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Epidemiology of Prostate Cancer: The Case of Ethnic German Migrants from the Former Soviet Union

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1. Introduction

1.1 Epidemiology of prostate cancer

1.1.1 Situation in Germany

In Germany, prostate cancer is the leading cause of cancer (26%) and the third leading cause of death from cancer in males (10%). The mean age of disease and of death due to prostate cancer is 70.1 years and 77.5 years, respectively (Ziegler et al., 2009). Few people are diagnosed before the age of 50 years. A 70-year old man has a 6% risk of developing prostate cancer within the next ten years, whereas, the risk for a 40-year-old man is 0.1% (RKI, 2010). In 2006, approximately 238,500 men were diagnosed with prostate cancer during the previous five years in Germany.

Currently, there is a statutory screening programme for prostate cancer in Germany. All men aged 45 years and over are asked once a year by their physician if they have any symptoms. This screening also includes an examination of the sexual organs, the lymph nodes, as well as a palpation examination of the prostate via the rectum. Presently, the prostate-specific antigen (PSA) blood test is not part of the statutory screening.

1.1.2 Longitudinal trends in Germany

During the 1970s incidence was stable around 50 per 100,000 persons (Ziegler et al., 2009). Since 1980, the incidence has increased (see Figure 1). The yearly number of new prostate cancer cases in Germany has risen by 200% (from 1980-2006), which may partly be due to the demographic change. During the same period the age-standardized incidence rate (standardized to the European standard population) also increased by 110%. In 2006, the age-standardized incidence rate was 110.1 per 100,000 men (RKI, 2010). This increase is mainly due the use of new diagnostic methods, e.g. testing for PSA. Earlier diagnosis, in terms of both the cancer's stage of development and the patient's age, has led to much higher incidence rates in the age group 50- to 69-years and lower rates among over-75-year-olds. Additionally, the mean age at onset fell from 73 years in 1980 to 70 years in 2006 (RKI, 2010).

On the other hand, age-standardized mortality rates have been more or less stable during the last decades and began to fall slightly since 1995. In 2006, the age-standardized mortality

rate was 21.2 per 100,000 men. The 30% increase in the number of deaths since 1980 is a result of demographic change.

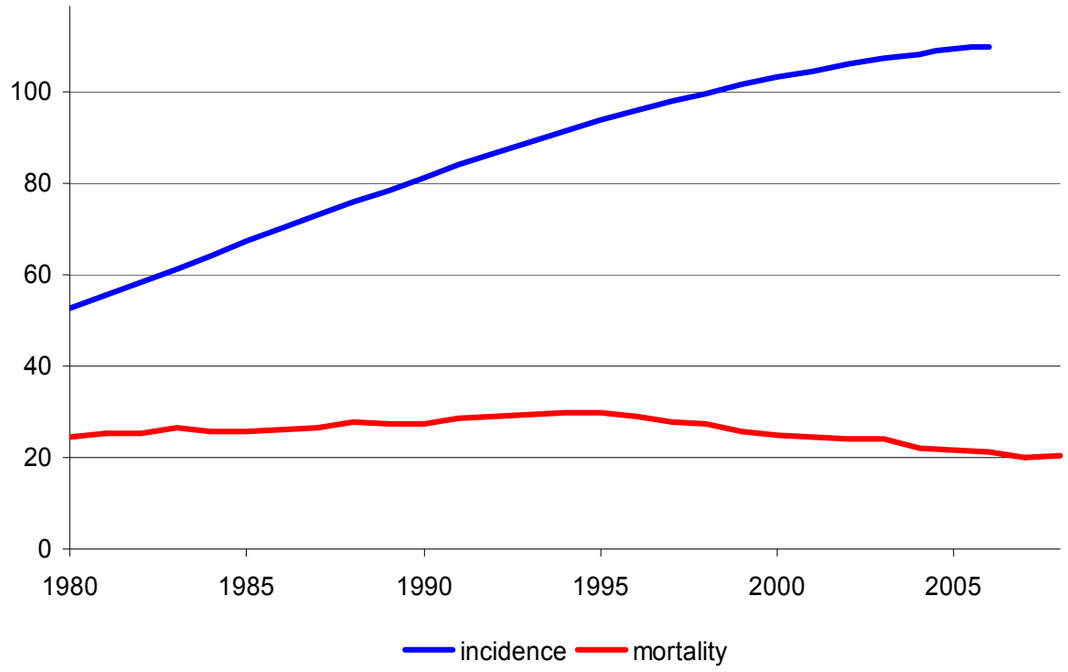


Fig. 1. Age-standardized prostate cancer incidence and mortality rates per 100,000 (European Standard) in Germany (RKI, 2011)

Between 1984 and 1998, the 5-year survival rate in Germany was 82% (RKI, 2008). Currently, relative 5-year survival rates are about 90% (Ziegler et al., 2009). However, whether this slight improvement in survival is a result of earlier diagnosis due to screening in the last years is not clear. With regards to prognosis, a distinction must be made between slowly progressing forms and aggressive metastasizing forms, which occur in greater proportions among younger men (under 60).

1.1.3 International comparison

An international comparison of German prostate cancer mortality and incidence to selected international countries is displayed in Figure 2. The cancer mortality rate in Germany is among the lowest in Europe, whereas the incidence is around the European average. Internationally, some of the lowest prostate cancer rates with regard to mortality and incidence are seen in Hong Kong. Scandinavian countries are among those with the highest prostate cancer mortality worldwide. Prostate cancer mortality rates are also estimated to be very high in some African and South American countries (Ferlay, 2010). A country-specific comparison shows that high prostate cancer mortality rates do not necessarily mean high incidence rates and vice versa (RKI, 2010).

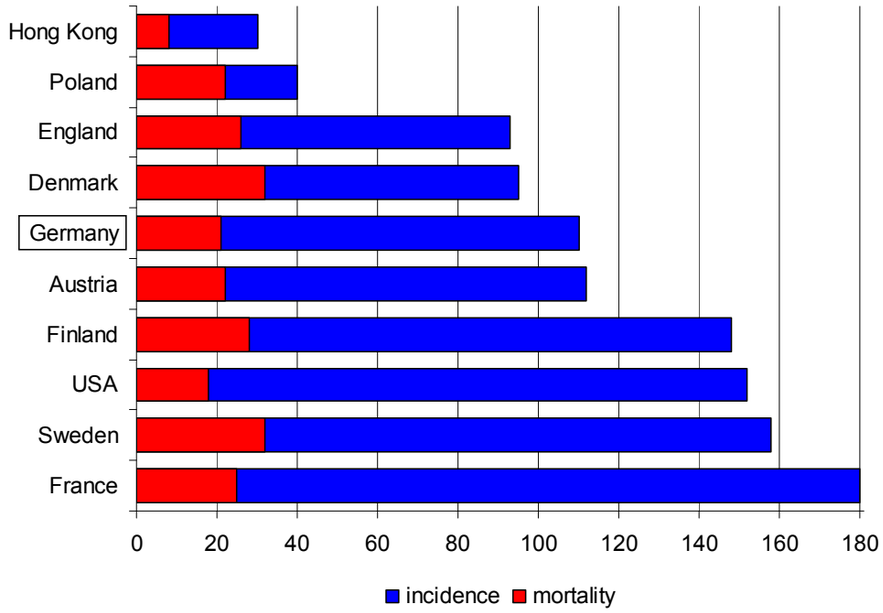


Fig. 2. Age-standardized prostate cancer incidence and mortality rates per 100,000 (European Standard) in Germany in 2006 compared internationally (except France in 2005) (RKI, 2010)

1.1.4 Risk factors

Risk factors and factors affecting disease progression are basically unknown. Clearly, male sex hormones play a role, without them prostate cancer would not develop. In addition, the aging process contributes to the development of prostate cancer as it does for all cancer sites. Cellular repair mechanisms become more and more error prone with age, which contributes to the development of malignancies.

A genetic predisposition has been discussed, because of a higher incidence in several ethnic groups and disease at a younger age. A clustering of the disease among close relatives has also been shown, although there is no consensus on which inheritable genetic defects are involved. In spite of extensive research, reliable findings on risk factors relating to lifestyle, diet or the environment remain elusive. Possible lifestyle risk factors are high intakes of α-linolenic acid (a polyunsaturated fatty acid in vegetables and dairy products) and calcium. Common risk factors for various cancer sites such as tobacco smoking, alcohol consumption and low physical activity do not seem to affect prostate cancer risk (Grönberg, 2003; Patel & Klein, 2009).

1.2 Migration and health

1.2.1 General aspects

Worldwide, there are many epidemiological studies of migrant populations that lead to new findings on the etiology of diseases (McCredie, 1998). Additionally, these studies help to develop targeted cancer prevention and early detection strategies for migrant groups.

In general, research on migrants focuses on topics that are related to selection. There are push and pull factors influencing the migration process. Push factors make people more

willing to leave their country of origin, for example a poor economy, or political or religious persecution. Pull factors on the other hand attract migrants to a country like a good employment situation, labour demand, higher wages, higher living standards, political and religious freedom.

It has been suggested that migrants are not representative samples of their population of origin. Migrants are likely to be positively selected when they respond to pull factors in the country of destination and negatively selected in respond to push factors in the country of origin (Lee, 1966). With regards to health, this leads to the so called "healthy migrant effect". In general, people that are younger and healthier are more willing and able to migrate (Jasso et al., 2004). The elderly and people that are ill tend to stay in their country of origin. So, this selection results in migrants that tend to be healthier than their population of origin. It has been shown, that the healthy migrant effect diminishes dramatically with time (Fennelly, 2007).

In general, many different factors affect the health of migrant populations (Marmot et al., 1984): First, the migration itself can have an impact on health. This refers to positive or negative selective factors and to mental stress. Second, disease risk profiles in the country of origin may differ from the host country due to environmental factors for example, which may lead to disease. Third, destination effects which include physical and social environments, for example the integration politics in the destination country may influence migrant health strongly by making health care services easily accessible for migrant populations.

1.2.2 Migration and cancer incidence & mortality

Cancer is one of the leading causes of deaths in the industrialized world (World Health Organization [WHO], 2004) and the second leading cause of death in Germany (Federal Statistical Office of Germany [DeStatis], 2007). It has been demonstrated that migrant cancer incidence and mortality differs in general from cancer patterns in the respective host population.

Cancer is known to have a long latency period between exposure and disease onset. Important exposure factors can be traced back to childhood and young adulthood. This means short and medium term cancer mortality among first generation migrants is mainly influenced by country-of-origin factors (Parkin & Khlat, 1996).

The longer migrants live and adapt to their destination country, the more their cancer rates converge towards those in that country. This has been shown for stomach, colon and prostate cancer (McKay, 2003). Migrants from non-western countries to Europe were found to be more prone to cancers that are related to infections experienced in early life, such as liver, cervical and stomach cancer. In contrast, migrants of non-western origin were less likely to suffer from cancers related to a western lifestyle, e.g. colorectal and breast cancer (Arnold et al., 2010).

Evidence was found for a transition of cancer incidence and mortality patterns towards the host population among Turkish migrants in Germany (Zeeb et al., 2002). Convergence may occur due to diet acculturation, adaptation of new lifestyles or utilization of often superior health services. Higher mortality from cancers where incidence can be reduced by effective screening programs and those where survival depends on availability of treatment options, may decrease in a relatively shorter time. Another study analyzed differences in cancer rates between first and second generation migrants relative to the host country, stratified by

country of origin, showing cancer site specific patterns for succeeding generations (Thomas & Karagas, 1987).

Results of an American study support the theory of a rather strong genetic influence on risk of prostate cancer. The study compared patterns of prostate cancer among black and white men (Chu et al., 2003). Black Americans had substantially higher prostate cancer rates than white Americans, but the longitudinal trends such as decreasing mortality, increasing incidence and survival were similar. Although this was not a typical migrant study, it compared different ethnic and thus genetic and lifestyle factors in a known risk pattern environment.

1.3 Ethnic German migrants in Germany - background on the study population

In the year 2005, only 2.9% of the global population were migrants, but migration is unequally distributed throughout the world. In past years, migration flows have shifted and in some cases, international migration is actually decreasing. Only two areas in the world have seen an increase in migration – North America and the Former Soviet Union (FSU) (International Organization for Migration, 2005).

Germany has long been a country of immigration. At present, there are two big groups of migrants, the Turks and ethnic Germans from countries of the FSU. We study disease patterns, focusing on cancer incidence and mortality, in the latter group.

The 'Aussiedler' are ethnic German migrants and represent a unique group of diaspora migrants. Since 1993, the officially correct term for Aussiedler is Spätaussiedler, however for ease of presentation we will use the term Aussiedler throughout the text.

The first Aussiedler came to Russia when Peter I (1689–1725) changed his politics towards Europe. They were the beginning of the urban German population in Russia. Tsarina Katharina II (1762–1796) promised the Aussiedler tax exemptions for 30 years, exoneration from military service, freedom of religion, autonomy and subsidy for resettlement. Many Germans living in regions still suffering from war migrated to Russia under these terms. During the first half of the 19th century approximately 55,000 German colonists settled in the Black Sea region. With time the Aussiedler lost several of the rights they were promised.

For centuries these ethnic Germans lived abroad and were a relatively closed group of people. After the start of World War I the laws of liquidation were implemented. On the basis of these laws more than 200,000 German colonists were driven away. In 1922, after the October-revolution and civil war the Union of Soviet Socialist Republics (USSR) was founded. When the Nazi Party came into power in Germany the situation of the Germans in the USSR worsened. Seen as an internal enemy, Stalin restricted their rights.

Soon after the German aggression against the USSR in 1941 the deportation of the German population started. Following Stalin's decree about 1,200,000 ethnic Germans were deported into the eastern parts of the Soviet Union, predominantly to Siberia, Kazakhstan and in the Urals. Their civil rights were disregarded; they were detained and forbidden to speak German. Most had to work in labour camps in inhumane conditions. An estimated 700,000 Germans died due to bad working and living conditions and inadequate medical treatment. In particular, the Stalinism destroyed the independent German culture in Russia. In 1955, the discrimination was subsided, and the ethnic Germans were allowed to change their residence, but not to their former colony areas. The Aussiedler became partly assimilated in the last decades of the USSR.

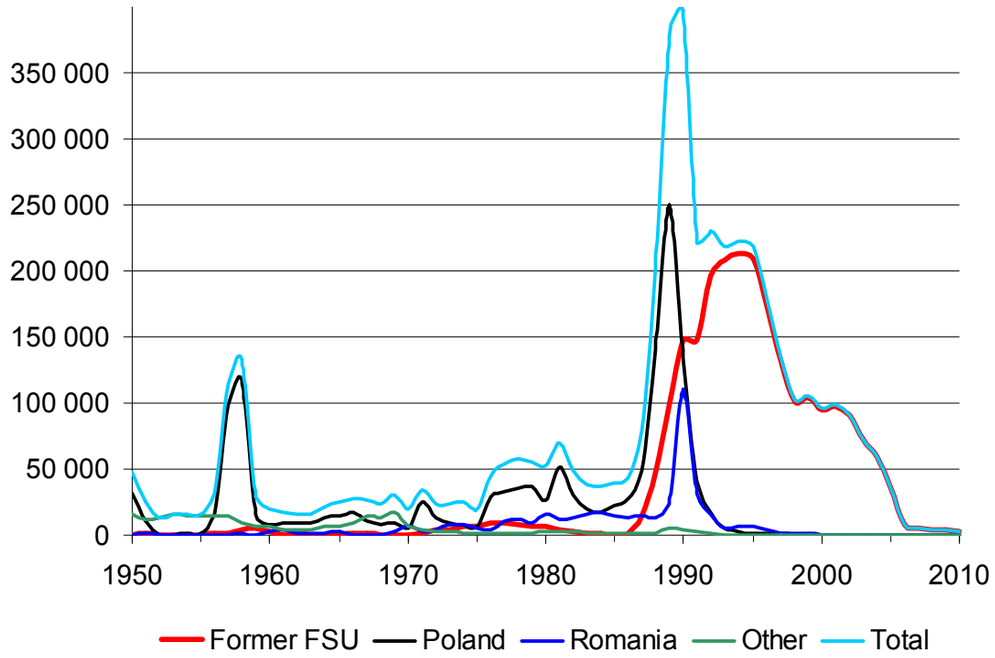


Fig. 3. Immigration of the Aussiedler over time by country of origin (Federal Ministry of the Interior, 2009; Federal Office of Administration, 2011)

When the iron curtain fell around 1990, a wave of migration to Germany started (see Figure 3). Since then more than two million Aussiedler migrated to Germany from countries of the FSU, with most coming from Kazakhstan and the Russian Federation. There are few examples of a large migration of one ethnic group from one country to another in a similarly short period of time.

In 1993, the German government began to restrict the immigration of Aussiedler by implementing annual quotas, which were further reduced in 1996. In parallel the government eliminated several benefits previously offered to Aussiedler, e.g. special credits and unemployment benefits.

The number of Aussiedler immigrating to Germany has fallen rapidly in recent years. In 2010, only 2,350 Aussiedler migrated to Germany (Federal Office of Administration, 2011). Today, the Aussiedler comprise about 2.5% of the German population, representing a relatively large group within German society (Destatis, 2008a; Destatis, 2008b).

More information on the history of the Aussiedler can be found elsewhere (Federal Central Office for Political Education, 2000; Bade & Olmert, 1999; Eisfeld, 1999; Pohl, 2001).

1.4 Comparing German incidence and mortality to the Former Soviet Union

The health situation in the FSU has changed dramatically during the last thirty years. Since the late 1980s the FSU has been experiencing a mortality crisis, in temporal association with massive social changes.

In Russia between 1987 and 1994, increases were observed for all major causes of death, except for cancer (Leon et al., 1997). Age-standardized mortality for all causes of death rose from 1140 in 1987 to 1600 per 100,000 persons in 1994 (adjusted to Segi). Development was

very similar in Kazakhstan and in Ukraine. After a dip, the excess mortality increased sharply following the economic crisis of 1998. Mortality is largely due to vascular and external causes of death in adults (Men et al., 2003). In 2006, mortality was still high with about 1300 per 100,000 people. During the same period in Germany, all cause mortality declined continuously from around 850 to 650 per 100,000 people (WHO, 2011a).

In 2008, the age-standardised mortality rate per 100,000 males for all cancers was 181.3 in Kazakhstan and 180.7 in the Russian Federation (Ferlay, 2010). In Germany, mortality for all cancer sites combined in the respective year was much lower with 133.2 per 100,000 males. An important reason for the lower cancer mortality in Germany compared to countries of the FSU is better survival. However, longitudinal trends in mortality for all cancer sites developed in parallel between Germany and the FSU.

A comparison of cancer incidence rates between Germany and the Aussiedler's countries of origin show much lower rates in the Former Soviet Union. However, it is likely that incidence rates are underestimated in the FSU as evidenced by mortality patterns and differences in diagnosis and treatment.

Mortality from prostate cancer in FSU countries is lower compared to Germany, however, during recent years this difference has diminished (see Figure 4). In 2006, the age-standardised mortality rate per 100,000 males was 12.3 in Germany, 5.7 in Kazakhstan, 10.1 in the Russian Federation, and 9.3 in Ukraine (WHO, 2011b).

Incidence from prostate cancer is also much lower compared to Germany. In 2008, the age-standardised incidence rate was estimated to be 82.7 in Germany, 10.9 in Kazakhstan, 26.1 in the Russian Federation, and 20.3 in Ukraine (Ferlay, 2010). Low incidence in countries of the FSU is likely due to less prostate specific antigen (PSA) testing and may also represent a general underestimation of cancer incidence. This results in an incidence : mortality ratio of 7 in Germany and only 2 in Kazakhstan, 2.5 in the Russian Federation, and 2 in Ukraine.

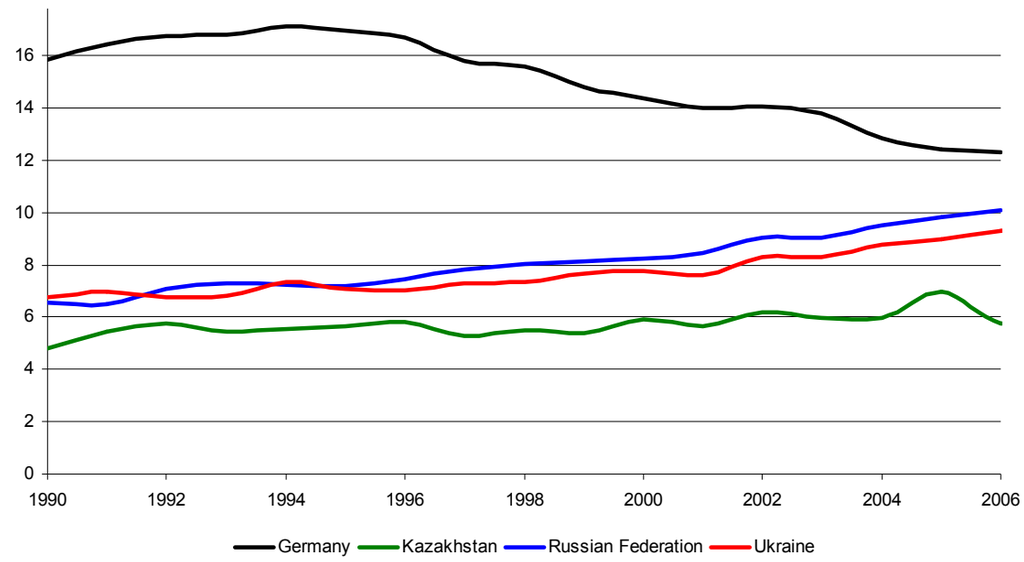


Fig. 4. Age-standardized prostate cancer mortality rates per 100,000 (Segi Standard) (WHO, 2011b)

1.5 Aims of the study and expected findings

Our studies focus on the health profile of ethnic German migrants from the Former Soviet Union in Germany. The presented work focuses on mortality and incidence of prostate cancer.

We compare two cohorts of Aussiedler to the autochthonous German population to investigate the Aussiedler's overall health status with regard to all cause mortality, and overall cancer and prostate cancer incidence and mortality. For prostate cancer we also consider the influence of age and length of stay in Germany in order to differentiate between the effects of genetic versus life-style dependent factors.

The two study cohorts are located in different Federal States of Germany. The Saarland cohort provides information on cancer incidence and mortality of the Aussiedler, whereas the North Rhine Westphalian cohort provides information on mortality only.

Aussiedler are exposed to different kinds of risk factors in different times of their lives. Before migration they are exposed to risk factors in their countries of origin, which have different disease patterns than Germany. Later, the Aussiedler are exposed to the migration process itself which can cause mental stress and, finally, they are exposed to the German pattern of risk factors.

Since most Aussiedler migrated to Germany at the beginning of the 1990s the mortality crisis in countries of the FSU could have influenced their health status. High mortality rates in their countries of origin and physical as well as psychological stress caused by migration was thought to negatively affect the general health of the Aussiedler. On the other hand, the better health care system in Germany may have improved their health status, if they have access to it. Additionally, social integration may also influence their health status.

A previous study confirmed the hypothesis that Aussiedler experienced higher mortality only for specific causes of death. In contrast, overall mortality of the Aussiedler was lower compared to the German population (Becher et al., 2007).

In general, few migrant studies assess cancer incidence and even fewer investigate both cancer incidence and mortality. Most investigations that do are occupational cancer studies, which describe health risks associated with workplace exposures only.

Aussiedler are likely to have higher mortality rates for all cancers due to country of origin effects. With regards to prostate cancer, a slighty lower mortality compared to Germany is expected, and incidence rates should confirm the observed mortality pattern. A previous study showed no differences in incidence and mortality for all cancers and confirmed expectations for prostate cancer, although it had incomplete follow up (Winkler et al., 2009). It is likely that incidence and mortality rates of the Aussiedler and the German population converge with time. This has already been shown for stomach cancer (Ronellenfitsch et al., 2009).

2. Materials and methods

2.1 Study population

2.1.1 North Rhine Westphalian cohort

In 2001, the North Rhine Westphalian (NRW) cohort was established (Ronellenfitsch et al., 2004). In brief, routine information from the Aussiedler reception centre of NRW was collected to setup a cohort. The original dataset included all Aussiedler from countries of the FSU who settled in NRW between 1990 and 2001.

The dataset contains information on name, date of birth, date of arrival in Germany, sex, country of origin, first city of residence and a unique code that identified members of the same family. After sample size calculation the cohort was restricted to a representative sample of 34,393 Aussiedler who were at least 15 years old when they migrated to Germany.
To ascertain vital status of each cohort member until the 31st December 2005 a follow up procedure was performed: Letters were sent to local registry offices in the cities of residence. In case of someone moving to another city, the registry provided the new city of residence and date of moving. The registry of the new city was then contacted until the individual was located. Changes of residence were recorded in a database with the exact date of moving. In the case of death, date and city of death were provided by the local registry office.
Cause of death was either ascertained through a record linkage system of the NRW regional statistical office or through the local health offices. The record linkage system has been described in detail by Klug and colleagues (2003). Local health offices provided an anonymous copy of the relevant death certificate. All copies of death certificates were then professionally coded at the Saarland Cancer Registry by International Classification of Diseases (ICD).

2.1.2 Saarland cohort

The Aussiedler reception centre of the Saarland could not provide a dataset with the standard information on the Aussiedler as in NRW. As an alternative, all local refugee offices of the Saarland were contacted to ask for access to their available data on the Aussiedler. In order to be eligible for the Saarland cohort, migrants must have arrived in Germany between 1990 and 2005 from countries of the FSU.
All together information on 26,384 Aussiedler (more than 90% of all Aussiedler who settled in the Saarland during the respective period) was available. The dataset contains name, date of birth, date of German passport as an approximation for date of migration, sex, country of birth for about 70% of the cohort, and first city of residence. The final cohort consisted of a sample of 18,619 individuals without missing data.
Follow up and cause of death ascertainment used the same method as for the NRW cohort. Follow up for cancer incidence was done directly by the Saarland cancer registry. Most individuals were identified by name, sex and date of birth. However, many Aussiedler change names during the first years of stay in Germany complicating simple identification by name. To minimize this problem the name matching procedure was done phonetically. For some individuals, city of residence was used as an additional variable to ensure correct identification. 43 cases were excluded from the analysis because they were already diagnosed in their country of origin.
All analyses were restricted to the first cancer diagnosis; multiple tumours per individual were not considered.

2.1.3 Data for comparison

For evaluation of the Aussiedler's cancer incidence and mortality in comparison to the autochthonous German population, rates for comparison are needed. To analyse mortality, rates of the German population were used. Although these rates include the

Aussiedler as a part of the German population, this should not bias the results of the comparison. For cardiovascular disease mortality it has been shown that the Aussiedler's influence on German mortality is limited to approximately 1% (Deckert et al., 2010). German mortality rates were calculated using the WHO mortality database (WHO, 2011b). Before 1998 causes of death are coded with 9th revision of ICD, thereafter the 10th is used in Germany.
A comparison to German incidence is not possible for the period between 1990 and 2005, since nation-wide information on cancer incidence is not available. For those years German incidence is estimated on basis of the Saarland Cancer Registry. Therefore, we directly compare cancer incidence of the Saarland Aussiedler cohort to the Saarland population. The Saarland Cancer Registry provided data on Saarland population figures and number of cancer cases (Saarland Cancer Registry, 2008). Cancer incidence data is coded in ICD9 only.

2.2 Statistical methods

2.2.1 Calculation of person-time

In most cohort studies it is necessary to calculate the actual time-at-risk for each individual as person-time. The person-time is used to either calculate mortality or incidence rates of the cohort or to perform indirect standardization or multivariate analysis.
Person-time was calculated in person-years (PY) by a SAS® macro. The macro uses the three time variables of age, length of stay in Germany and calendar-year. The macro calculates and distributes the person-years exactly to the day. Age and length of stay are categorized in one year intervals. Afterwards age is categorized into five year age groups up to 85 and older.

2.2.2 Indirect standardization

For comparing Aussiedler incidence and mortality with the German/Saarland population, indirect standardization was used. Compared to the method of direct standardization, the indirect method is advantageous when the stratum-specific rates of one of the populations to be compared are based on small numbers. In this case one can use the more stable rates of the larger population for the indirect standardization, thus gaining robustness with regard to sampling variation (Breslow and Day, 1987).
The standardized mortality ratio (SMR), and the standardized incidence ratio (SIR) are given by the observed number of events O (incident cases or number of deaths) divided by the number of events which one would expect E if the cohort had the mortality rate of the population used for standardization. Equation 1 shows the SMR as an example.

$$SMR = \frac{O}{E} = \frac{\sum_{i=1}^{i} O_i}{\sum_{i=1}^{i} py_i \lambda_i} \tag{1}$$

O_i gives the number of deaths in stratum i of the cohort. py_i gives the person-years in stratum i and λ_i the rate stratum j of the population used for standardization. All 95% confidence intervals (95% CI) were calculated using the exact method (Breslow and Day, 1987).

2.2.3 Multivariate analysis: Poisson regression

It is possible to measure effects of different covariables e.g. age, length of stay in Germany, etc. on the SMR and SIR by categorization, but this method is limited because of small sample sizes in subcategories. Another approach classically used in cohort studies is a Poisson regression model, which assesses the effects of different covariables simultaneously. It is based on the Poisson distribution, which is an approximation of the binomial distribution applied in large samples where the probability of the outcome is small.

After transformation, the Poisson model estimating the SMR and the SIR can be written as given in equation 2. α is the intercept, β_i is the regression coefficient, and x_i is the vector of covariable i.

$$\log(O_i) = \log(E_i) + \alpha + \beta_i x_i \quad (2)$$

The Poisson model is a generalized linear model characterized by the dependence of the outcome on a linear predictor through a non-linear link function. The predictors β_i can be estimated by maximum likelihood estimation.

More detailed information on the statistical methods can be found elsewhere (Breslow and Day, 1987). Data management was done by using Microsoft Access® and analysis was performed with SAS® version 9.2.

3. Results

3.1 Descriptive results

Descriptive characteristics of both cohorts and results of the follow up procedure are presented in Table 1. The Saarland cohort was approximately half the size of the cohort in NRW. Females were slightly overrepresented in both cohorts. The arrival period for entering the cohort was four years longer for the Saarland cohort. The NRW study population was restricted by age at migration of 15 years or older, whereas the Saarland cohort had no age restriction. Thus, the Saarland cohort was on average younger. Country of origin distribution was similar for both cohorts: around 55% of the Aussiedler came from Kazakhstan, 37% from the Russian Federation. Other countries of the FSU contributed each less than 5%.

Overall, the NRW cohort accumulated 344,486.1 PY and the Saarland cohort 147,165.2 PY. Follow up of the NRW cohort was complete for 96.7% of the cohort members with a mean follow up time of 10.1 years. Overall 2,580 (7.5%) cohort members died. Causes of death were known for 94.8% of deceased persons. 1,138 (3.3%) persons were lost to follow-up within the observation period, which means their last date of contact was censored. Individuals were lost follow-up due to different reasons, if they moved abroad or moved to an unknown destination.

Vital status was known for 77.4% of individuals in the Saarland cohort. Mean follow up time was 8 years. 87% of individuals lost to follow-up were censored on the day of leaving the study area because they moved to another Federal State. Since the Saarland is a relatively small state people are much more likely to move into another state than in the NRW. During the observation period 780 (4.2%) persons died. Cause of death is known for all types of cancer. Between 1990 and 2005, 448 members of the Saarland cohort were diagnosed with a malignant neoplasm (ICD-9: 140-208; except 173).

	Migrant cohort in the Federal State of NRW	Migrant cohort in the Federal State of Saarland
Number of cohort members	34,393	18,619
Males (%)	16,734 (48.7%)	8,977 (48.2%)
Females (%)	17,659 (51.3%)	9,642 (51.8%)
Immigration period	1990-2001	1990-2005
1990-1993	14,728	6,933
1994-1997	11,441	6,536
1998-2001/5	8,224	5,150
Age restriction	15+	-
Mean age at migration (standard deviation; range)	40.0 (17.0; 15-97)	32.4 (19.8; 0-103)
Males	38.4 (16.0; 15-93)	30.9 (19.0; 0-95)
Females	41.5 (17.7; 15-97)	33.8 (20.4; 0-103)
Descriptive results of the follow-up procedure		
End of follow-up date	31-12-2005	31-12-2005
Mean time of follow-up	10.1 years	8.0 years
Person-years	346,671.5	148,313.1
Males	167,882.0	71703.4
Females	178,789.4	76,609.6
Alive	89.2%	73.2%
Dead	7.5%	4.2%
Lost to follow-up	3.3%	22.6%

Table 1. Descriptive results of the two Aussiedler cohorts, from North-Rhine Westphalia and Saarland

During the observation period, 28 men died due to prostate cancer in both cohorts. Their mean age of deaths was 76.9 years (Range: 60.8 - 92.1). In the Saarland cohort 35 men were diagnosed with prostate cancer. Mean age of diagnosis was 67.6 years (Range: 45.3 - 85.8;). Figure 5 displays all 35 incident prostate cancer cases, starting with their migration to Germany, their age at diagnosis and their final status. Most cases were alive at the end of the observation period. Two cases moved out of the study area and nine died during the

observation. Three of the deceased men died from prostate cancer, one case (no. 30) was not diagnosed before death, and the cause of death is known from the death certificate only (DCO).

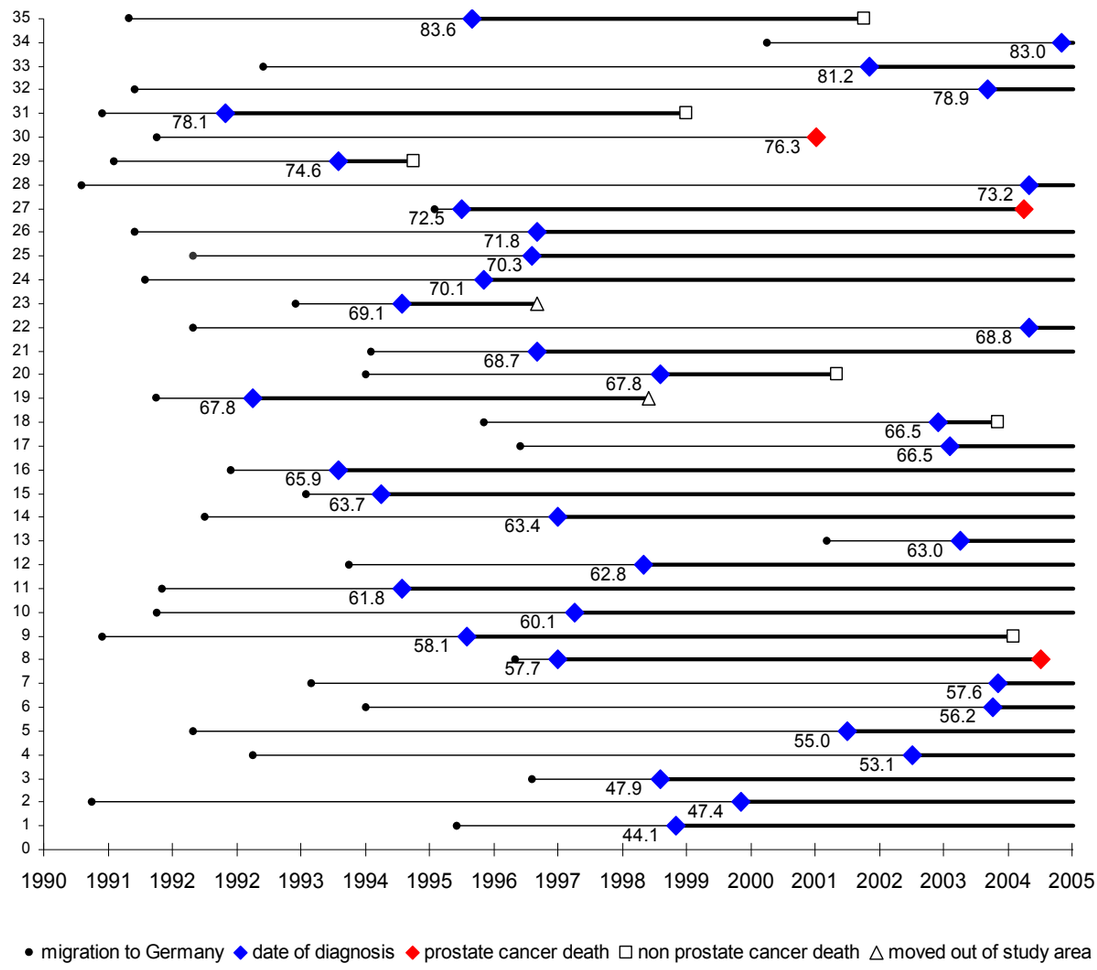


Fig. 5. Overview of all 35 incident prostate cancer cases with age at diagnosis from the Saarland cohort

3.2 Comparing mortality and incidence of the Aussiedler to Germany

This analysis of the Aussiedler in Germany focuses on prostate cancer. However, to place this in context of the Aussiedler's general health situation all cause mortality and mortality and incidence for all malignant neoplasms is presented. SMR is calculated for both cohorts together in comparison to the German population. SIR is based on the Saarland cohort in comparison to the Saarland population. Figure 6 shows SMR and SIR calculated for the whole observation period.

All cause mortality is significantly reduced for both sexes of the Aussiedler. In contrast, the mortality from all neoplasms is also reduced among females, but equal to the German population for males. Incidence of all cancer sites is somewhat lower for males compared to females, but not significantly reduced for either sex in comparison to the Saarland population.

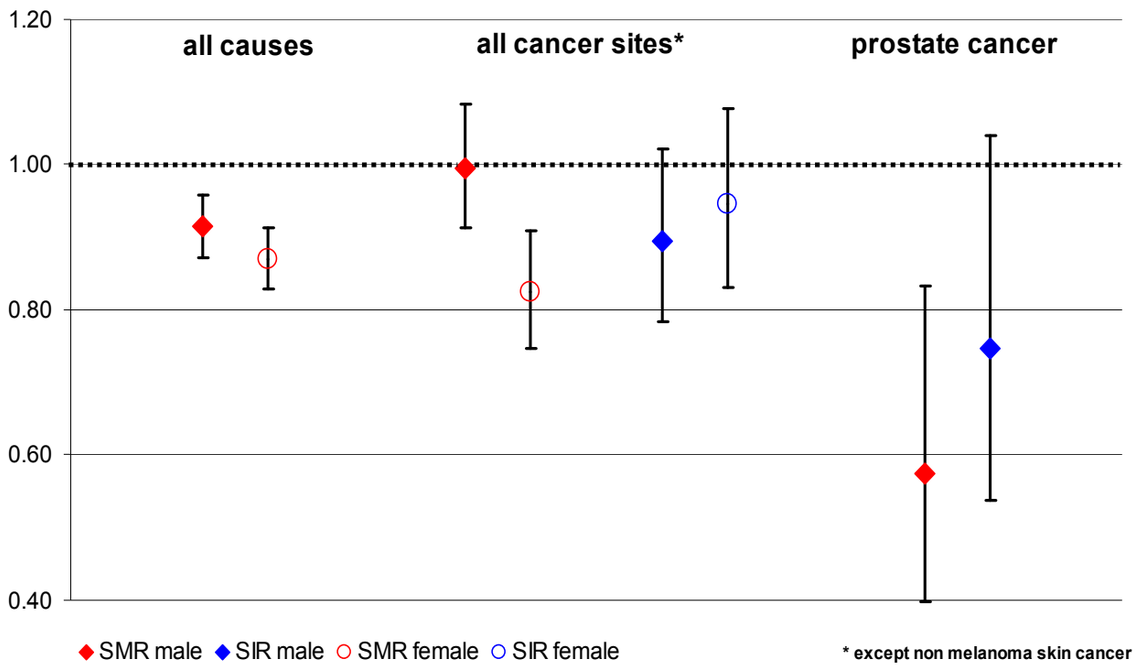


Fig. 6. Standardized mortality (SMR) and incidence (SIR) ratios for all causes, all cancer sites (except non melanoma skin cancer), and prostate cancer of the Aussiedler

Mortality from prostate cancer is strongly reduced among male Aussiedler with an SMR of 0.58 (95% CI: 0.40-0.83) for both cohorts combined. Cohort specific analysis shows a somewhat higher mortality among the NRW cohort compared to the Saarland cohort. In both cohorts mortality due to prostate cancer is significantly reduced.
Prostate cancer incidence is also reduced among the Aussiedler, however, the result is not significant with 0.75 (95% CI: 0.54-1.04).

3.3 Longitudinal effects on prostate cancer mortality and incidence of the Aussiedler

Results from the univariate analysis of prostate cancer mortality and incidence do not take into account the effect of different covariables, which might influence the SMR and SIR. Various covariables where considered to model longitudinal effects: age, calendar year, year of immigration, length of stay in Germany; cohort was considered for the analysis of mortality.
Multivariate Poisson regression did not show any significant effect of the considered covariables on mortality (data not shown). This is in contrast to the analysis of prostate cancer incidence. While the covariables length of stay and year of immigration did not reveal significant effects on the SIR, calendar year was nearly significant (estimate: -0.1213; p-value: 0.0650). Age, however, influenced the SIR. Table 2 shows the result of a model considering age as a dichotomised variable (age below 60 and over 60 years). The modelled SIR of Aussiedler being older than 60 years is 0.63 (exp(-0.47)). In contrast, the SIR of males aged below 60 years is 1.43 (exp(-0.46+0.83)).

	Estimate	*p*-value
intercept	-0.47	0.0165
age		
younger than 60 years	0.83	0.0401
older than 60 years*	0	-

*reference category

Table 2. Parameter estimates of the multivariable Poisson Model for the SIR function of prostate cancer

4. Discussion

The aim of the study was to analyse prostate cancer mortality and incidence among ethnic German migrants who came to Germany from the FSU after 1990. Additionally, we highlighted some general aspects of the Aussiedler's health profile to place prostate cancer incidence and mortality into a broader context. We analyzed two cohorts of migrants in terms of all cause mortality, overall cancer and prostate cancer mortality and incidence including longitudinal and age effects.

Methodological aspects of the cohorts and the statistical analysis have been discussed in detail elsewhere, they have been shown to be representative samples of the Aussiedler. representative (Klug et al., 2003; Ronellenfitsch et al., 2004; Becher et al., 2007; Winkler et al., 2009). In brief, both cohort studies have the pros and cons of historical cohort studies. It is possible to give valid estimates of Aussiedler mortality and incidence in terms of SMR and SIR. Indirect standardization is more appropriate for rare outcomes than direct standardization, resulting in the calculation of rates (McMichael and Giles, 1988). A limitation of this study is that we did not have access to information on potentially important risk factors such as lifestyle.

Results for all causes of deaths were significantly lower compared to the autochthon German population. Overall SMR is reduced for the Aussiedler, therefore, they seem to be healthier or more resistant than the Germans and therefore they are much healthier than populations of countries from the FSU.

Whether this is due to the healthy migrant effect is not immediately clear. For groups like the Aussiedler who have a legal right to migrate to Germany without fulfilling any prerequisites (at least in times when the majority immigrated), it may be assumed that the impact of self-selection on mortality trends is attenuated due to the small number of people staying in the country of origin. The assumption that almost all ethnic Germans migrated to Germany is supported by the continuously declining numbers of newly arriving Aussiedler. On the other hand, declining numbers of migrants may also be due to changes in German law. In addition, there are no official statistics about the number of ethnic Germans for the USSR nor for the FSU and estimations are highly controversial. There are estimates that approximately one million ethnic Germans live in the FSU (Ohliger, 1998). However, an analysis of family size in the NRW cohort shows that the Aussiedler tend to migrate with their whole complete family. Therefore, we think the healthy migrant theory is not applicable to this group of migrants.

The lower overall mortality is largely due to lower cardiovascular disease mortality, which is the predominant cause of death. Reasons for the reduced mortality remain unclear, but may be the result of genetic selection. For centuries the Aussiedler lived as a relatively closed group of people, which was only partly assimilated in the last decades of the USSR.

Among males, incidence and mortality due to all malignant neoplasms is neither different from the autochthon population nor different from each other. However, male cancer incidence is lower compared to mortality and to female cancer incidence. A possible explanation may be that in general males do not utilize health services as well as females. This may also lead to lower mortality among females.

Additionally, smaller differences between SIR and SMR may be explained by differences in the underlying populations for comparison. SMR was calculated on the basis of German rates and SIR on the basis of rates from the Saarland population.

Overall cancer incidence and mortality of the Aussiedler is comparable to the German population. Although there are larger differences for specific cancer sites (data not shown). Mortality for all cancer sites among females is lower, which is largely due to low mortality due to breast and lung cancer

The analysis of prostate cancer mortality and incidence revealed several interesting points. First, there was no difference between the mean age of death from prostate cancer in the Aussiedler and the Saarland population, at 76.9 and 77.5 years of age, respectively. However, mean age of diagnosis was 2.5 years earlier among Aussiedler, but this difference was not significant, which might be due to the limited number of observations.

Overall evaluation of prostate cancer shows lower mortality in Aussiedler than in the German population. Multivariate analysis did not reveal any longitudinal trends or differences in age patterns of dying from prostate cancer. However, this could be due to the relatively small number of observed deaths.

Prostate cancer diagnosis is lower among Aussiedler, but clearly higher than mortality. Poisson regression also revealed that Aussiedler below 60 have significantly more prostate cancer diagnoses than the Saarland population of this age. Longitudinal covariables had no significant effect on the SIR.

5. Conclusion

The Aussiedler are a unique group of diaspora migrants. There are few examples in the world of the migration of a large ethnic group from one country to another in a similarly short time period. Kazakhstan and Russia, the main countries of origin, have very different disease patterns than Germany, which may influence the risk profile of the Aussiedler. Studying the health risks of the Aussiedler not only helps to improve the health care they receive in Germany but also has wider implications for understanding the etiology of disease. The strength of this study is its cohort design. However, the retrospective cohort design relies on data from public registries and does not include information on individual risk factors such as lifestyle, which may also be important.

Results were in contrast to expectations based on country of origin data. Aussiedler have a lower mortality due to all causes of death, which cannot yet be explained completely. Cancer mortality and cancer incidence also differ from FSU countries, but are relatively equal to German rates, however, there are big differences in cancer site specific rates.

Prostate cancer mortality and incidence is lower among the Aussiedler and somehow reflects the situation in the FSU. Analysis did not reveal any short-term convergence of the Aussiedler's prostate cancer to German rates as would be expected in lifestyle driven cancer sites. Therefore, our results support the hypothesis of a relatively strong genetic influence on the development of prostate cancer.

6. Acknowledgment

Many thanks to Robin Nesbitt for language editing and critical thoughts on the manuscript.

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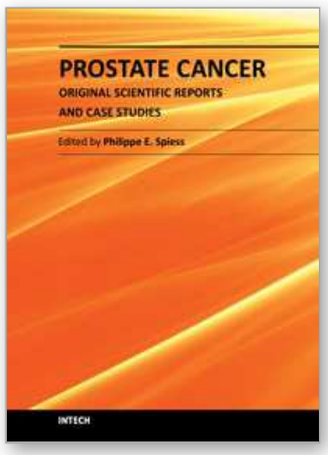
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Edited by Dr. Philippe E. Spiess

ISBN 978-953-307-342-2
Hard cover, 238 pages
Publisher InTech
Published online 21, November, 2011
Published in print edition November, 2011

This book encompasses three sections pertaining to the topics of cancer biology, diagnostic markers, and therapeutic novelties. It represents an essential resource for healthcare professionals and scientist dedicated to the field of prostate cancer research. This book is a celebration of the significant advances made within this field over the past decade, with the hopes that this is the stepping stone for the eradication of this potentially debilitating and/or fatal malignancy.

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Volker Winkler and Heiko Becher (2011). Epidemiology of Prostate Cancer: The Case of Ethnic German Migrants from the Former Soviet Union, Prostate Cancer - Original Scientific Reports and Case Studies, Dr. Philippe E. Spiess (Ed.), ISBN: 978-953-307-342-2, InTech, Available from: http://www.intechopen.com/books/prostate-cancer-original-scientific-reports-and-case-studies/epidemiology-of-prostate-cancer-the-case-of-ethnic-german-migrants-from-the-former-soviet-union

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