CONTEXTUAL AND INDIVIDUAL ASPECTS OF USE OF MEDICATION

Multilevel studies on anxiolytic-hypnotic drug use, social context, adherence to medication, and disability pension

Kristina Johnell

Stockholm 2005
No man is an island, entire of itself
every man is a piece of the continent, a part of the main

John Donne (1624)
ABSTRACT

Aims Public health research today is greatly interested in individuals and the context in which they live, e.g., the area or neighborhood of residence. People living within the same area may be more similar to each other than to people living in other areas. Similar people may move to similar areas, and they also share area specific economic, lifestyle, and social factors, and health care availability, which might influence health and health-related behavior, beyond individual characteristics. We aimed to study contextual and individual aspects of use of medication, with special reference to anxiolytic-hypnotic drug (AHD) use, social context, adherence to medication, and disability pension, by applying multilevel analysis. **Study I:** (i) to identify and quantify a hypothesized collective effect of the neighborhood on women’s AHD use, and (ii) to analyze the general impact of neighborhood social participation on use of these medicines. **Study II:** (i) to investigate whether women living in the same neighborhood have similar propensity for disability pension that relates to neighborhood social participation, and (ii) whether there is an association between AHD use and disability pension in women that is modified by the neighborhood context. **Study III:** to investigate (i) whether the contextual component of the miniaturization of community concept (i.e., area high social participation and low trust) is associated with individual AHD use, and (ii) whether people living in the same area share a similar probability of AHD use, and if so, how large this contextual phenomenon is. **Study IV:** to investigate (i) whether any of the individual characteristics age, educational level, financial strain, self-rated health, social participation, and trust in the health care system are associated with primary non-concordance with medication (i.e., non-redemption of prescription), and (ii) whether people living in the same area have similar probability of primary non-concordance with medication that relates to area social participation. **Study V:** to examine (i) whether individual low social participation is associated with low adherence to antihypertensive medication, and (ii) whether this possible association is modified by the municipality of residence.

Methods We used multilevel logistic regression analysis with individuals at the first level and areas (neighborhoods) at the second level. Both fixed effects (measures of association) and random effects (measures of variation) were investigated.

In Study I and II, we used baseline data from The Malmö Diet and Cancer Study, a prospective cohort study performed in Malmö, Sweden. The 17 388 women, aged 45-73 years, who participated in the cohort, represented 41% of all women born 1923-1950 living in Malmö during the baseline period 1991-1996. A questionnaire and a 7-day personal diary were used to obtain information on relevant characteristics of the women, including use of medication. **Study I:** Of the 17 388 women in the cohort, 89% (n=15 456), with complete information on the variables studied, were included. **Study II:** Of the 17 388 women in the cohort, 70% (n=12 156), aged less than 65 years and with complete information on the studied variables, were included. In Study III and IV, we used data from the Life & Health year 2000 survey. A random sample of 70 044 people, aged 18-79 years living in central Sweden, had the opportunity to answer the postal questionnaire and 46 636 (67%) returned the questionnaire. **Study III:** Of the 46 636 participants, 82% (n=39 195 women and 17 850 men) had complete information on all the studied variables, and were therefore included. **Study IV:** Of the 46 636 participants, we included the 34% who reported having visited an emergency department, a physician at a hospital department, a primary care physician, or been admitted to a hospital during the last 3 months, and with
complete information on all the variables studied (n=9 070 women and 6 795 men). In Study V, we used data from The Health Survey in Scania 2000, which was a postal questionnaire sent out to a random sample of 23 437 people aged 18-80 years living in Scania, Sweden. Study V: We included the 9.6% of the participants who indicated use of antihypertensives during the last year and who had complete information on all the variables studied (n = 1 288).

**Results** Study I: Overall, 1.7% of the total individual differences in the probability of using AHDs were explained by the neighborhood level. This percentage, however, differed between different groups of individuals. Neighborhood rate of low social participation was associated with higher probability of AHD use (odds ratio (OR)= 3.10 (95% confidence interval (CI) 1.51-6.41)), independently of individual age, social participation, education, and living alone. This association decreased (OR= 2.01 (95% CI 0.97-4.14)) after additional adjustment for individual disability pension, self-rated health, self-reported stress, and medication for somatic disorders. Study II: Both AHD use (OR= 2.09 (95% CI 1.65-2.65)) and neighborhood rate of low social participation (OR=11.85 (95% CI 5.09-27.58)), 80% interval odds ratio 7.49-18.74, were associated with higher propensity for disability pension, after adjustment for individual characteristics. The association between AHD use and disability pension was not modified by the neighborhood context. The median odds ratio was 1.44 after adjusting for individual characteristics and 1.27 after additional adjustment for neighborhood social participation. Study III: The contextual component of the miniaturization of community concept was associated with individual AHD use (ORwomen = 1.39 (95% CI 1.19-1.63), 80% interval odds ratio 1.05-1.86, and ORmen = 1.26 (95% CI 1.03-1.54), 80% interval odds ratio 0.89-1.78), after adjustment for the individual variables age, education, and financial strain. Additional adjustment for the combinations of individual social participation/trust did not substantially weaken the association (ORwomen = 1.34 (95% CI 1.15-1.56), 80% interval odds ratio 1.02-1.75, and ORmen = 1.22 (95% CI 0.99-1.49), 80% interval odds ratio 0.86-1.73). The variation in AHD use between the areas was fairly small. Study IV: Younger age, financial strain, low self-rated health, and low trust in the health care system were associated with primary non-concordance with medication. However, area social participation was not related to primary non-concordance, and the variation in primary non-concordance between the areas was small. Study V: Individual low social participation was associated with lower adherence to antihypertensives (OR = 2.05, 95% CI 1.05–3.99), after adjustment for age, sex, and education. However, after additional adjustment for self-rated health and psychological health, the association was not conclusive (OR = 1.80, 95% CI 0.90–3.61). Furthermore, the association between low social participation and low adherence to antihypertensives varied among municipalities in Scania (i.e., cross-level interaction).

**Conclusions** In the Swedish setting, our results indicate that the social context seems to influence individual use of AHD and disability pension, possibly through individual characteristics. However, administrative area boundaries seem to play a minor role in understanding individual AHD use. On the contrary, women living in the same neighborhood appear to have similar propensity for disability pension, beyond individual characteristics. In addition, AHD use might increase the propensity for disability pension in women. People with younger age, financial difficulties, low self-rated health, and low trust in the health care system may have a higher probability of primary non-concordance with medication. However, the area of residence—as defined by administrative boundaries—seems to play a minor role for primary non-concordance. Also, individual
low social participation seems to be associated with low adherence to antihypertensives, and this association may vary between different municipalities.

**Keywords** adherence to medication, anxiolytic-hypnotic drugs, disability pension, miniaturization of community, multilevel analysis, pharmacoepidemiology, social capital, social participation, trust
LIST OF PUBLICATIONS


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<td>Confidence interval</td>
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<td>ICC</td>
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1 INTRODUCTION
1.1 PHARMACOEPIDEMIOLOGY

Pharmacoepidemiology has been described as the study of the use and the effects of medication in a large number of people. The word pharmacoepidemiology contains two components: “pharmaco” and “epidemiology”, indicating that pharmacoepidemiology combines the fields of clinical pharmacology and epidemiology.\textsuperscript{1} It has been suggested that pharmacoepidemiology should more often investigate medication use within the context of cultural and social settings (Figure 1),\textsuperscript{2,3} which is the focus of this thesis.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{pharmaepi_overview.png}
\caption{Medication use in society: the need for a multidisciplinary approach}
\end{figure}

Source: Sterky et al. (1988).\textsuperscript{4}
1.2 CONTEXTUAL ASPECTS

Public health research today is greatly interested in individuals and the context in which they live, e.g., the area or neighborhood of residence.\(^5\)–\(^7\) People living within the same area may be more similar to each other than to people living in other areas. Similar people may move to similar areas, and they also share area specific economic, lifestyle and social factors, and health care availability, which might influence health and health-related behavior, beyond individual characteristics.\(^5\) Based on the ideas of the French sociologist Emile Durkheim (1858-1917),\(^9\) these contextual aspects were developed in Geoffrey Rose’s seminal work on the importance of distinguishing between the causes of individual cases of disease within a population, and the causes of differences in the rates of disease across populations.\(^10\)–\(^13\)

There is a large body of literature showing contextual effects,\(^14\) related to one’s area of residence, on health-related behavior, such as smoking,\(^15\)–\(^17\) obesity,\(^18\)–\(^19\) and physical activity,\(^18\) and also on diseases, such as coronary heart disease,\(^20\)–\(^22\) and mental disorders,\(^23\) and on self-rated health,\(^16\)–\(^24\)–\(^28\) and mortality.\(^29\)–\(^36\) However, there seems to be only a limited number of multilevel studies on contextual effects on medication use.\(^8\),\(^37\) Although many studies have shown contextual effects on health and health-related behavior, there are also other studies that have not found any contextual effects on mental health,\(^38\)–\(^40\) self-rated health,\(^41\) and physical activity.\(^42\) In addition, other types of contextual effects can be studied in public health research besides those related to the area of residence. In primary care research, investigators have tried to disentangle the effects of patient, physician, and health care facilities on different aspects of care-related outcomes.\(^43\)–\(^48\) Most studies in the field of research on contextual effects are observational. However, experimental data from families who moved from high-poverty neighborhoods to more affluent neighborhoods have shown that families who moved to the more affluent neighborhoods experienced less mental and physical health problems.\(^49\)\(^,\)\(^50\)

Use of medication is responsive to culture, history, and social context.\(^2\),\(^51\) Medication use may be determined by other factors than those strictly related to medical and pharmacological circumstances, such as the individual patient’s beliefs\(^52\) and expectations, and socioeconomic resources,\(^2\),\(^53\),\(^54\) and those kind of factors may be shaped by the area environment. Living in a disadvantaged area may affect the physical and mental health by increasing vulnerability directly or indirectly through diverse mechanisms like access to health services and other amenities, reduced opportunities for physical activity, stress, normative attitudes towards health, insecurity, social support, transmission of health information, and adaptation to health-behavior norms.\(^55\)–\(^58\) Such factors, related to the context in which you live, might, in turn, condition individual medication use, beyond individual characteristics.\(^8\)\(^,\)\(^37\)

Results from the limited number of published studies on contextual effects on anxiolytic-hypnotic drug (AHD) use have pointed in different directions, possibly because of the different statistical methods used. A multilevel regression study on benzodiazepine use showed only a small contextual effect.\(^37\) Two single level individual analyses with area variables did not find any significant contextual effects.\(^54\),\(^59\) One single level individual study found that rural location positively influenced AHD prescribing.\(^60\) Two single level ecological studies suggested an association between AHD use and area deprivation.\(^61\),\(^62\) “Contextual effects” is actually a rather vague
concept that, among many things, depends on the outcome under study (e.g., behavioral, medical), the geographical units (e.g., neighborhoods, municipalities, countries), and the statistical method used. This vagueness is especially apparent when comparing results from different studies. Therefore, in the studies in this thesis, we have tried to be clear about the materials and methods used regarding the contextual aspects.

1.2.1 Social capital and social participation

One aspect of the social context is the concept of social capital, which can be traced back to the work of the sociologist Durkheim. He emphasized the relationship between society and individual health, and aimed to explain individual pathology as a function of social dynamics. However, it is not clear who developed the first explicit definition of social capital. Nevertheless, Pierre Bourdieu and James Coleman were among the first social scientists who tried to define social capital. Bourdieu’s (1986) concept of social capital puts the emphasis on group membership and social networks, connected with his theoretical ideas on social class. According to Coleman in 1988, social capital consists of those features of social structures that facilitate collective action. In political science, the most prominent name regarding the social capital theory has been Robert Putnam who claimed the declining post-war social capital as explained by the disappearance of civic America. Social capital has since been defined as social structures and social relationships in a society, such as levels of trust, reciprocity, and interactions between inhabitants (group membership).

Further, social capital has been suggested to affect individual health by influencing health-related behavior, through diffusion of health information, maintenance of healthy norms, acting as a buffer against stressful life events, various forms of social support, and by exerting social control over deviant behavior. However, social capital may not always generate better health outcomes. Portes has pointed out four examples of negative consequences of social capital: exclusion of outsiders from social networks, free-riding problems when less hard-working members of the group enforce on the more successful all kinds of demands, demands for conformity and thereby restriction on individual freedom, and when group solidarity is cemented by a common feeling of opposition to mainstream society.

There is to date no consensus about how social capital should be measured and operationalized. Hence, the concept of social capital is criticized for being undertheorized and vague. Nevertheless, The Swedish National Committee for Public Health has proposed strengthening of the social capital and to give people opportunities for social participation as a health-political goal in Sweden. Also National Institutes of Health in the USA have mentioned social capital as an area where research should be expanded to enhance the understanding of social dimensions of health.

However, there is an ongoing debate about whether social capital should be a major focus of health and social policy. In particular, there have been discussions between proponents of a psychosocial versus a material explanation, where the former believes in the social capital theory and the latter is critical. The psychosocial explanation proposes that psychosocial factors, such as stress caused by exposure to daily adverse life circumstances, is the link between social capital and health. On the other
hand, the material explanation instead considers access to tangible material conditions and the distribution of private and public resources, i.e., macro level social and economic processes, to be what is really the explanation of epidemiological findings of connections between social capital and health. The main criticism the material explanation has against social capital is that social capital’s popularity and the psychosocial explanation have turned research on health inequalities away from social class and welfare, and “blames the victim” at the community level.

Moreover, a distinction between what is called bonding, bridging, and linking social capital has been suggested. It has been argued that this framework can help to reconcile the psychosocial and the material perspective on social capital. Bonding social capital refers to relations between members of networks who are similar. Bridging social capital, by contrast, refers to relations between people who are not alike in some socio-demographic sense (e.g., age, ethnic group, social class). Linking social capital, finally, refers to relations between people across formal power and authority.

Social participation describes how actively a person takes part in formal and informal activities, groups, and associations in society. Further, social participation is important for understanding the influence of social factors on individual health, and has been associated with smoking cessation, physical activity, coronary heart disease, self-rated health, and mortality. The neighborhood level of social participation has been considered as a structural component within the concept of social capital, and has been associated with use of hormone replacement therapy and mortality.

People with low socioeconomic status have been reported to have low levels of social participation, and, therefore, it is important to control for socioeconomic status in the analyses of the influence of social participation on health and health-related behavior.

### 1.2.2 Miniaturization of community

Another aspect of the social context related to social capital is what the historian Francis Fukuyama names “the miniaturization of community”, which is the phenomenon of high social participation combined with low trust. The idea of miniaturization of community may be an answer to the inconsistency in results regarding the association between social capital and health, caused by social relationships in a community that are not always beneficial to health. Also, the concept of miniaturization of community emphasizes that, both at the individual and at the community level, a high level of social participation can be accompanied by a low level of trust, which may, in turn, result in social disorder and lack of social cohesion. This social disorder may eventually be detrimental to health. Durkheim discussed these ideas already in 1897 in his work, *Suicide*, where he states, “Suicide varies inversely with degree of integration of the social groups of which the individual forms a part”.

Putnam argues that in the USA, social capital has declined during the late 20th century because people are less inclined to join large organizations for the benefit of small-scale activities. These new forms of social participation seem to be more individualistic than before and are practiced in more exclusive social networks, which do not particularly contribute to greater trust in other people. Fukuyama explains that over the past decades, groups and group membership have increased and trust in
other people has declined. Moreover, Fukuyama suggests that the radius of trust is diminishing, i.e., the circle that people trust is narrower. This results in a miniaturization of, and individualization within, the community.

The miniaturization of community concept has been empirically tested regarding tobacco smoking, cannabis smoking, self-rated health, patient satisfaction with primary health care, and consumption of home-made and smuggled liquor. Further, AHDs are mainly used to treat insomnia and anxiety disorders, conditions that may be affected by the miniaturization of community. When the radius of trust diminishes, the society becomes more disordered and people may tend to feel more insecure and anxious. Use of AHDs could thus be a coping strategy.

The concept of miniaturization of community has both an individual and a contextual component, to be compared with the discussion about the different levels of social capital. People who live in an area with a high level of miniaturization might experience impaired health, regardless of their own personal characteristics including their own level of social participation and trust.

1.3 INDIVIDUAL ASPECTS

As mentioned before, medication use may be determined by other factors than those strictly related to medical and pharmacological circumstances, such as the individual patient's beliefs and expectations, and socioeconomic resources.

1.3.1 Anxiolytic-hypnotic drug use

In the research literature, the reported prevalence of AHD use varies between 2% and 19%. This wide variation in reported prevalence of AHD use can largely be explained by different settings, definitions of AHD use, and observation periods. AHDs, mainly benzodiazepines, have been surrounded by much controversy during the last decades, foremost due to the associations between these drugs and tolerance, abuse, dependence, and abstinence problems. Therefore, AHD use should be monitored closely. Nevertheless, short-term therapy of insomnia, anxiety disorders, and withdrawal symptoms during alcohol detoxification is regarded as safe and effective, whereas long-term therapy should be avoided.

Besides these diagnoses related to mental health, other factors not directly related to formal medical indications have been reported as predictors for AHD use, such as age, sex, socioeconomic status, and somatic morbidity. Research has shown that AHD use increases with age and AHD use also seems to be twice as common among women as among men. However, the literature on the association between AHD use and socioeconomic status is not consistent. Most studies suggest that lower socioeconomic status positively correlates with AHD use. On the other hand, some studies have found the opposite relationship, or no association at all.

Also, use of AHDs can be a coping strategy. However, AHD use has been suggested to be an inappropriate coping strategy and may even decrease people’s capacity to cope with stress.
In addition, patients sometimes seem to obtain these drugs for somatic symptoms, such as back pain, headache, hypertension, and coronary heart disease, indications that lack scientific support. On the contrary, AHD use may have negative effects on health, mainly related to cognitive deterioration, impairment of driving skills, psychomotor function impairment, falls, and fractures.

### 1.3.2 Adherence to medication

The term adherence has been defined as ‘the extent to which a person’s behavior coincides with medical or health advice’. The terms compliance, adherence, and concordance have been used alternatively, although their meaning is somewhat different. Compliance was the first term used, but has been criticized for having negative connotations by suggesting submission and obedience by the patient, and an authoritarian and controlling role of the doctor. The term adherence, as used in study V, is widely used today, and reduces attribution of greater power to the doctor in the doctor-patient relationship and includes cooperation and partnership. We used the newest term concordance in study IV because we wanted to focus on trust and the term concordance implies agreement, trust, and harmony between patient and doctor, and acknowledges the patient as a decision maker, and a cornerstone is professional empathy.

Further, patient non-adherence may be divided into primary non-adherence, where the patient does not redeem the prescription, and secondary non-adherence, where the patient does not take the redeemed medication as prescribed. Most studies have focused on secondary non-adherence. Nevertheless, it is crucial to determine whether patients actually redeem their prescriptions from the pharmacy, because this is the first step in the complex phenomenon of adherence. Studies on primary non-adherence have reported non-redemption rates between 2% and 33%. However, these studies vary greatly regarding assessment of primary non-adherence, participants, and setting.

Adherence rates for long-term medication are estimated to be about 50%. The fact that about half of the patients do not take their medication as prescribed is a major public health problem that imposes a considerable financial burden on the health care system. Low adherence to medication weakens therapeutic effectiveness, increases health care service utilization, and may also generate adverse reactions. The World Health Organization (WHO) states that ‘Poor adherence is the primary reason for sub-optimal clinical benefit. It causes medical and psychosocial complications of disease, reduces patients’ quality of life, and wastes health care resources’. Patients’ reasons for not taking their medication as prescribed has been reported in qualitative studies to be, e.g., forgetfulness, reluctance to take drugs, fear of adverse effects of drugs, and drugs being a reminder of illness, and non-adherent patients have been reported to use more escape/avoidance coping strategies (e.g., escaping from the stressful situation, hoping for a miracle to happen, denial, disengagement) than adherent patients.

Despite the comprehensive research on adherence during the last decades, determinants of low adherence remain largely elusive and deserve further investigation. Individual socio-demographic factors, such as age, educational level,
and social support have been discussed as determinants of adherence to medication, however, the results are inconsistent.\textsuperscript{161, 162, 186-189} By contrast, the influence of contextual factors, related to one’s area of residence, have been scarcely investigated. Yet, over and above individual characteristics, patients’ adherence to medication might be related to the environment in which they live.\textsuperscript{161, 190}

Interventions to enhance patients’ adherence to medication have had modest effects.\textsuperscript{191, 192} Some of the most promising interventions have been complex, including information, counseling, reminders, and support by a health care provider.\textsuperscript{191, 193} Further, to achieve the best possibilities for patient adherence to medication, a multidisciplinary approach is needed where the physician, nurse, and pharmacist work together as partners.\textsuperscript{177, 194, 195}

1.3.3 Disability pension

The general idea of disability pension is to ensure the individual the right to economical security in case of impaired working capacity.\textsuperscript{196} The increasing number of people on disability pension in Sweden is of concern for Swedish policy makers. Data from the Swedish National Social Insurance Board show that over 500 000 people were on disability pension in 2003 compared to a labor force of about 4 million people.\textsuperscript{197} Further, in Sweden, expenditures for disability pension were about 50.2 billion SEK in 2001,\textsuperscript{196} which together with the costs for sickness absence equals the costs for the Swedish health care system.\textsuperscript{199} Also, it has been reported that men on disability pension continue to have increased health care utilization, unrelated to their retirement diagnosis, for a long time after receiving disability pension.\textsuperscript{200} Yet, despite the importance of disability pension, both for the individual and for the society, only a limited amount of research has been done in this field.\textsuperscript{201} There is a need for more research and a better understanding of the phenomenon and the mechanisms behind disability pension.\textsuperscript{202-204}

In 1995, musculoskeletal diseases accounted for 44\% of the disability pensions, mental disorders for 20\%, and diseases of the circulatory system for 11\%.\textsuperscript{196} In addition to conventional risk factors for disease, environmental characteristics, such as legislation, labor market, organizational characteristics and downsizing, physical and psychosocial work environment,\textsuperscript{205-208} and individual factors, such as sex,\textsuperscript{206, 209-212} socioeconomic status,\textsuperscript{205, 206, 210, 211, 213-217} social support,\textsuperscript{218} life dissatisfaction,\textsuperscript{219} physical fitness,\textsuperscript{220} and health-related lifestyle\textsuperscript{205, 221} may influence the probability for an individual to become a disability pensioner.\textsuperscript{196} Disability pension has also been suggested to be related to a high use of prescribed medicines.\textsuperscript{222-224}

Moreover, concepts of work, disease, illness, and disability are to a great extent culturally defined and, consequently, influenced by the social structure in the community.\textsuperscript{196, 211, 225} Disability pension may thus be affected by factors at different levels, e.g., factors in the labour market and in communities, and by individual factors.\textsuperscript{204} Therefore, contextual factors, related to one’s area of residence, could be placed upstream\textsuperscript{9} in the chain of events leading to disability pension. Two Norwegian studies have found that the level of deprivation in the area is related to disability pension.\textsuperscript{226, 227} In addition, a Swedish study observed that there appear to be variations in praxis of rejection of applicants for disability pension between Social Insurance boards in different geographical areas, due to other reasons than medical.\textsuperscript{228}
Furthermore, the Swedish National Social Insurance Board has reported that the differences in expenditure for disability pension and sickness benefit in Swedish municipalities can be explained to about 50% by demographic and socio-economic composition and the labour market in the municipalities. The Swedish National Social Insurance Board suggests that the answer to the unexplained 50% of the differences may be found in regional variations in culture and attitudes. This Scandinavian research suggests that different aspects of the environment can affect the probability of disability pension.

Moreover, researchers in the multidisciplinary field of occupational health suggest that women have been less often studied in occupational health and encourage more research where sex is not merely treated as a confounder, but rather that men and women are studied separately.

AHDs are often used to treat mental disorders and withdrawal symptoms during alcohol detoxification. In addition, patients sometimes seem to obtain these drugs for somatic symptoms such as back pain, headache, hypertension and coronary heart disease. All these diagnoses are, as mentioned before, main causes of disability pension in Sweden. However, previous longitudinal research in middle aged men has indicated that AHD use may predict future disability pension. This observation may reflect not only that AHD use is a proxy for disease, eventually leading to disability pension, but also that these drugs may have an independent negative effect on health and increase the probability of disability pension.

1.4 MULTILEVEL MODELING

Data in public health research are frequently ordered in a hierarchical fashion. For example, people live in areas, patients are managed by physicians, and physicians practice within primary health care centers or hospitals. Multilevel analysis deals with hierarchically structured data, such as in this thesis, a hierarchy of two levels with individuals at level 1 and areas (neighborhoods) at level 2.

In recent years, public health research has become more and more interested in analyzing the connections between individuals and the context in which they live, e.g., the area or neighborhood of residence. However, the insight that where you live makes a difference to your health is not new. The main interest nowadays has been whether the context in itself is directly of importance for health, i.e., “contextual” effects. Conversely, variations in individual health status between different geographical areas may arise from the tendency for particular people, who may be more likely to become ill due to their individual characteristics, to live in particular places, i.e., “compositional” effects. Thus, the key question is not only whether variations between different areas exist but what is their origin. Nevertheless, it has been argued that the distinction between people and areas, composition and context, is somewhat artificial. As Macintyre and Ellaway emphasize “People create places, and places create people”. Many of the individual variables controlled for as compositional confounders in contextual analyses, may in fact be mediators on the pathway between area and individual health.

Multilevel modeling techniques can separate contextual from compositional effects, because multilevel modeling handles both people and context simultaneously within one model. In contrast, traditional statistical modeling techniques only operate at one
single level. There are two possible single level approaches, which both have their problems when analyzing contextual effects. Single level ecological analyses use only aggregated data, and can, therefore, be susceptible to the “ecological fallacy”, i.e., when aggregate level associations are wrongly inferred to exist at the individual level.\(^5^,\, ^6\) In the second single level approach, only individual level data are used, which is prone to the “atomistic fallacy”, i.e., when individual level associations are wrongly inferred to exist at the aggregated level.\(^5\)\(^,\)\(^241\) Besides the problem with the atomistic fallacy, only using individual level data is also associated with a statistical problem in determining the significance of associations. If the outcome varies across areas, individuals cannot be considered as independent observations. Ignoring the lack of independence in the observations may result in underestimation of the standard error and, hence, in false statistical significant associations.\(^6\)\(^,\)\(^233\)\(^,\)\(^242\)\(^\text{-}\)\(^244\) Moreover, ignoring relevant area level variables in a study of individual level associations may lead to the “psychologistic fallacy”, i.e., assuming that individual level outcomes can be explained exclusively in terms of individual level characteristics. Analogously, ignoring the role of individual level characteristics in a study of areas may lead to the “sociologistic fallacy”, i.e., assuming that area level outcomes can be explained exclusively in terms of area level characteristics.\(^7\) Studies that have compared multilevel analysis with traditional statistical modeling have found that the measures of association (e.g., beta coefficients, odds ratios) are overestimated and the standard errors are underestimated in traditional statistical modeling.\(^233\)\(^,\)\(^245\)\(^,\)\(^246\) Furthermore, multilevel analysis can also examine the variance between areas and, therefore, investigate whether the area of residence matters for an individual outcome.\(^246\)

To simplify, one may separate the multilevel analysis into two parts: the fixed effects and the random effects.\(^244\) The fixed effects show the strength of the association (e.g., beta coefficient, odds ratio) between variables. The random effects display the geographical differences and variance at different levels in the multilevel analysis.\(^243\),\(^246\) Multilevel models are not only concerned with the “average” or “fixed effects”, but about how people and areas vary (health variation), and encourage us to think along the lines of “who you are depends on where you are”.\(^247\) Unfortunately, though, measures of health variation (i.e., the random effects, for example, the area variance, the intraclass correlation, clustering) have been underused in multilevel epidemiology. The analysis of health variation convey that people living within the same area may be more similar to each other than to people living in other areas regarding health outcome variables.\(^13\)

The power to detect the random effects in a multilevel analysis is affected by the number of areas and the number of individuals per area in a different manner than the power to detect the fixed effects. Thus, a study may have insufficient power to detect the random effects and yet have sufficient power to detect the fixed effect of an area variable. Therefore, one should be wary of concluding that contextual or area effects are not present based on the statistical significance of the area variance.\(^244\)\(^,\)\(^248\) A small variance between areas may give enough contrast of exposure to detect an association between an area variable and an individual outcome.\(^13\) Also, a small area variance may hide that the magnitude of a contextual effect may differ for different groups of people.\(^249\) Further, an area variance of zero does not automatically mean that the area context is not important for the individual outcome under study. Rather, an alternative explanation could be that the geographical boundaries used to define the areas in a
study do not correspond to the boundaries that shape the environment relevant to the individual outcome. Moreover, as individual level explanatory variables are entered into the multilevel model, the area variance may increase, meaning that in the adjusted models the between-area differences can actually become more pronounced. Therefore, it may be rash to decide whether between-area differences are present based on the area variance in the empty model where no individual variables are included.

In multilevel linear regression, the partition of variance between different levels and the computation of measures of clustering have more intuitive interpretations than in the multilevel logistic regression. The area-level variance and the individual-level variance in the multilevel logistic regression are not directly comparable because the area-level variance is on the logistic scale and the individual-level variance is on the probability scale. Despite this difficulty, methods and measures have been developed in multilevel logistic regression to obtain interpretable information on area-level variance and clustering within areas. Two of these methods are a) the simulation method; and b) the linear threshold method, or latent variable method. The simulation method translates the area-level variance from the logistic to the probability scale in order to have both components of variance on the probability scale. The linear threshold model or latent variable method converts the individual-level variance from the probability scale to the logistic scale in order to have both components of variance on the logistic scale.

The studies in this thesis have used four measures of the random effects in multilevel logistic regression: area variance, intraclass correlation (ICC), median odds ratio (MOR), and interval odds ratio (IOR). Area variance describes the differences between the areas regarding average estimates of an outcome in the respective areas. The ICC is a measure of the degree of resemblance between individuals living in the same area. It can also be defined as the proportion of the variance in the outcome that is between the areas. The MOR measures the area variance as an odds ratio and can be compared with other odds ratios in the analysis. The IOR integrates random effects (i.e., the area variance) in the measurement of fixed effects (i.e., the area variable). In addition, we performed random slope analysis, which gives information about whether the association between the individual explanatory variable and the individual outcome varies among the areas (i.e., cross-level interaction). If random slope variance is present in the multilevel analysis, the area variance becomes a function of individual variables. For a more detailed description of these measures of random effects, see the Methods section.

The generalized estimating equations (GEE) method has been suggested as an alternative in epidemiological research with different levels. This method, however, aims to provide acceptable estimates for the standard error around the point estimate (e.g., odds ratio), treating the existence of any random effects as a ‘nuisance’ that needs to be adjusted for in the analysis, but not explicitly investigated. Nevertheless, second order GEE has been used for analysis of variance and clustering.
2 AIMS

2.1 GENERAL AIM

To study contextual and individual aspects of use of medication, with special reference to AHD use, social context, adherence to medication, and disability pension, by applying multilevel analysis.

2.2 SPECIFIC AIMS

2.2.1 Study I

The aims of this study are (i) to identify and quantify a hypothesized collective effect of the neighborhood on women’s AHD use, and (ii) to analyze the general impact of neighborhood social participation on use of these medicines.

2.2.2 Study II

The aims of this study are to investigate (i) whether women living in the same neighborhood have similar propensity for disability pension that relates to neighborhood social participation, and (ii) whether there is an association between AHD use and disability pension in women that is modified by the neighborhood context.

2.2.3 Study III

The aims of this study are to investigate (i) whether the contextual component of the miniaturization of community concept (i.e., area high social participation and low trust) is associated with individual AHD use, and (ii) whether people living in the same area share a similar probability of AHD use, and if so, how large this contextual phenomenon is.

2.2.4 Study IV

The aims of this study are to investigate (i) whether any of the individual characteristics age, educational level, financial strain, self-rated health, social participation, and trust in the health care system are associated with primary non-concordance with medication (i.e., non-redemption of prescription), and (ii) whether people living in the same area have similar probability of primary non-concordance with medication that relates to area social participation.

2.2.5 Study V

The aims of this study are to examine (i) whether individual low social participation is associated with low adherence to antihypertensive medication, and (ii) whether this possible association is modified by the municipality of residence.
3 MATERIALS

3.1 THE MÅLÖ DIET AND CANCER STUDY

In Study I and II, we used baseline data from The Malmö Diet and Cancer Study, a prospective cohort study performed in the city of Malmö in southern Sweden. The city had a population of about 250,000 inhabitants in 1995 and was administratively divided into 110 neighborhoods. We included 95 neighborhoods, leaving out 15 neighborhoods which each had less than 20 participants in the The Malmö Diet and Cancer Study. We set an arbitrary limit of 20 participants to reduce bias regarding the measurement of information about the neighborhoods.

People were requested to participate in the The Malmö Diet and Cancer Study by letters of invitation, information through advertisements in the local media, and collaboration with major employers in Malmö. In total, letters of invitation provided 80% of the participants.

The 17,388 women, aged 45-73 years, who participated in the The Malmö Diet and Cancer Study cohort, represented 41% of all women born 1923-1950 living in Malmö during the baseline period 1991-1996.

A self-administered questionnaire and a 7-day personal diary were used to obtain information on relevant characteristics of the women, including use of medication. Each participant completed both information sources at home within one to two weeks between the first and the second consecutive baseline visits to the project office. All participants in Study I and II gave information in both the questionnaire and the diary.

A detailed description of the design and aims of the cohort study is given elsewhere.

3.1.1 Study sample in Study I

Of the 17,388 women in the cohort, 89% (n=15,456) were included in this study. Reasons for exclusion were lack of information on the studied variables and living in neighborhoods with less than 20 participants in the The Malmö Diet and Cancer Study.

3.1.2 Study sample in Study II

Of the 17,388 women in the cohort, 70% (n=12,156) were included in this study. Reasons for exclusion were age over or equal to the official retirement age in Sweden of 65 years, lack of information on the studied variables, and living in neighborhoods with less than 20 participants in the The Malmö Diet and Cancer Study.
3.2 THE LIFE & HEALTH YEAR 2000 SURVEY

In Study III and IV, we used data from the Life & Health year 2000 survey, a postal questionnaire administered by Statistics Sweden. A random sample of 70,044 people, aged 18-79 years from 58 municipalities in six regions in central Sweden (Södermanland, Uppsala, Värmland, Västmanland, and Örebro county, and south Dalarna), had the opportunity to participate in the survey and 46,636 (67%) returned the questionnaire. The survey had the purpose of generating self-reported information about people’s life and health in the area and was complemented with register data on age, sex, place of residence, and educational level.263

The areas in Study III and IV correspond to municipalities, except for Uppsala, Västerås, and Örebro (the three largest cities in the sample region), which were divided into ten, eight, and five smaller urban areas, respectively. In total, there were 78 areas.

3.2.1 Study sample in Study III

Of the 46,636 participants, 82% (n=20,319 women and 17,850 men) had complete information on all the variables studied, and were therefore included.

3.2.2 Study sample in Study IV

Of the 46,636 participants, we included the 34% who reported having visited an emergency department, a physician at a hospital department, a primary care physician, or been admitted to a hospital during the last 3 months, and with complete information on all the variables studied (n=9,070 women and 6,795 men).

3.3 THE HEALTH SURVEY IN SCANIA 2000

In Study V, we used data from The Health Survey in Scania 2000, a postal questionnaire sent out to a random sample of 23,437 individuals aged 18-80 years. The purpose of the survey was to obtain information about health conditions and different types of health hazards among the inhabitants of Scania.264 The province of Scania in southern Sweden had a population of about 1.2 million inhabitants in 2000 and was divided into 33 municipalities. In total, 13,715 (59%) participated, of which 98% had complete information about medication use.

3.3.1 Study sample in Study V

We included the 9.6% of the participants who indicated use of antihypertensives during the last year and who had complete information on all the variables studied (n = 1,288).
4 METHODS

4.1 OUTCOME VARIABLES

4.1.1 Study I

Anxiolytic-hypnotic drug (AHD) use
We obtained information on medication use from both the self-administered questionnaire and the 7-day personal diary. In the self-administered questionnaire, women listed brand name(s) of the drug(s) they used regularly, and in the 7-day personal diary the medicines they used during the week. Thereafter, all brand names were classified in accordance with the 1997 version of the Anatomical Therapeutic Chemical classification system (ATC-97).\textsuperscript{265,266} AHD use (dichotomous) was defined by the codes N05B (anxiolytics), N05C (hypnotics and sedatives), and N03AE (benzodiazepine derivatives).

4.1.2 Study II

Disability pension
Disability pension (dichotomous) was defined by self-reported retirement when being 64 years old or younger.

4.1.3 Study III

Anxiolytic-hypnotic drug use
Anxiolytic-hypnotic drug use (dichotomous) was assessed by the question “During the last 2 weeks, have you used a prescribed tranquillizer or sleeping medicine?”

4.1.4 Study IV

Primary non-concordance with medication
Primary non-concordance (dichotomous) was assessed by the question “During the last 3 months, have you received a prescription for medicine, but not redeemed the medicine?”

4.1.5 Study V

Low adherence to antihypertensives during the last two weeks
Use of antihypertensives was based on an affirmative answer to the question "Have you during the last year used medicine, which was bought at the pharmacy...?" and indicating "Medication for high blood pressure"
Low adherence to antihypertensives during the last two weeks (dichotomous) was based on the question "Have you used (this) medicine during the last year, but not during the last 2 weeks?" Those participants who answered yes were considered to have low adherence.

4.2 EXPLANATORY VARIABLES

Age
Study I: Age was categorized into four groups: 45-49 (reference), 50-59, 60-69, and 70-73 years.
**Study II**: Age was categorized into four groups: 45-49 (reference), 50-54, 55-59, and 60-64 years.

**Study III and IV**: Age was categorized into four groups: 18-34 (reference Study III), 35-49, 50-64, and 65-79 years (reference Study IV).

**Study V**: Age was categorized into five groups: 18-34 (reference), 35-44, 45-54, 55-64, and 65-80 years.

*Individual social participation*

**Study I, II, and V**: Individual social participation was defined by possible involvement in 13 formal or informal activities (study circle/course at work place, other study circle/course, union meeting, meeting of other organizations, theatre/cinema, arts exhibition, church, sports event, letter to editor of a newspaper/journal, demonstration, night club/entertainment, large gathering of relatives, private party), which the respondent might have participated in during the previous 12 months. Items were summed, and participants with involvement in three or fewer activities (lowest quartile) were classified as having low social participation (dichotomous).

**Study III and IV**: Individual social participation was defined by active membership in a labor union, political party, council/board, community center, sports association, cultural association/choir/orchestra/theater group, etc., religious association/community, or other association. Participants without any active membership in any of these associations were considered to have low social participation, otherwise seen as having high social participation (dichotomous).

*Neighborhood social participation*

**Study I and II**: Neighborhood low social participation was assessed by the proportion of women in the neighborhood who were classified as having individual low social participation.

*Area social participation*

**Study III and IV**: Area low social participation was based on a larger sample from the Life & Health year 2000 survey (20 715 women and 18 190 men), and established by the proportion of participants in the area who were classified as having individual low social participation. Area low social participation was then divided into tertiles.

*Individual trust*

**Study III**: The participants indicated whether they thought people living in their area could be trusted, by responding to the statement “The people in my area can be trusted”. Individual trust was then dichotomized into low trust (“do not agree”/“do not particularly agree”) and high trust (“agree”/“agree to some extent”).

*Area trust*

**Study III**: Area low trust was based on a larger sample from the Life & Health year 2000 survey (20 715 women and 18 190 men), and established by the proportion of participants in the area who were classified as having individual low trust. Area low trust was then divided into tertiles.
The individual component of the miniaturization of community concept

**Study III**: The individual combinations of social participation and trust resulted in four categories: (i) high social participation/high trust (used as reference); (ii) high social participation/low trust (the individual component of the miniaturisation of community concept); (iii) low social participation/high trust; and (iv) low social participation/low trust.110

The contextual component of the miniaturization of community concept

**Study III**: Area high social participation/low trust (the contextual component of the miniaturization of community concept) was based on the larger sample from the Life & Health year 2000 survey (20,715 women and 18,190 men), and established by the proportion of participants in the area who were classified as having individual high social participation/low trust (the individual component of the miniaturization of community concept). Area high social participation/low trust was then divided into tertiles.

Trust in the health care system

**Study IV**: Trust in the health care system was assessed by a categorical question and dichotomized into “not particularly high trust/no trust/have no opinion” (low trust in the health care system) and “very high trust/fairly high trust”.

Educational level

**Study I and II**: Low educational level (dichotomous) was defined as <9 years of education.

**Study III, IV, and V**: Low educational level (dichotomous) was defined as ≤9 years of education.

Financial strain

**Study III and IV**: Financial strain was assessed by a negative answer to the question, “Would you manage to raise 18 000 SEK in 1 week?” (dichotomous).

Living alone

**Study I and II**: Participants reported whether they were living alone (dichotomous).

Self-rated health

**Study I and II**: An ordinal scale ranging from 1 (“Very bad”) to 7 (“Very good”) determined self-rated health. Low self-rated health (dichotomous) was defined as a value of <4 on this scale.8

**Study IV**: Self-rated health was assessed by a categorical question and dichotomized into “neither good nor bad/bad/very bad health” (low self-rated health) and “good/very good health”.

**Study V**: Poor self-rated health (dichotomous) was defined as a value of ≤3 on an ordinal self-rated health scale ranging from 1 (“Very bad”) to 7 (“Very good”).269

Psychological health

**Study V**: Poor psychological health (dichotomous) was determined by giving three or more affirmative answers to the 12 items composing the Standardized General Health Questionnaire (GHQ-12).270
Use of medication for somatic disorders
Study I and II: Medication for somatic disorders (dichotomous) was defined as use of any pharmaceutical drug except those in the ATC-group N (nervous system).

Self-reported stress
Study I: Participants reported whether or not they felt psychological stress outside the work place (dichotomous).

Disability pension
Study I: (see section 4.1.2 above)

Anxiolytic-hypnotic drug use
Study II: (see section 4.1.1 above)

4.3 STATISTICAL ANALYSIS
4.3.1 Multilevel logistic regression analysis
We used multilevel logistic regression analysis with individuals at the first level and areas (neighborhoods) at the second level.

4.3.1.1 Modeling
Study I: We constructed four models. The first model, an empty model, was without the explanatory variables (i.e., simple component of variance analysis). The second model contained age together with one other variable at a time. The third model was created to observe whether neighborhood social participation affected individual AHD use, over and above the individual variables age, low educational level, low social participation, and living alone. The fourth model included all the studied variables.

Study II: We constructed four models. The first model was an empty model. The second model contained age together with AHD use. The third model also included low social participation, low educational level, living alone, low self-rated health, and use of medication for somatic disorders, as these individual factors may be confounders in the association between AHD use and disability pension. The fourth model was created to observe whether neighborhood low social participation affected individual disability pension, beyond the individual factors age, AHD use, low social participation, low educational level, living alone, low self-rated health, and use of medication for somatic disorders.

Study III: We performed four sets of analyses. In the first set of analyses (model i), we analyzed separate age-adjusted models with individual low social participation, individual low trust, and the combinations of these. In the second set of analyses (model ii), we analyzed separate models similar to those in model i, with the additional adjustment for education and financial strain. In the third set of analyses (model iii), we separately investigated the influence of the three area level variables, especially the influence of the contextual component of the miniaturization of community concept (i.e., the proportion of participants with high social participation/low trust) on individual AHD use, after adjusting for the individual characteristics age, education,
and financial strain. In the fourth set of analyses (model iv), we separately analyzed the area level variables, after adjusting for age, education, financial strain, and the combinations of individual social participation and trust.

**Study IV**: We constructed three models. The first model i was an empty model. In model ii, we included the individual variables age, education, financial strain, self-rated health, social participation, and trust in the health care system. In model iii, we added the area variable area low social participation.

**Study V**: We constructed three models. The first model i was created to study the influence of individual low social participation on low adherence to antihypertensives during the last two weeks, after adjusting for age and sex. The second model ii was extended to also include low educational level, because low educational level could be a confounder in the association between low social participation and low adherence to antihypertensives during the last two weeks. The third model iii additionally contained poor self-rated health and poor psychological health, because these variables may confound the association between low social participation and low adherence.

4.3.1.2 **Fixed effects (measures of association)**

The results are shown as odds ratios (ORs) with 95% confidence intervals (CIs).

4.3.1.3 **Random effects (measures of variation)**

The intraclass correlation (ICC)

**Study I, II, III, and IV**: We examined whether the area (neighborhood) environment affected the general probability of the individual outcomes (AHD use, disability pension, and primary non-concordance), beyond individual characteristics. This possible contextual effect was measured by the intraclass correlation (ICC). The ICC represents the percentage of the total variance in the probability of the individual outcome that is related to the area level, and is also used as a measure of clustering of the outcome in the areas. The ICC is a simple form of the ‘variance partition coefficient’ (VPC). 254

For dichotomous variables, e.g., use of AHD, the ICC can be calculated by the linear threshold method (latent variable method) according to the formula used by Snijders and Bosker244 (pp. 223-226):

\[
\text{ICC} = \frac{V_n}{V_n + \frac{\pi^2}{3}}
\]

\(V_n = \) neighborhood (area) variance

Calculated in this way, the ICC represents the average ICC for all individuals.254, 272 A high ICC in the empty model would indicate high clustering of the outcome, e.g., AHD use, in the areas and a strong area effect on the individual outcome. A low intraclass correlation, on the other hand, would express the existence of a weak area influence on the individual outcome.

In Study I, in separate models, we performed several multilevel logistic regression analyses with the individual variables (i.e., low social participation, low educational
level, living alone, disability pension, low self-rated health, self-reported stress, missing information on stress, and medication for somatic disorders) as dependent variables. Analyses of the ICC allowed quantification of the degree to which these individual socioeconomic and health-related factors were clustered within the areas.

The Median odds ratio (MOR)

Study II, III, and IV: We examined whether the area (neighborhood) of residence had a contextual effect on the individual outcomes (disability pension, AHD use, and primary non-concordance), in other words, if people living in the same area had a similar probability of the outcomes, beyond individual characteristics. This hypothesized contextual effect was measured by the MOR. Following the ideas of Larsen et al. and of Larsen and Merlo on area effects, we wanted to report the random effects in the multilevel logistic regression in terms of odds, as one of the advantageous properties of the logistic regression is that it allows associations (i.e., fixed effects) to be presented as odds ratios. The MOR measures the area variance as an odds ratio. If MOR is equal to one, there is no area variance. Conversely, the higher the MOR, the more important are the contextual effects for understanding the probability of the individual outcomes.

The MOR estimates the probability of the individual outcomes that can be attributed to the area context. In simple terms, the MOR indicates how much (in median) the probability of a dichotomous outcome would increase if an individual would move to another area with a higher prevalence of the outcome.

Because MOR is in the form of an odds ratio, it can be compared with other odds ratios in the analysis. This possibility of comparisons with other odds ratios makes the MOR understandable and useful in epidemiological terms. The MOR is theoretically calculated by doing pair-wise comparisons between individuals from different areas. If area variance is present, one of the individuals in the pair will have a higher OR for disability pension. If we perform all possible combinations of pair-wise comparisons we will get a distribution of pair-wise ORs. The MOR is the median of this distribution. In practice, it is not necessary to calculate all possible pair-wise comparisons of individuals from different areas. The MOR directly depends on the area level variance and can be computed with the following formula:

\[
MOR = \exp\left[\sqrt{(2 \times V_n)} \times 0.6745\right] \approx \exp(0.95 \times \sqrt{V_n})
\]

where \(V_n\) is the second level (neighborhood or area) variance and 0.6745 is the 75th percentile of the standard normal distribution with mean zero and variance one.

The interval odds ratio (IOR)

The IOR integrates random effects (i.e., the area variance) in the measurement of fixed effects (i.e., the area variable). Consider two individuals with different values of an area variable, \(x_1\) and \(x_2\) (e.g., low and high area social participation). The IOR is theoretically calculated by doing pair-wise comparisons, based on the area variable, estimated as odds ratios. The 80% IOR then forms an interval around the odds ratio for the area variable, covering the mid 80% of the pair-wise odds ratios. In practice, it is not necessary to calculate all possible pair-wise comparisons of individuals from different areas.
The lower and upper limits of the 80% IOR can be computed with the following formula:

\[
\text{IOR}_{\text{lower}} = \exp[\beta + \sqrt{2 \times V_n} \times (-1.2816)] \approx \exp(\beta - 1.81 \times \sqrt{V_n})
\]

\[
\text{IOR}_{\text{upper}} = \exp[\beta + \sqrt{2 \times V_n} \times (1.2816)] \approx \exp(\beta + 1.81 \times \sqrt{V_n})
\]

where \(V_n\) is the second level (neighborhood or area) variance, and -1.2816 and 1.2816 are the 10th and 90th percentiles of the standard normal distribution with mean zero and variance one.

The IOR is narrow when the between-area variance is small, and it is wide when the between-area variance is large. If the IOR contains one, the remaining unexplained area variance is large compared with the effect of the area variable. If the IOR does not contain one, the effect of the area variable is large compared with the unexplained variance between areas. According to the model, the odds ratios can take any value between zero and infinity. However, to make the IOR useful and understandable, it has been suggested to report an 80% interval, because it covers a large fraction of the odds ratios. Note that the IOR is not a confidence interval.

An extended explanation of the MOR and the 80% IOR can be found elsewhere.252, 253

Random slope analysis

**Study I, II, and V:** We analyzed cross-level interactions by letting the slopes of the associations between the individual explanatory variables and the individual outcomes vary at the area level. Random slope variance indicates whether the association between the explanatory variable and the outcome is different in different areas, and whether the area level modifies associations between individual level variables.

In Study V, we also calculated the covariance between intercept and slope residuals. The covariance gave information about whether the association between low social participation and low adherence to antihypertensives during the last two weeks depended on the prevalence of low adherence in the different municipalities.

**4.3.1.4 Parameter estimation**

**Study I, II, III, and V:** Parameters were estimated using the restricted iterative generalized least squares (RIGLS) and penalized quasilikelihood (PQL). Extra-binomial variation was explored systematically in all models and we found no evidence of under- or over-dispersion. The MLwiN software255, 273 was used for the analyses.

**Study IV:** Parameters were estimated using the Markov Chain Monte Carlo (MCMC) procedure. The MCMC procedure is regarded to give a more accurate estimate of the area variance than the maximum likelihood or the penalized quasilikelihood methods.274-276 The Deviance Information Criterion (DIC) was used as a measure of how well our different models fitted the data. A lower value on DIC indicates a better fit of the model.275 The MLwiN software, version 2.0, 273 was used for the analyses.
4.4 ETHICS

The ethical committee in Lund approved the study proposal of the The Malmö Diet and Cancer Study (Dnr LU 51-90, 1990), the proposal of our studies on the Life & health year 2000 survey (Dnr 788/2004, 2004), and the study proposal of The Health Survey in Scania 2000 (Dnr LU 179-99, 1999).
5 MAIN RESULTS

5.1 STUDY I

The prevalence of AHD use was 5.5% in the study sample.

AHD users had an impaired health and socioeconomic profile, with lower social participation (Table 2). The median (1st-3rd quartile) neighborhood low social participation was 29.3% (22.9%-36.7%). Table 2 shows that as the percentage of women with low social participation within the neighborhoods increased from low (Group 1) to high (Group 4), the women’s health, behavior, and socioeconomic profiles were impaired. Further, on average, there was a modest neighborhood clustering of AHD use (ICC=1.7%). However, Table 2 suggests socioeconomic clustering in the neighborhoods as illustrated by the ICC for the individual variables living alone (ICC=20.3%), low educational level (ICC=14.5%), low social participation (ICC=7.0%), and disability pension (ICC=8.9%). In contrast, the clustering was very small (ICC around 1% or less) regarding the health-related variables.

Fixed effects

In Model $ii$, neighborhood social participation and individual social participation were associated with higher individual probability of AHD use (Table 3). Model $iii$ showed that, independently of each other, both individual and neighborhood social participation were associated with AHD use. After inclusion of all the individual variables in model $iv$, the association between the neighborhood variable and AHD use was weakened and not conclusive (OR=2.01 (95% CI 0.97-4.14)).

Further, I have made additional analyses with a division of the neighborhood rate of low social participation into tertiles. In model $ii$, living in the tertile of neighborhoods with the highest compared to the lowest rates of low social participation was associated with higher individual probability of AHD use (age adjusted OR=1.38 (95% CI 1.14-1.66)), and also in model $iii$ (OR=1.24 (95% CI 1.04-1.48)), after adjusting for individual low social participation, low educational level, and living alone. However, the association between living in the tertile of neighborhoods with the highest compared to the lowest rates of low social participation and individual probability of AHD use was not conclusive in model $iv$ (OR=1.13 (95% CI 0.95-1.35)), after adjustment for all the individual variables.

Random effects

Model $i$ (empty model) revealed that only a relatively small percentage of the total individual variability in the probability of using AHD was attributable to the neighborhood level (ICC= 1.7%, see Table 3).

The multilevel technique is still under development, and in the time of submission of Study I, we did not use the MOR or the IOR. However, the MOR, calculated in retrospect, in model $i$ indicated that, hypothetically, a woman would (in median) increase her probability of AHD use with 25% (MOR=1.25) if she moved to a neighborhood with higher rate of AHD use. In model $ii$, with age, self-reported stress, and missing information on self-reported stress, the MOR was 1.18 for those who were not stressed and 1.84 for those who did not answer the question on stress. In model $iii$,
the MOR was 1.00 and in model iv, with all the variables in the same model, the MOR was 1.03 (Table 4).

The IOR, calculated in retrospect, did not include one in model ii, iii or iv and, hence, the effect of the neighborhood rate of low social participation was large compared with the unexplained variance between the neighborhoods (Table 3).

The random slope analysis suggested that the neighborhood modified the association between certain individual level variables and AHD use (Figure 2 and 3). Figure 3 shows the predicted probability of using AHD in function of self-reported stress. Both the women who reported stress (ICC=2.1%) and those who did not answer this question (ICC=11.1%) had a higher probability of AHD use, compared with women who were not stressed. The strength of the association was, however, different for different neighborhoods.
Table 2. Characteristics of the 15 456 women residing in 95 neighborhoods in the city of Malmö, Sweden (1991-1996). Values are percentages unless otherwise indicated.

<table>
<thead>
<tr>
<th></th>
<th>ICC*</th>
<th>Use of AHD</th>
<th>Neighborhood quartile groups of increasing rate of low social participation (mean %)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Use of AHD</td>
<td>1.7</td>
<td>94.5</td>
<td>5.5</td>
</tr>
<tr>
<td>Age</td>
<td>6.0</td>
<td>57.3</td>
<td>60.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mean years</td>
<td>mean years</td>
</tr>
<tr>
<td>Low social participation</td>
<td>7.0</td>
<td>29.5</td>
<td>42.6</td>
</tr>
<tr>
<td>Low educational level</td>
<td>14.5</td>
<td>38.7</td>
<td>42.6</td>
</tr>
<tr>
<td>Living alone</td>
<td>20.3</td>
<td>27.7</td>
<td>41.7</td>
</tr>
<tr>
<td>Disability pension</td>
<td>8.9</td>
<td>4.9</td>
<td>12.9</td>
</tr>
<tr>
<td>Low self-rated health</td>
<td>1.3</td>
<td>27.8</td>
<td>61.4</td>
</tr>
<tr>
<td>Self-reported stress</td>
<td>0.8</td>
<td>30.9</td>
<td>54.1</td>
</tr>
<tr>
<td>Not answering the question on stress</td>
<td>0.1</td>
<td>5.2</td>
<td>10.2</td>
</tr>
<tr>
<td>Medication for somatic disorders</td>
<td>0.2</td>
<td>61.7</td>
<td>83.0</td>
</tr>
</tbody>
</table>

* Intraclass (i.e., intra-neighborhood) correlation (ICC). The ICC measures the percentage of the total variance of the individual variable that is related to the neighbourhood level. It gives information about the clustering of the individual characteristics in the neighborhoods.
### Table 3. Intraclass correlation (ICC), interval odds ratio (IOR), and fixed effects results from separate models showing odds ratios (ORs) with 95% confidence intervals (95% CIs) for neighborhood and individual variables regarding use of anxiolytic-hypnotic drugs among 15,456 women residing in 95 neighborhoods in the city of Malmö, Sweden (1991-1996).

<table>
<thead>
<tr>
<th>Model</th>
<th>ICC (%)</th>
<th>Neighborhood intercept variance (standard error)</th>
<th>OR (95% CI)</th>
<th>Neighborhood slope variance (standard error)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model i (empty model)</td>
<td>1.7</td>
<td>0.056 (0.025)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age adjusted models</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model ii</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-49 ref</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>1.94</td>
<td>(1.54-2.45)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td>2.95</td>
<td>(2.34-3.72)</td>
<td>0.044 (0.067)</td>
<td></td>
</tr>
<tr>
<td>70-73</td>
<td>2.98</td>
<td>(2.27-3.92)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Low social participation (yes vs. no)</td>
<td>1.54</td>
<td>(1.33-1.78)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Low educational level (yes vs. no)</td>
<td>0.93</td>
<td>(0.79-1.10)</td>
<td>0.084 (0.076)</td>
<td></td>
</tr>
<tr>
<td>Living alone (yes vs. no)</td>
<td>1.70</td>
<td>(1.45-1.99)</td>
<td>0.081 (0.075)</td>
<td></td>
</tr>
<tr>
<td>Disability pension (yes vs. no)</td>
<td>3.02</td>
<td>(2.42-3.77)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Low self-rated health (yes vs. no)</td>
<td>4.29</td>
<td>(3.67-5.01)</td>
<td>0.057 (0.070)</td>
<td></td>
</tr>
<tr>
<td>Stress</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-reported stress (yes vs. no)</td>
<td>3.19</td>
<td>(2.69-3.79)</td>
<td>0.104 (0.079)</td>
<td></td>
</tr>
<tr>
<td>Missing information on self-reported stress (yes vs. no)</td>
<td>2.95</td>
<td>(2.16-4.04)</td>
<td>0.435 (0.264)</td>
<td></td>
</tr>
<tr>
<td>Medication for somatic disorders (yes vs. no)</td>
<td>2.91</td>
<td>(2.38-3.56)</td>
<td>0.107 (0.119)</td>
<td></td>
</tr>
<tr>
<td>Neighborhood rate of low social participation</td>
<td>5.02</td>
<td>(2.39-10.55)</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Model iii</td>
<td></td>
<td></td>
<td>80% IOR</td>
<td></td>
</tr>
<tr>
<td>Low social participation (yes vs. no)</td>
<td>1.56</td>
<td>(1.34-1.81)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low educational level (yes vs. no)</td>
<td>0.81</td>
<td>(0.70-0.95)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living alone (yes vs. no)</td>
<td>1.60</td>
<td>(1.38-1.86)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neighborhood rate of low social participation</td>
<td>3.10</td>
<td>(1.51-6.41)</td>
<td>3.10-3.10</td>
<td></td>
</tr>
<tr>
<td>Model iv</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All variables in the model</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neighborhood rate of low social participation</td>
<td>2.01</td>
<td>(0.97-4.14)</td>
<td>1.90-2.13</td>
<td></td>
</tr>
</tbody>
</table>

### Table 4. Neighborhood variance and median odds ratio (MOR) regarding use of anxiolytic-hypnotic drugs among 15,456 women residing in 95 neighborhoods in the city of Malmö, Sweden (1991-1996).

<table>
<thead>
<tr>
<th>Model</th>
<th>Model ii (empty model)</th>
<th>Model ii</th>
<th>Model iii</th>
<th>Model iv</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2nd level variance (standard error)</td>
<td>0.056 (0.025)</td>
<td>0.411 (0.243)</td>
<td>0.030 (0.022)</td>
<td>0</td>
</tr>
<tr>
<td>MOR</td>
<td>1.25</td>
<td>1.84</td>
<td>1.18</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Figure 2. Age adjusted probability of using anxiolytic-hypnotic drugs, and specific intraclass correlation (black squares), in function of individual social participation among 15,456 women residing in 95 neighborhoods in the city of Malmö, Sweden (1991-1996).

Figure 3. Age adjusted probability of using anxiolytic-hypnotic drugs, and specific intraclass correlation (black squares), in function of self-reported stress among 15,456 women residing in 95 neighborhoods in the city of Malmö, Sweden (1991-1996). Women who reported not being stressed are compared with those who reported being stressed and those who abstained from answering this question.
5.2 STUDY II

The prevalence of disability pension and AHD use was 6.8% and 4.9%, respectively, in the study sample. The median (1st-3rd quartile) neighborhood low social participation was 28.3% (22.8-36.7%).

**Fixed effects**

Women who used AHD had on average about a threefold higher propensity for disability pension than women who did not use AHD, after adjusting for age (Table 5). The association between AHD use and disability pension persisted after additional adjusting for low social participation, low educational level, living alone, low self-rated health, and use of medication for somatic disorders (OR = 2.15 (95% CI 1.69-2.72)). The addition of neighborhood low social participation did not considerably affect the association between AHD use and disability pension. In addition, individual low social participation was also associated with disability pension.

Moreover, neighborhood rate of low social participation was also associated with disability pension, after adjusting for the individual variables, age, AHD use, low social participation, low educational level, living alone, low self-rated health, and medication for somatic disorders (OR = 11.85 (95% CI 5.09-27.58)) (see Table 5).

Further, I have made additional analyses with a division of the neighborhood rate of low social participation into tertiles. In model iv, living in the tertile of neighborhoods with the highest compared to the lowest rates of low social participation was associated with higher individual probability of disability pension (OR=1.72 (95% CI 1.33-2.21)), after adjusting for the individual variables, age, AHD use, low social participation, low educational level, living alone, low self-rated health, and medication for somatic disorders.

**Random effects**

The neighborhood intercept variance decreased by 55% when all the individual variables were entered into model iii, compared with model i (empty model). However, model iv with neighborhood rate of low social participation decreased the intercept variance by further 25 percentage points (80% decrease compared with model i) (Table 5).

The MOR in model i could indicate that, hypothetically, a woman may (in median) increase her propensity for disability pension with 72% (MOR=1.72) if she moved to a neighborhood with a higher rate of disability pension. The ICC in model i was 9.0%. After adjusting for the individual variables (model iii), the MOR decreased to 1.44 and the ICC to 4.3%. The inclusion of the neighborhood rate of low social participation (model iv) further reduced the MOR to 1.27 and the ICC to 1.9% (Table 5).

The IOR did not include one and, hence, the effect of the neighborhood rate of low social participation was large compared with the unexplained variance between the neighborhoods (Table 5).

We found no conclusive random slope variance in the association between AHD use and disability pension. In other words, the association between AHD use and disability pension was similar in all the neighborhoods.
Table 5. Neighborhood variance and odds ratios (OR) with 95% confidence intervals (95% CI) for individual variables and neighborhood low social participation regarding disability pension among 12,156 women residing in 95 neighborhoods in the city of Malmö, Sweden (1991-1996).

<table>
<thead>
<tr>
<th>Fixed effects</th>
<th>Model i (empty model)</th>
<th>Model ii</th>
<th>Model iii</th>
<th>Model iv</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
</tr>
<tr>
<td>45-49 Ref</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>50-54</td>
<td>2.26 1.76-2.90</td>
<td>1.96 1.54-2.50</td>
<td>1.97 1.54-2.51</td>
<td>1.97 1.54-2.51</td>
</tr>
<tr>
<td>55-59</td>
<td>4.72 3.75-5.94</td>
<td>3.93 3.12-4.95</td>
<td>3.95 3.14-4.97</td>
<td>3.95 3.14-4.97</td>
</tr>
<tr>
<td>60-64</td>
<td>2.53 1.98-3.23</td>
<td>1.79 1.39-2.29</td>
<td>1.80 1.40-2.30</td>
<td>1.80 1.40-2.30</td>
</tr>
<tr>
<td>AHD use (yes vs. no)</td>
<td>2.99 2.38-3.77*</td>
<td>2.15 1.69-2.72*</td>
<td>2.09 1.65-2.65*</td>
<td>2.09 1.65-2.65*</td>
</tr>
<tr>
<td>Low social participation (yes vs. no)</td>
<td>2.25 1.93-2.63</td>
<td>2.17 1.86-2.53</td>
<td>2.17 1.86-2.53</td>
<td>2.17 1.86-2.53</td>
</tr>
<tr>
<td>Low educational level (yes vs. no)</td>
<td>1.82 1.55-2.13</td>
<td>1.71 1.46-2.01</td>
<td>1.71 1.46-2.01</td>
<td>1.71 1.46-2.01</td>
</tr>
<tr>
<td>Living alone (yes vs. no)</td>
<td>1.12 0.95-1.32</td>
<td>1.09 0.93-1.28</td>
<td>1.09 0.93-1.28</td>
<td>1.09 0.93-1.28</td>
</tr>
<tr>
<td>Low self-rated health (yes vs. no)</td>
<td>2.67 2.29-3.10</td>
<td>2.63 2.26-3.06</td>
<td>2.63 2.26-3.06</td>
<td>2.63 2.26-3.06</td>
</tr>
<tr>
<td>Medication for somatic disorders</td>
<td>1.34 1.14-1.57</td>
<td>1.35 1.15-1.59</td>
<td>1.35 1.15-1.59</td>
<td>1.35 1.15-1.59</td>
</tr>
<tr>
<td>Neighborhood rate of low social</td>
<td>11.85 5.09-27.58</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>participation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80% Interval odds ratio (IOR)</td>
<td></td>
<td>7.49-18.74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random effects</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept variance (standard error)</td>
<td>0.326 (0.072)</td>
<td>0.278 (0.065)</td>
<td>0.148 (0.045)</td>
<td>0.064 (0.030)</td>
</tr>
<tr>
<td>Median Odds Ratio (MOR)</td>
<td>1.72 1.65</td>
<td>1.44 1.27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraclass correlation (%)</td>
<td>9.0 7.8</td>
<td>4.3 1.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Random slope analysis gave no evidence of slope variance.
5.3 STUDY III

The prevalence of AHD use was 7.8% for women and 5.0% for men. The median (first to third quartile) number of participants in the areas was 256 (228-271) women and 224 (201-238) men. Area low trust ranged from 3% to 36%, area low social participation ranged from 45% to 63%, and area high social participation/low trust ranged from 1% to 12%.

*Fixed effects*

In model i, for both men and women, there was an association between individual high social participation/low trust (the individual component of the miniaturization of community concept) and AHD use, after adjustment for age (ORwomen = 1.43 (95% CI 1.06-1.95) and ORmen = 1.68 (95% CI 1.16-2.44)) (Tables 6 and 8). In model ii, after additional adjustment for education and financial strain, the association was reduced, and remained conclusive for men (ORwomen = 1.24 (95% CI 0.92-1.69) and ORmen = 1.44 (95% CI 1.00-2.09)) (Tables 6 and 8). In model iii, area high social participation/low trust (the contextual component of the miniaturization of community concept) was also associated with individual AHD use for both men and women (above third tertile of area high social participation/low trust ORwomen = 1.39 (95% CI 1.19-1.63) and ORmen = 1.26 (95% CI 1.03-1.54)), after adjustment for the individual variables age, education, and financial strain (Tables 7 and 9). Additional adjustment for the combinations of individual social participation/trust did not substantially weaken the association.

*Random effects*

The area intercept variance in the different analyses was similar and fairly small, ranging from 0.022 to 0.044 (Tables 6-9). Accordingly, the MOR and the ICC were also small, the MOR ranging from 1.15 to 1.22 and the ICC ranging from 0.7% to 1.3%.

Moreover, the 80% IOR indicated that, at least for women (Table 7), the influence of area high social participation/low trust (the contextual component of the miniaturization of community concept) on AHD use was large compared with the unexplained difference between the areas.
Table 6. Area variance and odds ratios (ORs) with 95% confidence intervals (95% CIs) for individual variables regarding use of anxiolytic-hypnotic drugs among 20,319 women from the Life & Health year 2000 survey, Sweden

<table>
<thead>
<tr>
<th></th>
<th>Model ia</th>
<th></th>
<th>Model iib</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>Area intercept variance (SE)</td>
<td>MOR</td>
</tr>
<tr>
<td>Low social participation (yes vs. no)</td>
<td>1.26</td>
<td>(1.13-1.40)</td>
<td>0.041 (0.016)</td>
<td>1.21</td>
</tr>
<tr>
<td>Low trust (yes vs. no)</td>
<td>1.94</td>
<td>(1.64-2.28)</td>
<td>0.032 (0.014)</td>
<td>1.19</td>
</tr>
<tr>
<td>Social participation/trust</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High/high</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High/low (miniaturization)</td>
<td>1.43</td>
<td>(1.06-1.95)</td>
<td>0.032 (0.014)</td>
<td>1.19</td>
</tr>
<tr>
<td>Low/high</td>
<td>1.17</td>
<td>(1.05-1.32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low/low</td>
<td>2.52</td>
<td>(2.07-3.07)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Model ii

<table>
<thead>
<tr>
<th></th>
<th>Model ii</th>
<th></th>
<th>Model iic</th>
<th></th>
</tr>
</thead>
<tbody>
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<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>Area intercept variance (SE)</td>
<td>MOR</td>
</tr>
<tr>
<td>Low social participation (yes vs. no)</td>
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<td>(1.07-1.33)</td>
<td>0.040 (0.015)</td>
<td>1.21</td>
</tr>
<tr>
<td>Low trust (yes vs. no)</td>
<td>1.66</td>
<td>(1.40-1.96)</td>
<td>0.033 (0.014)</td>
<td>1.19</td>
</tr>
<tr>
<td>Social participation/trust</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>High/high</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High/low (miniaturization)</td>
<td>1.24</td>
<td>(0.92-1.69)</td>
<td>0.033 (0.014)</td>
<td>1.19</td>
</tr>
<tr>
<td>Low/high</td>
<td>1.13</td>
<td>(1.00-1.26)</td>
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<td></td>
</tr>
<tr>
<td>Low/low</td>
<td>2.09</td>
<td>(1.70-2.55)</td>
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<td></td>
</tr>
</tbody>
</table>

aSeparate analyses adjusted for age; bSeparate analyses adjusted for age, education, and financial strain.

Table 7. Area variance and odds ratios (ORs) with 95% confidence intervals (95% CIs) for area variables regarding use of anxiolytic-hypnotic drugs among 20,319 women from the Life & Health year 2000 survey, Sweden

<table>
<thead>
<tr>
<th></th>
<th>Model iii</th>
<th></th>
<th>Model iv</th>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>Area intercept variance (SE)</td>
<td>MOR</td>
</tr>
<tr>
<td>Area low social participation in tertiles</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.16</td>
<td>(0.98-1.38)</td>
<td>0.81-1.66</td>
<td>0.039 (0.015)</td>
</tr>
<tr>
<td>3</td>
<td>1.03</td>
<td>(0.87-1.22)</td>
<td>0.72-1.47</td>
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</tr>
<tr>
<td>Area low trust in tertiles</td>
<td></td>
<td></td>
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<td>Ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.15</td>
<td>(0.98-1.36)</td>
<td>0.83-1.60</td>
<td>0.033 (0.014)</td>
</tr>
<tr>
<td>3</td>
<td>1.28</td>
<td>(1.08-1.51)</td>
<td>0.92-1.78</td>
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</tr>
<tr>
<td>Area high social participation/low trust in tertiles (miniaturization)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.22</td>
<td>(1.04-1.43)</td>
<td>0.92-1.63</td>
<td>0.025 (0.013)</td>
</tr>
<tr>
<td>3</td>
<td>1.39</td>
<td>(1.19-1.63)</td>
<td>1.05-1.86</td>
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<td>Area low social participation in tertiles</td>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.14</td>
<td>(0.96-1.35)</td>
<td>0.82-1.58</td>
<td>0.033 (0.014)</td>
</tr>
<tr>
<td>3</td>
<td>1.02</td>
<td>(0.86-1.20)</td>
<td>0.73-1.41</td>
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</tr>
<tr>
<td>Area low trust in tertiles</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.14</td>
<td>(0.97-1.34)</td>
<td>0.84-1.56</td>
<td>0.029 (0.014)</td>
</tr>
<tr>
<td>3</td>
<td>1.22</td>
<td>(1.04-1.44)</td>
<td>0.90-1.66</td>
<td></td>
</tr>
<tr>
<td>Area high social participation/low trust in tertiles (miniaturization)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.21</td>
<td>(1.04-1.42)</td>
<td>0.93-1.59</td>
<td>0.022 (0.012)</td>
</tr>
<tr>
<td>3</td>
<td>1.34</td>
<td>(1.15-1.56)</td>
<td>1.02-1.75</td>
<td></td>
</tr>
</tbody>
</table>

aSeparate analyses adjusted for age, education, and financial strain; bSeparate analyses adjusted for age, education, financial strain, and the combinations of individual social participation/trust.
Table 8. Area variance and odds ratios (ORs) with 95% confidence intervals (95% CIs) for individual variables regarding use of anxiolytic-hypnotic drugs among 17,850 men in the Life & Health year 2000 survey, Sweden

<table>
<thead>
<tr>
<th>Model</th>
<th>OR</th>
<th>95% CI</th>
<th>Area intercept variance (SE)</th>
<th>MOR</th>
<th>ICC (%)</th>
</tr>
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<tbody>
<tr>
<td>Model ia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low social participation (yes vs. no)</td>
<td>1.50</td>
<td>(1.31-1.72)</td>
<td>0.041 (0.021)</td>
<td>1.21</td>
<td>1.2</td>
</tr>
<tr>
<td>Low trust (yes vs. no)</td>
<td>2.05</td>
<td>(1.66-2.54)</td>
<td>0.037 (0.021)</td>
<td>1.20</td>
<td>1.1</td>
</tr>
<tr>
<td>Social participation/trust</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High/high</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High/low (miniaturization)</td>
<td>1.68</td>
<td>(1.16-2.44)</td>
<td>0.037 (0.020)</td>
<td>1.20</td>
<td>1.1</td>
</tr>
<tr>
<td>Low/high</td>
<td>1.43</td>
<td>(1.24-1.65)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low/low</td>
<td>3.04</td>
<td>(2.34-3.95)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model iib</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Low social participation (yes vs. no)</td>
<td>1.42</td>
<td>(1.24-1.63)</td>
<td>0.043 (0.022)</td>
<td>1.22</td>
<td>1.3</td>
</tr>
<tr>
<td>Low trust (yes vs. no)</td>
<td>1.72</td>
<td>(1.39-2.14)</td>
<td>0.041 (0.021)</td>
<td>1.21</td>
<td>1.2</td>
</tr>
<tr>
<td>Social participation/trust</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High/high</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High/low (miniaturization)</td>
<td>1.44</td>
<td>(1.00-2.09)</td>
<td>0.041 (0.021)</td>
<td>1.21</td>
<td>1.2</td>
</tr>
<tr>
<td>Low/high</td>
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<td>(1.18-1.58)</td>
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</tr>
<tr>
<td>Low/low</td>
<td>2.47</td>
<td>(1.89-3.22)</td>
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</tbody>
</table>

*separate analyses adjusted for age, education, and financial strain.

Table 9. Area variance and odds ratios (ORs) with 95% confidence intervals (95% CIs) for area variables regarding use of anxiolytic-hypnotic drugs among 17,850 men in the Life & Health year 2000 survey, Sweden

<table>
<thead>
<tr>
<th>Model iii a</th>
<th>OR</th>
<th>95% CI</th>
<th>80% IOR</th>
<th>Area intercept variance (SE)</th>
<th>MOR</th>
<th>ICC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low social participation in tertiles</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>1</td>
<td>Ref</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.17</td>
<td>(0.96-1.44)</td>
<td>0.81-1.70</td>
<td>0.042 (0.022)</td>
<td>1.22</td>
<td>1.3</td>
</tr>
<tr>
<td>3</td>
<td>1.08</td>
<td>(0.88-1.32)</td>
<td>0.74-1.56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low trust in tertiles</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Ref</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.14</td>
<td>(0.93-1.40)</td>
<td>0.78-1.67</td>
<td>0.044 (0.022)</td>
<td>1.22</td>
<td>1.3</td>
</tr>
<tr>
<td>3</td>
<td>1.14</td>
<td>(0.93-1.40)</td>
<td>0.78-1.67</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>High social participation/low trust in tertiles (miniaturization)</td>
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<tr>
<td>1</td>
<td>Ref</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.22</td>
<td>(1.00-1.49)</td>
<td>0.86-1.73</td>
<td>0.037 (0.021)</td>
<td>1.20</td>
<td>1.1</td>
</tr>
<tr>
<td>3</td>
<td>1.26</td>
<td>(1.03-1.54)</td>
<td>0.89-1.78</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*separate analyses adjusted for age, and financial strain.

Model iv b

| Area low social participation in tertiles | | | | | | |
| 1 | Ref | | | | | |
| 2 | 1.16 | (0.95-1.42) | 0.81-1.67 | 0.040 (0.021) | 1.21 | 1.2 |
| 3 | 1.05 | (0.86-1.29) | 0.73-1.52 | | | |
| Area low trust in tertiles | | | | | | |
| 1 | Ref | | | | | |
| 2 | 1.13 | (0.92-1.38) | 0.78-1.63 | 0.042 (0.021) | 1.22 | 1.3 |
| 3 | 1.09 | (0.89-1.34) | 0.75-1.58 | | | |
| Area high social participation/low trust in tertiles (miniaturization) | | | | | | |
| 1 | Ref | | | | | |
| 2 | 1.21 | (0.99-1.47) | 0.85-1.71 | 0.037 (0.020) | 1.20 | 1.1 |
| 3 | 1.22 | (0.99-1.49) | 0.86-1.73 | | | |

*separate analyses adjusted for age, education, financial strain, and the combinations of individual social participation/trust.
5.4 STUDY IV

The prevalence of primary non-concordance with medication was 7.6% for women and 6.5% for men in the study sample. The median (first to third quartile) number of participants in the areas was 115 (102-126) women and 86 (72-94) men. Area low social participation ranged from 45% to 63%.

Fixed effects

In model ii, the association between age and primary non-concordance with medication was inversed (Table 10 and 11). Further, we did not find any association between educational level and primary non-concordance, but between financial strain and primary non-concordance (OR\text{women}=1.87 (95% CI 1.58-2.22) and OR\text{men}=2.24 (95% CI 1.82-2.75)). Also low self-rated health (OR\text{women}=1.38 (95% CI 1.16-1.63) and OR\text{men}=1.58 (95% CI 1.28-1.95)) and low trust in the health care system (OR\text{women}=1.33 (95% CI 1.12-1.58) and OR\text{men}=1.37 (95% CI 1.11-1.69)) were related to primary non-concordance. The lower DIC value in model ii indicated a better fit than in model i (the empty model).

In model iii, area low social participation was not associated with primary non-concordance. Furthermore, the DIC showed that the addition of area low social participation did not improve the fit.

Random effects

The area intercept variance in the different analyses was small, ranging from 0.012 to 0.036 (Table 10 and 11). Accordingly, the MOR and the ICC were also small, the MOR ranging from 1.11 to 1.20 and the ICC ranging from 0.4% to 1.1%.

Moreover, the 80% IORs included one for area low social participation, and thereby confirmed the low importance, in this study, of this area characteristic for primary non-concordance with medication.
### Table 10. Area variance and odds ratios (ORs) with 95% confidence intervals (95% CIs) for individual variables and area low social participation regarding primary non-concordance with medication among 9,070 women from the Life & Health year 2000 survey, Sweden

<table>
<thead>
<tr>
<th>Fixed effects</th>
<th>Model i (empty model)</th>
<th>Model ii</th>
<th>Model iii</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-79 years</td>
<td>Ref</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>50-64 years</td>
<td>1.58 (1.16-2.15)</td>
<td>1.55 (1.18-2.03)</td>
<td></td>
</tr>
<tr>
<td>35-49 years</td>
<td>2.49 (1.82-3.43)</td>
<td>2.46 (1.88-3.22)</td>
<td></td>
</tr>
<tr>
<td>18-34 years</td>
<td>3.22 (2.36-4.39)</td>
<td>3.17 (2.41-4.17)</td>
<td></td>
</tr>
<tr>
<td><strong>Low educational level (yes vs. no)</strong></td>
<td>0.85 (0.71-1.03)</td>
<td>0.85 (0.71-1.03)</td>
<td></td>
</tr>
<tr>
<td><strong>Financial strain (yes vs. no)</strong></td>
<td>1.87 (1.58-2.22)</td>
<td>1.85 (1.57-2.18)</td>
<td></td>
</tr>
<tr>
<td><strong>Low self-rated health (yes vs. no)</strong></td>
<td>1.38 (1.16-1.63)</td>
<td>1.37 (1.16-1.62)</td>
<td></td>
</tr>
<tr>
<td><strong>Low social participation (yes vs. no)</strong></td>
<td>0.87 (0.74-1.02)</td>
<td>0.86 (0.73-1.02)</td>
<td></td>
</tr>
<tr>
<td><strong>Low trust in the health care system</strong></td>
<td>1.33 (1.12-1.58)</td>
<td>1.34 (1.13-1.58)</td>
<td></td>
</tr>
<tr>
<td><strong>Area low social participation in tertiles</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.22 (0.99-1.50)</td>
<td>0.98-1.51</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.10 (0.89-1.35)</td>
<td>0.88-1.36</td>
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</tr>
<tr>
<td><strong>Random effects</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Area intercept variance (SE)</td>
<td>0.014(0.015)</td>
<td>0.012(0.013)</td>
<td>0.014(0.015)</td>
</tr>
<tr>
<td>Median odds ratio</td>
<td>1.12</td>
<td>1.11</td>
<td>1.12</td>
</tr>
<tr>
<td>Intraclass correlation</td>
<td>0.4%</td>
<td>0.4%</td>
<td>0.4%</td>
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<tr>
<td>Deviance information criterion</td>
<td>4888</td>
<td>4686</td>
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</table>

### Table 11. Area variance and odds ratios (ORs) with 95% confidence intervals (95% CIs) for individual variables and area low social participation regarding primary non-concordance with medication among 6,795 men from the Life & Health year 2000 survey, Sweden

<table>
<thead>
<tr>
<th>Fixed effects</th>
<th>Model i (empty model)</th>
<th>Model ii</th>
<th>Model iii</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-79 years</td>
<td>Ref</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>50-64 years</td>
<td>1.57 (1.18-2.09)</td>
<td>1.57 (1.17-2.09)</td>
<td></td>
</tr>
<tr>
<td>35-49 years</td>
<td>2.23 (1.64-3.04)</td>
<td>2.19 (1.61-2.98)</td>
<td></td>
</tr>
<tr>
<td>18-34 years</td>
<td>2.29 (1.67-3.13)</td>
<td>2.26 (1.62-3.16)</td>
<td></td>
</tr>
<tr>
<td><strong>Low educational level (yes vs. no)</strong></td>
<td>0.87 (0.69-1.10)</td>
<td>0.87 (0.70-1.09)</td>
<td></td>
</tr>
<tr>
<td><strong>Financial strain (yes vs. no)</strong></td>
<td>2.24 (1.82-2.75)</td>
<td>2.25 (1.84-2.76)</td>
<td></td>
</tr>
<tr>
<td><strong>Low self-rated health (yes vs. no)</strong></td>
<td>1.58 (1.28-1.95)</td>
<td>1.58 (1.29-1.93)</td>
<td></td>
</tr>
<tr>
<td><strong>Low social participation (yes vs. no)</strong></td>
<td>0.85 (0.69-1.03)</td>
<td>0.85 (0.69-1.03)</td>
<td></td>
</tr>
<tr>
<td><strong>Low trust in the health care system</strong></td>
<td>1.37 (1.11-1.69)</td>
<td>1.38 (1.11-1.72)</td>
<td></td>
</tr>
<tr>
<td><strong>Area low social participation in tertiles</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.07 (0.80-1.43)</td>
<td>0.76-1.51</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0.83 (0.62-1.11)</td>
<td>0.59-1.17</td>
<td></td>
</tr>
<tr>
<td><strong>Random effects</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Area intercept variance (SE)</td>
<td>0.034(0.033)</td>
<td>0.034(0.033)</td>
<td>0.036(0.025)</td>
</tr>
<tr>
<td>Median odds ratio</td>
<td>1.19</td>
<td>1.19</td>
<td>1.20</td>
</tr>
<tr>
<td>Intraclass correlation</td>
<td>1.0%</td>
<td>1.0%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Deviance information criterion</td>
<td>3288</td>
<td>3148</td>
<td>3148</td>
</tr>
</tbody>
</table>
5.5 STUDY V

The prevalence of low adherence to antihypertensives during the last two weeks was 11% in the study sample.

**Fixed effects**

Participants with low social participation had on average a more than twofold higher probability of reporting low adherence to antihypertensives during the last two weeks than those who did not have low social participation (OR = 2.28 (95% CI 1.16-4.49)), after adjustment for age and sex (Table 12). This association between individual low social participation and low adherence to antihypertensives during the last two weeks persisted after additional adjustment for low educational level (OR= 2.05 (95% CI 1.05-3.99)). However, after additional adjustment for poor self-rated health and poor psychological health, the association between individual low social participation and low adherence to antihypertensives during the last two weeks was not conclusive (OR= 1.80 (95% CI 0.90-3.61)).

**Random effects**

We observed a variance between the municipalities in both low adherence to antihypertensives during the last two weeks (intercept variance) and in the association between individual low social participation and low adherence to antihypertensives during the last two weeks (slope variance) (Table 12 and Figure 4). The negative covariance between intercepts and slopes (Table 12) suggested that the associations between low social participation and low adherence to antihypertensives during the last two weeks (slopes) in the 33 municipalities depended on the different prevalence of low adherence to antihypertensives during the last two weeks in the different municipalities. The association between low social participation and low adherence to antihypertensives during the last two weeks (slope) was weaker in municipalities with higher prevalence than in municipalities with lower prevalence of low adherence to antihypertensives during the last two weeks (i.e., cross-level interaction).
Table 12. Municipality variance and age adjusted odds ratios (ORs) with 95% confidence intervals (95% CIs) for individual variables regarding low adherence to antihypertensives during the last two weeks among 1,288 participants from The Health Survey in Scania 2000, Sweden

<table>
<thead>
<tr>
<th>Model</th>
<th>OR</th>
<th>95% CI</th>
<th>OR</th>
<th>95% CI</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Model i</td>
<td></td>
<td>Model ii</td>
<td></td>
<td>Model iii</td>
</tr>
<tr>
<td>Women vs. men</td>
<td>1.21</td>
<td>(0.82-1.78)</td>
<td>1.15</td>
<td>(0.78-1.69)</td>
<td>1.17</td>
<td>(0.78-1.77)</td>
</tr>
<tr>
<td>Low social participation (yes vs. no)</td>
<td>2.28</td>
<td>(1.16-4.49)</td>
<td>2.05</td>
<td>(1.05-3.99)</td>
<td>1.80</td>
<td>(0.90-3.61)</td>
</tr>
<tr>
<td>Low educational level (yes vs. no)</td>
<td>1.87</td>
<td>(1.18-2.96)</td>
<td>1.76</td>
<td>(1.09-2.84)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor self-rated health (yes vs. no)</td>
<td></td>
<td>1.45</td>
<td>(0.83-2.54)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor psychological health (yes vs. no)</td>
<td>1.54</td>
<td>(0.92-2.59)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variance (SE)</th>
<th>Variance (SE)</th>
<th>Variance (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Municipality variance in low adherence to antihypertensives (intercept variance)</td>
<td>0.801 (0.461)</td>
<td>0.776 (0.450)</td>
</tr>
<tr>
<td>Municipality variance of the association between low social participation and low adherence to antihypertensives (slope variance)</td>
<td>1.812 (0.889)</td>
<td>1.720 (0.857)</td>
</tr>
<tr>
<td>Municipality covariance between intercepts and slopes</td>
<td>-1.163 (0.609)</td>
<td>-1.116 (0.591)</td>
</tr>
</tbody>
</table>
Figure 4. Slope variance in the association between individual low social participation and low adherence to antihypertensives during the last two weeks among 33 municipalities in Scania, Sweden.
6 DISCUSSION
6.1 CONTEXTUAL ASPECTS

Our results in Study I suggest that the level of low social participation in the neighborhood of residence may influence AHD use among women, beyond individual social participation, educational level, and living alone. This association decreased, however, after additional adjustment for self-reported stress, self-rated health, disability pension, and use of medication for somatic disorders.

The observed weakening of the association between neighborhood social participation and women’s use of AHD after we adjusted for the individual health-related variables may be an expression for compositional confounding, i.e., women with impaired health move to certain neighborhoods. However, the observed reduction of the association may instead be telling us that these individual level variables were on the pathway between neighborhood social environment and use of AHD. Contextual factors, related to one’s neighborhood of residence, can be upstream factors affecting individual factors, which in turn influence health, and the individual factors which are controlled for as confounders in contextual studies may in fact be intervening factors (mediators) on the pathway between area and health.

As Diez Roux states, a key challenge in research on area effects on individual health is the adjustment for individual confounders. Some individual variables may be both confounders and mediators, and, therefore, unadjusted estimates of contextual effects may be affected by residual compositional confounding and adjusted estimates of contextual effects may underestimate the true effect. This problem is a general concern in observational epidemiology and can be resolved with longitudinal data combined with well-elaborated theoretical framework.

Oakes questions whether people from two different neighborhoods are “exchangeable”, even after controlling for individual variables. However, uncontrolled confounding due to omitted variables is not unique to multilevel models of area effects, but rather a concern in all observational research. Further, Oakes is concerned whether data is extrapolated too far when there might not be sufficient data in all “cells” in a multilevel regression analysis of area effects. However, we had a large study sample in our analysis, and in Table 2, one can see that all the studied individual characteristics were represented across the different values on the neighborhood variable. Also, the number of variables was not so large and the size of the individual sample in each neighborhood reduced the risk of having many empty cells in the analyses.

Although neighborhood social participation was associated with AHD use in Study I, individual AHD use was on average rather homogeneous all over the city of Malmö. That is, only 1.7% of the individual differences in the probability of using AHD seemed to have contextual reasons. In other words, there existed a contextual phenomenon influencing AHD use, but it explained only a minor part (i.e., only 1.7%) of the individual variation in the propensity for using AHD. Although it may seem somewhat counterintuitive, neighborhood level variables can be strongly associated with individual health-related outcomes, even when the between-neighborhood variance is very small. In other words, a small variance between areas may give enough...
contrast of exposure to detect an association between an area variable and an individual outcome.\textsuperscript{13}

In contrast to medication use, there was a stronger clustering for some social variables, like for example living alone, low educational level, and disability pension.\textsuperscript{8} The results of cross-sectional multilevel analyses often demonstrate a higher neighborhood clustering of socioeconomic and behavioral outcomes than of biological and medical variables.\textsuperscript{280} This observation is also supported by the larger clustering of disability pension in Study II than of AHD use in Study I. Probably, socioeconomic and behavioral variables are more susceptible to current contextual influences than life-course determined biomedical variables. If contextual factors do affect biomedical outcomes, these effects need to be investigated by longitudinal, rather than cross-sectional, multilevel analysis.

The random slope analysis in Study I suggested that the neighborhood environment modified the association between certain individual level variables and AHD use. The impact of the neighborhood on AHD use, as expressed by the ICC and the MOR, was larger for stressed women and for those who abstained from answering this specific question on stress, than for women without stress. That is, on average, the neighborhood level explained a modest part of the individual differences in the probability of using AHD, but this average measure hid larger neighborhood effects for certain groups of women. The women with missing information on stress reported the same use of AHD as the women reporting stress (i.e., 9% and 10% respectively). It is possible, therefore, that women with missing information on this question were in fact women suffering from stress.

The MOR derived from study II suggests that when comparing two women with similar characteristics, but from different neighborhoods in Malmö, one of the women may hypothetically, in median, have a 44% higher probability of disability pension only because she lived in a different neighborhood. That is to say that beyond individual characteristics, there seems to be a contextual phenomenon influencing women living in the same neighborhood to have a similar probability of disability pension.

Over and above individual characteristics, neighborhood social participation explained a considerable part of the neighborhood variance and had an impact on the propensity for disability pension. The IOR indicated that the effect of neighborhood social participation was large compared with the unexplained variance between the neighborhoods. In a public health perspective, our results suggest that neighborhood social participation is relevant for understanding the individual propensity for disability pension, beyond individual characteristics such as age, low social participation, low educational level, living alone, low self-rated health, and use of medication for somatic disorders. Concepts of work, disease, and disability are to a great extent culturally defined and may, consequently, be influenced by the social structure in the community.\textsuperscript{211}

Our results in Study III indicate that, in central Sweden, a high level of miniaturization of community in the area (i.e., area high social participation and low trust) seems to be associated with an increased probability of individual AHD use, after adjustment for individual characteristics. As Fukuyama points out, when the radius of trust diminishes and the society is miniaturized and individualized, the social disorder that follows is measurable in statistics on for example crime.\textsuperscript{108} In this
study, we provide empirical results that suggest that the influence of miniaturization of community may also be measurable in terms of higher probability of AHD use.

A consequence of an individualistic lifestyle in the community is that people engage in social participation but share less with other people from outside their radius of trust. Even though participation in social activities may increase, the circle that people trust is narrower, which results in a miniaturization of community. The subsequent social disorder increases the general level of stress and anxiety, and people may turn to AHD use as a coping strategy. Nevertheless, AHD use has been suggested to be an inappropriate coping strategy. These drugs can negatively affect cognitive function, induce dependence, and may even decrease people’s capacity to cope with stress.

Although we found an association between high level of miniaturization of community in the area and individual AHD use, it is not evident that miniaturization of community is a highly relevant contextual variable for understanding AHD use. The area variance was low, which indicates that the administrative boundaries defining the municipalities in central Sweden were not so essential for understanding individual AHD use in the study sample. Consequently, the MOR was small and the ICC suggested that only about 1% of the differences between individuals in the probability of using AHD was at the area level. Moreover, this contextual variable did not fully explain the difference between areas regarding AHD use.

However, even though the variability between the areas regarding AHD use was fairly low, we were still able to detect an association between miniaturization of community at the area level and individual AHD use, especially for women. As mentioned before, area level variables can be strongly associated with individual health-related outcomes even when the between-area variance is very small.

A previous multilevel study has found a complex interaction between individual trust and community trust. Therefore, we tested for an interaction between individual high social participation/low trust (the individual component of the miniaturization of community concept) and area high social participation/low trust (the contextual component of the miniaturization of community concept). However, we did not find any interaction, suggesting that the association between area high social participation/low trust and AHD use seems to be independent of individual high social participation/low trust status.

Further, area social participation was not associated with primary non-concordance with medication in Study IV. This low importance of the area of residence—as defined by administrative boundaries—is further supported by the low area variances and, hence, the low MORs in the analyses, which indicate that the area of residence, as measured in this study in central Sweden, does not seem to have an impact on primary non-concordance. Nevertheless, an alternative explanation could be that the choice of areas in this study as municipalities and the way we measured the aggregated variable area social participation did not capture the context important for primary non-concordance with medication. Indeed, related research suggests that social capital plays a role in how health care is perceived by citizens and people’s trust in their physicians may be influenced by contextual variables.
Our finding in Study V that the association between individual low social participation and low adherence to antihypertensives during the last two weeks may vary between municipalities in Scania gives empirical support to the existence of cross-level interactions (i.e., between municipality and individual) associated with health-related behaviors, such as low adherence to medication. These behaviors may be a result of the interaction between a person and his or her area of residence. In a previous study, both individual and neighborhood social participation have been associated with impaired health and with use of hormone replacement therapy in women.8

Moreover, Study V shows that multilevel regression analysis can be used for investigation of geographical variation in health and health-related behavior (e.g., adherence to medication), without analyzing any specific area characteristic.243 In multilevel analysis, area effects can be investigated by measures of variance and by examining how area boundaries modify individual level associations (i.e., cross-level interactions).13

Living in a disadvantaged area, e.g., with low social capital, may negatively affect individual low social participation,284 health-related behavior,17, 21, 56 and health status,16, 25, 285 which in turn could have an impact on health-related outcomes. The area environment may influence the individual propensity for health-related outcomes through diverse mechanisms, such as accessibility to health services,53 local practice habits of practitioner,286-292 health-related life-style,293 lack of access to amenities, stress, shared norms around health and health-related behavior, transmission of health information, health behavior norms, and social control of deviant health-related behavior.56, 72, 294, 295 Inhabitants in deprived areas may have less availability of resources like shops, banks, health-care services and transportation, and they therefore have to spend more time and effort on addressing basic tasks of living. In addition, they may be exposed to chronic stress due to higher crime rates, poorer housing, greater crowding, and exposure to noise. Because disadvantaged areas have fewer facilities and resources, the adoption of public health recommendations such as obtaining a healthy diet and regular exercise sometimes cannot be met. The stress that can be experienced by inhabitants in a deprived area can lead to health-damaging behaviors that act as efforts to cope with stress, such as smoking, alcohol consumption, and drug abuse.296

As mentioned in the Introduction, there is an ongoing debate about whether social capital should be a major focus of health and social policy. In particular, there have been discussions between proponents of a psychosocial versus a material interpretation.73, 81-83 In my opinion, both access to tangible material conditions and psychosocial pathways contribute to contextual effects on health. The pathway between context and health is complex and multifaceted, and it is difficult to disentangle different effects from one another.73, 75, 83, 297

6.2 INDIVIDUAL ASPECTS

Individual low social participation was associated with AHD use, disability pension, and low adherence to antihypertensives during the last two weeks (Study I, II, III, and V). It is a widespread opinion that low social participation may have direct negative effects on health via biologic pathways.9, 298 Research on humans and animals indicate that social isolation has negative effects on health,9, 299-302 and anxiety,303-306 possibly through affecting cardiovascular9, 307 and neuroendocrine9, 299-302 activity, sleep,307 and
the immune system. Nevertheless, social relationships may also have indirect effects on health through access to a wide range of resources supportive of health, such as medical referral networks, job opportunities, high-quality health care, and housing. In addition, social relationships may beneficially affect health through shared norms, especially around health-promoting behaviors and health-damaging behaviors. It has been suggested that social networks may be more effective in supporting recovery after illness has occurred than in preventing the incidence of new disease, which supports the idea that social networks may influence health and health-related behavior (e.g., adherence to medication) by facilitating access to resources rather than by direct biological processes.

Further, in Study V, the association between low social participation and low adherence to antihypertensives during the last two weeks was weakened after additional adjustment for poor self-rated health and poor psychological health. The weakening of the association between low social participation and low adherence to antihypertensives during the last two weeks after we adjusted for poor self-rated health and poor psychological health may be an expression for confounding. Impaired health may negatively affect both social participation and adherence to antihypertensives. On the other hand, the observed reduction of the association may instead be telling us that physical and mental health are on the pathway between low social participation and low adherence to antihypertensives during the last two weeks. Social participation may be considered as an early factor on the causal pathway that determines individual health-related behavior, such as low adherence to medication.

Our results from Study II indicate that, as among men, AHD use in women is associated with disability pension. The association remained after adjusting for age, low social participation, low educational level, living alone, low self-rated health, medication for somatic disorders, and neighborhood low social participation. Information on AHD use may be a simple method for predicting future disability pension, and use of these drugs could also have an independent negative effect on health. AHD use has been suggested as an inappropriate coping strategy and use of these drugs could impair rather than improve people’s coping possibilities, maybe by affecting the cognitive function negatively and by decreasing people’s capacity to cope with stress.

In Study III, there was an association between the individual component of the miniaturization of community concept (i.e., individual high social participation and low trust) and use of AHDs, although, after adjustment for educational level and financial strain, this association was only conclusive in men. Previous studies have reported associations between the individual component of the miniaturization of community concept and tobacco smoking, cannabis smoking, self-rated health, patient satisfaction in primary health care, and consumption of home made and smuggled liquor.

Our findings in Study IV indicate that the individual characteristics younger age, financial strain, low self-rated health, and low trust in the health care system are associated with primary non-concordance with medication. Our finding that younger age is associated with higher primary non-concordance is in line with previous research on primary non-concordance. Moreover, research on education and concordance has been inconclusive, and we did not either find an association.
between educational level and primary non-concordance. However, there was a relation between educational level and primary non-concordance. All residents in Sweden who have spent 1800 SEK on medication within the preceding 12 months are entitled to free prescribed medicines.\textsuperscript{312} Despite this subsidy, participants in this study who experienced financial strain seemed to have difficulties redeeming their medication. It has been reported that financial barriers contribute to non-concordance,\textsuperscript{166, 171, 172, 186, 312-314} and also that people who restrict their use of medication because of cost have worse health outcomes.\textsuperscript{315} Also, we observed an association between low self-rated health and primary non-concordance. Nonetheless, previous studies on self-rated health and concordance have given different results.\textsuperscript{188} Furthermore, we found a relation between low trust in the health care system and primary non-concordance. There is an ongoing discussion about the lack of people’s trust in the health care system and health care professionals.\textsuperscript{316-322} It is known that trust and the quality of the doctor-patient relationship are important determinants of concordance with medication.\textsuperscript{162, 318, 323-325} Possible ways to enhance patient trust have been suggested to be continuity of care from a regular doctor\textsuperscript{326} and provision of patient centred care where the patient gets enough attention.\textsuperscript{327}

\section*{6.3 STRENGTHS}

Data from The Malmö Diet and Cancer Study have been used in many different papers\textsuperscript{8, 246, 284, 328, 329} and the study cohort may be regarded as fairly representative of the general population, at least in relation to the main sociodemographic variables.\textsuperscript{330} In addition, the reliability (test-retest stability) of the social participation index has been found to be rather high (kappa= 0.70)\textsuperscript{331} and the internal consistency of the items in the social participation index may be regarded as fairly satisfactory with a Cronbach’s alpha\textsuperscript{332}= 0.61 in both Study I and Study II. There is also a high agreement between the data from the self-administered questionnaire and the personal diary.\textsuperscript{262}

The Life & Health year 2000 survey was the largest population-based survey that had ever been done in central Sweden and the response rate was fairly high (67%).\textsuperscript{263}

The respondents of The Health Survey in Scania 2000 have been reported to have about the same distribution as the total population in Scania regarding age, sex, education, and health care utilization when compared to official registers.\textsuperscript{115, 264, 333} The internal consistency of the items in the social participation index may be regarded as fairly satisfactory with a Cronbach’s alpha= 0.64 in Study V. In addition, data from The Health Survey in Scania 2000 have been used in many studies.\textsuperscript{110, 112-115, 334}

The questions on social participation and trust used in the above-mentioned investigations have been used in previous research and may be regarded as standardized questions.\textsuperscript{29, 267, 268}

Multilevel analysis with random effects has been used throughout this thesis, which is the correct statistical method to use when investigating contextual effects on individual health.\textsuperscript{5, 6, 240, 246, 250, 335}
6.4 LIMITATIONS

The cross-sectional design of the studies in this thesis is a weakness, because the direction of causality is impossible to determine. In other words, it is difficult to discern whether the explanatory variables predict the outcomes in the studies, or if the outcomes predict the explanatory variables.

6.4.1 Selection bias

The participation rate (median; first - third quartile) in The Malmö Diet and Cancer Study in the different neighborhoods was low (42 %; 32 %-50 %). Hence, the cohort may not be representative for the whole female population, which may reduce the external validity of our results.

The rather low participation rate (59%) in Study V may increase the risk of selection bias and reduce the ability to generalize the results and compare them to other populations. Nevertheless, the participation rate for participants aged 51-80 was about 65% and the participants using antihypertensives had a mean age of 63 years.

The study sample in Study IV consisted of those who had visited an emergency department, a physician at a hospital department, a primary care physician, or been admitted to a hospital. With this definition of population at risk we tried to include individuals that had had some contact with the health care system and therefore could have received a prescription. However, this definition may not adequately capture people “at risk” of not redeeming a prescription for medicine.

Unfortunately, we had no information about how long the participants in the studies had lived in their respective areas, neighborhoods, or municipalities, which would have given information about the exposure time to their specific areas and to the area variables.

The selection of geographical units in Study I and II should not be a source of selection bias, as we only left out the 15 least populated neighborhoods. Multilevel analysis can be performed even when the number of people in each area is very different, because areas with a small number of people will provide less information to the analysis than areas with a higher number of people.\textsuperscript{13, 244}

Non-response to the surveys used in this thesis and to specific questions in the questionnaires could have introduced selection bias. Non-response to health surveys has been reported to correlate with psychological disorders, lower socioeconomic status, and disability pension.\textsuperscript{336-339} This possible selection bias could indicate a higher exposure to the explanatory variables and to the outcomes among the non-respondents, which may have resulted in an underestimation of the associations between the explanatory variables and the outcomes.

6.4.2 Information bias

The areas used in the analyses were defined by administrative boundaries, which may not adequately capture the social context important for individual health.\textsuperscript{340} This issue is supported by the, in general, low area variances found.

All the area variables used in this thesis are aggregated variables based on individual characteristics. Although we did not use integral area variables that described
characteristics of the areas that were not derived from individual characteristics, aggregated variables can provide information that is not captured by their individual level analogues. Furthermore, we controlled for the individual level analogues in the analyses.

In Study II, we defined the outcome disability pension among the 45-64 year-old women as self-reported retirement. Among those women who reported retirement, there could be those who were on early age pension. However, more than 95% of retired 45-64 year-old women in Sweden were on disability pension in December 2002. In addition, the age group with the highest propensity for disability pension in Study II was 55-59 years old. If early age pension was common, the age group with the highest propensity for disability pension would be expected to be 60-64 years old.

Compared with a previous study investigating the association between the individual component of the miniaturization of community concept (individual high social participation/low trust) and self-rated health in Scania, in southern Sweden, the prevalence of individual high social participation/low trust was lower and the prevalence of individual low social participation/high trust (which has been referred to as “traditionalism”) was higher in Study III. This discrepancy may be due to the definitions of “social participation” and “trust”. Social participation in the Life & Health year 2000 survey was assessed by a question concerning active membership in various associations, while the social participation variable in the previous study also included informal activities, such as private parties and other forms of entertainment. The question on trust in the Life & Health year 2000 survey dealt with trust in people “in your area”, as opposed to the previous study, where the question was about general trust in other people. In addition, the Life & Health year 2000 survey was done in central Sweden and the previous study was performed in Scania in southern Sweden. The differences in prevalence of high social participation/low trust and low social participation/high trust between the two studies may reflect more miniaturization of community in southern Sweden and more traditional attitudes to society (i.e., traditionalism) in central Sweden. Furthermore, the participation rate was higher in the Life & Health year 2000 survey (67%) than in The Health Survey in Scania 2000 (59%), which could also indicate a higher social capital and trust in central Sweden. People’s inclination to participate in health surveys may, similarly to their inclination to participate in political elections, demonstrate a general level of trust, and therefore be related to the concept of miniaturization of community.

Information on AHD use in this thesis was self-reported, which seems to be a valid method of measuring current drug use. The framing of the AHD question in Study III as “use during the last 2 weeks” might have limited recall bias regarding use of these drugs.

We used self-reported adherence to medication in both Study IV and V, which has been found to correlate with other measures of adherence and with clinical measures of disease activity. Further, self-report offers a convenient and non-invasive estimate of adherence behaviour. However, the procedure of measuring adherence is controversial. Self-report can be subject to self-presentational and recall biases. People may overestimate their adherence and their memory may be inaccurate. We might have reduced memory bias by restricting the recall time to 2 weeks in Study V. However, the prevalence of current low adherence (11%) in Study V is lower than low
adherence reported in a longer period of time, which may be as high as 50%,\textsuperscript{342, 347} even though other studies have found similar adherence rates for antihypertensives as we found.\textsuperscript{173, 348, 349} Our results may underestimate the association between individual social participation and low adherence to antihypertensives. It is possible that some participants with high adherence in the last two weeks had low adherence in other periods of the year. If this kind of misclassification would be more frequent among participants with low social participation, there would be differential misclassification, and the association between low social participation and adherence to antihypertensives could be underestimated. Non-differential misclassification would also underestimate the association between low social participation and low adherence to antihypertensives. Other ways of measuring adherence may be more appropriate, such as Morisky’s four-item scale,\textsuperscript{350} which was used in The Health Survey in Scania 2004. Our preliminary results from analyses on The Health Survey in Scania 2004 indicate that younger age is strongly associated with low adherence to medication, based on the Morisky’s scale, and that the area of residence—as defined by administrative boundaries—seems to matter less for low adherence.

\section*{6.4.3 Confounding}

Arguably, the considerable neighborhood variance found in Study II might be a result of residual individual confounding (i.e., compositional confounding).\textsuperscript{8} However, we would like to emphasize that if neighborhood factors influence health by operating as upstream determinants (i.e., larger socioeconomic, cultural, and environmental conditions) of individual characteristics,\textsuperscript{9, 351} adjusting for many downstream individual characteristics in the analyses may over-adjust and diminish the true effect of the context.\textsuperscript{8, 277, 335}

An important issue in multilevel research is that it may be difficult to differentiate between individual level variables as confounders or mediators.\textsuperscript{238, 248} If the latter, then adjusting for the individual level variable will lead to overlooking contextual effects.\textsuperscript{238} As mentioned before, some individual variables may be both confounders and mediators, and, therefore, unadjusted estimates of contextual effects may be affected by residual compositional confounding and adjusted estimates of contextual effects may underestimate the true effect. This problem is a general concern in observational epidemiology and can be resolved with longitudinal data combined with well-elaborated theoretical framework.\textsuperscript{278}

\section*{6.5 CONCLUSIONS}

This thesis has attempted to investigate aspects of use of medication within the social context, as suggested in the Introduction.\textsuperscript{2} Our results give empirical support to the idea that contextual factors related to aspects of the area environment may contribute to differences in aspects of medication use.\textsuperscript{8}

In concrete, our results suggest that a low level of social participation in the neighborhood, a main aspect within the concept of social capital,\textsuperscript{72} seems to be related to individual AHD use and to disability pension in Malmö. In a multilevel way of thinking, neighborhood social participation could be placed upstream in the causal
pathway determining individual health and it may affect downstream individual characteristics, which in turn influence the use of AHD and disability pension. However, neighborhoods in Malmö were on average rather homogeneous regarding individual use of AHD. Nevertheless, neighborhoods seem to play a larger role in explaining AHD use for certain groups of women, like those reporting stress. This heterogeneity need to be considered when analyzing contextual effects on individual health. Moreover, women living in the same neighborhood in Malmö appear to have a similar propensity for disability pension, beyond their individual characteristics. Also, living in an area with a high level of miniaturization of community (high social participation/low trust) in central Sweden seems to be associated with individual AHD use, beyond people’s individual characteristics including their own level of social participation and trust. The concept of miniaturization of community proposed by Fukuyama may be an extension of the classic concept of social capital since it includes two main components of social capital—social participation and trust. Consequently, the concept of the miniaturization of community may increase our understanding of contextual effects on health. Further, our results regarding adherence to medication indicate that people in central Sweden with younger age, financial difficulties, low self-rated health, and low trust in the health care system may have a higher probability of primary non-adherence to medication. Future studies of why some people have low trust in the health care system and how this trust can be enhanced are needed. However, the area of residence—as defined by administrative boundaries—seems to play a minor role for primary non-concordance with medication in central Sweden. Further, individual low social participation seems to be associated with low adherence to antihypertensives during the last two weeks, independently of low educational level. In addition, the association between low social participation and low adherence to antihypertensives during the last two weeks seems to vary between the municipalities in Scania, which gives empirical support to the existence of cross-level interactions (i.e., between municipality and individual) associated with health-related behaviors, such as low adherence to medication. Future studies aimed at investigating health-related behaviors in general and low adherence to medication in particular might benefit if they consider that area of residence may modify associations between individual variables.

6.6 IMPLICATIONS

At a political level, it may be emphasized that living in an unfavorable social context seems to go hand in hand with higher use of AHD and higher propensity for disability pension. However, administrative boundaries do not seem to best capture the social environment influencing individual health. Overall, contextual effects, related to one’s area of residence, appear to have some impact on health outcomes, and health policies could therefore focus on both areas and individuals, which make health issues a public responsibility and not only an individual responsibility. Politicians may consider that the health of the citizens may depend on the context, which deserves to be investigated and accounted for when planning public health interventions. It is then important that political decisions and implications are grounded on results from appropriate analysis.
A person and his or her chances of a good health will be affected by the society and the social environment in which he or she lives. If this is not recognized, there is a risk of “blaming the victim”, when individuals are held responsible for their own health and blamed for their illnesses. Health inequalities are wrong simply because of aspects of fairness and basic human rights.
7 SUMMARY IN SWEDISH

Bakgrund

Personer som bor inom samma område kan vara mer lika varandra än om man jämför personer som bor i olika områden. Människor som liknar varandra kan vara benägna att flytta till samma område, och de delar också samma ekonomiska, sociala och livsstilsrelaterade egenskaper, som är specifika för området. Dessa specifika egenskaper för området kan påverka hälsa och hälsorelaterat beteende hos invånarna, oberoende av deras individuella egenskaper.

Användning av läkemedel kan påverkas av andra faktorer än sådana som är strikt relaterade till diagnos, t ex patientens förväntningar och socioekonomiska resurser, och dessa slags faktorer kan i sin tur påverkas av området man bor i. Att bo i ett nedgånget område kan ha inverkan på den fysiska och mentala hälsan genom att öka sårbarheten direkt eller indirekt genom diverse mekanismer såsom tillgång till hälso- och sjukvård och andra resurser, stress, socialt stöd, överföring av hälsoinformation och anpassning till de hälsorelaterade beteendenormer som råder i området. Dessa kontextuella faktorer, som hänger samman med bostadsområdet, kan i sin tur påverka individens hälsa och hälsorelaterat beteende, t ex användning av läkemedel, oberoende av individens egenskaper.

Ett centralt begrepp inom forskning kring områdets inverkan på individen är socialt kapital, som betecknar sociala relationer i ett samhälle. Ett exempel på uttryck för socialt kapital är socialt deltagande, som betecknar medverkan i gemensamma aktiviteter i samhället, såsom aktivt medlemskap i olika typer av formella och informella sammanslutningar. Nivån av socialt deltagande i området kan således användas som ett mått på socialt kapital i området.

Ett möjligt alternativ till socialt kapital kan vara vad historikern Fukuyama kallar ”miniatyrisering av samhället”. Detta begrepp innefattar både socialt deltagande och tillit till andra människor, vilka är två dimensioner av social kapital.

Den statistiska metod som använts i denna doktorsavhandling heter multilevel analys (flernivåanalys). Denna metod har under de senaste åren börjat användas inom forskning kring hur bostadsområdet påverkar individens hälsa, eftersom metoden kan separera individuella effekter från kontextuella effekter.

Syften

Att studera kontextuella (som hänger samman med bostadsområdet) och individuella aspekter av användning av läkemedel med multilevel analys.

Studie I: (i) att analysera en hypotetisk kontextuell effekt från bostadsområdet på kvinnors användning av lugnande medel och sömnmedel, och (ii) att undersöka påverkan av nivån av socialt deltagande i bostadsområdet på kvinnors användning av dessa läkemedel.

Studie II: att studera (i) om kvinnor i samma bostadsområde har liknande benägenhet för förtidspension, som hänger samman med nivån av socialt deltagande i bostadsområdet, och (ii) om det finns ett samband mellan användning av lugnande medel och sömnmedel och förtidspension, som kan förändras av bostadsområdet.
**Studie III:** att undersöka (i) om en miniaturisering av samhället (dvs en kombination av högt socialt deltagande och låg tillit i området) är associerad med användning av lugnande medel och sömnmedel, och (ii) om personer som bor i samma område har liknande sannolikhet för användning av lugnande medel och sömnmedel.

**Studie IV:** att analysera (i) om någon av de individuella egenskaperna ålder, utbildning, ekonomiska svårigheter, självsatt hälsa, socialt deltagande och förtroende för sjukvården har samband med att hämta ut läkemedel (följsamhet till läkemedelsordinationen), och (ii) om personer som bor i samma område har liknande sannolikhet för att hämta ut läkemedel, som händer samman med nivån av socialt deltagande i området.

**Studie V:** att studera (i) om lågt social deltagande har samband med låg följsamhet till blodtryckssänkande läkemedel, och (ii) om detta eventuella samband är olika i olika kommuner.

**Material**

**Malmö Kost Cancer (MKC) studien**

I Studie I och II använde vi tvärsnittsdata från Malmö Kost Cancer (MKC) studien. Malmö är administrativt indelad i 110 bostadsområden. Vi inkluderade 95 av dessa bostadsområden, som hade 20 eller fler deltagare i MKC.

Boende i Malmö tillfrågades om de ville delta i MKC genom brev, reklamkampanjer i lokala media och genom samarbete med större arbetsgivare i Malmö.


Alla deltagare gav skriftligt informerat samtycke till att delta i studien.

**Studie I:** Av de 17388 kvinnorna i MKC inkluderades 89% (n=15456) i denna studie. Anledningar för exkludering var ofullständig information om studievariablerna och att bo i ett bostadsområde med färre än 20 deltagare i MKC.

**Studie II:** Av de 17388 kvinnorna i MKC inkluderades 70% (n=12156) i denna studie. Anledningar för exkludering var ålder över eller lika med den officiella svenska pensionsåldern 65 år, ofullständig information om studievariablerna och att bo i ett bostadsområde med färre än 20 deltagare i MKC.

**Liv & hälsa år 2000 undersökningen**

I Studie III och IV använde vi tvärsnittsdata från Liv & hälsa år 2000 undersökningen, en enkätundersökning administrerad av Statistiska Centralbyrån. Ett slumpmässigt urval av 70044 personer, 18-79 år från 58 kommuner i 6 regioner i Mellansverige (Södermanlands, Uppsala, Värmlands, Västmanlands och Örebro län samt södra Dalarna), hade möjlighet att besvara enkäten, vilket två av tre (67%) gjorde. Syftet med undersökningen var att få självrappporterad information om människors liv och hälsa i
området och kompletterades med registerdata om ålder, kön, folkbokföringsort samt utbildningsnivå. Områdena i Studie III och IV motsvarar kommuner, förutom de tre största kommunerna Uppsala, Västerås och Örebro, som delades in i 10, 8 och 5 delområden. Totalt blev det 78 områden.

Studie III: Av de 46636 deltagarna i Liv & hälsa år 2000 inkluderades 82% (n=20319 kvinnor och 17850 män), som hade komplett information om alla variablerna som användes i studien.

Studie IV: Av de 46636 deltagarna i Liv & hälsa år 2000 inkluderade vi de 34% som hade besökt en akutmottagning, läkare på annan sjukhusmottagning, läkare på vårdcentral eller blivit inlagd på sjukhus under de senaste 3 månaderna, och som hade komplett information om alla variablerna som användes i studien (n=9070 kvinnor och 6795 män).

Folkhälsoenkät Skåne 2000
I Studie V använde vi tvärsnittsdata från Folkhälsoenkät Skåne 2000, en enkätundersökning som skickade ut till ett slumpmässigt urval av 23437 personer mellan 18-80 år boende i Skåne. Syftet med undersökningen var att få information om hälsa och olika typer av hälsorisker bland skåningar. Skåne hade ca 1,2 miljoner invånare år 2000 och delades in i 33 kommuner. Totalt svarade 59% (13715) på enkäten.

Studie V: Av de 13715 deltagarna i Folkhälsoenkät Skåne 2000 inkluderades de som angett användning av blodtryckssänkande läkemedel samt med komplett information om alla variablerna som användes i studien (n=1288).

Metoder
Vi använde multilevel logistisk regression med individer på första nivån och områden på andra nivån. Både mått på samband och mått på varians undersöktes.

Studie I: Utfallsvariabel var användning av lugnande medel och/eller sömnmedel. Förklarande variabler var ålder, socialt deltagande, utbildningsnivå, en samboende, förtidspension, självskattad hälsa, självrapporterad stress, användning av somatiska läkemedel samt nivån av socialt deltagande i bostadsområdet.

Studie II: Utfallsvariabel var förtidspension. Förklarande variabler var ålder, användning av lugnande medel och/eller sömnmedel, låg socialt deltagande, låg utbildningsnivå, ensamboende, låg självskattad hälsa, användning av somatiska läkemedel samt nivån av socialt deltagande i bostadsområdet.

Studie III: Utfallsvariabel var användning av lugnande medel och/eller sömnmedel. Förklarande variabler var ålder, socialt deltagande, tillit, utbildningsnivå, ekonomiska svårigheter samt graden av miniatyrisering av området (dvs en kombination av högt socialt deltagande och låg tillit i området).

Studie IV: Utfallsvariabel var uthämtning av läkemedel (följsamhet till läkemedelsordinationen). Förklarande variabler var ålder, socialt deltagande, utbildningsnivå, ekonomiska svårigheter, självskattad hälsa, förtroende för sjukvården samt nivån av socialt deltagande i området.
Studie V: Utfallsvariabel var följsamhet till blodtryckssänkande läkemedel. Förklarande variabler var ålder, kön, socialt deltagande, utbildningsnivå, självskattad hälsa och psykisk hälsa.

Resultat

Studie I: Generellt förklarade bostadsområdet 1,7% av de totala skillnaderna mellan kvinnorna vad gällde benägenheten att använda lugnande medel och sömnmedel. Denna procentandel varierade dock mellan olika grupper av kvinnor. Låg nivå av socialt deltagande i bostadsområdet hade samband med högre benägenhet för användning av lugnande medel och sömnmedel (odds kvot= 3,10 (95% konfidentsintervall 1,51-6,41)), oberoende av ålder, individuellt lågt socialt deltagande, låg utbildningsnivå och ensamstående. Sambandet försvagades (odds kvot= 2,01 (95% konfidentsintervall 0,97-4,14)) efter utökad justering för förtidspension, låg självskattad hälsa, självrapporterad stress och användning av somatiska läkemedel.

Studie II: Både användning av lugnande medel och sömnmedel (odds kvot= 2,09 (95% konfidentsintervall 1,65-2,65)) och nivån av socialt deltagande i bostadsområdet (odds kvot= 11,85 (95% konfidentsintervall 5,09-27,58)) hade samband med ökad benägenhet för förtidspension, efter justering för de förklarande variablerna. Sambandet mellan användning av lugnande medel och sömnmedel och förtidspension försvagades inte av bostadsområdet. Hypotetiskt sett, kunde en kvinna i den här studien öka sin sannolikhet för förtidspension med 72% i median om hon flyttade till ett annat bostadsområde med högre andel förtidspensionerade.

Studie III: Att bo i ett område med en hög grad av miniatyrisering av samhället (dvs en kombination av högt socialt deltagande och låg tillit i området) var associerat med användning av lugnande medel och sömnmedel (för kvinnor: odds kvot= 1,34 (95% konfidentsintervall 1,15-1,56), för män: odds kvot= 1,22 (95% konfidentsintervall 0,99-1,49)), efter justering för de förklarande variablerna. Det var dock endast små skillnader mellan områdena vad gällde den individuella användningen av lugnande medel och sömnmedel.

Studie IV: Lägre ålder, ekonomiska svårigheter, låg självskattad hälsa och lågt förtroende för sjukvården var associerade med lägre sannolikhet för att hämta ut läkemedel. Nivån av socialt deltagande i området inverkade inte på benägenheten att hämta ut läkemedel, och det var endast små skillnader mellan områdena vad gällde den individuella uthämtningen av läkemedel.

Studie V: Lågt socialt deltagande hade samband med låg följsamhet till blodtryckssänkande läkemedel (odds kvot = 2,05 (95% konfidentsintervall 1,05-3,99)), oberoende av ålder, kön och utbildningsnivå. Sambandet försvagades (odds kvot=1,80 (95% konfidentsintervall 0,90-3,61)) efter utökad justering för självskattad hälsa och psykisk hälsa. Sambandet mellan socialt deltagande och följsamhet till blodtryckssänkande läkemedel varierade mellan olika kommuner i Skåne.
Slutsatser

Nivån av socialt deltagande i bostadsområdet och graden av miniatyrisering av samhället i området tycks kunna påverka användningen av lugnande medel och sömnmedel, möjligtvis via inverkan på individuella egenskaper. Våra studier pekar dock på endast små skillnader mellan områden inom Malmö och inom Mellansverige vad gäller individuell användning av lugnande medel och sömnmedel.

Kvinnor som bor i samma bostadsområde i Malmö verkar ha liknande benägenhet för förtidspension, oberoende av deras individuella egenskaper. Denna kontextuella effekt verkar till stor del kunna förklaras av nivån av socialt deltagande i bostadsområdet. Användning av lugnande medel och sömnmedel verkar vara associerat med förtidspension bland kvinnor, möjligtvis på grund av att dessa läkemedel har en negativ påverkan på hälsan.

Individuella egenskaper hos dem som bor i Mellansverige som kan påverka benägenheten att inte hämta ut läkemedel verkar vara lägre ålder, ekonomisk stress, låg självskattad hälsa och lågt förtroende för sjukvården. Dessutom verkar lågt socialt deltagande ha samband med låg följsamhet avseende blodtryckssänkande läkemedel, och detta samband kan sannolikt variera mellan olika kommuner i Skåne.
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10 STUDY I-V