Diplomarbeit

Clinical presentation of Puumala virus infections in Styria in the "peak year" 2012 compared to 2007-2011

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Ort, Datum (Unterschrift)

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Acknowledgement

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Kurzusammenfassung

2012 wurde in der Steiermark ein Ausbruch von Hantavirus Infektionen beobachtet. Bis zu diesem Zeitpunkt waren noch nie so hohe Fallzahlen von Nephropathia epidemica (NE) in Österreich registriert worden. Ziel der Arbeit war es, in einer retrospektiven Untersuchung herauszufinden, ob es Unterschiede in der Klinik, der Epidemiologie, der notwendigen Behandlungsform, den Laborparametern sowie dem Outcome der Patienten zwischen dem „Peakjahr" 2012 und den „normalen" Jahren 2007-2011, gab.

In die Untersuchung eingeschlossen wurden alle Patienten über 18 Jahre mit mittels Reagena® POC Puumala IgM Test bestätigter Diagnose einer NE, durchgeführt im Mikrobiologischen Labor der Universitätsklinik für Innere Medizin, Graz, zwischen 1. Januar 2007 und 31. Dezember 2012. In Gruppe 1 (2007-2011) wurden 40, in Gruppe 2 (2012) wurden 42 Patienten inkludiert.

Im Jahr 2012 wurde die Diagnose signifikant schneller gestellt als in 2007-2011. In Gruppe 1 konnte eine signifikante Häufung der Erstsymptome „Verschlechterung des Allgemeinzustandes" und „Arthromyalgie" beobachtet werden. In Gruppe 2 litten signifikant mehr Patienten an Lumbago. Tendenziell entwickelten mehr Patienten in Gruppe 1 petechiale Blutungen. Der 1. gemessene Wert des Hämoglobins, des Hämatokrits und der ALT waren in Gruppe 1 durchschnittlich signifikant höher. Thrombozytopenie war 2007-2011 tendenziell stärker ausgeprägt als 2012, ebenso zeigte sich eine Tendenz zu höheren CRP-und Harnstoff-Werten in diesen Jahren. 2012 wurden signifikant weniger Patienten dialysiert als in den Vorjahren.

Das klinische Bild von Hantavirus Infektionen scheint zu variieren, wie sich anhand der unterschiedlichen Symptomausprägung zeigt. Die schnellere Diagnosestellung im Jahr 2012 könnte aus eine gesteigerte Sensibilisierung hinsichtlich dieser Infektionskrankheit von Ärzten und Patienten resultieren, wodurch es zu einer schnelleren Behandlung und somit zur Vermeidung von Dialysebehandlungen kam. Andererseits ist auch ein allgemein leichterer Verlauf der Erkrankung im Jahr 2012 denkbar.

Abstract

In 2012, an outbreak of hantavirus infections was observed in Styria. Never before have so many cases of Nephropathia epidemica (NE) been recorded in Austria. The aim of this study was to investigate differences in epidemiology, clinical presentation, laboratory results, treatment, and outcome between the peak year 2012 and the “normal” years 2007-2011.

Therefore a retrospective analysis of clinical data was performed. Inclusion criteria were confirmed diagnosis by Reagena® POC Puumala IgM Test and/or ELISA testing by the Medical University of Vienna, Department of Virology, age older than 18 years, and hospitalization or consultation of a physician at the Department of Internal Medicine, Medical University of Graz. The period of investigation was January, 1st, 2007 until December 31st, 2012. Group 1 (2007-2011) included 40 patients, group 2 (2012) was formed out of 42 patients.

In 2012, patients were diagnosed significantly faster than in the past years. Worsening of general condition and arthromyalgia were significantly more frequent in group 1 while more patients were found to suffer from back pains in group 2. Petechial bleeding was found to be more frequent in 2007-2011. First measured levels of haemoglobin, haematocrit and ALT were significantly higher in group 1. Tendencies showing lower levels of thrombocytes as well as higher levels of CRP and urea have bee found in the years 2007-2011. Patients needed dialysis significantly more often in 2007-2011 than in 2012.

Clinical presentation of hantavirus disease shows slight variations in the different years, as the expression of symptoms varies. Possible explanations for a faster diagnosis and the low rate of patients being put on dialysis in 2012 are a heightened public awareness, leading to faster diagnosis and treatment making dialysis unnecessary, or that course of illness was less severe in 2012.

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Glossary and list of Abbreviations

A. agrarius	Apodemus agrarius
A. flavicollis	Apodemus flavicollis
ALT	Alanine aminotransferase
aPTT	activated partial thromboplastin time
ARDS	Acute respiratory distress syndrome
AST	Aspartate aminotransferase
CPAP	Continuous positive airway pressure
CRP	C-reactive protein
DOBV	Dobrava-Belgrade virus
ELISA	Enzyme-linked Immunosorbant Assay
GFR	Glomerulary filtration rate
Hb	Hämoglobin
HCPS	Hantavirus cardio-pulmonary syndrome
HFRS	Haemorrhagic fever with renal syndromes
HKT	Hämatokrit
HPS	Hantavirus pulmonary syndrome
ICU	Intensive care unit
IgG	Immunglobulin G
IgM	Immunglobulin M
kb	kilobit
KHF	Korean haemorrhagic fever
L	large
LDH	Lactate dehydrogenase
M	medium
MDRD	Modification of diet in renal disease
MEDOCS	Electronic communication and information system of the styrian state hospitals and the University

	Hospital of Graz
mRNA	messenger Ribonucleic acid
n	number
NE	Nephropathia epidemica
NS	Non structural protein
p	probability
POC	Point of care
POCT	Point of care test
PUUV	Puumala virus
R. norvegicus	Rattus norvegicus
RNA	Ribonucleic acid
RT-PCR	Reverse transcription polymerase chain reaction
S	small
SAAV	Saaremaa virus
SD	Standard deviation
SEM	Standard error of mean
SEOV	Seoul virus
TULV	Tula virus

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1 Introduction

1.1 A short history of Hantaviruses

Even if the symptoms of hantavirus infections have been known for hundreds of years in eastern Asia, the aetiology remained unknown until the 20th century (1). When during the Korean War (1950-1952) thousands of US troops contracted a disease marked by haemorrhagic fever and acute renal failure with shock, hantavirus infection with renal syndrome (HFRS) became better known to western medicine, too. However, the aetiological agent causing the disease remained a mystery (2).
In 1978, the Korean researcher H. W. Lee isolated a unique Orthobunya virus from field mice (A. agrarius) found near the Hantaan river in Korea (2,3). The virus was identified as the cause of haemorrhagic fever with renal syndrome, as the lung tissues of the mice contained specific antigens reactive with serum samples of HFRS patients. The new virus was named after the place of its discovery, the Hantaan river, the Hantaan virus. Since then, several related viruses have been found all over the world by a similar approach, each associated with different species of rodents, causing HFRS related diseases like Nephropathia epidemica (NE) and others (1,2,4,5).

1.2 Genome

Hantaviruses are members of the family of Bunyaviridae, encapsulated RNA-viruses, named after their prototype, the Bunyamwera virus, found in Bunyamwera, a locality in Uganda (3,4). The family includes over 100 members in five genera, Hantavirus is the only genus of Bunyaviridae, which is not an arbovirus (2,3).

Bunyaviridae (2,3)**:**

- Genus: Orthobunyavirus (Bunyamwera supergroup)
- Genus: Phlebovirus (Sandfly fever viruses)
- Genus: Nairovirus (Nairobi sheep disease-like viruses)
- Genus: Topsovirus (Tomato spotted wilt virus)
- Genus Hantavirus (Haemorrhagic fever with renal syndrome viruses)

Orthobunya-, Phlebo-, Nairo-, and Hantavirus are known to be pathogenic for humans. The Bunyaviruses have an average size of 80-120 nm in diameter, a spherical form and a lipid envelop, which is interrupted by stubby spikes made out of glycoprotein (4). The genome of Bunyavirus is a negative-sensed single stranded RNA in three segments, associated with three nucleocapsid-proteins (2,6). The three segments are L (large), M (medium) and S (small), with sizes of 7, 4 and 2 kb. The total length of genome is 11-19 kb (3). A schematic drawing of a Bunyavirus is shown in Figure 1.

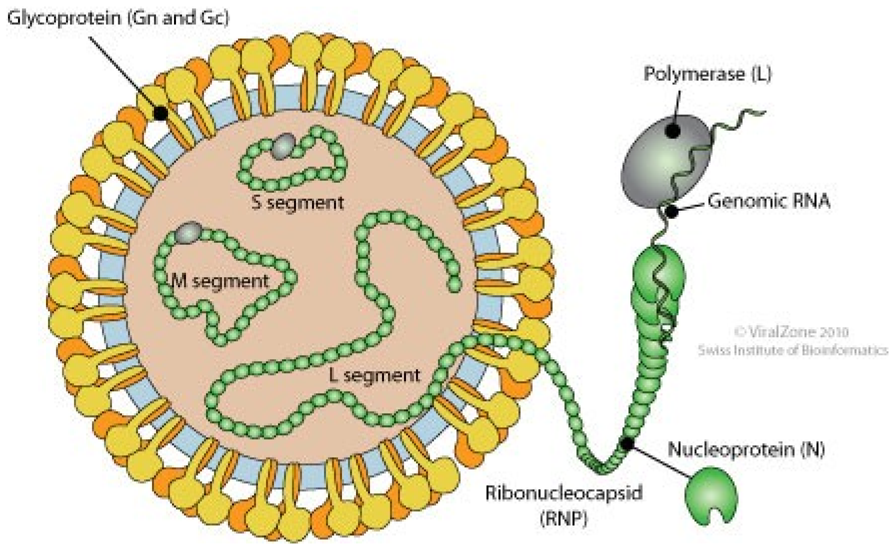

Figure 1: Schematic drawing of a Bunyavirus (7).

Replication takes place by attachment of the viruses to a cellular receptor via glycoproteins. After endocytosis, the helical nucleocapsids are invading cytoplasm by fusion with endosomal membrane (3,6). Virus transcription and translation entirely takes place in cytoplasm. First, the virion transcriptase transcribes sugenomic mRNA from each of the three virion RNA segments (L, M, S), while still associated with their nucleocapsids. This process can begin as soon as nucleocapsids are set free into cytoplasm. After translation of these mRNAs, replication of the virion RNA can occur (2–4). The large segment (L) encodes for the RNA polymerase, the medium segment for two envelop glycoproteins and the S-segment encodes the nucleocapsids as well as, in some genera, the non structural protein NS (2,4). Maturation and accumulation takes place in the Golgi apparatus, releasing occurs by exocytosis or cellular lysis (6). Table 1 shows the five genera of Bunyaviridae and some of the serotypes with their resulting diseases, hosts, vectors and the distribution.

Genus/ Virus	Host/ disease	Vector	Distribution
Orthobunyavirus			
Oropouch virus	Human: Fever	Midge, mosquito, sloths, monkeys	S. America
La Crosse virus	Human: Encephalitis	Mosquito, squirrels, chipmunks	N. America
Akabane virus	Cattle: Abortion and congenital defects	Midge, mosquito	Africa, Asia, Australia
Hantavirus			
Hantaan virus	Human: Severe haemorrhagic fever with renal syndrome (HFRS)	Field mice	Asia, Eastern Europe
Puumala virus	Human: Mild HFRS, Nehropathia epidemica (NE)	Bank voles	Western Europe, Scandinavia
Sin Nombre virus	Human: Hanta virus pulmonary syndrome	Deer mice	North and South America
Dobrava-Belgrade virus	Human: HFRS, NE	Yellow-necked-mice	Balkans, Central Europe
Seoul virus	Human: NE, HFRS	Rats	Worldwide

Table 1: Genera of Bunyaviridae with their most important serotypes, vectors and distribution (1,2,6,8).

Genus/ Virus	Host/ disease	Vector	Distribution
Nairovirus			
Crimean-Congo haemorrhagic fever virus	Human: Haemorrhagic fever	Tick, sheep, cattle, goats	Eastern Europe, Asia, Africa
Nairobi sheep disease virus	Sheep, goats: Fever, haemorrhagic gastroenteritis, abortion	Tick	Eastern Africa
Phlebovirus			
Rift Valley virus	Human: Encephalitis, haemorrhagic fever, retinitis	Mosquito,buffalo, goats, sheep, cattle	Africa
Sandfly fever virus	Human: Fever	Sandfly	Europe, Africa, Asia
Tospovirus			
Tomato spoted wilt virus	Plants: Various symptoms in more than 600 plant species	Thrips	Worldwide

Table 1 cont'd.: Genera of Bunyavirus with their most important serotypes, vectors and distribution (1,2,6,8).

1.3 **Virus-host relationship**

At least 11 human pathogenic and in total 22 serotypes of Hantavirus are known, five of these are common in Europe (1,6). Unlike other Bunyaviruses, the Hantavirus is not spread to humans by arthropod vectors such as sand flies, mosquitoes or ticks, but by rodent hosts (6). The infection is a zoonotical one, the virus causes persistent infections in rodents (8). A reservoir may be provided also by birds or other mammalians (6). For the rodent vectors, the infection is absolutely apathogenic, even if the virus load is high in lungs and kidneys of infected animals, and persists lifelong. The virus is shedded by saliva, urine and excreta. Transmission to humans occurs by inhaling the aerosolized excretions (9), as shown in Figure 2. Notably, a person-to-person transmission of Hantavirus does not occur. The only exception is probably the serotype of Andes virus in South America (8,10).

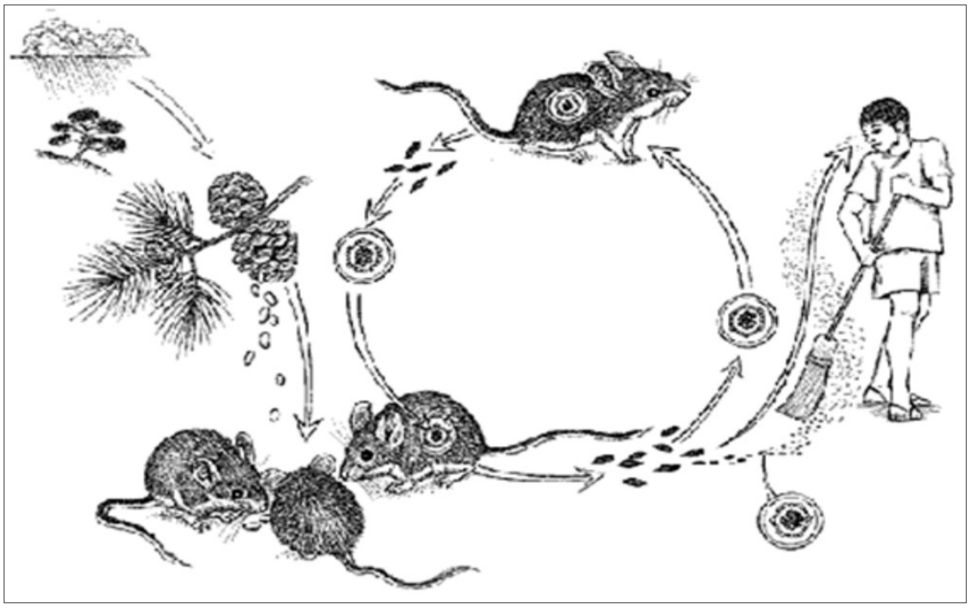

Figure 2: Transmission of Hantaviruses (11).

Each serotype of Hantavirus is normally carried by its own specific host; the virus coevolves with its carrier (compare Table 2). As more rodent species are studied, the number of serotypes of Hantaviruses will probably increase, too (1,5,8,9).

Virus/ serotype	Carrier rodent	Disease	Distribution
Hantaan	Apodemus agrarius, Apodemus flavicollis	HFRS, Korean haemorrhagic fever (KHF)	South-eastern Asia
Seoul	Rattus norvegicus, Rattus rattus	HFRS, mild KHF	Worldwide
Puumala	Myodes glareolus	HFRS, NE	Western and central Europe, Scandinavia
Dobrava- Belgrade	Apodemus flavicollis	HFRS, severe KHF	Central and eastern Europe, Balkans
Saareema	Apodemus agrarius	mild HFRS	Eastern and northern Europe
Sin Nombre	Peromyscus maniculatus	Hantavirus pulmonary syndrome (HPS)	Western and middle USA
Bayou	Oryzomys palustris	HPS	N. America, USA
New York	Peromyscus leukopus	HPS	N. America, Mexico
Black creek canal	Sigmodon hispidus	HPS	South-eastern USA
Andes	Oryzomys longicaudatus	HPS	S. America, Chile, Argentina
Laguna Negra	Calomys laucha	HPS	S. America, Paraguay

Table 2: Serotypes of Hantavirus. Vectors, caused disease and distribution (2,6,8).

1.4 **Epidemiology**

The viruses were named after the different geographic locations they were found in. Puumala virus was identified in bank voles (Myodes glareolus, formerly also known as Clethrionomys glareolus (9)) in Puumala, Finland. The Seoul virus was found in rats (Rattus rattus, Rattus norvegicus) in Korea. The Dobrava-Belgrade virus, a further distinct European Hantavirus, was isolated from yellow-necked mice near the Slovenian village Dobrava. Later, a related virus was found in field mice (A. agrarius) at the Saaremaa island, Estonia. The Tula virus, found in Microtus arvalis, the European common vole, in Tula, Russia, was not definitely shown to be associated with disease (1,2,8,12).

In the Americas, Hantavirus was unknown until 1993, when a mysterious outbreak of a new disease occurred in the south-western states of the USA. Influenza-like symptoms, with a rapid aggravation leading to acute respiratory distress and a mortality rate of 50% were mostly observed in healthy young adults. Serological and epidemiological findings showed a virus implicated to Hantaviruses but differing genetically from those causing HFRS. This new virus, called the Sin Nombre virus (formerly also known as Muerto canyon virus (2,13)), was found to be predominantly in northern and southern America, carried by Peromyscus maniculatus, the deer mouse (8). Subsequently, the virus was discovered in many states of the Americas in various other rodent species (Andes virus, Laguna Negra virus in South America, Bayou, New York and Black Creek Canal virus in North America). All of these viruses belong to the genus Hantavirus (1,2,4,8).

Epidemiologically, there are three different patterns of disease according to the place of acquirement: rural, urban and laboratory acquired. Each comes along with a different carrier-virus combination.

Concerning urban and laboratory-acquired infections, Seoul virus, widespread among common rats (Rattus rattus and R. norvegicus) all over the world, has been identified as the cause. Common, especially in seaports, the disease is transmitted to caretakers of animals and research personnel (2).

The rural type is the most common one. In China and Asia it is predominantly caused by the Hantaan virus carried by field mice, in the Americas it is caused by the Andes and the Sin Nombre virus, transmitted by the long tailed-rice mice and the deer mice. In South and Eastern Europe the Dobrava-Belgrade virus carried by the yellow-necked mice and finally the Puumala virus in western and northern Europe, carried by the bank vole are considered to be the most frequent causes of rural infection. Hence, geographical distribution of the viruses varies with the prevalence of the different rodent carriers (1,2,4,8).

In Europe, at least five serotypes of Hantaviruses can be found: Puumala virus (PUUV), Dobrava virus (DOBV), Saaremaa virus (SAAV), Tula virus (TULV) and Seoul virus (SEOV). Depending on the virus type, infections are characterized by mild (for example the Seoul virus) to severe (Dobrava-Belgrade virus) forms of haemorrhagic fever with renal syndrome. Nephropathia epidemica (NE), counting to mild HFRS, is caused by Puumala virus (14). The geographical distribution of Hantaviruses in Europe is shown in Table 3.

European countries	Puumala virus	Dobrava-Begrade-virus	Saaremaa virus	Tula virus	Seoul virus
Austria	x	x(2012)	x(2012)	x	
Belgium	x			x	x
Bosnia and Herzigovina	x	x			
Bulgaria	x	x			
Cyprus					
Czech Republic	x	x		x	
Denmark	x				
Estonia	x		x		
Finland	x		x	x	
France	x			x	x
Germany	x	x	x	x	
Greece		x			
Hungary	x	x	x	x	
Italy					
Ireland	x				x
Lithuania	x	x	x	x	
Luxembourg	x				
Netherlands	x			x	
Norway	x				
Poland	x	x			

Table 3: Distribution of Hantavirus serotypes in Europe (12).

European countries	Puumala virus	Dobrava-Begrade-virus	Saaremaa virus	Tula virus	Seoul virus
Portugal					x
Romania	x	x			
Russia	x	x	x	x	x
Slovakia	x	x	x		
Slovenia	x	x	x	x	
Spain					
Sweden	x				
Switzerland					
Turkey	x	x			
United Kingdom					

Table 3 cont'd.: Distribution of Hantavirus serotypes in Europe (12).

Human epidemiology of HFRS and NE varies according to the rodents dynamics. Furthermore, epidemics are spatially associated with the habitats of Hantavirus carrying rodents.

In northern Europe, population density cycles of 3-4 years for bank voles are common. As a covered RNA virus, Hantaviruses are surprisingly stable to temperature. They can survive >10 days at room temperature and >18 days at +4°C to -20°C. Together with the population cycles of the rodents in northern European countries, this explains the human epidemic peaks in northern Europe (1,10).

In temperate Europe, the population of bank voles but also of other forest rodents is more stable. Due to temperate climate there is a short lasting peak at the end of autumn. As forests are more fragmented in central Europe, local patches of high population densities of rodents are found. Consequently, in these areas outbreaks of forest rodents such as the bank vole and the yellow-necked mouse (A. flavicollis) are following mast years, warm summers with heavy beech, oak and acorn crops. Additionally, it has to be considered that it takes 1-2 years for a rodent peak to develop. Accordingly, current climate conditions during an epidemic are not the primary cause even though they may contribute to it. Cycles of 3-5 years are observed also in central Europe. Unlike in the northern parts, in western and central Europe rodent peaks are reached in spring or summer with a minor one in autumn and early winter. This occurs because after mastening in the autumn, the winter survival is good, breeding is started earlier and the highest density of population is reached earlier in the year (1,8,10).

1.5 **Hantavirus infection: Clinical presentation**

Of the two hantaviral diseases, the haemorrhagic fever with renal syndrome (HFRS) and the hantavirus (cardio) pulmonary syndrome (HCPS or HPS), only the first, the HFRS, is caused by European Hantaviruses (8,15,16).

1.5.1 Haemorrhagic fever with renal syndromes

HFRS and NE severity ranges from mild (NE) to severe (HFRS) infection, the mortality is at about 5%. Typical onset symptoms are influenza-like, malaise, cephalea and fever, followed by abdominal and back pain, nausea, vomiting, diarrhea and finishing in hypotension and haemorrhagia, accompanied by acute renal failure. Laboratory findings include thrombocytopenia, proteinuria and increase of urea and renal parameters. More rarely, but very typical, impairment of vision (acute myopia) occurs. Pulmonary involvement and multiorganic failure is possible(10,17). The patients are mainly male (1,2,4,8,17).

1.5.2 Hantavirus (cardio-) pulmonary syndrome

HCPS, also known as HPS, is characterized by interstitial pneumonitis with oedema and pleural effusion, dyspnoea, tachycardia, hypotension and eventual cardiogenic shock. The onset happens very sudden. The first symptoms are unspecific and influenza-like. Thrombocytopenia is common but without severe haemorrhagia. Development of hepatitis is possible. Death is due to acute respiratory failure or cardiogenic shock. Mortality is very high with rates of 40-60%. The distribution of sex is described as equivalent (4,8).

1.6 Hantavirus infection: Diagnosis and treatment

Hantavirus infection should be suspected if high fever is accompanied by acute renal failure, head or backache, thrombocytopenia, leucocytosis and ocular findings. Because of the variety of symptoms, the diagnosis should be confirmed serologically via ELISA (IgM, IgG), RT-PCR or immunofluorescence tests on infected Vero cells. IgG increase can persist for decades and infection is thought to cause a lifelong immunity (1,4,8,10,18).

Therapy of hantavirus infections is mostly supportive. Especially maintaining the fluid and electrolyte balance is of critical importance. In case of acute renal failure, refractory to conservative management, dialysis may be necessary. Some studies reported the benefit of early antiviral treatment with Ribavirin, showing reduced rates of mortality and severity of symptoms. Generally, antiviral therapy is not necessary in NE (1,4,8,17).

Vaccines based on inactivated viruses were developed and used in Korea, China and widely across Asia, but are not yet available in Europe (1,8,10,17).

According to the prevalence, avoiding the exposition is of highest importance. The risk of transmission is more evident indoors, where rodents are seeking food or shelter, than outdoors. Particular risk is associated with opening, occupying and cleaning structures such as wood shelters, summer cottages, stables, barns, cellars and attics but even with simple rural work in gardens and woods. Especially farmers, hunters and soldiers are exposed to a higher risk of hantavirus infections because of rural environment with potential contact to rodents' excrements, urine and saliva. Infections may be avoided by using masks. Rodent control and rodent-proof buildings in endemic areas prevents them from shedding viruses and can reduce morbidity(1,2,5,8,10).

1.7 Hantavirus infections in Austria

In Austria, the predominant serotype of the Hantavirus is the Puumala virus (PUUV), carried by the bank vole Myodes glareolus (12,19), as shown in Figure 3.


Figure 3: Clethrionomys glareolus, now Myodes glareolus, the bank vole (20).

As mentioned above, the virus causes NE, the mildest form of HFRS, with a rate of mortality between 0,1%-0,2%. In Austria, three cases of death caused by Hantavirus have been reported so far (21). The seroprevalence in Austria ranges from 0,08% to 1,8%. NE was diagnosed for the first time in Austria in 1993, but it has to be considered that NE infections were most probably underestimated in the past (9,22). In the late nineties, hotspots of Puumala virus infections were located in Carinthia, especially in the Lavanttal, the area around Wolfsberg, some areas in Styria and Lower Austria(19). However, the geographical distribution shifted, as more and more infections were diagnosed in Styria, which can be seen in Figure 4 (21,23).

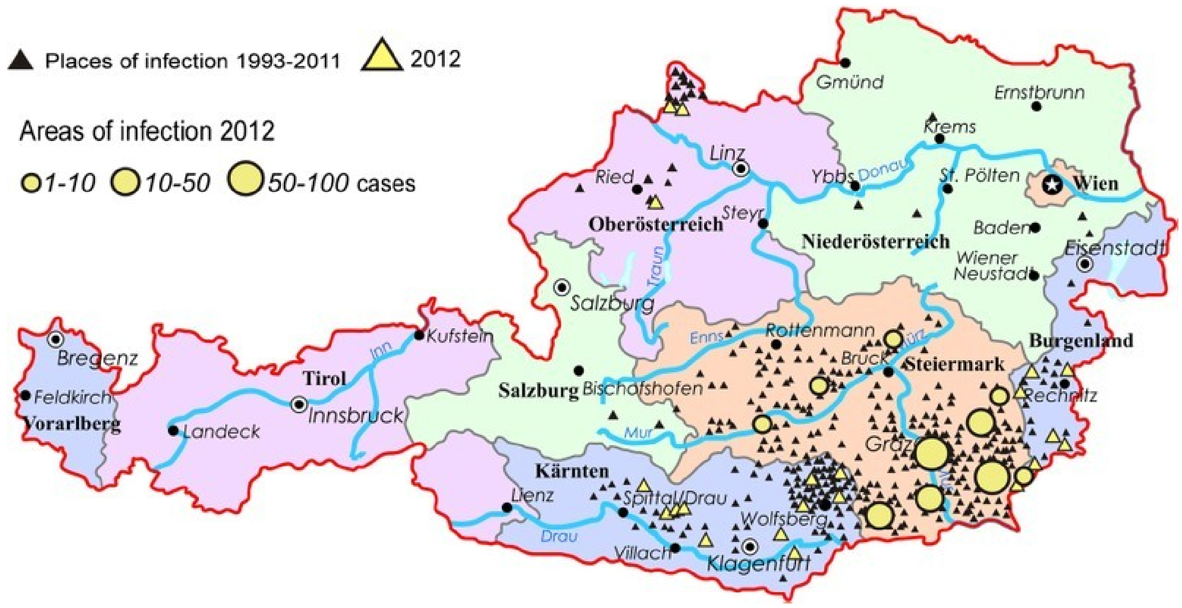

Figure 4: Hantavirus infections acquired in Austria (21).

In the past, the average infection rate was 20 cases of NE per year. In 2007, a peak was observed (78 cases in Austria, 47 cases of infection in Styria), until then the year with the highest infecton rate since beginning of surveillance. Similarly, there was a slight increase in 2011 with a total of 44 patients (n=29 in Styria) (23,24). As in 2011 the peak was found to be in February, an unexpected cold at the end of January 2011 was supposed to be the reason of an increased sheltering in houses and barns and consequently virus shedding of the bank voles. Simultaneously, Germany, which was also touched by the extreme cold, reported increased rates of NE-cases (23). One patient with verified Dobrava virus infection was hospitalized at the University Hospital of Graz in 2011. The case is assumed to be the first autochton infection with the Dobrava-Belgrade virus in Austria (23).

In 2012, a massive outbreak of Puumala virus infections took place in Austria. 264 cases were reported, which means more than seven times the annual average of 2011. Again, the hotspot of infections was located in Styria: 232 cases (88%) were diagnosed in this region. Interestingly, two cases of autochton Dobrava virus infections occurred in 2012 and another so far in 2013. One case of autochton Saaremaa virus infection was observed in 2012. As in the past years, the patients of infection were mostly male (73% in 2012), and rather young (the average was 41 years in 2012). Neither Austria nor Slovenia, where a similar outbreak has been reported, have observed a comparable number of hantavirus infections ever before. An astonishing high number of hantavirus disease infection in 2012 was also reported from Germany, as well as an epidemic of Sin Nombre virus in the United States in summer 2012 (16,21).

1.8 **Aims**

The aim of this retrospective study was to investigate differences in epidemiology, clinical presentation, laboratory results, treatment, and outcome of Puumala virus infections in the Graz region, diagnosed and treated at the Department of Internal Medicine, Medical University of Graz. Forty-two patients of the peak year 2012 were compared to patients of the ″normal” years 2007-2011 where an average of eight infections were observed.

2 Methods

The study was carried out at the Department of Internal Medicine, Medical University of Graz. Therefore, only patients above the age of 18 years diagnosed with Puumala virus infections using point of care Puumala and Hantaan IgM test (Reagena, Toivala, Finland) at the microbiology laboratory, Department of Internal Medicine, Medical University of Graz between January 1, 2007 and December 31, 2012 were included. Patients younger than 18 years of age are diagnosed and treated at the Department of Paediatrics. Patients with an indeterminate result of the Reagena® IgM test but confirmed diagnosis of Puumala virus infection by IgM and IgG ELISA-testing on Puumala virus done by the Department of Virology of the Medical University of Vienna were included in the investigation.

All patients with diagnosed NE between 2007 and 2011 that were regarded as “normal” years, considering the number of infected patients in each of those years, formed group 1. We chose a period of five years with an average of eight cases a year. This was done to achieve approximately the same sample size as 2012. All patients with diagnosed Puumala virus infection in 2012 were assigned to group 2. 2012 was regarded as a peak year because of an extraordinary number of infections (232 cases in all Austria) compared to the former Austrian annual mean (20 cases). Group 1 (patients from 2007-2011) included 40, group 2 (patients from 2012 only) 42 patients.

Patient data was retrieved from the clinical computational system MEDOCS, as not all data for all patients was available or documentation was inaccurate, the number of patients for the different results may vary.

For recruitment, all patients between 2007 and 2012, who had been tested on Hantavirus at the University Hospital of Graz, were selected. This research was done by checking the record of the laboratory, as we presumed every patient who has passed the testing on Puumala virus to be registered.

The main including criteria were already determined before starting the group assignment. Because we did not expect any differences in clinical presentation and outcome regarding the sex, during assignment of groups it was not considered a relevant criterion on differentiation during observation of clinical presentation.

Furthermore, the number of cases was too small to allow any further division, and still obtain sensible statistical results.

2.1 Parameters of evaluation

To investigate differences in clinical presentation, epidemiology and outcome between the patients of "normal" years of hantavirus infections (2007-2011) and those of the overshooting peak year 2012 should be investigated. Therefore, the following parameters were evaluated in both groups:

1) The distribution of patients' characteristics such as sex, age and a potential comorbidity were evaluated. Concerning comorbidity we investigated for a major risk of a more severe manifestation of disease at the basis of comorbidity. Comorbidities were evaluated by calculating the Charlson Comorbidity Index Score Calculator.

2) Epidemiological data: The probable environment - according to the accomplished activity - at the time of virus exposition and the way of virus' transmission as well as the most likely place of acquiring Puumala virus infection was evaluated for each patient. For the first parameter, the most probable environment of virus exposition, we classified into "free time activities", "domestic work", "job-related" and "unknown". Concerning the most likely way of virus' transmission, "unknown", "airborne", "transmission by bite" and "transmission by skin contact" were determined. Furthermore, we tried to localize the assumed place of virus transmission by reviewing the patients' history. Therefore, we did a demographic mapping of the cases of infections in the various political districts of Styria. Based on these data and the patients' description of first symptoms, a presumed time of incubation was determined. Additionally, a figure of the monthly course of Puumala virus infection rate was drawn, according to the date of patients' first visitation of a physician.

3) Data on diagnosis: The period between patients' first perception of signs of illness and the date of first consultation of a physician with symptoms leading to diagnosis was evaluated. The date of Reagena® POC, the results of the test and the period between first consultation until diagnosis (via Reagena® POC) was analyzed. According to documentation in the patients' clinical record, the number of cases

mentioning “Puumala virus infection“ or “hantavirus infection“ as main differential diagnosis after the first clinical examination was evaluated by simple calculation.

4) Clinical presentation and symptoms: The first six symptoms, urging each of the 82 patients to go to hospital, were recorded, according to the clinical case reports. The objective clinical severity of symptoms was not decisive for recording, but the subjective report of patients in first history:
Fever, cephalea and retroocular pains, decrease of general condition, respiratory symptoms like cough and other infections of the respiratory tract coming along with dyspnoea, arthromyalgia, shivering, back pain, renal and flank's hurting were remarked. Further, trigger mechanism of Herpes labialis, vision disorders, gastrointestinal discomfort including worse abdominal pain, nausea, vomiting, diarrhea, meteorism, constipation and gastro-oesophageal reflux, dizziness, urinary changes like oliguria, anuria and macroscopic haematuria; and finally, fatigue, faintness and lassitude were described by the patients.

5) Signs on first clinical examination: Concerning the first clinical examination, ten parameters of clinical significance were chosen to be investigated, according to their frequency and importance in Puumala virus infections (5,9,12,18,25). Patients’ case reports were checked for initially measured blood pressure, temperature, petechial bleeding, oedema of either face or extremities, shade-loving and meningism, conjunctival bleeding, scleral bleeding, conjunctivitis, impaired vision in the sense of a Puumala virus infection typical pseudomyopic shift and irregularities of renal function at the time of first hospital consultation.

6) Clinical signs and symptoms in the course of the disease: For a better overview of the general condition and state of illness of the patients, the clinical findings from first clinical examination mentioned above (petechial bleeding, conjunctival bleeding, scleral bleeding, conjunctivitis, impaired vision and renal irregularities), were followed up during the whole hospital stay of patients.

7) Data on diagnostic work up: To complete clinical examination, specifics in thoracic radiology (X-ray or computer tomography) as well as abdominal radiology (sonography or computer tomography) were inquired. The radiological investigation referred to organs of whom pathological radiologic findings were already reported such as the

kidneys, spleen and lungs (1,18,26). To undertake statistical interpretation, groups of radiological findings were assigned. In thoracic radiological diagnostic, five groups were formed:

- No X-ray or computer tomography was done.
- No atypical finding was shown by the performed method.
- Pleural effusions were observed
- Pleural effusions coming along with pulmonal infiltrations were described.
- Appearance of the last two mentioned together with pneumothorax.

Concerning abdominal radiology, we divided the findings into the following eight groups to become statistically recorded:

- No abdominal radiology performed
- No conspicuous changes found
- Splenomegaly
- Alterations of the kidneys
- Abdominal effusion (ascites) coming along with splenomegaly
- Splenomegaly seen together with changes of the kidneys
- Splenomegaly, ascites and kidney's alterations
- Ascites and alteration of kidneys in abdominal sonography.

8) Laboratory results at first presentation: The most typical laboratory findings in the acute phase of Puumala virus infection are already well-established (4,17,18,25,26). Reportedly common are leucocytosis, thrombocytopenia, atypical lymphocytes, increased serum levels of C-reactive protein (CRP) and creatinine, as well as haematuria and proteinuria (17,18). Furthermore, white blood cells, haematocrit, urea and GFR (calculated by MDRD), LDH, levels of liver parameters ALT and AST and aPTT have been observed. For this investigation, all those seemed to be interesting for evaluating the patients' state of illness, and important to interpret the course of disease.

9) Maximum and minimum values of laboratory results: The pathological peak values of C-reactive protein, creatinine, urea, haematuria and proteinuria were investigated.

Furthermore, the minimum values of thrombocytes and GFR (MDRD) were investigated. The parameters were chosen because of being assumed to be the most fitting ones for description of the course of Puumala virus infection.

10) Data on treatment: Due to our intention of observing the follow up of the patients infected with Puumala virus, the duration of stay in hospital was calculated out of the data. For evaluating the way of treatment, the number of patients who were treated outpatient and just needed an outpatient control as long as diseases' complete cure was confirmed, was analyzed. Furthermore, the number of patients who needed to stay in hospital was investigated. If outpatient treatment had taken place, the number of times the patient had to come to an outpatient visit at the hospital was taken into account. Concerning the inpatients, an eventual outpatient control after dismission of the hospital was not taken into account, being no point of interest for this work.
In addition, the number of patients who needed intensive care at the ICU during their hospital stay and their average duration of stay at the Intensive care unit were evaluated. Furthermore, parameters of needed intensive care were allocated: Dialysis, artificial ventilation, meaning intubation and respiratory support like CPAP (Continuous Positive Airway Pressure) and application of oxygen.

11) Data on outcome: The overall outcome was divided into the subgroups complete healing, consequential damage or death of the patient.

2.2 **Statistical analysis**

For statistical analysis, IBM SPSS Statistics 20 was used. Initially, all data was divided in nominal, ordinal and metric values. Data on gender distribution, clinical presentation, diagnostic workup, epidemiology, data on treatment and outcome are expressed as percentage. Other data are expressed as mean value± standard error of mean (SEM).
All numeric parameters which were characterized by more than one variable and did not make any predication on comparison of the average were analyzed by Chi-square test and described in percentage and numerical data. If three variables or more have been used, symmetric measures were evaluated by Phi-Cramer V test.
For all data which were determined to compare the means of each group, we did the Kolmogorov-Smirnov-Z-pretesting. If significance could be shown, non-normal

distribution was assumed and Mann-Whitney U test was used. In cases of a non-significant result of the Kolmogorov-Smirnov-Z-pretest, Student’s t-test for independent control was used.

3 Results

Between 2007 and 2011, 59 of 651 tests on Puumala virus had positive results. During the same period, 481 patients out of 651 patients were also tested on Hantaan virus. Six of 481 performed tests on Hantaan virus were positive. Of note, all patients positive for Hantaan virus were positive for Puumala virus, too.
In seven cases, patients, who's POCT had been Puumala virus positive, were also tested on Dobrava virus. One of those showed a slightly elevated level of Dobrava IgM, which meant for this case a positive POCT on Puumala virus, Hantaan virus and Dobrava virus.

Seven patients had to be excluded of group assignment because of confirmation of a diagnosis other than Puumala virus infection, or contradiction of the POCT result by negative ELISA-testing on the Department of Virology of the Medical University of Vienna. Another 12 patients were excluded because of age under 18 years.

Consequently, the group representing the "normal" infection years 2007-2011 was formed by 40 patients, older than 18 years, positive Puumala virus point of care test at the microbiology laboratory, of the Department of Internal Medicine, Medical University of Graz. If the result of the POCT was not explicit, patients were also included when diagnosis was confirmed by ELISA testing at the Department of Virology of the Medical University of Vienna.

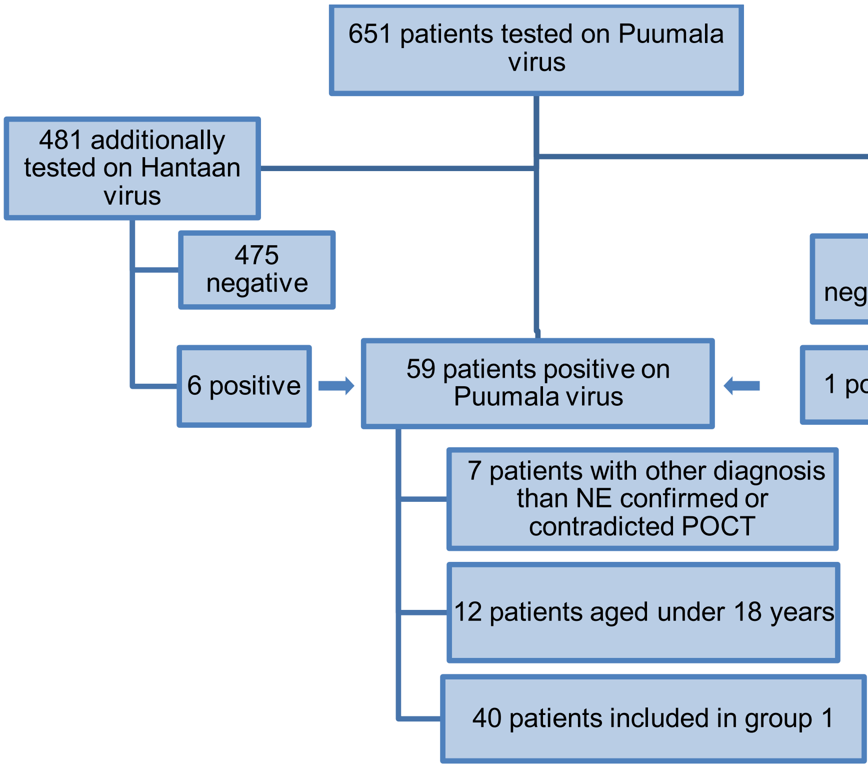

Figure 5: Assignment of group 1 (2007-2011).

The same procedure was used for all patients, who had been tested on Puumala virus in 2012. In this peak year of infections, 124 POCT's on Puumala virus occurred at the Department of Internal Medicine of Graz, 50 of these turned out to be positive.

In 88 among these 124 tested patients, it was found that also a Hantaan virus POCT had been done. In 2012, none of these were positive. Likewise, none of the two patients tested on Dobrava virus showed a positive result for Dobrava IgM in 2012.
In retrospective investigation of the clinical case reports, it was not possible to find a systematic proceeding in the accomplishment of point of care tests on the different virus species.
Since eight of the 50 patients positive for Puumala virus dropped out because of age beneath eighteen, 42 patients remained with ELISA- confirmed Puumala virus infection in group 2.

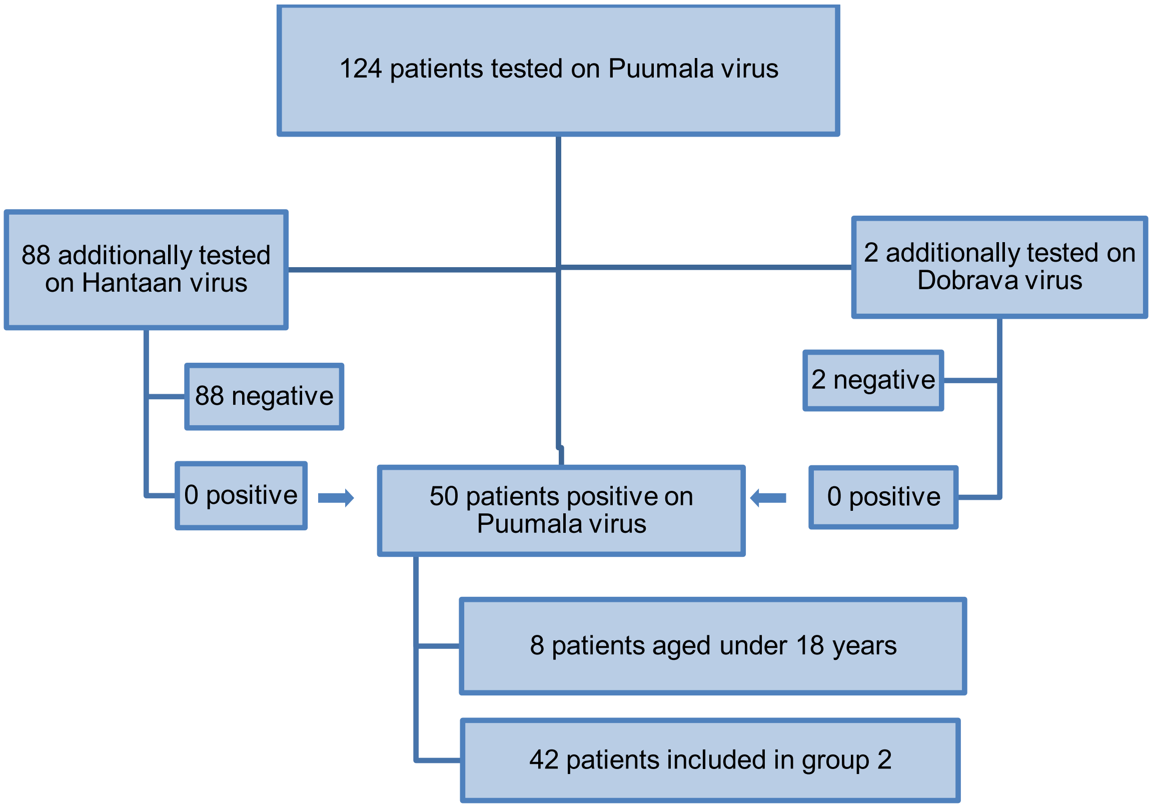

Figure 6: Assignment of group 2.

This difference in annual number of infections between 2007-2011 and 2012 was highly significant with p<0.0005 (see also Figure 7).

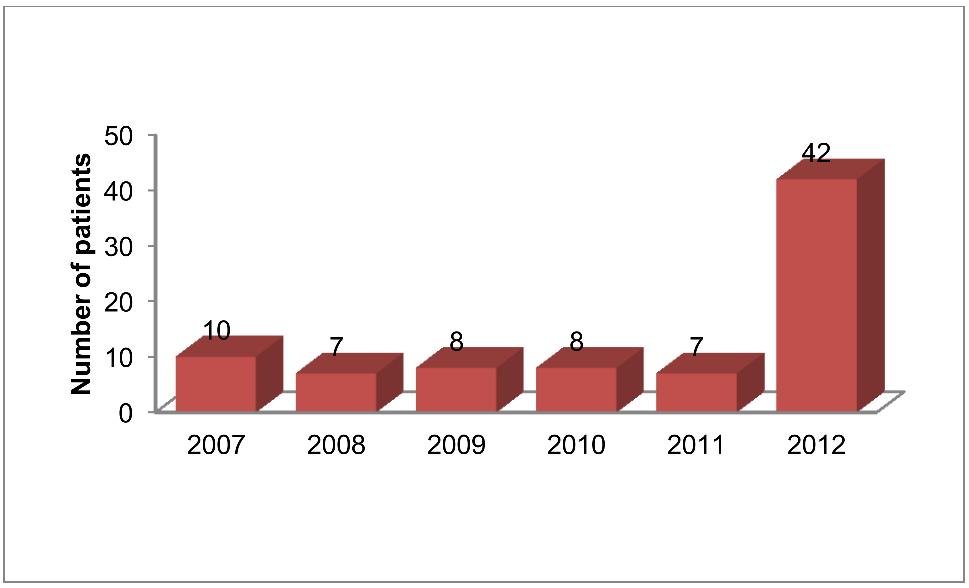

Figure 7: Number of patients infected with Puumala virus in 2007-2012, included to clinical research.

3.1 Statistical evaluation of patients' characteristics

The distribution of sex, age and comorbidities of patients were statistically evaluated.

3.1.1 Gender distribution

Focusing on the gender distribution, following data was found for the years 2007 to 2012 (see Table 4).

Group/Year	Sex		p-value (Chi-square)
	Female	Male	
Group 1 (2007-2011), n=40	11 (27.50%)	29 (72.50%)	0.522
Group 2 (2012), n=42	9 (21.40%)	33 (78.60%)	
Sum (2007-2012) n=82	20 (24.40%)	62 (75.60%)	

Table 4: Distribution of sex.

There was no significant difference found in the distribution of sex. Of note, in the overall an evident predominance of male patients can be observed (see Figure 8).

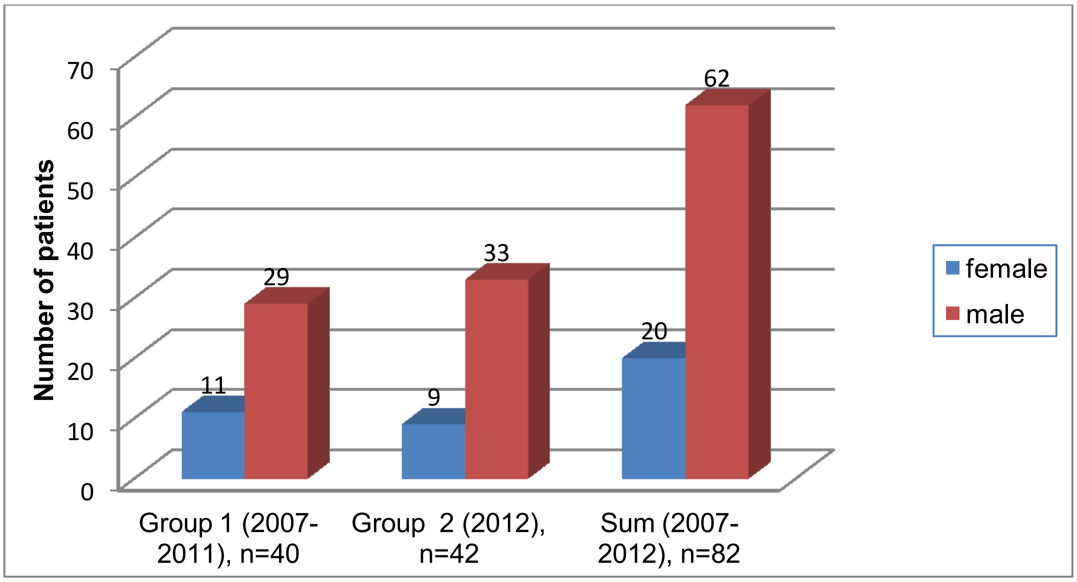

Figure 8: Gender distribution of Puumala virus infectons in 2007-2012.

3.1.2 Distribution of age

The average age in both groups was 39.78 years (SEM=±1.34). There was no significant difference between group 1 and group 2 (40.8±1.9 vs. 38.9±1.9 years, *p*=0.484).

3.1.3 Comorbidities

There was no significant difference in the distribution of the age adjusted Charlson score. However, a slight trend could be remarked, showing a difference in the distribution of age adjusted Charlson score between the two groups (*p*=0.133, Phi-Cramer V=0.266, see also Figure 9).

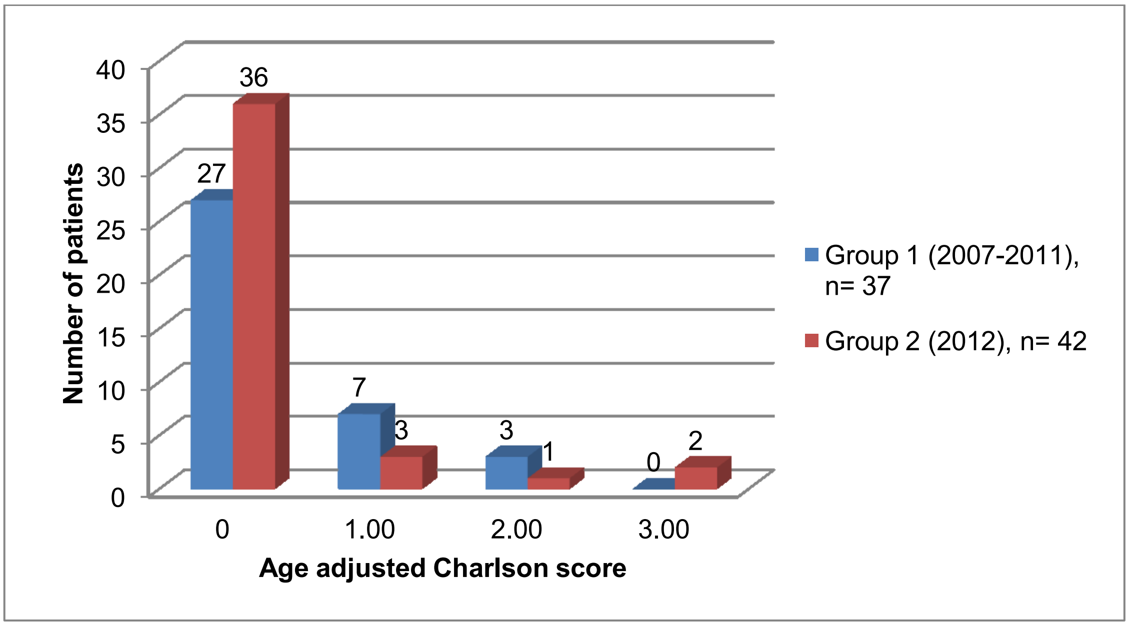

Figure 9: Age adjusted Charlson score.

Additionally, the collective mean (mean value=0.3, SEM=±0.1) and the annual mean of the score results were calculated (Table 5). The Mann-Whitney U test showed no significant difference (*p*=0.207).

Group	Mean value of Charlson score	Standard deviation	Standard error of mean	Kolmogorov-Smirnov Z	p-value (Mann-Whitney U test)
Group 1 (2007-2011), n=37	0.35	0.63	0.10	<0.0005	0.207
Group 2 (2012), n=42	0.26	0.11	0.73		

Table 5: Annual mean value of the age adjusted Charlson score.

3.2 Evaluation of epidemiologic data

Epidemiologic key data was statistically analyzed: the place of infection, the activity performed at the assumed moment of virus acquiring, the way of virus transmission, incubation time and the month of first consultation of a physician.

3.2.1 Place of infection

The distribution of the assumed places of infections between 2007 and 2012, according to political districts of Styria, are shown in Table 6. There was no significant difference shown in Chi-square between the groups (*p*=0.356, Phi-Cramer V=0.367).

Political district	Group 1 (2007-2012), n=40	Group 2 (2012), n=42	Sum (2007-2012), n=82
Graz	3 (7.5%)	3 (7.1%)	6 (7.3%)
Graz- Umgebung	13 (32.5%)	14 (33.3%)	27 (32.9%)
Weiz	2 (5%)	2 (5%)	4 (4.9%)
Voitsberg	2 (5%)	0.00	2 (2.4%)
Deutschlandsberg	1 (2.5%)	4 (9.5%)	5 (6.1%)
Leibnitz	4 (10%)	0.00	4 (4.9%)
Feldbach	4 (10%)	3 (7.1%)	7 (8.5%)
Hartberg- Fürstenfeld	1 (2.5%)	1 (2.4%)	2 (2.4%)
Judenburg	1 (2,5%)	0.00	1 (1.2%)
Liezen	0.00	1 (2.4%)	1 (1.2%)
Unknown	9 (22.5%)	14 (33.3%)	23 (28%)

Table 6: assumed places of Puumala virus infection in Styria between 2007 and 2012.

Figures 10, 11 and 12 depict the demographic distribution of the locations where infections are assumed to be acquired in 2007 to 2011, 2012 only and the overall (2007-2012).

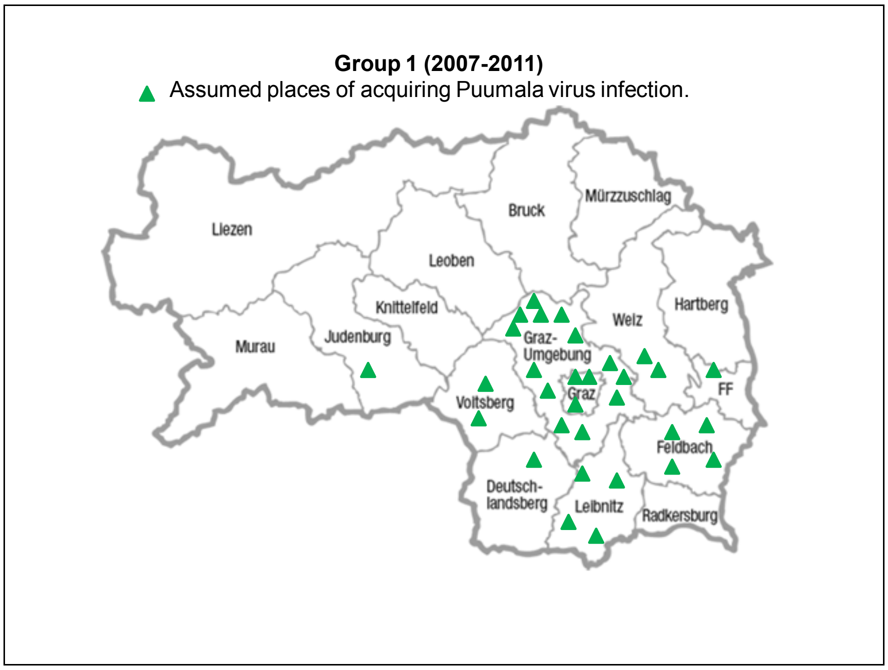

Figure 10: Demographic distribution of assumed locations of Puumala virus acquiring 2007-2011.

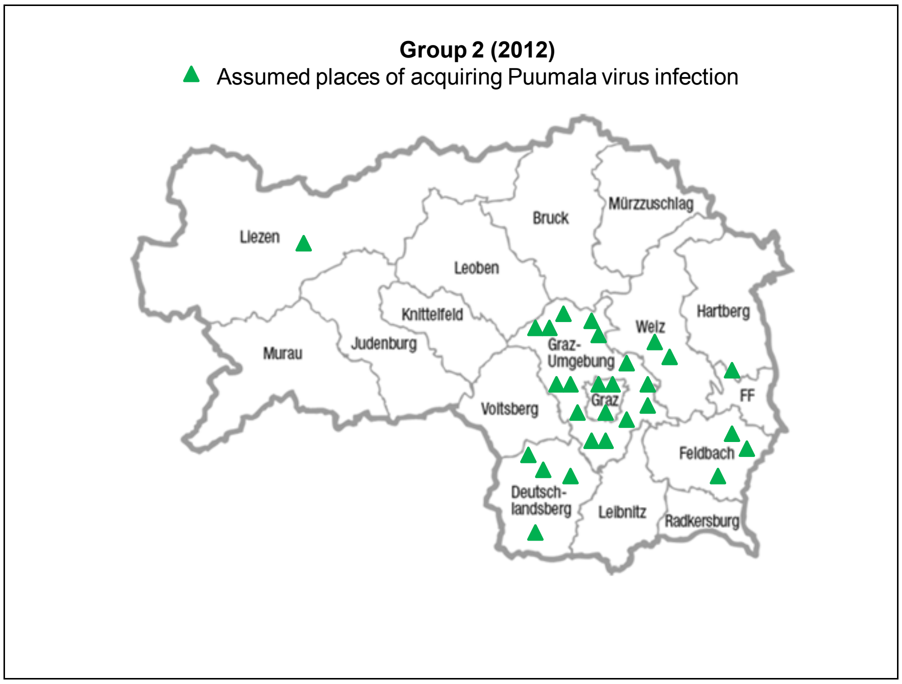

Figure 11: Demographic distribution of assumed locations of Puumala virus acquiring 2012.

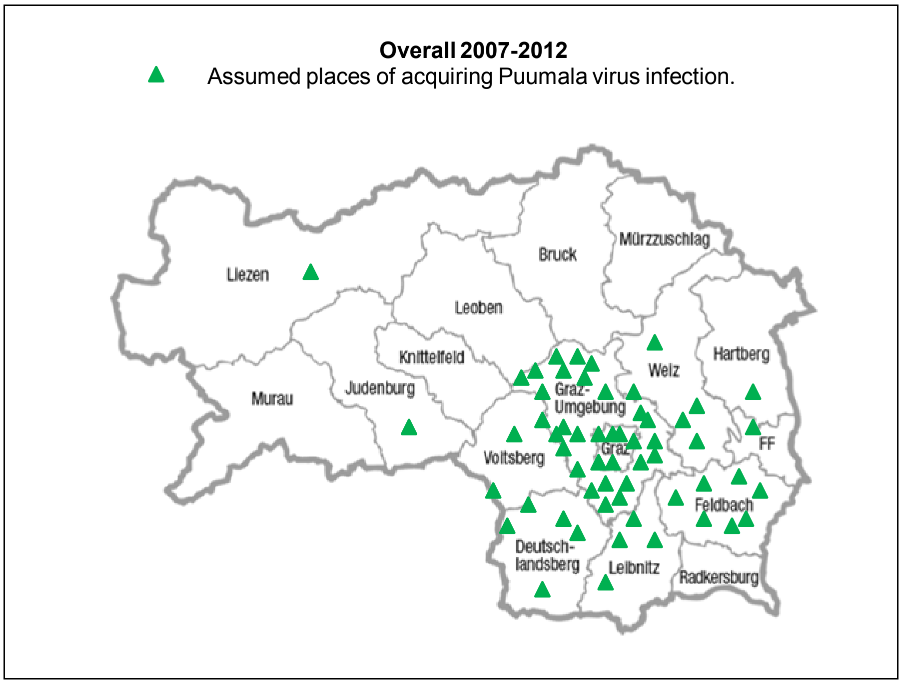

Figure 12: Demographic distribution of assumed locations of acquiring Puumala virus infections (2007–2012).

3.2.2 Activity leading to infection

In group 1, it was found that 22.5% (9 out of 40) of the patients were most probably exposed to Puumala virus when doing domestic work, 22.5% (9 out of 40) during professional work and 30.0% (12 out of 40) while their free time activities, as hiking, mountain biking, jogging and others. For 25.0% (10 out of 40) of the patients, the environment of viral exposure could not be determined.

In 2012, 16.7% (7 out of 42) were doing domestic work and 21.4% (9 out of 42) doing their professional work while being exposed to Puumala virus. Whereas, 26.2% (11 out of 42) were doing free time activities. For 35.0% (15 out of 42), the activity responsible for virus acquiring remained unknown. There is no significant difference between the two groups (p=0.742, Phi-Cramer V test=0.123).

3.2.3 Route of infection

In group 1, it was found that 65.0% (26 out of 40) of patients acquired Puumala virus infection by airborne transmission. 2.5% (1 out of 40) each were infected either by bite or via skin contact. In 30.0% (12 out of 40), the way of infection remained unknown.

The results for group 2 were similar: Here, 69% (29 out of 42) of the patients were found to have been probably infected by airborne route of transmission, while for 31.0% (13 out of 42), the way of virus acquiring could not be identified. In this group, none of the patients seemed to have acquired Puumala virus by skin contact or bite. There was no significant difference between the groups in Chi-square testing (p=0.541, Phi-Cramer V=0,162).

3.2.4 Time of incubation

The average time of incubation could be investigated in 11 of 82 cases, nine out of group 1 and two out of group 2. We calculated a general average of incubation time of 21.64 days, with SEM=±1.99.

The average incubation time of group 1 was 21 days (SEM=±2.33). In group 2, incubation time was not significantly higher (24.5 days, SEM=±3.5, Kolmogorov-Smirnov-Z=0.419, p=0.527).

3.2.5 Month of first consultation of a physician

A peak of infections occurred in April 2012, as 21% of all the first consultations occurred in this month (9 out of 42 patients). In the years of 2007-2011, a similar peak was evaluated, but beginning one month later, in May (6 out of 40 patients) and finally reached in June (7 out of 40 patients). Another short peak could be observed for group 1 in early autumn, as in August, another 15% (6 out of 40 patients) of the cases of this group were observed (see also Figure 13).

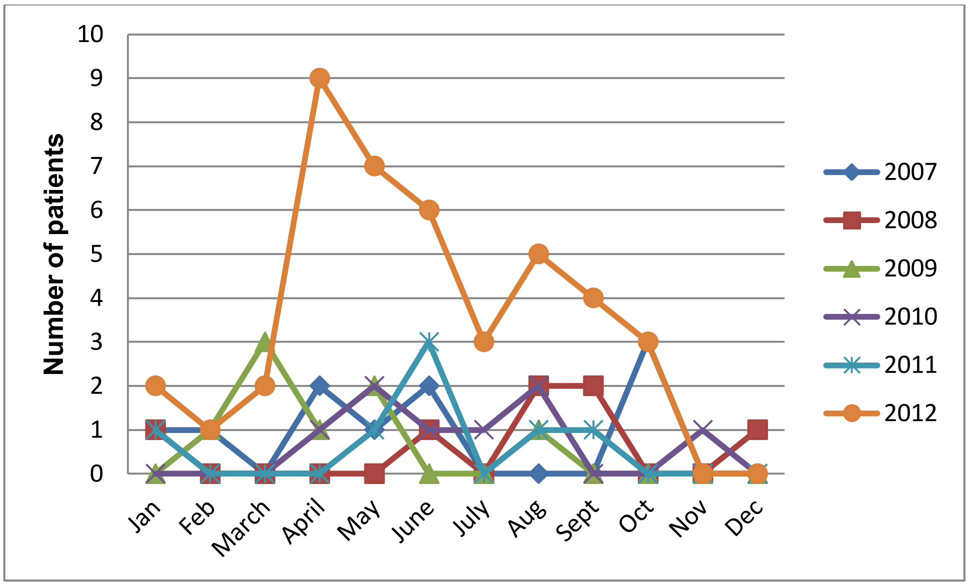

Figure 13: Number of infections per month 2007-2012, according to date of first consultation.

3.3 **Evaluated data on diagnosis**

Procedure of first diagnosis as well as the results of POCT was analyzed.

3.3.1 Time between first consultation and confirmation of diagnosis

The period between first consultation of a physician and the date of POCT diagnosis was calculated. Shown in Table 7, there was a significantly shorter loss of time in 2012 compared to 2007-2011 (1.3±0.2 vs. 2.7±0.4, p=0.01). The general mean was two days (SEM=±0.2).

Group	Average gap (days)	Standard deviation	Standard error of mean	Kolmogorov-Smirnov Z	p-value (Mann-Whitney U test)
Group 1 (2007-2011), n=40	2.7	2.8	0.4	0.002	0.01
Group 2 (2012), n=42	1.3	1.2	0.2		

Table 7: Average gap between first consultation of a physician and diagnosis.

3.3.2 Time between first symptoms and first contact with a physician

In the overview of 2007 to 2012, it took in average five days (SEM=±0.48) between the date of the first subjectively perceived symptoms of illness and the consultation of a physician. Regarding the results for each group of interest separately, the mean time was six days for group 1 (SEM=±0.94) versus 4.1 days for group 2 (SEM=±0.28). In group 1, calculation was done with n=35, as data was not available for five patients, in group 2, same was done with n=39 and data of three patients missing. The difference was not significant (p=0.322).

3.3.3 Results of the point of care test

During January 1st 2007 and December 31st 2011, 92.5% of the patients (n=40) showed a positive result on Puumala virus by Reagena®. For 2 patients (2.5%), the test results were found to be positive for Puumala virus as well as for Hantaan. Furthermore, one patient was also positively tested for Dobrava virus.

In group 2, Reagena® testing was positive for Puumala virus by 100% of the patients. This was found not to be significantly different in Chi-square test (p=0.195).

3.3.4 First suspected diagnosis

Finally, of the 82 cases of diagnosed Puumala virus infections, 42 were suggested to be NE after the first clinical examination, before conducting the Reagena® point of care test. For group 1, Puumala virus infection was the first mentioned diagnosis in 17 out of 40 cases (42.5%). In group 2, 24 patients out of 42 (57.1%) were diagnosed with NE before the POCT was done. This meant no significant difference (*p*=0.185).

3.4 Statistical evaluation of symptoms at first presentation

Symptoms at first presentation at a hospital are described below.

3.4.1 Arthromyalgia

Significantly more patients complained of arthromyalgia in 2007-2011 compared to 2012. In group 1 (2007-2011), 10 patients out of 40 described arthromyalgia at first examination while in group 2, three patients out of 42 did so (25% vs. 7.1%, *p*=0.027), see also Figure 14.

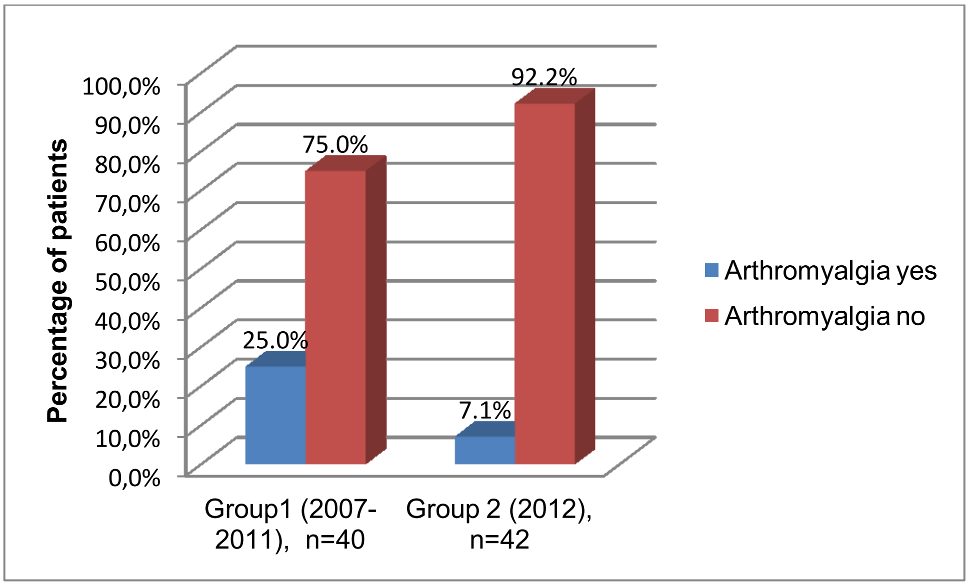

Figure 14: Arthromyalgia as a first symptom.

3.4.2 Lumbago

Significantly more patients complained of lumbago in 2012 (see also Figure 15). In group 2, nine out of 42 patients (21.4%) reported back pain to their treating physician during first consultation. In group 1 (2007-2011) only 2 out of 40 patients (5.0%) complained of back ache. This means a statistically significant difference of *p*=0.029.

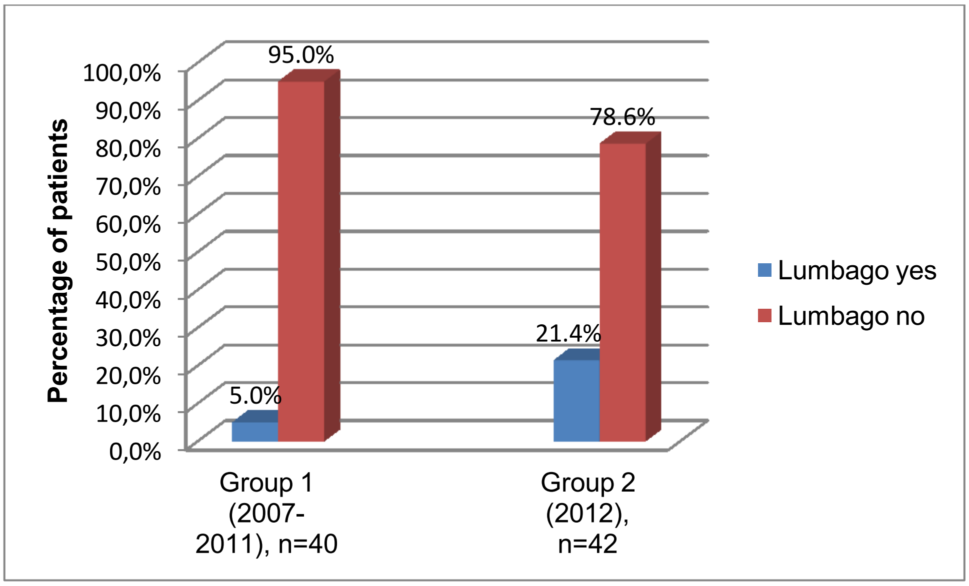

Figure 15: Lumbago as a first symptom.

3.4.3 Fever

Regarding the next clinical sign, fever, all of the 82 patients were considered. The behaviour of 2007-2011 patients was found to be almost equivalent (*p*=0.942) to those of 2012. 36 of 40 patients of group 1 (90.0%) reported about fever as one of the reasons for searching a physician's consult. Likewise, in group 2, 38 of 42 patients (90.5%), had fever before or at the time of consulting the hospital.

3.4.4 Cephalea and retroocular pain

Further, no statistical significant difference for cephalea and retroocular pains could be found in the two groups (*p*=0.837). In 2007-2011, we found that 21 out of 40 patients (52.5%) of the examined patients came to hospital with headache, whereas in 2012, even 23 out of 42 (54.8%) suffered from headache.

3.4.5 Worsening of general condition

Of note, a significant difference could be observed in decrease of general condition. While in group 1 25% (10 out of 40) of the patients described a massive worsening of their general condition during the period of their illness, nobody of the second group mentioned this in the year 2012 (p=0.001, see also Table 8).

Groups	Worsening of general condition		p-value (Chi-square)
	yes	no	
Group 1 (2007-2011), n=40	10 (25%)	30 (75%)	0.001
Group 2 (2012), n=42	0	42 (100%)	

Table 8: Worsening of general condition as a first symptom.

3.4.6 Respiratory symptoms

There was no significant difference concerning dyspnoea, cough and other symptoms of infections of the respiratory tract like sinusitis or angina tonsillaris (p=0.221).

In the “normal” years, 25% of the patients (10 out of 40) complained about one of these symptoms, while in the peak year 2012, there were only 14.3% (6 out of 42 patients).

3.4.7 Shivering

Shivering can be assumed as a rather rare reason for consulting a physician, in both groups together (2007-2012), we found that 12.2% complained about it; 7.5% (three out of 40) in 2007-2011 and 16.7% (7 out of 42) in 2012. The difference in number was not significant (p=0.205).

3.4.8 Renal or flanks’ pain

There were seven out of 40 patients (17.5%) in group 1, who reported decidedly of renal or flanks' pain, on the contrast to lower back pain. In group 2 (2012), six patients (14.3%) did so. With p=0.690, the result was not significant.

3.4.9 Herpes labialis triggering

Similarly, five percent of the first group had a triggering of herpes labialis in course of their infection (2 of 40 patients). In 2012 (group 2), we could observe one patient of 42 who showed herpetical lesions during his illness (2.4%). The small difference found in number did not confer to any statistical significance (*p*=0.528).

3.4.10 Impaired vision

In group 1, 22.5% of the patients (9 out of 40) reported of blurred vision before coming to hospital, whereas in 2012, 28.6% patients (12 out of 42) did so. The slight difference shown in the comparison of the two groups was not significant in Chi-square (*p*=0.529).

3.4.11 Gastro-intestinal symptoms

Regarding the percentage of patients with gastro-intestinal symptoms, 18 out of 40 patients in group 1 (45.0%), complained of either diarrhea, nausea, constipation, meteorism, vomiting, severe abdominal pain or gastro-oesophageal reflux. In comparison, 25 out of 42 patients (59.5%) described at least one of these symptoms in the peak year 2012. The rather big difference of more than 10 percent did not find expression in statistical significance, *p*=0.188.

3.4.12 Vertigo

Compared with other clinical signs, we found vertigo to be rather rare. Only 10.0% (4 out of 40) of the patients in the “normal” years of Puumala virus infections, reported of troubling dizziness as one of the distinguishing marks in the early phase of illness.

In the second group, 4.8% (two out of 42 patients) complained of vertigo or dizziness. The result was not significant, *p*=0.363.

3.4.13 Renal symptoms

As acute renal failure is one of the most pathognomonic symptoms of Puumala virus infections (1,8,17), a particular interest was taken in how many patients had already renal irregularities when coming to hospital. In the group of 2007-2011, 25% (10 out of 40) of the patients mentioned either oligo-anuria or changes in colour of urine as well as painful mictation. In the second group, 26.2% (11 out of 42 patients) reported the same complaints to their treating physician in hospital. With p=0.902, we could find an approaching to equality (see also Figure 16).

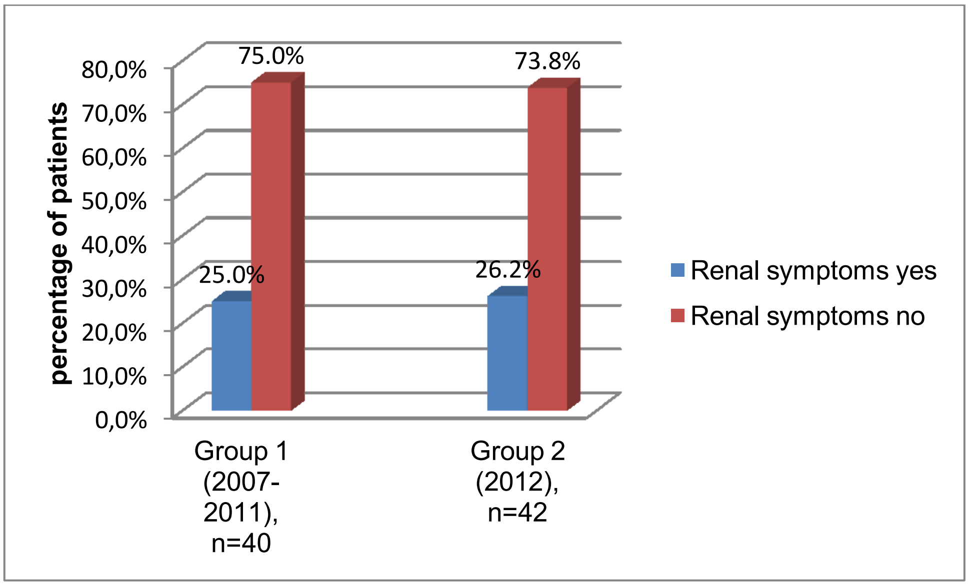

Figure 16: Percentage of patients with renal syptoms among first symptoms.

3.4.14 Fatigue, faintness, lassitude

Similarly, we observed an approximately equality with p=0.900 in the symptomatic complex of fatigue, faintness and lassitude. Here, 25.0% of the patients described these complaints in 2007-2007, while 23.8% in 2012 did so. In sum, nearly a quarter, 24.4%, of all the patients with Puumala virus infection from 2007 of 2012 reported of fatigue, faintness and lassitude among the first symptoms of illness.

3.5 **Statistical evaluation of clinical signs on first clinical examination**

Clinical signs present at first clinical examination were analyzed.

3.5.1 Petechial bleeding

Knowing thrombocytopenia as one of the main modification in biochemical laboratory parameters (17,27), the existence of petechial bleeding in first clinical examination was investigated. In 2012, no patient presented with petechiae, whereas in the previous years, 7.5% (three out of 40) did. This difference is according to a statistical trend (p=0.071, see also Table 9).

3.5.2 Oedema

Regarding oedema, a non-significant difference of 5% (p=0.142) can be observed. In group 1, we collected data of two patients with visible oedema, corresponding to 5%, whereas nobody in group 1 was hospitalized with signs of oedema at the first examination.

3.5.3 Ocular manifestation

Notably, neither in group 1 nor in group 2, conjunctival bleeding or scleral bleeding was found at first clinical examination after hospitalization.

Conjunctivitis was uncommon in both groups, just 2.4% (one patient out of 42) in group 2 (2012) complained about it. This signifies no statistically significant difference (p=0.326).

We found that 22.5% patients (nine out of 40) between 2007 and 2011 and 23.8% (10 out of 42) in 2012 had a blurred vision at first clinical examination (p=0.888).

3.5.4 Renal irregularities approved by clinical examination

In contrast to the number of patients with subjective perceived renal troubles (changes in either oligo-anuria, colour of urine or painful mictation), as mentioned above, we found proved (by clinic and results of laboratory parameters) renal irregularities in half of the cases (20 out of 40 patients) during 2007-2011. In 2012, even 57.1% (24 out of 42) of patients were admitted with renal dysfunction (Table 9).

3.5.5 Meningeal symptoms

Among the patients between 2007 and 2011, one patient showed meningism and sensitiveness to light during first clinical examination. This made up 2.5% of the 40 patients of group 1. In 2012, three cases were identified to have these symptoms, respectively 7.1% of the 42 members of the group. No statistical significance of the difference could be remarked.

Parameters of first clinical examination	**Group 1 (2007-2011), n=40**	**Group 2 (2012),n=42**	**p- value (Chi-square)**
Petechial bleeding	3 (7.5%)	0	0.071
Oedema (face, body or extremities)	2 (5%)	0	0.142
Conjunctival bleeding	0	0	
Scleral bleeding	0	0	
Conjunctivitis	0	1 (2.4%)	0.326
Blurred vision/ troubles of refraction	9 (22.5%)	10 (23.8%)	0.888
Renal findings	20 (50%)	24 (57.1%)	0.517
Meningeal symptoms	1 (2.5%)	3 (7.1%)	0.329

Table 9: Findings at first clinical examination.

3.5.6 Blood pressure

For 61 out of 82 patients, we found the systolic and diastolic blood pressure to be documented.

3.5.6.1 Systolic blood pressure

A mean value of 130.2 mmHg (SEM=±4.3) was calculated for group 1, while the annual mean of group 2 was 130.5 mmHg (SEM=±4.1). In the comparison of the mean values by Students' t-test, no significant difference was found. Systolic blood pressure is supposed to be approximately equal in group 1 and group 2 (see Table 10).

3.5.6.2 Diastolic blood pressure

Looking at the diastolic parameter, the mean values calculated for group 1 and group 2 separately resulted in 81.5±2.1 mmHg vs. 84.1±2.3 mmHg. Here, the Students' t- test did not show a significant result, shown in Table 10.

3.5.6.3 Temperature °C

Among 47 of 82 cases, the first measured temperature at clinical examination was registered. Comparing group 1 and 2, no significant difference was found. Of note, an approximately equal temperature could be observed between the groups (Table 10).

Parameters	Mean value	Standard deviation	SEM	Kolmogorov Smirnov- Z	p-value (T-Test)
Systolic blood pressure (mmHg)					
Group 1 (2007-2011), n=23	130.2	20.78	4.3	0.905	0.961
Group 2 (2012), n=38	130.5	25.49	4.1		
Diastolic blood pressure (mmHg)					
Group 1 (2007-2011), n=23	81.5	9.96	2.1	0.177	0.446
Group 2 (2007-2012), n=38	84.1	14.35	2.3		
Temperature (°C)					
Group 1 (2007-2011), n=17	37.6	0.76	0.2	0.938	0.380
Group 2 (2012), n=30	37.3	1.08	0.2		

Table 10: Findings at first clinical examination.

3.6 **Data on diagnostic workup**

Comparing results of thoracic radiology (X-ray or computer tomography) and abdominal sonography or computer tomography, no significant difference was found between the two groups of interest, as shown in Table 11.

Parameters	Group 1 (2007-2011), n=40	Group 2 (2012), n=42	p-value (Chi-square)	Phi-Cramer V
Thoracic radiology (X-ray or CT)				
Not done	10 (25%)	17 (40.5%)	0.421	0.218
Inconspicuous	16 (40.0%)	15 (35.7%)		
Pleural effusions	11 (27.5%)	7 (16.7%)		
Pleural effusion and pulmonary infiltrations	2 (5.0%)	3 (7.1%)		
Pleural effusion, pulmonary infiltrations and pneumothorax	1 (2.5%)	0		
Abdominal radiology (sonography or CT)				
Not done	9 (22.5%)	11 (26.2%)	0.171	0.355
Inconspicious	8 (20.0%)	10 (23.8%)		
Splenomegaly	5 (12.5%)	2 (4.8%)		
Sonographic changes of renal parenchyma	7 (17.5%)	12 (28.6%)		
Splenomegaly and ascites	2 (5.0%)	0		
Sonographic changes of renal parenchyma and ascites	4 (10.0%)	0		
Sonographic changes of renal parenchyma and splenomegaly	3 (7.5%)	6 (14.3%)		
Splenomegaly, sonographic changes of renal parenchyma and ascites	2 (5.0%)	1 (2.4%)		

Table 11: Comparison of findings in thoracic and abdominal radiology.

3.7 Laboratory results at first clinical examination

Concerning the first evaluated biochemical parameters, a significant difference for haemoglobin (*p*=0.023), haematocrit (*p*=0.018) and ALT (*p*=0.051) was found between group 1 and group 2. While a slight trend for AST and an approximately equality for aPTT was observed, the results for all of the other parameters did not show any significant difference (see Table 12). Unfortunately, proteinuria and haematuria had to be dismissed previously as variable because of irregularities in documentation.

Parameters	Mean value	SD	SEM	Kolmogorov-Smirnov-Z	p-value (t-test)	p-value (Mann-Whitney U test)
1. Leucocytes (G/l)						
Group 1 (2007-2011), n=40	10.78	5.63	0.89	0.032		0.571
Group 2 (2012), n=42	9.51	3.59	0.55			
1. Haemoglobin (g/dl)						
Group 1 (2007-2011), n=40	15.99	1.86	0.29	0.933	0.023	
Group 2 (2012), n=42	15.03	1.88	0.29			
1. Haematocrit (%)						
Group 1 (2007-2011), n=40	44.43	4.60	0.73	0.998	0.018	
Group 2 (2012), n=42	41.95	4.70	0.73			

Table 12: Average values of first laboratory results.

Parameters	Mean value	SD	SEM	Kolmogorov-Smirnov-Z	p-value (t-test)	p-value (Mann-Whitney U test)
1. Thrombocytes (G/l)						
Group 1 (2007-2011), n=40	85.7	64.61	10.22	0.017		0.653
Group 2 (2012), n=42	83.88	44.31	6.84			
1. Lymphocytes (%)						
Group 1 (2007-2011), n=40	17.20	5.82	0.92	0.693	0.190	
Group 2 (2012), n=42	19.7	7.50	1.16			
1. Creatinine (mg/dl)						
Group 1 (2007-2011), n=40	2.03	1.62	0.26	<0.0005		0.519
Group 2 (2012), n=42	2.47	2.30	0.35			
1. Urea (mg/dl)						
Group 1 (2007-2011), n=40	68.9	58.62	9.27	0.007		0.777
Group 2 (2012), n=42	68.05	54.65	8.43			
1. GFR (MDRD)						
Group 1 (2007-2011), n=40	50.20	29.79	4.71	0.257	0.682	
Group 2 (2012), n=42	53.03	32.37	4.99			

Table 12 cont'd.: Average values of first laboratory results.

Parameters	Mean value	SD	SEM	Kolmogorov-Smirnov-Z	p-value (t-test)	p-value (Mann-Whitney U test)
1. LDH (U/l)						
Group 1 (2007-2011), n=40	322.93	142.81	22.58	<0.0005		0.305
Group 2 (2012), n=42	411.29	816.93	126.06			
1. ALT (U/l)						
Group 1 (2007-2011), n=40	57.43	41.03	6.49	<0.0005		0,051
Group 2 (2012), n=42	58.71	120.16	18.54			
1. AST (U/l)						
Group 1 (2007-2011), n=40	61.2	41.41	6.55	<0.0005		0.101
Group 2 (2012), n=42	83.02	263.75	40.70			
1. aPTT (sec)						
Group 1 (2007-2011), n=39	38.77	5.34	0.85	0.450	0.935	
Group 2 (2012), n=41	38.64	8.39	1.31			
1. CRP (mg/l)						
Group 1 (2007-2011), n=40	77.03	65.34	10.33	0.003		0.189
Group 2 (2012), n=42	60.82	61.35	9.47			

Table 12 cont'd.: Average values of first laboratory results.

3.8 **Clinical signs and symptoms in the course of Puumala virus infection**

Clinical findings and symptoms during the course of infection were evaluated.

3.8.1 Petechial bleeding

Of the 40 patients of group 1, we found two (5.0%), who had petechial bleeding in the course of their illness. In 2012, one person of 42 (2.4%) was found to have developed petechial lesions while being sick. For one person in group 2, a follow up could not be done because of lack of information. In Chi-square testing, we found *p*=0.513, respectively, no significant difference.

3.8.2 Oedema

Among nine out of 40 patients between 2007 and 2011 (22.5%), the development of oedema during the course of disease could be observed. In group 2 (2012 only), nine patients out of 42 (16.7%), with one patient's data missing, were afflicted by oedema. Obtained data did not show any significant difference between the two groups (*p*=0.512).

3.8.3 Ocular manifestation

Conjunctival lesions, corresponding to bleeding, were found among 5% of the patients of group 1 during their period of illness. In contrast there was no patient in group 2 who ever suffered of conjunctival bleeding. Although there is a difference in number, statistically, there is none, Chi-square test resulted in *p*=0.216.

Approximately the same results were found for scleral bleeding. With two patients (5.0%) of group 1 being positive for scleral bleeding during the course of illness and nobody in group 2, no significant difference was found, *p*=0.216. For conjunctival as well as for scleral bleeding, the data of one person of group 2 was missing because of prohibited access to data.

Conjunctivitis was observed for 7 of 40 patients in group 1 (17.5%) during their time of illness, in comparison to 2 of 42 (4.8%) members of group 2, who had the same clinical symptom while being diseased. Again, the data of 1 patient of the year 2012 was missing. A slight trend was remarked (*p*=0.121).

Regarding the appearance of blurred vision in the course of disease, we found 47.5% of the patients between 2007 and 2011 affected. In 2012, 42.9% of the patients were discovered to have troubles of vision while being ill. No evaluation could be done for 1 patient of group 2, again, because of missing data. According to Chi-square test, no significant difference was found (*p*=0.586).

3.8.4 Renal irregularities during course of Puumala virus infection

Renal symptoms such as oligo-anuria and painful mictation as well as irregularities in biochemical parameters of renal function were observed among 29 out of 40 patients (72.5%) of group 1 during the follow up, while in group 2, 35 out of 42 patients (83.3%) developed these symptoms. The difference was not statistically significant (*p*=0.225). A total of 64 patients with renal irregularities (78.0%) during the course of illness was found between 2007 and 2012.

3.9 **Maximum and minimum values of pathologic laboratory findings**

The averages of pathologic maximum and minimum values of laboratory findings are shown in Table 13. There was no significant difference found between the maximum values of CRP, urea, and creatinine as well as the minimum values of thrombocytes and GFR (MDRD). Minimum levels of thrombocytes tended to be lower in 2007-2011 compared to 2012 (69.45±9.46 vs. 77.0±6.77 G/l), although the difference did not reach statistical significance (*p*=0.116). Maximum levels of CRP tended to be higher in group 1 compared with group 2 (95.63±11.04 vs. 80.0±11.79 mg/l, *p*=0.143).The difference was statistically not significant. Maximum levels of urea showed a trend to statistical significance with higher values in 2007-2011 (114.48±12.14 vs. 91.07±9.46 mg/dl, *p*=0.130). There was no significant difference in maximum values of creatinine and minimum values of GFR (MDRD).

Parameters	Mean value	SD	SEM	Kolmogorov-Smirnov-Z	p- value (t-test)	p- value (Mann-Whitney U test)
Minimum thrombocytes						
Group 1 (2007-2011), n=40	69.45	59.80	9.46	0.015		0.116
Group 2 (2012), n=42	77.00	43.86	6.77			
Maximum CRP						
Group 1 (2007-2011), n=40	95.63	69.83	11.04	0.031		0.143
Group 2 (2012), n=42	80.00	76.41	11.79			
Maximum urea						
Group 1 (2007-2011), n=40	114. 48	76.76	12.14	0.086	0.130	
Group 2 (2012), n=42	91.07	61.28	9.46			
Maximum creatinine						
Group 1 (2007-2011), n=40	3.86	3.28	0.52	<0.0005		0.963
Group 2 (2012), n=42	3.69	3.17	0.49			
Minimum GFR (MDRD)						
Group 1 (2007-2011), n=40	34.87	27.23	4.30	0.145	0.931	
Group 2 (2012), n=42	34.37	25.33	3.91			

Table 13: Comparison of maximum and minimum mean values of laboratory results.

3.10 Statistical evaluation of data on treatment

3.10.1 Hospitalization and outpatient visits

Particular attention was paid as to whether patients have been hospitalized or treated outpatient. The presented data refers to 7.5% (three out of 40) patients treated as outpatient in group 1 versus 7.1% (three out of 42) in group 2. The difference is not significant and corresponds to an approximation on equality (p=0.951), as shown in Table 14.

Groups	Hospitalization		p- value (Chi-square)
	yes	no	
Group 1 (2007-2011), n=40	37 (92.5%)	3 (7.5%)	0.951
Group 2 (2012), n=42	39 (92.9%)	3 (7.1%)	

Table 14: Number and percentage of patients treated inpatient.

Patients who were not admitted tended to need more outpatient visits in 2012 compared with 2007-2011. In group 1, patients came 1.33 times to an outpatient control, whereas in group 2, it was 3.67 times (SEM=±0.33 vs. ±0.88, p-value=0.069).

3.10.2 Length of stay in hospital

The mean value of length at stay at hospital was evaluated. Therefore, inpatients' data was reviewed on their length of stay at hospital. For three patients of group 1 and four patients of group 2, data could not be obtained. Statistically, no significant difference was found, as one can see in Table 15.

Groups	Length of stay in hospital-mean value (days)	SD	SEM	Kolmogorov-Smirnov Z	p-value (Mann-Whitney U test)
Group 1 (2007-2011), n=37	9.24	3.996	0.657	0.371	0.229
Group 2 (2012), n=38	7.87	2.713	0.440		

Table 15: Mean values of length of stay at hospital.

3.10.3 Need of intensive care

Additionally, five out of the 40 patients of group 1 (12.5%), needed a further treatment at intensive care unit (ICU). Among group 2, two patients (4.8%) had to be treated at ICU. The difference was not statistically significant (Table 16).

Groups	Hospitalization at ICU		p-value (Chi-square)
	yes	no	
Group 1 (2007-2011), n=40	5 (12.5%)	35 (87.5%)	0.210
Group 2 (2012), n=42	2 (4.8%)	40 (95.2%)	

Table 16: Number and percentage of patients needing a hospitalization at ICU.

3.10.4 Length of stay at ICU

There was no significant difference in the length of stay at ICU between the two groups (4.40±1.66 vs. 3.50±2.50 days, p=0.782), as shown in Table 17.

Groups	Length of stay at ICU-mean values (days)	SD	SEM	Kolmogorov-Smirnov-Z	p-value (t-test)
Group 1 (2007-2011), n=5	4.40	3.72	1.66	0.371	0.782
Group 2 (2012), n=2	3.50	3.54	2.50		

Table 17: Mean value of needed length of stay at ICU.

Among 82 patients, four needed respiratory support, either by oxygen application via oxygen mask, CPAP or intubation. Three of these cases were included in group 1. The difference was not shown to be significant (*p*=0.546, see also Table 18).

Groups	Respiratory support					p-value (Chi-square)	Phi-Cramer V
	unknown	none	Oxygen mask	CPAP	Intubation		
Group 1 (2007-2011), n=40	0	37 (9.5%)	1 (2.5%)	1 (2.5%)	1 (2.5%)	0.546	0.193
Group 2 (2012), n=42	1 (2.4%)	40 (95.2%)	0	1 (2.4%)	0		

Table 18: Number and percentage of patients with supportive respiratory therapy during course of illness.

3.10.5 Dialysis

Significantly more patients required dialysis in the years 2007-2011 compared with the year 2012 (eight out of 40 patients, 20.0% vs. one out of 42 patients, 2.4%, *p*=0.011). See also Table 19.

Groups	Dialysis		p-value (Chi-square)
	yes	no	
Group 1 (2007-2011), n=40	8 (20.0%)	32 (80.0%)	**0.011**
Group 2 (2012), n=42	1 (2.4%)	41 (97.6%)	

Table 19: Number and percentage of patients needing dialysis treatment.

3.11 Statistical evaluation of patients' outcome

As all patients showed full recovery of renal function, investigation was divided into "healing" and "death". However, no significant difference was observed between the two groups. In group 1, one patient deceased, respectively 2.5%. 100.0% of the patients out of group 2 recovered completely (Figure 17).

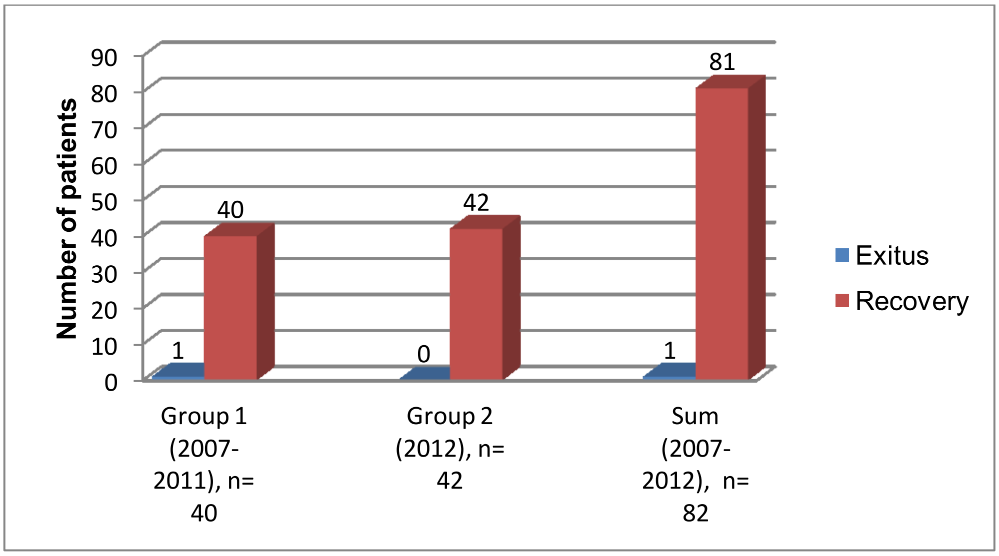

Figure 17: Comparison of patients' outcome.

4 Discussion

As the epidemic profile of hantavirus disease is closely related to growth and population of their reservoir (9), in Austria the common bank vole, the outbreak in 2012 can be explained by an increased population of these rodents in this year. Patients reported a massive appearance of rodents in their surroundings in 2012 (21). This increase could have been due to unusually warm weather in late autumn and winter 2011 leading to better breeding conditions for rodents as described before (1,28).

The massive increase of bank voles and resulting NE is also shown by the numbers of adults with confirmed diagnosis hospitalized at the Department of Internal Medicine, Medical University of Graz. In 2007-2011 (group 1), 40 patients were treated with confirmed diagnosis Puumala virus infection at the Department of Internal Medicine, Medical University of Graz. With n=42 in 2012 alone, we found the case number four times as high as in group 1.

Convenient to the theory of an increased bank vole population because of climate changes is the particularity that in 2012, outbreak of Hantavirus disease occurred mostly in April, one month before the former annual peak's rising, May to June. Due to better food supplies because of high temperatures in summer, the bank vole population starts to breed earlier, which causes an earlier shedding of virus and following, earlier rise of numbers of infections (10,12,16,23,24). A second peak of infection outbreak in autumn, like it occurred in August and September 2012, has already been described for northern European countries (10).

A shift of Austrian bank vole population has to be assumed, as in the late nineteen-nineties, infection hotspots were located in certain parts of Carinthia (Upper Lavanttal), while in 2012 and already in 2011, most of the cases were diagnosed in Styria (88% in 2012, 29 of 35 cases in 2011) (19,21). Geographically, a peak of infectional distribution for both groups of interest in the direct area around Graz, the political district Graz-Umgebung was found in this study (32.9% of all the infections).

As already described previously in other reviews, most of the infected patients were male in both groups (72.5 vs. 78.6%) (8). These numbers are comparable to results of former publications (72% male, 29% female) (29). In keeping with review reports, the average age of patients ranges from 38.9 to 40.8 years, probably reflecting the age

group most active performing work like cleaning attics, cellars, shelters, barns, working in the woods and fields (8,10,12,17,19,29).
In the peak year 2012, patients were diagnosed significantly faster than in former years of investigation 2007-2011. We assume a heightened public awareness by physicians and patients, caused by reports in public media, to be responsible for this development. In addition, fewer patients needed to be put on dialysis (2.4%) in 2012. A review from Germany described that about 5% of hospitalized patients require temporary dialysis (16), similar results were mentioned in other publications (1,25). Possible explanations for the low rate of dialysis in our patients in 2012 are: either patients were diagnosed faster and were hence treated with intravenous fluids earlier making dialysis unnecessary or that the course of the disease was less severe in 2012 compared with previous years.
The suggestion that the disease was less severe in 2012 is supported by the fact that only two patients needed to be treated at the ICU in 2012 although this finding did not reach statistical significance. Furthermore, in 2012 no patient developed petechiae, whereas 7.5% did in previous years (p=0.07), also suggesting a less severe course of disease. Additionally, significantly more patients complained about worsening of general condition in 2007-2011, which may suggest a more severe disease in these years. Furthermore, in 2007-2011 we found a tendency for thrombocytopenia, C-reactive protein and urea to be more pronounced compared to 2012. Taken together, these findings support the interpretation that the course of disease was less severe in 2012.

Patients complained more often about lower back pain in 2012, whereas they reported arthromyalgias more frequently in previous years as well as a higher tendency to develop conjunctivitis. These findings emphasize that the clinical presentation of Puumala infections may vary seasonally, as it was described previously (5).

The occurrence of clinical findings in our study are similar to previously published results (1). In a publication of 2003, fever is described as one of the most frequent symptoms of NE (97-100%). This correlates approximately with the results of our study, showing fever to be the most frequent symptom (90.0% in 2007-2011, 90.5% in 2012). Furthermore, the rates of headache, backache as well as abdominal pains, nausea, vomiting and conjunctival infection during the course of disease are reported to be similar to our study (1). The number of patients needing dialysis in 2007-2011 shows an elevated percentage in our study in comparison with the review of 2003 (20.0% vs. 5-7%) (1). In 2012, the number patients put on dialysis was lower compared with the review of 2003 (2.4% vs. 5-7%). Furthermore, we found comparable results in radiological pulmonary and renal manifestations. Of interest, blurred vision was observed more often in the patients of our study, compared to the review of 2003 (45.1% vs. 10-36%) (1).

Of interest, a German publication of 2012 mentioned a comparable length of stay in hospital (8 days vs. 8.1 days in the present study) (16). In contrast, the rate of hospitalization was higher in our study. In the German publication, 50-65% of patients were hospitalized, in this study, the percentage of patients being admitted to hospital was 92.7% (16). These differences may be explained by structural differences in the Austrian and German health care systems.

The laboratory findings on admission were similar in our study compared to a German study published in 2010 (29). First values of leucocytes, haemoglobin, haematocrit and creatinine showed comparable results. Of interest, a difference can be observed in values of CRP (68.73±63.46 mg/dl vs. 5.8±0.4 mg/dl) The same publication reports of one case of death due to pulmonary complications, comparable to the present investigation. As limiting factor, it has to be considered that in the former study children older than 16 years were included for research (29).

This present investigation has several limitations. Firstly, because of the low number of cases, conclusions have to be drawn with caution. Due to irregularities in documentation, several parameters of clinical importance could not be evaluated, such as proteinuria and haematuria in urinary bandlette test. Further, a bias of information could not be avoided, as especially data on epidemiology are depending on the non-standardized first history and the subjective reports of patients. Further, data was collected from already existing, non-standardized documentation, possible errors of subjective understanding in extraction of data are possible, which may also cause an origin of bias of information.

In conclusion, 2012 was a peak year of NE in Styria. Of five main symptoms at admission, two were found significantly more (lumbago) or less (arthromyalgia) frequent when compared to 2007-2011. Patients were diagnosed significantly faster which may be due to increased public awareness through reports in newspapers, journals, and TV channels. In addition, patients required significantly less dialysis treatments in 2012. Possible explanations for the low rate of dialysis include the faster diagnosis followed by earlier specific treatment and a less severe course of the disease in 2012.

5 References

1. Vapalahti O, Mustonen J, Lundkvist A, Henttonen H, Plyusnin A, Vaheri A. Hantavirus infections in Europe. Lancet Infect Dis. 2003 Oct;3(10):653-61.

2. White D.O., Fenner F.J. Medical Virology. 4th Edition. San Diego: Academic Press; 1994.

3. Acheson N.H. Fundamentals of Molecular Virology. 2nd Edition. Hoboken: John Wiley& Sons, Inc.; 2011.

4. Collier L., Oxford J., Kellam P. Human Virology. 4th Edition. New York: Oxford University Press Inc.; 2011.

5. Loyen M., Helmchen U.,Hofmann J., Krüger D.H., Clasen W. Von Mäusen auf Menschen - Erkenntnisse aus der Hantavirus-Epidemie 2010 From mice to men - insights from the hantavirus epidemic in 2010. Dtsch Med Wochenschr. 2012;(137(07)):309–13.

6. Mims C., Dockrell H.M., Goering R.V., Roitt I., Wakelin D., Zuckermann M. Medizinische Mikrobiologie Infektiologie. 1. deutsche Auflage. München: Elsevier GmbH; 2006.

7. Bunyaviridae - home [Internet]. [zitiert 18. Juni 2013]. Verfügbar unter: http://bunyaviridae.wikispaces.com/

8. Marre R., Mertens T.,Trautmann M., Zimmerli W. Klinische Infektiologie. 2nd Edition. München: Elsevier GmbH; 2008.

9. Klempa B, Radosa L, Kruger DH. The broad spectrum of hantaviruses and their hosts in Central Europe. Acta Virol. 2013;57(2):130–7.

10. Vaheri A, Henttonen H, Voutilainen L, Mustonen J, Sironen T, Vapalahti O. Hantavirus infections in Europe and their impact on public health. Rev Med Virol. 1. Januar 2013;23(1):35–49.

11. hanatvirus-cycle.gif (GIF-Grafik, 450 × 308 Pixel) - Skaliert (80%) [Internet]. [zitiert 11. Juni 2013]. Verfügbar unter: http://www.sdnhm.org/archive/fieldguide/zoonoses/images/hanatvirus-cycle.gif

12. Heyman P., Ceianu C.S.,Christova I.,Tordo N., Beersma M., João Alves M., Lundkvist A., Hukic M., Papa A., Tenorio A., Zelená H., Eßbauer S., Visontai I., I Golovljova I., Connell J., Nicoletti L., Van Esbroeck M., Gjeruldsen Dudman S., Aberle S.W., Avšić-Županc T., Korukluoglu G., Nowakowska A., Klempa B., Ulrich R.G., Bino S., Engler O., Opp M., Vaheri A. A five-year perspective on the situation of haemorrhagic fever with renal syndrome and status of the hantavirus reservoirs in Europe, 2005-2010. Eurosurveillance Vol 16 Issue 36 08 Sept 2011.

13. Modrow S., Falke D., Schatzl H.,Truyen U. Molekulare Virologie. 3. Auflage. Heidelberg: Spektrum Akademischer Verlag; 2010.

14. Heyman P, Thoma BR, Marié JL, Cochez C, Essbauer SS. In Search for Factors that Drive Hantavirus Epidemics. [Internet]. Front. Syst. Biol. 2012. Verfügbar unter: http://han.medunigraz.at/han/pubmed/www.frontiersin.org/Systems_Biology/10.3389/fphys.2012.00237/abstract

15. Watson D.C., Sargianou M. ,Papa A., Chra P., Starakis I., Panos G.,. Epidemiology of Hantavirus infections in humans: A comprehensive, global overview. [Internet]. [zitiert 8. Juli 2013]. Verfügbar unter: http://han.medunigraz.at/han/pubmed/informahealthcare.com/doi/abs/10.3109/1040841X.2013.783555

16. Krautkrämer E., Kruger D.H., Zeier M. Recent outbreaks of hantavirus disease in Germany and in the United States. Kidney Int. 2012;(82):1243–5.

17. Herold G. et al. Herold Innere Medizin. Köln: Herold, Gerd; 2013.

18. Sargianou M, Watson DC, Chra P, Papa A, Starakis I, Gogos C, u. a. Hantavirus infections for the clinician: From case presentation to diagnosis and treatment. Crit Rev Microbiol. November 2012;38(4):317–29.

19. Aberle SW, Lehner P, Ecker M, Aberle JH, Arneitz K, Khanakah G, Radda A, Radda I, Popow-Kraupp T, Kunz C, Heinz FX. Eur J Clin Microbiol Infect Dis. Nephropathia Epidemica Puumala Virus Austria. (1999 Jul;18(7)):467–72.

20. Bank Vole (Clethrionomys Glareolus) Seen From The Side Royalty Free Stock Photo, Pictures, Images And Stock Photography. Image 11645103. [Internet]. [zitiert 18. Juni 2013]. Verfügbar unter: http://www.123rf.com/photo_11645103_bank-vole-clethrionomys-glareolus-seen-from-the-side.html

21. Aberle S. Medizinische Universität Wien - Virologie - Virus-Epidemiologie - Virusepidemiologische Information - 2013 [Internet]. 2013 [zitiert 13. Juni 2013]. Verfügbar unter: http://www.virologie.meduniwien.ac.at/home/virus-epidemiologie/virusepidemiologische-information/2013/lang_1-content.html

22. Acham-Roschitz B., Aberle S.W., Pirker N., Kaulfersch W., Boehm M., Roedl S., Zenz W., Ring E.,Mache C. J. Nephropathia Epidemica (Puumala Virus Infection) in Austrian Children. Pediatr Infect Dis J. September 2010;(Issue: Volume 29(9)):pp 874–876.

23. Aberle S. Medizinische Universität Wien - Virologie - Virus-Epidemiologie - Virusepidemiologische Information - 2012 [Internet]. 2012 [zitiert 13. Juni 2013]. Verfügbar unter: http://www.virologie.meduniwien.ac.at/home/virus-epidemiologie/virusepidemiologische-information/2012/lang_1-content.html

24. Aberle S. Medizinische Universität Wien - Virologie - Virus-Epidemiologie - Virusepidemiologische Information - 2011 [Internet]. 2011 [zitiert 13. Juni 2013]. Verfügbar unter: http://www.virologie.meduniwien.ac.at/home/virus-epidemiologie/virusepidemiologische-information/2011/idart_82-lang_1-content.html

25. Turčinov D., Puljiz I., Markotić A., Kuzman I., Begovac J. Clinical and laboratory findings in patients with oliguric and non-oliguric Hantavirus haemorrhagic fever with renal syndrome: an analysis of 128 patients. Clin Microbiol Infect. Juli 2012;19(7):674–9.

26. Moßhammer D., Reichert E., Reichert W. Nephropathia epidemica durch Hantavirus-Infektion vom Puumala-Typ Ein Fallbericht aus dem ambulanten Sektor. Dtsch Med Wochenschr. 2010;(135(50)):2518–22.

27. Denecke B., Bigalke B., Haap M., Overkamp D.,Lehnert H., Haas C.S. Hantavirus Infection: A Neglected Diagnosis in Thrombocytopenia and Fever? [Internet]. 2010 [zitiert 21. Mai 2013]. Verfügbar unter: http://han.medunigraz.at/han/pubmed/www.ncbi.nlm.nih.gov/pmc/articles/PMC2966365/

28. Zentralanstalt für Meteorologie und Geodynamik — ZAMG [Internet]. ZAMG Zentralanstalt Für Meterologie Geodyn. [zitiert 12. September 2013]. Verfügbar unter: http://www.zamg.ac.at/cms/de/aktuell

29. Braun N, Haap M, Overkamp D, Kimmel M, Alscher MD, Lehnert H, Haas CS. Characterization and outcome following Puumala virus infection: a retrospective analysis of 75 cases. Nephrol Dial Transplant. 11. März 2010;25(9):2997–3003.

Annex –Output tables

Year of infection

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Year * Year of infection	82	100,0%	0	0,0%	82	100,0%

Year * Year of infection Kreuztabelle

Anzahl

		Year of infection						Gesamt
		2007	2008	2009	2010	2011	2012	
Year	2007-2011	10	7	8	8	7	0	40
	2012	0	0	0	0	0	42	42
Gesamt		10	7	8	8	7	42	82

Chi-Quadrat-Tests

	Wert	df	Asymptotische Signifikanz (2-seitig)
Chi-Quadrat nach Pearson	82,000[a]	5	,000
Likelihood-Quotient	113,627	5	,000
Zusammenhang linear-mit-linear	57,377	1	,000
Anzahl der gültigen Fälle	82		

a. 9 Zellen (75,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 3,41.

Symmetrische Maße

		Wert	Näherungsweise
Nominal- bzgl. Nominalmaß	Phi	1,000	,000
	Cramer-V	1,000	,000
Anzahl der gültigen Fälle		82	

a. Die Null-Hyphothese wird nicht angenommen.

b. Unter Annahme der Null-Hyphothese wird der asymptotische Standardfehler verwendet.

Statistical evaluation of patients' characteristics

Sex

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Geschlecht	82	100,0%	0	0,0%	82	100,0%

Jahr * Geschlecht Kreuztabelle

			Geschlecht		Gesamt
			weiblich	männlich	
Jahr	2007-2011	Anzahl	11	29	40
		% innerhalb von Jahr	27,5%	72,5%	100,0%
	2012	Anzahl	9	33	42
		% innerhalb von Jahr	21,4%	78,6%	100,0%
Gesamt		Anzahl	20	62	82
		% innerhalb von Jahr	24,4%	75,6%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische Signifikanz (2-seitig)	Exakte Signifikanz (2-seitig)	Exakte Signifikanz (1-seitig)
Chi-Quadrat nach Pearson	,410[a]	1	,522		
Kontinuitätskorrektur[b]	,146	1	,702		
Likelihood-Quotient	,410	1	,522		
Exakter Test nach Fisher				,611	,351
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 9,76.

b. Wird nur für eine 2x2-Tabelle berechnet

Age

Statistiken

Alter

N	Gültig	82
	Fehlend	0
Mittelwert		39,78
Standardfehler des Mittelwertes		1,343
Standardabweichung		12,159

Kolmogorov-Smirnov-Anpassungstest

		Alter
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	39,78
	Standardabweichung	12,159
Extremste Differenzen	Absolut	,059
	Positiv	,059
	Negativ	-,039
Kolmogorov-Smirnov-Z		,538
Asymptotische Signifikanz (2-seitig)		,934

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Gruppenstatistiken

	Jahr	N	Mittelwert	Standardabwei	Standardfehler
Alter	2007-2011	40	40,75	11,860	1,875
	2012	42	38,86	12,511	1,930

Test bei unabhängigen Stichproben

		Levene-Test der		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	95%	
									Untere	Obere
Alter	Varianze	,907	,344	,702	80	,484	1,893	2,695	-3,470	7,256
	Varianze			,703	79,99	,484	1,893	2,691	-3,463	7,249

Comorbidities

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Age adjusted	79	96,3%	3	3,7%	82	100,0%

Jahr * Age adjusted Charlson Score Kreuztabelle

Anzahl

		Age adjusted Charlson Score				Gesamt
		,00	1,00	2,00	3,00	
Jahr	2007-2011	27	7	3	0	37
	2012	36	3	1	2	42
Gesamt		63	10	4	2	79

Chi-Quadrat-Tests

	Wert	df	Asymptotische Signifikanz (2-seitig)
Chi-Quadrat nach	5,592 (a)	3	,133
Likelihood-Quotient	6,438	3	,092
Zusammenhang linear-	,334	1	,563
Anzahl der gültigen Fälle	79		

a 5 Zellen (62,5%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 94.

Symmetrische Maße

		Wert	Näherungsweise Signifikanz
Nominal- bzgl. Nominalmaßg	Phi	,266	,133
	Cramer-V	,266	,133
Anzahl der gültigen Fälle		79	

a. Die Null-Hyphothese wird nicht angenommen.

b. Unter Annahme der Null-Hyphothese wird der asymptotische Standardfehler

Statistiken

Age adjusted Charlson Score

2007-2011	N	Gültig	37
		Fehlend	3
	Mittelwert		,3514
	Standardfehler des Mittelwertes		,10409
	Standardabweichung		,63317
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		,2619
	Standardfehler des Mittelwertes		,11334
	Standardabweichung		,73450

Age adjusted Charlson Score

Year			Häufigkeit	Prozent	Gültige	Kumulierte
2007-2011	Gültig	,00	27	67,5	73,0	73,0
		1,00	7	17,5	18,9	91,9
		2,00	3	7,5	8,1	100,0
		Gesamt	37	92,5	100,0	
	Fehlend	System	3	7,5		
	Gesamt		40	100,0		
2012	Gültig	,00	36	85,7	85,7	85,7
		1,00	3	7,1	7,1	92,9
		2,00	1	2,4	2,4	95,2
		3,00	2	4,8	4,8	100,0
		Gesamt	42	100,0	100,0	

Kolmogorov-Smirnov-Anpassungstest

		Age adjusted Charlson Score
N		79
Parameter der Normalverteilung(a,b)	Mittelwert	,3038
	Standardabweichung	,68602
Extremste Differenzen	Absolut	,469
	Positiv	,469
	Negativ	-,329
Kolmogorov-Smirnov-Z		4,164
Asymptotische Signifikanz (2-seitig)		,000

a Die zu testende Verteilung ist eine Normalverteilung.

b Aus den Daten berechnet.

Ränge

	Year	N	Mittlerer Rang	Rangsumme
Age adjusted Charlson Score	2007-2011	37	42,43	1570,00
	2012	42	37,86	1590,00
	Gesamt	79		

Statistik für Test (a)

	Age adjusted Charlson Score
Mann-Whitney-U	687,000
Wilcoxon-W	1590,000
Z	-1,262
Asymptotische Signifikanz (2-seitig)	,207

a Gruppenvariable: Year

Evaluation of epidemiolocig data

Place of infection

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * political district	82	100,0%	0	,0%	82	100,0%

Jahr * political district Kreuztabelle

			political district											Gesamt
			unknown	Graz	Graz Umgebung	Weiz	Voitsberg	Deutschlandsberg	Leibnitz	Feldbach	Hartberg-Fürstenfeld	Judenburg	Liezen	
Jahr	2007-2011	Anzahl	9	3	13	2	2	1	4	4	1	1	0	40
		% von Jahr	22,5%	7,5%	32,5%	5,0%	5,0%	2,5%	10,0%	10,0%	2,5%	2,5%	,0%	100,0%
	2012	Anzahl	14	3	14	2	0	4	0	3	1	0	1	42
		% von Jahr	33,3%	7,1%	33,3%	4,8%	,0%	9,5%	,0%	7,1%	2,4%	,0%	2,4%	100,0%
Gesamt		Anzahl	23	6	27	4	2	5	4	7	2	1	1	82
		% von Jahr	28,0%	7,3%	32,9%	4,9%	2,4%	6,1%	4,9%	8,5%	2,4%	1,2%	1,2%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische
Chi-Quadrat nach Pearson	11,025 (a)	10	,356
Likelihood-Quotient	14,245	10	,162
Zusammenhang linear-mit-linear	1,234	1	,267
Anzahl der gültigen Fälle	82		

a 18 Zellen (81,8%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 49.

Symmetrische Maße

		Wert	Näherungsweise Signifikanz
Nominal- bzgl. Nominalmaß	Phi	,367	,356
	Cramer-V	,367	,356
Anzahl der gültigen Fälle		82	

a Die Null-Hyphothese wird nicht angenommen.

b Unter Annahme der Null-Hyphothese wird der asymptotische Standardfehler verwendet.

Activity leading to infection

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Expositionsumgebung	82	100,0%	0	0,0%	82	100,0%

Jahr * Expositionsumgebung Kreuztabelle

			Expositionsumgebung				Gesamt
			unbekannt	Freizeit	berufliche	Heimarbeiten	
Jahr	2007-2011	Anzahl	10	12	9	9	40
		% innerhalb von	25,0%	30,0%	22,5%	22,5%	100,0%
	2012	Anzahl	15	11	9	7	42
		% innerhalb von	35,7%	26,2%	21,4%	16,7%	100,0%
Gesamt		Anzahl	25	23	18	16	82
		% innerhalb von	30,5%	28,0%	22,0%	19,5%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische Signifikanz (2-seitig)
Chi-Quadrat nach Pearson	1,245[a]	3	,742
Likelihood-Quotient	1,252	3	,741
Anzahl der gültigen Fälle	82		

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 7,80.

Symmetrische Maße[c]

		Wert	Näherungsweise Signifikanz
Nominal- bzgl. Nominalmaß	Phi	,123	,742
	Cramer-V	,123	,742
Anzahl der gültigen Fälle		82	

a. Die Null-Hyphothese wird nicht angenommen.

b. Unter Annahme der Null-Hyphothese wird der asymptotische Standardfehler verwendet.

c. Die Korrelations-Statistik ist nur für numerische Daten verfügbar.

Route of infection

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Übertragungsart	82	100,0%	0	0,0%	82	100,0%

Jahr * Übertragungsart Kreuztabelle

			Übertragungsart				Gesamt
			unbekannt	aerogen	Biss	Hautkontakt	
Jahr	2007-2011	Anzahl	12	26	1	1	40
		% innerhalb von Jahr	30,0%	65,0%	2,5%	2,5%	100,0%
	2012	Anzahl	13	29	0	0	42
		% innerhalb von Jahr	31,0%	69,0%	0,0%	0,0%	100,0%
Gesamt		Anzahl	25	55	1	1	82
		% innerhalb von Jahr	30,5%	67,1%	1,2%	1,2%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische
Chi-Quadrat nach Pearson	2,156[a]	3	,541
Likelihood-Quotient	2,928	3	,403
Anzahl der gültigen Fälle	82		

a. 4 Zellen (50,0%) haben eine erwartete Häufigkeit kleiner 5. Die

Symmetrische Maße[c]

		Wert	Näherungsweise
Nominal- bzgl. Nominalmaß	Phi	,162	,541
	Cramer-V	,162	,541
Anzahl der gültigen Fälle		82	

a. Die Null-Hyphothese wird nicht angenommen.

b. Unter Annahme der Null-Hyphothese wird der asymptotische Standardfehler verwendet.

c. Die Korrelations-Statistik ist nur für numerische Daten verfügbar.

Time of incubation

Kolmogorov-Smirnov-Anpassungstest

		Incubation time
N		11
Parameter der Normalverteilung(a,b)	Mittelwert	21,64
	Standardabweichung	6,607
Extremste Differenzen	Absolut	,266
	Positiv	,266
	Negativ	-,189
Kolmogorov-Smirnov-Z		,881
Asymptotische Signifikanz (2-seitig)		,419

a Die zu testende Verteilung ist eine Normalverteilung.
b Aus den Daten berechnet.

T-Test

Gruppenstatistiken

	Year	N	Mittelwert	Standardabweichung	Standardfehler des Mittelwertes
Incubation time	2007-2011	9	21,00	7,000	2,333
	2012	2	24,50	4,950	3,500

Test bei unabhängigen Stichproben

		Levene-Test der Varianzgleichheit		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standard fehler der Differenz	95% Konfidenzintervall der Differenz	
									Untere	Obere
Incubation time	Varianzen sind gleich	,102	,756	-,658	9	,527	-3,50	5,318	-15,530	8,530
	Varianzen sind nicht gleich			-,832	2,036	,492	-3,50	4,206	-21,295	14,295

Statistiken

Incubation time

N	Gültig	11
	Fehlend	71
Mittelwert		21,64
Standardfehler des Mittelwertes		1,992
Standardabweichung		6,607

Incubation time

		Häufigkeit	Prozent	Gültige Prozente	Kumulierte Prozente
Gültig	14	3	3,7	27,3	27,3
	21	5	6,1	45,5	72,7
	28	2	2,4	18,2	90,9
	35	1	1,2	9,1	100,0
	Gesamt	11	13,4	100,0	
Fehlend	System	71	86,6		
Gesamt		82	100,0		

Month of first diagnosis

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Year of infection * assumed	82	100,0%	0	0,0%	82	100,0%

		assumed month of infection according to date of first consultation												Gesamt
		january	february	march	april	may	june	july	august	september	october	november	december	
Year of infection	2007	1	1	0	2	1	2	0	0	0	3	0	0	10
	2008	1	0	0	0	0	1	0	2	2	0	0	1	7
	2009	0	1	3	1	2	0	0	1	0	0	0	0	8
	2010	0	0	0	1	2	1	1	2	0	0	1	0	8
	2011	1	0	0	0	1	3	0	1	1	0	0	0	7
	2012	2	1	2	10	6	6	3	5	4	3	0	0	42
Gesamt		5	3	5	14	12	13	4	11	7	6	1	1	82

Evaluated data on diagnosis

Time between first consultation and confirmation of diagnosis

Statistiken

Dauer 1.Arztbesuch-Schnelltest

N	Gültig	82
	Fehlend	0
Mittelwert		1,96
Standardfehler des Mittelwertes		,244
Standardabweichung		2,208

Statistiken

Dauer 1.Arztbesuch-Schnelltest

2007-2011	N	Gültig	40
		Fehlend	0
	Mittelwert		2,68
	Standardfehler des Mittelwertes		,438
	Standardabweichung		2,768
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		1,29
	Standardfehler des Mittelwertes		,181
	Standardabweichung		1,175

Kolmogorov-Smirnov-Anpassungstest

		Dauer 1.Arztbesuch-
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	1,96
	Standardabweichung	2,208
Extremste Differenzen	Absolut	,205
	Positiv	,205
	Negativ	-,187
Kolmogorov-Smirnov-Z		1,859
Asymptotische Signifikanz (2-seitig)		,002

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
Dauer 1.Arztbesuch-Schnelltest	2007-2011	40	48,30	1932,00
	2012	42	35,02	1471,00
	Gesamt	82		

Statistik für Test[a]

	Dauer 1.Arztbesuch-Schnelltest
Mann-Whitney-U	568,000
Wilcoxon-W	1471,000
Z	-2,591
Asymptotische Signifikanz (2-seitig)	,010

a. Gruppenvariable: Jahr

Time between first symptoms and first contact with a physician

Statistiken

Beschwerdedauer vor 1. Arztbesuch,in Tagen

N	Gültig	74
	Fehlend	8
Mittelwert		5,00
Standardfehler des Mittelwertes		,479
Standardabweichung		4,121

Statistiken

Beschwerdedauer vor 1. Arztbesuch,in Tagen

2007-2011	N	Gültig	35
		Fehlend	5
	Mittelwert		6,00
	Standardfehler des Mittelwertes		,944
	Standardabweichung		5,584
2012	N	Gültig	39
		Fehlend	3
	Mittelwert		4,10
	Standardfehler des Mittelwertes		,277
	Standardabweichung		1,729

Kolmogorov-Smirnov-Anpassungstest

		Beschwerdedauer vor 1.
N		74
Parameter der Normalverteilung[a,b]	Mittelwert	5,00
	Standardabweichung	4,121
Extremste Differenzen	Absolut	,246
	Positiv	,246
	Negativ	-,166
Kolmogorov-Smirnov-Z		2,118
Asymptotische Signifikanz (2-seitig)		,000

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
Beschwerdedauer vor 1. Arztbesuch,in Tagen!	2007-2011	35	40,09	1403,00
	2012	39	35,18	1372,00
	Gesamt	74		

Statistik für Test[a]

	Beschwerdedauer vor 1. Arztbesuch,in
Mann-Whitney-U	592,000
Wilcoxon-W	1372,000
Z	-,991
Asymptotische Signifikanz (2-seitig)	,322

a. Gruppenvariable: Jahr

Results of the point of care test

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Ergebnis des	82	100,0%	0	0,0%	82	100,0%

Jahr * Ergebnis des Schnelltestes Kreuztabelle

			Ergebnis des Schnelltestes			Gesamt
			puumala	puumala+	alle 3	
Jahr	2007-2011	Anzahl	37	2	1	40
		% innerhalb von Jahr	92,5%	5,0%	2,5%	100,0%
	2012	Anzahl	42	0	0	42
		% innerhalb von Jahr	100,0%	0,0%	0,0%	100,0%
Gesamt		Anzahl	79	2	1	82
		% innerhalb von Jahr	96,3%	2,4%	1,2%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische
Chi-Quadrat nach Pearson	3,270[a]	2	,195
Likelihood-Quotient	4,427	2	,109
Anzahl der gültigen Fälle	82		

a. 4 Zellen (66,7%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 49.

Symmetrische Maße[c]

		Wert	Näherungsweise
Nominal- bzgl. Nominalmaß	Phi	,200	,195
	Cramer-V	,200	,195
Anzahl der gültigen Fälle		82	

a. Die Null-Hyphothese wird nicht angenommen.

b. Unter Annahme der Null-Hyphothese wird der asymptotische Standardfehler verwendet.

c. Die Korrelations-Statistik ist nur für numerische Daten verfügbar.

First suspected diagnosis

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Year * Puumalainfektion	82	100,0%	0	,0%	82	100,0%

Year * Puumalainfektion as 1. diagnosis Kreuztabelle

			Puumalainfektion as 1. diagnosis		Gesamt
			other than	Puumala/Hant	
Year	2007-2011	Anzahl	23	17	40
		% von Year	57,5%	42,5%	100,0%
	2012	Anzahl	18	24	42
		% von Year	42,9%	57,1%	100,0%
Gesamt		Anzahl	41	41	82
		% von Year	50,0%	50,0%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	1,757 (b)	1	,185		
Kontinuitätskorrektur (a)	1,220	1	,269		
Likelihood-Quotient	1,763	1	,184		
Exakter Test nach Fisher				,269	,135
Zusammenhang linear-mit-..	1,736	1	,188		
Anzahl der gültigen Fälle	82				

a Wird nur für eine 2x2-Tabelle berechnet

b 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 20,00.

Symmetrische Maße

			Wert	Asymptoti	Näherungs	Näherungs
Intervall-	bzgl.	Pearson-R	,146	,109	1,324	,189 (c)
Ordinal-	bzgl.	Korrelation nach	,146	,109	1,324	,189 (c)
Anzahl der gültigen Fälle			82			

a Die Null-Hyphothese wird nicht angenommen.

b Unter Annahme der Null-Hyphothese wird der asymptotische Standardfehler verwendet.

c Basierend auf normaler Näherung

Statistical evaluation of clinical presentation

Arthromyalgia

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Arthromyalgien	82	100,0%	0	0,0%	82	100,0%

Jahr * Arthromyalgien Kreuztabelle

			Arthromyalgien		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	30	10	40
		% innerhalb von Jahr	75,0%	25,0%	100,0%
	2012	Anzahl	39	3	42
		% innerhalb von Jahr	92,9%	7,1%	100,0%
Gesamt		Anzahl	69	13	82
		% innerhalb von Jahr	84,1%	15,9%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	4,897[a]	1	,027		
Kontinuitätskorrektur[b]	3,650	1	,056		
Likelihood-Quotient	5,105	1	,024		
Exakter Test nach Fisher				,035	,027
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 6,34.

b. Wird nur für eine 2x2-Tabelle berechnet

Lumbago

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Lumbago	82	100,0%	0	0,0%	82	100,0%

Jahr * Lumbago Kreuztabelle

			Lumbago		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	38	2	40
		% innerhalb von Jahr	95,0%	5,0%	100,0%
	2012	Anzahl	33	9	42
		% innerhalb von Jahr	78,6%	21,4%	100,0%
Gesamt		Anzahl	71	11	82
		% innerhalb von Jahr	86,6%	13,4%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische Signifikanz (2-seitig)	Exakte Signifikanz (2-seitig)	Exakte Signifikanz (1-seitig)
Chi-Quadrat nach Pearson	4,761[a]	1	,029		
Kontinuitätskorrektur[b]	3,451	1	,063		
Likelihood-Quotient	5,122	1	,024		
Exakter Test nach Fisher				,049	,029
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 5,37.

b. Wird nur für eine 2x2-Tabelle berechnet

Fever

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Fieber	82	100,0%	0	0,0%	82	100,0%

Jahr * Fieber Kreuztabelle

			Fieber		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	4	36	40
		% innerhalb von Jahr	10,0%	90,0%	100,0%
	2012	Anzahl	4	38	42
		% innerhalb von Jahr	9,5%	90,5%	100,0%
Gesamt		Anzahl	8	74	82
		% innerhalb von Jahr	9,8%	90,2%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	,005[a]	1	,942		
Kontinuitätskorrektur[b]	,000	1	1,000		
Likelihood-Quotient	,005	1	,942		
Exakter Test nach Fisher				1,000	,616
Anzahl der gültigen Fälle	82				

a. 2 Zellen (50,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 3,90.

b. Wird nur für eine 2x2-Tabelle berechnet

Cephalea and retroocular pain

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Kopf- und	82	100,0%	0	0,0%	82	100,0%

Jahr * Kopf- und Bulbusschmerzen, retrobulbärer Schmerz Kreuztabelle

			Kopf- und Bulbusschmerzen,		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	19	21	40
		% innerhalb von Jahr	47,5%	52,5%	100,0%
	2012	Anzahl	19	23	42
		% innerhalb von Jahr	45,2%	54,8%	100,0%
Gesamt		Anzahl	38	44	82
		% innerhalb von Jahr	46,3%	53,7%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	,042[a]	1	,837		
Kontinuitätskorrektur[b]	,000	1	1,000		
Likelihood-Quotient	,042	1	,837		
Exakter Test nach Fisher				1,000	,506
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 18,54.

b. Wird nur für eine 2x2-Tabelle berechnet

Worsening of general condition

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * AZ-verschlechterung	82	100,0%	0	0,0%	82	100,0%

Jahr * AZ-verschlechterung Kreuztabelle

			AZ-verschlechterung		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	30	10	40
		% innerhalb von Jahr	75,0%	25,0%	100,0%
	2012	Anzahl	42	0	42
		% innerhalb von Jahr	100,0%	0,0%	100,0%
Gesamt		Anzahl	72	10	82
		% innerhalb von Jahr	87,8%	12,2%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	11,958[a]	1	,001		
Kontinuitätskorrektur[b]	9,738	1	,002		
Likelihood-Quotient	15,824	1	,000		
Exakter Test nach Fisher				,000	,000
Anzahl der gültigen Fälle	82				

a. 1 Zellen (25,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 4,88.

b. Wird nur für eine 2x2-Tabelle berechnet

Respiratory symptoms

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Husten, Atemnot,	82	100,0%	0	0,0%	82	100,0%

Jahr * Husten, Atemnot, Respirationstrakt Kreuztabelle

			Husten, Atemnot, Respirationstrakt		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	30	10	40
		% innerhalb von Jahr	75,0%	25,0%	100,0%
	2012	Anzahl	36	6	42
		% innerhalb von Jahr	85,7%	14,3%	100,0%
Gesamt		Anzahl	66	16	82
		% innerhalb von Jahr	80,5%	19,5%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	1,498[a]	1	,221		
Kontinuitätskorrektur[b]	,893	1	,345		
Likelihood-Quotient	1,508	1	,219		
Exakter Test nach Fisher				,271	,172
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 7,80.

b. Wird nur für eine 2x2-Tabelle berechnet

Shivering

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Schüttelfrost	82	100,0%	0	0,0%	82	100,0%

Jahr * Schüttelfrost Kreuztabelle

			Schüttelfrost		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	37	3	40
		% innerhalb von Jahr	92,5%	7,5%	100,0%
	2012	Anzahl	35	7	42
		% innerhalb von Jahr	83,3%	16,7%	100,0%
Gesamt		Anzahl	72	10	82
		% innerhalb von Jahr	87,8%	12,2%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	1,608[a]	1	,205		
Kontinuitätskorrektur[b]	,866	1	,352		
Likelihood-Quotient	1,652	1	,199		
Exakter Test nach Fisher				,313	,177
Anzahl der gültigen Fälle	82				

a. 1 Zellen (25,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 4,88.

b. Wird nur für eine 2x2-Tabelle berechnet

Renal or flanks' pain

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Nieren-und	82	100,0%	0	0,0%	82	100,0%

Jahr * Nieren-und Flankenschmerz Kreuztabelle

			Nieren-und Flankenschmerz		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	33	7	40
		% innerhalb von Jahr	82,5%	17,5%	100,0%
	2012	Anzahl	36	6	42
		% innerhalb von Jahr	85,7%	14,3%	100,0%
Gesamt		Anzahl	69	13	82
		% innerhalb von Jahr	84,1%	15,9%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	,159[a]	1	,690		
Kontinuitätskorrektur[b]	,009	1	,924		
Likelihood-Quotient	,159	1	,690		
Exakter Test nach Fisher				,768	,461
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 6,34.

b. Wird nur für eine 2x2-Tabelle berechnet

Meningeal symptoms

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr *	82	100,0%	0	0,0%	82	100,0%

Jahr * Lichtscheue/Meningismus Kreuztabelle

			Lichtscheue/Meningismus		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	39	1	40
		% innerhalb von Jahr	97,5%	2,5%	100,0%
	2012	Anzahl	39	3	42
		% innerhalb von Jahr	92,9%	7,1%	100,0%
Gesamt		Anzahl	78	4	82
		% innerhalb von Jahr	95,1%	4,9%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	,952[a]	1	,329		
Kontinuitätskorrektur[b]	,214	1	,644		
Likelihood-Quotient	,998	1	,318		
Exakter Test nach Fisher				,616	,327
Anzahl der gültigen Fälle	82				

a. 2 Zellen (50,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 1,95.

b. Wird nur für eine 2x2-Tabelle berechnet

Herpes labialis triggering

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Herpes labialis	82	100,0%	0	0,0%	82	100,0%

Jahr * Herpes labialis Triggerung Kreuztabelle

			Herpes labialis Triggerung		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	38	2	40
		% innerhalb von Jahr	95,0%	5,0%	100,0%
	2012	Anzahl	41	1	42
		% innerhalb von Jahr	97,6%	2,4%	100,0%
Gesamt		Anzahl	79	3	82
		% innerhalb von Jahr	96,3%	3,7%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	,399[a]	1	,528		
Kontinuitätskorrektur[b]	,002	1	,966		
Likelihood-Quotient	,405	1	,525		
Exakter Test nach Fisher				,611	,481
Anzahl der gültigen Fälle	82				

a. 2 Zellen (50,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 1,46.

b. Wird nur für eine 2x2-Tabelle berechnet

Troubles of vision

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Sehstörungen	82	100,0%	0	0,0%	82	100,0%

Jahr * Sehstörungen Kreuztabelle

			Sehstörungen		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	31	9	40
		% innerhalb von Jahr	77,5%	22,5%	100,0%
	2012	Anzahl	30	12	42
		% innerhalb von Jahr	71,4%	28,6%	100,0%
Gesamt		Anzahl	61	21	82
		% innerhalb von Jahr	74,4%	25,6%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	,396[a]	1	,529		
Kontinuitätskorrektur[b]	,142	1	,707		
Likelihood-Quotient	,398	1	,528		
Exakter Test nach Fisher				,616	,354
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 10,24.

b. Wird nur für eine 2x2-Tabelle berechnet

Gastro-intestinal symptoms

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * GIT-Symptome	82	100,0%	0	0,0%	82	100,0%

Jahr * GIT-Symptome Kreuztabelle

			GIT-Symptome		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	22	18	40
		% innerhalb von Jahr	55,0%	45,0%	100,0%
	2012	Anzahl	17	25	42
		% innerhalb von Jahr	40,5%	59,5%	100,0%
Gesamt		Anzahl	39	43	82
		% innerhalb von Jahr	47,6%	52,4%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	1,733[a]	1	,188		
Kontinuitätskorrektur[b]	1,199	1	,273		
Likelihood-Quotient	1,739	1	,187		
Exakter Test nach Fisher				,269	,137
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 19,02.

b. Wird nur für eine 2x2-Tabelle berechnet

Vertigo

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Vertigo	82	100,0%	0	0,0%	82	100,0%

Jahr * Vertigo Kreuztabelle

			Vertigo		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	36	4	40
		% innerhalb von Jahr	90,0%	10,0%	100,0%
	2012	Anzahl	40	2	42
		% innerhalb von Jahr	95,2%	4,8%	100,0%
Gesamt		Anzahl	76	6	82
		% innerhalb von Jahr	92,7%	7,3%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	,829[a]	1	,363		
Kontinuitätskorrektur[b]	,236	1	,627		
Likelihood-Quotient	,841	1	,359		
Exakter Test nach Fisher				,427	,315
Anzahl der gültigen Fälle	82				

a. 2 Zellen (50,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 2,93.

b. Wird nur für eine 2x2-Tabelle berechnet

Renal symptoms

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Harnveränderungen	82	100,0%	0	0,0%	82	100,0%

Jahr * Harnveränderungen jeglicher Art Kreuztabelle

			Harnveränderungen jeglicher Art		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	30	10	40
		% innerhalb von Jahr	75,0%	25,0%	100,0%
	2012	Anzahl	31	11	42
		% innerhalb von Jahr	73,8%	26,2%	100,0%
Gesamt		Anzahl	61	21	82
		% innerhalb von Jahr	74,4%	25,6%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische Signifikanz (2-seitig)	Exakte Signifikanz (2-seitig)	Exakte Signifikanz (1-seitig)
Chi-Quadrat nach Pearson	,015[a]	1	,902		
Kontinuitätskorrektur[b]	,000	1	1,000		
Likelihood-Quotient	,015	1	,902		
Exakter Test nach Fisher				1,000	,552
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 10,24.

b. Wird nur für eine 2x2-Tabelle berechnet

Fatigue, faintness, lassitude

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * MMA	82	100,0%	0	0,0%	82	100,0%

Jahr * MMA Kreuztabelle

			MMA		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	30	10	40
		% innerhalb von Jahr	75,0%	25,0%	100,0%
	2012	Anzahl	32	10	42
		% innerhalb von Jahr	76,2%	23,8%	100,0%
Gesamt		Anzahl	62	20	82
		% innerhalb von Jahr	75,6%	24,4%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	,016[a]	1	,900		
Kontinuitätskorrektur[b]	,000	1	1,000		
Likelihood-Quotient	,016	1	,900		
Exakter Test nach Fisher				1,000	,552
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 9,76.
b. Wird nur für eine 2x2-Tabelle berechnet

Statistical evaluation of first clinical examination

Petechial bleeding

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Petechien bei	82	100,0%	0	0,0%	82	100,0%

Jahr * Petechien bei Aufnahme Kreuztabelle

			Petechien bei Aufnahme		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	37	3	40
		% innerhalb von Jahr	92,5%	7,5%	100,0%
	2012	Anzahl	42	0	42
		% innerhalb von Jahr	100,0%	0,0%	100,0%
Gesamt		Anzahl	79	3	82
		% innerhalb von Jahr	96,3%	3,7%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	3,270[a]	1	,071		
Kontinuitätskorrektur[b]	1,488	1	,223		
Likelihood-Quotient	4,427	1	,035		
Exakter Test nach Fisher				,112	,112
Anzahl der gültigen Fälle	82				

a. 2 Zellen (50,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 1,46.

b. Wird nur für eine 2x2-Tabelle berechnet

Oedema

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Ödeme bei Aufnahme	82	100,0%	0	0,0%	82	100,0%

Jahr * Ödeme bei Aufnahme Kreuztabelle

			Ödeme bei Aufnahme		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	38	2	40
		% innerhalb von Jahr	95,0%	5,0%	100,0%
	2012	Anzahl	42	0	42
		% innerhalb von Jahr	100,0%	0,0%	100,0%
Gesamt		Anzahl	80	2	82
		% innerhalb von Jahr	97,6%	2,4%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	2,153[a]	1	,142		
Kontinuitätskorrektur[b]	,564	1	,453		
Likelihood-Quotient	2,924	1	,087		
Exakter Test nach Fisher				,235	,235
Anzahl der gültigen Fälle	82				

a. 2 Zellen (50,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 98.

b. Wird nur für eine 2x2-Tabelle berechnet

Ocular manifestation

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * konjunktivale	82	100,0%	0	0,0%	82	100,0%

Jahr * konjunktivale Blutungen bei Aufnahme Kreuztabelle

			konjunktivale	Gesamt
			nein	
Jahr	2007-2011	Anzahl	40	40
		% innerhalb von Jahr	100,0%	100,0%
	2012	Anzahl	42	42
		% innerhalb von Jahr	100,0%	100,0%
Gesamt		Anzahl	82	82
		% innerhalb von Jahr	100,0%	100,0%

Chi-Quadrat-Tests

	Wert
Chi-Quadrat nach Pearson	.[a]
Anzahl der gültigen Fälle	82

a. Es werden keine Statistiken berechnet, da konjunktivale Blutungen bei Aufnahme eine Konstante ist

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * sklerale Blutungen bei	82	100,0%	0	0,0%	82	100,0%

Jahr * sklerale Blutungen bei Aufnahme Kreuztabelle

			sklerale Blutungen bei	Gesamt
			nein	
Jahr	2007-2011	Anzahl	40	40
		% innerhalb von Jahr	100,0%	100,0%
	2012	Anzahl	42	42
		% innerhalb von Jahr	100,0%	100,0%
Gesamt		Anzahl	82	82
		% innerhalb von Jahr	100,0%	100,0%

Chi-Quadrat-Tests

	Wert
Chi-Quadrat nach Pearson	.[a]
Anzahl der gültigen Fälle	82

a. Es werden keine Statistiken berechnet, da sklerale Blutungen bei Aufnahme eine Konstante ist

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Konjunktivitis bei	82	100,0%	0	0,0%	82	100,0%

Jahr * Konjunktivitis bei Aufnahme Kreuztabelle

			Konjunktivitis bei Aufnahme		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	40	0	40
		% innerhalb von Jahr	100,0%	0,0%	100,0%
	2012	Anzahl	41	1	42
		% innerhalb von Jahr	97,6%	2,4%	100,0%
Gesamt		Anzahl	81	1	82
		% innerhalb von Jahr	98,8%	1,2%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	,016[a]	1	,900		
Kontinuitätskorrektur[b]	,000	1	1,000		
Likelihood-Quotient	,016	1	,900		
Exakter Test nach Fisher				1,000	,552
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 9,76.

b. Wird nur für eine 2x2-Tabelle berechnet

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Myopie bei Aufnahme	82	100,0%	0	0,0%	82	100,0%

Jahr * Myopie bei Aufnahme Kreuztabelle

			Myopie bei Aufnahme		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	31	9	40
		% innerhalb von Jahr	77,5%	22,5%	100,0%
	2012	Anzahl	32	10	42
		% innerhalb von Jahr	76,2%	23,8%	100,0%
Gesamt		Anzahl	63	19	82
		% innerhalb von Jahr	76,8%	23,2%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	,020[a]	1	,888		
Kontinuitätskorrektur[b]	,000	1	1,000		
Likelihood-Quotient	,020	1	,888		
Exakter Test nach Fisher				1,000	,549
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 9,27.

b. Wird nur für eine 2x2-Tabelle berechnet

Renal troubles approved by clinical examination

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * NINS bei Aufnahme	82	100,0%	0	0,0%	82	100,0%

Jahr * NINS bei Aufnahme Kreuztabelle

			NINS bei Aufnahme		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	20	20	40
		% innerhalb von Jahr	50,0%	50,0%	100,0%
	2012	Anzahl	18	24	42
		% innerhalb von Jahr	42,9%	57,1%	100,0%
Gesamt		Anzahl	38	44	82
		% innerhalb von Jahr	46,3%	53,7%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	,420[a]	1	,517		
Kontinuitätskorrektur[b]	,182	1	,669		
Likelihood-Quotient	,421	1	,517		
Exakter Test nach Fisher				,658	,335
Anzahl der gültigen Fälle	82				

a. 0 Zellen (,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 18,54.

b. Wird nur für eine 2x2-Tabelle berechnet

Blood pressure

Systolischer Blutdruck

Deskriptive Statistiken

	N	Mittelwert	Standardabweich	Minimum	Maximum
systolischer Blutdruck bei	61	130,41	23,643	78	194

Kolmogorov-Smirnov-Anpassungstest

		systolischer
N		61
Parameter der Normalverteilung[a,b]	Mittelwert	130,41
	Standardabweichung	23,643
Extremste Differenzen	Absolut	,073
	Positiv	,073
	Negativ	-,069
Kolmogorov-Smirnov-Z		,567
Asymptotische Signifikanz (2-seitig)		,905

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Gruppenstatistiken

	Jahr	N	Mittelwert	Standardabweic	Standardfehler
systolischer Blutdruck bei Aufnahme	2007-2011	23	130,22	20,776	4,332
	2012	38	130,53	25,492	4,135

Test bei unabhängigen Stichproben

		Levene-Test der		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	95% Konfidenzintervall der Differenz	
									Untere	Obere
systolischer Blutdruck bei Aufnahme	Varianzen sind gleich	,953	,333	-,049	59	,961	-,309	6,299	-12,913	12,295
	Varianzen sind nicht gleich			-,052	53,800	,959	-,309	5,989	-12,317	11,699

Diastolic blood pressure

Deskriptive Statistiken

	N	Mittelwert	Standardabweich	Minimum	Maximum
diastolischer Blutdruck bei	61	83,15	12,842	53	120

Kolmogorov-Smirnov-Anpassungstest

		diastolischer Blutdruck
N		61
Parameter der Normalverteilung[a,b]	Mittelwert	83,15
	Standardabweichung	12,842
Extremste Differenzen	Absolut	,141
	Positiv	,116
	Negativ	-,141
Kolmogorov-Smirnov-Z		1,100
Asymptotische Signifikanz (2-seitig)		,177

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Gruppenstatistiken

	Jahr	N	Mittelwert	Standardabweic	Standardfehler
diastolischer Blutdruck bei Aufnahme	2007-2011	23	81,52	9,963	2,077
	2012	38	84,13	14,345	2,327

Test bei unabhängigen Stichproben

		Levene-Test der Varianzgleichheit		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	95% Konfidenzintervall der Differenz	
									Untere	Obere
diastolischer Blutdruck bei Aufnahme	Varianzen sind gleich	1,860	,178	-,767	59	,446	-2,610	3,405	-9,422	4,203
	Varianzen sind nicht gleich			-,837	57,769	,406	-2,610	3,120	-8,855	3,635

Temperature

Deskriptive Statistiken

	N	Mittelwert	Standardabweich	Minimum	Maximum
Temperatur °C bei Aufnahme	47	37,4085	,97620	35,70	39,80

Kolmogorov-Smirnov-Anpassungstest

		Temperatur °C bei
N		47
Parameter der Normalverteilung[a,b]	Mittelwert	37,4085
	Standardabweichung	,97620
Extremste Differenzen	Absolut	,078
	Positiv	,078
	Negativ	-,053
Kolmogorov-Smirnov-Z		,534
Asymptotische Signifikanz (2-seitig)		,938

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Gruppenstatistiken

	Jahr	N	Mittelwert	Standardabweic	Standardfehler
Temperatur °C bei Aufnahme	2007-2011	17	37,5765	,76119	,18462
	2012	30	37,3133	1,07983	,19715

Test bei unabhängigen Stichproben

		Levene-Test der Varianzgleichheit		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	95% Konfidenzintervall der Differenz	
									Untere	Obere
Temperatur °C bei Aufnahme	Varianzen sind gleich	3,456	,070	,886	45	,380	,26314	,29704	-,33514	,86142
	Varianzen sind nicht gleich			,974	42,678	,335	,26314	,27009	-,28168	,80795

Data on diagnostic workup

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Thorax Röntgen	82	100,0%	0	0,0%	82	100,0%

Jahr * Thorax Röntgen Kreuztabelle

			Thorax Röntgen					Gesamt
			keines	unauffällig	Pleura-erguss	Pleuraerguss +Infiltrate	Pleuraerguss +Infiltrat	
Jahr	2007-2011	Anzahl	10	16	11	2	1	40
		% innerhalb von Jahr	25,0%	40,0%	27,5%	5,0%	2,5%	100,0%
	2012	Anzahl	17	15	7	3	0	42
		% innerhalb von Jahr	40,5%	35,7%	16,7%	7,1%	0,0%	100,0%
Gesamt		Anzahl	27	31	18	5	1	82
		% innerhalb von Jahr	32,9%	37,8%	22,0%	6,1%	1,2%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische
Chi-Quadrat nach Pearson	3,889[a]	4	,421
Likelihood-Quotient	4,303	4	,367
Anzahl der gültigen Fälle	82		

a. 4 Zellen (40,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 49.

Symmetrische Maße[c]

		Wert	Näherungsweise
Nominal- bzgl. Nominalmaß	Phi	,218	,421
	Cramer-V	,218	,421
Anzahl der gültigen Fälle		82	

a. Die Null-Hyphothese wird nicht angenommen.

b. Unter Annahme der Null-Hyphothese wird der asymptotische Standardfehler verwendet.

c. Die Korrelations-Statistik ist nur für numerische Daten verfügbar.

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Abdomen Sono	82	100,0%	0	0,0%	82	100,0%

Jahr * Abdomen Sono Kreuztabelle

			Abdomen Sono								Gesamt
			keines	unauffällig	Splenomegalie	Veränderungen der Nieren	Splenomegalie +Ascites	Splenomegalie +Veränderungen der Niere	Splenomegalie +Ascites +Veränderungen der Niere	Ascites +Veränderungen der Niere	
Jahr	2007-2011	Anzahl	9	8	5	7	2	3	2	4	40
		% innerhalb von Jahr	22,5%	20,0%	12,5%	17,5%	5,0%	7,5%	5,0%	10,0%	100,0%
	2012	Anzahl	11	10	2	12	0	6	1	0	42
		% innerhalb von Jahr	26,2%	23,8%	4,8%	28,6%	0,0%	14,3%	2,4%	0,0%	100,0%
Gesamt		Anzahl	20	18	7	19	2	9	3	4	82
		% innerhalb von Jahr	24,4%	22,0%	8,5%	23,2%	2,4%	11,0%	3,7%	4,9%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische Signifikanz (2-seitig)
Chi-Quadrat nach Pearson	10,314[a]	7	,171
Likelihood-Quotient	12,711	7	,079
Anzahl der gültigen Fälle	82		

a. 10 Zellen (62,5%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 98.

Symmetrische Maße[c]

		Wert	Näherungsweise
Nominal- bzgl. Nominalmaß	Phi	,355	,171
	Cramer-V	,355	,171
Anzahl der gültigen Fälle		82	

a. Die Null-Hyphothese wird nicht angenommen.

b. Unter Annahme der Null-Hyphothese wird der asymptotische Standardfehler verwendet.

c. Die Korrelations-Statistik ist nur für numerische Daten verfügbar.

Laboratory results at first clinical examination

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
1. Leukos	82	10,1280	4,71316	3,83	25,27

Statistiken

1. Leukos

2007-2011	N	Gültig	40
		Fehlend	0
	Mittelwert		10,7825
	Standardfehler des Mittelwertes		,89041
	Standardabweichung		5,63144
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		9,5048
	Standardfehler des Mittelwertes		,55429
	Standardabweichung		3,59222

Kolmogorov-Smirnov-Anpassungstest

		1. Leukos
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	10,1280
	Standardabweichung	4,71316
Extremste Differenzen	Absolut	,159
	Positiv	,159
	Negativ	-,121
Kolmogorov-Smirnov-Z		1,439
Asymptotische Signifikanz (2-seitig)		,032

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
1. Leukos	2007-2011	40	43,03	1721,00
	2012	42	40,05	1682,00
	Gesamt	82		

Statistik für Test[a]

	1. Leukos
Mann-Whitney-U	779,000
Wilcoxon-W	1682,000
Z	-,566
Asymptotische Signifikanz (2-seitig)	,571

a. Gruppenvariable: Jahr

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
1.HB	82	15,4939	1,91919	10,60	21,20

Kolmogorov-Smirnov-Anpassungstest

		1.HB
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	15,4939
	Standardabweichung	1,91919
Extremste Differenzen	Absolut	,060
	Positiv	,059
	Negativ	-,060
Kolmogorov-Smirnov-Z		,540
Asymptotische Signifikanz (2-seitig)		,933

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

T-Test

Gruppenstatistiken

	Jahr	N	Mittelwert	Standardabweic	Standardfehler
1.HB	2007-2011	40	15,9850	1,86253	,29449
	2012	42	15,0262	1,87552	,28940

Test bei unabhängigen Stichproben

		Levene-Test der		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	95% Konfidenzintervall der Differenz	
									Untere	Obere
1.HB	Varianzen sind gleich	,035	,852	2,322	80	,023	,95881	,41296	,13699	1,78063
	Varianzen sind nicht gleich			2,322	79,856	,023	,95881	,41289	,13711	1,78051

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
1.HKT	82	43,1622	4,79170	30,90	54,70

Kolmogorov-Smirnov-Anpassungstest

		1.HKT
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	43,1622
	Standardabweichung	4,79170
Extremste Differenzen	Absolut	,042
	Positiv	,041
	Negativ	-,042
Kolmogorov-Smirnov-Z		,384
Asymptotische Signifikanz (2-seitig)		,998

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

T-Test

Gruppenstatistiken

	Jahr	N	Mittelwert	Standardabweic	Standardfehler
1.HKT	2007-2011	40	44,4300	4,60486	,72809
	2012	42	41,9548	4,70413	,72586

Test bei unabhängigen Stichproben

		Levene-Test der		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	95% Konfidenzintervall der Differenz	
									Untere	Obere
1.HKT	Varianzen sind gleich	,029	,866	2,406	80	,018	2,47524	1,02864	,42817	4,52231
	Varianzen sind nicht gleich			2,408	79,937	,018	2,47524	1,02810	,42922	4,52125

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
1. Thrombos	82	84,7683	54,81446	16,00	370,00

Statistiken

1. Thrombos

2007-2011	N	Gültig	40
		Fehlend	0
	Mittelwert		85,7000
	Standardfehler des Mittelwertes		10,21564
	Standardabweichung		64,60936
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		83,8810
	Standardfehler des Mittelwertes		6,83752
	Standardabweichung		44,31220

Kolmogorov-Smirnov-Anpassungstest

		1. Thrombos
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	84,7683
	Standardabweichung	54,81446
Extremste Differenzen	Absolut	,170
	Positiv	,170
	Negativ	-,117
Kolmogorov-Smirnov-Z		1,543
Asymptotische Signifikanz (2-seitig)		,017

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
1. Thrombos	2007-2011	40	40,29	1611,50
	2012	42	42,65	1791,50
	Gesamt	82		

Statistik für Test[a]

	1. Thrombos
Mann-Whitney-U	791,500
Wilcoxon-W	1611,500
Z	-,450
Asymptotische Signifikanz (2-seitig)	,653

a. Gruppenvariable: Jahr

Deskriptive Statistiken

	N	Mittelwert	Standardabweichun	Minimum	Maximum
1. Lymphos%	82	18,2087	6,76473	4,00	38,00

Kolmogorov-Smirnov-Anpassungstest

		1. Lymphos%
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	18,2087
	Standardabweichung	6,76473
Extremste Differenzen	Absolut	,079
	Positiv	,079
	Negativ	-,055
Kolmogorov-Smirnov-Z		,711
Asymptotische Signifikanz (2-seitig)		,693

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

T-Test

Gruppenstatistiken

	Jahr	N	Mittelwert	Standardabweichu	Standardfehler des
1. Lymphos%	2007-2011	40	17,2015	5,81995	,92021
	2012	42	19,1679	7,50035	1,15733

Test bei unabhängigen Stichproben

		Levene-Test der		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	95% Konfidenzintervall der Differenz	
									Untere	Obere
1. Lymphos%	Varianzen sind gleich	1,028	,314	-1,322	80	,190	-1,96636	1,48768	-4,92693	,99422
	Varianzen sind nicht gleich			-1,330	76,911	,187	-1,96636	1,47858	-4,91065	,97793

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
1. Crea	82	2,2555	1,99469	,60	10,60

Statistiken

1. Crea

2007-2011	N	Gültig	40
		Fehlend	0
	Mittelwert		2,0308
	Standardfehler des Mittelwertes		,25599
	Standardabweichung		1,61903
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		2,4695
	Standardfehler des Mittelwertes		,35426
	Standardabweichung		2,29585

Kolmogorov-Smirnov-Anpassungstest

		1. Crea
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	2,2555
	Standardabweichung	1,99469
Extremste Differenzen	Absolut	,230
	Positiv	,230
	Negativ	-,210
Kolmogorov-Smirnov-Z		2,079
Asymptotische Signifikanz (2-seitig)		,000

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
1. Crea	2007-2011	40	39,76	1590,50
	2012	42	43,15	1812,50
	Gesamt	82		

Statistik für Test[a]

	1. Crea
Mann-Whitney-U	770,500
Wilcoxon-W	1590,500
Z	-,645
Asymptotische Signifikanz (2-seitig)	,519

a. Gruppenvariable: Jahr

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
1.Harnst	82	68,4634	56,27253	13,00	300,00

Statistiken

1.Harnst

2007-2011	N	Gültig	40
		Fehlend	0
	Mittelwert		68,9000
	Standardfehler des Mittelwertes		9,26856
	Standardabweichung		58,61950
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		68,0476
	Standardfehler des Mittelwertes		8,43317
	Standardabweichung		54,65321

Kolmogorov-Smirnov-Anpassungstest

		1.Harnst
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	68,4634
	Standardabweichung	56,27253
Extremste Differenzen	Absolut	,186
	Positiv	,186
	Negativ	-,162
Kolmogorov-Smirnov-Z		1,685
Asymptotische Signifikanz (2-seitig)		,007

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
1.Harnst	2007-2011	40	40,74	1629,50
	2012	42	42,23	1773,50
	Gesamt	82		

Statistik für Test[a]

	1.Harnst
Mann-Whitney-U	809,500
Wilcoxon-W	1629,500
Z	-,283
Asymptotische Signifikanz (2-seitig)	,777

a. Gruppenvariable: Jahr

Deskriptive Statistiken

	N	Mittelwert	Standardabweichun	Minimum	Maximum
1. GFR MDRD	82	51,6467	30,97916	7,90	133,55

Kolmogorov-Smirnov-Anpassungstest

		1. GFR MDRD
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	51,6467
	Standardabweichung	30,97916
Extremste Differenzen	Absolut	,112
	Positiv	,112
	Negativ	-,079
Kolmogorov-Smirnov-Z		1,013
Asymptotische Signifikanz (2-seitig)		,257

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

T-Test

Gruppenstatistiken

	Jahr	N	Mittelwert	Standardabweichu	Standardfehler des
1. GFR MDRD	2007-2011	40	50,1978	29,79009	4,71023
	2012	42	53,0267	32,37053	4,99488

Test bei unabhängigen Stichproben

		Levene-Test der		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	95% Konfidenzintervall der Differenz	
									Untere	Obere
1. GFR MDRD	Varianzen sind gleich	,312	,578	-,411	80	,682	-2,82892	6,87957	-16,51969	10,86185
	Varianzen sind nicht gleich			-,412	79,910	,681	-2,82892	6,86550	-16,49193	10,83410

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
1.LDH	82	368,1829	591,27425	140,00	5539,00

Statistiken

1.LDH

2007-2011	N	Gültig	40
		Fehlend	0
	Mittelwert		322,9250
	Standardfehler des Mittelwertes		22,58081
	Standardabweichung		142,81356
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		411,2857
	Standardfehler des Mittelwertes		126,05566
	Standardabweichung		816,93404

Kolmogorov-Smirnov-Anpassungstest

		1.LDH
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	368,1829
	Standardabweichung	591,27425
Extremste Differenzen	Absolut	,350
	Positiv	,329
	Negativ	-,350
Kolmogorov-Smirnov-Z		3,167
Asymptotische Signifikanz (2-seitig)		,000

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
1.LDH	2007-2011	40	44,26	1770,50
	2012	42	38,87	1632,50
	Gesamt	82		

Statistik für Test[a]

	1.LDH
Mann-Whitney-U	729,500
Wilcoxon-W	1632,500
Z	-1,025
Asymptotische Signifikanz (2-seitig)	,305

a. Gruppenvariable: Jahr

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
1. ALT	82	58,0854	90,10997	12,00	802,00

Statistiken

1. ALT

2007-2011	N	Gültig	40
		Fehlend	0
	Mittelwert		57,4250
	Standardfehler des Mittelwertes		6,48775
	Standardabweichung		41,03212
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		58,7143
	Standardfehler des Mittelwertes		18,54161
	Standardabweichung		120,16336

Kolmogorov-Smirnov-Anpassungstest

		1. ALT
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	58,0854
	Standardabweichung	90,10997
Extremste Differenzen	Absolut	,305
	Positiv	,289
	Negativ	-,305
Kolmogorov-Smirnov-Z		2,758
Asymptotische Signifikanz (2-seitig)		,000

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
1. ALT	2007-2011	40	46,75	1870,00
	2012	42	36,50	1533,00
	Gesamt	82		

Statistik für Test[a]

	1. ALT
Mann-Whitney-U	630,000
Wilcoxon-W	1533,000
Z	-1,949
Asymptotische Signifikanz (2-seitig)	,051

a. Gruppenvariable: Jahr

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
1.AST	82	72,3780	190,15417	14,00	1747,00

Statistiken

1.AST

2007-2011	N	Gültig	40
		Fehlend	0
	Mittelwert		61,2000
	Standardfehler des Mittelwertes		6,54787
	Standardabweichung		41,41237
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		83,0238
	Standardfehler des Mittelwertes		40,69807
	Standardabweichung		263,75363

Kolmogorov-Smirnov-Anpassungstest

		1.AST
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	72,3780
	Standardabweichung	190,15417
Extremste Differenzen	Absolut	,379
	Positiv	,359
	Negativ	-,379
Kolmogorov-Smirnov-Z		3,436
Asymptotische Signifikanz (2-seitig)		,000

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
1.AST	2007-2011	40	45,91	1836,50
	2012	42	37,30	1566,50
	Gesamt	82		

Statistik für Test[a]

	1.AST
Mann-Whitney-U	663,500
Wilcoxon-W	1566,500
Z	-1,638
Asymptotische Signifikanz (2-seitig)	,101

a. Gruppenvariable: Jahr

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
1.aPTT	80	38,7025	7,02473	24,60	75,10

Kolmogorov-Smirnov-Anpassungstest

		1.aPTT
N		80
Parameter der Normalverteilung[a,b]	Mittelwert	38,7025
	Standardabweichung	7,02473
Extremste Differenzen	Absolut	,096
	Positiv	,096
	Negativ	-,084
Kolmogorov-Smirnov-Z		,860
Asymptotische Signifikanz (2-seitig)		,450

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

T-Test

Gruppenstatistiken

	Jahr	N	Mittelwert	Standardabweichung	Standardfehler des
1.aPTT	2007-2011	39	38,7692	5,33633	,85450
	2012	41	38,6390	8,39041	1,31036

Test bei unabhängigen Stichproben

		Levene-Test der Varianzgleichheit		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	95% Konfidenzintervall der Differenz	
									Untere	Obere
1.aPTT	Varianzen sind gleich	1,738	,191	,082	78	,935	,13021	1,58124	-3,01780	3,27821
	Varianzen sind nicht gleich			,083	68,260	,934	,13021	1,56436	-2,99120	3,25162

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
1.CRP	82	68,7280	63,46018	1,00	266,40

Statistiken

1.CRP

2007-2011	N	Gültig	40
		Fehlend	0
	Mittelwert		77,0325
	Standardfehler des Mittelwertes		10,33107
	Standardabweichung		65,33945
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		60,8190
	Standardfehler des Mittelwertes		9,46650
	Standardabweichung		61,34996

Kolmogorov-Smirnov-Anpassungstest

		1.CRP
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	68,7280
	Standardabweichung	63,46018
Extremste Differenzen	Absolut	,200
	Positiv	,200
	Negativ	-,147
Kolmogorov-Smirnov-Z		1,808
Asymptotische Signifikanz (2-seitig)		,003

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
1.CRP	2007-2011	40	45,04	1801,50
	2012	42	38,13	1601,50
	Gesamt	82		

Statistik für Test[a]

	1.CRP
Mann-Whitney-U	698,500
Wilcoxon-W	1601,500
Z	-1,313
Asymptotische Signifikanz (2-seitig)	,189

a. Gruppenvariable: Jahr

Clinical signs and symptoms in the course of disease

Petechial bleeding

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Petechien im Verlauf	82	100,0%	0	0,0%	82	100,0%

Jahr * Petechien im Verlauf Kreuztabelle

			Petechien im Verlauf			Gesamt
				nein	ja	
Jahr	2007-2011	Anzahl	0	38	2	40
		% innerhalb von Jahr	0,0%	95,0%	5,0%	100,0%
	2012	Anzahl	1	40	1	42
		% innerhalb von Jahr	2,4%	95,2%	2,4%	100,0%
Gesamt		Anzahl	1	78	3	82
		% innerhalb von Jahr	1,2%	95,1%	3,7%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische
Chi-Quadrat nach Pearson	1,337[a]	2	,513
Likelihood-Quotient	1,729	2	,421
Anzahl der gültigen Fälle	82		

a. 4 Zellen (66,7%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 49.

Oedema

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Ödeme im Verlauf	82	100,0%	0	0,0%	82	100,0%

Jahr * Ödeme im Verlauf Kreuztabelle

			Ödeme im Verlauf			Gesamt
				nein	ja	
Jahr	2007-2011	Anzahl	0	31	9	40
		% innerhalb von Jahr	0,0%	77,5%	22,5%	100,0%
	2012	Anzahl	1	34	7	42
		% innerhalb von Jahr	2,4%	81,0%	16,7%	100,0%
Gesamt		Anzahl	1	65	16	82
		% innerhalb von Jahr	1,2%	79,3%	19,5%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische
Chi-Quadrat nach Pearson	1,340[a]	2	,512
Likelihood-Quotient	1,727	2	,422
Anzahl der gültigen Fälle	82		

a. 2 Zellen (33,3%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 49.

Ocular manifestation

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * konjunktivale	82	100,0%	0	0,0%	82	100,0%

Jahr * konjunktivale Blutungen im Verlauf Kreuztabelle

			konjunktivale Blutungen im Verlauf			Gesamt
				nein	ja	
Jahr	2007-2011	Anzahl	0	38	2	40
		% innerhalb von Jahr	0,0%	95,0%	5,0%	100,0%
	2012	Anzahl	1	41	0	42
		% innerhalb von Jahr	2,4%	97,6%	0,0%	100,0%
Gesamt		Anzahl	1	79	2	82
		% innerhalb von Jahr	1,2%	96,3%	2,4%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische
Chi-Quadrat nach Pearson	3,067[a]	2	,216
Likelihood-Quotient	4,224	2	,121
Anzahl der gültigen Fälle	82		

a. 4 Zellen (66,7%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 49.

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Konjunktivitis im	82	100,0%	0	0,0%	82	100,0%

Jahr * Konjunktivitis im Verlauf Kreuztabelle

			Konjunktivitis im Verlauf			Gesamt
				nein	ja	
Jahr	2007-2011	Anzahl	0	33	7	40
		% innerhalb von Jahr	0,0%	82,5%	17,5%	100,0%
	2012	Anzahl	1	39	2	42
		% innerhalb von Jahr	2,4%	92,9%	4,8%	100,0%
Gesamt		Anzahl	1	72	9	82
		% innerhalb von Jahr	1,2%	87,8%	11,0%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische
Chi-Quadrat nach Pearson	4,232[a]	2	,121
Likelihood-Quotient	4,780	2	,092
Anzahl der gültigen Fälle	82		

a. 4 Zellen (66,7%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 49.

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Myopie im Verlauf	82	100,0%	0	0,0%	82	100,0%

Jahr * Myopie im Verlauf Kreuztabelle

			Myopie im Verlauf			Gesamt
				nein	ja	
Jahr	2007-2011	Anzahl	0	21	19	40
		% innerhalb von Jahr	0,0%	52,5%	47,5%	100,0%
	2012	Anzahl	1	23	18	42
		% innerhalb von Jahr	2,4%	54,8%	42,9%	100,0%
Gesamt		Anzahl	1	44	37	82
		% innerhalb von Jahr	1,2%	53,7%	45,1%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische
Chi-Quadrat nach Pearson	1,070[a]	2	,586
Likelihood-Quotient	1,455	2	,483
Anzahl der gültigen Fälle	82		

a. 2 Zellen (33,3%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 49.

Renal failure

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * NINS im Verlauf	82	100,0%	0	0,0%	82	100,0%

Jahr * NINS im Verlauf Kreuztabelle

			NINS im Verlauf			Gesamt
				nein	ja	
Jahr	2007-2011	Anzahl	0	11	29	40
		% innerhalb von Jahr	0,0%	27,5%	72,5%	100,0%
	2012	Anzahl	1	6	35	42
		% innerhalb von Jahr	2,4%	14,3%	83,3%	100,0%
Gesamt		Anzahl	1	17	64	82
		% innerhalb von Jahr	1,2%	20,7%	78,0%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische
Chi-Quadrat nach Pearson	2,986[a]	2	,225
Likelihood-Quotient	3,393	2	,183
Anzahl der gültigen Fälle	82		

a. 2 Zellen (33,3%) haben eine erwartete Häufigkeit kleiner 5. Die

Maximum and minimum values of pathologic laboratory findings

Deskriptive Statistiken

	N	Mittelwert	Standardabweichun	Minimum	Maximum
Thrombos max	82	73,3171	52,05313	8,00	323,00

Statistiken

Thrombos max

2007-2011	N	Gültig	40
		Fehlend	0
	Mittelwert		69,4500
	Standardfehler des Mittelwertes		9,45461
	Standardabweichung		59,79621
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		77,0000
	Standardfehler des Mittelwertes		6,76707
	Standardabweichung		43,85564

Kolmogorov-Smirnov-Anpassungstest

		Thrombos max
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	73,3171
	Standardabweichung	52,05313
Extremste Differenzen	Absolut	,173
	Positiv	,173
	Negativ	-,107
Kolmogorov-Smirnov-Z		1,568
Asymptotische Signifikanz (2-seitig)		,015

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
Thrombos max	2007-2011	40	37,26	1490,50
	2012	42	45,54	1912,50
	Gesamt	82		

Statistik für Test[a]

	Thrombos max
Mann-Whitney-U	670,500
Wilcoxon-W	1490,500
Z	-1,573
Asymptotische Signifikanz (2-seitig)	,116

a. Gruppenvariable: Jahr

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
CRP max	82	87,6244	73,24779	1,00	365,30

Statistiken

CRP max

2007-2011	N	Gültig	40
		Fehlend	0
	Mittelwert		95,6250
	Standardfehler des Mittelwertes		11,04134
	Standardabweichung		69,83157
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		80,0048
	Standardfehler des Mittelwertes		11,79096
	Standardabweichung		76,41415

Kolmogorov-Smirnov-Anpassungstest

		CRP max
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	87,6244
	Standardabweichung	73,24779
Extremste Differenzen	Absolut	,159
	Positiv	,159
	Negativ	-,120
Kolmogorov-Smirnov-Z		1,443
Asymptotische Signifikanz (2-seitig)		,031

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
CRP max	2007-2011	40	45,45	1818,00
	2012	42	37,74	1585,00
	Gesamt	82		

Statistik für Test[a]

	CRP max
Mann-Whitney-U	682,000
Wilcoxon-W	1585,000
Z	-1,466
Asymptotische Signifikanz (2-seitig)	,143

a. Gruppenvariable: Jahr

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
Crea max	82	3,7750	3,20408	,60	11,94

Statistiken

Crea max

2007-2011	N	Gültig	40
		Fehlend	0
	Mittelwert		3,8620
	Standardfehler des Mittelwertes		,51829
	Standardabweichung		3,27798
2012	N	Gültig	42
		Fehlend	0
	Mittelwert		3,6921
	Standardfehler des Mittelwertes		,48908
	Standardabweichung		3,16960

Kolmogorov-Smirnov-Anpassungstest

		Crea max
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	3,7750
	Standardabweichung	3,20408
Extremste Differenzen	Absolut	,235
	Positiv	,235
	Negativ	-,164
Kolmogorov-Smirnov-Z		2,125
Asymptotische Signifikanz (2-seitig)		,000

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Jahr	N	Mittlerer Rang	Rangsumme
Crea max	2007-2011	40	41,38	1655,00
	2012	42	41,62	1748,00
	Gesamt	82		

Statistik für Test[a]

	Crea max
Mann-Whitney-U	835,000
Wilcoxon-W	1655,000
Z	-,046
Asymptotische Signifikanz (2-seitig)	,963

a. Gruppenvariable: Jahr

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
HST max	82	102,4878	69,82946	17,00	300,00

Kolmogorov-Smirnov-Anpassungstest

		HST max
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	102,4878
	Standardabweichung	69,82946
Extremste Differenzen	Absolut	,139
	Positiv	,139
	Negativ	-,110
Kolmogorov-Smirnov-Z		1,254
Asymptotische Signifikanz (2-seitig)		,086

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

T-Test

Gruppenstatistiken

	Jahr	N	Mittelwert	Standardabweichun	Standardfehler des
HST max	2007-2011	40	114,4750	76,75836	12,13656
	2012	42	91,0714	61,28000	9,45571

Test bei unabhängigen Stichproben

		Levene-Test der Varianzgleichheit		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	95% Konfidenzintervall der Differenz	
									Untere	Obere
HST max	Varianzen sind gleich	6,052	,016	1,530	80	,130	23,40357	15,30135	-7,04708	53,85422
	Varianzen sind nicht gleich			1,521	74,578	,132	23,40357	15,38527	-7,24830	54,05545

Deskriptive Statistiken

	N	Mittelwert	Standardabweichung	Minimum	Maximum
GFR max	82	34,6154	26,11246	4,77	108,13

Kolmogorov-Smirnov-Anpassungstest

		GFR max
N		82
Parameter der Normalverteilung[a,b]	Mittelwert	34,6154
	Standardabweichung	26,11246
Extremste Differenzen	Absolut	,127
	Positiv	,112
	Negativ	-,127
Kolmogorov-Smirnov-Z		1,146
Asymptotische Signifikanz (2-seitig)		,145

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

T-Test

Gruppenstatistiken

	Jahr	N	Mittelwert	Standardabweichun	Standardfehler des
GFR max	2007-2011	40	34,8733	27,23053	4,30552
	2012	42	34,3698	25,33048	3,90858

Test bei unabhängigen Stichproben

		Levene-Test der Varianzgleichheit		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	95% Konfidenzintervall der Differenz	
									Untere	Obere
GFR max	Varianzen sind gleich	,740	,392	,087	80	,931	,50349	5,80467	-11,04817	12,05514
	Varianzen sind nicht gleich			,087	78,837	,931	,50349	5,81503	-11,07140	12,07838

Statistical evaluation of data on treatment

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Behandlungsart	82	100,0%	0	0,0%	82	100,0%

Jahr * Behandlungsart Kreuztabelle

			Behandlungsart		Gesamt
			ambulant	stationär	
Jahr	2007-2011	Anzahl	3	37	40
		% innerhalb von Jahr	7,5%	92,5%	100,0%
	2012	Anzahl	3	39	42
		% innerhalb von Jahr	7,1%	92,9%	100,0%
Gesamt		Anzahl	6	76	82
		% innerhalb von Jahr	7,3%	92,7%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische Signifikanz (2-seitig)	Exakte Signifikanz (2-seitig)	Exakte Signifikanz (1-seitig)
Chi-Quadrat nach Pearson	,004[a]	1	,951		
Kontinuitätskorrektur[b]	,000	1	1,000		
Likelihood-Quotient	,004	1	,951		
Exakter Test nach Fisher				1,000	,639
Anzahl der gültigen Fälle	82				

a. 2 Zellen (50,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 2,93.

b. Wird nur für eine 2x2-Tabelle berechnet

Statistiken

Aufenthaltsdauer

N	Gültig	75
	Fehlend	7
Mittelwert		8,55
Standardfehler des Mittelwertes		,399
Standardabweichung		3,454

Statistiken

Aufenthaltsdauer

2007-2011	N	Gültig	37
		Fehlend	3
	Mittelwert		9,24
	Standardfehler des Mittelwertes		,657
	Standardabweichung		3,996
2012	N	Gültig	38
		Fehlend	4
	Mittelwert		7,87
	Standardfehler des Mittelwertes		,440
	Standardabweichung		2,713

Kolmogorov-Smirnov-Anpassungstest

		Aufenthaltsdauer
N		75
Parameter der Normalverteilung (a,b)	Mittelwert	8,55
	Standardabweichung	3,454
Extremste Differenzen	Absolut	,163
	Positiv	,163
	Negativ	-,087
Kolmogorov-Smirnov-Z		1,411
Asymptotische Signifikanz (2-seitig)		,037

a Die zu testende Verteilung ist eine Normalverteilung.

b Aus den Daten berechnet.

Mann-Whitney-Test

Ränge

	Year	N	Mittlerer Rang	Rangsumme
Aufenthaltsdauer	2007-2011	37	41,04	1518,50
	2012	38	35,04	1331,50
	Gesamt	75		

Statistik für Test (a)

	Aufenthaltsdauer
Mann-Whitney-U	590,500
Wilcoxon-W	1331,500
Z	-1,203
Asymptotische Signifikanz (2-seitig)	,229

a Gruppenvariable: Year

Kolmogorov-Smirnov-Anpassungstest

		Outpatien control
N		6
Parameter der Normalverteilung (a,b)	Mittelwert	2,5000
	Standardabweichung	1,64317
Extremste Differenzen	Absolut	,286
	Positiv	,286
	Negativ	-,181
Kolmogorov-Smirnov-Z		,701
Asymptotische Signifikanz (2-seitig)		,709

a Die zu testende Verteilung ist eine Normalverteilung.

b Aus den Daten berechnet.

Gruppenstatistiken

	Year	N	Mittelwert	Standardabweichung	Standardfehler des
Outpatien control	2007-2011	3	1,3333	,57735	,33333
	2012	3	3,6667	1,52753	,88192

Test bei unabhängigen Stichproben

		Levene-Test der Varianzgleichheit		T-Test für die Mittelwertgleichheit						
									95% Konfidenzintervall der Differenz	
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	Untere	Obere
Outpatien control	Varianzen sind gleich	2,571	,184	-2,475	4	,069	-2,3333	,94281	-4,95099	,28432
	Varianzen sind nicht gleich			-2,475	2,560	,104	-2,3333	,94281	-5,64770	,98104

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * ICU- Aufenthalt	82	100,0%	0	0,0%	82	100,0%

Jahr * ICU- Aufenthalt Kreuztabelle

		ICU- Aufenthalt		Gesamt
		nein	ja	
Jahr 2007-2011	Anzahl	35	5	40
	% innerhalb von Jahr	87,5%	12,5%	100,0%
Jahr 2012	Anzahl	40	2	42
	% innerhalb von Jahr	95,2%	4,8%	100,0%
Gesamt	Anzahl	75	7	82
	% innerhalb von Jahr	91,5%	8,5%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische Signifikanz (2-	Exakte Signifikanz (2-	Exakte Signifikanz (1-
Chi-Quadrat nach Pearson	1,571[a]	1	,210		
Kontinuitätskorrektur[b]	,736	1	,391		
Likelihood-Quotient	1,613	1	,204		
Exakter Test nach Fisher				,259	,196
Anzahl der gültigen Fälle	82				

a. 2 Zellen (50,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 3,41.

b. Wird nur für eine 2x2-Tabelle berechnet

Statistiken

Aufenthaltsdauer ICU

N	Gültig	7
	Fehlend	75
Mittelwert		4,14
Standardfehler des Mittelwertes		1,280
Standardabweichung		3,388

Kolmogorov-Smirnov-Anpassungstest

		Aufenthaltsdauer ICU
N		7
Parameter der Normalverteilung[a,b]	Mittelwert	4,14
	Standardabweichung	3,388
Extremste Differenzen	Absolut	,346
	Positiv	,346
	Negativ	-,177
Kolmogorov-Smirnov-Z		,916
Asymptotische Signifikanz (2-seitig)		,371

a. Die zu testende Verteilung ist eine Normalverteilung.

b. Aus den Daten berechnet.

T-Test

Gruppenstatistiken

	Jahr	N	Mittelwert	Standardabweichung	Standardfehler des Mittelwertes
Aufenthaltsdauer ICU	2007-2011	5	4,40	3,715	1,661
	2012	2	3,50	3,536	2,500

Test bei unabhängigen Stichproben

		Levene-Test der Varianzgleichheit		T-Test für die Mittelwertgleichheit						
		F	Signifikanz	T	df	Sig. (2-seitig)	Mittlere Differenz	Standardfehler der Differenz	95% Konfidenzintervall der Differenz	
									Untere	Obere
Aufenthaltsdauer ICU	Varianzen sind gleich	,007	,937	,292	5	,782	,900	3,079	-7,014	8,814
	Varianzen sind nicht gleich			,300	1,982	,793	,900	3,002	-12,131	13,931

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Dialyse	82	100,0%	0	0,0%	82	100,0%

Jahr * Dialyse Kreuztabelle

			Dialyse		Gesamt
			nein	ja	
Jahr	2007-2011	Anzahl	32	8	40
		% innerhalb von Jahr	80,0%	20,0%	100,0%
	2012	Anzahl	41	1	42
		% innerhalb von Jahr	97,6%	2,4%	100,0%
Gesamt		Anzahl	73	9	82
		% innerhalb von Jahr	89,0%	11,0%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	6,509[a]	1	,011		
Kontinuitätskorrektur[b]	4,831	1	,028		
Likelihood-Quotient	7,261	1	,007		
Exakter Test nach Fisher				,013	,012
Anzahl der gültigen Fälle	82				

a. 2 Zellen (50,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist 4,39.

b. Wird nur für eine 2x2-Tabelle berechnet

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Beatmungspflichtigkeit	82	100,0%	0	0,0%	82	100,0%

Jahr * Beatmungspflichtigkeit Kreuztabelle

			Beatmungspflichtigkeit					Gesamt
				keine	O2-Brille	CPAP	Intubation	
Jahr	2007-2011	Anzahl	0	37	1	1	1	40
		% innerhalb von Jahr	0,0%	92,5%	2,5%	2,5%	2,5%	100,0%
	2012	Anzahl	1	40	0	1	0	42
		% innerhalb von Jahr	2,4%	95,2%	0,0%	2,4%	0,0%	100,0%
Gesamt		Anzahl	1	77	1	2	1	82
		% innerhalb von Jahr	1,2%	93,9%	1,2%	2,4%	1,2%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische Signifikanz (2-seitig)
Chi-Quadrat nach Pearson	3,070[a]	4	,546
Likelihood-Quotient	4,227	4	,376
Anzahl der gültigen Fälle	82		

a. 8 Zellen (80,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 49.

Symmetrische Maße[c]

		Wert	Näherungsweise
Nominal- bzgl. Nominalmaß	Phi	,193	,546
	Cramer-V	,193	,546
Anzahl der gültigen Fälle		82	

a. Die Null-Hyphothese wird nicht angenommen.

b. Unter Annahme der Null-Hyphothese wird der asymptotische Standardfehler verwendet.

c. Die Korrelations-Statistik ist nur für numerische Daten verfügbar.

Statistical evaluation of patients' outcome

Verarbeitete Fälle

	Fälle					
	Gültig		Fehlend		Gesamt	
	N	Prozent	N	Prozent	N	Prozent
Jahr * Outcome	82	100,0%	0	0,0%	82	100,0%

Jahr * Outcome Kreuztabelle

			Outcome		Gesamt
			Exitus	Heilung	
Jahr	2007-2011	Anzahl	1	39	40
		% innerhalb von Jahr	2,5%	97,5%	100,0%
	2012	Anzahl	0	42	42
		% innerhalb von Jahr	0,0%	100,0%	100,0%
Gesamt		Anzahl	1	81	82
		% innerhalb von Jahr	1,2%	98,8%	100,0%

Chi-Quadrat-Tests

	Wert	df	Asymptotische	Exakte	Exakte
Chi-Quadrat nach Pearson	1,063[a]	1	,303		
Kontinuitätskorrektur[b]	,001	1	,980		
Likelihood-Quotient	1,449	1	,229		
Exakter Test nach Fisher				,488	,488
Anzahl der gültigen Fälle	82				

a. 2 Zellen (50,0%) haben eine erwartete Häufigkeit kleiner 5. Die minimale erwartete Häufigkeit ist, 49.

b. Wird nur für eine 2x2-Tabelle berechnet