Urban-rural differences in distal forearm fractures - Cohort Norway.

Søgaard AJ [1, 2], Gustad TK [2,1], Bjertness E [2], Tell GS[3], Schei B[4], Emaus, N[5], Meyer HE [2,1]

on behalf of the Norwegian Epidemiological Osteoporosis Studies (NOREPOS) Research Group *

ajso@fhi.no t.k.gustad@studmed.uio.no espen.bjertness@medisin.uio.no h.e.meyer@medisin.uio.no nina.emaus@ism.uit.no berit.schei@ntnu.no grethe.tell@helse-bergen.no

[1] Division of epidemiology, Norwegian Institute of Public Health, Oslo, Norway

[2] Institute of General Practice and Community Medicine, Section for Preventive Medicine and Epidemiology, University of Oslo, Oslo, Norway

[3] Department of Public Health and Primary Health Care, University of Bergen, Bergen, Norway.

[4] Department of Community Medicine, Norwegian University of Science and Technology, Trondheim, Norway.

[5] Institute of Community Medicine, University of Tromsø, Norway

* The NOREPOS Research Group – *Core Research Group (in alphabetic order):*
Nina Emaus (Tromsø), Haakon E. Meyer (Oslo), Berit Schei (Nord-Trøndelag), and Grethe S. Tell (Bergen).

Local collaborators: (in alphabetic order)
Bergen: Gjesdal CG, Tell GS
Nord-Trøndelag: Forsén L, Forsmo S, Langhammer A, Schei B
Oslo: Falch JA, Meyer HE, Søgaard AJ
Tromsø: Berntsen GKR, Emaus N, Fønnebø V, Joachimsen RM

Address for correspondence and reprints:

Anne Johanne Søgaard
Norwegian Institute of Public Health
P.O.Box 4404 Nydalen, 0403 Oslo, Norway
Phone +47 23 40 81 87
Fax +47 23 40 82 60
E-mail: ajso@fhi.no

Running title: Forearm fracture and urbanization.

Word count: Abstract: 199, Paper: 3,488

Abbreviations:

CONOR= The collaborative Norwegian study "Cohort Norway"

BMD=Bone Mineral Density

BMI=Body Mass Index

SD=Standard Deviation

OR=Odds Ratio

CI=Confidence Interval

ABSTRACT

The purpose of this study was to investigate possible urban-rural gradients in self-reported forearm fractures, and assess the contribution of lifestyle or socio-demographic factors to such gradients. The collaborative Norwegian study "Cohort Norway" comprises ten population-based surveys inviting altogether 309,832 individuals aged 20 years and above. All the 181,891 participants underwent a standardized examination and answered 50 common questions on socio-demographic conditions, risk factors and diseases, including one question concerning former forearm/wrist fractures. Based on the home-addresses, participants' were divided into three population density groups – cities, densely and sparsely populated areas. The analyses are limited to the 162,286 participants 30 years and above, of whom 21,661 reported a forearm fracture. The prevalence increased with increasing degree of urbanization for both genders. After adjustment for age and potential explanatory factors, the odds ratio of having sustained a forearm fracture in men living in densely populated areas and in cities were 1.12 (95% confidence interval: 1.04, 1.21) and 1.38 (95% confidence interval: 1.30, 1.46), respectively, compared to rural areas. Similar odds ratios were observed among women. A higher proportion of self-reported fractures were found in urban compared to rural areas, with an evident urbanization gradient not explained by other factors.

Key words: Epidemiology, forearm, fractures, osteoporosis, rural population, urban population, urbanization, wrist

The Norwegian incidence rates of distal forearm fractures are the highest ever reported (1-3). The capital city of Oslo still had a higher incidence than elsewhere when the analyses were restricted to the summer months without snow and ice (1). Although not among the fractures with the most serious consequences for the individual, distal forearm fracture is nevertheless an indicator of postmenopausal osteoporosis (4-6). Almost every second woman and every third man 50 years or older with a low energy wrist fracture have osteoporosis (t-score $\leq$ 2.5) (7), and wrist fractures are an important predictor of suffering a subsequent osteoporotic fracture (8-9). Pooled data from existing studies displayed more than a 2-fold risk of future fracture given a history of prior wrist fracture (9). In elderly women, prior wrist fracture is a risk factor for vertebral fractures also after adjustment for bone mineral density (10).

In contrast to hip fractures, only a limited number of studies have identified risk factors for distal forearm-/wrist fractures. Whereas reports from Norway and other Western countries suggest a universally higher incidence of hip fractures among city dwellers compared to rural populations (11-23), only a few studies have examined whether a corresponding urban-rural difference exists for other types of fractures – including distal forearm-/wrist fractures (17, 23-25). These studies report a higher *overall* fracture rate in urban compared to rural areas, also when hip fractures are excluded. Only one of these studies found a statistically significant urban–rural difference in wrist fractures (23), however this study did not have access to individual data on possible confounding factors. The etiology of urban-rural differences is not known, although physical activity, work load and other lifestyle- and environmental factors have been posed as possible explanatory factors (11, 17, 19, 24-25).

The aim of this study was to investigate possible urban-rural gradients in self-reported forearm fractures, and whether such gradients could be attributed to lifestyle or socio-demographic factors. The very large population-based collaborative Norwegian study “Cohort Norway” (CONOR) offered the opportunity to examine these issues.

MATERIALS AND METHODS

CONOR is a large collaborative project between epidemiological centers at the University of Tromsø, the Norwegian University of Science and Technology in Trondheim, the University of Bergen, the University of Oslo and the Norwegian Institute of Public Health (26-27). Regional data from 10 epidemiological studies have been merged into a national database for the purpose of examining environmental, genetic, cultural and social exposures on rare conditions and diseases.

Invitation and procedures

The location of the study sites are shown in figure 1 and the web site for each study contains more detailed information (see Table 1). Altogether 309,832 individuals were invited to participate (Table 1), based on addresses from the Population Registry of Norway. Some of the studies invited all subjects above a specific age, whereas others invited all subjects in selected age groups. In all CONOR surveys, the data collection followed a standard procedure, described in more details on CONOR’s web site (28).

Letters of invitation were mailed about 2 weeks before the time of appointment. Included were a questionnaire and a brochure with information about the aims of the study, examinations and procedures. The main questionnaire was brought to the screening station, where heart rate, systolic and diastolic blood pressures, weight, height, and waist and hip circumferences were measured, and a non-fasting blood sample was drawn and analyzed for serum total- and HDL cholesterol, glucose and triglycerides. Another sample of whole blood was stored at minus 80 degrees Celsius. At most study sites, participants were given supplementary questionnaires to fill in at home and return by mail in pre addressed envelopes.

All the surveys used 50 common questions which are available at CONOR's web site (28). The CONOR-questions include self-reported health and selected diseases, various risk factors, socio-demographic factors, use of medications and reproductive history (women).

CONOR participants

Altogether 181,891 subjects participated, among these 7,460 participated in more than one surveys (Table 1). For the latter group, information from the last survey only is included, yielding a total number of 174,430 participants. The attendance rate varied between study sites, declined slightly throughout the study-period 1994-2003 and was higher in sparsely/densely populated areas than in cities.

The age distribution of the CONOR participants is shown in table 2. In this paper we have limited the analyses to the 162,286 participants 30 years and above with valid information on place of residence (79,101 men and 83,185 women).

Ethics and approvals

At each study site, the study protocol was evaluated by the Regional Committee for Medical Research Ethics and approved by the Norwegian Data Inspectorate. All participants signed an informed declaration of consent form.

Variables used in this paper

In addition to the variables from the invitation file – i.e. gender, age, address, country of birth (in this study dichotomized by having been born in Norway or not), and marital status (dichotomized into married versus not), the following variables are used in this paper:

Forearm fracture. The participants were asked: Have you ever broken (fractured) your wrist/forearm. If yes, indicate the age at the last occasion.

Population density. Based on information on place of residence (municipality) from the invitation file, the participants were divided into three population density groups – i.e. inhabitants living in sparsely populated areas (municipalities with less than 10,000 inhabitants), densely populated areas (municipalities with 10,000-19,999 inhabitants), or cities (municipalities with 20,000 or more inhabitants). The municipality of Tromsø encompasses a large geographic area (2.558 km^2) and was divided in two – those living in the urban areas of Tromsø were classified to the city area, the others were classified as living in rural areas. Statistics Norway contributed information about the size of all municipalities in Norway.

Covariates. As possible confounding or explanatory factors we considered variables known to be associated with fractures – i.e. age, gender, marital status, country of birth, length of education, smoking, consumption of alcohol, physical activity during leisure time and during work hours, height, body mass index (BMI) and postmenopausal hormone therapy (women only).

Number of years of education was used as a continuous variable in the multivariate analyses, or dichotomized into 10 years or less vs. 11 years or more. Smoking was classified as current daily smoking vs. previous/never. Consumption of alcohol was dichotomized into drinking 4-7 times per week vs. less, and the question regarding number of hours of vigorous leisure time physical activity during an average week was dichotomized into no such activity (=inactive) vs. more. Physical activity at work was dichotomized into mainly sedentary work (desk work, assembly work) vs. work involving a lot of walking, lifting or heavy physical work.

Postmenopausal hormone therapy was categorized as never-/previous use vs. current use. In addition we have used the measures height (in cm) and body mass index (kg/m^2).

Statistical analyses

All analyses were conducted using SPSS. Comparisons between background characteristics and the population density groups were done by F-tests for continuous- and by chi-square tests for categorical variables. Standard deviations are reported for crude means. The age-adjusted figures were compared using variance analysis and tested by F-test.

Logistic regression was employed to estimate the association between forearm fractures and population density groups – and to study whether adjustment for other factors would change the association. The full model was also tested for trend.

RESULTS

Characteristics of participants 30 years and older, stratified by the three population density groups are shown in table 3. Men and women living in rural areas were the oldest, but the difference between the three groups was 3.5 years at the most. A higher proportion of participants residing in cities were single, had more than 10 years of education, consumed alcohol 4-7 times a week and had sedentary type of work compared to participants from the two less populated areas. The city dwellers had lower proportions of smokers and women with sedentary leisure time physical activity. Adjusting for age did not substantially change the results and the crude figures are thus shown in table 3.

Altogether 149,725 participants 30 years and over with information on place of residence (92.3 percent) answered the question about forearm fracture. A similar proportion of men (n=10,585; 14.5 percent) and women (n=11,076; 14.4 percent) reported to have suffered a forearm fracture, and the prevalence increased with increasing degree of urbanization for both genders (table 4). The crude- and age-adjusted results were almost similar (table 4). Compared to rural areas the age-adjusted prevalence of forearm fractures was 13 percent higher in densely populated areas and 37 percent higher in city areas - in both men and women. The urbanization gradient was present in all age groups for both genders ($p \leq 0.001$) (figure 2a and 2b). The difference between rural and urban areas increased with increasing age.

Because CONOR includes information about place of residence at one year of age, we redid the analyses for those ca. 50,000 participants (>=30 years) who lived in the same municipality the first year after birth and at the time of the study. The differences between the three population density areas were, in both genders, similar to those shown in table 4 (Data not shown).

The age adjusted odds ratio of sustaining a forearm fracture among men living in densely populated and in city-areas were 1.13 (95 percent confidence interval (CI): 1.05, 1.22) and 1.42 (95 percent CI: 1.35, 1.50), respectively, compared to rural area (table 5). The odds ratios for women were almost identical. The odd ratios were slightly reduced after multivariate adjustment, but the associations remained statistically significant. Test for trend showed p <0.001 for both genders. Analyses excluding all participants born outside Norway (n=9,852) gave similar results.

Because the question about physical activity at work (type of work) was asked to a sub-population only (see footnote table 3), we did a separate analysis with additional adjustment for this variable. The associations between fractures and population density were similar with and without this additional adjustment.

The analyses shown in table 5 were repeated including only participants 50 years and over who had suffered their last forearm fracture at the age of 50 years or later. Adjusted for age and explanatory variables, the differences between rural- and city-areas became larger for both men (odds ratio=1.61, 95 percent CI: 1.34, 1.93) and women (odds ratio=1.52, 95 percent CI: 1.37, 1.68), but odds ratio for forearm fractures in the densely populated area was not statistically significant different from the rural area. The statistical power was strongly reduced in this sub-sample (n= 27,938 men and n=20,393 women in the logistic regression analyses).

The CONOR database does not contain information about falls, but three of the sub-studies (HUBRO, OPPHED, TROFINN – see table 1, figure 1) provided information about falls in participants 75-76 years old. About 25 percent of men and almost 30 percent of women reported at least one fall during the last year, irrespective of place of living. The only exception was women in Oslo (HUBRO), where the percent of falls was 34.

DISCUSSION

The proportion of men and women reporting to have suffered a distal forearm fracture increased with increasing degree of urbanization. Adjusted for age, men living in city-areas were 37 percent more likely to have sustained a forearm fracture compared with men living in rural areas; the corresponding figure for men in densely populated areas was 13 percent. The figures for women were similar. To our knowledge, this is the first time a relationship between forearm fractures and *degree* of urban-rural living has been reported, although this has been previously reported for hip fractures (11).

Strength and weaknesses

A strength of this population-based study is the large number of participants and fractures, the representation from ten different studies from around the country, and the standardized procedures and questions used at all sites. However, the study also has its methodical problems and limitations. The participation was lower in some of the cities compared to the more rural areas. The possible problem of bias because of non-attendance in population-based studies has been analyzed in the Oslo Health Study (29). Even though unhealthy persons attended to a lesser degree than healthy individuals, self-selection had little impact on prevalence estimates of risk factors and self-reported diseases. Most of the associations between outcome- and exposure variables (available for both attendees and non-attendees) were found to be unbiased (29).

Self-report of fracture

Self-reports are not optimal regarding information about forearm fractures. However, several studies have compared self-reports with official hospital registries/medical records and found fairly high validity. In one of the CONOR sites, the Tromsø Study, 85 percent of all forearm fractures registered in the X-ray registry at the Tromsø University Hospital, were also self-reported (30). Very few cases of over-reporting were found. In an Australian study, the false positive rate was 2.2 percent for wrist fractures (31). In a Danish validation-study the positive predictive value was 84 percent for wrist fractures, and false positive reports introduced only modest bias in fracture risk estimates and tended to dilute the association between exposure and fracture (32).

The Women's Health Initiative also supports a high validity of self-reports for forearm-/wrist fractures with 81 percent agreement between self-reports and review of medical records (33). Two prospective studies made similar conclusions regarding self-reports of forearm fractures

(34, 35). We therefore conclude that self-report is a relatively accurate method of obtaining information about the occurrence of distal radius fractures.
An important question in our study is whether those living in rural areas report differently compared to inhabitants in more densely populated areas and cities. A Swedish study found that subjects in the city of Malmø had forgotten more of their fractures compared to subjects living in the small village of Sjöbo in the same region (36). If this is the case in Norway as well, the fracture differences between the three areas would be even larger than those reported here.

Other limitations

The lower prevalence of forearm fractures in sparsely populated areas could reflect longer distance to physicians with radiographic service and thus lower rates of established diagnosed fractures. If this factor explained the difference, there would be a considerable number of undiscovered fractures in Norway. This is unlikely given our well developed public health service where almost all expenses for the consultation and the referral to an x-ray clinic are covered by social security.

To verify our findings, we were able to obtain unpublished data on forearm fractures from the Fracture Registry at the University Hospital in Tromsø. A higher 5 year incidence of forearm fractures was found in the urban vs. rural part of the Municipality of Tromsø both among men and women above 30 years participating in the Tromsø Study during 1994-95. The urban versus rural rates per 10,000 person-years were 12.3 vs. 8.7 in men and 53.0 vs. 43.6 in women (Dr. Luai Awad Ahmed, University of Tromsø, personal communication, 2005).

Our main exposure variable, level of urbanization, is constructed based on the number of inhabitants in the municipality. Although this is a crude variable, we nevertheless found an increase in forearm fractures by increasing degree of urbanization. If anything, this lack of precision in the exposure measurement should cause an under-, rather than over-estimation of the association in question.

Other studies have reported higher risk of forearm fractures in white Caucasian women than in other ethnic groups (37). The vast majority of the participants in CONOR were ethnic Norwegians (i.e. Caucasian). Only the city of Oslo has a moderate proportion of non-Caucasian immigrants. Excluding individuals born outside Norway did not change the main findings.

Our study is cross-sectional with its implied weaknesses. The reported fractures may have happened a long time ago, when the participants were living in another area than the present residence. While we do not know the potential impact of such misclassification, we believe that it could probably weaken the associations. We do not have information about the residential history of our participants. However when we analyzed only those who lived in the same municipality the first year after birth and at the time of the study, the fracture prevalence in the three population density areas were similar as the main findings.

The fracture mechanism is furthermore unknown. Although we included only individuals 30 years and older to avoid the more prevalent high-energy fractures in younger age groups, such fractures may nevertheless be included. It seems, however, that also high-energy fractures are associated with low bone mineral density (9). In an Australian study the bone mineral density (BMD z-scores) were reduced in both the low- and the high trauma groups - and the odds ratios for having osteoporosis (t-score $\leq$ -2.5) were 2.7 and 3.1, respectively, when compared to a group without fractures (38). This may indicate that our results would not have differed if only low-energy fractures had been included.

Possible causes of the differences

In a large study in Southern Tasmania, all fractures were identified from radiologists' reports (23). The rate ratios of wrist fractures in urban vs. rural areas were 1.8 in men and 1.7 in women (all ages), but they did not have access to individual data on risk factors.

When we adjusted for known risk factors for forearm fractures in our study, the odds ratios were only slightly reduced. If we assume that the risk factors are measured adequately, there must be other, unmeasured, factors that could explain the association, e.g. BMD, environmental factors like air- or water pollution, or icy road conditions during winter. Several studies have documented a higher incidence of forearm fractures in the winter than in the summer months (1, 2, 39-40). In a Norwegian city, more than half the distal radial fractures occurred while out walking (2). It is not unlikely that the pavements and streets in the cities are more slippery than roads in more sparsely populated areas, although we have no data to document this.

Fractures are caused by a combination of low bone mass/bone quality and fall/trauma. More falls in urban compared to rural areas could have been one reason for our findings. Although we have no information about falls in CONOR overall, data from 75/76 year-old participants in three of the CONOR-studies indicated no association between falls and degree of urbanization, except for a higher percent of falls in Oslo-women (HUBRO). This slightly higher fall rate could hardly explain our findings.

Some of the CONOR-studies have included BMD measures in ancillary studies – forming the Norwegian Epidemiological Osteoporosis Studies (NOREPOS). Higher BMD was found in rural compared with urban areas (41), which may explain parts of the association between forearm fracture and degree of urbanization in our study. The BMD differences corresponded to an increased risk of forearm fracture of 12-20 percent in cities vs. rural areas. Thus, there must be additional unknown factors contributing to the association we found in our study. Two other studies confirm higher bone mineral density in rural compared to urban dwellers (42-43), the first has analyzed forearm BMD, the other femoral neck.

Even though we adjusted for physical activity, we cannot rule out the possible effect of long time exposure to physical activity in daily life. Our questions about physical activity were limited to last year – and do not ask for "everyday" activity (house-cleaning, walking to neighbors/ school/ work/ store, climbing stairs etc). Our question about type of work was only asked to a sub-sample, which was not totally comparable to the total sample. In a Swedish study both men and women in a rural area had significantly higher work load and were more physically active during leisure time compared to an age-matched group in the city of Malmø, suggesting that the higher prevalence of fractures in Malmø could be explained by a less physically active lifestyle (44). Further, elderly women in Malmø participating in long-term moderate exercise programs for more than 20 years, performed significantly better in all functional tests and sustained fewer fractures than age-matched controls from the same city, but not statistically significant different compared to rural controls (45). The possible effect of every day physical activity on the fracture difference between rural and urban area should be investigated more thoroughly.

Several studies have reported higher hip fracture rates in urban compared with rural areas (11-23). A few studies have reported a corresponding difference in all fractures (17, 23-25), and one in wrist fractures (23). As far as we are aware, no study has yet observed an association between forearm fractures and *degree* of urbanization. Our finding of a "dose-response" relationship strengthens the suggestion of a real association between risk of forearm fractures and population density. The consistent findings across gender and age support this suggestion.

Conclusion

We found a statistically significant gradient in the proportion of self-reported forearm fractures from cities to densely populated rural areas to sparsely populated rural areas in both genders. The differences persisted after adjusting for possible explanatory factors. Further studies are needed to verify whether the differences might be explained by lower bone mineral density, lower lifetime workload and/or more falls in urban compared to rural areas.

ACKNOWLEDGEMENT

All data used in this paper were obtained from Cohort Norway. The authors wish to acknowledge the services of CONOR and the contributing research centres delivering data to CONOR. Our sincerely thank to all the participants and all the staff-members dealing with collection of the health surveys contributing to the CONOR database.

We would like to thank dr. PhD Luai Awad Ahmed, Institute of Community Medicine, University of Tromsø, Norway for his preliminary analyses of forearm fractures from the Fracture Registry at the University Hospital in Tromsø, and professor Svetlana Skurtveit, the Norwegian Institute of Public Health for her preliminary analyses of falls in the Oppland and Hedmark Health Study (OPPHED).

REFERENCES

1. Falch JA. Epidemiology of fractures of the distal forearm in Oslo, Norway. Acta Orthop Scand 1983;54:291-5.

2. Hove LM, Fjeldsgaard K, Reitan R, et al. Fractures of the distal radius in a Norwegian city. Scand J Plast Reconstr Surg Hand Surg 1995;29:263-7.

3. O'Neill TW, Cooper C, Finn JD, et al. Incidence of distal forearm fracture in British men and women. Osteoporos Int. 2001;12:555-8.

4. Eastell R. Forearm fracture. Bone 1996;18 (Suppl 3):2035-75.

5. Earnshaw SA, Caute SA, Worley A, et al. Colles' fracture of the wrist as an indicator of underlying osteoporosis in postmenopausal women: a prospective study of bone mineral density and bone turnover rate. Osteoporos Int 1998;8:53-60.

6. Cuddihy MT, Gabriel SE, Crowson CS, et al. forearm fractures as predictors of subsequent osteoporotic fracture. Osteoporos Int 1999;9:469-75.

7. Haugeberg G, Gjesdal CG, Gulseth HC. Application of the Norwegian Medicines Agency Osteoporosis Treatment Guidelines on male and female patients with wrist fractures in Norway (Abstract). J Bone Miner Res 2005;20(Suppl 1):S266.

8. Barrett-Connor E, Siris E, Miller P, et al. Association of wrist fracture with subsequent hip, spine, rib, and wrist or forearm fractures in postmenopausal women: Results from the National Osteoporosis Risk Assessment (NORA) (Abstract). J Bone Miner Res 2005;20(Suppl 1):S267.

9. Klotzbuecher CM, Ross PD, Landsman PB. Patients with prior fractures have an increased risk of future fractures: A summary of the literature and statistical synthesis. J Bone Miner Res 2000;15:721-739.

10. Schousboe JT, Fink HA, Taylor BC, et al. Association between self-reported prior wrist fractures and risk of subsequent hip and radiographic vertebral fractures in older women: a prospective study. J Bone Miner Res 2005;20:100-6.

11. Finsen V, Benum P. Changing incidence of hip fractures in rural and urban areas of central Norway. Clin Orthop Relat Res 1987;218:104-10.

12. Finsen V, Johnsen LG, Tranø G, et al. Hip fracture incidence in Central Norway: A follow-up study. Clin Orthop 2004;419:173-8.

13. Bulajic-Kopjar M, Wiik J, Nordhagen R. Regional differences in the incidence of hip fracture in Norway (Norwegian). Tidsskr Nor Lægeforen 1998;118:30-3.

14. Larsson S, Eliasson P, Hansson LI. Hip fractures in northern Sweden 1973-1984. Acta Orthop Scand 1989;60:567-71.

15. Falch JA, Ilebekk A, Slungaard U. Epidemiology of hip fractures in Norway. Acta Orthop Scand 1985;56:12-6.

16. Madhok R, Melton LJ III, Atkinson E, et al. Urban vs rural increase in hip fracture incidence. Acta Orthop Scand 1993;64:543-8.

17. Sanders KM, Nicholson GC, Ugoni AM, et al. Fracture rates lower in rural than urban communities: The Geelong Osteoporosis Study. J Epidemiol Community Health 2002;56:466-470.

18. Falch JA, Kaastad TS, Bohler G, et al. Secular increase and geographical differences in hip fracture incidence in Norway. Bone 1993;14:643-5.

19. Mannius S, Mellstrom D, Oden A, et al. Incidence of hip fracture in western Sweden 1974-1982. Comparison of rural and urban populations. Acta Orthop Scand 1987;58:38-42.

20. Sernbo I, Johnell O, Andersson T. Differences in the incidence of hip fracture. Comparison of an urban and a rural population in southern Sweden. Acta Orthop Scand 1988;59:382-5.

21. Chevalley T, Herrmann FR, Delmi M, et al. Evaluation of the age-adjusted incidence of hip fractures between urban and rural areas: the difference is not related to the prevalence of institutions for the elderly. Osteoporos Int 2002;13:113-8.

22. Norton R, Yee T, Rodgers A, et al. Regional variation in the incidence of hip fracture in New Zealand. N Z Med J 1997;110:78-80.

23. Cooley HM, Jones G. Symptomatic fracture incidence in southern Tasmania: does living in the country reduce your fracture risk? Osteoporos Int 2002;13:317-22.

24. Jonsson B, Gardsell P, Johnell O, et al. Differences in fracture pattern between an urban and a rural population: a comparative population-based study in southern Sweden. Osteoporos Int 1992;2:269-73.

25. Melton LJ 3rd, Crowson CS, O'Fallon WN. Fracture incidence in Olmsted County, Minnesota: comparison of urban with rural rates and changes in urban rates over time. Osteoporos Int 1999;9:29-37.

26. Engeland A, Søgaard AJ. CONOR (Cohort NORway) - an overview of a unique research material (Norwegian – English abstract). Nor J Epidemiol 2003;13:73-77.

27. Magnus, P, Arnesen E, Holmen J, et al. CONOR - Cohort NORway: history, purpose and potential (Norwegian). Nor J Epidemiol 2003;13:79-82.

28. Norwegian Institute of Public Health, Oslo, Norway. CONOR. July 2006. (http://www.fhi.no/artikler/?id=28138).

29. Søgaard AJ, Selmer R, Bjertness E, et al. The Oslo Health Study. The impact of self-selection in a large, poulation-based survey. Int J Equity Health 2004; 3:3. Online: http://www.equityhealthj.com/content/3/1/3

30. Joakimsen RM, Fonnebø V, Søgaard AJ, et al. The Tromsø Study: registration of fractures, how good are self-reports, a computerized radiographic register and a discharge register? Osteoporos Int 2001;12:1001-5

31. Ivers RQ, Cumming RG, Mitchell P, et al. The accuracy of self-reported fractures in older people. J Clin Epidemiol 2002;55:452-7.

32. Hundrup YA, Hoidrup S, Obel EB, et al. The validity of self-reported fractures among Danish female nurses: comparison with fractures registered in the Danish National

Hospital Register. Scand J Public Health 2004;32:136-43.

33. Chen Z, Kooperberg C, Pettinger MB, et al. Validity of self-report for fractures among a multiethnic cohort of postmenopausal women: results from the Women's Health Initiative observational study and clinical trials. Menopause 2004;11:264-74.

34. Nevitt MC, Cummings SR, Browner WS, et al. The accuracy of self-report of fractures in elderly women: evidence from a prospective study. Am J Epidemiol 1992;135:490-9.

35. Ismail AA, O'Neill TW, Cockerill W, et al. Validity of self-report of fractures: results from a prospective study in men and women across Europe. EPOS Study Group. European Prospective Osteoporosis Study Group. Osteoporos Int 2000;11:248-54.

36. Jonsson B, Gardsell P, Johnell O, et al. Remembering fractures: fracture registration and proband recall in southern Sweden. J Epidemiol Community Health 1994;48:489-90.

37. Barrett-Connor E, Siris E, Wehren LE, et al. Osteoporosis and fracture risk in women of different ethnic groups. J Bone Miner Res 2005;20:185-94. Epub 2004 Oct 18.

38. Sanders KM, Pasco JA, Ugoni AM, et al. The exclusion of high trauma fractures may underestimate the prevalence of bone fragility fractures in the community: the Geelong Osteoporosis Study. J Bone Mineral Res 1998;13:1337-42.

39. Wareham K, Johansen A, Stone MD, et al. Seasonal variation in the incidence of wrist and forearm fractures, and its consequences. Injury 2003;34:219-22.

40. Thompson PW, Taylor J, Dawson A. The annual incidence and seasonal variation of fractures of the distal radius in men and women over 25 years in Dorset, UK. Injuy 2004;35:462-6.

41. Meyer HE, Berntsen GKR, Søgaard AJ, et al. Higher bone mineral density in rural compared with urban dwellers: the NOREPOS study. Am J Epidemiol 2004;160:1039-46.

42. Gardsell P, Johnell O, Nilsson BE, et al. Bone mass in an urban and a rural population: a comparative, population-based study in southern Sweden. J Bone Miner Res 1991;6:67-75. Erratum in: J Bone Miner Res 1991;6:428.

43. Pongchaiyakul C, Nguyen T, Kosulwat V, et al. Effect of urbanization on bone mineral density: A Thai epidemiological study. BMC Musculoskelet Disord 2005;6:5. Online: http://www.biomedcentral.com/1471-2474/6/5.

44. Jonsson B, Gardsell P, Johnell O, et al. Life-style and different fracture prevalence: a cross-sectional comparative population-based study. Calsif Tissue Int 1993;52:425-33.

45. Ringsberg K, Gardsell P, Johnell O, et al. The impact of long-term moderate physical activity on functional performance, bone mineral density and fracture incidence in elderly women. Gerontology. 2001;47:15-20.

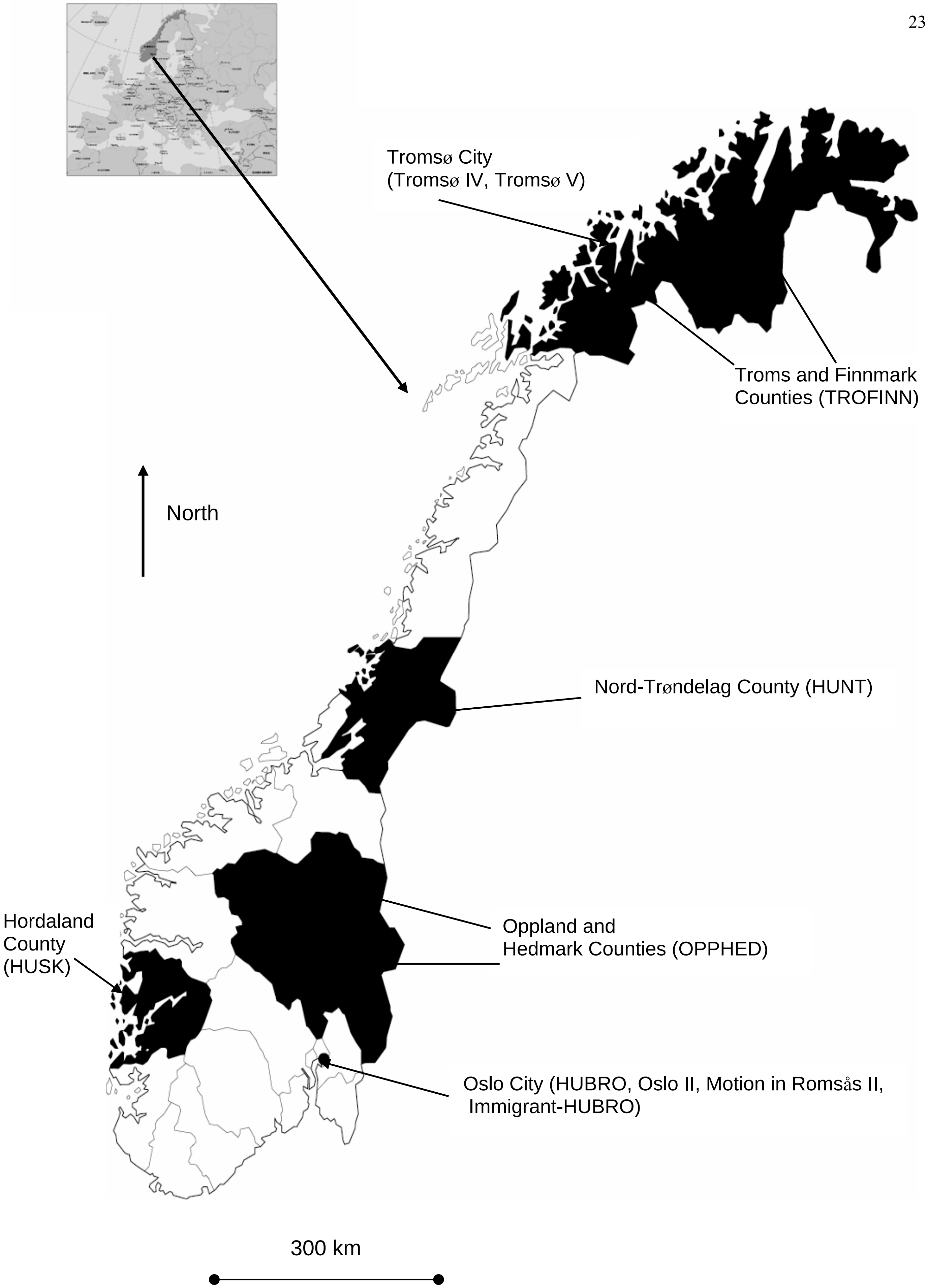
Tromsø City
(Tromsø IV, Tromsø V)
Troms and Finnmark Counties (TROFINN)
North
Nord-Trøndelag County (HUNT)
Hordaland County (HUSK)
Oppland and Hedmark Counties (OPPHED)
Oslo City (HUBRO, Oslo II, Motion in Romsås II, Immigrant-HUBRO)
300 km

FIGURE LEGEND

FIGURE 1. Map of Norway, as part of Europe, showing the geographic location of the ten surveys constituting Cohort Norway (CONOR) 1994-2003.

FIGURE 2a and b. The proportion of men (2a) and women (2b) 30 years or more reporting to have ever sustained a forearm fractures according to age-group in rural areas, densely populated areas and city areas. Cohort Norway (CONOR), 1994-2003.

TABLE 1. Number of invited and participating subjects in Cohort Norway (CONOR) 1994-2003.

Name of the study	Year of survey	Number invited†	Invited age-groups in years‡	Number of participants * Men	Women	Total	Web address
Tromsø IV (The fourth Tromsø Study)	1994-1995	37,582	25 +	12,797	14,128	26,925	http://uit.no/tromsoundersokelsen/tromso4/2
HUNT II (The second North-Trøndelag Study)	1995-1997	94,196	20 +	30,442	34,576	65,018	http://www.hunt.ntnu.no/
HUSK (The Hordaland Study)	1997-1999	38,587	40-44, 46-47, 70-72	11,678	13,852	25,530	http://www.uib.no/isf/husk/
Oslo II (The second Oslo Study)	2000	14,209§	48-77	6,919		6,919	http://www.fhi.no/artikler/?id=54685
HUBRO (The Oslo Health Study)	2000-2001	58,660#	30, 31, 40, 45, 46, 59/ 60, 75/ 76	9,751	12,264	22,015	http://www.fhi.no/artikler/?id=54464
OPPHED (The Oppland and Hedmark Health Study)	2000-2001	22,327	30, 40, 45, 60, 75	5,650	6,752	12,402	http://www.fhi.no/artikler/?id=28233
Tromsø V (The fifth Tromsø Study)	2001	10,419	30 +	3,491	4,586	8,077**	http://uit.no/tromsoundersokelsen/tromso5/2
I-HUBRO (The Oslo Immigrant Health Study)	2002	12,088††	20-60	1,915	1,768	3,683	http://www.fhi.no/artikler/?id=28217
TROFINN (The Troms and Finnmark Health Study) ‡‡	2002	16,229	30-77	4,318	5,009	9,327	http://www.fhi.no/artikler/?id=28261
MoRo II (The second part of the Romsås in Motion Study)	2003	5,535	34-70	899	1,096	1,995	http://www.fhi.no/artikler/?id=28254
CONOR (Cohort Norway)	1994-2003	309,832	20-103	87,157	92,928	181,891*	http://www.fhi.no/artikler/?id=28138

* Number of participants equals those who attended the survey and/or answered at least one questionnaire and signed a written consent. 7,460 persons participated in a second CONOR survey and 1 person participated in a third. Thus, the total numbers of participants with consent were 174,430.

† The numbers include all individuals invited. The individual surveys could have published papers with slightly different total numbers.

‡ HUSK: All 40-44 years and those participating in a study in 1992-93 born 1950-51 and 1925-27; Oslo II: All those invited to the Oslo Study 1972-73, except those invited to HUBRO and MoRo I (Invited in 1972/73: all men born 1923-32 and 7% random sample of those born 1933-52); Tromsø V: All 30, 40, 45, 60, 75 years and all those participating in phase II in Tromsø IV - which included: all born 1920-1939, 5-10% sample of other age groups attending phase I, all women born 1940-44; I-HUBRO: 30% random sample of people born in Pakistan, all born in Turkey, Sri Lanka, Iran, Vietnam - except those invited to HUBRO; MoRo II: All those participating in a study in 2 local districts in Oslo in 2000 (MoRo I) born 1933-1969 – except those participating in HUBRO; TROFINN: All 30, 40, 45, 60, 75 years and all those participating in three Finnmark studies in the period 1974-1988 – which included: All born 1925-1947, all born 1948-1968 invited to Finnmark I, II or III.

§ 2,515 more men who belonged to the Oslo II cohort, also belonged to the HUBRO cohort, and were only invited to HUBRO. Of these 1,320 men participated. They are only counted as participants in HUBRO.

Include 17,308 invitees (31 and 46 years – additional cohorts) who were not reminded. The attendance-rate of these was low.

** 6,967 of these participated also in Tromsø IV.

†† Include 4,116 persons (20-30 years – additional cohort) who were not reminded. The attendance-rate of these was very low.

‡‡ Include 18 of 25 municipalities in Troms and 10 of 19 municipalities in Finnmark. The other municipalities participated in Tromsø V and in SAMINOR, i.e. a health survey in communities with Sámi and Norwegian population, at the same time.

TABLE 2. Number of participants in Cohort Norway (1994-2003)
According to gender and age (at the time they attended the screening station).
If participating in more than one study, only the last one is counted.

	Men	Women	Total
Age	N	N	N
≤ 29	5,377	6,593	11,970
30-34	8,036	9,838	17,874
35-39	5,041	5,524	10,565
40-44	15,267	17,409	32,676
45-49	12,997	15,109	28,106
50-54	5,185	4,637	9,822
55-59	5,106	5,349	10,455
60-64	6,594	6,909	13,503
65-69	5,587	3,879	9,466
70-74	8,336	5,688	14,024
75-79	5,472	6,341	11,813
80-84	1,104	1,685	2,789
85+	514	853	1,367
Total	84,616	89,814	174,430

TABLE 3. Baseline characteristics of men and women 30 years and older according to population density. Cohort Norway 1994-2003.

	Men (79,101)						Women (83,185)					
	Rural (< 10,000 inh)		Densely populated (10-19,999 inh)		City (≥ 20,000 inh)		Rural (< 10,000 inh)		Densely populated (10-19,999 inh)		City (≥ 20,000 inh)	
Number	20,537		16,256		42,308		22,792		18,654		41,739	
	Mean/%	(SD)	Mean/%	(SD)	Mean/%	(SD)	Mean/%	(SD)	Mean/%	(SD)	Mean/%	(SD)
Age (mean, years)	53.6	(14.4)	51.4	(14.0)	52.8	(14.8)	53.7	(15.0)	51.7	(14.5)	50.2	(14.5)
Height (mean, cm)	176.2	(7.0)	177.4	(6.7)	177.2	(7.1)	163.2	(6.6)	164.1	(6.3)	164.1	(6.8)
BMI (mean, units)	26.9	(3.7)	26.7	(3.4)	26.2	(3.5)	26.7	(4.8)	26.1	(4.4)	25.4	(4.5)
Daily smoking %	32.0		30.5		28.9		31.4		30.8		29.8	
Not married %	33.0		29.1		34.8		35.4		33.1		43.7	
Education ≤ 10 years %	70.7		66.7		41.4		68.7		66.7		46.4	
Drinking alcohol 4-7 times per week %	1.5		1.3		5.8		0.5		0.4		2.4	
Sedentary physical activity during leisure time % *	36.1		30.8		34.1		49.7		43.3		41.8	
Sedentary work % †	31.3		37.6		55.0		29.6		29.0		47.6	
Current use of postmenopausal hormone therapy %							8.5		8.2		8.8	

p (homogeneity - two-sided chi-square- and F-tests) between the population density areas were less than 0.01 for all variables except for use of postmenopausal hormone in women p=0.03.

* Sedentary physical activity during leisure time = no vigorous physical activity at all per week.

† This question was not asked in 2 of the 10 CONOR-studies (Oslo II & MoRo II) and not asked to those 75/67 years in HUBRO, OPPHED, Tromsø V, Immigrant HUBRO and TROFINN. Answered by 62.0 % (100,674) of all participants 30 years and above.

SD=standard deviation.

Inh=inhabitants.

TABLE 4. The number and prevalence of men and women 30 years and above reporting forearm/wrist fracture according to population density. Cohort Norway 1994-2003.

	Number of participants*	Number of fractures	Crude prevalence†	Age-adjusted prevalence‡
Men				
Rural	19,050	2,233	11.7	11.8
Densely populated	14,967	1,995	13.3	13.3
City	39,018	6,330	16.2	16.2
Women				
Rural	21,220	2,778	13.1	11.9
Densely populated	17,099	2,287	13.4	13.4
City	38,371	6,004	15.6	16.3

* Participants who answered the question about fracture among those allocated to the population density areas.

† The difference between the population density areas: Pearson chi square two-sided p <0.001 for both genders.

‡ The difference between the population density areas: F-test: p <0.001 for both genders.

TABLE 5. Odds ratio (OR) for forearm/wrist fracture in densely populated- and city area compared to rural area (reference) - adjusted for confounding factors in men and women. Cohort Norway 1994-2003.*

	OR†	95% confidence interval	OR‡	95% confidence interval
Men				
Rural	Reference		Reference	
Densely populated	1.13	1.05, 1.22	1.12	1.04, 1.21
City	1.42	1.35, 1.50	1.38	1.30, 1.46
			trend:	p <0.001
Women				
Rural	Reference		Reference	
Densely populated	1.13	1.04, 1.22	1.12	1.03, 1.21
City	1.44	1.36, 1.53	1.37	1.29, 1.45
			trend:	p <0.001

* Complete data were available for 61,041 men and 59,575 women for outcome, exposure and all covariates. Both the age-adjusted analyses and the analyses adjusted for all confounding factors are restricted to these numbers. The number of fractures included is 8,959 in men and 8,060 in women.

† Odds ratio - adjusted for age.

‡ Odds ratio - adjusted for age, height, BMI, smoking, marital status, education, consumption of alcohol, vigorous physical activity during leisure time, and use of postmenopausal hormone therapy (women only).

FIGURE 2a

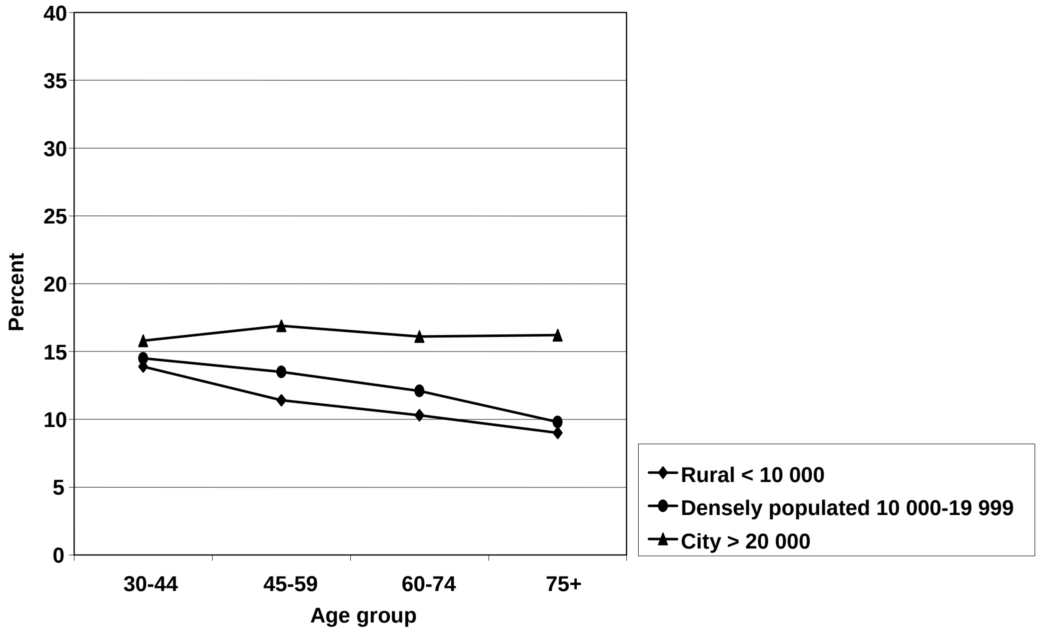

FIGURE 2b