded 16,402 patients without previous inhaled maintenance pharmacotherapy (see Assessment of Variables, below) between 1st January 2006 and 31st December 2010. For this purpose, we used the SPDR, which records all medications dispensed by the Swedish pharmacies, excluding storage in hospitals and nursing homes. Finally, we excluded 3640 patients who died during 2011 and 330 patients who had resided in Sweden for less than 5 years at baseline.

In summary, the study population consisted of 49,019 patients with a hospital COPD diagnosis. The patients were 35–80 years old and had resided in Sweden for at least 6 years by 31st December 2011. All patients had complete information on demographic and socioeconomic variables and were using inhaled maintenance pharmacotherapy before 31st December 2010 (Figure 1).

Ethical Statement

The Regional Ethics Review Board in southern Sweden (no. 2012/637), as well as the data safety committees from the

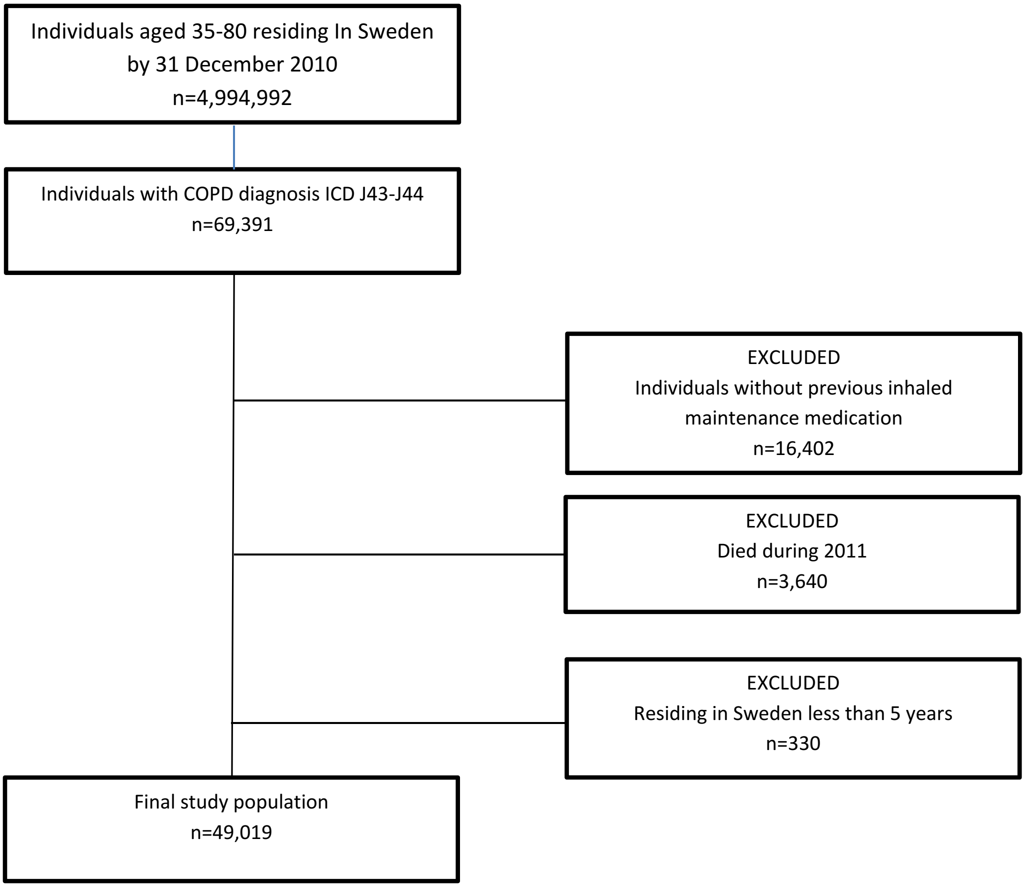

Figure 1 Flowchart indicating the selection of patients in the study sample.

National Board of Health and Welfare and from Statistics Sweden, approved the construction of the database.

Data Accessibility

The original databases are available from the Swedish National Board of Health and Welfare, and Statistics Sweden. In Sweden, register data are protected by strict rules of confidentiality[23] but can be made available for research after a special review that includes approval of the research project by both an Ethics Committee and the authorities' own data safety committees. The Swedish authorities under the Ministry of Health and Social Affairs do not provide individual-level data to researchers abroad. Instead, they normally advise researchers in other countries to cooperate with Swedish colleagues and analyse data in collaboration according to standard legal provisions and procedures.

Assessment of Variables

Discontinuation of Inhaled Maintenance Medication (the Outcome Variable)

We first retrieved information from the SPDR. Thereafter, we defined inhaled maintenance medication as any dispensation of the following substances: long-acting β_2-agonists (LABA), including salmeterol, formoterol and indacaterol; long-acting muscarinic antagonists (LAMA), including tiotropium bromide; and combinations of LABA and inhaled corticosteroids (LABA-ICS), including formoterol and budesonide, salmeterol and fluticasone, and formoterol and beclometasone. We specify the Anatomical

Therapeutic Chemical Classification system (ATC) codes of these substances in the supplementary material. The Stata do-file can easily be adapted by readers for use on their own data.

Based on the Swedish guidelines at the time of the study,[7] we assumed that the patients in our sample fulfilled the criteria for inhaled maintenance medication since they all had a COPD diagnosis in the NPR as well as previous inhaled maintenance medication in the SPDR. We defined "discontinuation" as the absolute lack of retrieval from a pharmacy of inhaled maintenance medication between 1st January and 31st December 2011.

Sociodemographic Variables

We defined three age categories: 35–49, 50–64 and 65–80 years. These cut-off values were chosen to create three groups with a similar age-span and to separate individuals aged 65 and older, as 65 years is the official age of retirement. Gender was defined in a binary manner according to legal sex as male or female. We used information on individualized disposable family income for the years 2000, 2005 and 2010 to compute a cumulative measurement that is more stable to temporary fluctuations in income than single measurements.[24] We used information on absolute income, which takes into account the size of the household and the consumption weight of the individuals. In each of the three years, income was categorized into 25 groups (coded 1–25) by quantiles using the complete Swedish population. The groups from the three years were then summed up, so a patient could have a value between 3 (always in the lowest income group) and 75 (always in the highest income group). Thereafter, we categorized the cumulative income in three groups by tertiles. Individuals with missing values for income during 2000 or 2005 (N=381) were assigned the tertile values of the year 2010. No individuals in our study population had missing income data for 2010.

Finally, we created a multicategorical sociodemographic variable composed of 18 sociodemographic contexts consisting of all possible combinations of categories of gender, age and income-level variables (2×3×3).

Geographical Information

At the time of our study, Sweden was divided into 21 counties, and each patient was assigned to the county where the individual resided on 31st December 2010.

Multicategorical Geographical and Sociodemographic Matrix

For the purpose of the cross-classified multilevel analyses (see the description in the following subsection), we created a multicategorical matrix with 372 strata defined by the unique combinations of the 18 sociodemographic contexts and the 21 counties (ie, 18×21 minus 6 empty strata).

Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (MAIHDA)

Two-Way Cross-Classified Multilevel Model

We analysed the risk of discontinuation of the patients using cross-classified multilevel logistic regression models with COPD patients simultaneously nested within 18 sociodemographic contexts and within 21 counties. Underneath these two higher levels of analysis, there were the 372 strata.

To avoid giving a higher weight to patient categories with a large number of individuals, as in the case of a traditional single-level analysis, we calculated the average proportion of discontinuation across the geographical and sociodemographic categories. We also considered the reliability and precision of the strata information by using multilevel models, as they are based on reliability-weighted strata residuals (ie, shrunken residuals) and average proportions.[25]

In addition, crude geographical (eg, county) differences in discontinuation may be confounded by the different composition of the counties in relation to the demographic and socioeconomic characteristics of the patients. Analogously, sociodemographic categories may be confounded by the different health-care management policies of the counties where the patients reside. Ideally, to investigate county and sociodemographic differences, they should be disentangled from one another. Therefore, we performed a two-way cross-classified multilevel model that decomposes the higher level variance into county and sociodemographic components. Let y_i denote the number of patients who discontinue in stratum i $(i = 1, \ldots, 372)$. The model is written as

$$y_i \sim \text{Binomial}(n_i, \pi_i)$$

$$\text{logit}(\pi_i) \equiv \log\left(\frac{\pi_i}{1-\pi_i}\right) = \beta_0 + v_k + u_j$$

$$v_k \sim N\left(0, \sigma_v^2\right)$$

$$u_j \sim N\left(0, \sigma_u^2\right) \quad 1$$

where n_i denotes the total number of patients in that stratum, π_i denotes the probability of discontinuation, β_0 denotes the intercept, u_j denotes the random effect for sociodemographic context j ($j = 1, \ldots, 18$) and v_k denotes the random effect for county of residence k ($k = 1, \ldots, 21$). The random effects are assumed to be normally distributed with mean 0 and variances σ_v^2 (between counties), σ_u^2 (between sociodemographic contexts). The intercept, β_0, is the average proportion (on the log-odds scale) of discontinuation (ie, grand mean) across all counties and sociodemographic categories, defined as the 372 strata.

This model has three purposes:

1. Mapping county and sociodemographic differences in discontinuation risk

The first purpose was to obtain an improved mapping of how the individual risk of discontinuation is distributed across counties and sociodemographic strata. We use the predicted random effects (ie, shrunken residuals) from the multilevel regression to calculate the absolute risk (AR) of discontinuation and its 95% credible interval (CI) in each sociodemographic context and county. To do so, we transformed the predicted logit of discontinuation into predicted proportions.

For the county-level prediction, we used the following formula, and calculated the absolute risk (AR_C):

$$AR_C \equiv \pi_k = \mathrm{logit}^{-1}(\beta_0 + v_k) \equiv \frac{\exp(\beta_0 + v_k)}{1 + \exp(\beta_0 + v_k)} \quad 2$$

For the sociodemographic context prediction, we used the following formula:

$$AR_{SD} \equiv \pi_j = \mathrm{logit}^{-1}\left(\beta_0 + u_j\right) \equiv \frac{\exp\left(\beta_0 + u_j\right)}{1 + \exp\left(\beta_0 + u_j\right)} \quad 3$$

Observe that in Formulas 2 and 3, the predictions isolate the county and sociodemographic differences while holding the other source of differences constant and, in this way, the values are adjusted for each other.

An advantage of multilevel modelling is that in the presence of higher level units with a small number of patients, the shrunken residuals enable one to obtain precision-weighted AR predictions and also to overcome the limitation of model convergence in the presence of small groups.[25,26]

The graphical or tabulated representation of the ARs facilitates the evaluation of how the individual risk of discontinuation is distributed across counties of residence and sociodemographic contexts. However, this information is based on differences between average ARs, and it does not inform us about individual patient heterogeneity around such averages.[14] Therefore, for a complete evaluation, the mapping of risk needs to be accompanied by measures of county, sociodemographic context and individual patient components of variance and/or discriminatory accuracy.

2. Evaluating the components of variance: the variance partition coefficient (VPC)

The second purpose, therefore, was to take into account the individual heterogeneity around the averages and quantify the share of the total individual differences in the latent propensity of discontinuation that existed at the different levels of the analysis. Consequently, we calculated a VPC based on the latent response formulation of the model, as it is an approach widely adopted in applied work.[27–29]

The VPC for the county level (VPC_C) informs on the share of the total individual differences in the underlying propensity for discontinuation that existed at the county level. The VPC_C expresses what has been called the general contextual effect;[14] that is, the potential ceiling influence of the geo-administrative boundaries of the counties on the individual outcome without any other specific county-level information. The higher the VPC_C , the higher the county general contextual effect; in other words, the more relevant the county context for understanding individual variation in the latent risk for discontinuation. We computed the VPC_C as

$$VPC_C = \frac{\sigma_v^2}{\sigma_v^2 + \sigma_u^2 + \frac{\pi^2}{3}} \quad 5$$

where π denotes the mathematical constant 3.1416, and $\frac{\pi^2}{3} = 3.29$ is the variance of the standard logistic distribution. We then multiplied the VPC_C by 100 and interpreted it as a percentage.

Analogously, the VPC for the sociodemographic level (VPC_{SD}) can be calculated as

$$VPC_{SD} = \frac{\sigma_u^2}{\sigma_v^2 + \sigma_u^2 + \frac{\pi^2}{3}} \quad 6$$

The VPC_C and the VPC_{SD} can be directly compared with each other in order to evaluate the relative relevance of geographical versus sociodemographic factors when it comes to understanding patient differences in the latent propensity of discontinuation.

3. Evaluating the discriminatory accuracy (DA) of the information on county of residence and sociodemographic context

A well-known measure of DA is the area under the receiver operating characteristics curve (AUC).[14,30] The AUC measures the accuracy of geographical and/or sociodemographic information for discriminating patients according their treatment status (discontinuing or not).

The AUC_C computed for the county level obtained from Formula 2 and the AUC_{SD} computed for the sociodemographic level from Formula 3 provide complementary information to the VPC_C and VPC_{SD}.[14,31] One advantage of the use of the AUC is that this measure is already an established concept in clinical epidemiology.

Software and Estimation Methods

All models were run in MLwiN 3.02,[32] called from Stata 14.1 using the runmlwin command.[33] We note that MLwiN can equally be called from within R using the R2MLwiN package,[34] and so our analysis can also be replicated by readers in that statistical package.

We performed all estimations via Markov chain Monte Carlo (MCMC) methods with diffuse (vague, flat or minimally informative) prior distributions for all parameters. We used quasi-likelihood methods to provide starting values for all parameters. For each model, the burn-in length and monitoring chains were set to 5000 and 10,000 iterations. We analysed the parameter chains and standard MCMC convergence diagnostics to evaluate whether the model was adequate.

An advantage of the MCMC is that the resulting parameter chains can be used to construct 95% credible intervals (CI) for all model predictions to communicate statistical uncertainty. MCMC is easy to apply using available software.[32,35,36]

An advantage of our approach is that the multilevel analyses can be performed using a simple table or matrix with the 372 strata. The only information necessary for the analysis is the number of patients and the number of cases with discontinuation in each stratum. This aggregated approach maintains the joint distribution of the socioeconomic strata and the counties and provides exactly the same model results (parameter estimates, predictions and standard errors) as when analysing the underlying individual-level data. The aggregated approach allows a large number of patients to be analysed in just a few hundred strata, which leads to computationally efficient (fast) estimation. In addition, working with tabulated data reduces ethical problems of confidentiality (statistical disclosure).

The Stata do-file used for our analysis is available as supplementary material.

Auditing Sociodemographic and Geographical Differences in Discontinuation of Inhaled Maintenance Medication

In traditional analysis, geographical (ie, county) differences are evaluated by means of figures (eg, league tables) and sociodemographic differences are appraised by measures of association such as odds ratios or relative risks (ie, socioeconomic gradients). In both cases, the information is only based on differences between group averages. However, as explained in a previous publication,[17] in order to perform an improved epidemiological evaluation of sociodemographic and geographical differences in discontinuation, we need at least two types of information.

First, we need a predetermined benchmark or target value informing on the highest percentage of patients with discontinuation that is considered as acceptable. Ideally, this target value should be zero, since there are no formal reasons for discontinuation once maintenance with inhaled therapy is indicated. However, based on standards of ≥90% treatment proposed among Danish COPD patients with documented dyspnoea[37] and findings of a prevalence of non-adherence of 5% among patients attending pulmonary outpatient clinics in Denmark,[11] we propose a benchmark of 10%, which could be acceptable considering that in some cases medication can be discontinued because of side effects or because the COPD diagnosis was incorrect. Therefore, we propose that a percentage under 10% should be considered as a full achievement, between 10% and 15% as a close achievement and >15% as an insufficient achievement. However, further studies are needed to establish an appropriate benchmark level and the level of achievement. In our study, rather than the country proportion of discontinuation, we used the average proportion (ie, grand mean) across the 372 strata defined in the multicategorical geographical and sociodemographic matrix.

The main questions that we asked in the evaluation were: Has the benchmark value been insufficiently, closely or fully reached? What is the size of the inequities between the counties and between sociodemographic groups? To answer these questions, we created a framework (Table 1) with 15 scenarios combining benchmark value achievement and the size of the county/sociodemographic difference measures according to the VPC and the AUC. First, we located the overall achievement in relation to the predefined benchmark value of acceptable prevalence of discontinuation. Second, we quantified the size of the county and sociodemographic differences expressed as VPC and AUC.

Those scenarios can be used to orient the interpretation of an analysis.

Results

Table 2 presents the characteristics of the 49,019 COPD patients and absolute risk of discontinuation by county of residence, and Table 3 by sociodemographic category. There was a slight overrepresentation of women, and the mean age was around 68 years. In the whole country as well as in all counties except Stockholm, low income was overrepresented in the COPD patient population.

Overall in Sweden, 8998 patients discontinued inhaled maintenance medication during 2011, giving a national prevalence close to 18%. However, the crude county averages ranged between 14% in Värmland and 21% in Stockholm. The national average percentage of discontinuation across the geographical and sociodemographic strata and accounting for the reliability of the information was 21.9% (95% CI 19.1–25.0%). Table 4 illustrates the results from the cross-classified multilevel model of discontinuation.

According to the framework presented in Table 1, the county differences were very small since the VPC_v was only 0.4% and the AUC_v was 0.54. The differences between the sociodemographic categories were higher than the geographical differences but still those differences were small, as the VPC_u was 5.0% and the AUC_u value was 0.57.

The cross-classified multilevel model provided information on the predicted average risk of discontinuation for the 21 counties and the 18 sociodemographic contexts simultaneously adjusted for each other. The adjusted county average risk of discontinuation ranged between 19% in the county of Värmland and 26% in the county of Stockholm (Figure 2). The sociodemographic differences were more pronounced than the geographical ones. They varied between 14% in 65–80-year-old women with high income and 34% in 35–49-year-old men with low income (Figure 3). Discontinuation decreased with age, but we did not find clear income gradients. The pattern of discontinuation across sociodemographic categories was similar in men and women, with men having a marginally higher proportion of discontinuation. This difference was not obvious in young patients. However, it was conclusive for patients aged 50–64 and 65–80 years across all three income categories.

An appropriate interpretation of the observed county and sociodemographic differences in Figures 2 and 3 needs to be made in the light of the information provided by the VPC and the AUC (Tables 1 and 4 and Figure 4). Figure 4 shows the AUCs for the county and the sociodemographic information, and it illustrates very clearly their low discriminatory accuracy.

In summary, at the time of our study, there were very small county differences and the sociodemographic inequalities were small, but the proportion of discontinuation was unjustifiably high overall in Sweden. Geographical differences in discontinuation of inhaled maintenance medication can be placed in scenario C and the sociodemographic differences in scenario F (see Table 1) in the framework that we propose.

Table 1 Framework for Evaluating Continuity of Maintenance Medication Among COPD Patients

Size of the County/ Sociodemographic Differences			Benchmark Value Achievement		
			Full	**Close**	**Insufficient**
	VPC (%)	AUC	<10%	10–15%	>15%
Absent/very small	0–1	0.50–0.55	A	B	C
Small	1–5	0.55–0.61	D	E	F
Moderate	5–10	0.61–0.66	G	H	I
Large	10–20	0.66–0.72	J	K	L
Very large	>20	>0.72	M	N	O

Notes: The table outlines a two-dimensional evaluation of continuity with maintenance medication. First, we locate the overall achievement in relation to a predefined benchmark value. Second, we quantify the size of county and sociodemographic differences expressed as variance partition coefficient (VPC) and area under the receiver operating characteristics curve (AUC). Combining this information, we obtain 15 different scenarios (A–O) useful to the evaluation.

Discussion

We aimed to evaluate geographical and sociodemographic differences in discontinuation of maintenance with inhaled medication therapy. As far as we know, our study is original in this area and it demonstrates a high prevalence of discontinuation in Sweden. The discontinuation rate across all geographical and sociodemographic categories was 21.86% and, overall, around 18% of the COPD patients who should be on maintenance therapy were not dispensed any such medication during a whole year. While we found statistically significant average differences between both county and sociodemographic strata, those differences only explained very small (geographical case) and small (sociodemographic case) proportions of the individuals' propensities for discontinuation. Both the VPC and the AUC indicated that discontinuation presented a homogeneous distribution across counties in Sweden.

Table 2 Characteristics by County

County	Number of Patients	AR-D Crude (%)	AR-D Adjusted[a] (%)	Female (%)	Mean Age (Years)	Income Group (%)		
						High	Middle	Low
Stockholms län	10,028	21.01	25.80	57.14	67.50	31.46	36.35	32.19
Uppsala län	1699	16.48	20.77	54.97	67.25	22.66	37.08	40.26
Södermanlands län	1604	16.77	21.21	56.80	67.76	21.32	37.66	41.02
Östergötlands län	2264	15.28	19.73	55.30	67.72	20.32	36.75	42.93
Jönköpings län	1759	15.86	20.31	53.21	67.96	18.65	38.26	43.09
Kronobergs län	909	16.17	20.93	53.91	68.07	19.47	40.26	40.26
Kalmar län	1330	17.74	21.94	53.83	67.88	17.74	36.54	45.71
Gotlands län	331	20.24	22.74	50.45	67.35	13.90	34.44	51.66
Blekinge län	850	18.12	22.09	53.06	67.76	17.06	41.06	41.,88
Skåne län	8034	17.70	21.84	56.97	67.28	21.55	35.69	42.77
Hallands län	1523	16.41	21.17	55.88	68.31	24.43	37.16	38.41
Västra Götalands län	7567	19.65	24.21	57.31	68.11	19.41	36.91	43.68
Värmlands län	1161	13.87	19.15	53.66	68.57	15.93	33.76	50.30
Örebro län	1597	17.41	21.36	54.16	67.17	16.91	35.82	47.28
Västmanlands län	1324	18.88	22.67	56.34	67.19	18.96	38.44	42.60
Dalarnas län	1394	17.29	21.60	55.24	67.97	16.43	39.38	44.19
Gävleborgs län	1358	17.82	22.12	57.73	68.22	17.45	36.16	46.39
Västernorrlands län	1083	16.99	21.35	56.14	67.85	19.85	34.44	45.71
Jämtlands län	602	18.44	22.54	58.80	68.26	16.94	37.38	45.68
Västerbottens län	1150	18.00	22.39	57.83	68.70	17.48	39.91	42.61
Norrbottens län	1452	19.28	23.54	55.65	68.44	19.70	41.18	39.12
Sweden	49,019	18.36	21.86	56.25	67.75	22.08	36.91	41.01

Notes: Characteristics of the 49,019 COPD patients by county of residence and sociodemographic factors, as well as absolute risk for discontinuation (AR-D) of inhaled maintenance medication in 2011. Values are percentages if not otherwise indicated. [a]Estimated from the cross-classified MAIHDA.

Sociodemographic categorizations appeared to have a higher relevance than counties as determinants of discontinuation.

Our results indicate that measures to reduce the discontinuation of inhaled maintenance medication could be improved among COPD patients in Sweden. Using our proposed benchmark of 10%, the prevalence of discontinuation was double the desired level. However, neither counties nor sociodemographic factors seem relevant to understanding patient discontinuation. Other geographical and sociodemographic contexts may play a more relevant role for understanding patients' adherence to inhaled medication. For example, the clinics where patients are treated on a regular basis and even physician-prescribing behaviour have been shown to be relevant for adherence to other medications, such as statins.[38,39] In addition, in countries with different health-care systems, counties and sociodemographic factors may have a larger influence on adherence.

The prevalence of discontinuation in our study was similar to that observed in previous publications,[40–42] in spite of different definitions of medication adherence/discontinuation being used. Haupt et al[41] saw that among patients who had received any inhaled medication, 24% received it only once during a 5-year period. However, short-acting pharmacological agents that may be prescribed for non-chronic conditions were included in that study. In another study, Sundh et al[40] found that 22% of COPD patients treated at hospitals lacked prescribed maintenance medication. Those results concerning discontinuation, low-dosage coverage or no maintenance treatment on discharge from hospital are in line with our findings.

The high prevalence of discontinuation may have several explanations. Compliance with COPD medication is influenced by many different factors. One possible reason for the high prevalence of discontinuation is offered by publications suggesting a considerable prevalence of COPD overdiagnosis.[43,44] If COPD was erroneously diagnosed, the patient would not benefit from maintenance medication and discontinuation would be an adequate response to an incorrect diagnosis. In this scenario, discontinuation of therapy could be a relevant process indicator of COPD health-care quality.

Table 3 Number of Patients and Absolute Risk of Discontinuation by Sociodemographic Category

Sociodemographic Group	Number of Patients (N)	AR-D Crude (%)	AR-D Adjusted[a] (%)
65–80 male high	3530	17.65	16.71
65–80 male middle	5913	17.74	17.07
65–80 male low	5731	18.79	18.22
50–64 male high	1528	21.53	20.59
50–64 male middle	1831	24.30	23.39
50–64 male low	2288	26.79	25.61
35–49 male high	115	29.57	26.54
35–49 male middle	161	34.78	31.58
35–49 male low	347	36.60	34.05
65–80 female high	3555	14.74	13.81
65–80 female middle	7070	15.30	14.56
65–80 female low	7813	15.33	14.85
50–64 female high	2026	15.20	14.55
50–64 female middle	2904	17.84	17.24
50–64 female low	3091	21.51	20.72
35–49 female high	68	23.53	21.79
35–49 female middle	214	32.24	29.58
35–49 female low	834	31.77	30.46
Total	49,019	18.36	21.86

Notes: Number of patients by sociodemographic group, as well as crude and adjusted absolute risk for discontinuation (AR-D) of inhaled maintenance medication in 2011. Values are percentages if not otherwise indicated. [a]Estimated from the cross-classified MAIHDA.

Table 4 Results (95% Confidence Intervals) from the Multilevel Cross-Classified Analysis of County and Sociodemographic Context in Relation to Discontinuation of Inhaled Maintenance Medication in 2011, Among 49,019 Patients with COPD

Variance	
County level	0.012 (0.005–0.026)
Sociodemographic category	0.174 (0.082–0.352)
VPC (%)	
County level	0.35 (0.15–0.75)
Sociodemographic context	4.98 (2.42–9.63)
AUC	
County level (AUC_v)	0.54 (0.53–0.54)
Sociodemographic context (AUC_u)	0.57 (0.56–0.57)

Abbreviations: VPC, variance partition coefficient; AUC, area under the receiver operating characteristics curve.

The negative association between age and therapy discontinuation could be explained by the findings by Ingebrigtsen et al[11] that adherence and use of maintenance therapy increase with the increased severity of COPD, since COPD is often more severe among older patients. Tottenborg et al presented similar results regarding the relationship between young age and non-use of maintenance therapy, in a Danish cohort study of COPD patients.[10]

As indicated in Figure 3, and while not statistically significant in all age categories, we found men to have a higher absolute risk of therapy discontinuation than women, which is in line with previous research.[40,45] Possible explanations include findings that the lung function of female smokers deteriorates more rapidly than among male smokers, causing more severe COPD[46,47] and, thereby, increased adherence with maintenance therapy. However, we need more research on gender disparities in COPD maintenance treatment.

Finally, we did not find obvious income gradients in discontinuation, except among middle-aged women. This observation is in line with findings of small differences in adherence across income groups in Denmark.[10] The absence of effect of income on propensity of discontinuation could be explained by the Swedish reimbursement scheme for prescription medication, which is available for all individuals residing in Sweden, and has a co-payment ceiling that by 2011 was at SEK 1800 (~EUR 180) in a given 12-month period. It is also possible that higher disease severity among patients with low income increases adherence and counterbalances a possible income gradient. However, we did not have access to information on COPD severity. In any case, because of the limited success in reducing socioeconomic disparities achieved by behavioural interventions,[48] socioeconomic determinants of health higher up in the causal pathway should be addressed in order to reduce inequalities.

It is possible that using only three categories of age and income may result in an underestimation of the variance attributed to the sociodemographic level and wider credible interval. Therefore, we performed a sensitivity analysis using, besides the two categories of sex, nine categories of age and 25 categories of income. In this analysis, the VPC=2.7% (CI: 2.0–3.5%) was lower than in the primary analysis. In absolute terms, our conclusion on the low/moderate relevance of the sociodemographic context remains in both analyses. Using the AUC rather than the VPC values indicates that a finer categorization (ie, AUC=0.59) does not improve the discriminatory accuracy of the original sociodemographic categorization (ie, AUC= 0.57). However, a more detailed categorization would result in more empty cells.

As a supplementary analysis, we also investigated potential interaction effects between county of residence and sociodemographic strata by constructing a third

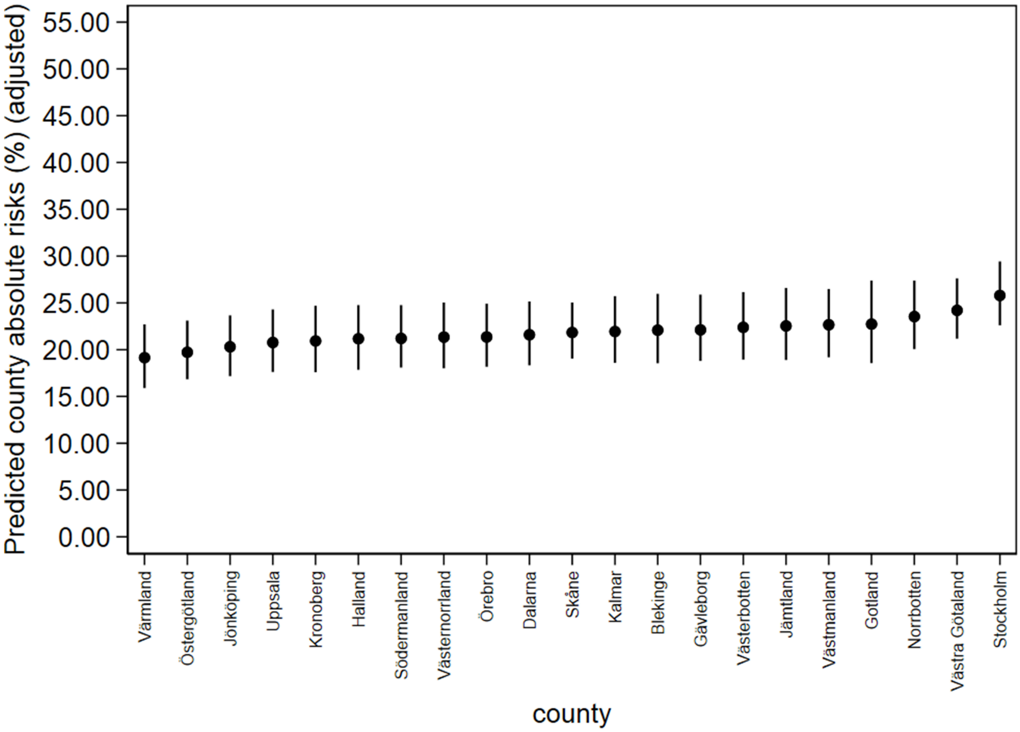

Figure 2 Adjusted absolute risk differences by county. Adjusted differences between the 21 counties in discontinuation of inhaled maintenance medication among 49,019 COPD patients according to the cross-classified multilevel model.

interaction model (see elsewhere for details and an empirical example[49]). However, we did not find any obvious interaction, suggesting that the degree of sociodemographic inequalities varies across different counties.

Strengths and Limitations

The major limitation of this observational register study is the lack of information on the disease stage and COPD severity of the patients. Since both overdiagnosis and underdiagnosis of COPD are common problems, it is likely that we have both missed COPD patients who ideally should be included and included some patients with erroneous COPD diagnoses. According to the guidelines in Sweden at 2010, all individuals with COPD stages 2, 3 and 4 should be prescribed a bronchodilator as maintenance therapy.[7] The study population consisted of individuals treated at hospitals, and with previous prescriptions of LAMA, LABA or LAMA/LABA. Therefore, we assumed that all COPD patients included in our study had COPD stage 2 or higher and needed maintenance therapy. While our assumption seems very probable, we need further studies with exact information on COPD stage since patients with more severe disease have better adherence compared to those with milder cases.[50] We did not have information on the type of inhaler or the frequency of dosing, which also influence adherence.[51] Another limitation is that patients who are treated only in primary health care are not covered by the NPR.

Overall, the data used in this study are of high quality since all socioeconomic parameters are based on national registers. A total of 3636 individuals died during 2011 and it cannot be ruled out that this fact introduces a selection bias. Since follow-up was only one year and the proportion of patients who died during the follow-up time accounted for 6.9% of the study population, we do not think that it would alter our conclusions if we ran a survival analysis instead. In a sensitivity analysis where the patients who died during 2011 were not excluded, we found similar

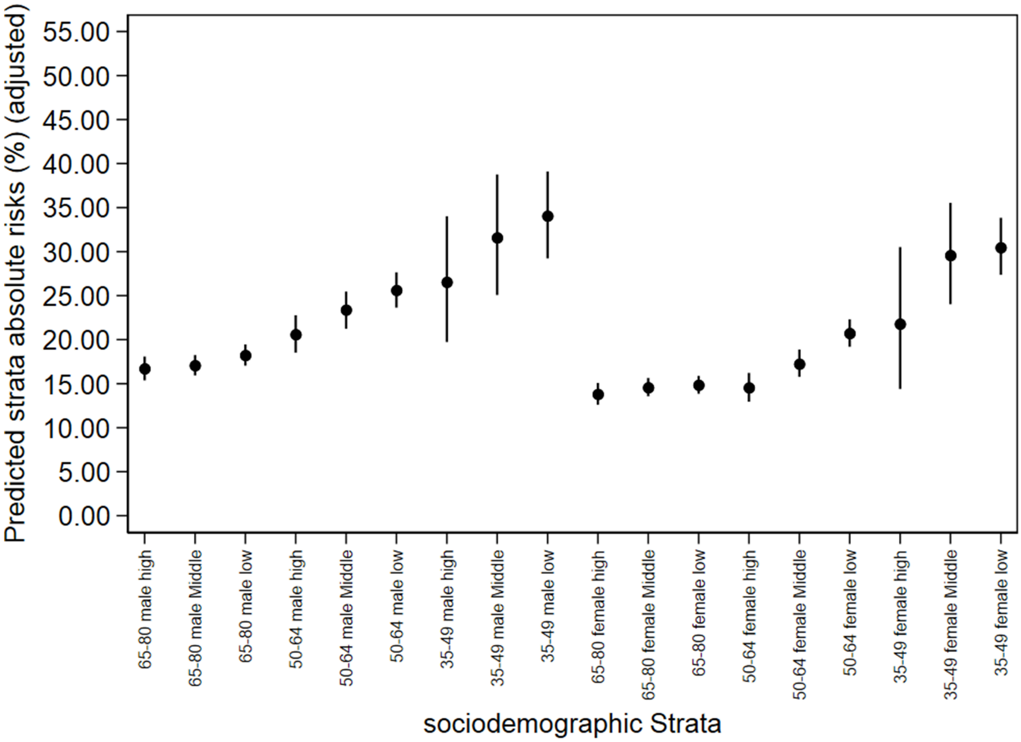

Figure 3 Adjusted absolute risk differences by sociodemographic category. Adjusted differences between the 18 sociodemographic categories in discontinuation of inhaled maintenance medication among 49,019 COPD patients according the cross-classified multilevel model.

results. Our results are based on a large database comprising all patients with COPD diagnosed at hospital wards or specialist outpatient clinics. The validity of the ICD diagnoses of COPD has been judged to be suitable for epidemiological research.[52]

Another strength of this study is the application of measurements of discriminatory accuracy for investigating socioeconomic and geographical inequities in both public health[16,53] and health-care epidemiology.[14,54] For instance, in order to assess whether it would be preferable to target certain groups (eg, counties or sociodemographic strata) or to perform a universal intervention, we need measures of general contextual effects. If the general contextual effect is low, targeting only those counties or strata with a high average risk may lead to inefficient interventions, and also raises ethical issues related to risk communication and the perils of stigmatization of individuals from specific strata.[55]

Multilevel models have a number of advantages compared to traditional single-level models and we refer to previous publications for extended explanations.[28,29,56–61] However, the present study emphasizes the advantage of using average proportions based on the reliability-weighted strata rather than on the population of individuals, especially when the interest focuses on measuring the proportion of patients with a specific quality indicator (eg, discontinuation of maintenance medication in our case) in relation to geographical and sociodemographic categories.[25] The crude proportion of patients with discontinuation may provide information on the burden of discontinuation in, for instance, the country, but it is less representative of the county and sociodemographic contexts of interest in this study.

Implications and Conclusions

The MAIHDA methodology used in this study converges with the current movement of precision (ie, individualized, personalized, stratified) medicine, and its efforts towards understanding not only differences between group averages but also individual heterogeneity around such averages.

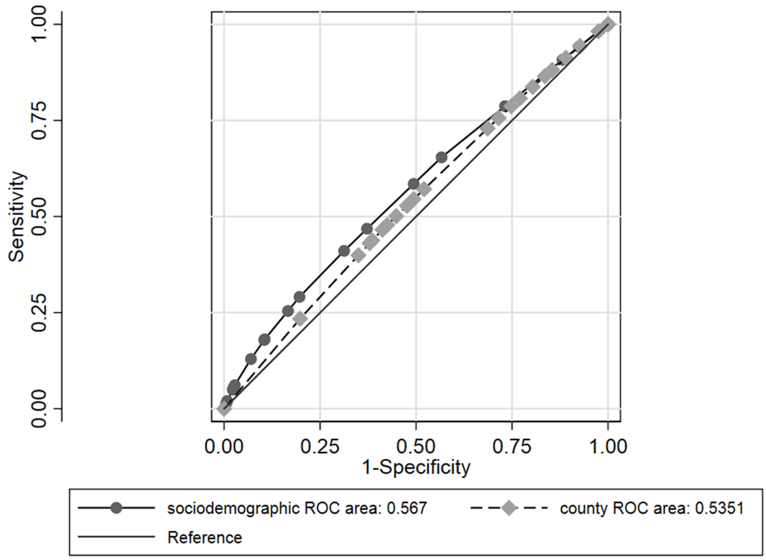

Figure 4 Area under the receiver operating characteristics curve (AUC) for the county and for the sociodemographic information as predictors of discontinuation of inhaled maintenance medication among COPD patients in Sweden with previous maintenance treatment.

Nevertheless, a fundamental conceptual distinction exists between the MAIHDA and individualized medicine: rather than considering only individual characteristics, MAIHDA tries to identify the components of individual heterogeneity in health that are at different contextual levels of analysis. The fundamental statement is that individual and population health are not dislocated study objects. Rather, we need to consider the existence of a continuous distribution of individual outcome heterogeneity that can be articulated at different levels of analysis.[15,18]

One key question for policy makers is to what degree public health interventions should be universal (ie, similarly directed towards the whole population) or targeted to specific groups. The framework outlined in this study provides a tool to guide such decisions. If the insufficient overall achievement had been accompanied by large disparities, as in scenario O in Table 1, targeted health interventions would be justified for categories above the benchmark value. For the case of discontinuation of COPD maintenance medication (scenarios C and F), our results support the public health concept of proportionate universalism.[62,63] Since the overlap between both county and sociodemographic strata is substantial, interventions to improve adherence need to be universal and not exclusively target those groups with increased risk of discontinuation. However, the existence of small sociodemographic disparities and even smaller county-level disparities means that interventions should be proportionately more intense among sociodemographic strata with higher average risk of discontinuation, and to a lesser extent in counties with increased risk of discontinuation. One example of an efficient universal intervention is presented by Tottenborg et al,[64] who showed how a systematic quality improvement initiative managed to eliminate socioeconomic inequalities in COPD health care. Such universal incentives should be initiated in sociodemographic strata and counties with higher risk of discontinuation. Our study demonstrates the use of MAIHDA to assess differences between geographical areas (ie, counties) and between sociodemographic contexts. Evaluations of geographical differences in health-care performance should always consider sociodemographic factors, and MAIHDA is an appropriate tool to perform such analyses.

Abbreviations

AUC, area under the receiver operating characteristics curve; COPD, chronic obstructive pulmonary disease; CI, confidence interval; DA, discriminatory accuracy; NPR, National Patient Register; SPDR, Swedish Prescribed Drug Register; GCE, general contextual effect; MAIHDA, multilevel analysis of individual heterogeneity and discriminatory accuracy; VPC, variance partition coefficient.

Disclosure

The authors report no conflicts of interest in this work.

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Paper IV

BMJ Open

Understanding the complexity of socioeconomic disparities in smoking prevalence in Sweden: a cross-sectional study applying intersectionality theory

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ABSTRACT

Objectives Socioeconomic disparities in smoking prevalence remain a challenge to public health. The objective of this study was to present a simple methodology that displays intersectional patterns of smoking and quantify heterogeneities within groups to avoid inappropriate and potentially stigmatising conclusions exclusively based on group averages.

Setting This is a cross-sectional observational study based on data from the National Health Surveys for Sweden (2004–2016 and 2018) including 136 301 individuals. We excluded people under 30 years of age, or missing information on education, household composition or smoking habits. The final sample consisted on 110 044 individuals or 80.7% of the original sample.

Outcome Applying intersectional analysis of individual heterogeneity and discriminatory accuracy (AIHDA), we investigated the risk of self-reported smoking across 72 intersectional strata defined by age, gender, educational achievement, migration status and household composition.

Results The distribution of smoking habit risk in the population was very heterogeneous. For instance, immigrant men aged 30–44 with low educational achievement that lived alone had a prevalence of smoking of 54% (95% CI 44% to 64%), around nine times higher than native women aged 65–84 with high educational achievement and living with other(s) that had a prevalence of 6% (95% CI 5% to 7%). The discriminatory accuracy of the information was moderate.

Conclusion A more detailed, intersectional mapping of the socioeconomic and demographic disparities of smoking can assist in public health management aiming to eliminate this unhealthy habit from the community. Intersectionality theory together with AIHDA provides information that can guide resource allocation according to the concept proportionate universalism.

Strengths and limitations of this study

- We present an intersectional approach to study the multidimensional socioeconomic disparities in smoking prevalence in Sweden.
- In addition to differences between averages of intersectional strata, we quantify individual heterogeneities around those averages by presenting measurements of discriminatory accuracy.
- Our method is simpler but share crucial advantages with multilevel analysis of individual heterogeneity and discriminatory accuracy (AIHDA), such as improved health mapping and assessment of intersectional interaction.
- We use pooled data from Swedish National Health Survey with participation rates spanning from 60.8% 2004 to 42.1% 2018.
- AIHDA is a suitable tool to inform whether interventions to reduce socioeconomic health disparities should be universal or target-specific groups.

INTRODUCTION

A higher prevalence of smoking among individuals with low socioeconomic position (SEP) compared with higher SEP has been reported in several studies in Sweden[1] and globally.[2–5] The higher prevalence results both from higher rates of initiation[6] and lower rates of successful smoking cessation.[7] In addition to this, other factors like country of birth,[8] household composition,[9] age and gender influence the probability of smoking.[10] Overall, socioeconomic determinants of smoking are multidimensional but few studies have empirically confronted this heterogeneity using an intersectional perspective.[11–15]

Intersectionality theory, proportionate universalism and the analysis of individual heterogeneity and discriminatory accuracy

Structural interventions including raised tobacco taxes and smoking-free zones can reduce smoking prevalence,[16] most among people with low SEP.[17] In UK, healthcare-based smoking cessation aid has reduced disparities in smoking rates between privileged and socioeconomically deprived areas, although this effect was modest.[18] However, a review of the efficacy of non-healthcare interventions targeting behavioural factors among people with low education[19] concludes that there is a lack of evidence that such interventions oriented towards individual determinants of health are efficient when it comes to reducing socioeconomic disparities in smoking.[20] Marmot and Bell claim[21] that interventions to reduce socioeconomic health disparities need to address all levels of society and not only those who are worst off. They argue that an efficient approach may be proportionate universalism[21 22] where interventions are universal, that is, directed towards the whole population (such as tobacco taxes, smoking bans in public) but proportionately more intense among population subgroups with augmented needs where targeted interventions can be launched (ie, information campaigns in specific neighbourhoods or populations such as pregnant women). However, as argued elsewhere[22–24] successful and efficient implementation of proportionate universalism requires development and application of appropriate theories and epidemiological methodologies.

Intersectionality theory is a critical social theory[25] that stresses the need for simultaneous consideration of different social dimensions such as racialised identity, gender and class in order to properly understand the social context acting on individuals. According to intersectionality theory, the social reality is shaped by overlapping systems of oppression that influence distribution of resources and power in society.

The inclusion of intersectionality in epidemiology and public health has been promoted by several scholars.[26–29] A direct consequence of this approach in quantitative analyses is the study of multiple intersectional strata defined by combinations of different social dimensions, since the effect of each social dimension on an individual is intrinsically dependent on other social identities of that person. This contrasts with the common approach considering one social dimension at the time. Thereby, the intersectional approach may enrich public health research by providing an improved mapping of socioeconomic health disparities.[26 30] Such socioeconomic heterogeneity can be analysed by quantifying differences between intersectional strata averages. However, we[23 28 29 31 32] and other scholars[33–35] stress the added relevance of simultaneously quantifying the discriminatory accuracy (DA) of the intersectional categorisation for specific outcomes. An intersectional map combined with information on its DA provides an improved picture of the socioeconomic heterogeneity existing in the society. This approach can be used to inform interventions according to the concept of proportionate universalism. The extent to which a universal intervention needs to be proportional can be evaluated by the DA of the intersectional strata. A low DA suggests the need for universal interventions while a high DA supports more selective interventions. This idea aligns with the distinctions made by McCall between anticategorical, and intercategorical intersectional approaches.[36] According to the anticategorical intersectionality, the categorisations adopted in quantitative research are simplified and contribute to stereotypes and perpetuations of inequalities. The intercategorical intersectionality, on the other hand, accepts categorisations since they can be useful in the study of intersectional inequities. The finding of a low DA would support the anticategorical standpoint that the categorisations lack relevance for the studied outcome. If the DA is high, this would rather support the intercategorical standpoint that intersectional matrix provides worthy information. A moderate DA does not give full support to neither the anticategorical nor intercategorical intersectionality.

Adopting a quantitative perspective, in the present study, we aim to illustrate how a more precise intersectional categorisation combined with analysis of individual heterogeneity and DA (AIHDA) improves our understanding of smoking prevalence and facilitates the application of proportionate universalism.

METHODS

Study population

In this cross-sectional observational study, we used data from all the 14 National Health Surveys (NHS) for Sweden for the years 2004–2016 and 2018 (https://www.folkhalsomyndigheten.se/the-public-health-agency-of-sweden/public-health-reporting/). The NHS is an ongoing collaborative project between the Public Health Agency of Sweden and the Swedish Association of Local Authorities and Regions. The NHS record self-reported information on health, lifestyle and living conditions. The study has been conducted annually between 2004 and 2016 and comprised a random sample of 20 000 individuals aged 16–84 years. After 2016 the survey is conducted biannually but with a random sample of 40 000 individuals. Response rates span from 60.8% 2004 to 42.1% 2018. Using a unique personal identification number, the Swedish authorities linked the sample surveys to national register administered at Statistics Sweden to obtain demographical and socioeconomic information.

For our study, we pooled the data from the last 14 surveys, which rendered a sample of 136 301 individuals. Thereafter, we excluded people younger than 30 years. The lower age limit of 30 years was chosen since most individuals in Sweden that will complete a 3-year education after high school do so before this age[37] and educational status was the indicator of SEP chosen in this study. We also excluded people with missing information on education, household composition or smoking habits. The final sample consisted on 110 044 individuals or 80.7% of the original sample (figure 1).

Patient and public involvement

All data from NHS provided to researchers is anonymised, so study participants cannot be identified. The study participants were not involved in the research process.

Assessment of variables

Smoking status was assessed based on the answer to the question ‘Do you smoke?’, if the person answered ‘yes’

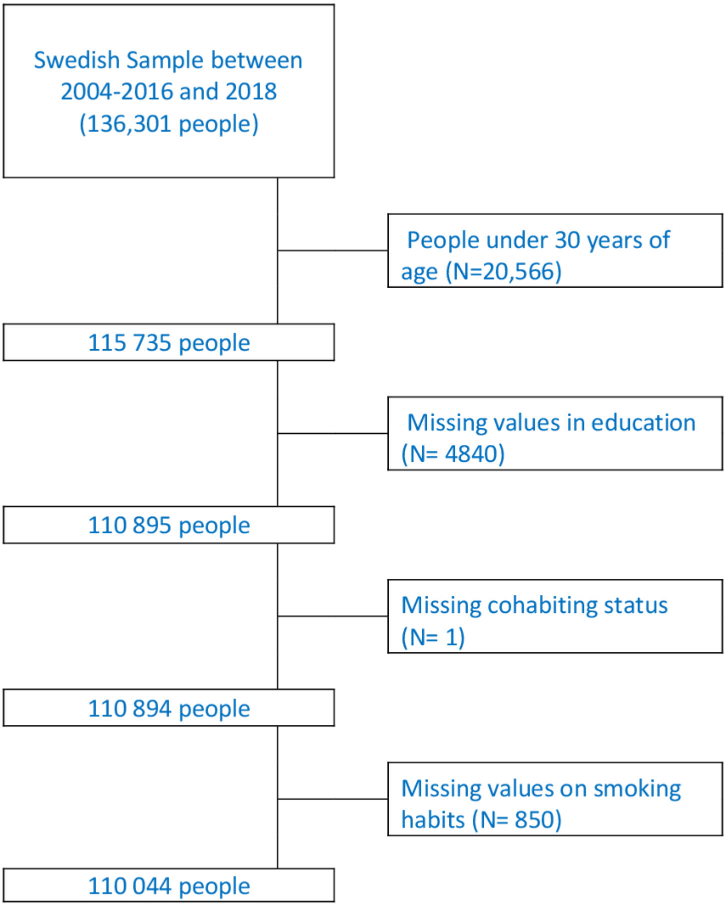

Figure 1 Flow chart showing the selection of the study population.

or 'yes, sometimes', the individual was categorised as a smoker, if the respondent answered 'no' the individual was considered a non-smoker.

We categorised age into three groups: 30–44, 45–64 and 65–84year-old. We classified gender as a binary variable distinguishing between men and women as more specific information on gender was not available in the questionnaire. We classified educational achievement into three categories, as low if the respondent had not completed 3years of high school education, as middle if they had high school education but less than 3years of education after high school and high if the respondent had at least 3years of education after high school. Throughout 2008–2016 respondents were asked 'with whom do you share household?', we defined household composition as living alone if the respondent answered 'with no one', otherwise as living with other(s). In 2018 that question was not asked so individuals were defined in the same way according to the linked information provided by Statics Sweden. We classified migration status as native (ie, born in Sweden) or immigrant.

As a way of operationalising intersectional contexts, we created 72 strata by combining the three categories of age, the two of gender, the three of educational achievement, the two of migration status and the two categories of household composition. We used 30–45years old native men living with other(s) and with high educational achievement as the reference in the comparisons, as this group was assumed to occupy the position of greatest structural privilege. This choice was based on unidimensional assumptions of structural privilege for young compared with old,[38] men compared with women, high SEP compared with low SEP,[39] natives compared with immigrants[40] and those living with other(s) compared with people living alone.[41] We also included the survey year of the participants using 2018 as reference in all comparisons.

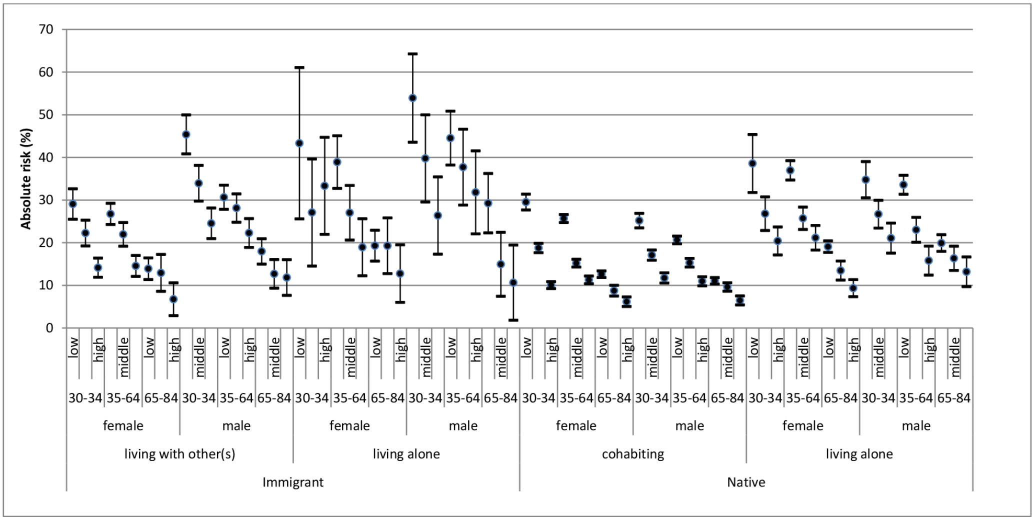

Figure 2 Absolute risk (ie, prevalence) and 95% CIs of smoking in different intersectional strata according the National health survey in Sweden between 2004 and 2018.

Statistical analyses

The first step in our analysis was to obtain the trends in smoking prevalence and the trends in socioeconomic and demographic gradients in smoking between 2004 and 2018 (see online supplemental material 1). Thereafter, we performed a stratified analysis aimed to provide a detailed map of the prevalence (ie, absolute risk) and 95% CIs of smoking across the intersectional strata. This stratification allows comparing the prevalence of smoking in different strata without any reference (figure 2).

Thereafter, we performed seven consecutive regression analyses, modelling smoking as the dependent variable and survey year as well as the different demographical and socioeconomic dimensions alone and in combination as explanatory variables. The use of logistic regression to obtain ORs is common but the OR is a good estimation of the relative risk only when the prevalence of the outcome is very small (rare event assumption).[42] Therefore, for the analysis, rather than logistic regression to obtain ORs, we used Cox proportional hazards regression with a constant follow-up time equal to one to obtain prevalence ratios (PR)[43] with 95% CI.

Model 1 included only survey year, model 2 added age, model 3 added gender, model 4 added educational achievement, model 5 added migration status and model 6 added household composition and thus included all the variables that defined the intersectional strata. Finally, the intersectional model 7 included the same variables as model 6 but in the form of a multicategorical variable with 72 intersectional strata. Here, we used the 30–45 years old, native men living with other(s) and with high educational achievement as the reference in the comparison.

For each model, we quantified its DA by means of the area under the receiver operator characteristics curve (AUC).[44] The AUC measures the accuracy of the information provided by the variables in the model for discriminating individuals who smoke from those who do not. The AUC takes a value between 0.5 and 1, where 1 indicates perfect discrimination and 0.5 means that the studied variables have no DA at all. The AUC can even be used to qualify the size of the intersectional differences. Rather than evaluating the absolute risk differences between strata, using the AUC we assess the overlapping of the individual risk predictions (based on the intersectional strata) between smokers and non-smokers.

There is no fully established practical guideline for the interpretation of the size of the AUC as a measure of DA when analysing intersectional inequalities. However, based on the cut-off values provided by Hosmer and Lemeshow[45] but using more neutral denominations we qualify intersectional inequalities according to the DA as (1) 'absent or very small' (AUC=0.5–0.6), (2) 'moderate' (AUC >0.6–≤0.7), (3) 'large' (AUC >0.7–≤0.8) and (4) 'very large' (AUC >0.8). Evaluating intersectional differences using only strata prevalence is insufficient as it does not consider any overlapping between the strata. Therefore, the AUC provides fundamental information for evaluation of group differences.[46]

We further calculated the incremental change in the AUC value (Δ-AUC) between the models. The Δ-AUC quantifies the improvement in the DA obtained by a model, in relation to the previous model.[24] The categorical intersectional variable in model 7 allows for the capturing of interaction of effects. If any such interaction exists, the DA of model 7 will increase in comparison with model 6 and the Δ-AUC will thus be positive.

We used STATA V.15.1 and IBM SPSS V.25 for PC to perform all statistical analyses.

RESULTS

Over the whole study period, the prevalence of smoking was 18%. The visual analysis of the trends indicated that the prevalence of smoking monotonically decreased in Sweden from 25.0% in 2004 to around 11.1% in 2018. While sex-differences were small throughout the period and the sex-category with highest smoking prevalence changed, we observed consistent differences between groups defined by age, country of birth, educational achievement and household composition. In absolute terms, the gaps between subgroups were static except for differences between age categories that narrowed in later years (see online supplemental material 1).

Table 1 presents the prevalence of smokers and non-smokers across the included socioeconomic and demographic variables as well as across survey years. It indicates that the prevalence of smoking was higher in individuals aged 45–64 years (20.6%) than in both younger (19.8%) and older people (12.4%). Women and men had similar prevalence of smoking (17.9% vs 17.8%). As expected, smoking was more common among people with low (21.7%) and medium (17.0%) educational achievement compared with people with high educational achievement (11.9%). The prevalence of smoking was higher among immigrants (23.9%) than among natives (17.0%) and the same was true for individuals living alone (24.1%) compared with those who were living with other(s) (16.5%).

Figure 2 shows the prevalence of smoking across the intersectional strata. We observed the highest prevalence (54%) among 30–44 years old immigrant men with low educational achievement and living alone, and the lowest prevalence (6%) among 65–84 years old native women with high educational achievement and living together. The reference stratum (ie, 30–45 years old, native men living with other(s) and with high educational achievement) used in the relative comparisons (table 2) presented a smoking prevalence of about 12%.

The table 3 informs that the PR of smoking decreases with age, being lowest in the old population. This age gradient is clear after adjustment for the other variables in the model 6. Low educational achievement, being immigrant and living alone was associated with a higher smoking risk. However, there were no age-adjusted gender differences. The AUC in the model including only survey year was 0.58. In the age adjusted model 2, the AUC was 0.60 and it did not increase when gender was included in model 3. The AUC increased by 0.04

Table 1 Distribution (prevalence) of smokers across categories of age, gender, education, migration and household composition in the 110 044 participants in the Swedish National Health Surveys (2004–2018)

	Non-smokers (%)	Smokers (%)
30–44	22 799 (80.23)	5618 (19.77)
45–64	38 024 (79.41)	9862 (20.59)
65–84	29 575 (87.65)	4166 (12.35)
Female	48 782 (82.08)	10.653 (17.92)
Male	41 616 (82.23)	8993 (17.77)
Low	38 791 (78.32)	10 738 (21.68)
Middle	27 716 (83.02)	5670 (16.98)
High	23 891 (88.06)	3238 (11.94)
Immigrant	10 410 (76.07)	3274 (23.93)
Native	79 988 (83.01)	16 372 (16.99)
Living with other(s)	75 625 (83.48)	14 964 (16.52)
Living Alone	14 773 (75.93)	4682 (24.07)
2004	6803 (75.03)	2264 (24.97)
2005	3339 (75.90)	1060 (24.10)
2006	3450 (77.62)	995 (22.38)
2007	3272 (77.81)	933 (22.19)
2008	6525 (79.07)	1727 (20.93)
2009	6123 (79.22)	1606 (20.78)
2010	6718 (80.59)	1618 (19.41)
2011	6760 (82.56)	1428 (17.44)
2012	6893 (82.68)	1444 (17.32)
2013	6770 (83.10)	1377 (16.90)
2014	6845 (83.74)	1329 (16.26)
2015	6978 (84.21)	1308 (15.79)
2016	7086 (88.13)	954 (11.87)
2018	12 836 (88.90)	1603 (11.10)

Values are number (and percentage) of individuals.

units when including education. It did not increase when adding migration status but further increased by 0.01 units when including household composition. The AUC of intersectional model 7 was 0.66, with 95% CI overlapping the AUC of model 6 indicating no conclusive intersectional interaction.

Table 2 shows the 10 strata with the lowest and the 10 strata with the highest PRs of smoking using the strata of young native men with high educational achievement and living with other(s) as reference. The lowest PR=0.55 was observed in older native women with high educational achievement and living with other(s) and the highest PR=4.45 was observed in young immigrant men with low educational achievement and living alone. When comparing with the reference stratum of native young men with high educational achievement and living with other(s), we observed that low educational achievement, being immigrant and living alone were, respectively,

Table 2 Results from the intersectional model 7 indicating the 10 strata with lowest and the 10 strata with highest prevalence ratios (PR) with 95% CIs of smoking across intersectional strata in the Swedish population using the stratum of young, native, men with high education that were living with other(s) (LWO) as reference in the comparisons

Age	Gender	Educational achievement	Migration status	Household composition	PR (95% CI)
65–84	Female	High	Native	LWO	0.55 (0.45 to 0.69)
65–84	Male	High	Native	LWO	0.58 (0.48 to 0.71)
65–84	Female	High	Immigrant	LWO	0.61 (0.33 to 1.11)
65–84	Female	Middle	Native	LWO	0.80 (0.66 to 0.96)
65–84	Female	High	Native	Living alone	0.83 (0.64 to 1.06)
65–84	Male	Middle	Native	LWO	0.85 (0.73 to 0.99)
30–44	Female	High	Native	LWO	0.86 (0.74 to 0.98)
65–84	Male	High	Immigrant	Living alone	0.91 (0.38 to 2.21)
45–64	Male	High	Native	LWO	0.92 (0.8 to 1.07)
65–84	Male	Low	Native	LWO	0.96 (0.84 to 1.11)
30–44	Male	High	Native	LWO	Reference
30–44	Female	High	Immigrant	Living alone	2.87 (1.86 to 4.42)
30–44	Female	Low	Native	Living alone	2.95 (2.29 to 3.78)
45–64	Female	Low	Native	Living alone	2.99 (2.61 to 3.41)
45–64	Male	Middle	Immigrant	Living alone	3.10 (2.26 to 4.26)
45–64	Female	Low	Immigrant	Living alone	3.22 (2.56 to 4.06)
30–44	Male	Middle	Immigrant	Living alone	3.33 (2.35 to 4.71)
30–44	Female	Low	Immigrant	Living alone	3.41 (1.96 to 5.94)
45–64	Male	Low	Immigrant	Living alone	3.61 (2.90 to 4.50)
30–44	Male	Low	Immigrant	LWO	3.66 (3.07 to 4.35)
30–44	Male	Low	Immigrant	Living alone	4.45 (3.29 to 6.03)
AUC					0.66 (0.65 to 0.66)
∆AUC compared with model 6					0.01

AUC, area under the curve.

present in 7, 8 and 9 of the 10 strata with the highest risk of smoking (see online supplemental material 2 for the complete list of PR values).

DISCUSSION

Main findings

Our study provides an improved mapping of the distribution of the smoking habit in Sweden compared with unidimensional analyses. Rather than focusing on single socioeconomic and demographical variables, we use an intersectional AIHDA analysis that uncovers the socioeconomic and demographical heterogeneity existing in the country. We also applied the AUC to obtain information on the accuracy of the intersectional grouping for identifying individuals according to their smoking status. We found a moderate AUC=0.66, which indicates that individual risk of smoking considerably overlaps between the intersectional strata and that neither the anticategorical nor the intercategorical intersectionality approaches are fully supported. We found that the stratum-specific risks were due to the main effects of the different variables used to define the intersectional strata without any conclusive interactive component.

We found intersectional strata with a rather high prevalence of smoking. For instance, the prevalence of smoking in young immigrant men with low educational achievement and living alone was 54%. Interestingly, while high educational achievement generally prevents smoking, young immigrant women that lived alone had a PR of 2.87 (95% CI 1.86 to 4.42) despite their high educational achievement. This indicates that the protective effect of high education may depend on other variables such as migration status and gender. Our finding could hypothetically reflect both smoking culture in the country of birth of the individual or that discrimination on the basis of gender or migration status may contribute to making education a poorer indicator of SEP in this group.

Relation to previous studies

In spite of the use of different definitions and measurements of smoking habits as well as the use of different indicators of SEP, many previous publications have shown the existence of socioeconomic, ethnic and

Table 3 Prevalence ratios (PR) and 95% CI, of smoking among people aged 30–84 included in the National Health Surveys between 2004 and 2018 in relation to survey year, age, gender, education, migration statis and household composition

		Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
	2004	2.25 (2.11–2.40)	2.07 (1.95–2.21)	2.08 (1.95–2.21)	1.85 (1.74–1.98)	1.88 (1.76–2.00)	1.84 (1.73–1.97)
	2005	2.17 (2.01–2.35)	2.01 (1.86–2.17)	2.01 (1.86.2.17)	1.83 (1.69–1.98)	1.85 (1.71–2.00)	1.83 (1.69–1.98)
	2006	2.02 (1.86–2.18)	1.87 (1.72–2.02)	1.87 (1.72–2.02)	1.70 (1.57–1.84)	1.71 (1.58–1.85)	1.68 (1.55–1.82)
	2007	2.00 (1.84–2.17)	1.86 (1.71–2.01)	1.86 (1.71–2.01)	1.71 (1.57–1.85)	1.65 (1.54–1.77)	1.70 (1.56–1.84)
	2008	1.89 (1.76–2.02)	1.76 (1.64–1.88)	1.76 (1.64–1.88)	1.64 (1.53–1.75)	1.66 (1.55–1.78)	1.63 (1.52–1.74)
	2009	1.87 (1.75–2.01)	1.75 (1.64–1.89)	1.76 (1.64-1-88)	1.65 (1.54–1.77)	1.62 (1.51–1.73)	1.63 (1.52–1.75)
	2010	1.75 (1.63–1.87)	1.70 (1.58–1.82)	1.70 (1.58–1.82)	1.61 (1.50–1.72)	1.46 (1.36–1.57)	1.59 (1.48–1.70)
	2011	1.57 (1.46–1.69)	1.53 (1.43–1.64)	1.53 (1.43–1.64)	1.45 (1.35–1.56)	1.47 (1.37–1.58)	1.43 (1.33–1.54)
	2012	1.56 (1.45–1.68)	1.53 (1.42–1.64)	1.53 (1.42–1.64)	1.47 (1.37–1.57)	1.45 (1.35–1.56)	1.44 (1.34–1.55)
	2013	1.52 (1.42–1.64)	1.49 (1.39–1.60)	1.49 (1.39–1.60)	1.45 (1.35–1.55)	1.45 (1.35–1.56)	1.42 (1.32–1.52)
	2014	1.47 (1.36–1.75)	1.45 (1.35–1.56)	1.45 (1.35–1.56)	1.41 (1.31–1.52)	1.42 (1.32–1.53)	1.39 (1.30–1.50)
	2015	1.42 (1.32–1.53)	1.40 (1.30–1.51)	1.40 (1.30–1.51)	1.37 (1.27–1.47)	1.38 (1.28–1.48)	1.35 (1.26–1.46)
	2016	1.07 (0.99–1.16)	1.06 (0.97–1.14)	1.06 (0.97–1.14)	1.04 (0.96–1.13)	1.05 (0.97–1.13)	1. 03 (0.95–1.11)
Year	2018	Reference	Reference	Reference	Reference	Reference	Reference
	30–44		Reference	Reference	Reference	Reference	Reference
	45–64		1.06 (1.03–1.10)	1.06 (1.03–1.10)	0.94 (0.91–0.97)	0.94 (0.91–0.98)	0.93 (0.90–0.96)
Age	65–84		0.68 (0.65–0.71)	0.68 (0.65–0.71)	0.56 (0.54–0.58)	0.57 (0.55–0.59)	0.53 (0.51–0.56)
	Male			Reference	Reference	Reference	Reference
Gender	Female			1.00 (0.97–1.02)	1.02 (0.99–1.05)	1.02 (0.99–1.05)	1.01 (0.98–1.04)
	Low				1.96 (1.88–2.04)	1.96 (1.88–2.04)	1.93 (1.86–2.01)
	Middle				1.42 (1.36–1.48)	1.43 (1.37–1.49)	1.42 (1.36–1.49)
Education	High				Reference	Reference	Reference
	Native					Reference	Reference
Born in Sweden	Immigrant					1.39 (1.34–1.45)	1.39 (1.24–1.44)
	Living alone						1.53 (1.48–1.58)
Living alone	living with other(s)						Reference
AUC		0.58 (0.58–0.59)	0.60 (0.60–0.61)	0.60 (0.60–0.61)	0.64 (0.63–0.64)	0.64 (0.64–0.65)	0.65 (0.65–0.66)
ΔAUC		–	0.02	0.00	0.04	0.00	0.01

Model 7 includes the same variables as model 6 but as a multicategorical variable, the PRs and AUC for model 7 are presented in the table 2. AUC values with 95% CI representing the discriminatory accuracy and ΔAUC values of the models are also presented.
AUC, area under the curve.

demographical differences in smoking.[2 4 47] However, as far we known, only a few have considered the intersectional approach.[11 14 15] The heterogeneous distribution of smoking prevalence we found in Sweden is in accordance with recent intersectional research on smoking cessation in the US adult population.[15]

High education may influence smoking through both direct effects, such as increased understanding of detrimental health effects of smoking, and indirect effects such as social and material circumstances.[48] Educational achievement is the preferred indicator of SEP in previous public health reports in Sweden.[49] We performed a sensitivity analysis where we included income instead of education and the results were very similar and are provided as online supplemental material 3.

In a comparison of the relative importance of low education on smoking prevalence across age and gender groups in Denmark and Sweden, Eek *et al*[1] found that the effect of low education on smoking prevalence and continuation of smoking was strongest among younger women in Sweden, indicating a failure of tobacco prevention interventions to reach this group. While immigrant men were clearly overrepresented among the strata with highest prevalence of smoking, this was not the case for women. This pattern was also found by Lindström and Sundquist[8] in a study from southern Sweden showing lower rates of smoking among men born in Sweden, but higher rates of smoking among women born in Sweden compared with men and women from most other country groups. These differences were attributable to different smoking prevalence in the countries of origins of the immigrants, potentially representing different stages of the smoking transition. The distribution of smoking prevalence across age groups we found is similar to the pattern observed by Ali *et al*[50] in a study from southern Sweden.

Strengths and limitations

The cross-sectional and observational character of this study prevents causal conclusions. However, the variables included in our analyses are to a little extent effected by smoking status, so the causal direction can be presumed to go from sociodemographic variables towards smoking rather than the opposite.

A weakness in our study is that the participation rates were rather low, especially during the last years. An analysis of the non-participants performed by Statistics Sweden shows that people with low income, people born outside Sweden and people living alone were less likely to be responders.[51] Therefore, if the prevalence of smoking is higher in non-participants, our analysis may have underestimated the existing socioeconomic differences. In a sensitivity analysis, we used data that had been weighted by Statistics Sweden in order to reduce skewness resulting from non-participating individuals. The variables used to perform the weighting were age, gender, educational level, country of birth, household composition and urban/rural.[52] These results were very similar, which was expected since the intersectional variable included all weighting variables except rural/urban. Our study represents the Swedish circumstances so the AIHDA-approach should be replicated in different contexts.

A further limitation of this study is the simple categorisations of the dimensions incorporated in the intersectional matrix. Gender was binary defined which neglects the existence of numerous gender identities. Migration status was binary defined as natives and immigrants, which may hide heterogeneity in smoking prevalence. A more detailed classification with four categories (ie, Sweden, Nordic countries, Europe and Outside Europe) shows that all the categories except women born outside Europe had a higher prevalence than the individuals born in Sweden (see online supplemental material 4). The used categorisations stem in part from the information available in the survey and in part from the aim of presenting a parsimonious intersectional model that is easier to adopt in public health analyses and by the fact that several strata would be empty or contain very few individuals if the intersectional matrix was expanded.

We also performed a sensitivity analysis excluding 'sometimes smokers' from the smoker category. As expected, overall prevalence was lower, 11% compared with 18%, and intersectional disparities larger. The AUC of the intersectional model 7 was 0.70 compared with 0.66 in the main analysis. Our main results combined with the results from the sensitivity analysis reflect the existence of socioeconomic disparities not only in prevalence, but also in intensity, of smoking.[53] Our results, therefore, may underestimate the intersectional disparities in health hazards attributable to smoking.

Implications and future studies

There is a growing body of literature focusing on how to perform quantitative intersectional research,[27 36] with the emergence of multilevel AIHDA (MAIHDA) as a recent example.[28 29 34] However, in spite of providing complementary information,[34] the fixed effects AIHDA approach we use in our study is rather accessible and share crucial advantages of the MAIHDA. First, the AIHDA provides an intersectional mapping that is more appropriate than unidimensional analyses to identify specifically vulnerable population groups in which interventions could be effective. Second, by going beyond average probabilistic measurements (ie, prevalence) and also analysing DA we get a quantification of the heterogeneity around the averages.[46] From the AIHDA, we found that the DA of our intersectional model was only moderate which indicates the necessity for universal interventions due to a large unexplained heterogeneity. However, we also identified that the three most vulnerable groups (ie, strata) included immigrant men with low education younger than 65 years. This finding suggests that special preventive measures should be directed to these groups. Furthermore, research methods that actively involves members of marginalised groups and has the explicit purpose to result in public health improvements are developing and could be one way forward.[54]

Interventions to reduce smoking prevalence should address Social Determinants of Health (SDH) at all levels. Examples targeted directly at smoking include increased tobacco taxation, smoke-free zones and public antismoking campaigns.[55] Stigmatisation is a negative side effect of such interventions that need to be taken into account, especially for low SEP groups.[56] Qualitative intersectional research has provided important insights into how the stigma of smoking interacts with identities of low class, country of birth, being a bad mother and may be in conflict with norms of femininity.[57]

Equal access to education, housing and healthy recreation, regardless of gender, socioeconomic status, migration status and household composition, is important to reduce smoking prevalence. Therefore, institutions outside the healthcare system play an important role to redistribute resources and access to SDH,[58 59] in order to counterweight the accelerating tendency of accumulation of resources among a very rich minority that characterises modern capitalism.[60] This requires political decisions that prioritise population health aims more than market-oriented reforms that exacerbate health inequities.[61] Health politics should adopt an intersectional perspective when redistributing resources in order to reduce the complex disparities in smoking revealed in this study.

CONCLUSIONS

Compared with studies focused on single variables, the intersectional AIHDA offers a better mapping of the socioeconomic and demographical distribution of smoking in Sweden. However, the moderate DA found in the AIHDA analysis suggested the existence of substantial unexplained heterogeneity in smoking risk within the different intersectional strata defined by age, gender, education, household composition and migration status. An intersectional AIHDA approach is necessary to understand the existing socioeconomic and demographic complexity influencing smoking behaviour. Future studies should identify preventive measures that are guided by proportionate universalism to find practical ways forwards to reduce intersectional disparities in smoking prevalence.

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