DISSERTATIONES GEOGRAPHICAE UNIVERSITATIS TARTUENSIS
36

DISSERTATIONES GEOGRAPHICAE UNIVERSITATIS TARTUENSIS
36

MARE REMM

Geographic aspects of enterobiasis in Estonia

TARTU UNIVERSITY
PRESS

Department of Geography, Institute of Ecology and Earth Sciences, Faculty of Science and Technology, University of Tartu, Estonia

Dissertation is accepted for the commencement of the degree of *Doctor philosophiae* in geography at the University of Tartu on June 18, 2009 by the Council of the Institute of Ecology and Earth Sciences, University of Tartu

Supervisor: Senior researcher Kalle Remm, University of Tartu, Estonia

Opponent: Prof. Markku Löytönen, University of Helsinki, Finland

Commencement: Scientific Council room (204) in University main building, Ülikooli 18, Tartu; on August 26, 2009, at 10.15 a.m.

The publication of this dissertation is granted by Department of Geography, University of Tartu

The investigation was supported by the Doctoral School of Ecology and Environmental Science and by the Estonian Ministry of Education and Science (target financing project no SF0180052s07)

Toetab Euroopa Liit

RAK
Eesti Riiklik Arengukava

ISSN 1406–1295
ISBN 978–9949–19–173–4 (trükis)
ISBN 978–9949–19–174–1 (PDF)

Tartu Ülikooli Kirjastus
www.tyk.ee
Tellimus nr 268

CONTENTS

LIST OF ORIGINAL PUBLICATIONS 6
Interactions between the papers.. 7

1. INTRODUCTION.. 9
1.1. Parasitic worm *Enterobius vermicularis* 9
1.2. Diagnosis of enterobiasis 11
1.3. Enterobiasis and diagnosis in Estonia 12
1.4. Space and risk factors of enterobiasis 14
1.5. Risk estimation and prediction.. 15

2. OBJECTIVES OF THE STUDY 17

3. MATERIALS AND METHODS 19
3.1. Studies of nursery schools and children.. 19
3.2. Methods of data collection.. 21
3.3. Data processing 23

4. RESULTS.. 25
4.1. The prevalence and possible risk factors of enterobiasis.................. 25
4.2. The benefit of repeated examinations and prevalence estimations compared to the results of a single anal swab examination 29
4.3. The effectiveness of individual-based risk estimations, comparison of prediction methods and the effect of sample size 30
4.4. Enterobiasis related to geographical region and settlement size, spatial autocorrelation of prevalence 32

5. DISCUSSION 34

6. CONCLUSIONS 39

SUMMARY IN ESTONIAN 41

REFERENCES.. 43

ACKNOWLEDGEMENTS 47

PUBLICATIONS 49

LIST OF ORIGINAL PUBLICATIONS

The thesis is based on the following publications, in the text referred to by their Roman numerals.

I Remm, M., 2006. Distribution of enterobiasis among nursery school children in SE Estonia and of other helminthiases in Estonia. Parasitology Research 99, 729–736.

II Remm, M., Remm, K., 2008. Case-based estimation of the risk of enterobiasis. Artificial Intelligence in Medicine. 43 (3), 167–177.

III Remm, M., Remm, K., 2009. Effectiveness of repeated examination to diagnose enterobiasis in nursery school groups. Accepted by The Korean Journal of Parasitology.

IV Remm, K., Remm, M., 2009. Geographic aspects of enterobiasis in Estonia. Submitted to Health and Place.

Author's contribution

First paper	–	all parts of the investigation.
Second paper	–	data collection and laboratory analyses in full amount; data analysis, interpretation of results and writing the paper in cooperation with the second author.
Third paper	–	data collection and laboratory analyses in full amount; data analysis, interpretation of results and writing the paper in cooperation with the second author.
Forth paper	–	data collection and laboratory analyses in full amount; data analysis, interpretation of results and writing the paper in cooperation with the first author.

Interactions between the papers

The collection of parasitological examinations and other data for this study took quite a long time (2002–2007). As the first three papers were written while the data collection was going on, it was not possible to use the final sample in these papers. Only the fourth paper could use information from all observations.

Four keywords can be highlighted to characterize the interactions between the papers: 1) prevalence of enterobiasis, 2) risk factors and risk estimation, 3) methods for multivariate risk estimation and 4) distribution of enterobiasis depending on geographical location (Fig.1).

The treatment of prevalence and risk factors started with the first paper using only univariate methods. Data from only two counties was collected while the first paper was prepared. The number of counties investigated increased by one for the second paper. The analysis of risk factors and the estimation of risk levels continued using a multivariate approach. The comparison and testing of different multivariate risk estimation methods started with the second paper.

The effectiveness of repeated examination of enterobiasis was the focus of attention in the third paper. Only nurseries from three counties (Põlva, Hiiu and Valga) were included in the sample where repeated examinations were carried out. As repeated examinations improve the results of a single examination, the keywords for this paper were again prevalence and multivariate risk estimation methods.

The collection of data from eight counties was completed for the fourth paper. Thus, the comparison of geographical regions and generalizations about social and geographical factors became possible. The prevalence and risk factors of enterobiasis continued to be related to geographical regions. The comparison of risk estimation methods was also carried out. The new key idea in the fourth paper was the influence of geographical aspects on the distribution and prevalence of enterobiasis.

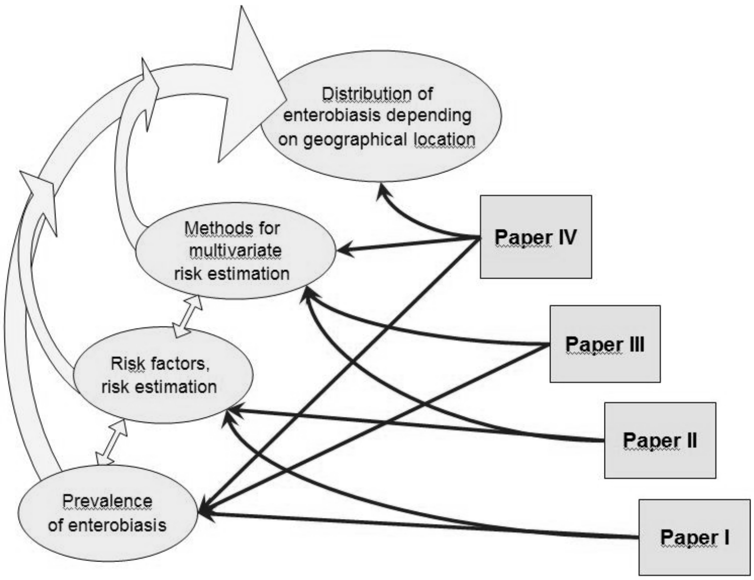

Figure 1. Interactions between the papers and themes

1. INTRODUCTION

1.1. Parasitic worm *Enterobius vermicularis*

Pinworm (*Enterobius vermicularis*) is a contact helminth causing enterobiasis. *E. vermicularis* is the most common helminth in temperate climate countries (Gale, 2002) and is common in tropical climates as well (Norhayati et al., 1994; Nithikathkul et al., 2001). Pinworm does not respect social status (Gale, 2002); it is prevalent both in developing and developed countries (Haswell-Helkins et al., 1987). It was a parasitic companion for humans already in ancient and prehistoric populations, both in the old and new world (Hugot et al., 1999; Horne, 2002; Kliks, 1990; Iñiguez, 2006).

Although successful and effective antihelminthic drugs have been available for decades, enterobiasis still remains among helminthic diseases of major public health importance, affecting approximately 1 billion people worldwide, predominantly preschool and school age children (Cook, 1994; Grencis and Cooper, 1996).

The main risk factors of enterobiasis are associated with indoor living conditions and close contact with other people, as pinworms primarily spread indoors directly from one human to another (Fig. 2). The most commonly infected are children, particularly in groups.

Four methods of transmission are known: 1) direct infection from the anal and perianal regions by fingernail contamination (autoinfection); 2) exposure to viable eggs on contaminated objects; 3) by contaminated dust containing embryonated eggs; 4) retro infection – after hatching on the anal mucosa, larvae migrate into the sigmoid colon and caecum (Cook, 1994).

Though often asymptomatic, the most common presentation of enterobiasis is perianal pruritus (Cook, 1994). Though the itching is usually most intense at night, this may be disturbing, especially during social communication, or even painful for children and also for adults during the whole day. The skin can be excoriated and secondarily infected by bacteria (Burkhart and Burkhart, 2005). Other symptoms attributed to enterobiasis occure rarely though cases are described. These are abdominal pain, irritability, restlessness, insomnia, dysuria, enuresis, vulvovaginitis and vaginal discharge in females (Burkhart and Burkhart, 2005). Whether *E. vermicularis* is causatively related to acute appendicitis, however, remains controversial (Cook, 1994). *E. vermicularis* could also be more frequent in children with allergic disease compared to nonallergic children (Herrström et al., 2001).

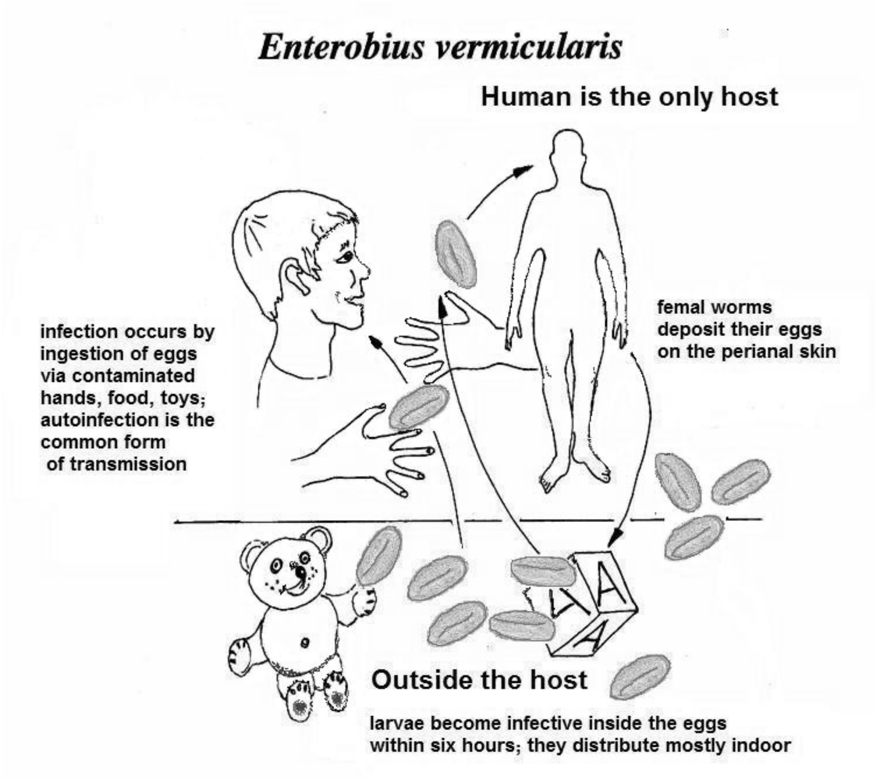

Figure 2. The life cycle of *E. vermicularis*

1.2. Diagnosis of enterobiasis

Due in part to the nature of the life cycle of *E. vermicularis* the correct diagnosis of this parasite is complicated. Though the life cycle takes place within the lumen of the gastrointestinal tract, microscopic examination of faecal samples is not recommended for diagnosis. Faecal samples give a positive diagnosis in only a few cases: 5–15% (Cook, 1994). Anal swab examination is the recommended method, although it also detects parasitism that has already been terminated (Cho and Kang, 1975). A positive result from an anal swab should not always be interpreted as a diagnostic criterion of a present infection since positive cases may not have intestinal *E. vermicularis*, although negative cases may (Cho et al., 1976). This results from peculiarities in the life cycle of *E. vermicularis*. The gravid worm migrates from the colon through the anus and expels eggs in the perianal region, after that the worm dies. Therefore, the already terminated parasitism is detected by the examinations.

Autoinfection is frequent, causing common co-occurrence of different life stages of the worms in the same child, but an anal swab cannot detect the young stages. The proportion of positive results from a single anal swab can be far less than the actual prevalence of *E. vermicularis* infections. Cho and Kang (1975) found that 81.3% of negative cases of single anal swabs had various developmental stages of *E. vermicularis* in the subject's intestine. The ratio between anal swab results and actual pinworm infection is affected by several factors, including the size of the parasite's brood, the intervals between re-infection, and the distribution of the *E. vermicularis* burden in the community being surveyed (Cho et al., 1976). Sadun and Melvin (1955) detected 60% positives using a single examination in a heavily-infected group, but only 37% positives in groups with a lower prevalence. A small number of egg-positive children in consecutive examinations may suggest that the worm burden in the positive children is low (Yoon et al., 2000).

The single anal swab method cannot accurately estimate the true prevalence of the *E. vermicularis* infection in a community as it reveals only a fraction of the existing infections (Sadun and Melvin, 1955). The increase in prevalence from repeated examinations has varied study by study. Fan and Chan (1990) found that the prevalence among nursery and kindergarten children increased from 17.3% and 34.6% from a single swab to 44.4% and 70.2% after eight consecutive swabs; the prevalence among primary school students increased from 59.9% in a single swab examination to 77.3% after four consecutive swabs. Kim et al (1991) found the increase of prevalence from 50.0–59.2% for single anal swabs to 70.8% from three anal swabs repeated at 4–5 day intervals. Two consecutive examinations may increase the egg detection rate by 4.2–4.8% for low (around 10%) enterobiasis prevalence (Yoon et al., 2000). The triple anal swab examinations presumably detect nearly 90% of infected individuals (Sadun and Melvin, 1955; Cook, 1994).

1.3. Enterobiasis and diagnosis in Estonia

Extensive prophylactic coprohelminthological studies of the Estonian population were started in 1956, lasting capaciously until 1989. A total of 41–55% of the entire population was examined every year from 1957 to 1986 (Jõgiste et al., 2001). The number of perianal swab studies to detect enterobiasis has increased greatly since 1972. The studies of perianal swabs engaged 11% of the population in 1972, increasing up to 21% of the population in 1984 (Fig. 3). All nursery school children were examined annually, which provided a good overview of infected children and the potential for prevention. Since the restoration of independence and reforms in the public health system in the 1990s, the number of helminthological studies has decreased noticeably in Estonia (Communicable …, 2000). As a result of long-term prophylactic programs the prevalence of helminthiases essentially decreased. From 1960 to 1989, the number of cases of ascariasis decreased 25 times, trichuriasis 30 times, diphyllobothriasis 4 times, *Taenia. solium* taeniasis 26, *T. saginata* taeniasis 17, and hymenolepiasis 10 times (Jõgiste and Barotov, 1993). In the 1990s, the most prevalent helminthiases remained: enterobiasis (92% from all registered cases), diphyllobothriasis (4%), and ascariasis (3%) (Communicable …, 2000).

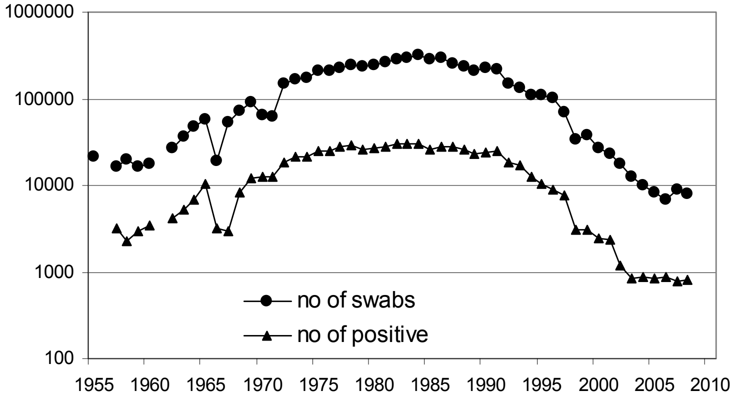

Figure 3. The number of examined swabs of enterobiasis and the number of positive results. Data from Communicable disease statistics in Estonia (2000; 2005; Nakkus-haigustesse …, 2009)

Table 1. Examination of enterobiasis in Estonia, 1999–2008 (Nakkushaigustesse …, 2009)

Year	Number of swabs	Number of cases	Prevalence per 100000	Per cent of positive swabs [%]
1999	37367	3025	209.2	8.1
2000	26600	2482	172.4	9.3
2001	23005	2361	173.1	10.3
2002	17572	1194	87.4	6.8
2003	12572	838	61.9	6.7
2004	9828	882	65.0	9.0
2005	8344	853	62.0	10.2
2006	6940	867	64.5	12.5
2007	8997	782	58.2	8.7
2008	8033	806	60.1	10.0

In spite of the prophylactic programs since the 1990s and effective antihelminthic drugs, enterobiasis is the most common helminthiasis in Estonia up to the present (Table 1), though the occurrence of cases has decreased from 30379 in 1983 to 806 cases in 2008. The number of anal swab examinations has decreased in the same period as well: from 321757 in 1984 to 8033 in 2008. The largest number of cases is characteristic of the age group 5–9 inclusively. As much as 35.3% of all cases were found in this age group in 2007. In the same year, 29.3% of all cases were found among nursery school children, yet there were more cases among school children (Communicable…, 2000; Nakkushaigustesse …, 2009).

The study of 18 parasitological laboratories in Estonia resulted in the conclusion that the most common parasite for laboratory examinations in Estonia is *E. vermicularis*. The common method for its examination is microscopic study of perianal swabs (Must, 2006). The cellophane tape method, the other method widely used around the world for examination of *E. vermicularis*, is little known in Estonia and not used in laboratories. This method was known only in one laboratory from seven examined and was not used even there, since the norm in Estonia is, as they said, the perianal swab method (Sommer, 2008). The perianal swab method was compared with the cellophane tape method and also the unstained tape-slide with stained tape-slide in the same study. Only a third of children, who were Enterobius-positive according to the tape method, were also positive using the perianal swab. More eggs were found from stained tape-slides than from unstained slides (Sommer, 2008). The recommended stain for the slides is lactophenol cotton blue (Parija et al., 2001).

1.4. Space and risk factors of enterobiasis

There is a long tradition of using cartography in helping to understand the epidemiology of soil-transmitted helminth diseases in tropical and subtropical countries (Brooker et al., 2003; Abrahams, 2006; Brooker et al., 2006). During the last decade, considerable progress has been made in the use of spatial analysis and geographical information systems (GIS) to better understand helminth ecology and epidemiology. These methods have enabled new insights into the geographical ecology of infection and have made it possible to predict spatial distributions of infection prevalence using statistical approaches (Brooker and Michael, 2000; Brooker et al., 2006). Still, GIS and remote sensing data can be applied for predictive mapping of helminth distribution if the helminth's development or any of its distributors depends on factors of the external environment.

The prevalence of helminthiases, which are mainly related to social factors including hygiene and are not directly dependent on natural conditions like soil, climate, and vegetation, is not so easy to map geographically. *E. vermicularis* is one of the helminthes associated with social factors. An understanding of a geographical region could still have a descriptive value since the risk of contamination depends on the overall prevalence of enterobiasis in a particular region. All people, especially children, are exposed to a higher risk if the parasite is common. In other words the probability of disease should have a positive autocorrelation in a geographical area. Also, the risk factors related to way of life are geographically and socially distributed – economic activity, dominant living conditions, traditions of social communication and family size depend on regions.

Therefore, the interpretation of geographical and social space and risk factors are related in enterobiasis studies. Environment, risk factors and the variability of the prevalence of enterobiasis have mostly been studied locally. The investigations have covered only a single country or its sub-regions. Urban and rural areas have been compared in several studies (Pezzani, 2004; Cazorla et al., 2006). Day-care centres in residential areas have been compared with those situated near traditional markets where the environment is not satisfactory in terms of public health (Song et al., 2003). In Sivas, Turkey, students living in an urban slum area and in an urban central area were examined (Çelíksöz et al., 2005). Two populations living and studying in different socioeconomic conditions as a result of an earthquake were also compared in Turkey (Öztürk et al., 2004). The risk associated with wastewater in transmitting intestinal helminth to a population living near an urban effluent was evaluated in Morocco (Moubarrad and Assobhei, 2005). The risk factors and prevalence of enterobiasis have been studied in different regions within Venezuela (Devera et al., 1998; Acosta et al., 2002; Cazorla et al., 2006), the Republic of Korea (Kim et al., 2003; Park et al., 2005) and in other countries.

Epidemiological risk factors consist of the characteristics of people and the environment that are related to a higher occurrence of a disease in a population. The main risk factors for enterobiasis are associated with indoor living conditions and close contact with other people. The hidden risk factors differ, and may be related to socio-economic and cultural differences. The socio-economic status of a family (Chan, 1985; Georgiev, 2001; Song et al., 2003; Öztürk et al., 2004; Artan et al., 2008; Wang et al., 2009), family size (Artan et al., 2008), living in non-apartment dwellings (Sung et al., 2001), poverty and overcrowding (Acosta et al., 2002; Cazorla et al., 2006), but also the educational level and employment status of parents (Artan et al., 2008) have been studied. Also, personal and communal hygiene (Norhayati et al., 1994; Chih et al., 1996; Herrström et al.,1997; Sung et al., 2001; Song et al., 2003), nail biting and thumb sucking (Chih et al., 1996; Herrström et al., 1997; Sung et al., 2001; Cazorla et al., 2006), gender (Acosta et al., 2002; Kim et al., 2003; Song et al., 2003; Astal, 2004; Çelíksöz et al., 2005; Park et al., 2005; Cazorla et al., 2006) and age (Acosta et al., 2002; Song et al., 2003; Park, 2005; Cazorla et al., 2006) together with some other factors have been revealed and estimated differently.

1.5. Risk estimation and prediction

Epidemiological risk can be estimated as the risk associated with an individual or with a particular group of people, or alternatively, as describing certain characteristics of the environment or people. The risk and risk factors of enterobiasis have been estimated using both univariate and multivariate methods in previous studies. The main method used to estimate the degree of influence of a single risk factor is the odds ratio (OR); the main methods for estimating the statistical significance of various risks analysed separately are the χ^2-test and the Mann-Whitney U-test. Univariate risk estimation methods have been used in a number of studies; for example, Sung et al. (2001), Song et al. (2003), Pezzani et al. (2004), Çelíksöz et al. (2005) and Artan et al. (2008).

Presumably, multivariate risk estimation is more reliable than univariate estimations, which analyse every factor separately. The main techniques used in predictive computational multivariate methods belong to statistical modelling, artificial intelligence (AI) methods and data mining.

Logistic regression has been the most common method of statistical modelling used for risk estimation, including epidemiological risks. It has often been used to estimate the risk of enterobiasis as well (Sung et al., 2001; Song et al., 2003; Pezzani, 2004).

It is necessary to find the best predictive combinations of explanatory variables for successful risk modelling and predicting. The indicator value of single characteristics can differ greatly if taken alone or if in combination with other explanatory variables since many characteristics are inter-correlated or duplicate each other. In most cases, it is sufficient to use only one explanatory variable from several similar variables. Multiple methods enable to search for effective combinations of variables.

There are two factors that add importance to predicting the prevalence of enterobiasis at a group level besides predicting at the individual level: the chance of an individual being infected is difficult to predict, and the infection of all members of groups depends on the prevalence in groups and all members of infected groups are endangered as pinworm is a contact helminth.

A case-based reasoning-system enables us to compare data on every child with database records and give similarity-based estimations of the infection risk. Individual level estimations can be summarized to the group level and form the basis for estimating group level prevalence.

The ultimate aim of the individual-based models for this study was not to predict the enterobius positive/negative status of a child but to estimate the enterobiasis prevalence in groups. We assumed that random biases in risk estimations should at least partially smooth out according to the law of large numbers. Risk models can be applied to different groups of children.

2. OBJECTIVES OF THE STUDY

Pinworm is a widespread parasitic risk factor for a healthy environment, in particular for children. It is usually considered a nuisance rather than a cause of serious disease, and its treatment is straightforward; however, the correct diagnosis of pinworm is complicated and the elimination of the parasite from a family group or institution often poses significant problems (Cook, 1994). Therefore, prevention of contamination is essential and knowledge in addition to medical treatment may play a key role in the prevention of enterobiasis (Nithikathkul, 2005).

The prevalence of enterobiasis was examined thoroughly and consistently from the late 1950s to the late1980s. Though, there is no reliable up-to-date information about the occurrence of *E. vermicularis* in Estonia – as enterobiasis is low symptomatic the examination occurred occasionally and these examinations did not always give accurate results.

Risk factors of enterobiasis have been investigated in many studies over the world, but not in Estonia. It is known that risk factors vary locally, depending upon social, cultural and geographical spatial factors, so some of these may be specific to Estonia. Knowing the risk factors would enable us to estimate the prevalence and distribution of enterobiasis in Estonia using a minimal number of direct examinations.

Univariate and multivariate risk estimation first of all using logistic regression have been conducted in numerous studies of enterobiasis. Methods that can be classified as applications of artificial intelligence have not been tested up to now according to our knowledge. Studies of enterobiasis have been local rather than observing larger regions or a whole country. The enterobiasis prevalence for all counties in every year was known in Estonia for the second half of last century. However, comparative treatments of enterobiasis prevalence and risk factors on the basis of geographical regions and generalizations about the variability of the risk factors for all Estonia were missing.

The present study had the following aims:

1. To investigate the prevalence and possible risk factors of enterobiasis among nursery school children of Estonia and to study correlations between the prevalence, children's households, habits, living conditions at home, and also personnel and indoor conditions in nursery school groups (paper **I**, **II**, **III** and **IV**).
2. To estimate the benefit from repeated examinations for the detection of enterobiasis in nursery school groups in Estonia and the possibility to predict the estimated prevalence for multiple examinations from the results of a single anal swab examination in nursery school groups (**III**).

3. To test the effectiveness of individual-based risk predictions using different methods including similarity-based reasoning, to compare the best methods for individual-based predictions of the prevalence of infection in groups and the effect of sample size (**II**, **III** and **IV**).
4. To find out how are the prevalence and the risk factors of enterobiasis related to geographical regions and settlement size in Estonia (**IV**).

3. MATERIALS AND METHODS

3.1. Studies of nursery schools and children

The investigation of enterobiasis was conducted among nursery school children in the capital Tallinn and seven counties (Tartu, Põlva, Pärnu, Järva, Hiiu, Ida-Viru, Valga) in Estonia over the period 2002–2007 (Fig. 4). The anal swab examination involved 3 131 children from 279 groups in 80 nursery schools (Table 2). Six hundred and four of the children were examined two times and 96 of them three times. The number of children investigated in groups varied from 1–26, the number of groups per nursery school from 1–12 (**IV** Fig. 1A).

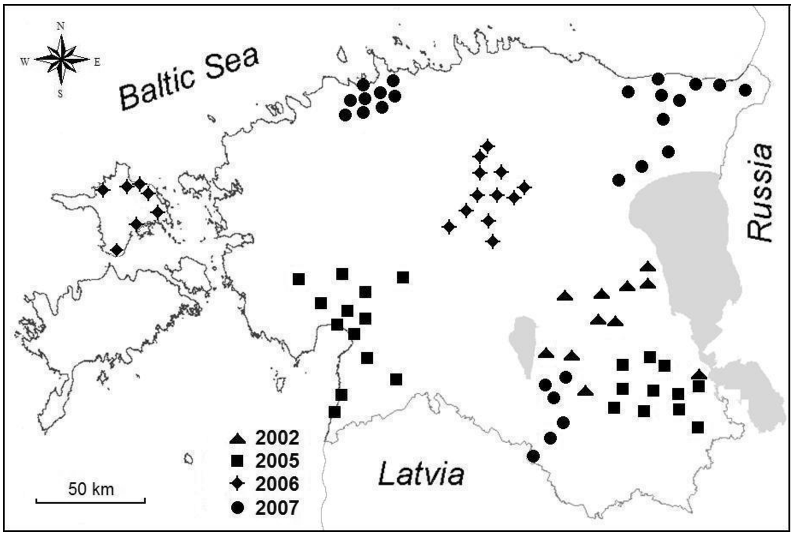

Figure 4. Studied nurseries: the location and year of sampling

Table 2. The number of observations by regional units

Regional units	Nurseries	Nursery school groups	Children	Swabs	Returned questionnaires (%)
Tartu county	9	31	442	442	337 (76)
Põlva county	12	31	468	804	400 (85)
Pärnu county	13	50	536	536	445 (83)
Järva county	12	37	414	414	374 (90)
Hiiu county	7	19	204	344	193 (95)
Ida-Viru county	11	43	387	387	356 (92)
Tallinn	9	53	491	491	395 (80)
Valga county	7	15	189	413	116 (61)
Total	**80**	**269**	**3131**	**3831**	**2616 (84)**

The following four principles were followed in the selection of nursery schools for our research: 1) selected nursery schools had to be spatially scattered in the studied county; 2) rural areas, small towns and larger towns (if present in a county) had to be represented; 3) consent from the head of a nursery school, from the child and from the parents to conduct the investigation was obligatory; 4) all children who were allowed to participate in the investigation and were present in the nursery school group on the day of sampling were examined.

Paper I

The research of enterobiasis among Southeast Estonian nursery school children was conducted in two parts. Children mainly from Tartu county were examined in 2002 and from Põlva county in 2005. We examined 954 children in total from 22 nursery schools.

There were 509 children examined in 2002 from Tartu county (in addition two nurseries, one from Otepää, another from Räpina) and 445 in 2005 from Põlva county (Fig. 5A).

Paper II

The investigation of enterobiasis was conducted among nursery school children in four counties in Estonia (Tartu, Põlva, Pärnu and Järva) from 2002 to 2006 (Fig. 5B). The total number of studied children was 1 905.

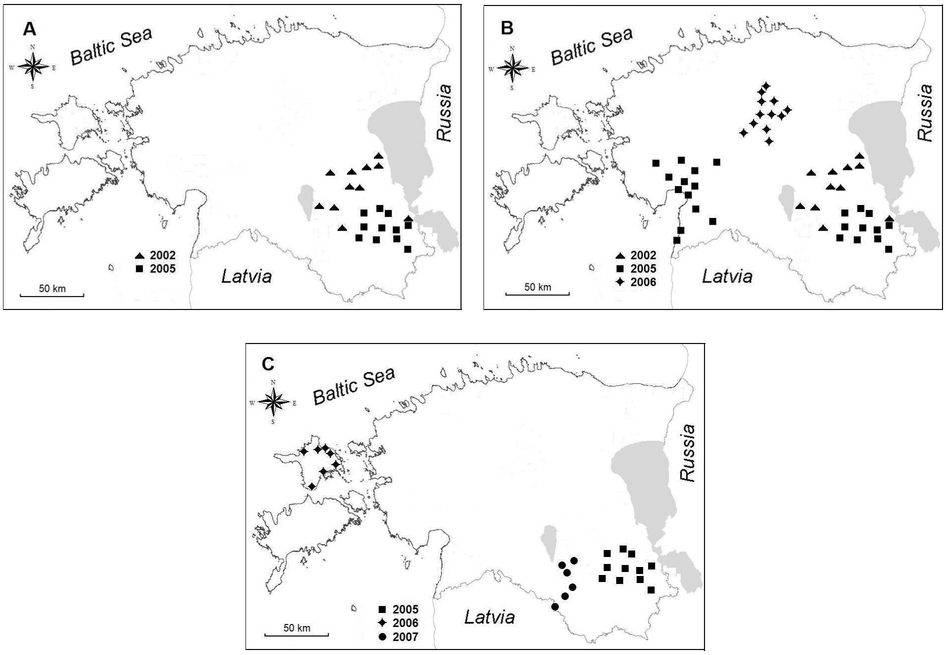

Figure 5. Studied nurseries by papers: A – paper I, B – paper II, C – paper III

Paper III
The investigation of enterobiasis was conducted among nursery school children in three counties (Põlva, Hiiu and Valga) in Estonia over the period 2005–2007 (Fig. 5C). The double swab examination in Põlva county was conducted in spring 2005, and in Hiiu county in autumn 2006. The triple swab examination in Valga county was conducted in spring and autumn 2007. The double swab examination involved 604 children from 57 groups in 23 nursery schools. Ninety-six children from 6 nursery schools in Valga county were investigated three times.

Paper IV
The investigation of enterobiasis was conducted among nursery school children in seven counties and Tallinn over the period 2002–2007 (Fig. 4). The anal swab examination involved 3 131 children from 279 groups in 80 nursery schools. Data from all examined children were included in this paper, yet only the results of the first swab from repeatedly examined children.

3.2. Methods of data collection

The data was obtained from three sources: 1) perianal swabs from children for the diagnosis of enterobiasis; 2) closed-ended questionnaires for children's parents; 3) observations of nursery schools and structured interviews with school staff.

Perianal swabs and examination
Infections of *E. vermicularis* were examined using the anal swab technique. The swabs were collected using sterile dry swab tubes that were moistened in a 50% solution of glycerol before sampling. Swabs were taken after breakfast just before the children went outside. One slide was prepared from each swab in the laboratory. The swab's stick was turned 360 degrees in a drop of physiologic saline on the microscope slide and then a 22×22 mm cover glass was mounted. The whole slide was examined systematically line-by-line using a 10× lens for 4 to 5 minutes. If needed, the finding was verified using a 40× lens. The presence or absence of *E. vermicularis* eggs was determined – the number of parasites was not determined (Fig. 6). Repeated anal swabs (paper III) were taken from children on the second or third day after the first swab.

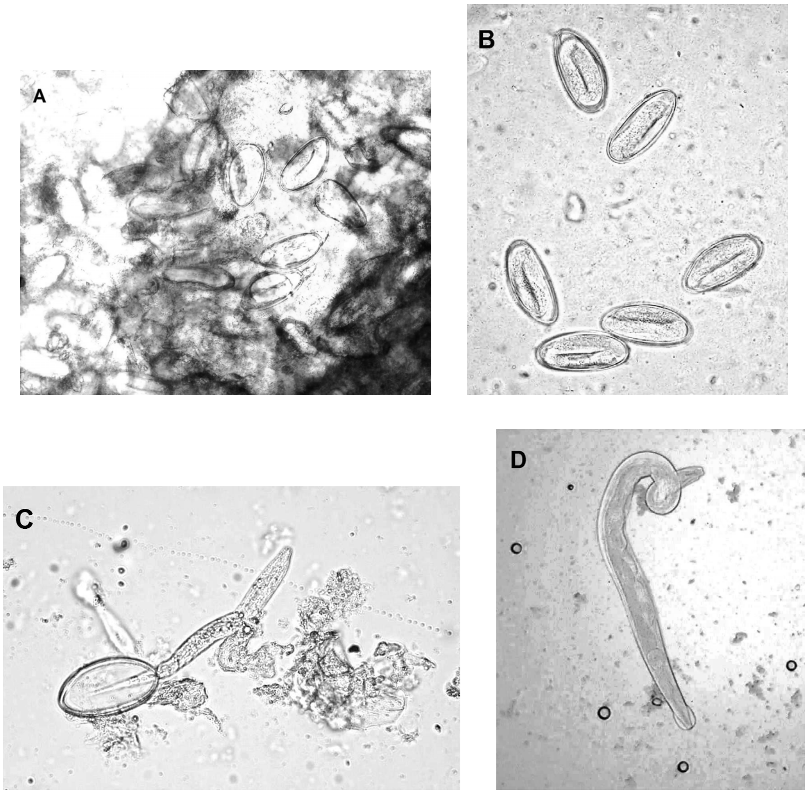

Figure 6. *Enterobius vermicularis* diagnostic stages: A, B – eggs; C, D – larvae

Questionnaires, interviews and observations

The data on possible risk factors were obtained from two sources: 1) closed-ended questionnaires for children's parents; 2) observations of nursery schools and structured interviews with school staff. The aim of the questionnaire was to identify possible factors of infection risk associated with children's households and homes. The questions addressed six topics (the number of questions in brackets): personal data (5), household members and pet animals (3), previous occurrence of helminthiases in the family (2), socioeconomic status of the household (2), living conditions at home (8), the child's habits and personal hygiene (3). A total of 2 616 (84%) questionnaires were returned (Table 2). Data on the children were included in the research even if their parents did not return the questionnaire. In this case, we still recorded the child's gender, presence/absence of the infection, and in most cases were able to determine the age of the child. The aim of the interviews and the observations was to identify possible infection risk factors in nursery groups. The observations took place only in those rooms where children spent considerable time: play rooms, eating rooms, bedrooms and washing rooms. The observations concerned the number, purpose, sanitary conditions and state of repair of the rooms. The interviews concerned sanitation and children's hygiene, their habits and cleanliness. Observations of rooms and interviews with supervisors took place in all nursery schools groups.

The results of the anal swab examinations, each child's personal data and the results of the interviews and questionnaires were recorded in a Microsoft Access database. The number of explanatory features in the database for every child reached 77. Seven features concerned the child's gender, age, habits and personal hygiene, 15 features, the household and family and 55, the nursery school.

3.3. Data processing

In **paper I,** the association of possible risk factors with the frequency of enterobiasis was only estimated using the $\chi 2$ test calculated in Statsoft Statistica 6; the significance level of 0.05 was applied.

In **paper II,** the machine learning and prediction software Constud (http://www.geo.ut.ee/CONSTUD), which applies similarity-based reasoning, was mainly used for the risk estimation. The introduction of Constud and its application on tabular data was first published in this paper. Also, this was the first application of Constud for processing epidemiological data. The probabilities of the statistical significance of the difference between proportions were calculated in Statsoft Statistica 6.1.

The risk of enterobiasis was also modelled using logistic regression and classification trees in Statistica 7.1 (Statsoft) for comparison with Constud. The fit of predictions obtained using different methods was compared using true skill statistic (TSS – the proportion of true positives plus the proportion of true negatives minus one). TSS was preferred to the commonly used positive predictive value (PPV) since TSS is not dependent on prevalence (Allouche et al., 2006). The best-fit, alternative to Constud, was obtained using a classification tree. These two tools were continually used in the subsequent parts of the study.

In order to model the risk of enterobiasis at individual level **(III**), Constud was compared with data mining methods in the Statistica 8 Data Miner (Statsoft) software package. Data mining methods that fit a binomial dependent variable and a large number of nominal and numerical explanatory variables, and are not sensitive to missing values in explanatory variables were compared: *k*-nearest neighbours, boosting classification trees (BCT), random forest classification (RF), support vector machine, Naïve Bayes classifier, advanced classification trees and automated neural network search. Random forest classification and boosting classification trees models were trained both in equal prior probabilities and estimated prior probabilities mode. The other methods do not accommodate prior probabilities.

Only the results of the first examination and all available characteristics on the children's homes and nursery groups were used as training data for all modelling methods not giving any preference to the main risk factors known from previous investigations where risk factors were compared one-by-one. Estimations derived from the results of the first examination were compared with the results of the following examinations. The fit of predictions was expressed as the proportion of correctly classified cases and as TSS.

In **paper IV,** two essentially different techniques that have been among the most effective methods in earlier comparative studies (Elith et al., 2006; Remm, 2004; paper III) were compared: 1) boosting classification trees (BCT) in Statsoft Statistica 8 Data Miner and 2) similarity-based learning of weights and predictions in Constud. BCT represents deductive – top-down classification, which gradually divides the solution space. Constud represents an extremely empirical case-based approach that, instead of generalizations, describes predictable classes according to exemplar-observations selected from the training data. Also, the most indicative set of features is selected during iterative learning of weights in Constud.

Missing data were replaced using mean values (numerical feature) or using an unused code (nominal feature) in building BCT models since otherwise the Data Miner software would ignore observations with missing data. Missing values do not hinder predictions in Constud; a feature that has a missing value is not taken into account in the calculation of similarity between two observations – instead the prediction is calculated using other features.

The correspondence between model-estimations of infection presence/ absence and the results of anal swab examinations were measured using TSS. The features more closely related to enterobiasis were selected and ordered using the feature selection and variable screening (FSVS) module in the Statsoft Statistica 8 Data Miner.

4. RESULTS

4.1. The prevalence and possible risk factors of enterobiasis

The prevalence

The prevalence was 21% according the whole study and 19% if only results from the first examination were included. The prevalence in all counties was similar, being mostly at 20–23%, except in Tallinn (nearly half lower than the prevalence in other counties) and in Ida-Viru county (a little lower than in other counties) (Table 3). This was higher due to repeated examinations. Regional samples varied little during the study. The prevalence from study **I** resulted a prevalence of 23% in Tartu county and 22% (26% according to repeated swabs) in the nurseries of Põlva county.

By nursery schools the prevalence ranged from zero to 57%. Zero-prevalence existed in five out of all 80 nurseries and only four if the results from the repeated examinations in three counties were included. Prevalence was more than 45% (according to the first examination) in five nurseries and 30–45% in 15 nurseries, and exceeded 30% in more nurseries after repeated examination (**IV** Fig 1). Prevalence did not reach such a high level in any nursery in Tallinn.

The variability of prevalence among nursery groups was higher than the variability between nurseries. The range was from zero (for 27% of groups per single and for 26% per double examination) to 61%. A prevalence of 45% or higher resulted from the first examination for 7% of groups and from repeated examinations for 9%; 30–45% for 17% and 18% respectively. The highest prevalence in a group in Tallinn was 44%.

From the children examined, 83% (2600) attended infected groups. The prevalence was 30% among children from infected groups according to the first examination, and 33% if the results from repeated examinations from three counties were included.

The whole sample was divided into seventeen small geographical units (**IV**) according to the combinations of the size of settlement and the geographical district (counties). The highest prevalence of enterobiasis was characteristic of rural units, except in Tartu county. The highest prevalence was in the Põlva rural unit – 32% according to the first examination, and in the Valga rural unit – 43% from double examination (Table 3).

Table 3. Prevalence by county and by settlement type in counties

County	Prevalence [%]		Prevalence [%] *		Location	Settlement type	No of obs.	Prevalence [%]	
	First exam	Repeated exams	In nurseries	In nursery groups				First exam	Repeated exams
Tallinn	10		0(2)–17	0(26)–44	Tallinn	large town	491	10	
Ida-Viru	17		5–57	0(16)–57	Ida-Viru	large town	173	13	
					Ida-Viru rural	rural	214	20	
Hiiu	23	27	8–35	0(5)–55	Kärdla	small town	58	17	17
					Hiiu rural	rural	146	25	31
Järva	22		0(1)–44	0(5)–55	Paide, Türi	small town	177	18	
					Järva rural	rural	237	24	
Tartu	22		12–46	0(4)–61	Tartu	large town	159	23	
					Elva	small town	71	18	
					Tartu rural	rural	212	22	
Põlva	22	27	0(1)–50	0(7)–50	Põlva, Räpina	small town	269	14	20
					Põlva rural	rural	199	32	37
Valga	22	33	0(1)–35	0(2)–50	Valga, Otepää	small town	92	17	22
					Valga rural	rural	97	27	43
Pärnu	20		12–53	0(8)–55	Pärnu	large town	176	16	
					Kilingi-Nõmme, Sindi	small town	154	16	
					Pärnu rural	rural	206	27	

* The number of zero-prevalence nurseries and groups in brackets

Risk factors

The different methods used in different parts of the study found similar factors as the most important risk factors – including features connected with the age of the children.

The frequency of enterobiasis was significantly related to the age of the child according to all data and also in all geographical units (**IV**). From the study in Tartu and Põlva county (**I**), the overall infection rate among children from 1 to 3 years was 16%, among 4-year-olds –16%, among 5-year-olds – 30%, among 6-year-olds – 30%, and among those from 7 to 8 years – 42%. From the study in Tartu, Põlva and Pärnu county (**II**), the prevalence was higher among older preschool children, being 13% among <4-year-old children, and 27% among older children. The similarity-based risk-estimations yielded an even greater difference, exaggerating the risk in the older group (**II** Fig. 2). The age-related features of groups: age of children in the nursery school group that the child attends (Fig. 7) and the range of age within the group, were also indicative. The prevalence of enterobiasis was different in groups consisting of children with little age difference, and in mixed-age nursery school groups (**II**). The feature, mixed-age or single-age group, had the highest indicator value (prevalence 18% in single-age groups and 38% in mixed-age groups) in small towns where both mixed and same-age groups were common (**IV**).

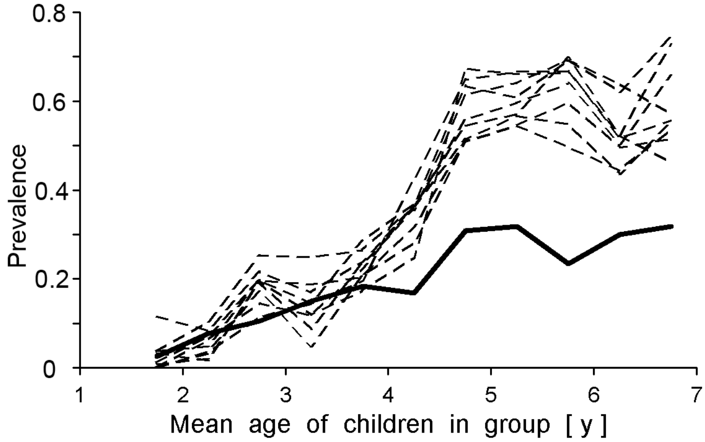

Figure 7. Infection rate in nursery school groups related to the mean age of children in the group according to single anal swab analyses – bold line, estimated risk of enterobiasis – dashed lines

The second group of risk factors – the number of communications and partners – are partially included in the age-related features: the mean and range of the children's age in a nursery school group. The score given to a nursery school group for the general cleanliness and neatness of the members appeared to be a good indicator of playmate-related risk. The infection rate of children from larger families was higher in Tartu and Põlva counties (*p*=0.005) (**I**), the existence and occupation of other children in the family was always selected as among the best predictive sets (**II** Table 2). The number of children in the family was an essential risk factor everywhere except in larger towns (**IV**). The risk-relevant communication partners at home were other children and pets (**II** Table 3).

The feature most closely related to the occurrence of enterobiasis according to the FSVS analysis of all data (**IV**) was the region according to a detailed division (17 types). The main presumption for the distribution of enterobiasis is the existence of infection and first of all, the occurrence of the parasite in the same unit. In other words, enterobiasis has a positive autocorrelation in the geographical area. Region, child age and range of ages in a nursery school group were also among the 13 most indicative attributes in all three models (Constud, BCT, RF) selected for predicting individual risks (**III** Table 5).

In some districts, the characteristics of personal hygiene and the cleanliness of rooms were estimated as being among the most indicative characteristics, although not according to the total sample.

In Tartu and Põlva county, the washing of hands after visiting the toilet as an aspect of personal habits was significantly related to infection rate (**I**). The need to wash hands before meals becomes evident when combined with other factors; for example, when considering children who do not always wash their hands before meals, the prevalence among children who also cuddle their pets was somewhat enhanced.

The prevalence and estimated risk were high in all cases if the child had any extra habit, be it a pet for cuddling, finger sucking, nail biting, or putting things into his or her mouth (**II**). Hand washing after toilet use was among the top 10 risk indicators in most of the investigated rural areas, and carefulness in hand washing was among the most indicative features in major towns (**IV**).

Family income was not among the top 10 indicators in any region of Estonia. The risk of enterobiasis also did not depend on the gender of the child or on the educational level of the mother.

4.2. The benefit of repeated examinations and prevalence estimations compared to the results of a single anal swab examination

Prevalence increased after double and triple examinations in all repeatedly examined districts (Table 3). The overall mean prevalence of enterobiasis for the entire sample of children twice examined increased 8% after double anal swabs (**III** Table 1). The average efficiency (**III**) of double examination for the entire data set was 37%.

The average prevalence of enterobiasis among nursery groups from two single examinations varied between 0 and 59%. The range of increase in prevalence resulting from double examination was 0–25% in groups. The overall mean increase in estimated prevalence was 7%. The efficiency of the double examination varied from 0 to 100% in groups, the mean value was 38.6% (Fig. 8). The prevalence increased in 79% of groups. The increase in the estimated prevalence was a function of the prevalence according to the mean single examination: less in groups having a lower prevalence and more in groups with a higher prevalence – except for groups where the preliminary prevalence was the highest (**III** Table 2).

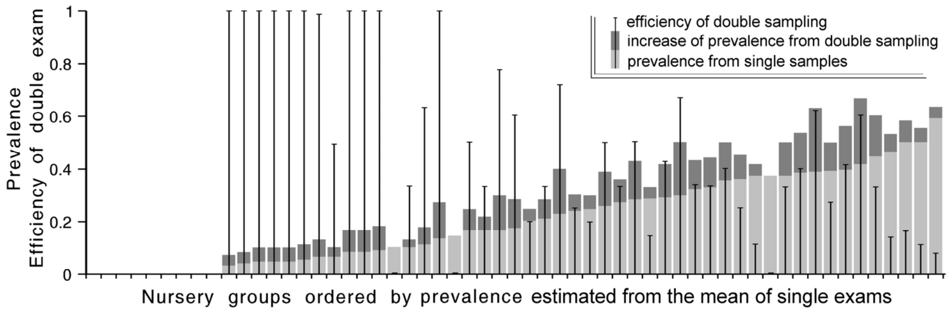

Figure 8. Increase in estimated prevalence after double examination in nursery school groups

In the sample of triple examined groups, prevalence increased in 10 groups out of 57 after double examination and continuously in 9 out of 12 triple examined groups (Fig. 9). The average prevalence among groups from two single examinations varied between 0 and 41%. The range of increase in prevalence from the double examination was 0–21% in groups, average increase 9%; the increase from the triple examination was 0–21%, average 7% (**III** Table 3).

8

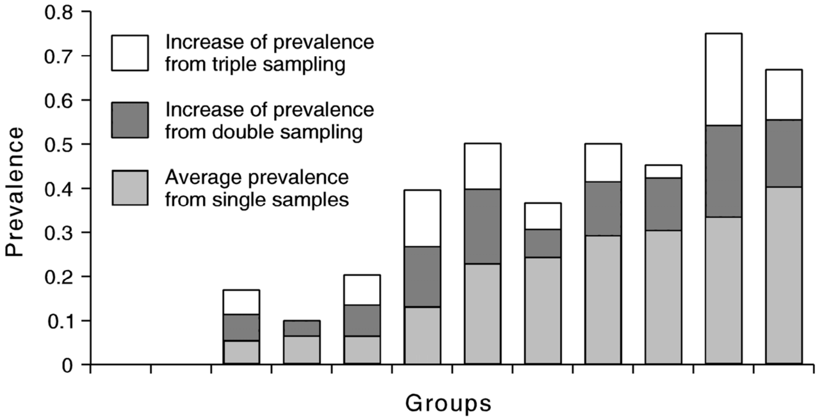

Figure 9. Increase in estimated prevalence after double and triple examination in triple examined groups

The three best methods for estimating individual risk levels (RF, BCT and Constud) were able to predict the actual results of the second examination – about two thirds correctly classified, TSS≈0.35. The best TSS results for the three methods for predicting individual risk were RF using equal prior probabilities (63.6% correctly classified, TSS=0.332), BCT using estimated prior probabilities (64.9%, TSS=0.338), and machine learning using Constud (73.8%, TSS=0.388). Constud was superior in recognizing true negative cases, while BCT and RF succeeded better in predicting true positive cases (**III** Table 4).

4.3. The effectiveness of individual-based risk estimations, comparison of prediction methods and the effect of sample size

In paper **II,** the highest TSS attained in the 10 machine learning processes using Constud was 0.381; the mean was 0.368. Nearly equally good estimations can be obtained from many different sets of explanatory features. The TSS training fit of the best logit-model was <0.244 in the simple training sample and 0.439 in the equalised training sample; the best validation fit remained at 0.237. The best classification tree estimated the risk at TSS=0.775 in the training data, 0.18 in the cross-validation sample and 0.35 in all data. Over fitting of the tree is obvious. Healthy children were predominantly correctly recognized by Constud, but about a half of the predicted cases of enterobiasis were not confirmed by the single anal swab laboratory analysis (**II** Fig. 1); that is, the number of false positive predictions was remarkable. The overall prevalence was 22.8%

according to the examinations. The case-based prevalence estimations varied between 34.5% and 47.8% (average 42.8%) in the results of 10 parallel estimations. The most similar exemplars for the largest number of children (79.3%) were all either exemplars of infected or non-infected children, 20.7% of children were similar in both categories to a certain degree.

In paper **III,** the estimated overall prevalence calculated using the three methods (Constud, BCT and RF) was 31.1% according to Constud, 43.7% according to BCT and 45.7% according to RF. The mean TSS-fit for Constud was lower in groups with more than ten children (TSS=0.295, versus TSS=0.587, n=31 and 28, p=0.002, Mann-Whitney U-test). Many small groups were not infected and the few children in these groups were commonly identified as not infected. The explanatory features selected by these three methods as the most useful for distinguishing positive and negative cases were not the same (**III** Table 5). The classification tree methods relied more on child and family characteristics, whereas Constud selected characteristics of nursery groups. Region, child age, and range of ages in nursery school groups were among the 13 most indicative attributes in all three models.

The prevalence estimations in groups calculated from individual level predictions varied between 0.17 and 1.0, but still correlated strongly with the results of single (R=0.666), double (R=0.613) and triple examination (R=0.583). Constud estimated 31.5% of detections (SD=0.268) for the mean prevalence in groups, which is greater than the result of 20.4% from single swab examinations (SD=0.162), 27.4% (SD=0.201) for double examination, and 29.1% (SD=0.216) for triple examinations.

The internal fit of Constud predictions depended on the size of the training sample. Constud reached high training accuracies when using small samples, but these accuracies were not valid outside the sample – a phenomenon of over fitting (**IV** Fig 2B, 3). The training accuracies of BCT models were generally lower – the BCT method may drastically fail in cross-predictions if the learning sample is less than 500 observations. The external fit of Constud predictions did not indicate any dependence on the size of the training sample.

Internal and external fit converged for both methods (BCT and Constud) when the training samples increased. The model derived from a larger training sample is more likely to be valid outside the training data; or in other words, is more universal. The high risk of over fitting in Constud, while using samples approximately less than 500 observations, also became evident when using random training samples of 5 to 50% of the size of all observations (**IV** Fig. 3). On the other hand, Constud was ineffective or at least time-expensive in finding a predictive set of weights for features and exemplars when the training sample was large (more than 1000 observations). BCT was much more efficient in finding a more generalized model from a large training sample.

4.4. Enterobiasis related to geographical region and settlement size, spatial autocorrelation of prevalence

The mean prevalence of enterobiasis according to geographical region in Estonia was 26% in the southeast, 20% in the southwest, 27% in the northwest, 17% in the northeast and 22% in the central part of Estonia; according to settlement type the mean prevalence was 14% in large towns, 19% in small towns and 28% in rural settlements (Table 3). Enterobiasis in the capital of Estonia, Tallinn, was remarkably less frequent (10%) than in other parts of Estonia (Table 3) (**IV** Fig. 1B). Prevalence in the other larger towns was 16% in Pärnu and 23% in Tartu; the prevalence of enterobiasis differed among small towns (13–32%) and rural settlements (20–43%). The dependence of prevalence on the most detailed geographical units (n=17) was more significant in southeast Estonia and among rural settlements, which both were represented by a larger number of sub-divisions (**IV**).

Differences in risk factors became evident in connection with the settlement type; this probably results from differences in social conditions or life style. The number of children in the family was an essential risk factor everywhere except in larger towns; also, the occupation of other children was not a significant factor in Tallinn and in the predominantly industrial towns of northeast Estonia, where the mean number of children per family was relatively small (**IV** Table 2). Mixed-age groups had the highest indicator value in small towns where both mixed and same-age groups were common. The prevalence of enterobiasis was remarkably higher in mixed-age groups in eastern and central Estonia.

The indicator value of some features depended on settlement type as well. In large towns, the general cleanliness of children in the nursery group was ranked first (FSVS in Statsoft Statistica Data Miner), and presence/absence of soft toys in the nursery and hand washing habits had a relatively high rank (**VI** Table 3). Carefulness of hand washing was also among the most indicative features in major towns.

Feature ranking in smaller geographical samples seems to be largely casual, and probably simply due to the smaller sample size. Hand washing after toilet use was among the top 10 risk indicators in most of the investigated rural areas. The number of rooms for a nursery group was related to the risk of enterobiasis mainly in Tartu where this figure is the lowest (average number rooms=1.2 in Tartu; in all data 1.9).

The fit of BCT cross-predictions was slightly higher if the distance between samples was less than 200 km; at larger distances the mean fit of BCT cross-predictions was lower than expected from the random assignment of the infection risk (mean values 0.040 and −0.001, p = 0.029, two-sided t-test). The mean fit of mutual cross-predictions was higher (over 0.1) between geographical subdivisions within southeast Estonia.

Spatial autocorrelation of the prevalence of enterobiasis in nurseries expressed as the Moran's I is generally low being significant at $p<0.01$ level

(I = 0.2217) only within distance up to 20 km (**VI** Fig. 5). This indicates some similarity of prevalence in nurseries within the same settlement and within the detailed spatial units used in this study but not at larger distances.

5. DISCUSSION

The prevalence found from this study was quite high, even more than 19% (**I**). In other words, one fifth of all nursery children in Estonia are infected. This may be nearly 10500 children if we consider the mean number of nursery children within a year during the period from 2002 to 2007. Prevalence may be even higher as this was the result from a single study, which shows only a part of the prevalence as a rule (**III**). Also, the method of examination was anal swabs, which is less productive than the tape method (Sommer, 2008). A high prevalence of enterobiasis, especially among children, from several other countries has also been reported. According to a review on parasitic diseases in the Republic of Korea, *E. vermicularis* infection is considered not to have reduced significantly; even in the 1980s and 1990s, the prevalence among children has remained approximately 30%–60% (Shin et al., 2008). Although some investigations in Korea have found a lower prevalence: 9.5% (Song et al., 2003) and 18.5% (Park et al., 2005). In Turkey, the prevalence has been 5.1% among preschool children aged 5–7 (Artan et al., 2008), according to other investigations among primary schools students 15.6% (Çelíksöz et al., 2005), in Argentina 41.4% (Pezzani, 2004), in Venezuela even so high as 57.8% (Acosta et al., 2002) and 63.2% (Cazorla et al., 2006). Prevalence is much lower among nursery school children in Bulgaria, 3.7–6.2% (1991–2000) (Kurdova, 2001) and 5.2% among 344 children examined in Finland (Kyrönseppä, 1993). In Sweden the prevalence was 37% among allergic children, compared to 23% in the no allergic control group (Herrström et al., 2001).

Only 230 cases of enterobiasis (0.4% from nursery children) are known among nursery children in Estonia according to the official statistics in 2007 (Nakkushaigustesse …, 2009). Of course, the data collection purposes and methods for research and official statistics differ, so it is not correct to compare these numbers. We can only conclude from the official data on enterobiasis in Estonia that there is insufficient monitoring at the present time.

Children belonging to the infected groups (83% of studied children) are endangered in the nursery environment first of all. The prevalence among children from infected groups was 30% according to single examinations. If we take into account the efficiency of triple examinations (**III**), the real prevalence could be 56% or higher. Such a high prevalence has also been found in Venezuela and Argentina (Acosta et al., 2002; Pezzani, 2004; Cazorla et al., 2006). The nursery group the child belongs to can be taken as an important risk factor. Only a quarter (27%) of all studied groups seemed to be non-infected.

Enterobiasis infection in a person cannot be detected for certain. For nursery children, the possibility of becoming infected depends on the prevalence within the group, as every child who belongs to an infected group can get enterobiasis at any time. The relatively high number of infected groups shows the danger even better than the prevalence among individuals.

The predicted prevalence was higher than found by the examination of swabs. The larger number of false-positive estimations can be attributed to the objective function, where the shares of true positive and true negative have equal weight, and by the lability of actual infection compared to the more stable risk of infection. The detected infection is even more difficult to predict since not all cases of infection are discovered by anal swab analysis (**II**). The case-based risk estimations enhanced differences, as is generally expected from an indicator – in general the differences in risks were much larger than the differences in prevalence. For instance, the risk was estimated to be five times higher in the groups that got a mark of poor for general cleanliness than in the groups assigned excellent – the prevalence was, however, barely two times higher (**II**).

The ultimate aim of the individual-based models in paper **III** was not to predict the positive/negative enterobius status of a child, but to estimate enterobiasis prevalence in groups. The results of study confirmed that individual-level modelled risk predictions can support or be an alternative for the estimation of the expected prevalence of enterobiasis (**III**).

One part of the investigation was to test the efficiency of case-based reasoning (CBR) system Constud in epidemiological predictions using tabular data. CBR has proved its strength in many weak-theory domains, in which a great number of single examples and case studies predominate over deduction, and in which large databases of previous cases exist, including medicine (Schmidt et al., 2001; Bichindaritz et al., 2006).

The main differences between Constud and traditional methods of statistical modelling are as follows.

1. The estimations in Constud are derived from the most similar feature vectors. Generalization in the form of a model, like in the case of traditional statistical methods, is not created.
2. Traditionally iterative model fitting in the case of advanced statistical methods complete when a given criterion is reached or a given number of iterations is passed. Search of the best solution in Constud is a continuous iterative process. Experience obtained during the process is saved in a knowledge base as values of actuality.
3. Features and cases can be added to and excluded from the knowledge base without interrupting the learning process. The hitherto best set of weights for features and exemplars can always be used for predictions. There is no need to generate a new model, like in the case of modelling, when additional observations or features have been added to the knowledge base. Supplementary machine learning involving new data is recommended but not obligatory.
4. Feature vectors, parameters, results of iterations and metadata are kept in a single relational knowledge base, which is not the case in most other software packages.

According to the methodological comparisons of this study there were three major advantages of Constud compared to the tested regression and classification tree models. Most statistical methods did not reach the prediction fit obtained by Constud.

1. Only the methods boosted classifications trees and random forest were at the same level according to the objective function TSS (**II**, **III**). Constud was able to yield the highest overall fit of individual-based predictions while boosting classification tree and random forest models were more effective in recognizing enterobius positive persons.
2. Leave-one-out cross validation does not demand exclusion of a large amount of observations from training data to a validation sample. A large number of explanatory features yields in many nearly equally effective sets of predictive features but does not hinder the calibration of a similarity-based prediction system.
3. Observations containing empty fields are not used in the calibration of regression models and in the classification tree methods in Statistica. Constud is unaffected by missing feature values. The similarity between two cases is calculated using only those features that have values (**II**).

The main present drawbacks hindering wider application of Constud are complicated using and the time spent for calculations. A shortage is also that predictive sets in Constud tend to be over fitted if the number of training observations is less than 500. The solution fits relatively well inside the training set yet is deceptive outside the learning sample. The internal and external fit of BCT predictions differs less in moderate size samples. Both methods failed to offer reasonable cross-predictions if the training sample is less than 300 observations (**IV**).

The predicting system can produce effective estimations in spite of the above mentioned shortages. Cooperation with additional infotechnology experts could develope the system more competitive.

Enterobiasis risk was universally related to children's age in all geographical units of Estonia (**I, II**, **IV**). Nursery age and younger school age are mentioned in numerous publications as the more common ages for enterobiasis. This study shows a significantly higher occurrence of enterobiasis among 5–8 year old children (**I**) who are the oldest children in nurseries. This is in agreement with other studies (Norhayati et al., 1994; Song et al., 2003). The causes of this trend could be: inadequate personal hygiene of older children, more physical contact with their friends and playing with dirty toys (Song et al., 2003). Another possible cause is iterative self-infection if an earlier infection has remained untreated.

In previous studies, the age of each child has predominantly been related to infection risk, not the mean age in their nursery school group. The extent of the variability of the age of children in a group has not been analysed until now according to our knowledge (**II**). Mixed-age groups with an age range over 4 years turned out to be a significant risk factor for the younger members of the group. Prevalence is usually low among children aged 1–4, in mixed-age groups they are likely to be infected by their older companions. The prevalence of enterobiasis was remarkably higher in mixed-age groups in eastern and central Estonia.

Family size was a significant risk factor of enterobiasis in our study and also in studies of Artan et al. (2008) – children from large families are infected more often (**I**) as a result of more frequent contact with other children. First of all, this factor has sprung up in regions where families of various sizes exist, mainly in rural settlements. Other investigations have not proved the significance of family size for the risk of enterobiasis (Chan, 1985; Norhayati et al., 1994; Song et al., 2003).

Risk and indicator factors vary by regions. As a rule, locally more variable factors have a higher indicator value for predictive models. For example, other children in the family, and especially other nursery children, are a major factor of enterobiasis risk mainly in the countryside where the prevalence of enterobiasis is higher. The number of children per family is less and children are at home less in large towns. Therefore, the probability of being with a contaminated person is distributed more equally among urban children, which gives personal hygiene (hand washing quality) a higher weight as a risk-reducing factor (**IV**).

The features of personal hygiene and the sanitary situation in rooms, which have been significant in some other studies (Norhayati et al., 1994; Chih et al., 1996; Herrström et al., 1997; Sung et al., 2001), were significant only in some regions in this study.

The prevalence of enterobiasis in Estonia is higher in rural settlements and lowest in the capital of Estonia, Tallinn; it is also low in the industrial towns of the northeastern part of the country (**IV**). A much lower prevalence of enterobiasis in urban areas than in rural communities has also been described by Cazorla et al. (2006) in Venezuela. The prevalence was quite low even in small towns in comparison with rural areas. However, the living conditions in small towns and in villages seem to be similar in Estonia contrary to Venezuela (Cazorla et al., 2006). The socioeconomic status of the family is mentioned as a risk factor of enterobiasis in publications (Çelíksöz et al., 2005; Cazorla et al., 2006; Wang et al., 2009, Artanet al., 2008). Ida-Viru county is among the lowest income regions of Estonia. So, a high prevalence was expected. Actually, the prevalence of enterobiasis in the industrial towns of northeastern Estonia was lower than in other areas, except Tallinn, while the prevalence of enterobiasis in the rural part of Ida-Viru was at the same level as in other rural areas (**IV**).

Differences in the prevalence of enterobiasis were statistically significant between the detailed geographical units. These units carry information on the distribution of the prevalence of enterobiasis, and possibly also about geographical differences in risk factors, since the prediction models worked out

10

for one geographical unit usually do not work for other units. If a local or environmental factor influencing the risk of contamination is constantly high in a region, it can be treated as a geographic characteristic of that region. Positive spatial autocorrelation at distances up to 20 km also indicates that first of all the smaller geographical units are related to the distribution of enterobiasis not larger regions. The distance up to 20 km is common for everyday movement and contacts of people. It is also about the radius of the detailed spatial units of this study (**IV**).

6. CONCLUSIONS

This investigation focused on the prevalence, prediction, risk factors and geographical aspects of enterobiasis in Estonia. *Enterobius vermicularis* is a widespread parasitic risk factor for a healthy environment, in particular for children. The correct diagnosis of pinworm is complicated and the elimination of the parasite from a family group or institution often poses significant problems though its treatment is straightforward. There was not reliable up-to-date information about the occurrence of *E. vermicularis* in Estonia. The main results of this study are as follows.

1. As a rule, the actual prevalence of enterobiasis is higher than indicated by a single examination. The group level estimation of prevalence deduced from risk predictions modelled at individual-level, repeated examinations and using the values of the mean increase in prevalence after double examinations found in this investigation are the options to get a more realistic estimation for prevalence.
2. From risk modelling methods, a similarity-based machine learning and prediction software Constud, random forest classification and boosting classification trees from the Statistica 8 Data Miner software package were successful. Detailed description of the software system Constud was published in an international journal for the first time.
3. Features as: region according to the detailed division, the age of the child, the mean age of the children in the nursery group, the range of children age in the nursery group, the general cleanliness of children in the nursery group, the number of children in the family, pets of the family, other children in the family attending a nursery or elementary school and features of individual hygiene were among the more indicative features for risk modelling. The family income, gender of the child and also educational level of child's mother had a low indicative value.
4. As a rule, the locally more variable factors have a higher indicator value for predictive models. The best indicator features differ in geographical space since the variability of features varies locally. Knowledge of the detailed region appeared to be a good indicator of infection – the prevalence of enterobiasis is positively autocorrelated in space.
5. The mean prevalence of enterobiasis according to settlement type varied being the lowest in the capital of Estonia – Tallinn and the highest in rural settlements. The overall mean prevalence from single examinations was 19%, the estimated mean prevalence in groups derived by Constud was much higher 31.5%. This estimation is still fitting with the results from triple swab examinations. As much as three quarters from all studied nursery school groups turned out to be infected. This indicates to the real infection threat for all children belonging to these groups, also for the family members and the staff of nurseries.

6. The prevalence of enterobiasis among nursery school children is high in Estonia. This can be even over 40% if to take into account the results from the multiple examination and calculated predictions. 83% of studied children belonged to the infected groups.

SUMMARY IN ESTONIAN

Enterobiaasi geograafilisi aspekte Eestis

Enterobiaasi põhjustaja, naaskelsaba (*Enterobius vermicularis*), on maailmas, sealhulgas paraskliima vööndis, laialtlevinud kontakthelmint, kellega nakatuvad eelkõige vanemas lasteaiaeas ja nooremas koolieas olevad lapsed. Parasiit on eriti levinud lastekollektiivides. Kuigi üks enamlevinud helmintidest ka arenenud riikides, on naaskelsaba diagnoosimine ja nakatatuse õige taseme kindlakstegemine sageli aeganõudev. Ravi on küll lihtne, kuid naaskelsabade tõrjumine perekonnast või lasterühmadest võib palju vaeva nõuda. Lihtsam on nakatumist vältida. Selleks on vajalik teave olemasolevast nakatatusest ja riskiteguritest. Naaskelsaba on oma elutsüklis väga tihedalt inimesega seotud parasiit. Kuna sotsiaalsed, majanduslikud, kultuurilised tingimused ja traditsioonid on maailma eri piirkondades varieeruvad, on seda ka enterobiaasi riskitegurid. Enterobiaasi esinemist, riskitegureid, ravi ja diagnoosimise tõhusust on uuritud paljudes maades. Suuremat territooriumi (kogu riiki) võrdlevalt käsitlevaid uuringuid ei ei ole autorile teada. Kirjeldatud on enterobiaasi lokaalset esinemist või võrreldud nakatatuse erinevusi üksikutes piirkondades.

Uuringu eesmärgid olid järgmised.

1. Kirjeldada enterobiaasi levikut ja riskitegureid Eesti lasteaiarühmades, välja selgitada nakatatuse seos erinevat tüüpi teguritega.
2. Hinnata kordusuuringu tõhusust enterobiaasi tuvastamisel lasteaiarühmades ja tegeliku nakatatuse hindamise võimalikkust lasteaiarühmade ühekordse uuringu tulemuste põhjal.
3. Välja selgitada erinevate meetoditega läbi viidud indiviidipõhise riskihindamise tõhusus, võrrelda parimaid meetodeid indiviidipõhise hindamise alusel rühma nakatatuse kindlakstegemisel ja selgitada õppevalimi suuruse mõju hinnangu edukusele.
4. Välja selgitada enterobiaasi nakatatuse ja riskitegurite seos geograafiliste piirkondadega ja asumisuurusega.

Uuringumaterjal koguti 2002–2007 aastal. Uuring toimus seitsmes Eesti maakonnas ja Tallinnas. Uuringusse haarati 279 rühma 80 lasteaiast. Kokku uuriti 3131 last, mis moodustas 5,8% uuringu ajavahemiku keskmisest aasta lasteaialaste hulgast. 604 last uuriti kahekordselt ja 96 last kolmekordselt. Kordusuuringute tõttu oli laboratoorselt uuritud perianaalkaabete arv 3831. Lapsevanematelt saadi tagasi 2616 täidetud ankeeti, kõikides rühmades viidi läbi rühmaruumide vaatlus ja struktureeritud intervjuu õpetaja või abiõpetajaga.

Vaatlused jagati geograafilisteks valimiteks kolmel viisil: 1) kuueks regiooniks vastavalt geograafilisele paiknemisele; 2) kolmeks lähtuvalt asumi suurusest: suured linnad, väikesed linnad, maapiirkond; 3) detailseteks piirkondadeks kombineerides asukohta ja asumi suurust (17 piirkonda).

Andmeanalüüsi abil selgitati välja enterobiaasi riski hindamiseks sobivad indikaatortunnused Eestis. Enterobiaasi hindamisel kasutati ja hindamise tõhususes võrreldi Statsoft Statistica andmekaevandamispaketti kuuluvaid meetodeid ja Tartu Ülikooli geograafia osakonnas arendatud tarkvara Constud.

Peamised tulemused ja järeldused olid järgmised.

1. Enterobiaasi esinemissagedus lasteaialaste seas on kõrge. Arvestades mitmekordseid uuringuid ja hinnanguid, võib nakatunud olla ligi 40% lastest. Kolmveerand uuritud rühmadest olid nakatunud. 83% uuritud lastest kuulub nakatunud rühmadesse. Kõigil nakatunud rühmadesse kuuluvatel lastel on suur tõenäosus nakatuda.
2. Suurema indikaatorväärtusega tunnused on: piirkond; lapse vanus; rühma vanuselised tunnused – laste vanus rühmas, vanusehaare rühmas; suhtluspartneritega seotud tunnused – rühma kuuluvate laste puhtus, laste arv peres, koduloomad, pere teiste laste tegevus; individuaalne hügieen; rühma ruumide puhtus. Väheolulisteks osutusid: pere sissetulek, lapse sugu ja ema haridustase.
3. Ühekordse uuringuga saadud enterobiaasi nakatatuse tulemused on reeglina puudulikud. Soovitav on kasutada mitmekordset uuringut või lisada rühma ühekordsest uuringust saadud nakatatusele käesolevas uuringus leitud topeltuuringutega lisanduv keskmine nakatatus või siis arvutada tegelik nakatatus mudelist.
4. Uuritud meetoditest olid rühma nakatatuse indiviidipõhisel hindamisel edukad *Random Forest Classification,, Boosting Classification Trees* ja Constud. Tarkvaraga Constud saadi mitmekordse uuringuga hästi kokkulangev rühma nakatatuse hinnang: 31,5%. Laboratoorsel uuringul saadi nakatatuseks: ühekordse kaape tulemusel 20,4% , kahekordse kaape tulemusel 27,4% ja kolmekordse kaape tulemusel 29,1%.
5. Tarkvara Constud kasutati esmakordselt tabelandmete ja epidemioloogiliste andmete töötlemisel, avaldati esmakordselt tarkvara kirjeldus rahvusvahelises ajakirjas.
6. Kõrgeim nakatatus esineb maapiirkondades, madalaim suurtes linnades (eriti Tallinnas ja Ida-Viru linnades). Detailsed piirkondlikud üksused on head nakatatuse indikaatorid, positiivne ruumiline autokorrelatsioon leiti 20 km ulatuses. Kui nakkus on piirkonnas olemas ja mida kõrgem see on, seda enam on kõik inimesed piirkonnas ohustatud.

Enterobiaasi ennetustöös lasteasutustes tuleks tähelepanu pöörata rühmade nakkusvabaks muutmisele ja nakkusvabana hoidmisele.

REFERENCES

Abrahams, P.W., 2006. Soil, geography and human disease: a critical review of the importance of medical cartography. Progress in Physical Geography 30 (4), 490–512.

Acosta, M., Cazorla, D., Garvett, M., 2002. Enterobiasis en escolares de una población rural del Estado Falcón, Venezuela y su relación con el nivel socio-económico. Inves. Clin 43, 173–181.

Allouche, O., Tsoar, A., Kadmon, R., 2006. Assessing the accuracy of species distribution models: prevalence, kappa and the true skill statistic (TSS). J Appl Ecol 43, 1223–1232.

Artan, M.O., Baukan, Z., Artan, C., 2008. Enterobiasis among preschool children: a study from Kayseri, Turkey. Jpn J Infect Dis 61,482–483.

Astal, Z., 2004. Epidemiological survey of the prevalence of parasites among children in Khan Younis governorate, Palestine. Parasitol Res 94, 449–451.

Bichindaritz, I., Marling, C., 2006. Case-based reasoning in the health sciences: what's next? Artif Intell Med 36,127–135.

Brooker, S., Michael, E., 2000. The potential of geographical information systems and remote sensing in the epidemiology and control of human helminth infections. Adv Parasitol 47, 245–88.

Brooker, S., Singhasivanon, P., Waikagul, J., Supavej, S., Kojima, S., Takeuchi, T., Luong, T.V., Looareesuwan, S., 2003. Mapping soil-transmitted helminths in Southeast Asia and implications for parasite control. Southeast Asian J Trop Med Public Health 34(1), 24–36.

Brooker, S., Clements, A.C., Bundy, D.A., 2006. Global epidemiology, ecology and control of soil-transmitted helminth infections. Adv Parasitol 62, 221–61.

Burkhart, C.N., Burkhart, C.G., 2005. Assessment of frequency, transmission, and genitourinary complications of enterobiasis (pinworms). Int J Dermatol 44(10), 837–840.

Cazorla, D., Acosta, M., García, E., Garvett, M., Ruiz, A., 2006. Enterobius vermicularis infection in preschool and schoolchildren of six rural communities from a semiarid region of Venezuela: a clinical and epidemiological study. Helminthologia 43(2), 81–85.

Çelíksöz, A., Aciöz, M., Değerli, S., Ali, A., Aygan, Ç., 2005. Egg positive rate of Enterobius vermicularis and Taenia spp. by cellophane tape method in primary school children in Sivas, Turkey. Korean J Parasitol 43(2), 61–64.

Chan, C.T., 1985. Enterobiasis among schoolchildren in Macao. Southeast Asian J Trop Med Public Health 16, 549–553.

Chih, H.W., Lin, H.S., Tang, K.S., Cheu, S.C., 1996. A study of multiple factors to Enterobius vermicularis infection among pre-school children in Ta-Liao district of Kaohsiung County. Kaohsiung J Med Sci 12, 538–543.

Cho, S.-Y., Kang, S.-Y., 1975. Significance of Scotch-tape anal swab technique in diagnosis of Enterobius vermicularis infection. Korean J Parasitol 13(2), 102–114.

Cho, S.-Y., Kang, S.-Y., Ryang, Y.-S., Seo, B.-S., 1976. Relationships between the results of repeated anal swab examinations and worm burden of Enterobius vermicularis. Korean J Parasitol 14(2), 109–116.

Cook, G., 1994. Enterobius vermicularis infection. Gut 35, 1159–1162.

Devera, R., Perez, C., Ramos, Y., 1998. Enterobiasis in students from Ciudad Bolivar, Venezuela. Bol Chil Parasitol 53, 14–18.
Elith, J., Graham, C.H., Anderson, R.P., Dudík, M., Ferrier, S., Guisan, A., Hijmans, R.J, Huettmann, F., Leathwick, J.R., Lehmann, A., Li, J., Lohmann, L.G., Loiselle, B.A., Manion, G., Moritz, C., Nakamura, M., Nakazawa, Y., Overton, J.McC., Peterson, A.T., Phillips, S.J., Richardson, K., Scachetti-Pereira, R., Schapire, R.E., Soberón, J., Williams, S., Wisz, M.S., Zimmermann, N.E., 2006. Novel methods improve prediction of species' distributions from occurrence data. Ecography 29, 129–151.
Fan, P., Chan, C., 1990. Consecutive examination by scotch-tape perianal swab in diagnosis of enterobiasis. Gaoxiong Yi Xue Ke Xue Za Zhi 6(12), 647–652.
Gale, E.A.M., 2002. A missing link in the hygien hypothesis? Diabetologia 45, 588–594.
Georgiev, V.S., 2001. Chemotherapy of enterobiasis (oxyuriasis). Expert Opin Pharmacother 2, 267–275.
Grencis, R., Cooper, E., 1996. Enterobius, Trichuris, Capillaria and hookworm. Gastroenterol. Clin. North. Am., 25, 579–596.
Haswell-Helkins, M., Elkins, D., Manjula, K., Michael, E., Anderson, R., 1987. The distribution and abundance of Enterobius vermicularis in a South Indian fishing community. Parasitology 95, 339–354.
Health Protection Inspectorate, 2000. Communicable disease statistics in Estonia. Part 9. Tervisekaitseinspektsioon, Tallinn.
Health Protection Inspectorate, 2005. Communicable disease statistics in Estonia. Part 13. Tervisekaitseinspektsioon, Tallinn.
Herrström, P., Friström, A., Karlsson, A., Högstedt, B., 1997. Enterobius vermicularis and finger sucking in young Swedish children. Scand J Prim Health Care 15(3), 146–148.
Herrström P., Henricson K.A., Råberg A., Karlsson A., Högstedt B., 2001. Allergic disease and the infestation of Enterobius vermicularis in Swedish children 4–10 years of age. J Investig Allergol Clin Immunol 11(3), 157–160.
Horne, P.D., 2002. First Evidence of Enterobiasis in Ancient Egypt. J Parasitol 88(5), 1019–1021.
Hugot, J.-P., Reinhard, K.J., Gardner, S.L., Morand, S., 1999. Human enterobiasis in evolution: Origin, specificity and transmission. Parasite 6, 201–208.
Iñiguez, A.M., Reinhard, K., Gonçøalves, M.L.C., Ferreira, L.F., Araújo, A., Vicente, A.C.P., 2006. SL1 RNA gene recovery from Enterobius vermicularis ancient DNA in pre-Columbian human coprolites. Int J Parasitol 36, 1419–1425.
Jõgiste, A., Barotov, O., Varjas, J., 2001. Ülevaade helmintiaaside tõrje tulemustest. Eesti Arst 80, 265–270.
Jõgiste, A., Barotov, O., 1993. Helmintoosid Eestis aastail 1960–1989. Eesti Arst 72, 251–254.
Kim, J., Lee, H., Ahn, Y., 1991. Prevalence of Enterobius vermicularis infection and preventive effects of mass treatment among children in rural and urban areas, and children in orphanages. Korean J Parasitol 29(3), 235–243.
Kim, B.J., Lee, B.Y., Chung, H.K., Lee, Y.S., Lee, K.H., Hung H.J., Ock M.S., 2003. Egg positive rate of Enterobius vermicularis of primary school children in Geoje island. Korean J Parasitol 41(1), 75–77.
Kliks, M.M., 1990. Helminths as Heirlooms and Souvenirs: a Review of New World PaleoparasitoIogy. Parasitol Today 6, 93–100.

Kyrönseppä H., 1993. The occurrence of human intestinal parasites in Finland. Scand J Infect Dis 25(5), 671–673.

Moubarrad, F.-Z.L., Assobhei, O., 2005. Impact of urban effluents on intestinal helminth infections in the wastewater discharge zone of the city of El Jadida, Morocco. Management of Environmental Quality 16(1), 6–16.

Nithikathkul, C., Changsap, B., Wannapinyosheep, S., Poiter, C., Boontan, P., 2001. The prevalence of enterobiasis in children attending mobile health clinic of Huachiew Chalermprakiet University. Southeast Asian J Trop Med Public Health 32, 138–142.

Nithikathkul, C., Akarachantachote, N., Wannapinyosheep, S., Pumdonming, W., Brodsky, M., Sukthana, Y., 2005. Impact of health educational programmes on the prevalence of enterobiasis in schoolchildren in Thailand. J Helminthol 79(1), 61–65.

Norhayati, M., Jayati, M.I., Oothuman, P., Azizi, O., Fatmah, M.S., Ismail, G., Minudin, Y., 1994. Enterobius vermicularis infection among children aged 1–8 years in a rural area in Malysia. Southeast Asian J Trop Med Public Health 25, 494–497.

Park, J.-H., Han, E.-T., Kim, W.-H., Shin, E.-H., Guk, S.-M., Kim, J.-L., Chai, J.-Y., 2005. A survey of Enterobius vermicularis infection among children on western and southern coastal islands of the Republic of Korea. Korean J Parasitol 43(4), 129–134.

Parija S.C., Sheeladevi C., Shivaprakash M.R., Biswal N., 2001. Evaluation of lactophenol cotton blue stain for detection of eggs of Enterobius vermicularis in perianal surface samples. Trop Doct 31(4), 214–215.

Pezzani, B.C., Minvielle, M.C., de Luca, M.M., Córdoba, M.A., Apezteguķa, M.C., Basualdo, J.A., 2004. Enterobius vermicularis infection among population of General Mansilla, Argentina. World J Gastroenterol 10(17), 2535–2539.

Remm, K., 2004. Case-based predictions for species and habitat mapping. Ecol Modell 177 (3–4), 259–281.

Sadun, E., Melvin, D., 1955. The value of repeated examination in diagnosis of infection with Enterobius vermicularis. J Parasitol 41(l), 41.

Schmidt, R., Montani, S., Bellazzi, R., Portinale, L., Gierl, L., 2001. Casedbased reasoning for medical knowledge-based systems. Int J Med Inform 64, 355–367.

Song, H.-J., Cho, C.-H., Kim, J.-S., Choi, M.-H., Hong, S.-T., 2003. Prevalence and risk factors for enterobiasis among preschool children in a metropolitan city in Korea. Parasitol Res 91, 46–50.

Sung, J.F.C., Lin, R.S., Huang, K.C., Wang, S.Y., Lu, Y.-J., 2001. Pinworm control and risk factors of pinworm infection among primary-school children in Taiwan. Am J Trop Med Hyg 65(5), 558–562.

Öztürk, C.E., Şahin, I., Yavuz, T., Öztürk, A., Akgünoğlu, M., Kaya, D.,2004. Intestinal parasitic infection in children in post-disaster situations years after earthquake. Pediatr Int 46, 656–662.

Wang, L.-C., Hwang, K.-P., Chen, E.-R., 2009. Enterobius vermicularis infection in schoolchildren: a large-scale survey 6 years after a population-based control. Epidemiol Infect 19, 1–9.

Yoon, H.-J., Choi, Y.-J., Lee, S.-U., Park, H.-Y., Huh, S., Yang, Y.-S,. 2000. Enterobius vermicularis egg positive rate of pre-school children in Chunchon, Korea (1999). Korean J Parasitol 38(4), 279–281.

Käsikirjad ja veebilehed

Must, H., 2006. Parasitoloogilised laboriuuringud Eestis. Diplomitöö, Tartu Tervishoiu Kõrgkool.

Nakkushaigustesse haigestumine Eestis, 2009. Health Protection Inspectorate. http://www.tervisekaitse.ee/?mid=136 14.04.09.

Sommer, S., 2008. Teibimeetod enterobiaasi laboratoorses diagnostikas. Diplomitöö, Tartu Tervishoiu Kõrgkool.

ACKNOWLEDGEMENTS

My deepest gratitude to my supervisor Kalle Remm for supporting me throughout my studies.

I am thankful to Tõnu Oja and Ülo Mander for their kind help and support in my studies.

I am grateful to students from Tartu School of Health Care: for participating in data collection and also to all directors and teachers of the studied nursery schools and the parents of the children for their kind cooperation.

All laboratory examinations were carried out at the laboratories of Tartu Health Care College. I am thankful for possibility to use laboratories and the equipment, and also to colleges for supporting me in this time, especially to Inga for motivation in evenings when the microscopy was already fatiguing and Helja for helping in the laboratory process.

My special thanks to all from my family who have accompanied me through the good and bad times.

The investigation was supported by the Doctoral School of Ecology and Environmental Science and by the Estonian Ministry of Education and Science (target financing project no SF0180052s07).

CURRICULUM VITAE

Mare Remm

Date and place of birth:	February 27, 1954, Tallinn
Citizenship:	Estonian
Contact:	Tartu Health Care College, Nooruse 9, 50411 Tartu, Estonia
E-mail	mareremm@nooruse.ee

Education

2004–	University of Tartu, Faculty of Science and Technology, Institute of Ecology and Earth Sciences, Ph. D. studies in geography
2001–2003	University of Tartu, Faculty of Medicine, Department of Public Health, Master of Public Health
1972–1977	University of Tartu, Faculty of Biology and Geography, Department of Biology, biologist, the teacher of biology and chemistry
–1972	Tallinn Secondary School No 4.

Professional experience

1982–present	Tartu Medical School, since 2005 Tartu School of Health Care, since 2009 Tartu Health Care College, teacher, since 1995 senior teacher, since 2005 coordinator for curricula of environmental health specialist and of bioanalyst
1977–1982	Tartu Secondary School No 7, teacher of biology

Scientific interest

Parasitology, environmental health

Publications

Peer-reviewed

M. Remm, K. Remm. (2008). Effectiveness of repeated examination and individual-based risk predictions to diagnose enterobiasis. Laboratorine medicina (Program and Abstracts Volume), 10, 34.

Remm, M., Remm, K. (2008). Case-based estimation of the risk of enterobiasis. Artificial Intelligence in Medicine, 4, 167–177.

Remm, M., Vipp, H. (2006). Distribution of enterobiasis among nursery children in Estonia and estimation of usefulness of recurrent sampling. Laboratorine Medicina (Program and Abstracts Volume), 1(29), 44.

Remm, M. (2006). Distribution of enterobiasis among nursery school children in SE Estonia and of other helminthiases in Estonia. Parasitology Research, 99, 729–736.

Remm, M. (2004). Helmintiaaside esinemine Tartu ja selle ümbruse lastepäevakodude lastel ning seda mõjutavad tegurid. Eesti Arst, 83, 148–153.

Others

Remm, M. 2008. Sanitaarvelskrite ja tervisekaitse spetsialistide õppest Tartu Meditsiinikoolis/Tartu Tervishoiu Kõrgkoolis. Eesti Tervisekaitse seltsi 54. konverentsi ettekannete kogumik. Tallinn.

Remm, M. 2007. Mitmekordse uuringu tõhusus enterobiaasi kindlakstegemisel. Eesti Tervisekaitse seltsi 53. konverentsi ettekannete kogumik. Tallinn.

Remm, M. 2006. 2005./2006. õppeaasta tervisekaitse spetsialistide õppes. Tervisekaitse 2005. Tallinn.

Remm, M., Orav, A., Aotäht, E. (2006). Bioanalüütiku kutseala ja haridus Eestis. Lege artis, apr.

Remm, M. 2005. 2004./2005. õppeaasta tervisekaitse spetsialistide õppes. Tervisekaitse 2004. Tallinn.

Remm, M. 2005. Enterobiaasi levimus Kagu-Eesti lasteaialaste seas ja seda mõjutavad tegurid. Eesti Tervisekaitse seltsi 51. konverentsi ettekannete kogumik. Tallinn.

Remm, M. 2004. Tervisekaitse eriala Tartu Meditsiinikoolis. Tervisekaitse 2003. Tallinn.

Conference presentations

Remm, M. The education of bioanalysts in Estonia. Oral presentation at General Governing Body Meeting and Students Forum of European Association for Professions in Biomedical Science, Bratislava, Slovakia, 2008.

Remm, M., Remm, K. Effectiveness of repeated examination and individualbased risk predictions to diagnose enterobiasis. Poster presentation at 9th Baltic Congress of Laboratory Medicine, Jurmala, Latvia, 2008.

Remm, M., Aotäht, E., Orav, O. Current and future education of bioanalysts in Estonia. Poster presentation at NML (Nordic Medical Laboratory) Congress, Helsinki, Finland, 2007.

Remm, M. Mitmekordse uuringu tõhusus enterobiaasi kindlakstegemisel. Oral presentation at 53th Conference of Estonian Society of Health Protection, Suure-Jaani, Estonia, 2007.

Remm, M., Vipp, H. Distribution of enterobiasis among nursery children in Estonia and estimation of usefulness of recurrent sampling. Poster presentation at 8th Baltic Congress of Laboratory Medicine, Vilnius, Lithuania, 2006.

Remm, M., Aotäht, E. The development of bioanalyst education in Estonia and research as an important part of it. Poster presentation at 8th Baltic Congress of Laboratory Medicine, Vilnius, Lithuania, 2006.

M. Remm. Enterobiaasi levimus Kagu-Eesti lasteaialaste seas ja seda mõjutavad tegurid. Oral presentation at 51th Conference of Estonian Society of Health Protection, Kuressaare, Estonia, 2005.

Professional membership

Estonian Society of Health Protection
Association of Estonian Biomedical Laboratory Sciencists

CURRICULUM VITAE

Mare Remm

Sünniaeg:	27 veebruar, 1954, Tallinn
Kodakondsus:	Eesti
Aadress:	Tartu Tervishoiu Kõrgkool, Nooruse 9, 50411 Tartu, Eesti
E-post	mareremm@nooruse.ee

Haridus

2004–	Tartu Ülikool, Loodus- ja tehnoloogiateaduskond, Ökoloogia ja Maateaduste Instituut, doktoriõpe geograafias
2001–2003	Tartu Ülikool, Arstiteaduskond, Tervishoiu instituut, rahvatervise kutsemagister
1972–1977	Tartu Ülikool, Bioloogia-Geograafia teaduskond, bioloogia osakond, bioloog, bioloogia ja keemia õpetaja diplom
–1972	Tallinn 4. Keskkool

Teenistuskäik

1982–praeguseni	Tartu Meditsiinikool, alates 2005 Tartu Tervishoiu Kõrgkool, õpetaja, alates 1995 vanemõpetaja, alates 2005 tervisekaitse spetsialisti ja bioanalüütiku õppekavade koordinaator
1977–1982	Tartu 7. Keskkool, bioloogia õpetaja

Uurimisvaldkond

Parasitoloogia, keskkonnatervis

Publikatsioonid

Eelretsenseeritud

M. Remm, K. Remm. (2008). Effectiveness of repeated examination and individual-based risk predictions to diagnose enterobiasis. Laboratorine medicina (Program and Abstracts Volume), 10, 34.

Remm, M., Remm, K. (2008). Case-based estimation of the risk of enterobiasis. Artificial Intelligence in Medicine, 4, 167–177.

Remm, M., Vipp, H. (2006). Distribution of enterobiasis among nursery children in Estonia and estimation of usefulness of recurrent sampling. Laboratorine Medicina (Program and Abstracts Volume), 1(29), 44.

Remm, M. (2006). Distribution of enterobiasis among nursery school children in SE Estonia and of other helminthiases in Estonia. Parasitology Research, 99, 729–736.

Remm, M. (2004). Helmintiaaside esinemine Tartu ja selle ümbruse lastepäevakodude lastel ning seda mõjutavad tegurid. Eesti Arst, 83, 148–153.

Muud

Remm, M. 2008. Sanitaarvelskrite ja tervisekaitse spetsialistide õppest Tartu Meditsiinikoolis/Tartu Tervishoiu Kõrgkoolis. Eesti Tervisekaitse seltsi 54. konverentsi ettekannete kogumik. Tallinn.

Remm, M. 2007. Mitmekordse uuringu tõhusus enterobiaasi kindlakstegemisel. Eesti Tervisekaitse seltsi 53. konverentsi ettekannete kogumik. Tallinn.

Remm, M. 2006. 2005./2006. õppeaasta tervisekaitse spetsialistide õppes. Tervisekaitse 2005. Tallinn.

Remm, M., Orav, A., Aotäht, E. (2006). Bioanalüütiku kutseala ja haridus Eestis. Lege artis, apr.

Remm, M. 2005. 2004./2005. õppeaasta tervisekaitse spetsialistide õppes. Tervisekaitse 2004. Tallinn.

Remm, M. 2005. Enterobiaasi levimus Kagu-Eesti lasteaialaste seas ja seda mõjutavad tegurid. Eesti Tervisekaitse seltsi 51. konverentsi ettekannete kogumik. Tallinn.

Remm, M. 2004. Tervisekaitse eriala Tartu Meditsiinikoolis. Tervisekaitse 2003. Tallinn.

Ettekanded konverentsidel

Remm, M. The education of bioanalysts in Estonia. Oral presentation at General Governing Body Meeting and Students Forum of European Association for Professions in Biomedical Science, Bratislava, Slovakia, 2008.

Remm, M., Remm, K. Effectiveness of repeated examination and individualbased risk predictions to diagnose enterobiasis. Poster presentation at 9th Baltic Congress of Laboratory Medicine, Jurmala, Latvia, 2008.

Remm, M., Aotäht, E., Orav, O. Current and future education of bioanalysts in Estonia. Poster presentation at NML (Nordic Medical Laboratory) Congress, Helsinki, Finland, 2007.

Remm, M. Mitmekordse uuringu tõhusus enterobiaasi kindlakstegemisel. Oral presentation at 53th Conference of Estonian Society of Health Protection, Suure-Jaani, Estonia, 2007.

Remm, M., Vipp, H. Distribution of enterobiasis among nursery children in Estonia and estimation of usefulness of recurrent sampling. Poster presentation at 8th Baltic Congress of Laboratory Medicine, Vilnius, Lithuania, 2006.

Remm, M., Aotäht, E. The development of bioanalyst education in Estonia and research as an important part of it. Poster presentation at 8th Baltic Congress of Laboratory Medicine, Vilnius, Lithuania, 2006.

M. Remm. Enterobiaasi levimus Kagu-Eesti lasteaialaste seas ja seda mõjutavad tegurid. Oral presentation at 51th Conference of Estonian Society of Health Protection, Kuressaare, Estonia, 2005.

Osalemine erialastes ühingutes

Eesti Tervisekaitse Selts

Eesti Bioanalüütikute Ühingu

DISSERTATIONES GEOGRAPHICAE UNIVERSITATIS TARTUENSIS

1. Вийви Руссак. Солнечная радиация в Тыравере. Тарту, 1991.
2. Urmas Peterson. Studies on Reflectance Factor Dynamics of Forest Communities in Estonia. Tartu, 1993.
3. Ülo Suursaar. Soome lahe avaosa ja Eesti rannikumere vee kvaliteedi analüüs. Tartu, 1993.
4. Kiira Aaviksoo. Application of Markov Models in Investigation of Vegetation and Land Use Dynamics in Estonian Mire Landscapes. Tartu, 1993.
5. Kjell Weppling. On the assessment of feasible liming strategies for acid sulphate waters in Finland. Tartu, 1997.
6. Hannes Palang. Landscape changes in Estonia: the past and the future. Tartu, 1998.
7. Eiki Berg. Estonia's northeastern periphery in politics: socio-economic and ethnic dimensions. Tartu, 1999.
8. Valdo Kuusemets. Nitrogen and phosphorus transformation in riparian buffer zones of agricultural landscapes in Estonia. Tartu, 1999.
9. Kalev Sepp. The methodology and applications of agricultural landscape monitoring in Estonia. Tartu, 1999.
10. Rein Ahas. Spatial and temporal variability of phenological phases in Estonia. Tartu, 1999.
11. Эрки Таммиксаар. Географические аспекты творчества Карла Бэра в 1830–1840 гг. Тарту, 2000.
12. Garri Raagmaa. Regional identity and public leaders in regional economic development. Tartu, 2000.
13. Tiit Tammaru. Linnastumine ja linnade kasv Eestis nõukogude aastatel. Tartu, 2001.
14. Tõnu Mauring. Wastewater treatment weltlands in Estonia: efficiency and landscape analysis. Tartu, 2001.
15. Ain Kull. Impact of weather and climatic fluctuations on nutrient flows in rural catchments. Tartu, 2001.
16. Robert Szava-Kovats. Assessment of stream sediment contamination by median sum of weighted residuals regression. Tartu, 2001.
17. Heno Sarv. Indigenous Europeans east of Moscow. Population and Migration Patterns of the Largest Finno-Ugrian Peoples in Russia from the 18th to the 20th Centuries. Tartu, 2002.
18. Mart Külvik. Ecological networks in Estonia — concepts and applications. Tartu, 2002.
19. Arvo Järvet. Influence of hydrological factors and human impact on the ecological state of shallow Lake Võrtsjärv in Estonia. Tartu, 2004.
20. Katrin Pajuste. Deposition and transformation of air pollutants in coniferous forests. Tartu, 2004.

21. Helen Sooväli. *Saaremaa waltz*. Landscape imagery of Saaremaa Island in the 20th century. Tartu, 2004.
22. Antti Roose. Optimisation of environmental monitoring network by integrated modelling strategy with geographic information system — an Estonian case. Tartu, 2005.
23. Anto Aasa. Changes in phenological time series in Estonia and Central and Eastern Europe 1951–1998. Relationships with air temperature and atmospheric circulation. Tartu, 2005.
24. Anneli Palo. Relationships between landscape factors and vegetation site types: case study from Saare county, Estonia. Tartu, 2005.
25. Mait Sepp. Influence of atmospheric circulation on environmental variables in Estonia. Tartu, 2005.
26. Helen Alumäe. Landscape preferences of local people: considerations for landscape planning in rural areas of Estonia. Tartu, 2006.
27. Aarne Luud. Evaluation of moose habitats and forest reclamation in Estonian oil shale mining areas. Tartu, 2006.
28. Taavi Pae. Formation of cultural traits in Estonia resulting from historical administrative division. Tartu, 2006.
29. Anneli Kährik. Socio-spatial residential segregation in post-socialist cities: the case of Tallinn, Estonia. Tartu, 2006.
30. Dago Antov. Road user perception towards road safety in Estonia. Tartu, 2006.
31. Üllas Ehrlich. Ecological economics as a tool for resource based nature conservation management in Estonia. Tartu, 2007.
32. Evelyn Uuemaa. Indicatory value of landscape metrics for river water quality and landscape pattern. Tartu, 2007.
33. Raivo Aunap. The applicability of gis data in detecting and representing changes in landscape: three case studies in Estonia. Tartu, 2007.
34. Kai Treier. Trends of air pollutants in precipitation at Estonian monitoring stations. Tartu, 2008.
35. Kadri Leetmaa. Residential suburbanisation in the Tallinn metropolitan area. Tartu, 2008.