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**Geographical variation in hip
fracture incidence in a Nordic
Population (Sweden):
A GIS study exploring the
covariation between UV radiation
and osteoporosis at different
latitudes**

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Applied Informatics and Environmental Modelling

Geographical variation in hip fracture incidence in a Nordic Population (Sweden): A GIS study exploring the covariation between UV radiation and osteoporosis at different latitudes.

Key words:

Hip fractures – Osteoporosis – UV radiation – Vitamin D – GIS – Nordic population – Latitude

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Abstract

Title

Geographical variation in hip fracture incidence in a Nordic Population (Sweden):
A GIS study exploring the covariation between UV radiation and osteoporosis at different latitudes.

Introduction

Scandinavian women have the highest incident rates of hip fractures in the world. Osteoporosis is a contributing factor to fragility fractures, which are very costly for the society. If we could identify persons at risk of osteoporosis or find the principal causes, we could more easily find ways to take care of these people, and give better quality of life for both patients and relatives, and reduce expenses for society. There are many indications that vitamin D and osteoporosis are correlated. Vitamin D is important for bone health, as the main purpose of vitamin D is to increase the intestinal absorption of calcium and phosphate. Vitamin D is synthesized in the skin under the influence of ultraviolet light or the sun. This thesis will take a closer look on the potential covariation of UV radiation and osteoporosis.

Aim

The aim of this study is to investigate the potential impact of UV exposure on the incidence of fragility fractures in a Nordic population (Sweden).

Material

The UV radiation data was calculated by the courtesy of the researchers Kåre Edvardsen and Ola Engelsen at Norwegian Institute for Air Research (NILU) in Tromsø, Norway.

The Swedish hip fracture data were provided by the *Swedish National Board of Health and Welfare*, Department of Statistics, Monitoring and Evaluation (former EpC, center of epidemiology)).

The standard population in this thesis is the Swedish population of January 2000, and is provided by Statistics Sweden (Statistiska centralbyrån).

Methods

GIS analysis, statistical methods (regression analysis), Kriging

Results

This master thesis demonstrates the covariation between UV radiation and osteoporosis.

Key words

Osteoporosis – Hip fractures – UV radiation – Vitamin D – GIS – Nordic population – Latitude – spatial analysis

Sammendrag

Tittel

Geografisk variasjon i forekomsten av hoftebrudd i en nordisk befolkning (Sverige):
En GIS-analyse av samvariasjon mellom UV-stråling og benskjørhet ved forskjellige breddegrader.

Introduksjon

Skandinaviske kvinner har den høyeste forekomsten av lårhalsbrudd i verden. Benskjørhet er en medvirkende årsak til lavenergibrudd, som er kostbart for samfunnet. Dersom vi kunne identifisere de individene som er i faresonen for å få benskjørhet, eller finne hovedårsakene til benskjørhet, kunne vi lettere kunne ta vare på disse individene, gi bedre livskvalitet til både pasienter og pårørende, og samtidig redusere samfunnets kostnader. Det er mange indikasjoner på at det er en sammenheng mellom vitamin D og benskjørhet. Vitamin D er viktig for benstrukturen, siden en av oppgavene til vitamin D er å bidra til kroppens kalsium- og fosfatopptak. Vitamin D blir produsert i huden etter påvirkning av sollys. Denne oppgaven vil se nærmere på den mulige sammenhengen mellom UV-stråling og benskjørhet.

Mål

Målet med denne studien er å undersøke hvorvidt det finnes en sammenheng mellom UV-stråling og benskjørhet i en nordisk befolkning (Sverige).

Materiale

UV-stråledata ble velvilligst beregnet av forskerne Kåre Edvardsen og Ola Engelsen ved Norsk institutt for luftforskning (NILU) i Tromsø, Norge.

Hoftebrudddataene ble skaffet fra Sosialstyrelsen i Sverige *Swedish National Board of Health and Welfare*, Department of Statistics, Monitoring and Evaluation (former EpC, center of epidemiology).

Standardbefolkningen i Sverige pr januar 2000 ble lastet ned fra nettsiden til Statistiska centralbyråen i Sverige.

Metoder

GIS analyse, statistiske metoder (regresjonsanalyse), Kriging

Resultat

Denne masteroppgaven viser at det er en signifikant samvariasjon mellom UV-stråling og benskjørhet

Nøkkelord

Osteoporose – Benskjørhet – Hoftebrudd – UV stråling – Vitamin D – GIS – Nordisk befolkning – breddegrad

Preface

I started to look for potential thesis material during the second year of my studies, as I wanted to find an area that I really wanted to look into, to avoid the situation that I might end up with a less interesting subject. Fortunately, I must say, as it turned out to be a rather tedious challenge to find something of interest. Professor Knut Kvaal, my former mentor and former co-adviser, was early involved in my master studies, and he had several suggestions regarding potential thesis material and advisers.

After looking around for a while, seeking out various researchers and topics of possible interest, I visited professor Owe Löfman. He is a medical doctor with a particular interest in public health, epidemiology and diseases like cancer and osteoporosis, besides being a professor in geomatics. I found his research and fields of study very interesting, partly because the professional content of his research suits my study profile, and partly because several areas of the potential thesis material is of particular personal interest to me.

Initially I wanted to study something dealing with GIS and the occurrence of specific types of cancer in certain areas or populations, but after careful consideration and several discussions with both my former advisers, we chose to go on with something related to GIS and public health. After more consideration and discussions, we decided to see if we could find a connection between osteoporosis and UV radiation. My initial interest in this specific topic was curiosity about the fact that Norwegians, and also Swedes, are at top of the global list of hip fracture incidents. I wondered what conditions may make Scandinavia such a bad scene for not only Scandinavian women, but also for Scandinavian men, regarding hip fracture incidents.

Originally we tried to get Norwegian hip fracture data, but it proved difficult, so we turned to Sweden as the next natural place to look for data, both because my former adviser is a Swedish MD, and knows the Swedish public health service from the inside, and because Sweden is immediate behind Norway on the global hip fracture incidence list.

Another factor that makes me want to look into this subject is the fact that bone fractures caused by osteoporosis is very costly for the society. Calculations show that Norway spend some NOK 2 billion on hip fractures every year (Nasjonalt folkehelseinstitutt 2015). If we could identify the persons at risk of osteoporosis or find the principal causes, we could more easily find cures or alternative ways to take care of people suffering from osteoporosis. This would give a better quality of life for both patients and relatives, reduced expenses for the society, hence better social economics (Osnes et al. 2004), as we could release assets for other important tasks.

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1 Introduction

The aim of this study is to investigate the potential impact of UV exposure on the incidence of fragility fractures (low energy/osteoporotic fractures) as resulting from varying bone mineral density (BMD) at different latitudes in Sweden.

1.1 Research question

There are many indications that vitamin D and osteoporosis are correlated. Our hypothesis is that there is a significant correlation between UV radiation and osteoporosis. Using hip fracture data (fx) as a proxy for osteoporosis, our specific research question is:

To what extent is UV exposure correlated to hip fractures in Sweden?

In search of adequate literature combining osteoporosis, hip fractures, vitamin D, UV radiation, spatial analysis and GIS analysis, we only found a few relevant articles. This is an indication that the coherence between these factors are not investigated or paid much attention to neither in medical nor spatial research.

The table in Figure 1 gives an overview over some of the available research on this topic.

Author / subject	Hip fractures	Epidemiology	Osteoporosis	Vit D	Sun exposure	Seasonal	UV radiation	Latitude	Spatial / geographic	Regional	GIS
Hip fractures cluster in space (de Pina et al. 2008)	X		X		X				X		X
Geographic variation in osteoporotic hip fracture incidence (Dhanwal et al. 2010)	X		X	X					X	X	
Seasonal variation of hip fracture at three latitudes (Douglas et al. 2000)	X					X		X	X		
Incidence and seasonal variation in hip fracture incidence among elderly women in Norway. The HUNT study. (Gronskog et al. 2010)	X	X	X			X		X	X	X	
Regional Variation in the Incidence of Hip Fracture (Jacobsen et al. 1990)	X								X		
Seasonal Variation in the Incidence of Hip Fracture among White Persons Aged 65 Years and Older in the United States 1984-1987 (Jacobsen et al. 1991)	X					X		X	X		
National variation in hip fracture rate in Sweden depends on latitude and season (Johnell et al. 2002)	X			X		X		X			
Latitude, socioeconomic prosperity, mobile phones and hip fracture risk (Johnell et al. 2007)	X							X			
Mortality following the first hip fracture in Norwegian women and men (1999–2008) (Omsland 2014)	X		X								
A comparison of hip fracture incidence rates among elderly in Sweden by latitude and sunlight exposure (Nilson 2014)	X	X			X		X	X			

Figure 1: An overview over some of the available research on this topic, showing the precious research on this topic is insufficient.

We would like to start by giving the necessary definitions in the fields which will be covered. The following chapters will give information about osteoporosis, hip fractures (fx), vitamin D, and UV radiation.

1.2 Osteoporosis

1.2.1 What is osteoporosis?

Osteoporosis is a very common disorder affecting the skeleton (eOrthopod 2005). Osteoporosis is diagnosed when body mineral density (BMD) is below a defined limit value (Löfman et al. 2007). BMD and fracture risk are closely connected to each other (Löfman et al. 2007). The BMD is at peak when about 25 years of age (eOrthopod 2005), after which it decreases as a natural part of aging. About 80 percent of people with osteoporosis are women (eOrthopod 2005), and every year adult Norwegians suffer from different kinds of fractures such as hip fractures (some 9 000), wrist fractures (some 15 000) and an additional number suffer from impacted fractures (Nasjonalt folkehelseinstitutt 2015). In Sweden there are some 70 000 osteoporotic fractures per year, of whom 17 000 - 18 000 are hip fractures (Lofman 2006).

Osteoporosis is a contributing factor to most fractures amongst elderly people. Females in Oslo are world leading in this miserable competition, making osteoporosis a public health problem (Nasjonalt folkehelseinstitutt 2015). Osteoporosis is present in roughly 100 000 Norwegian women, causing reduced ability to perform activities of daily life, and it comes with a huge cost, both economically and personally (Osnes et al. 2004). Vitamin D deficiency leads to reduced bone mass and increased risk of falls, which in turn increases the risk of fractures (Pettersson 2008).

Figure 1 and 2 illustrate normal and osteoporotic bone tissues.

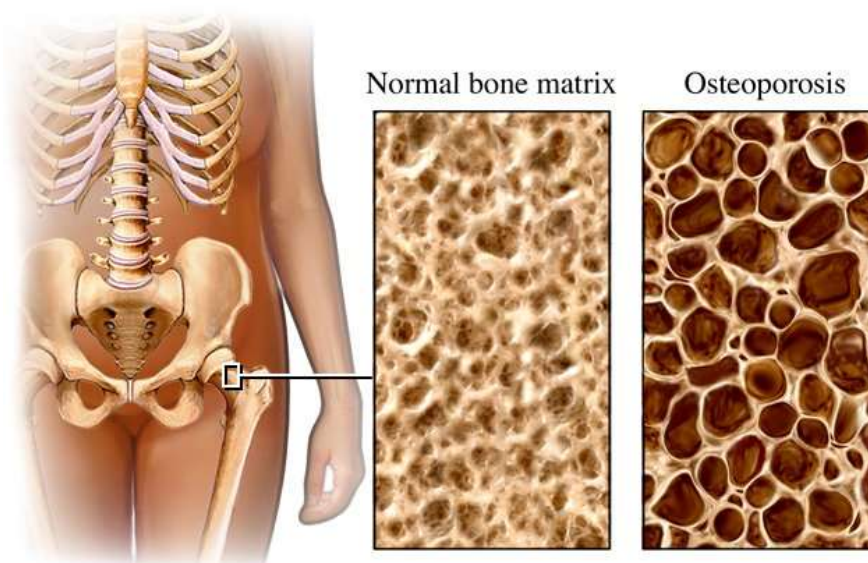


Figure 2: Illustrations from a hip. Normal bone tissues in the middle, osteoporotic bone tissues to the right. The structures are thinner and the cavities bigger in the osteoporotic tissues, frequently causing hip fractures in elderly people (Norwegian Institute of Public Health).

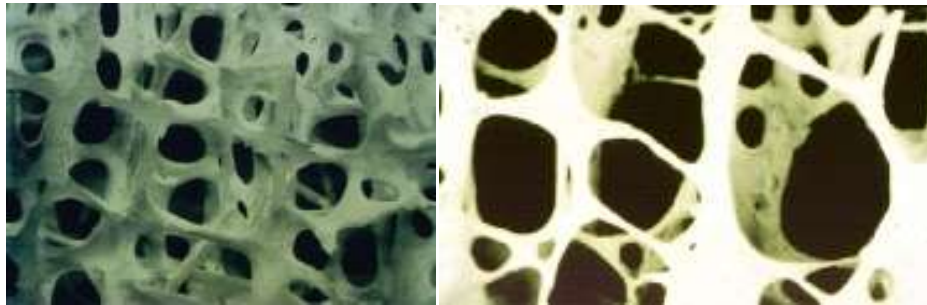


Figure 3: Normal, strong bone tissues (left) and osteoporotic bone tissues (right)
(Norwegian Institute of Public Health)

1.2.2 Causes and variations

Many factors are causing or preventing osteoporosis. Low bone tissue values in the first place, or losing bone tissues more rapidly than normal, are well-known risk factors. Other non-affectable factors are gender, age, previous fractures, early menopause, inheritance, and ethnicity. The incidences of osteoporosis show variations concerning gender, age (Lofthus et al. 2001; Osnes et al. 2004) and regional differences (Omsland et al. 2008). Omsland et al. did not reveal the reasons for the regional differences in Norway, but the paper states it should be explored in further studies.

Modern populations in Norway and England differ in their experience of osteoporosis. A comparative study shows that Norwegians have a lower bone mineral density (BMD) and a higher fragility fracture rate than the English have (S. Mays 2006). The results indicated that both peak BMD and age related loss of BMD were similar in medieval populations, suggesting that the differences are of recent origin, but the results will need further investigation to confirm this. Possible causes may be colder climate and greater frequency of hard surfaces.

1.2.3 How to predict osteoporosis

Osteoporosis can be proven by bone density measurements, but as these tests are not commonly performed unless osteoporosis is suspected, other factors come into consideration, such as heritage, use of cortisone, early menopause, smoking, low body weight and low energy fractures. A low energy fracture or a fragility fracture is when the fracture is a result from a fall from standing upright, or when there is no present trauma causing the fracture. Previous research has also found that there are six previously unknown gene variations that increase the risk of fractures (Snaprud 2012).

1.3 Hip fractures

Adults worldwide experience hip fractures, but the rate of incidents vary from low risk countries like Turkey and Chile, to high risk countries as Norway and Sweden (Kanis et al. 2002).

Figure 4 below shows variations in hip fracture probabilities.

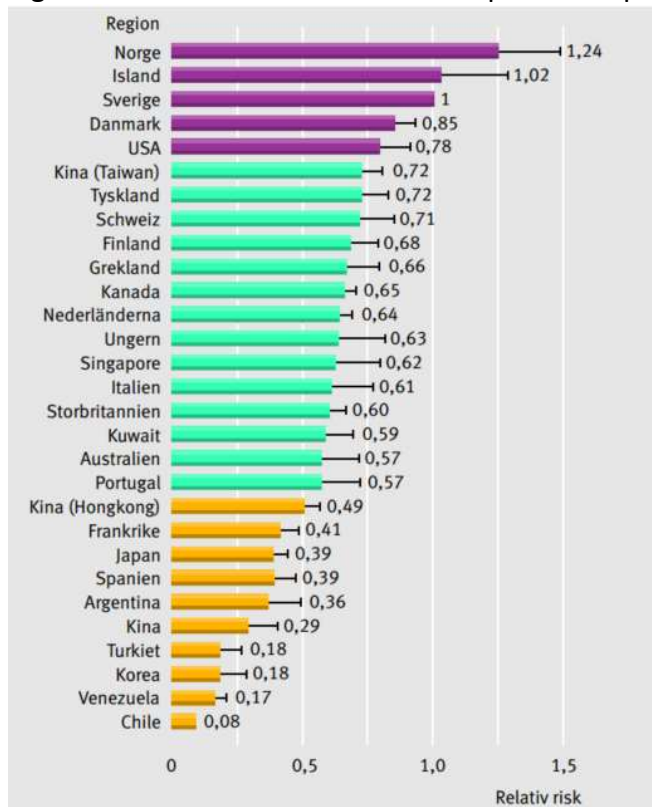


Figure 4 Ten-year probability of hip fracture amongst Swedish females compared to other countries. The risk in Sweden is set as 1. Norway has the risk 1.24, i.e. Norway has a 24 % higher risk than in Sweden. All other countries except Iceland has a lower risk (Lofman 2006).

Norwegian adults experience some 9 000 hip fractures and 15 000 wrist fractures a year (Nasjonalt folkehelseinstitutt 2015). In Sweden there are some 70 000 osteoporotic fractures per year, of whom 17 000 - 18 000 are hip fractures (Lofman 2006). The annual occurrence of new hip fractures is strongly increasing with age, as shown in the illustration in Figure 5. However, the overall trend is somewhat decreasing, according to two studies sited at (Norwegian Institute of Public Health).

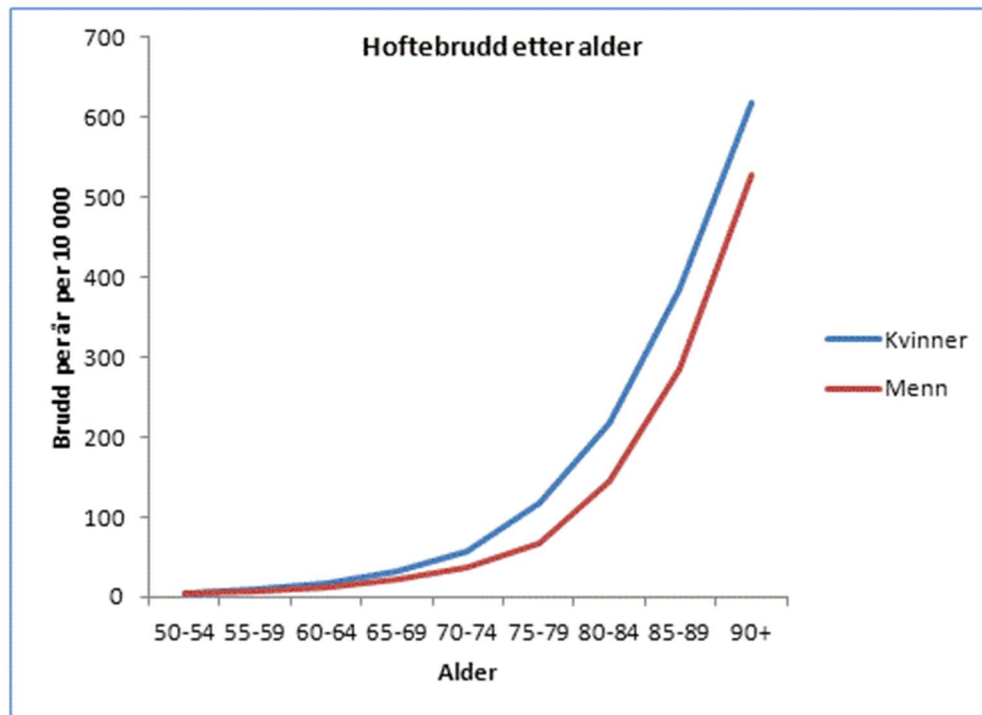


Figure 5: Annual (per år) incidence of hip fractures. The risk of hip fractures increases with age among both women (kvinner) and men (menn). The risk increases sharply after 70 years of age. (Figure: Norwegian Institute of Public Health /Omsland)

Still there is a variety of factors susceptible to influence. Amongst them are falling, exercising, smoking, alcohol consumption, food, medicines and cortisone, minerals, vitamins, physical activities and little or no sun (Nasjonalt folkehelseinstitutt).

People are also getting taller, a fact that may – or may not – be related to more frequent incidents of hip fractures and other fractures.

1.4 UV radiation

Ultra violet (UV) radiation is the part of the electromagnetic spectrum with wavelengths from 100 nm to 400 nm, where UV-A radiation ranges from 400 to 315 nm, UV-B ranges from 315 to 280 nm, and UV-C ranges from 280–100 nm.

Figure 6 The electromagnetic spectrum shows the electromagnetic spectrum of the UV radiation.

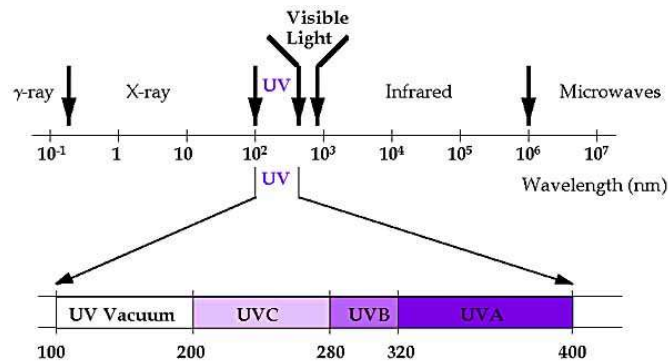


Figure 6 The electromagnetic spectrum (Bioscience.org 1997)

UV radiation is harmful to humans, and precautions must be made. The table from Yr shown in Figure 7, indicates how long a person with Nordic skin type can stay in the sun without damaging the skin.

Så lang tid tar det før huden din kan bli skadet

Styrke	UV- indeks	Tid før mulig hudskade	MED / time
Lav	1-2	1 dag	0,4-0,9
Moderat	3-5	1-2 timer	1,3-2,1
Sterk	6-7	0,5-1 time	2,6-30
Svært høy	8-10	15-30 min	3,4-4,3
Ekstrem	>11	5-15 min	>4,7

Figure 7: The table from the Norwegian meteorological department's public service Yr, shows the harmful levels of UV radiation. The table is valid for a Nordic (fair) skin type (Yr.no).

UV radiation is known to kill mite and bacteria, and is widely in use for industrial purposes. Commercial interests also try to benefit from the UV radiation's sanitation skills by providing different items to the public.

Figure 8 shows the UV radiation Kriging map. The radiation decreases northbound as the latitude increases.

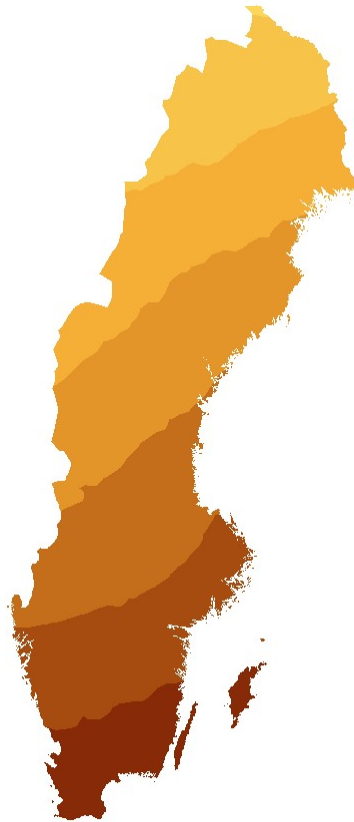


Figure 8: This Kriging map over Sweden shows a decreasing UV-value (Vit-D-weighted) to the more northern locations in accordance with the hypothesis. Does it fit the incidence data inversely?

1.4.1 UV exposure for Vitamin D

The dangers of overexposure to sunlight have been well publicised, but less attention has been given to an acknowledged benefit of exposure to ultraviolet radiation: cutaneous synthesis of vitamin D₃. (Webb & Engelsen 2006) define a standard vitamin D dose based upon recommended requirements for vitamin D that take account of its risk reduction role in a variety of diseases. Vitamin D₃ synthesis is not possible at high latitudes in the winter season, or the exposure time required to reach a standard dose is sometimes impractical. Where solar UV is sufficient, a risk benefit analysis of sunburn vs. vitamin D₃ synthesis shows that the best time for brief sun exposure is in the middle of the day. For low solar elevation angles common at high latitudes, a fine line exists between adequate UV exposure for vitamin D₃ synthesis and a risk of sun burn (Webb & Engelsen 2006)

UV radiation is strongest by the equator line and diminishes with increasing latitude. This means the contribution to the production of vitamin D in the human body is decreasing with increasing latitude.

1.5 Vitamin D

1.5.1 What is vitamin D?

Vitamin D is a prohormone wrongly classified as a vitamin in the early 1920s. Vitamin D is not really a vitamin, i.e., it is not an essential dietary factor, but is a prohormone that is produced photochemically in the skin. It is largely through a historical accident that vitamin D was classified as a vitamin rather than as a steroid hormone. Technically, vitamin D is a secosteroid¹ (Norman 1998). The main purpose of vitamin D is to increase the intestinal absorption of calcium and phosphate, and satisfy the mineralisation of the skeleton (Favus, p263; Waern). Vitamin D is indeed important for bone health, and may prevent some cancers e.g. in breast, prostate and colon as well. It may also inhibit some autoimmune diseases such as multiple sclerosis, diabetes-1, rheumatoid arthritis (Engelsen 2007) and psoriasis (Osmancevic 2009). Current research suggests that clinical interventions, such as vitamin D supplementation, exercise or physical therapy programs, and some comprehensive multifactorial fall assessment and management interventions, can reduce falls and are safe for community-dwelling older adults (Michael et al. 2010).

Vitamin D is essential to the body. Several surveys to investigate the impact of vitamin D and vitamin D deficiency have been carried out in the last decades. This applies especially to obtaining the prohormone from UV radiation, as the advice on sun awning and vitamin D obtaining often contradict. Further research is required.

1.5.2 Admission to the human body

Vitamin D is obtained in three ways (MedlinePlus 2011); from food, from supplements or it is synthesised in the skin during summer under the influence of ultraviolet light of the sun (Lips 2006). Vitamin D is actually rare in foods, but the major natural sources of vitamin D are fatty fish, such as salmon and mackerel, and fatty fish oils, including cod liver oil. Vitamin D can also be obtained from foods fortified with vitamin D, including some cereals, bread products, and milk. (Favus, p75). On the global level, the main source of vitamin D is the sun (Engelsen 2007; Jørgensen). Solar rays are in principle free, and toxic vitamin D levels from the sun are not possible (Engelsen 2007). Vitamin D₃, or cholecalciferol, is produced in the basal epidermis by ultraviolet radiation (290-315 nm) (Osmancevic 2009), but vitamin D production in human skin occurs only when incident UV radiation exceeds a certain threshold (Engelsen, O. et al. 2005).

Engelsen has done research on the relationship between UV exposure and vitamin D status (Engelsen 2007), and has made a fast simulation tool to determine the UV radiation at the earth's surface (Engelsen & Kylling 2005).

¹ A molecule similar to a steroid but with a "broken" ring (<http://en.wikipedia.org/wiki/Secosteroid>),

1.5.3 Metabolism of vitamin D

Vitamin D can be made in the skin by the action of sunlight. Vitamin D is biologically inert and must undergo two successive hydroxylations in the liver and kidney to become biological active 1,25-dihydroxyvitamin D (1,25(OH)₂D). The renal production of 1,25(OH)₂D is tightly regulated by serum calcium levels through the action of parathyroid hormone (PTH) and phosphorus (Favus, p 74). There are a wide variety of inborn and acquired disorders in the metabolism of vitamin D that can lead to both hypo- and hypercalcemic conditions (Favus, p 74). Vitamin D₂, which comes from yeasts and plants, and vitamin D₃, which is found in the fatty fish and cod liver oil, and is made in the skin, have the same biologic potency in humans. Once either vitamin D₂ or vitamin D₃ enters the circulation, it is bound to the vitamin-D-binding protein and transported to the liver, where the major circulating form of vitamin D, 25(OH)D, is formed. The measurement of this 25(OH)D is used to determine whether a patient is vitamin D deficient, vitamin D sufficient or vitamin D intoxicated (Favus, p 75).

Figure 9 illustrates the process of metabolism of vitamin D.

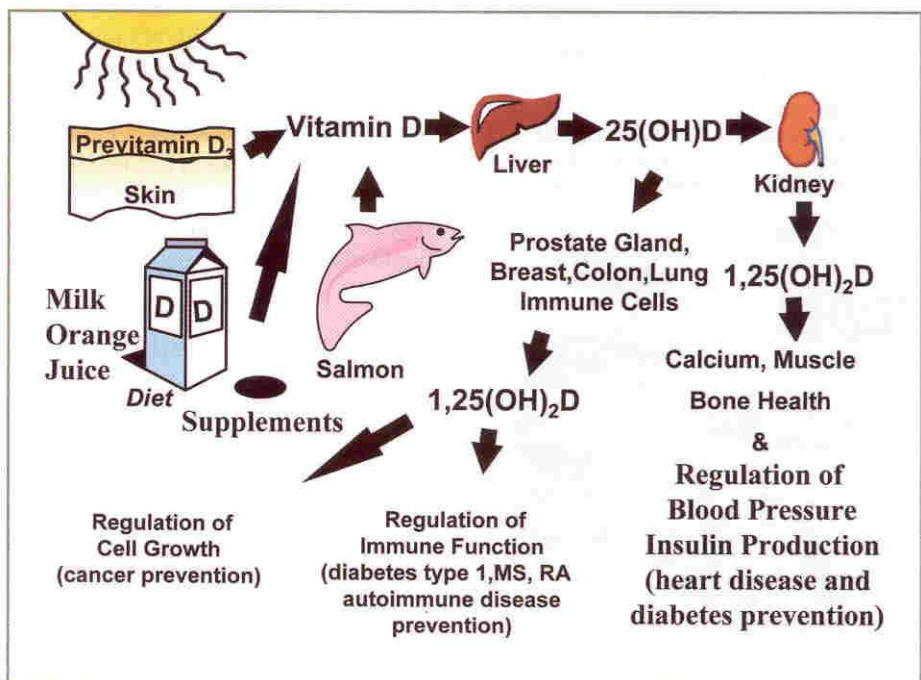


Figure 9: The metabolism of Vitamin D (Laurance Johnston Ph.D.)

1.5.4 Effects of Vitamin D and UV radiation exposure

Vitamin D and its metabolites form an important endocrine system, with effects on gene expression within most of our tissues, including neurons in the brain (Humble 2007).

W B Grant et al. state clearly that there is compelling evidence that low vitamin D levels lead to increased risk of developing rickets, osteoporosis and osteomaloma, 16 cancers (including cancers of breast, ovary, prostate and non-Hodgkin's lymphoma), and other chronic diseases such as psoriasis, diabetes mellitus, hypertension, heart disease, myopathy, multiple sclerosis, schizophrenia, hyperparathyroidism and susceptibility to tuberculosis. (Humble 2007) also shows that Vitamin D insufficiency may constitute an important risk factor for common cancers, diabetes, and cardiovascular, autoimmune and neuropsychiatric disorders.

Severe vitamin D deficiency causes rickets or osteomalacia, where the new bone, the osteoid, is not mineralised. Less severe vitamin D deficiency causes an increase of serum PTH leading to bone resorption, osteoporosis and fractures (Lips ; Waern), even low energy fractures (Mosekilde). It also leads to secondary hyperparathyroidism and osteomalacia, and both conditions are associated with fractures, the most severe being hip fracture (Bakhtiyarova et al.). Vitamin D deficiency even has negative effects on the muscle functions, thus also contributes further to the risk of fractures (Waern). When evaluating patients for hypo- and hypercalcemic conditions, it is appropriate to consider the patient's vitamin D status, as well as whether they suffer from either an acquired or inherited disorder in the acquisition and/or metabolism of vitamin D (Favus, p80).

Vitamin D plays a critically important role in the mineralisation of the skeleton at all ages. As the body depletes its stores of vitamin D because of lack of exposure to sunlight or a deficiency of vitamin D in the diet, the efficiency of intestinal calcium absorption decreases from approximately 30% to 50%, to no more than 15 % (Favus, pp 79-80). Epidemiological facts support the hypothesis about vitamin D as a protective agent against autoimmune diseases (Jørgensen 2007). Several epidemiological studies indicate increased frequency of certain autoimmune diseases when the distance from equator increases. As the dermal vitamin D production ascends with the extent of sun exposure, the vitamin D insufficiency is mentioned as a possible contributing factor to the development of autoimmune diseases (Jørgensen). Johnell et al. even found a significant association between latitude and 10-year hip fracture probability. Supplementation of vitamin D in elderly people with and without fracture might prevent secondary hyperparathyroidism, osteomalacia and fractures (Bakhtiyarova et al. 2006).

There are well documented beneficial as well as adverse effects of solar ultraviolet radiation exposure (Lucas & Ponsonby 2002). V. B. Grant claims that the health benefits of UVB radiation seem to outweigh the adverse effects, and that the risks can be minimised by avoiding sunburn, excess UV radiation exposure and by attention to dietary factors, such as antioxidants and limiting energy and fat consumption. In a doctoral thesis Osmancevic shows

that vitamin D production in psoriasis patients increased less with Narrowband UVB (NBUVB) than with broadband UVB phototherapy (Osmanovic 2009) .

Most public health statements regarding exposure to solar ultraviolet radiation (UVR) recommend avoiding it, especially at midday, and advocate using sunscreen. Excess UVR is a primary risk factor for skin cancers, premature photoageing and the development of cataracts. However, if applied uncritically, these guidelines may actually cause more harm than good.

In Figure 10, points A and C represent inappropriate UVR exposure. Europeans in Australia with high outdoor UVR exposure typify point A. Point C represents people with insufficient UVR exposure, whose dietary vitamin D intake will also be important in determining their vitamin D status. Point B represents optimal UVR exposure: a person with careful titration of correct UVR dose for skin type.

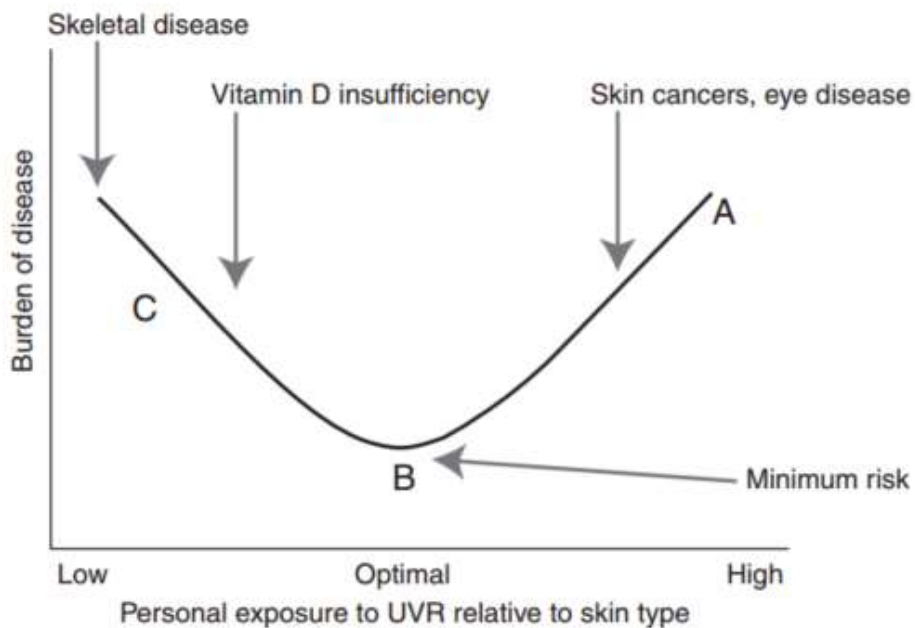


Figure 10: Schematic diagram of the relation between ultraviolet radiation (UVR) exposure and the burden of disease. (Lucas & Ponsonby 2002).

1.5.5 Recommended daily intake

Recommended vitamin D intake by The Norwegian Directorate of Health is 10 mcg per day for children under the age of two years and elderly over the age of 60. As for the adults and children over two years of age, the recommendation is 7,5 mcg per day (Helsedir. IS 1408 2006, p33). There is evidence of that the daily intake of vitamin D can be considerably increased without accompanying hypercalcaemia (Jørgensen 2007). The ideal Vitamin D level according to Norwegian health authorities is over 50 nmol/l (Helsedir. IS 1408 2006, p 48).

The American Academy of Dermatology is rather determined in its recommendation. It recommends that an adequate amount of vitamin D should be obtained from a healthy diet that includes foods naturally rich in vitamin D, foods/beverages fortified with vitamin D, and/or vitamin D supplements; it should not be obtained from unprotected exposure to ultraviolet (UV) radiation. It should be noted, however, that the currently recommended adequate intake levels established by the Institute of Medicine may be revised upward due to evolving research on the increasing clinical benefit of vitamin D (American Academy of Dermatology). It is anticipated, that increasing attention will be paid to the benefits of UVB radiation and vitamin D and that health guidelines will be revised in the future (W B Grant).

1.5.6 Risk factors

Vitamin D status is highly dependent on season: moreover, the relation between vitamin D intake and status is also seasonally dependent, being strong in the winter and negligible in the summer (Davies PS 1999).

Some groups in the population have increased risk of having vitamin D deficiency. The main cause is low exposure to sunlight (Waern). Risk factors for vitamin D deficiency are premature birth, skin pigmentation, low sunshine exposure, obesity, malabsorption and advanced age (Lips 2006).

Serum 25(OH)D levels decline with age. This is partly due to decreased solar exposure. Intestinal calcium absorption also decreases with age. Vitamin D supplementation in the elderly reduces fractures of all types (Favus 1996, p263).

Some risk factors may be harder to find, as they are not at all expected. An outbreak of hypercalcemia in eight patients was reported from the incorrect dosing of dairy milk with vitamin D, and, in addition, a defect was found in the concentrate used to fortify the milk (containing cholecalciferol [vitamin D3] rather than the expected ergocalciferol [vitamin D2]). These same investigators extended their measurements of the vitamin D content to both commercial dairy milks and fortified infant formulas, and they found that only 29% of the milks and formulas contained within 20% of the stated vitamin D content. These studies suggest that improved monitoring of the fortification process is mandatory. Such studies may explain the rare finding of clinical vitamin D deficiency in children drinking "fortified" milk (Favus, p 211).

2 Data capture and preparation

2.1 The process of collecting data

Due to strict Norwegian legislation on protection of personal information, professor Löfman had earlier experienced difficulties and delays in getting medical information in Norway. We therefore decided to start the data gathering as early as possible to avoid similar delays in our project. That turned out to be wise. We ended up with Swedish data though, partly due to the strict Norwegian personal information protection legislation, but partly also due to poor data on osteoporosis in Norway.

As mentioned, we started the effort to get the requisite medical data on hip fractures early. Our chase went on without results, when we by chance found that one of the researchers in an adequate research group at The Norwegian Institute of Public Health (Nasjonalt folkehelseinstitutt), was a previous collaborating partner of my former main adviser. This researcher was Dr. Jan Falch, and he and his group agreed to have a meeting with us. This meeting, revealed that the hip fracture data we needed did not yet exist in a researchable condition, and thus was unavailable at the time. The researcher group made us aware of the existence of a data base named CONOR (COhort NORway), which amongst other data contained data about radius fractures. The radius bone is the knucklebone at the thumb side of the forearm. If we could get access to this database, we could use the radius fractures for people above 50 years of age to predict the presence of osteoporosis in a patient. We decided this probably was the best we could hope for as an osteoporosis proxy, so we applied for such data. After five months, with several occasions of supplementary information to our application, we were finally accepted as receivers of data from the base. Shortly thereafter, I had a conversation with them, revealing that their data had neither dated nor located data as we needed. We kept on trying to get other, equivalent data from Norway, but all leads ended up where we started, at The Norwegian Institute of Public Health (Nasjonalt folkehelseinstitutt) and the not yet researchable data. Interrupted by absence due to sickness with both student and adviser, we finally managed to get satisfactory fracture data from Sweden. This is owing to my Swedish former adviser, who happens to be familiar with the Swedish health bureaucracy after many years of medical activities in his native country.

It would of course have been more satisfying to do research on Norwegian material, as that was my first interest in the project. The osteoporosis related fracture rate is very high in Norway, and I wanted to look into that matter to see if I could find any factor to explain this more than other factors. However, it turned out to be impossible to find applicable data from Norway, so to avoid too much futile work; we decided to change the aspects to regard Sweden instead. Luckily, the researchers at NILU in Tromsø were still able and willing to help us. With just some adjustments to their algorithms, they calculated the UV-data for Sweden in our study.

2.2 Description of the study area

The total Swedish population is some 9.8 million people as for March 2016 (Statistics Sweden). Our population of interest is all men and women aged 50 and above per January 2000, which includes 3 206 513 persons. The Swedish country covers a total area of 449 964 km², of which lakes and rivers cover 39 030km² (about 10%). The study area has land borders to Norway and Finland and comprises 290 municipalities (communes).

Figure 11 shows a map over Europe, with the Swedish border outlined.



Figure 11: Map over Europe, with the Swedish border outlined

The municipality names and identity numbers have altered during the period of research. However, this is not taken into consideration, as it is the geographical place that is of interest, not what the municipality was called or what identification number it had at the time in question. Thus, the chosen division in this thesis is the present division by Statistics Sweden (Statistiska centralbyrån, SCB), as the preferred presentation. All the data belonging to a municipality that has changed, has been carefully matched with the correct area in the present municipality organisation. In a few cases of doubt, some municipalities have been merged to a greater municipality, to make the areas the same throughout the whole research period.

Figure 12 shows the municipalities of Sweden. Please note that for municipalities near the sea, the borders of each municipality is extended into the sea.



Figure 12: The municipalities of Sweden. Please note that for municipalities near the sea, the borders of each municipality is extended into the sea.

2.3 The UV Radiation data

The UV radiation data was calculated for us by the courtesy of the researchers Kåre Edvardsen and Ola Engelsen at Norwegian Institute for Air Research (NILU), Tromsø, using the simulation tool FastRT. Originally the researchers would provide pre calculated data from Norway, but as we ended up not using Norwegian data, they offered to calculate Swedish data for us, an offer we were happy to accept.

The data came packed in 23 separate .dat-files, one for each year, from the period January 1st 1980 to August 31st 2002. Each of these years included daily records from 90 spots in a grid completely covering Sweden and the surrounding areas, a total of 745 110 records, including the five leap years of the period, namely 1980, 1984, 1988, 1992 and 1996. Year 2000 was not a leap year.

See Figure 13: .dat files from the NILU researchers. The difference in size is due to leap years.

Name	Type	Size
<input type="checkbox"/> VDaydose_Sweden_1980.dat	DAT File	1 770 KB
<input type="checkbox"/> VDaydose_Sweden_1981.dat	DAT File	1 765 KB
<input type="checkbox"/> VDaydose_Sweden_1982.dat	DAT File	1 765 KB
<input type="checkbox"/> VDaydose_Sweden_1983.dat	DAT File	1 765 KB
<input type="checkbox"/> VDaydose_Sweden_1984.dat	DAT File	1 770 KB
<input type="checkbox"/> VDaydose_Sweden_1985.dat	DAT File	1 765 KB
<input type="checkbox"/> VDaydose_Sweden_1986.dat	DAT File	1 765 KB

Figure 13: .dat files from the NILU researchers. The difference in size is due to leap years.

The files were opened in an Excel workbook for further preparation and aggregation, as shown in Figure 14: Importing the UV radiation data to an Excel file, one file at the time.

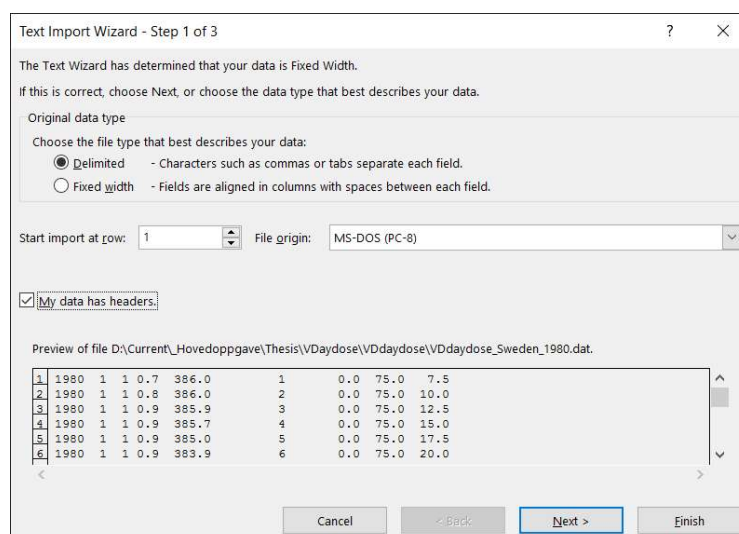


Figure 14: Importing the UV radiation data to an Excel file, one file at the time.

Prior to the actual import, it was essential to choose the right settings for the import itself, including choosing the right character set, punctuation marks and format of the original .dat-files. A typical blunder in this work was to let the cell format in Excel remain "standard", which would inevitably lead to converting the longitudes into dates, e.g. 7.5° E would turn into May 7th. The imported files were put into separate sheets according to the corresponding year in the same Excel workbook.

The mean values for vitamin D weighted daily dose [mJ/m²] were aggregated, point by point for the years 1980 – 2002, using Excel's average formula [=AVERAGE(F3:AB3)]. The aggregated value per point were then divided by the number of days (8279) in the period, thus ending up with the mean value per day per point in the 9 x 10 point grid covering the whole area of Sweden, and beyond, as shown in Figure 15. The calculations were taking into consideration that year 2002 only had records for eight months, and that there were only six leap years in the period, as year 2000 was not a leap year. See the calculations in the appendix.

Figure 15 shows a map over Sweden. The 90-point grid covers the whole of Sweden, and beyond.

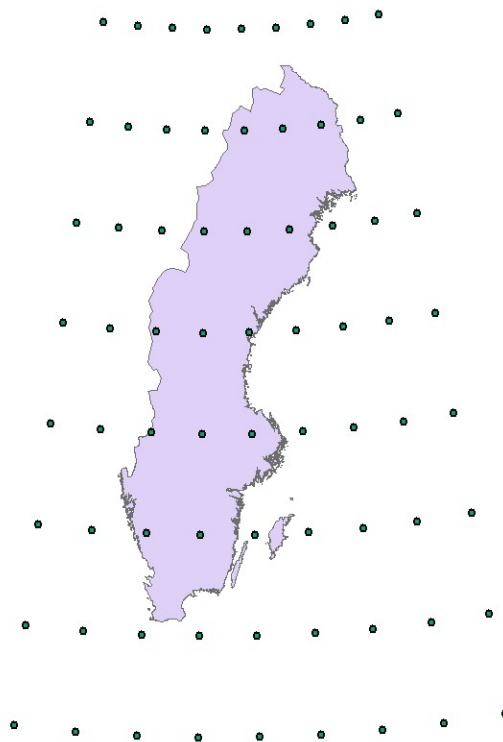


Figure 15: A map over Sweden showing the 90-point grid (RT90 25 gon V)

Vitamin D production in human skin occurs only when incident UV radiation exceeds a certain threshold. During some periods of the year, no cutaneous vitamin D production occurs at 51 degrees latitude and higher, and vitamin D can be absent for 5 months at 70 degrees latitude. At the equator, agents like clouds, aerosols and thick ozone events can reduce the duration of vitamin D synthesis considerably, and can even suppress the vitamin D synthesis completely (Engelsen, O. et al. 2005).

2.3.1 FastRT

Engelsen and Kylling has described FastRT, which is a popular, fast, yet accurate UV simulation tool that computes UV doses at the earth's surface, UV indices, and irradiances in the spectral range 290 to 400 nm (Engelsen & Kylling 2005).

The tool accounts for the main radiative input parameters, i.e., instrumental characteristics, solar zenith angle, ozone column, aerosol loading, clouds, surface albedo, and surface altitude. FastRT is based on look-up tables of carefully selected entries of atmospheric transmittances and spherical albedos, and exploits the smoothness of these quantities with respect to atmospheric, surface, geometrical, and spectral parameters. Applications of FastRT are diverse, ranging from operational simulation of UV doses to detailed reproduction of real UV measurements (Engelsen & Kylling 2005).

2.4 The hip fracture data

The Swedish hip fracture data were provided by the *Swedish National Board of Health and Welfare* (Socialstyrelsen), Department of Statistics, Monitoring and Evaluation (former EpC, center of epidemiology)). Duplicates were avoided due to precision/accuracy, thus allowing us to remove duplicate data, and by this create a very reliable data set. The data were standardised, using the direct standardisation method, which is the same as age-adjusted death rates (ADR) (Curtin & Klein 1995). This method is preferred when calculating a weighted average. This method is, however, not used when the age specific rates are unavailable, or the rates are not stable, due to a smaller number of events (approximately <100). In such cases, the indirect method is recommended.

Initially there were 22 years of hip fracture data from the period 1982-2003, containing roughly 700 000 hip fractures, of which some 350 000 duplicates were discarded. A duplicate was defined to be hip fractures occurring in one single patient within 6 months after the initial hip fracture. By doing this, incidents of patients transferred to another hospital, and by that registered in two or more times per hip fracture were excluded.

The standard population data were downloaded from the Statistics Sweden's (Statistics Sweden) website and grouped into ten year groups. This was later on changed to five year groups, as five year groups were found to be more visually suitable.

After producing maps based on the hip fracture data, and comparing them with maps of the UV radiation data, we found some anomalies in the maps we produced, compared to our expectations. These maps combined did not only confirm our theory, they actually showed far too much verification, which of course made us suspicious. There has been some restructuring (merging and splitting) of Swedish municipalities during this 22-year period, so we suspected that this could be the reason, but without finding any evidence of neither this, nor other possible biases, we could not prove anything.

We decided to go on with a more limited study period to see if we got the same results, and carefully selected a period of 13 years to investigate (1984-1996). This period was chosen because it gave the longest, assumed stable, study period within the 22-year period of our data, regarding the municipalities, and therefore the highest number of hip fractures to study, which of course would make the results more reliable. At the same time, we decided to group the data into five year groups instead of ten year groups, as we initially did.

While manually matching the municipality population data with the hip fracture data, we incidentally noticed that some of the municipalities had no fractures at all. This is not a reliable result, as the probability of no hip fractures at all in the whole population over 50 years old during a period of 13 years is infinitesimal. To see if there were some connections or mistakes made somewhere, we marked all the missing municipalities in a separate map. Then it became very clear that these municipalities not only were connected, they also belonged to the same few counties.

Figure 16 shows the missing municipalities in Skåne county, municipalities marked in red.



Figure 16: Maps showing counties of Sweden before and after merging Kristianstads län and Malmöhus län into Skåne län in January 1997. The municipalities missing in our data are marked in red. As we can see, these municipalities are all belonging to former Kristianstads län.

Figure 17 shows the missing municipalities in Västra Götalands county (län). The missing municipalities are marked in red.

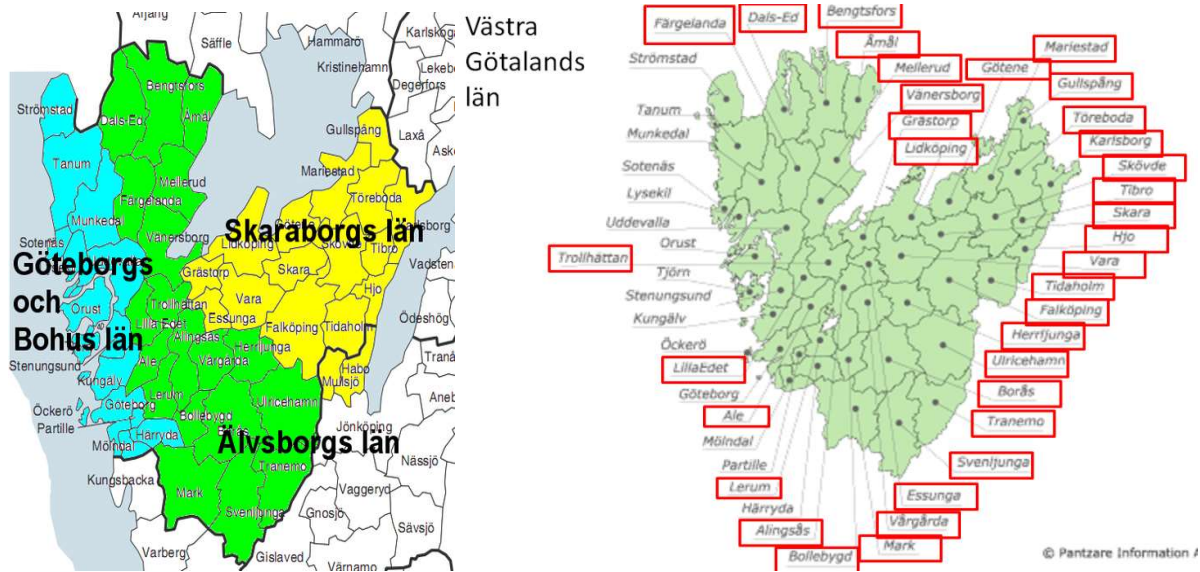


Figure 17: The maps shows the counties of Sweden before and after merging Göteborgs och Bohus county (län), Skaraborgs county (län) and Älvsborgs county (län) into Västra Götalands County (län) in January 1997. The municipalities missing in our data are marked in red. As we can see, these municipalities are all belonging to the three former counties.

After carefully checking where these data could have ended up, we found that our original raw data did not contain any hip fractures for these municipalities in the period chosen. This is believed to be related to the fact that these counties were changed in 1997 and 1998. We also believe that these missing data are the reason for our anomalies in the first round of calculations.

Still, the missing data has to be somewhere, but since we are not able to identify and extract them from the rest of the data, we once again wanted to change the study period to minimize, or even exclude, the risk of anomalies/errors. Our choice this time was the years 1998-2003. Over these six years we only have some 95 000 hip fractures, but it is still a substantial number, and the number is considerably higher than we could possibly have had for the same period in Norway. To make a comparison, as the Swedish population is roughly twice the population of Norway², these 95 000 hip fractures would approximately equal a study period of about 12 years of Norwegian data, which would be a quite considerable period. We know the figures in Norway and Sweden are not the same, but for all good purposes, this estimate will do.

² Population of Sweden as of 2000: 8 882 792 (www.scb.se).

Population of Norway as of January 1st 2000: 4 478 500 (www.ssb.no).

2.5 Population data

The population data is collected from the administrative agency Statistics Sweden (Statistiska centralbyrån, SCB), whose main purpose is to supply customers with statistics for decision making, debate and research (About Statistics Sweden). They provide a multitude of data open to the public. We chose data from the middle of our study period, so the population would constitute the mean population of the period. Our population data were acquired by Using the programme PC Axis³, a free program offered from Statistics Sweden.

The municipalities of Sweden is shown in Figure 18.

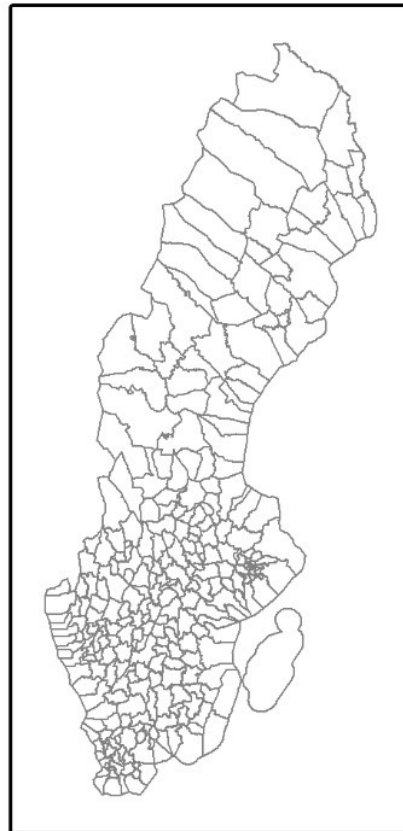


Figure 18: The municipalities of Sweden. Please note that for municipalities near the sea, the borders of each municipality is extended into the sea.

³ PC Axis was replaced by PX-Win 1.0, published June 21st 2016 <http://www.scb.se/pc-axis/pc-axis>

3 Methods

3.1 Background

3.1.1 Statistical methods

To ensure the hip fracture data could be compared, regardless of the different age distributions in the different Swedish municipalities, some kind of standardisation were necessary. To do this, the direct method was utilized, also called the age adjustment method. The terms "adjustment" and "standardisation" both refer to procedures for facilitating the comparison of summary measures across groups (Shoenbach 1999).

The goal of age adjustment is to modify the crude rates, so that any difference in incident rates due to differences in age distribution is eliminated. This method forces the comparison of the two populations to be made on a common age distribution, as the confounding factor age is removed by re-computing the rates substituting a common age distribution for the separate age distributions. The populations are then compared as if they had the same age structure. The common age distribution is determined by identifying a standard population (Kleinbaum et al. 2003 p92). The standard population in this thesis is the Swedish population of January 2000, and is provided by Statistics Sweden (Statistiska centralbyrån).

3.1.2 Geographical methods

In this work the geographical method ordinary Kriging is being used.

Kriging is an advanced geostatistical procedure that generates an estimated surface from a scattered set of points with z-values. Unlike other interpolation methods in the Interpolation toolset, to use the Kriging tool effectively involves an interactive investigation of the spatial behaviour of the phenomenon represented by the z-values before you select the best estimation method for generating the output surface. Kriging assumes that the distance or direction between sample points reflects a spatial correlation that can be used to explain variation in the surface. The Kriging tool fits a mathematical function to a specified number of points, or all points within a specified radius, to determine the output value for each location. Kriging is a multistep process; it includes exploratory statistical analysis of the data, variogram modelling, creating the surface, and (optionally) exploring a variance surface. Kriging is most appropriate when you know there is a spatially correlated distance or directional bias in the data. It is often used in soil science and geology.

Ordinary kriging is the most general and widely used of the kriging methods and is the default. It assumes the constant mean is unknown. This is a reasonable assumption unless there is a scientific reason to reject it (ArcGIS Desktop help).

3.1.3 Software

During the work, the following software has been used:

- **Microsoft Office**
MS Word 2007 / MS Word 2016 for the writing,
MS Excel 2007 / MS Excel 2016 for working with the data,
MS PowerPoint 2007 / MS PowerPoint 2016 for presentation,
MS Snipping Tool for screen shots.
- **EndNote X6/X7** for taking care of the references.
- **ESRI ArcGIS 10**, with the extensions Spatial Analyst and Geostatistical Analyst.
ArcGIS is a program made for handling, analysing and sharing geographic information.
- **PC-AXIS** for working with the standard population data.
PC-AXIS is freeware developed by Statistics Sweden (SCB) with contribution from other similar agencies, among others Statistics Norway and Statistics Denmark.
- **Notepad** for notes and for unformat formatted text.
- **Skype** for video talks with my former, main adviser while he was not present at campus.
- **SyncBack** for backup, which proved very useful when my laptop broke down.
- **Foxit Reader** for reading pdf files.

3.2 Workflow

The main scope of this thesis was to take the hip fractures, remove the irrelevant data, and compare them with the UV radiation data, as shown in Figure 19: The principal work flow of the thesis.

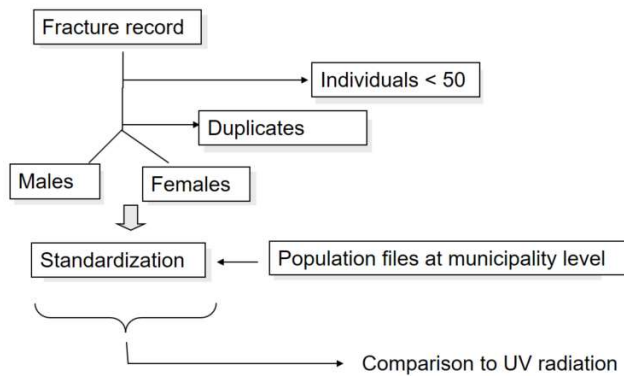


Figure 19: The principal work flow of the thesis.

To keep track of the two different methods in the comparison process, two different flow charts were made. The UV radiation data, the hip fracture data and the Swedish population data were the basis of these flow charts. When all the data were prepared, they were loaded into ESRI's ArcGIS 10 and converted to the map coordinate system Swedish grid RT90 (Rikets Nät RT90).

3.2.1 Method 1

In this method the UV and hip fracture data sets are linked to the municipality centroids. The flowchart in Figure 20 illustrates this work flow.

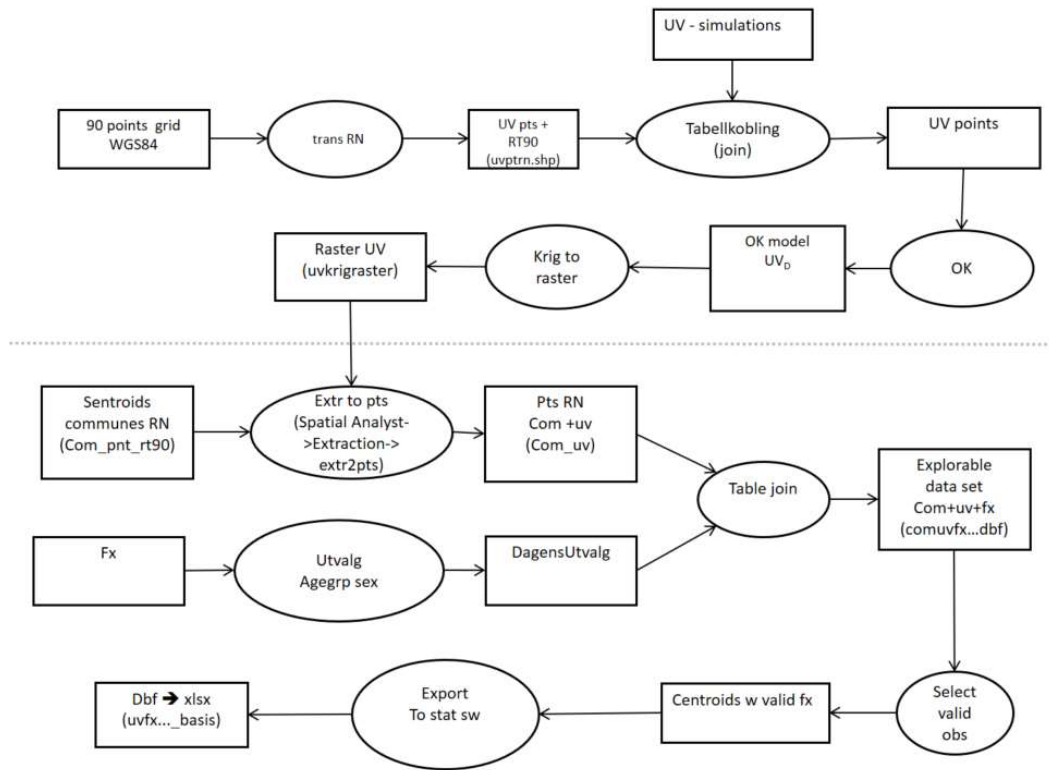


Figure 20 The flowchart of method 1, describing how we combined the UV radiation data and the hip fracture data (fx)

Centroids for the municipalities were generated from the municipality polygons using ArcGIS 10 Feature to Point. See Figure 21.

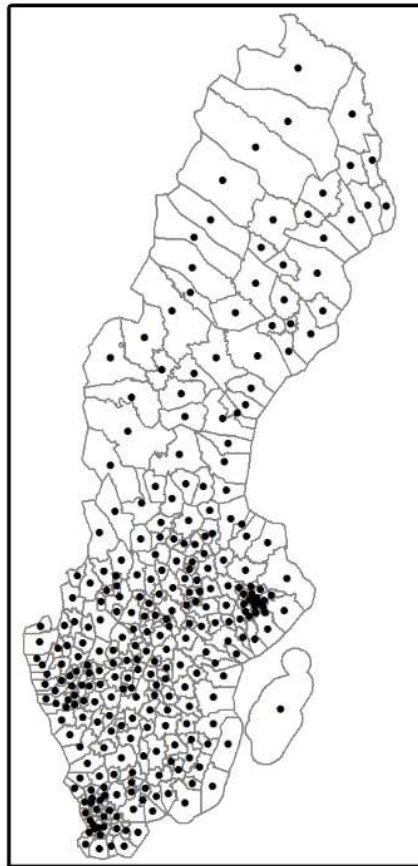


Figure 21 The Swedish municipalities with the Municipality centroids

In method 1, the UV data from the researchers from NILU were distributed as 2.5-degree point grid (9x10 points) covering the whole area of Sweden. The grid was transformed to the Swedish Rikets Nät (RT90 25 gon V), and the geographical interpolation method Ordinary Kriging was performed on the data, using the ArcGis 10 extension Geostatistical Analyst, to get the Kriging model for the vitamin D producing UV radiation, with the settings ordinary Kriging, transformation type: none, order of trend removal: none. See Figure 22 for the cross validation step in the process.

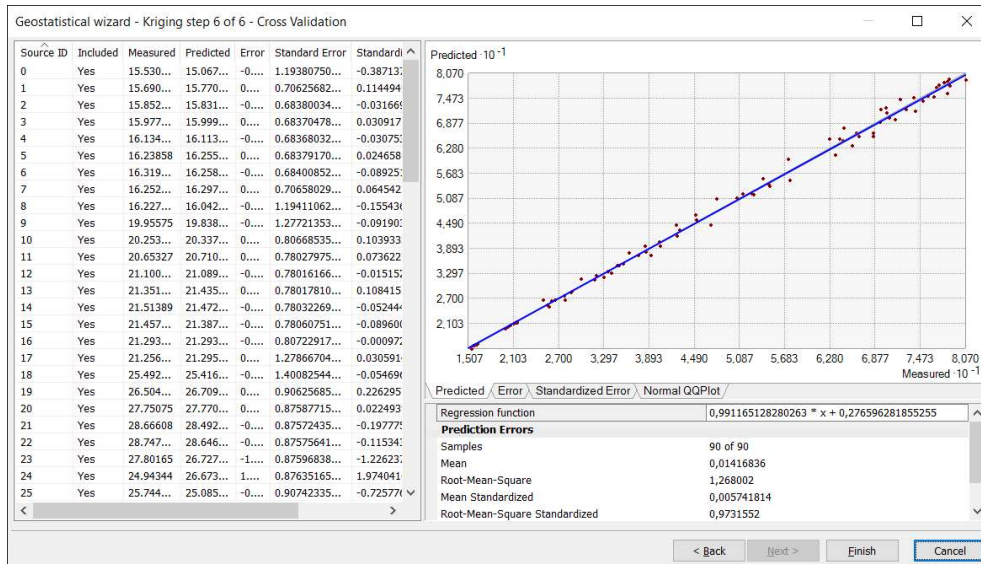


Figure 22: The cross validation of the UV data.

The resulting Kriging map is shown in Figure 23

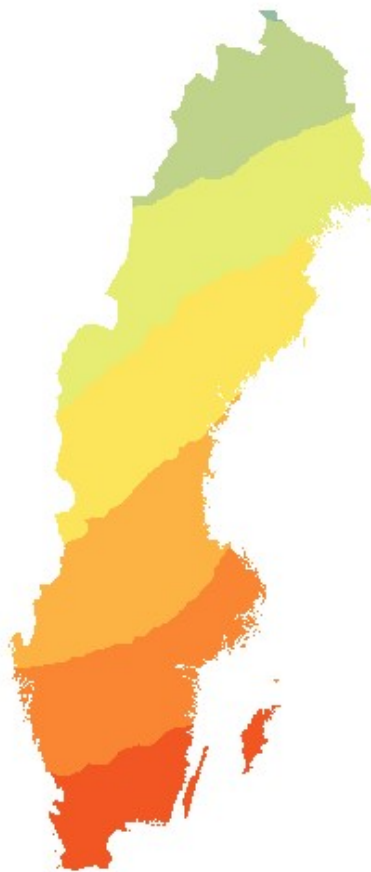


Figure 23 This Kriging map shows the distribution of the UV data, with a significant northbound trend, as expected.

The Kriging map was then transformed to a raster map, which we subsequently extracted to the municipality centroids, using the Spatial Analyst function Extract to points. Then we performed a table join on the selected hip fractures. This action resulted in an explorable data set consisting of both UV radiation data and hip fracture data for every municipality. As this set also included invalid data, i.e. zero values, we left these values out, to finally have a data set ready for export to any chosen analytical tool. See Figure 24 Rikets Nät (RT90 25 gon V). Municipalities with invalid data are marked with red points.

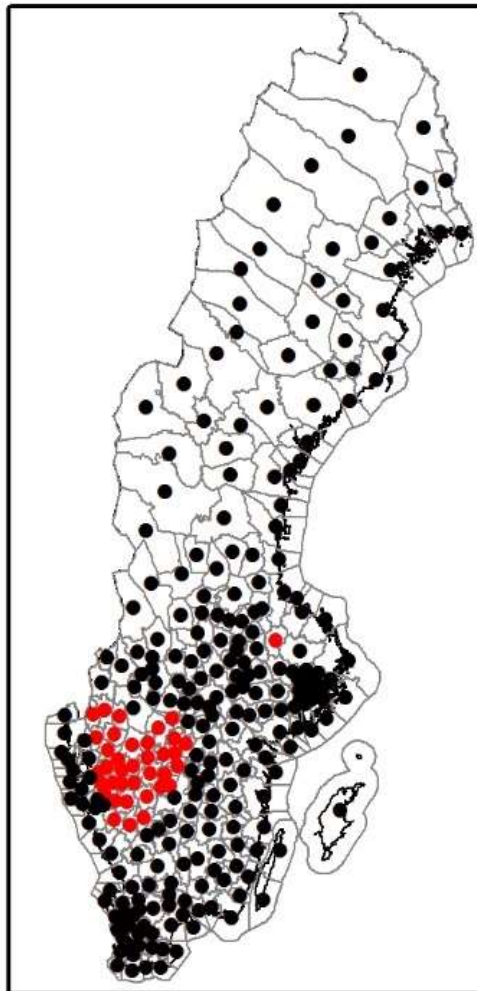


Figure 24 Rikets Nät (RT90 25 gon V)
Municipalities with invalid data are marked with red points.

3.2.2 Method 2

In this method the UV and hip fracture data (fx) data are interpolated and linked to a 10 km x 10 km fishnet grid. The flowchart of the work is illustrated in Figure 25.

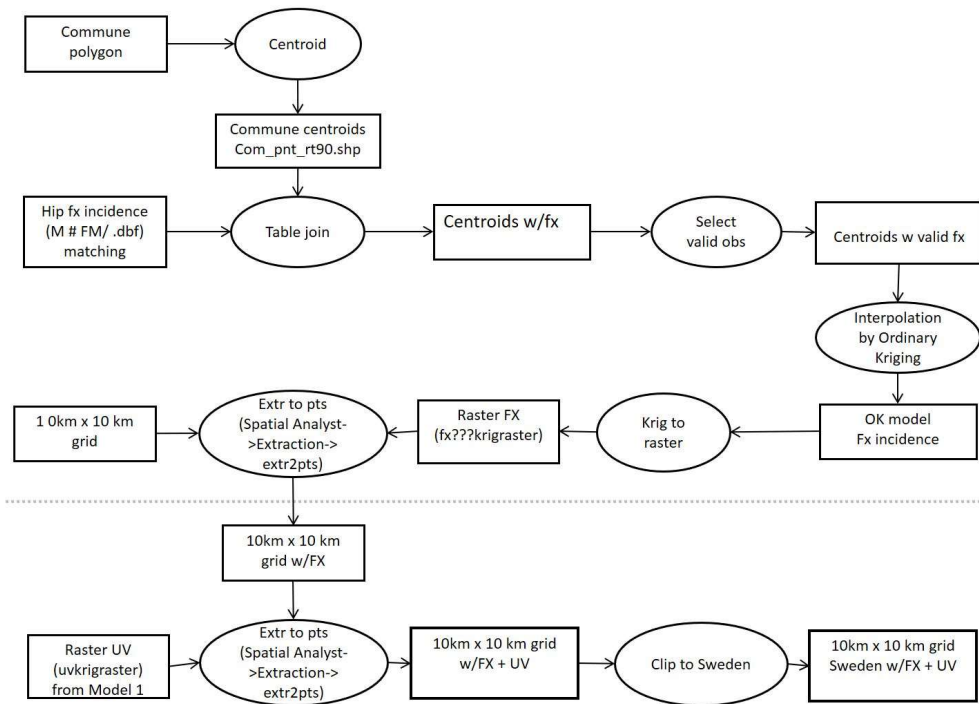


Figure 25. Method 2 – The work flow of Rastermap - grid

First we made municipality centroids for every municipality polygon. We then performed a table join with the hip fracture incidence data. Then we omitted the invalid zero-observations again, resulting in centroids with only valid observations. Interpolation by the geographical method Ordinary Kriging were then performed on these centroids, which gave us a Kriging model with hip fracture incidents. See Figure 26 Kriging map made from the hip fracture data and Figure 27 Kriging map made from the hip fracture data, and with the municipality centroids (with centroids included).

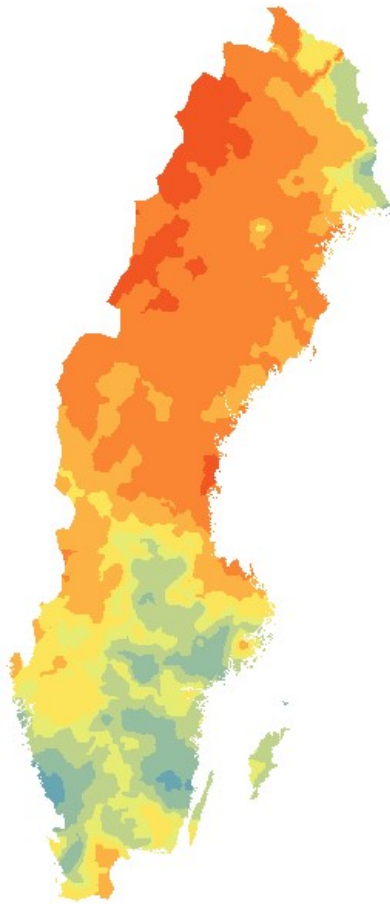


Figure 26 Kriging map made from the hip fracture data

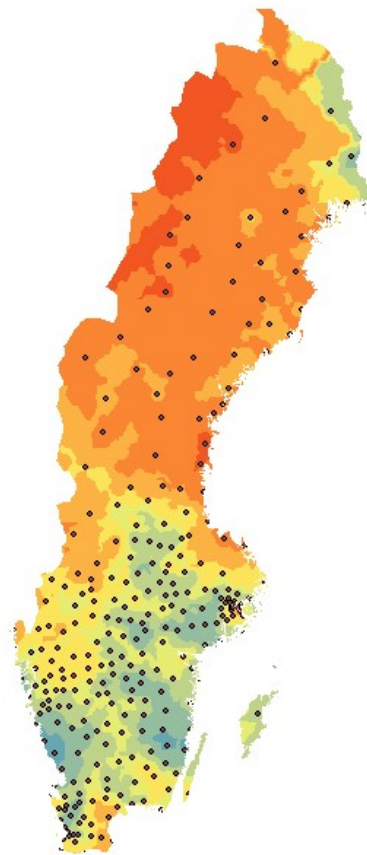


Figure 27 Kriging map made from the hip fracture data, and with the municipality centroids

For the UV data the interpolation was done the same way as in method 1. The Kriging maps were then saved as raster maps, values were extracted to a 10 km x 10 km grid, and clipped using the Sweden polygon. See Figure 28: The 10 km x 10 km grid covering Sweden.

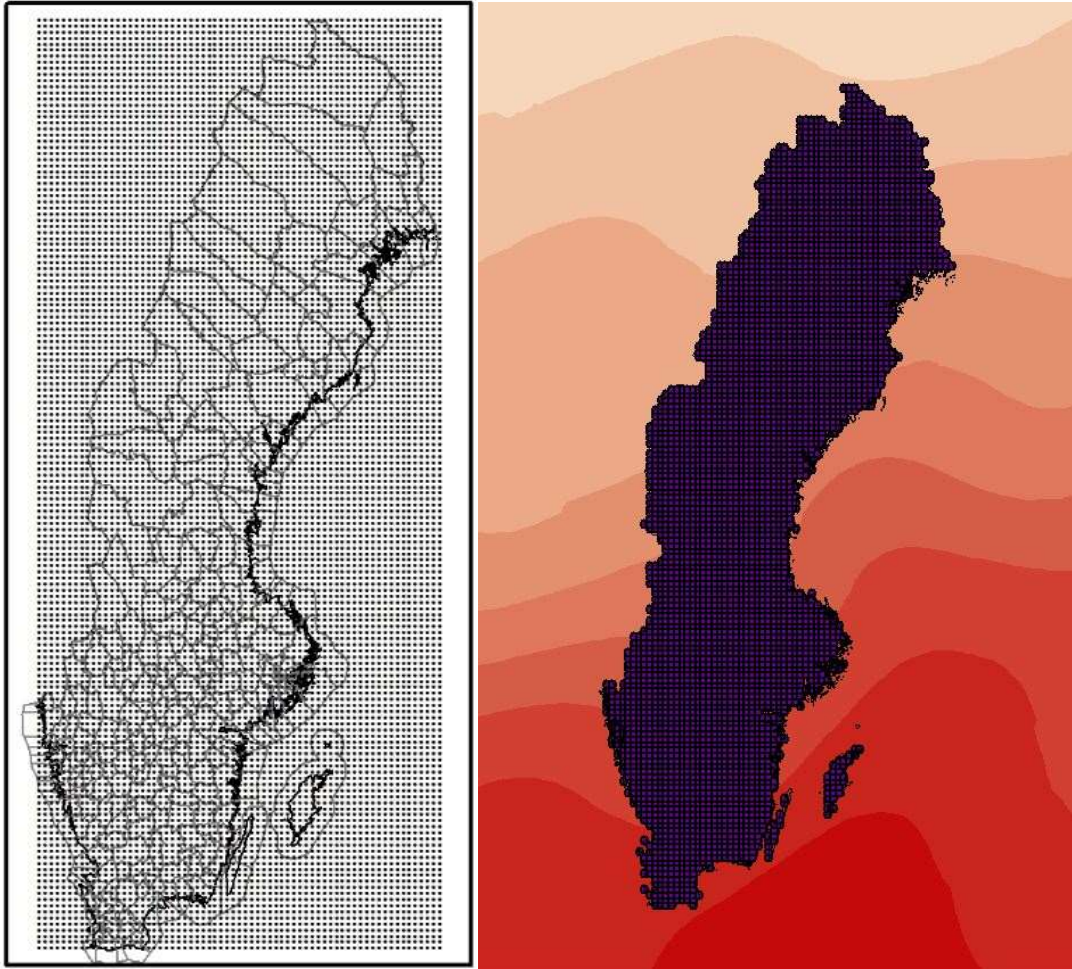


Figure 28: The 10 km x 10 km grid covering Sweden.
The map to the right also shows the UV radiation.

4 Results

In chapter 4 the results of the Kriging are shown, with selected illustrations.

The details of the Kriging interpolations are given in screen shots showing the course of the processes, in the appendix, chapter 8.

The UV Kriging maps are produced in ArcGIS 10.4, with Geostatistical Analyst, using the interpolation method Ordinary Kriging. The hip fracture data are interpolated separate for males and females, with and without trend removal.

4.1 The UV Kriging map

UV map, with first order trend removal, the other parameters are the defaults.

The semivariogram of the UV Kriging map is shown in Figure 29.

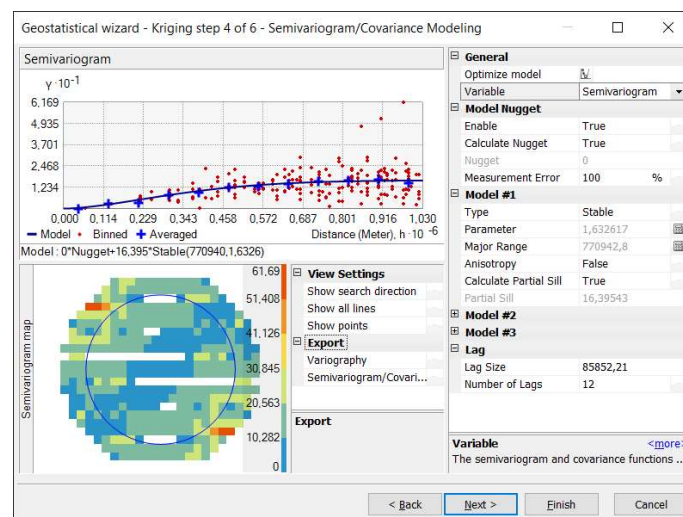


Figure 29: The semivariogram of the UV Kriging map

The method report is shown in Figure 30.

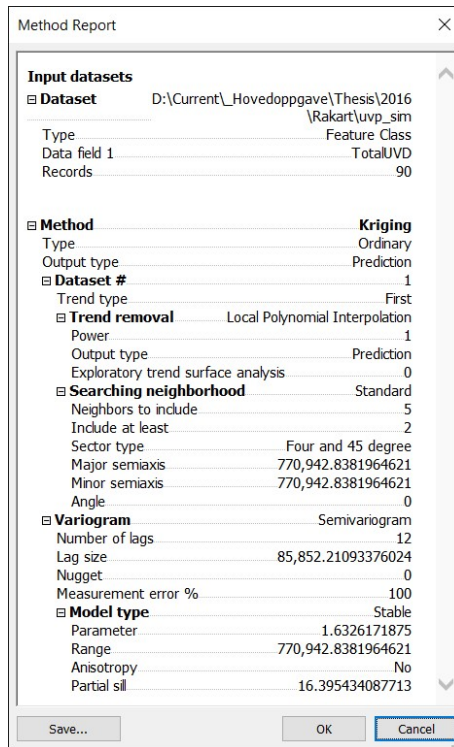


Figure 30: The Method Report of the UV Kriging map

The UV map in Figure 31 was made using the 90 data points and Ordinary Kriging with first order trend removal.

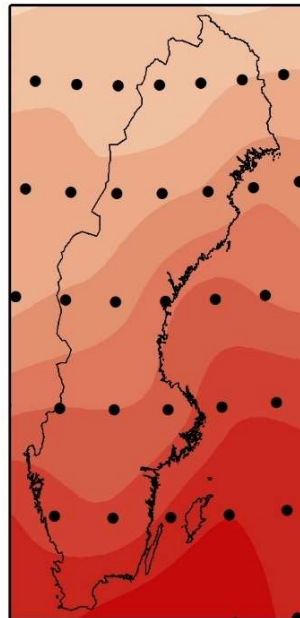


Figure 31: The resulting UV map from Ordinary Kriging, shown in a map together with the 90-point grid. The UV radiation is strongest by the equator line, and decreases by the latitude to the poles, as indicated by the northbound, fading colour. As this map clearly shows, the trend is significant from south to north. There is also a slight trend from east to west.

4.2 The hip fracture Kriging maps

4.2.1 Females, no trend removal

The semivariogram of the Kriging is shown in Figure 32 below.

In this step there were no trend removal.

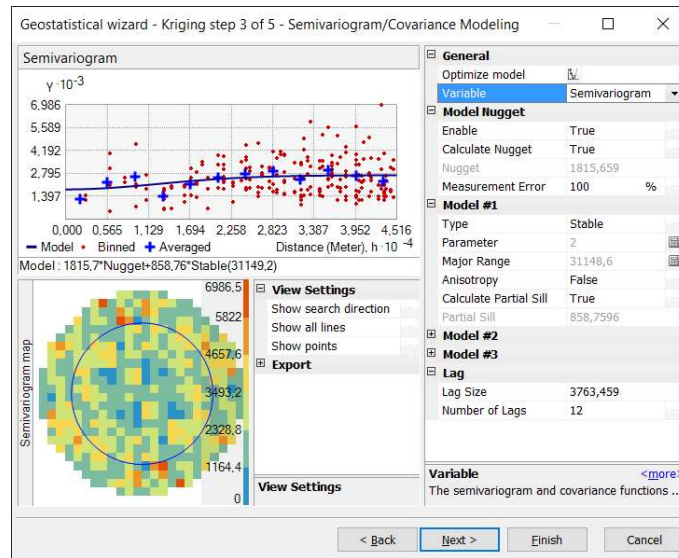


Figure 32: The semivariogram of the Kriging of the age adjusted female hip fracture incidences.

Figure 33 shows the cross validation of the Kriging of the age adjusted female hip fracture incidences.

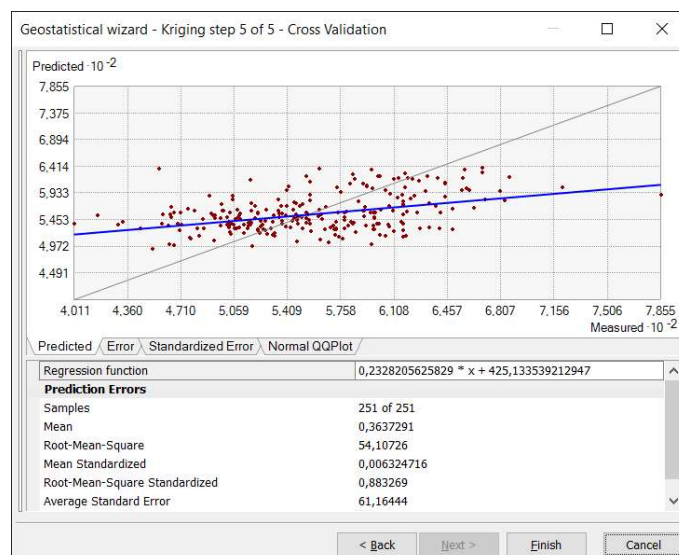


Figure 33: The illustration shows the cross validation of the Kriging of the age adjusted female hip fracture incidences.

Figure 34 shows the method report of the Kriging of age adjusted female hip fracture data.

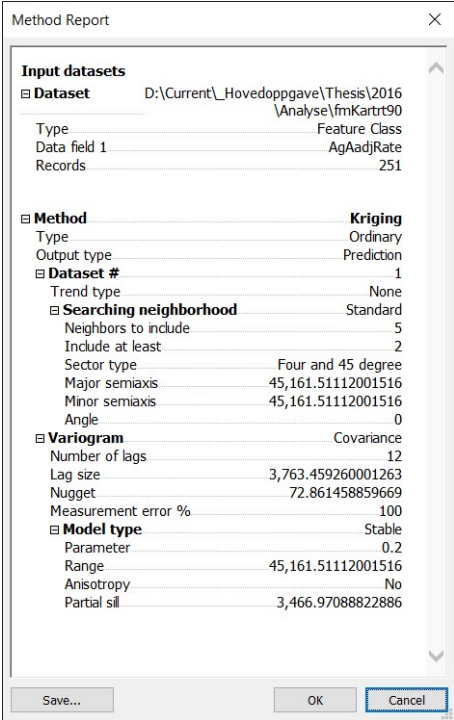


Figure 34 shows the method report of the Kriging of age adjusted female hip fracture data.

Figure 35 shows the resulting Kriging map made by age adjusted hip fracture data for females.

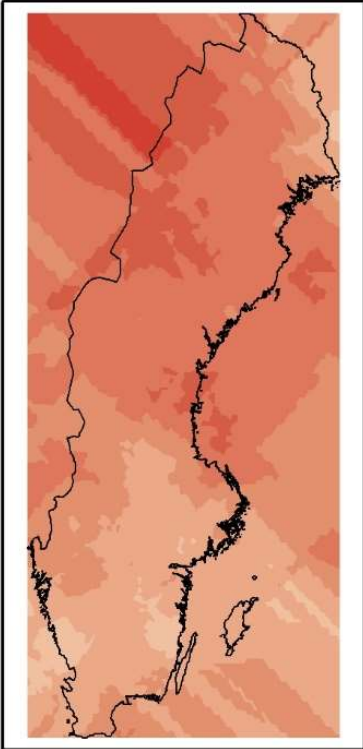


Figure 35: The resulting Kriging map made by age adjusted hip fracture data for females.

4.2.2 Females, first order trend removal

Figure 36 shows the semivariogram of the Kriging of the age adjusted female hip fracture incidences, with first order trend removal.

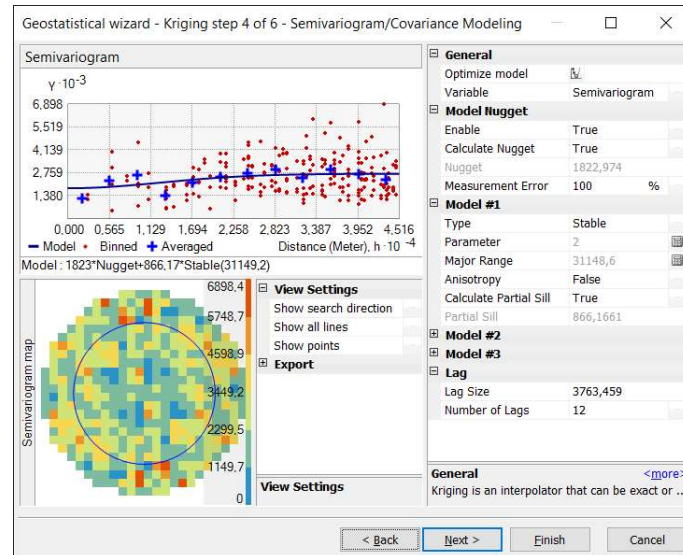


Figure 36: The semivariogram of the Kriging of the age adjusted female hip fracture incidences, with first order trend removal.

Figure 37 shows the cross validation of the Kriging of the age adjusted female hip fracture incidences, with first order trend removal

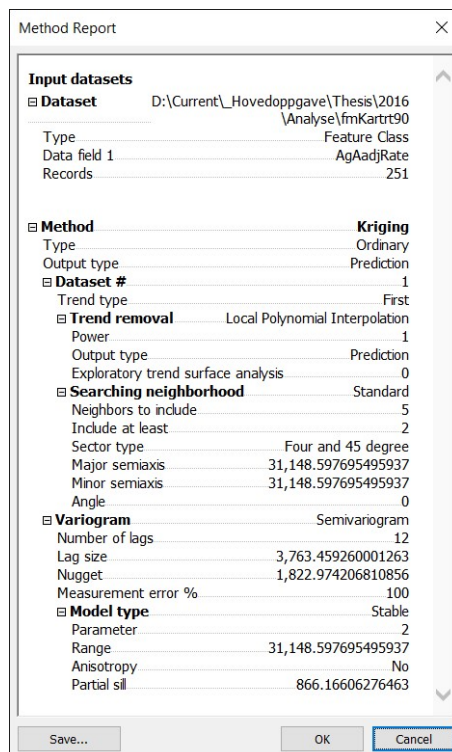


Figure 37: The cross validation of the Kriging of the age adjusted female hip fracture incidences, with first order trend removal.

Figure 38 shows the resulting Kriging map made by age adjusted hip fracture data for females, with first order trend removal.

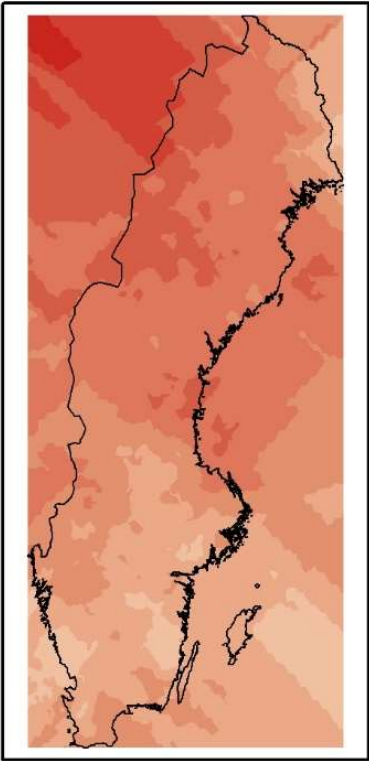


Figure 38: The resulting Kriging map made by age adjusted hip fracture data for females, with first order trend removal.

4.2.3 Males, no trend removal

Figure 39 shows the semivariogram of the Kriging of the age adjusted male hip fracture incidences.

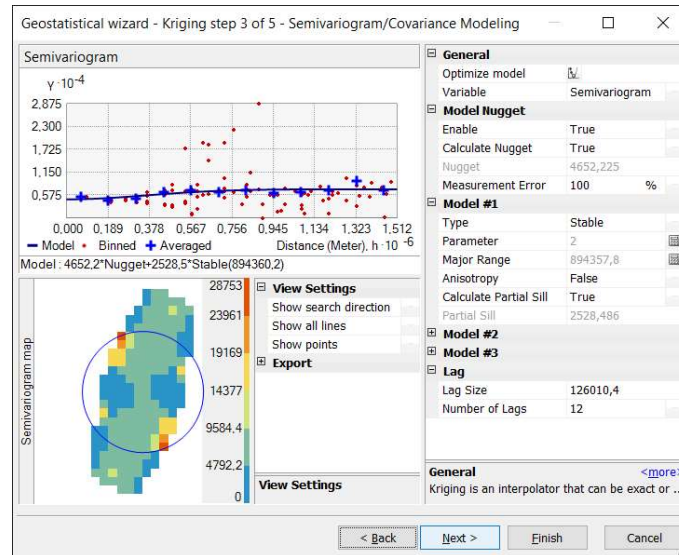


Figure 39: The semivariogram of the Kriging of the age adjusted male hip fracture incidences.

Figure 40 shows the method report of the Kriging of age adjusted male hip fracture data.

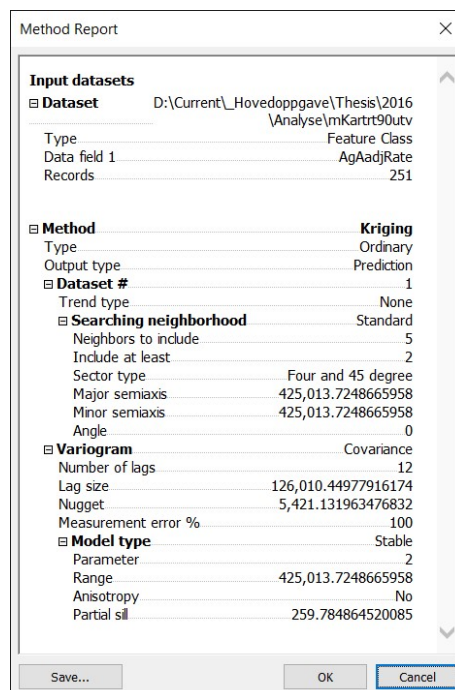


Figure 40: The method report of the Kriging of age adjusted male hip fracture data.

Figure 41 shows the resulting Kriging map made by age adjusted hip fracture data for males.

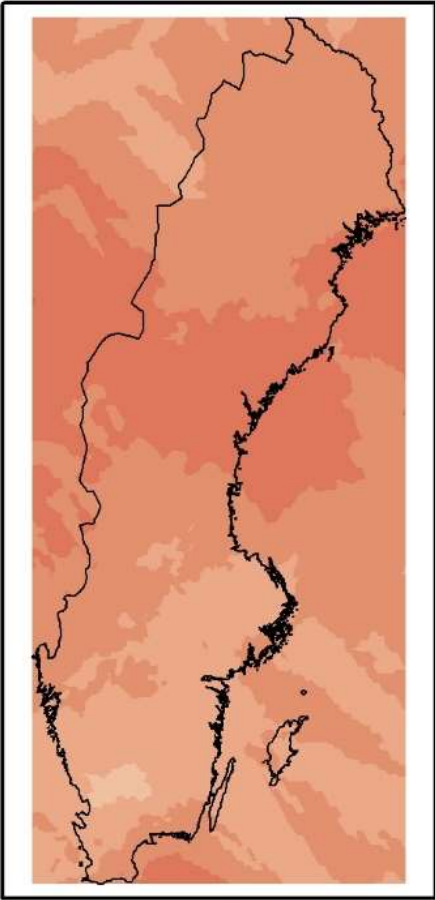


Figure 41: The resulting Kriging map made by age adjusted hip fracture data for males.

4.2.4 Males, first order trend removal

Figure 42 shows the semivariogram of the Kriging of the age adjusted male hip fracture incidences, with first order trend removal.

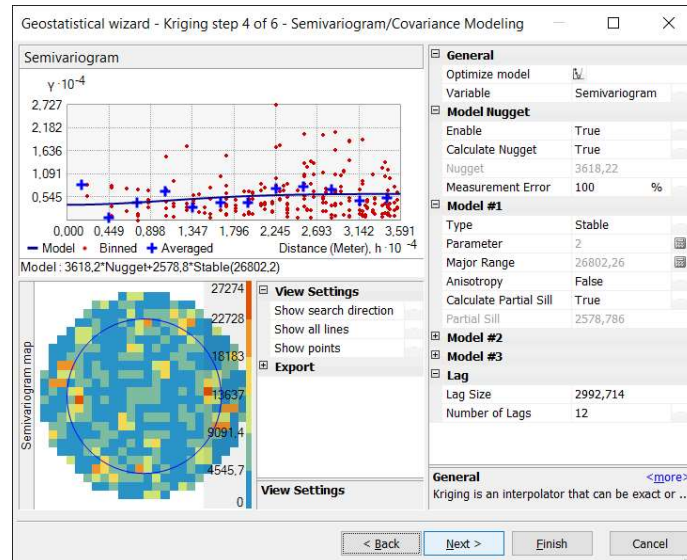


Figure 42: The semivariogram of the Kriging of the age adjusted male hip fracture incidences, with first order trend removal.

Figure 43 shows the method report of the Kriging of age adjusted male hip fracture data, with first order trend removal.

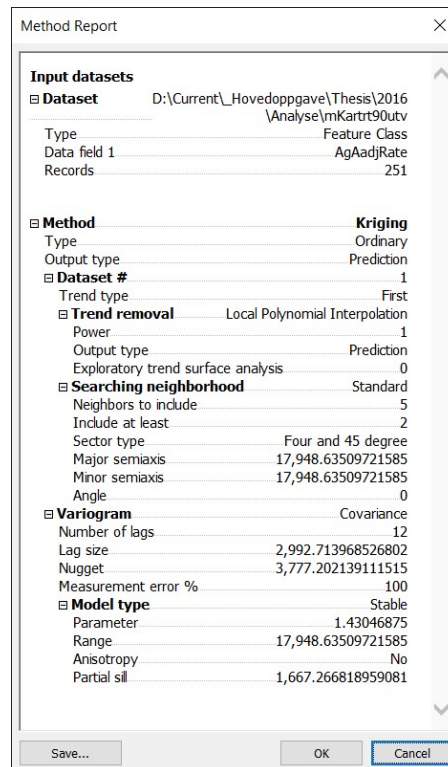


Figure 43: The method report of the Kriging of age adjusted male hip fracture data, with first order trend removal.

Figure 44 shows the resulting Kriging map made by age adjusted hip fracture data for females, with first order trend removal.

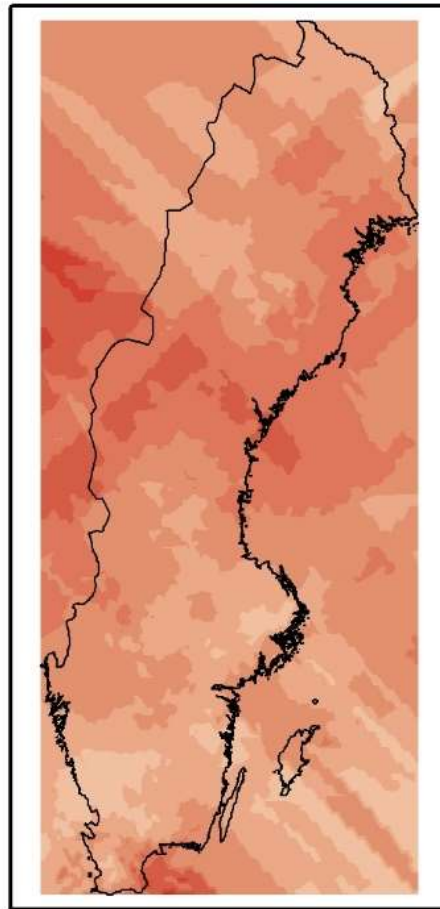


Figure 44: The resulting Kriging map made by age adjusted hip fracture data for females, with first order trend removal.

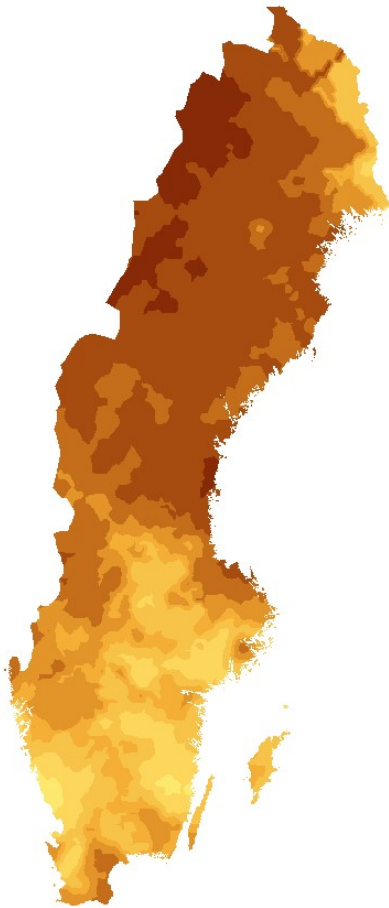


Figure 45: The hip fracture Kriging map. There is a significant trend from south to north, and from east to west.

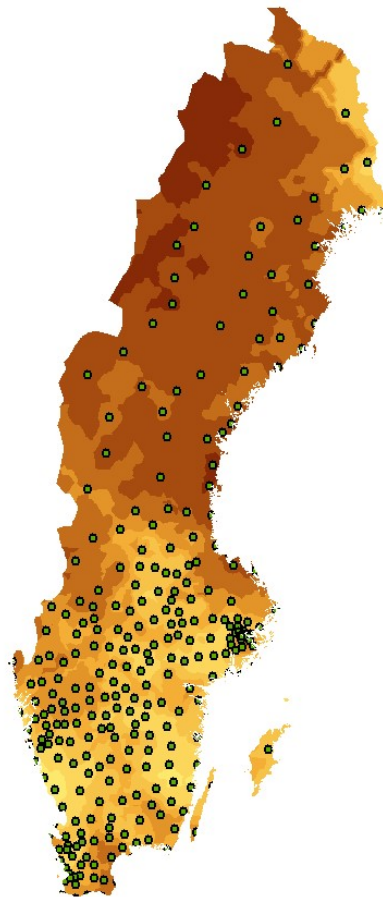


Figure 46: The hip fracture Kriging map with the municipality centroids. Due to the municipalities' dissemination into the sea some of the centroids are actually situated *in* the sea.

4.2.5 Statistical analyses

Figure 47 shows the results of the statistical analysis of Vitamin D vs female age adjusted incident rate (Kriging *without* trend removal, raster to point with interpolation).

SUMMARY OUTPUT								
Regression Statistics								
Multiple R	0,368108138							
R Square	0,135503601							
Adjusted R Square	0,132031728							
Standard Error	55,54054387							
Observations	251							
ANOVA								
	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>Significance F</i>			
Regression	1	120394,6679	120394,6679	39,02896161	1,79485E-09			
Residual	249	768103,2512	3084,752013					
Total	250	888497,9191						
	<i>Coefficients</i>	<i>Standard Error</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower 95%</i>	<i>Upper 95%</i>	<i>Lower 95,0%</i>	<i>Upper 95,0%</i>
Intercept	692,5556672	21,91612462	31,60027967	4,14687E-89	649,3910518	735,7202826	649,3910518	735,7202826
RASTERVALU_N,19,11	-2,26611694	0,362734463	-6,247316352	1,79485E-09	-2,980535837	-1,551698042	-2,980535837	-1,551698042

Figure 47: Regression analysis of Kriging without trend removal, raster to point with interpolation

Figure 48 shows the results of the statistical analysis of Vitamin D vs female age adjusted incident rate (Kriging with *first order* trend removal, raster to point with interpolation).

SUMMARY OUTPUT								
Regression Statistics								
Multiple R	0,344093564							
R Square	0,118400381							
Adjusted R Square	0,11485982							
Standard Error	8,951528967							
Observations	251							
ANOVA								
	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>Significance F</i>			
Regression	1	2679,634099	2679,634099	33,44113838	2,19263E-08			
Residual	249	19952,33784	80,12987084					
Total	250	22631,97194						
	<i>Coefficients</i>	<i>Standard Error</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower 95%</i>	<i>Upper 95%</i>	<i>Lower 95,0%</i>	<i>Upper 95,0%</i>
Intercept	89,42426956	5,323500749	16,79801953	7,48414E-43	78,93943857	99,90910055	78,93943857	99,90910055
AdjR	-0,054917346	0,009496619	-5,782831346	2,19263E-08	-0,073621287	-0,036213405	-0,073621287	-0,036213405

Figure 48: Regression analysis of Kriging with first order trend removal, raster to point with interpolation

Figure 49 shows the results of the statistical analysis of Vitamin D vs female age adjusted incident rate (Kriging *without* trend removal, raster to point with interpolation).

SUMMARY OUTPUT								
<i>Regression Statistics</i>								
Multiple R	0,203879293							
R Square	0,041566766							
Adjusted R Square	0,037702116							
Standard Error	74,2174031							
Observations	250							
<i>ANOVA</i>								
	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>Significance F</i>			
Regression	1	59244,43534	59244,43534	10,75563501	0,001188716			
Residual	248	1366039,285	5508,222924					
Total	249	1425283,72						
	<i>Coefficients</i>	<i>Standard Error</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower 95%</i>	<i>Upper 95%</i>	<i>Lower 95,0%</i>	<i>Upper 95,0%</i>
Intercept	479,1418569	29,83812234	16,05804318	2,89142E-40	420,3734176	537,9102962	420,3734176	537,9102962
31,85838318	-1,617158304	0,493099437	-3,279578481	0,001188716	-2,58835495	-0,645961657	-2,58835495	-0,645961657

Figure 49: Regression analysis of Kriging without trend removal, raster to point with interpolation

Figure 50 below shows the results of the statistical analysis of Vitamin D vs male age adjusted incident rate (Kriging with *first order* trend removal, raster to point with interpolation).

SUMMARY OUTPUT								
<i>Regression Statistics</i>								
Multiple R	0,162634604							
R Square	0,026450014							
Adjusted R Square	0,02252441							
Standard Error	74,11718841							
Observations	250							
<i>ANOVA</i>								
	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>Significance F</i>			
Regression	1	37013,24931	37013,24931	6,737818998	0,010001915			
Residual	248	1362352,689	5493,357617					
Total	249	1399365,938						
	<i>Coefficients</i>	<i>Standard Error</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower 95%</i>	<i>Upper 95%</i>	<i>Lower 95,0%</i>	<i>Upper 95,0%</i>
Intercept	458,6086572	29,40619964	15,59564523	1,11811E-38	400,6909223	516,5263921	400,6909223	516,5263921
69,6652985	-1,282197254	0,493963856	-2,595730918	0,010001915	-2,255096438	-0,309298069	-2,255096438	-0,309298069

Figure 50: Regression analysis of Kriging with first order trend removal, raster to point with interpolation.

Method 2: Kriging of both hip fracture data (*no trend removal*) and UV data (*first order trend removal*) (10km grid) – females.

SUMMARY OUTPUT								
<i>Regression Statistics</i>								
Multiple R	0,183053199							
R Square	0,033508474							
Adjusted R Square	0,033288216							
Standard Error	162,3163336							
Observations	4390							
<i>ANOVA</i>								
	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>Significance F</i>			
Regression	1	4008184,097	4008184,097	152,1329239	2,18736E-34			
Residual	4388	115608846,3	26346,59214					
Total	4389	119617030,4						
	<i>Coefficients</i>	<i>Standard Error</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower 95%</i>	<i>Upper 95%</i>	<i>Lower 95,0%</i>	<i>Upper 95,0%</i>
Intercept	714,3072869	10,8251998	65,98559841	0	693,0844312	735,5301426	693,0844312	735,5301426
X Variable 1	-2,651246398	0,214950513	-12,3342176	2,18736E-34	-3,072657901	-2,229834895	-3,072657901	-2,229834895

Figure 51: Regression analysis of Kriging with both hip fracture data for females (first order trend removal) and UV radiation data (10km grid)

We considered p-values less than 0.05 as statistical significant. The regression calculations have quite small p-values, all less than 0.01, and are therefore considered strongly statistical significant. This proves a statistical significant correlation between UV radiation and hip fractures in our data, which means that lack of UV radiation at higher latitudes probably contributes to the high numbers of hip fractures in Nordic populations (Sweden). Both the maps and the regression analysis clearly supports the hypothesis that Vitamin D producing UV radiation and the hip fracture incidents are correlated. We have also found that the incidents of female hip fractures show more distinct trends than the male incidents.

5 Discussion

5.1 Data uncertainties

The main data used in this work are considered very reliable. The UVD data are good, and the hip fracture incidents data are exquisite. At the same time, we are aware of other, confounding factors, which also might have an influence on the results. These factors are described in the chapters 1.3.1, 1.3.2 (Norwegian Institute of Public Health 2016) and 1.3.3.

5.1.1 Modifiable risk factors

Low bone mineral density, physical inactivity, lightweight, weight loss and possibly weight fluctuations. Obesity appears to somewhat increase the risk. Cortisone treatment. Increased risk of falls, poor muscle tone, poor vision, poor balance, poor mobility, urinary incontinence, sedatives, sleeping pills and factors as loose carpets and poor lighting affects the risk of falls. Smoking reduces bone density in both women and men. Thin, smoking females has the highest risk of hip fractures. High alcohol consumption. Minimal sun exposure, which is related to the production of vitamin D.

5.1.2 Non-modifiable risk factors

Advanced age, sex, previous fractures, early menopause, heredity, ethnicity and height. Certain diseases in the digestive system also contribute to higher fracture risk.

5.1.3 Other factors

Over the last decades, senior citizens are known to go to the Mediterranean countries for shorter or longer periods, mostly during winter. Our research has not taken that into account, as it would be very difficult and probably very expensive to investigate, if at all possible.

Another factor is that the ozone layer may be thinner at the poles. If so, does it allow more UV radiation? If yes, does this also mean that the body produces more vitamin D? If these questions are answered with "yes", will this weaken or strengthen our theory?

5.2 Recommendation

The results show there is a significant trend in the hip fracture data. This trend is from south to north, and from east to west in the hip fracture incidences. It is a matter of interest that the initial purpose of this thesis was to investigate the trend in Norway, and West of Sweden is Norway. This leads to a renewed interest in investigating hip fractures in Norway. Therefore, further investigation is strongly recommended, as the area is far from fully mapped.

One could also consider to put all the data into a data base, to make it easier to analyse parts of the data set, e.g. omit all ages above 85 years of age and so on.

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7 Figures

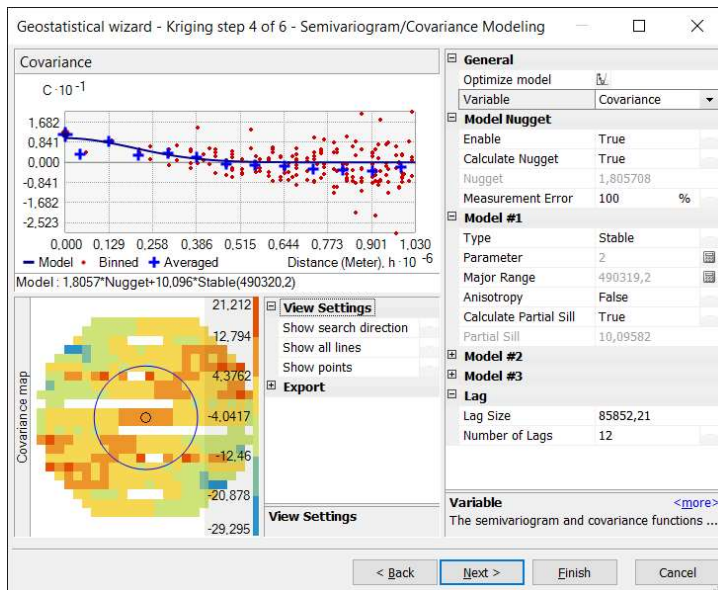
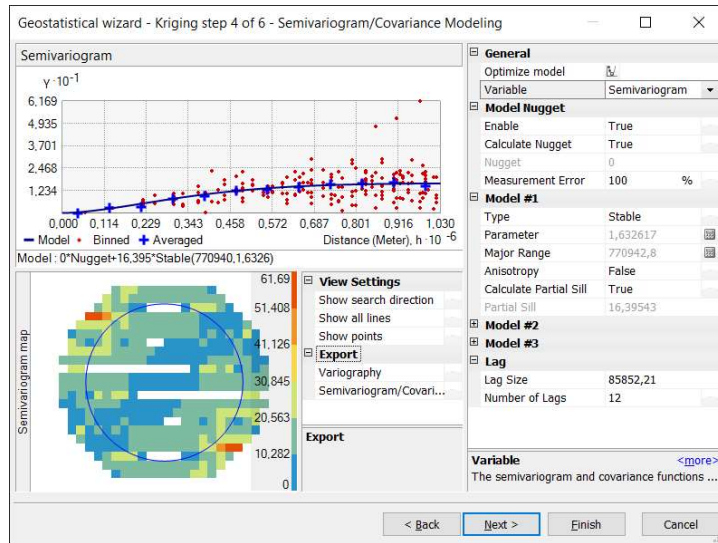
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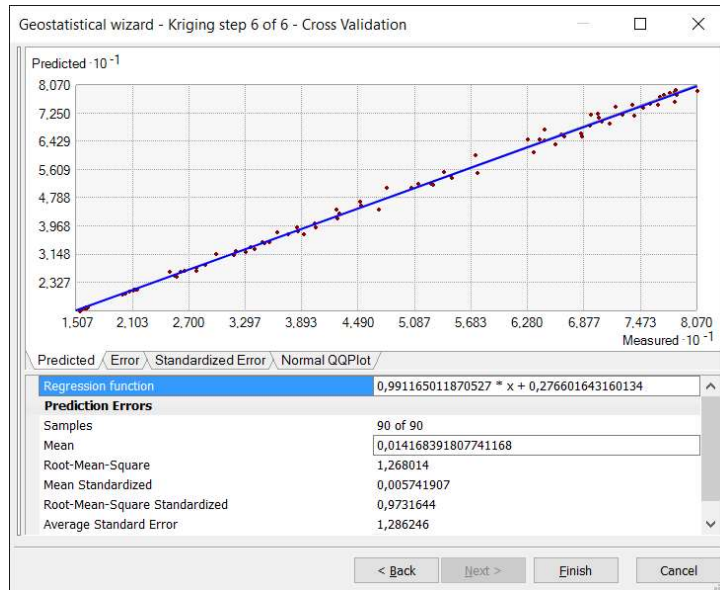
8 Appendix

8.1 Kriging for the UV data

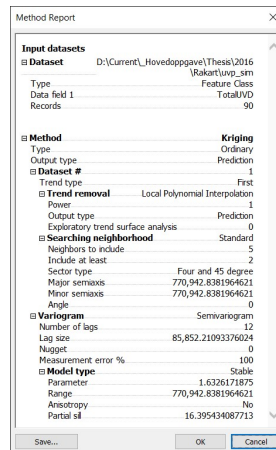
ArcGIS 10.4, Geostatistical Analyst, Ordinary Kriging, First order trend removal, defaults.



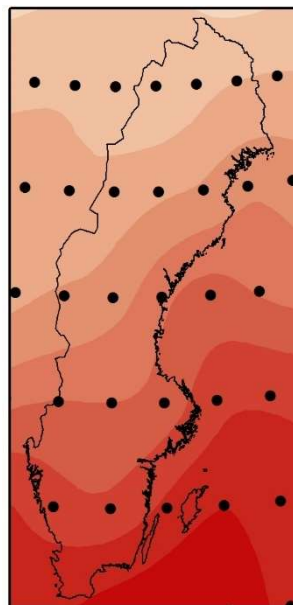
The prediction errors:



Method report:



Resulting map:

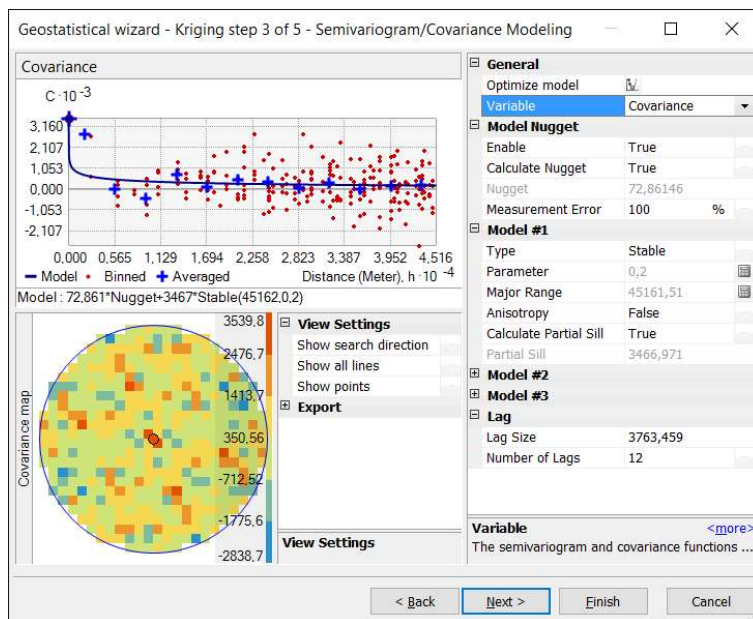
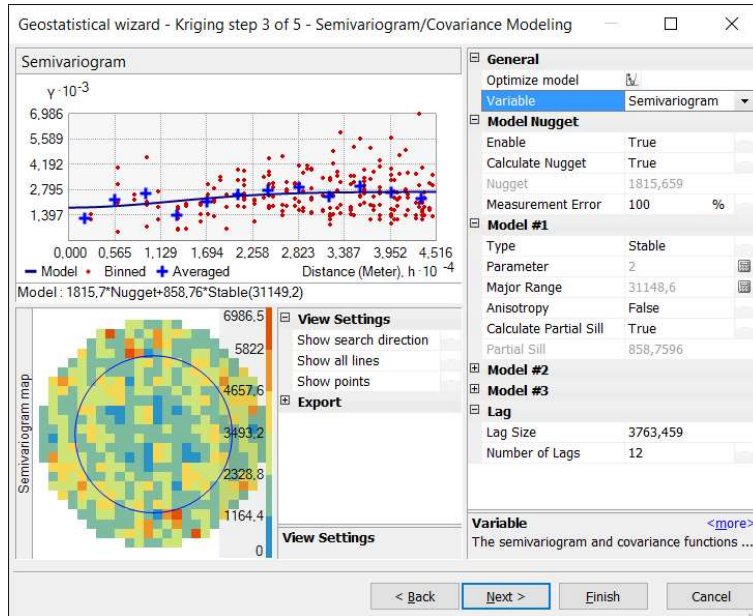


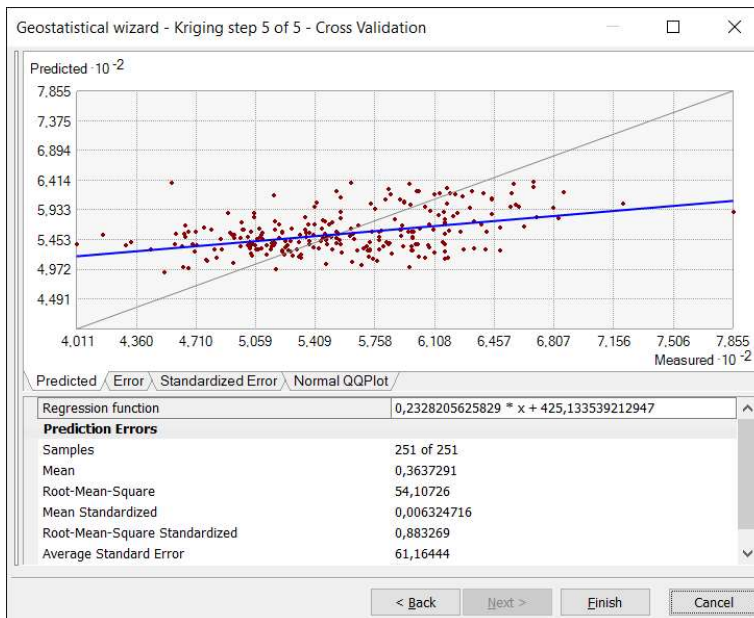
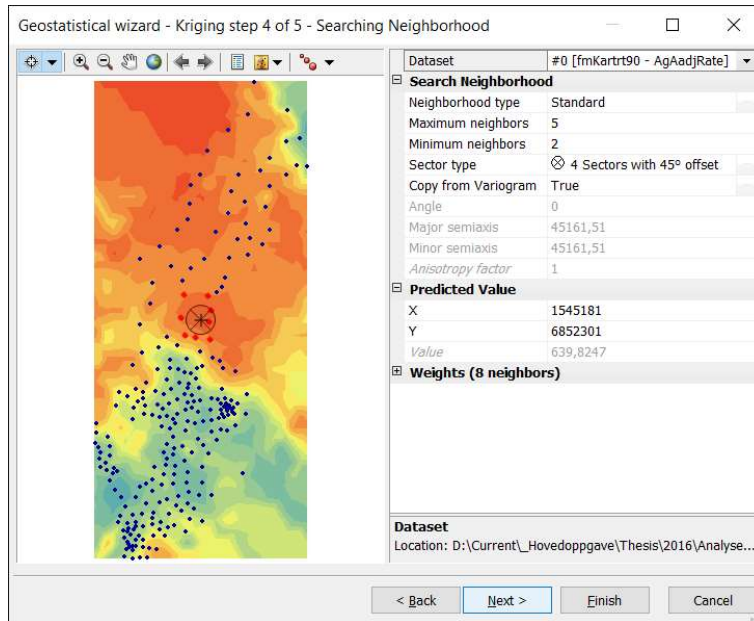
8.2 Kriging for the hip fracture data

8.2.1 Females

8.2.1.1 No trend removal, females

Fmkarttrt90utv, Age adjusted rate, ordinary Kriging,





Method Report

Input datasets

Dataset D:\Current_Hovedoppgave\Thesis\2016
 \Analyse\fmKarttrt90
 Type Feature Class
 Data field 1 AgAadRate
 Records 251

Method **Kriging**
 Type Ordinary
 Output type Prediction

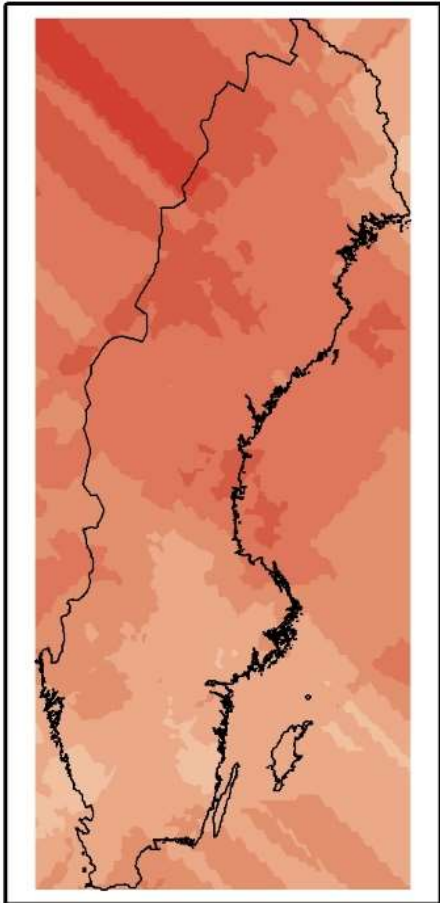
Dataset # 1
 Trend type None

Searching neighborhood Standard
 Neighbors to include 5
 Include at least 2
 Sector type Four and 45 degree
 Major semiaxis 45,161.51112001516
 Minor semiaxis 45,161.51112001516
 Angle 0

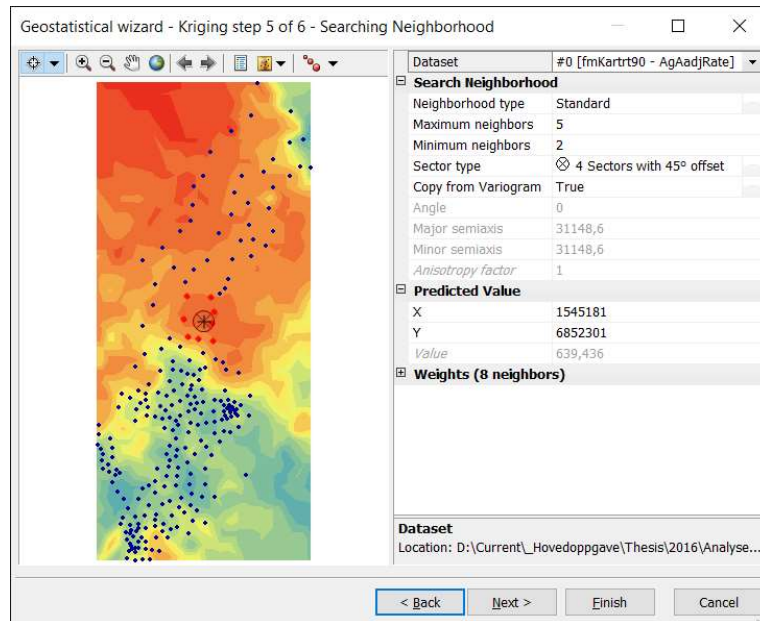
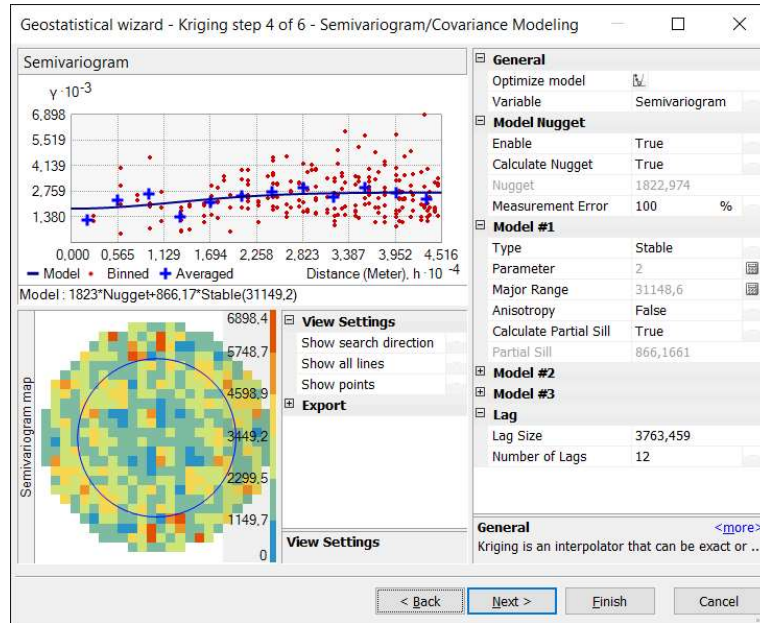
Variogram Covariance
 Number of lags 12
 Lag size 3,763.459260001263
 Nugget 72.861458859669
 Measurement error % 100

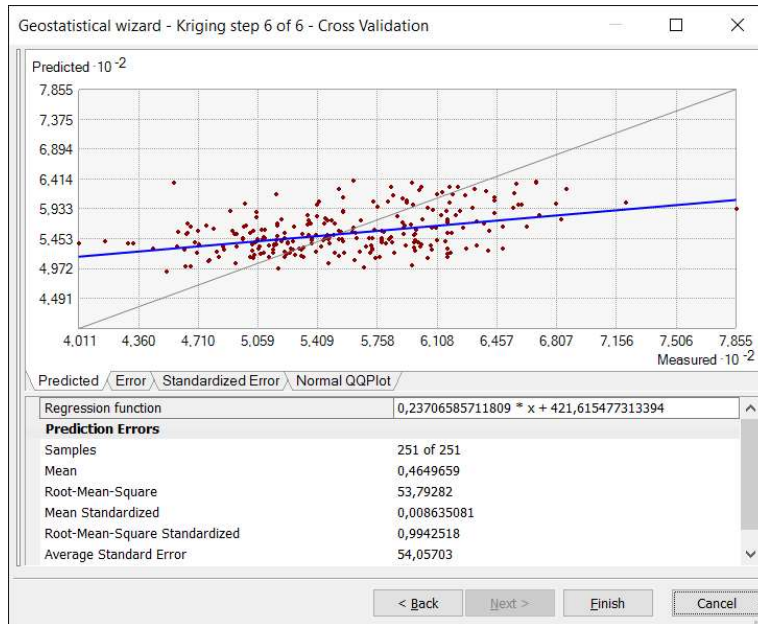
Model type Stable
 Parameter 0.2
 Range 45,161.51112001516
 Anisotropy No
 Partial sill 3,466.97088822886

Save... OK Cancel



8.2.1.2 First order trend removal, females

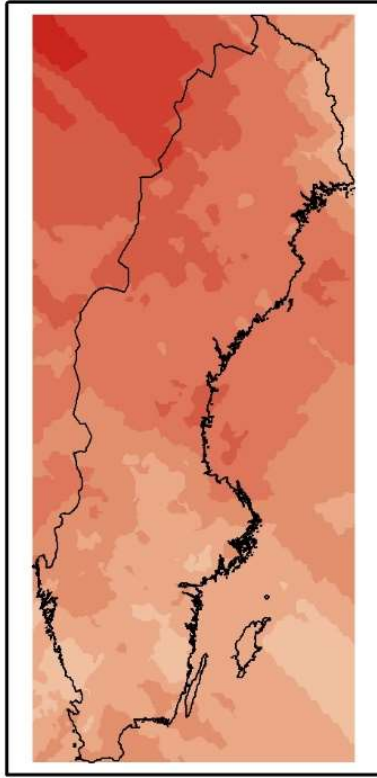




Method Report

Input datasets	
Dataset	D:\Current_Hovedoppgave\Thesis\2016\Analyse\fmKarttr90
Type	Feature Class
Data field 1	AgAdjRate
Records	251
Method Kriging	
Type	Ordinary
Output type	Prediction
Dataset #	1
Trend type	First
Trend removal	Local Polynomial Interpolation
Power	1
Output type	Prediction
Exploratory trend surface analysis	0
Searching neighborhood	Standard
Neighbors to include	5
Include at least	2
Sector type	Four and 45 degree
Major semiaxis	31,148.597695495937
Minor semiaxis	31,148.597695495937
Angle	0
Variogram	Semivariogram
Number of lags	12
Lag size	3,763.459260001263
Nugget	1,822.974206810856
Measurement error %	100
Model type	Stable
Parameter	2
Range	31,148.597695495937
Anisotropy	No
Partial sill	866.16606276463

Save... OK Cancel



8.2.2 Males

8.2.2.1 No trend removal, males

Geostatistical Wizard: Kriging / CoKriging

Methods

- ▣ **Deterministic methods**
 - Inverse Distance Weighting
 - Global Polynomial Interpolation
 - Radial Basis Functions
 - Local Polynomial Interpolation
- ▣ **Geostatistical methods**
 - Kriging / CoKriging**
 - Areal Interpolation
 - Empirical Bayesian Kriging
- ▣ **Interpolation with barriers**
 - Kernel Smoothing
 - Diffusion Kernel

Input Data

Dataset	Source Dataset	Data Field
Dataset 1	mKartrt90utv	AgAdjRate
Dataset 2	<none>	
Dataset 3	<none>	
Dataset 4	<none>	

Kriging / CoKriging

Kriging is an interpolator that can be exact or smoothed depending on the measurement error model. It is very flexible and allows you to investigate graphs of spatial auto- and cross-correlation. Kriging uses statistical models that allow a variety of output surfaces including predictions, prediction standard errors, probability and quantile. The flexibility of kriging can require a lot of decision-making. Kriging assumes the data come from a stationary stochastic process, and some methods

[About Kriging / CoKriging](#)

< Back **Next >** Finish Cancel

Geostatistical wizard - Kriging step 2 of 5

Kriging Type

- Ordinary**
- Simple
- Universal
- Indicator
- Probability
- Disjunctive

Output Surface Type

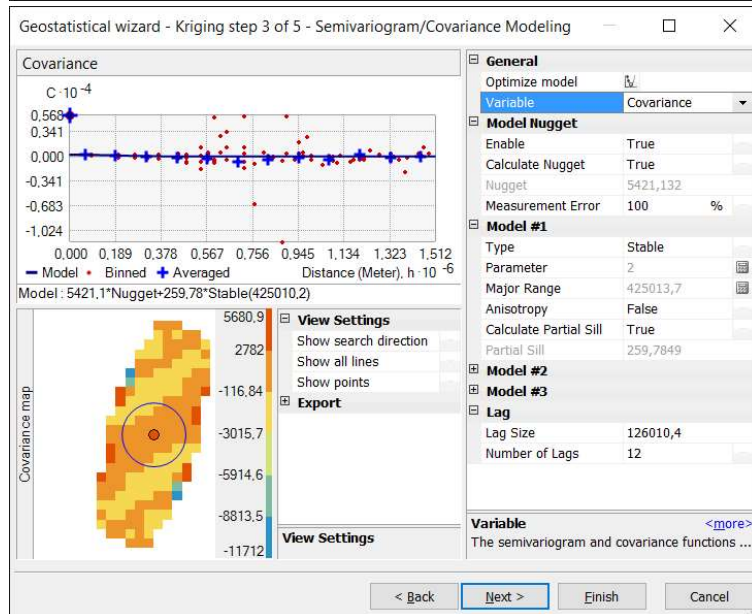
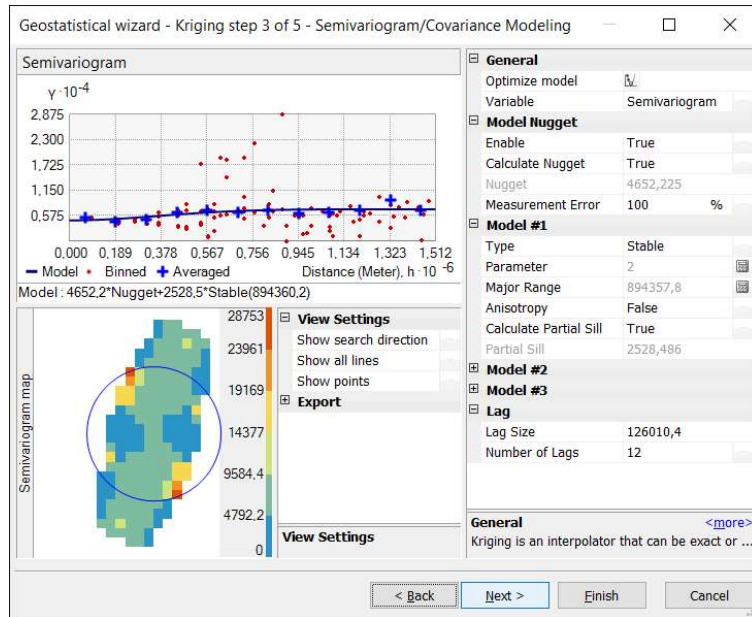
- Prediction**
- Quantile
- Probability
- Prediction Standard Error

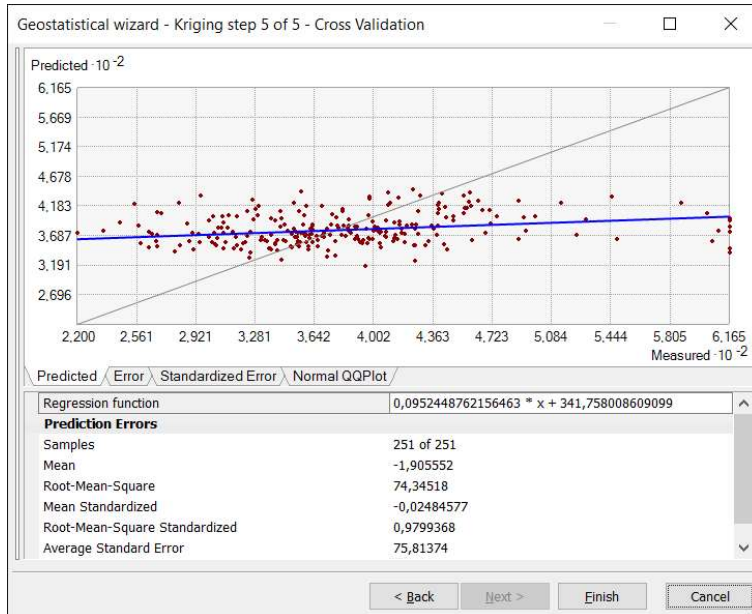
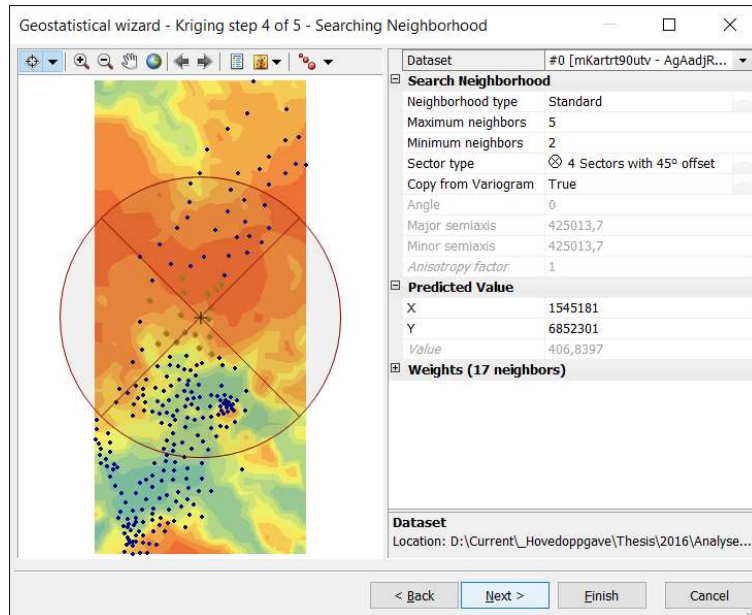
Dataset #1

Transformation type	None
Order of trend removal	None

Order of trend removal [<more>](#)
You may want to remove a surface trend from your data and use kriging or cokriging on the detrended (residual) data.

< Back **Next >** Finish Cancel





Method Report

Input datasets

Dataset D:\Current_Hovedoppgave\Thesis\2016
 \Analyse\mKartr90utv
 Type Feature Class
 Data field 1 AgAadjRate
 Records 251

Method **Kriging**

Type Ordinary
 Output type Prediction

Dataset # 1

Trend type None

Searching neighborhood Standard

Neighbors to include 5
 Include at least 2
 Sector type Four and 45 degree
 Major semiaxis 425,013.7248665958
 Minor semiaxis 425,013.7248665958
 Angle 0

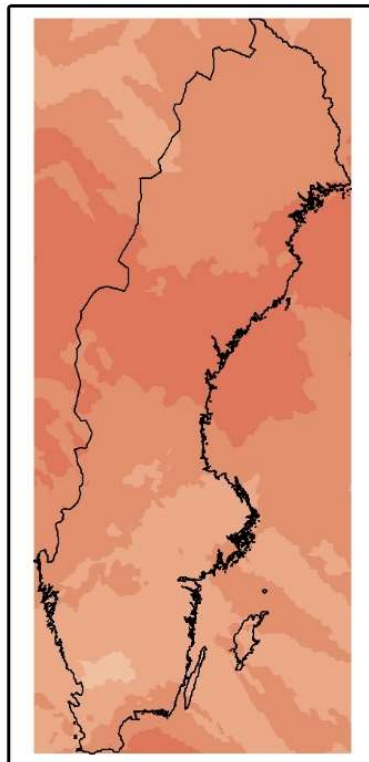
Variogram Covariance

Number of lags 12
 Lag size 126,010.44977916174
 Nugget 5,421.131963476832
 Measurement error % 100

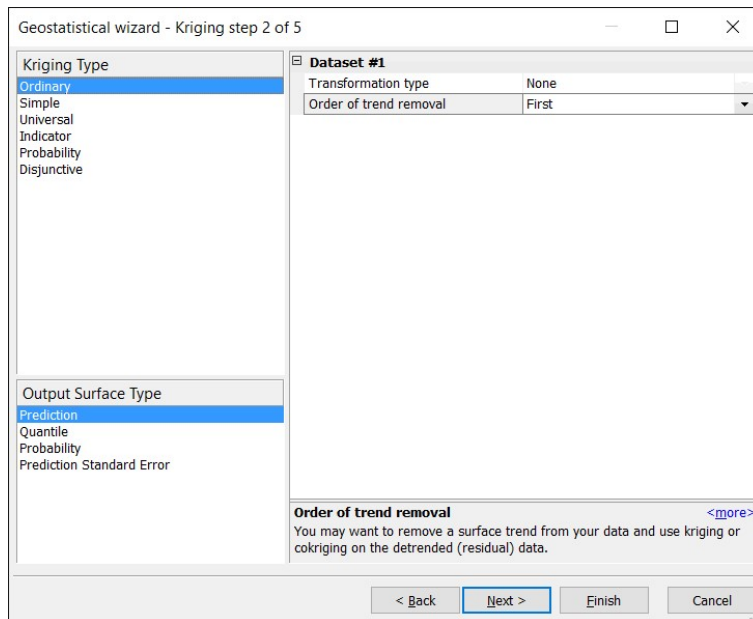
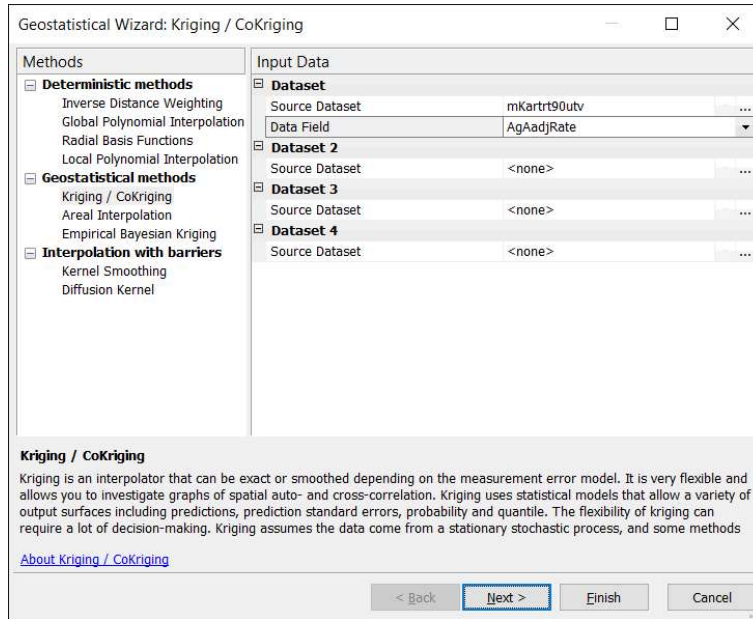
Model type Stable

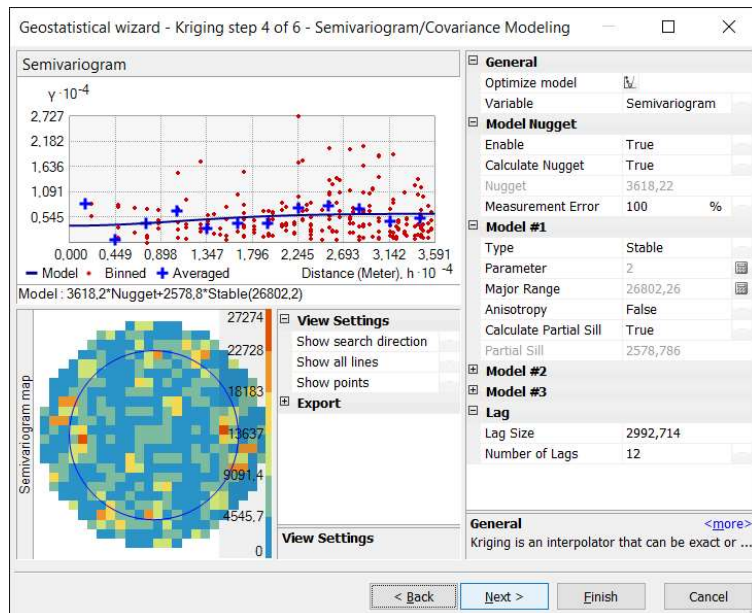
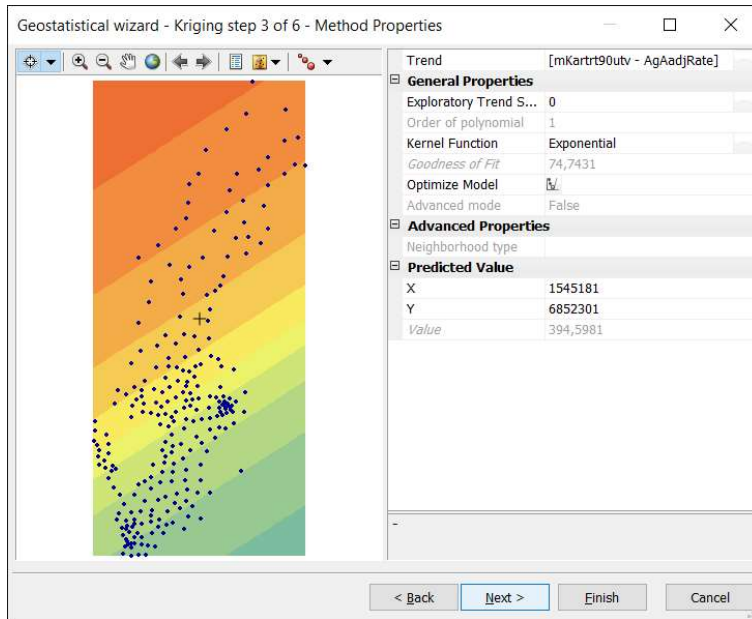
Parameter 2
 Range 425,013.7248665958
 Anisotropy No
 Partial sill 259.784864520085

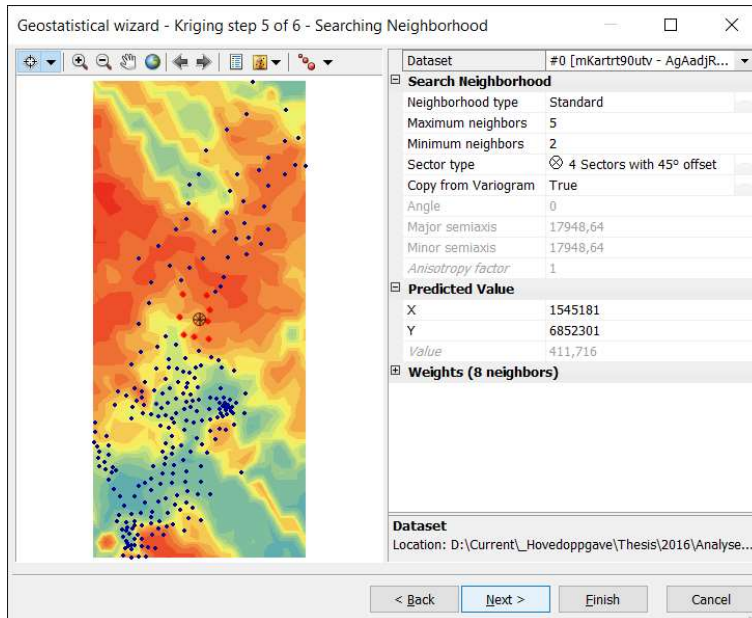
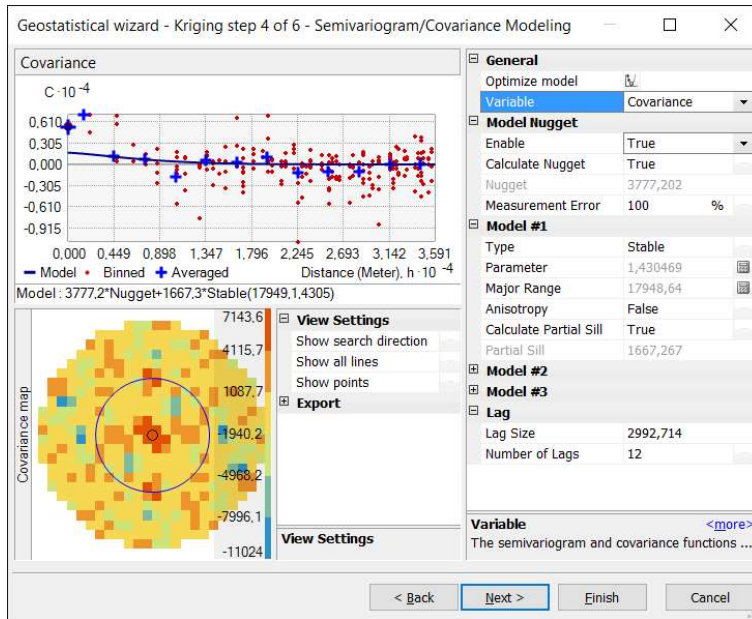
Save... OK Cancel

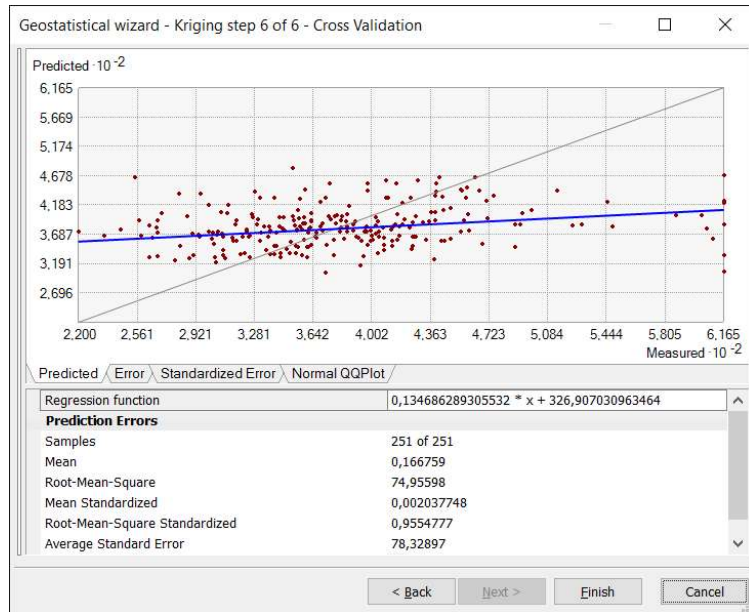


8.2.2.2 First order trend removal, males









Method Report

Input datasets

Dataset D:\Current_Hovedoppgave\Thesis\2016
 \Analyse\mKartrt90utv

Type Feature Class
 Data field 1 AgAdjRate
 Records 251

Method **Kriging**

Type Ordinary
 Output type Prediction

Dataset # 1

Trend type First

Trend removal Local Polynomial Interpolation

Power 1
 Output type Prediction
 Exploratory trend surface analysis 0

Searching neighborhood Standard

Neighbors to include 5
 Include at least 2
 Sector type Four and 45 degree
 Major semiaxis 17,948.63509721585
 Minor semiaxis 17,948.63509721585
 Angle 0

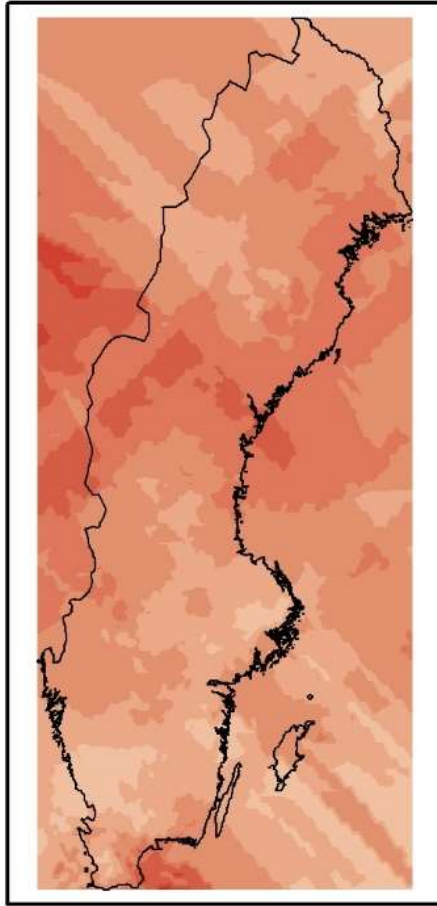
Variogram Covariance

Number of lags 12
 Lag size 2,992.713968526802
 Nugget 3,777.202139111515
 Measurement error % 100

Model type Stable

Parameter 1.43046875
 Range 17,948.63509721585
 Anisotropy No
 Partial sill 1,667.266818959081

Save... OK Cancel



8.3 Calculations

8.3.1 Number of days

The calculation of the number of days in the period 1980 – 2002 is shown in Figure 52

	#yrs	#days	Total #days
Years 1980-2001	22	365	=D5*E5
Leap years (yr 2000 excluded)	6	1	=D6*E6
Year 2002	1	=31*5+30*2+28*1	=D7*E7
Days Jan 1 2002-Aug 31 2002			=SUM(F5:F7)

Figure 52: The calculation of the number of days in the period 1980 – 2002

