Karolinska Institutet

Department of Medical Epidemiology and Biostatistics
and Osher Center for Integrative Medicine

Web-based studies of lifestyle factors and immune function

AKADEMISK AVHANDLING
som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Gard aulan, Smittskyddsinstitutet, Solna.

Fredagen den 4 februari, 2011, kl 09.00

av
Elinor Fondell
B.Sc.

Huvudhandledare:
Docent Katarina Bälter
Karolinska Institutet
Institutionen för Medicinsk Epidemiologi och Biostatistik

Bihandledare:
Docent Hans Gaines
Smittskyddsinstitutet

Docent Carl Johan Sundberg
Karolinska Institutet
Institutionen för Fysiologi och Farmakologi

Professor Kenneth J. Rothman
Boston University School of Public Health
Departments of Epidemiology and Medicine

Fakultetsopponent:
Docent Murray Mittleman
Harvard School of Public Health
Department of Epidemiology

Betygsnämnd:
Professor Anna Winkvist
Göteborgs Universitet
Institutionen för Medicin
Avd. f. Klinisk Näringslära

Professor Lars Alfredsson
Karolinska Institutet
Institutet för Miljömedicin
Enheten för Kardiovaskulär Epidemiologi

Professor Karl Ekdahl
European Centre for Disease Prevention and Control och Karolinska Institutet
Institutionen för Medicinsk Epidemiologi och Biostatistik

Stockholm 2011

Abstract
Upper respiratory tract infection (URTI), is estimated to cost $40 billion per year in the US, not including the cost of influenza, and is the most common reason for seeking primary care in many countries. Despite this, little is known about how to decrease susceptibility. Lifestyle factors such as physical activity, stress, sleep, and diet are important modulators of immune function and in this thesis, five papers evaluating the use of Internet for data collection, and the association of lifestyle factors to URTI and immune function in blood, are described.

In **Paper I,** the feasibility of using Web questionnaires compared with traditional paper questionnaires in a population-based setting was investigated. The use of interactive Web-based questionnaires resulted in lower initial response rate but similar total response-rates on follow-up questionnaires. Based on these findings, we conducted a population-based Web cohort study of 1509 Swedish men and women aged 20-60 with a follow-up period of four months (**Papers II-IV)**. Participants reported a total of 1181 occurrences of URTI. In **Paper II**, results show that high levels of physical activity (≥55 MET-hours/d, MET, metabolic equivalent task) were associated with an 18% reduced risk of self-reporting URTI compared with low levels of physical activity (<45 MET-hours/d) (IRR 0.82, 95% CI 0.69-0.98). In addition, highly stressed people, particularly men, appeared to benefit more from physical activity than those reporting lower stress levels. When studying intake of antioxidants and URTI risk in **Paper III**, we found that a high intake of vitamin C from food (>200 mg/d) was associated with a 31% lower risk of URTI compared with a low intake (<100 mg/d) (IRR 0.69, 95% CI 0.49-0.98) among women. This association was not seen among men, who overall had a lower intake of vitamin C than women. In **Paper IV**, we assessed adherence to the Nordic Nutrition Recommendations (NNR) as a measure of an overall healthy diet. The NNR include recommendations on macronutrients (e.g. saturated fat), micronutrients (vitamins and minerals), fiber, sodium, alcohol, and physical activity. Good adherence versus poor adherence to the NNR was not associated with risk of URTI in this study. In **Paper V** the natural variations of sleep duration, stress, physical activity, leukocyte numbers, and their function was examined in 36 men and women, aged 20-54. Results show that short sleep duration (<7h) prior to blood draw was associated with a 49% higher T cell function (95% CI 7/109%) in response to phytohemagglutinin (PHA) and 30% lower natural killer cell activity (NKCA) (95% CI -46/-8%) compared with normal prior sleep (7-9h). Results also indicate that high general perceived stress was associated with a 39% higher T cell function in response to PHA (95% CI 0/94%), and that high general physical activity was associated with an increased number of B cells and T cells, but general physical activity was not clearly associated with immune cell function.
In conclusion, we found that Web questionnaires can be useful for research purposes in populations with high proportion of Internet users, especially when multiple follow-ups are needed. **Paper II** and **III** conclude that lifestyle factors such as physical activity, stress, and diet are associated with risk of self-reported URTI. However, no association was seen between good adherence to the NNR and URTI, which may be explained by the fact that the participants were generally very well-nourished and with a limited variation in the NNR score (**Paper IV**). In **Paper V,** we found that lifestyle factors were related to immunological markers in blood. Natural short sleep duration was associated with lower NKCA, which might impair ability to fight infections.

ISBN 978-91-7457-177-6