

## Søknadsinformasjon

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Utlysning	Nordic Cancer Union Research Grant, 2015
Søknad	Lifestyle and occupational cancer risk - adjusting for alcohol and tobacco
Søknadsid	176677
Innsendt av	Kristina Kjærheim

## Oppgave: Progress report

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Tilordnet	Kristina Kjærheim
Status	Arkivert
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## RAPPORT

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### Briefly describe the project in a language understandable to non-scientists

In the present project, we have developed and tested a novel method to cope with the problem of unmeasured confounders, by using the observed pattern of cancer at sites associated with tobacco alone or alcohol and tobacco in combination as indicators of smoking and drinking. The underlying assumption is that the unobserved smoking pattern in an occupational group is reflected in the observed risk of cancer at sites with an established association to tobacco. If for instance, the standardized incidence ratio (SIR) for bladder cancer in a given occupation were elevated, while the other tobacco related cancers were not; one would commonly argue that this suggests the presence of an occupational carcinogen. With the proposed analytical method, based on the use of generalized models for confirmatory factor analysis, we aimed to formally evaluate this common-sense way of arguing.

### Summarize the major findings of the project

As an initial test of the suggested method, it was first applied (study 1) on a dataset restricted to Norwegian men identified from the 1970 census with follow-up for cancer through 1971–2001. Subsequently, the method was applied on men (study 2) and women (study 3), respectively, from the national censuses in Denmark, Finland, Norway, and Sweden in 1960, 1970, 1980 and/or 1990/91, followed-up for cancer from the year after inclusion until 2003/2005. Analyses were also done for all four countries combined. All studies produced estimates of cancer risk in occupational groups adjusted for tobacco and alcohol.

Separate factor models for tobacco smoking only and for the combined effect of alcohol and tobacco were found. The models included a latent common factor (tobacco, or alcohol and tobacco in combination) and unique (site-specific) factors that seemed necessary to include for achieving a correct picture of the relationship between the latent factor of main interest and incidence of cancer. In some cases, correlations between unique factors were included in the models. The models were finally used to predict the influence from latent factors for each occupational group, before adjusted expected numbers of cancer were calculated.

In the study on Norwegian men from the 1970 census (study 1), the estimated relative strength of the effect from tobacco and alcohol on relevant cancers was found to be in general accordance with what was expected based on prior knowledge. In occupations with few known and suspected carcinogens, the adjusted SIRs were closer to the expected values (i.e. the population average). The relative bias in the unadjusted estimates ( $[SIR_{unadjusted} - SIR_{adjusted}] / SIR_{adjusted}$ ) ranged between -50% and +65% for lung cancer and tobacco. For alcohol and tobacco related cancers of the upper aero-digestive tract, the relative bias was between -70% and +400%, although for 50 out of 52 occupational groups the bias was between -55% and +40%.

In the second part of the study, focusing on men (study 2) and women (study 3) in four Nordic countries, we examined the results of adjustment on both national and Nordic level for 53 defined occupational groups. To summarize, the results so far indicate that several occupational groups have different habits from the population average with respect to smoking and alcohol consumption, and that unadjusted SIRs might give a biased picture of occupational risks. We consider the method useful for achieving less confounded estimates of cancer risk in large cohort studies with no information on smoking and alcohol consumption.

Papers discussing the effect of adjustment for potential confounding on specific cancer sites (e.g. lung, bladder, nose) and for specific high or low risk groups are being drafted and will be submitted during 2017.

**Describe how the project has increased our knowledge of the prevention, cause and/or cure for cancer**

We consider this novel method of adjusting for alcohol and tobacco to increase the credibility and quality of results from register-based studies, and thus to enhance the possibility of identifying occupational risks at the national level with greater confidence. The identification of such risks is an important prerequisite for prevention, and the results may help for planning and priority questions in prevention, for instance in the discussion of preventive strategies aimed at regulating work conditions or reducing the consumption of tobacco and alcohol. The method is also applicable in studies of geographical or social distribution of cancer. Again, the purpose might be for planning of prevention, for planning of intervention or treatment facilities, or generally in the search for etiological clues. Reducing the risk of false positive conclusions is always useful, and the studies will add to the literature on potential confounding in etiological studies.

**Outline how Nordic cooperation has added value to this project**

The inclusion of the NOCCA data from all Nordic countries increased the number of persons included (15 mill) and gave a longer follow-up period (up to 45 years), and contributed the benefits of having data from several countries. The Nordic approach gave more stable estimates, and made it possible to evaluate possible national differences. The project also benefits scientifically from the long-standing collaboration within the Nordic work group with national expertise.

**List the publications resulting from the NCU research grant**

Author(s), title, journal and edition	PMID (8 digits, only if possible)
Haldorsen T, Martinsen JI, Kjærheim K, Grimsrud TK. Adjustment for tobacco smoking and alcohol consumption by simultaneous analysis. Cancer Causes Control. 2017 Feb;28(2):155-165. doi: 10.1007/s10552-016-0847-x. Epub 2017 Feb 2.	28155007

**Brief overview of expenditures for last year** 1 vedlegg (20170224 Brief overview of expenditures for 2016.docx)