



Key Statements

- The goal of early cancer detection is to recognise cancers as early as possible by means of simple, low-stress examinations in order to improve the patients' chances of survival and reduce mortality in the general population due to cancer.
- A decrease in mortality has been observed in recent years with cancer of the colon and rectum, prostate gland and cervix.
- Newly introduced early detection measures can lead to a temporary increase in incidence (e.g. with skin and breast cancer).
- A significant reduction in the incidence of cervical cancer can be recognised since the introduction of the Pap smear in the 1970s.
- To date, mammography screening is the only early detection programme in Germany in which invitations are extended in all parts of the country.

Epidemiology and Early Diagnosis of Common Cancers in Germany

With the general increase in the life expectancy of populations, the importance of cancer is also increasing in Germany and in all other industrialised countries. Despite significant improvements in cancer patients' chances of survival, the absolute number of annual deaths due to cancer has risen relatively continuously in the last 30 years. Due to the changed spectrum of the causes of death, every fourth death today is attributable to a form of cancer, as opposed to one in five deaths in 1980.

In addition to a reduction of the risk factors (primary prevention), such as tobacco consumption or certain infections, early cancer detection (secondary prevention) offers the chance of reducing the burden of disease in the general population. The early diagnosis measures (screening examinations) provided by the statutory health insurance funds in Germany currently apply to tumours of the skin, colon and rectum, the cervix and mammary gland with women and the prostate gland with men. They are free of charge for insured persons and are usually regulated via the directive on the early diagnosis of cancers issued by the Federal Joint Committee (G-BA 2011).

The objective of all early cancer detection (ECD) measures is to recognise cancers as early as possible by means of relatively simple, low-stress examinations in order to improve the success of the treatment and thereby the chances of survival of those affected by prescribing the suitable therapies. The actual screening examination often provides only suspicions which are then either substantiated or rejected in the course of more thorough examinations, such as a tissue sampling. With colorectal and cervical cancer in particular, a goal of early detection is the avoidance of invasive tumours which grow into and destroy the tissue through the recognition and treatment of preliminary stages of cancer (locally limited in-situ tumours).

The success of early cancer detection measures on the level of the general public depends on the quality of the procedures used and the manner in which they are conducted, as well as the willingness of each target group to participate. Fundamentally, however, early cancer detection also involves potential disadvantages either through the risks of the examination itself (e.g. low radiation levels during the mammography to detect breast cancer) or the physical or emotional consequences of false positive findings and the unnecessary diagnostic examinations this entails.

An »early cancer detection programme« (as defined by EU directives) is only said to exist when a certain organisational level has been reached with regard to screening, which must above all have a systematic invitation system and continuous quality assurance integrated into the programme. This programme characteristic has currently only been realised in Germany for mammography

screening of women aged between 50 and 69 years. The other early detection measures offered by the health insurance funds free of charge do not involve a special invitation process.

In the space of the last 10 years, early cancer detection has become more and more the focus of political and public discussion. During the same period, there were comprehensive changes to the existing methods in Germany. Nationwide mammography screening was established in all federal states between 2005 and 2008. Other ECD services (colon and rectum and skin cancer) were either modified or expanded.

The further development of early cancer detection is also one of the main goals of the National Cancer Plan, in which politics and associations are currently involved in a concerted action to improve the care of cancer patients (Federal Health Ministry (BMG) 2012).

When assessing the effects of early cancer detection on the level of the population in general, the epidemiological cancer registries, which have been set up all over the country in all federal states since 2009, play a vital role. By linking the registry data with the participant cohorts, the rate of tumours detected outside the screening examinations (interval carcinomas), which are an important quality indicator, can be determined on the one hand. In a similar manner, the death rate (mortality) attributable to cancer among the participants can be determined on the other hand and compared with the mortality rate among the entire population from the statistics on the causes of death. The data on the development of incidence (disease frequency) and tumour stage distribution also provide important information.

On a national government level, the data from the epidemiological cancer registries are regularly evaluated and published by the Centre for Cancer Registry Data (ZfKD) at the Robert Koch Institute.

For this reason, several important epidemiological parameters (see the box on P. 4) are presented in the following article on the cancer types for which the corresponding early

detection services currently exist in Germany. In addition to the ZfKD data, the official statistics on the causes of death of the Federal Statistical Office were used along with existing results on the use of early detection services, some of which were taken from the telephonic health survey »German Health Update« (GEDA) conducted by the Robert Koch Institute in 2010.

German Health Update (GEDA)

<i>Data owner:</i>	Robert Koch Institute
<i>Goals:</i>	Provision of updated data on health-related topics and the analysis of current developments and trends
<i>Survey method:</i>	Computer-assisted telephone interviews (CATI)
<i>Population:</i>	People resident in Germany aged 18 years and over
<i>Sample:</i>	22,050 women und men
<i>Cooperation rate:</i>	55.8 %
<i>Survey period:</i>	September 2009 to Juli 2010

Skin cancer

The measures for the early detection of all forms of skin cancer in the early cancer detection programme of the statutory health insurance funds in Germany were regulated anew in mid-2008. Since then, people of both sexes with compulsory health insurance aged 35 and over are entitled to a complete examination of their skin every two years by a physician (dermatologist, general practitioner etc.) with the requisite further training. In the years prior to this (from 1970), physical examinations were not yet a part of the complex preventive services offered.

With skin cancer, a difference is made between basal cell and cutaneous squamous cell carcinomas on the one hand and malignant melanomas of the skin on the other. Overall, skin cancer accounts for slightly more than 1 % of all deaths due to cancer in Germany (approx. 3,000 per year) with men and women. Of these, more than 80 % are attributable to malignant melanomas of the skin. In addition to this, people with malignant melanomas die an average of 10 years earlier than patients with basal cell and cutaneous squamous cell carcinomas (average age 71 as opposed to 82 years).

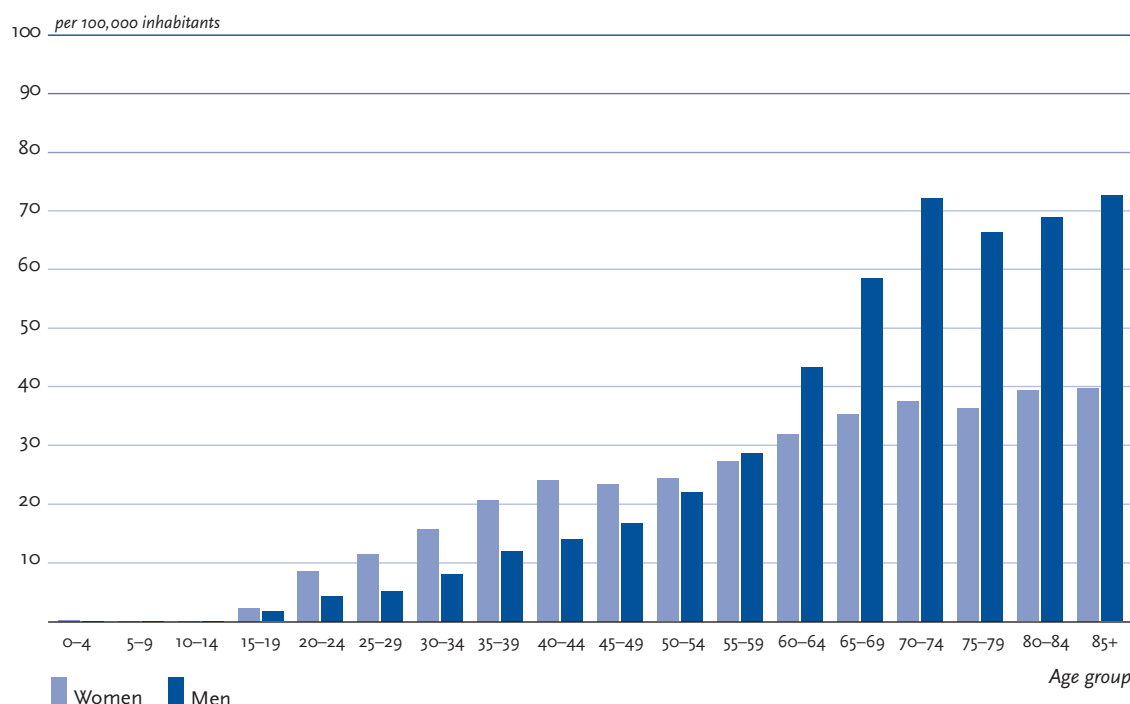
The proportion of malignant melanomas of the skin in all new cancer cases is roughly 4 %. Basal cell and cutaneous squamous cell carcinomas are much more common in Germany where more than 150,000 new cases can be expected every year. As is customary all over the world, the Centre for Cancer Registry Data only estimates in detail the frequency of malignant melanomas of the skin (RKI, GEKID 2012).

As in other European countries too, the rate at which people in Germany are diagnosed with malignant melanomas has been rising for decades. A sharp increase in incidence

Center for Cancer Registry Data

The Centre for Cancer Registry Data (ZfKD) was set up at the Robert Koch Institute (RKI) in the Epidemiology and Health Reporting department after the Federal Cancer Registry Data Act (2009) came into effect in January 2010. The ZfKD evaluates on a national level the data on new cases of cancer in the population recorded regionally in the epidemiological (population-related) cancer registries of each federal state. As several cancer registries are still being set up, the data on the number of new cases and survival rates for Germany published by the ZfKD are still estimations, even though they are made in line with an increasingly more reliable database. You will find more information on this on the internet at www.krebsdaten.rki.de.

Figure 1
Incidence of malignant melanomas of the skin (ICD-10: C43) in Germany 2008
Source: ZfKD



was observed in 2008, the year in which intensified measures for the early detection of skin cancer were introduced (RKI, GEKID 2012).

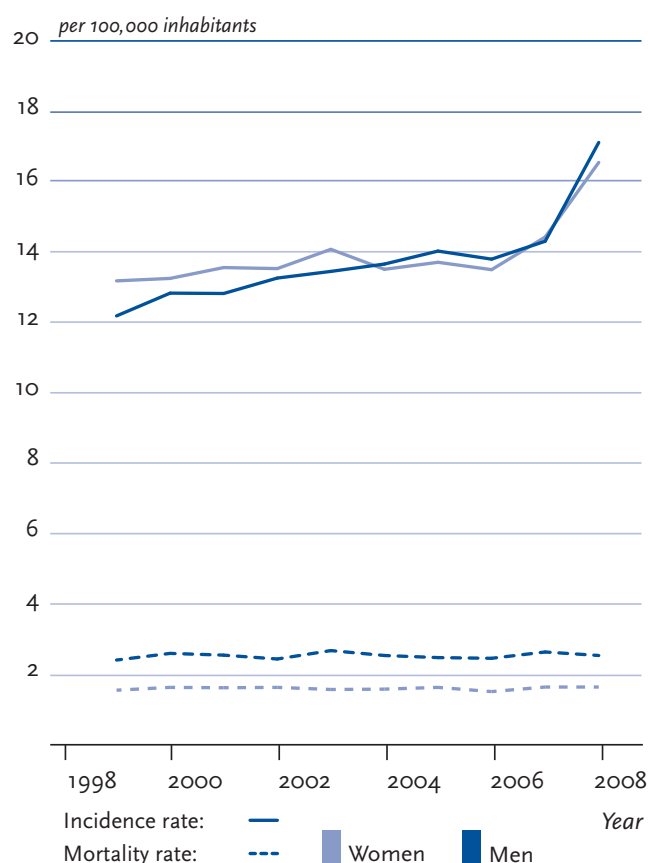
With women aged up to 55, malignant melanomas of the skin are diagnosed much more frequently than with men of the same age, but this ratio is reversed after the age of 55 (Figure 1). This means that with an median age of 60 years, women develop malignant skin melanomas earlier than men with an median age of 66.

The death rates for malignant skin melanomas are on roughly the same level with younger women and men. In contrast, however, considerably lower death rates are recorded for women aged 50 and over than for men (Figure 2). Whereas the age-standardised death rates among women have decreased by roughly 10 % since 1980, they have risen by roughly 10 % among men over the same period. The lower mortality rates among women with malignant melanomas is possibly attributable to the fact that on average, diagnosis is made earlier with prognostically more favourable tumour stages.

There is currently a very favourable relative 5-year survival rate of 91% for women with malignant melanomas of the skin in Germany, while at 87 %, this rate is only slightly worse for men. The tumour stage at which the melanoma is diagnosed makes it a major factor in this positive development of survival rates.

At least every second melanoma is discovered at an early tumour stage (T₁) so that the chances of successful treatment are good, with results once again being slightly better for women. The results of the latest GEDA Study 2010 show that women and men participate in equal measure

Figure 2
Age-standardised incidence and mortality rates, ICD-10 C43, in Germany 1999 – 2008
Source: ZfKD



in the early detection programme for skin cancer that was introduced in 2008. Whereas participation among women of all ages is slightly higher, more frequent participation has been determined for men, especially the more elderly (Table 1) (GEDA 2012).

Table 1
Participation in early skin cancer detection among respondents aged 35 and over
Database: GEDA 2010

Single/Multiple participation in early skin cancer detection		
	%	(95 %-CI)
Total	33.4	(32.4–34.3)
Total Women	32.9	(31.6–34.1)
Age group		
35 to 44	34.2	(32.1–36.4)
45 to 54	33.5	(31.3–35.7)
55 to 64	34.9	(32.3–37.7)
65 and over	30.5	(28.1–33.1)
Total Men	33.9	(32.5–35.4)
Age group		
35 to 44	27.5	(25.1–30.1)
45 to 54	30.4	(27.8–33.0)
55 to 64	32.3	(29.4–35.3)
65 and over	44.2	(41.1–47.3)

Cancer of the colon and rectum

Various examination methods for the early detection of cancer of the colon and rectum have been available for many years. People with statutory health insurance aged between 50 and 54 are entitled to an annual stool test (guaiac test / FOBT) for fecal occult blood. From the age of 55, the insured persons have the option of having an early detection colonoscopy performed (National Association of SHI Physicians (KBV) 2012). Of all measures, the colonoscopy has the highest sensitivity and specificity for the detection of neoplasms in the colorectum (Schmiegel et al. 2008). During this examination, colon polyps from which potentially malignant tumours can develop can also be removed if necessary. If there are no conspicuous findings, there is an entitlement to a repeat colonoscopy after ten years.

If the offered colonoscopy is not used, insured people aged 55 and over can have a stool blood test conducted as an alternative every two years. If the findings are conspicuous here, the insured person is entitled to have them clarified per colonoscopy. For persons with a higher morbidity risk (family history of colorectal cancer, chronic intestinal inflammation etc.), the recommended courses

of action differ and these should be discussed with the attending physician. Cancer of the colon and rectum is the second most common form of cancer with both men and women. Roughly 30,000 women and 35,000 men contracted the disease in 2008. As is customary, the very rare tumour of the small intestine was not included in this morbidity group.

The most recent age-standardised incidence rates showed a slight decline with women. They remained stable with men, although there was an increase in absolute case numbers due to demographic changes (RKI, GEKID 2012) (Figure 3).

In contrast to this, the age-standardised death rates have decreased by more than 20 % for both sexes in the last ten years. In 2008, roughly 3,000 fewer women died of colorectal cancer than in 1999, while the absolute number

Indicators

Incidence:

disease frequency, disease rate: annual number of new cases per 100,000 persons

Mortality:

Death rate; annual number of deaths per 100,000 persons

Age-specific rates:

These show the connection between age and incidence or mortality. The age-specific incidence and mortality rates are given as annual rates per 100,000 persons in each age group.

Age-standardised rates:

Age standardisation allows the comparison of rates in populations with different age structures. It indicates the incidence or mortality among a total of 100,000 persons of a predetermined, usually fictitious, age structure. The so-called Old European standard was used here.

Relative survival rates:

Survival rates describe average survival chances. Relative survival takes into account the fact that only a certain percentage of the deaths among cancer patients are attributable to cancer because a certain mortality rate among persons of the same age and sex has to be expected due to other underlying diseases. A relative 5-year survival rate of 80 %, for example, means that the percentage of cancer patients who still survive 5 years after the diagnosis equates to 80 % of the expected percentage of survivors from a population of the same age and sex without cancer.

Tumour stages:

Tumour stages classify the size of a tumour and are a component of TNM classification in which the tumour size (T), affected lymph nodes (N) and occurrence of distant metastasis (M) are classified. TNM classification is used to describe the spread of a solid malignant tumour at the time of diagnosis. Tumour sizes are given in four stages (T-1 to T-4), with T-1 being the early stage and T-4 the late stage.

of deaths among men remained more or less constant (Figure 3). Around half of the people who contract the disease are still alive five years after the initial diagnosis. This makes colorectal cancer one of the cancer types with medium prognosis. As symptoms such as blood in the stool and pain usually only occur at a later stage, early detection takes on a special significance.

Information on the acceptance of colonoscopy by persons aged 55 and over was collected in the GEDA Study 2010, in which colonoscopies performed for reasons other than early detection («curative colonoscopies») were deliberately included. The results show that the percentage of persons who subject themselves to at least one colonoscopy in the course of their life lies at roughly 58 % for both men and women. It can be seen here that a significant increase in participation is recorded for both sexes from the age of 65 (women approx. 60 %, men approx. 65 %) (Table 2) (RKI 2012).

The introduction of an organised invitation process, which has already enjoyed great success in other countries and within the scope of studies, is currently being discussed as the principal measure to increase the participation rate and thereby the early detection of colorectal cancer (BMG 2012).

Figure 3
Absolute number of new cases and deaths from colorectal cancer (ICD-10: C18-21) in Germany 1999–2008
Source: Zfkd

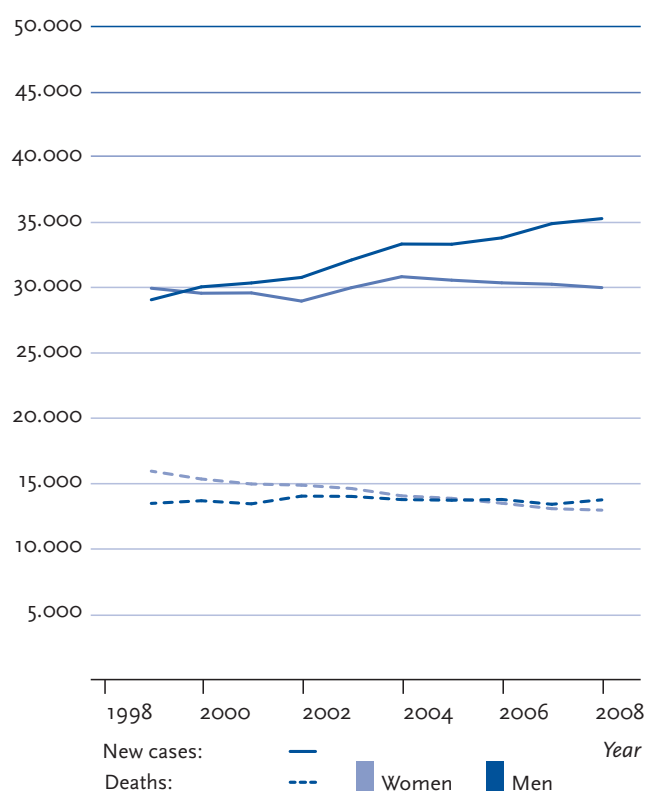


Table 2
Use of colonoscopy (various reasons, including early detection)
Database: GEDA 2010

Single/Multiple participation in colonoscopy		
	%	(95 %-CI)
Total	58.1	(56.6–59.6)
Total Women	57.5	(55.4–59.6)
Age group		
55 to 64	53.0	(50.1–55.8)
65 and over	59.8	(57.0–62.5)
Total Men	58.9	(56.6–61.2)
Age group		
55 to 64	50.0	(46.7–53.4)
65 and over	64.9	(61.8–67.8)

Prostate cancer

The early detection examination for prostate cancer is part of the early detection services of the statutory health insurance funds and currently comprises an annual examination of the external sexual organs and palpation of the prostate gland and related lymph nodes (digital-rectal examination, DRE) for men aged 45 and over.

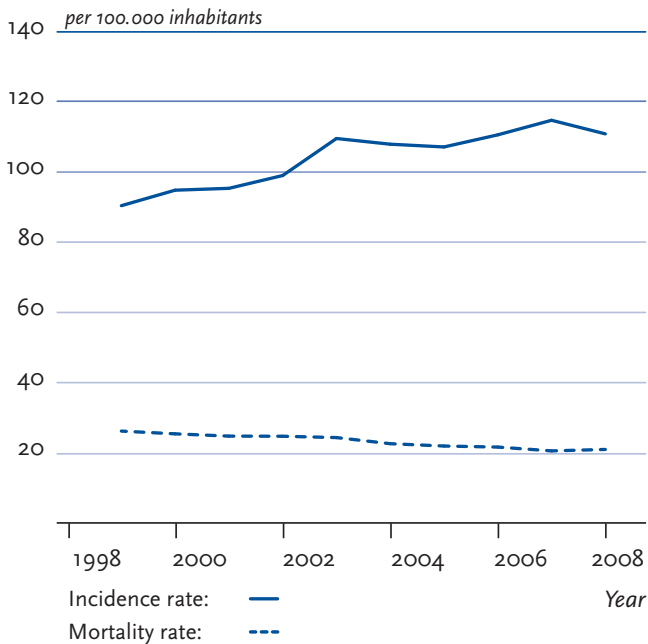
The use of the blood test for prostate-specific antigens (PSA test) for the early detection of prostate cancer is still the subject of international debate (Andriole et al. 2009, Schröder et al. 2009, Sandblom et al. 2011) as it leads to over-diagnosis which involves unnecessary treatments. For this reason, the PSA test is not a component of statutory early detection in Germany. It has to be paid for by the patients themselves as an individual health service (IGel-Monitor 2012).

With 26 %, prostate cancer is the most common form of cancer among men in Germany and with 10 % the third most frequent cause of death from cancer. The number of new cases has risen steadily in recent years and reached approx. 63,400 in 2008. This is also reflected in the age-standardised incidence rate, which has risen by almost 25 % since 1999 (Figure 4) (RKI, GEKID 2012).

An increase can be recognised in particular in the age group between 50 and 74 (Figure 5), although the overall increase does not appear to have continued since roughly 2003. Based on the latest population forecasts, which assume that the percentage of over 60-year-old men will almost double in Germany by 2050, it can be expected that the absolute number of prostate cancer cases will also increase significantly (DGU 2011).

In contrast to this, the age-standardised death rate has stayed on a relatively constant level over the years and has even shown a slight decline since 2003. This increase in the incidence rate with an unchanged death rate is attributable above all to increased use of the PSA test (RKI 2007) and can

Figure 4
Age-standardised incidence and mortality rates for prostate cancer (ICD-10: C61) in Germany 1999–2008
 Source: ZfKD



be observed in practically all western industrialised countries. This is linked with a drop in the median age from 73 in 1990 to 70 in 2008.

A representative population study of 11,778 men aged between 45 and 69 conducted in 2004 showed that almost two thirds of them had undergone the DRE test and almost half (46 %) had taken the DRE and PSA test. A third of those questioned, on the other hand, stated that they had never taken part in an early detection examination for prostate cancer (Sieverding et al. 2008). The percentage of non-participants is high in the younger age groups in particular, but it drops with increasing age with the result that roughly 80 % of 60 to 69 year-old men have subjected

themselves to at least one of the two examinations. Further analysis showed that participation in health checks in particular (e. g. Checkup 35) increases participation in ECD (Sieverding et al. 2008).

Cervical cancer (carcinoma of the cervix)

Within the scope of the early cancer detection schemes provided by the statutory health insurance funds, women in Germany aged 20 and over can have a cell smear of the cervix (PAP smear) carried out and evaluated once a year. In the vast majority of cases, cervical cancer is caused by a persistent infection with human papillomavirus (HPV).

For this reason, the German Standing Committee on Vaccination Recommendations (STIKO) recommended in March 2007 that all girls aged between 12 and 17 be vaccinated against two high-risk HPV types (HPV 16 and 18), which are responsible for around 70 % of all cervical carcinomas.

Despite this, the early detection smear test cannot be dispensed with because any changes to the cervix that have already occurred due to cancer cannot be prevented by the vaccination and infection with other HPV cannot be excluded. Since the introduction of the PAP smear test in the 1970s, a distinct decline in the incidence of cervical carcinomas and related mortality rate has been observed in Germany (RKI, GEKID 2012).

In recent years, however, this decline has slowed down considerably and both rates have remained mainly stable since roughly 2003. The exceptions here are the figures for mortality among younger women aged 35 to 50 and older women over 65 years of age, both of which showed a further decline after the year 2000 (Figure 6).

The highest incidence rates for invasive carcinomas are currently with women aged 40 to 49. The median age at diagnosis is 53 and therefore significantly lower than for cancers in general (69 years). On average, women are diagnosed with carcinoma in-situ, the preliminary stage which

Figure 5
Age-specific incidence rates of prostate cancer (ICD-10: C61) in Germany
 Source: ZfKD

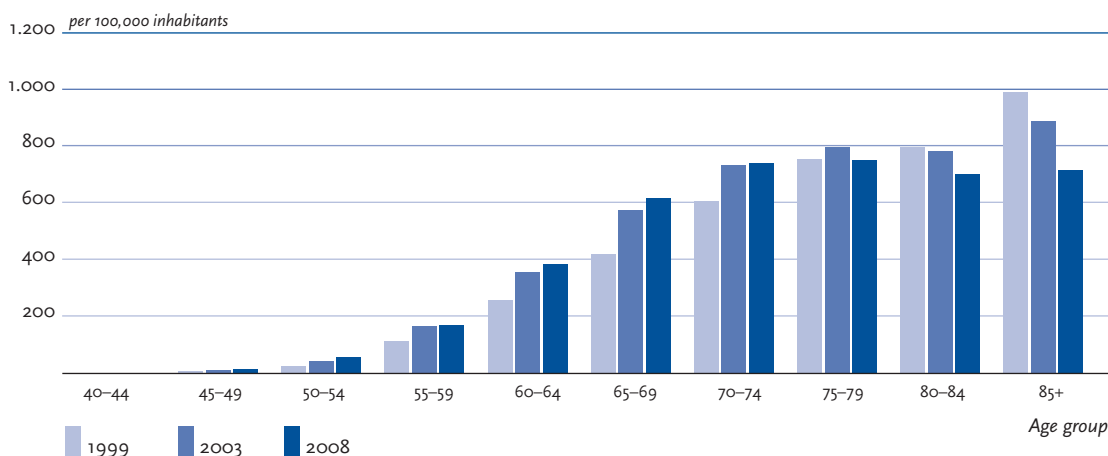
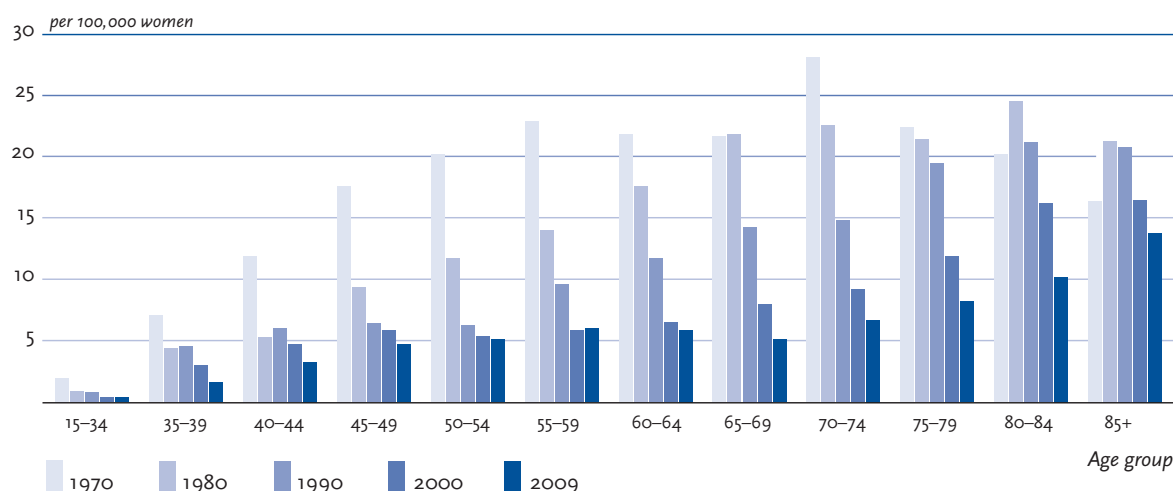


Figure 6
Age-specific mortality due to cervical cancer (ICD-10: C53) in Germany
 Source: ZfKD



is easier to treat, at the age of only 36. Carcinoma in-situ is diagnosed up to four times more often than invasive carcinomas. The early cancer detection programme of the statutory health insurance funds focuses in particular on the diagnosis and timely removal of preliminary stages of cervical cancer, the last stage of which is the carcinoma in-situ before the invasive carcinoma forms.

In contrast to mammography screening, women in the stipulated age group in Germany are not invited to early detection examinations for cervical cancer but despite this, many women make use of this early detection measure. A special evaluation of the years 2002 to 2004 conducted by the Central Research Institute of Ambulatory Health Care (Association of SHI Physicians North-Rhine and Bremen) showed that the participation rate among under 50-year-olds lies between 70 % and 80 % within a period of three years and more than 60 % of women aged under 65 make use of the offer (Table 3) (Kerek-Bodden et al. 2009).

Different recommendations are given in European guidelines, above all with regard to the examination interval and quality assurance. This has given good reason to think about further development in the early detection concept for cervical cancer within the scope of the National Cancer Plan (BMG 2012).

Breast cancer

Mammography screening was introduced in Germany's federal states between 2005 and 2008 following a Bundestag resolution from 2002 and the programme can be said to provide nationwide coverage since 2009. This makes it the first early detection measure in Germany with a programme character. Women aged between 50 and 69 receive a written invitation to participate in a standardised screening programme with extensive quality assurance measures every two years.

The prime objective of the programme is to reduce the breast cancer mortality rate in each affected age group. According to the results of controlled studies conducted in the 1980s and 1990s in Scandinavia and the UK (Anderson et al. 1988, Tabar et al. 1989, Roberts et al. 1990), a reduction of 20 % to 30 % appears to be possible, which would mean as many as 2,000 prevented deaths in Germany every year.

Another goal is to reduce the frequency of stressful therapy procedures (radical mastectomy, chemotherapy), which are usually necessary at advanced stages and which involve

Table 3
Participation in early cervical cancer detection within a 3-year period (2002–2004)
 Source: Kerek-Bodden et al. 2009

Participation in early cervical cancer detection	
Age group	%
20 to 24	79.0
25 to 29	81.1
30 to 34	79.3
35 to 39	76.7
40 to 44	73.5
45 to 49	71.7
50 to 54	69.2
55 to 59	65.7
60 to 64	61.7
65 to 69	54.4
70 to 74	42.2
75 to 79	31.3
80 and over	16.3

considerable side-effects, and enable the use of more gentle forms of treatment by recognising tumours at an early stage.

Possible disadvantages of the procedure are summarised under the catchwords »over-therapy« or »over-diagnosis«, implying that the regular examination of clinically healthy women would probably lead to a large number of tumours being detected and treated which would not otherwise have troubled the women in question due to the long growth period of the tumour. International estimates of the extent of this effect lie far apart (Jorgensen et al. 2009, Puliti et al. 2009, Kalager et al. 2012).

Whereas the effects of the programme on breast cancer mortality nationwide will probably only become apparent in 2015, the first effects on diagnosis rates can already be observed along with developments in the participation rate. Due to the restricted age group in the screening programme, the development of the age-specific incidence rates is of particular interest here (Figure 7).

Since 2005, the rate has increased by 16 % in the 50 to 59 year-old age group and by 31 % with the 60 to 69 year-olds. Although a slight increase of roughly 5 % was recognised over the same period in all other age groups not directly affected by screening, the trends from the years prior to 2005 have basically continued.

Thanks to systematic mammography screening, a particularly good data basis is available compared to the cancer types outlined above. This is distinguished by a high level of registration completeness as well as the completeness of data on the tumour stage (> 90 %) in virtually all federal states.

In this way, in addition to general incidence rates, incidences by the individual tumour stages (stage-specific incidence rates) can be estimated throughout the country

(Figure 8). A distinct increase in the incidence rate for T1 tumours (< 2 cm) can be recognised here. Whereas the morbidity rates for T2 and T3 tumours remain stable, a slight but continuous reduction which set in before screening was introduced can be recognised with T4 tumours.

The participation rates (percentage of participants from all women invited) in the mammography screening programme remained stable in the first few years at between 50 % and 55 %, but it should be taken into account that due to the step-by-step build-up of the programme, the number of women invited every year increased step by step too between 2005 and 2008 (Kooperationsgemeinschaft Mammographie 2011).

Overall, therefore, despite participation rates which have not been very high up to now, the first effects of organised mammography screening can be recognised in the nationwide data which at least prove that more smaller-sized tumours were detected in each age group in the first screening phase than was previously the case.

»Grey« screening (mammography examination after referral justified by unclear palpation findings or family history), which was probably fairly widespread at the time, could possibly be responsible for the decline in T4 tumours before 2005.

In the medium term, a more distinct reduction in the incidence of larger tumours (T2 to T4), in primary metastasised cases and ultimately in the mortality rates in the age group between 50 and 74 would be an indication of the success of the programme (Fracheboud et al. 2004).

Figure 7
Age-specific incidence rates of breast cancer (ICD-10: C50) for women in Germany from 1999 to 2008
Source: ZfKD

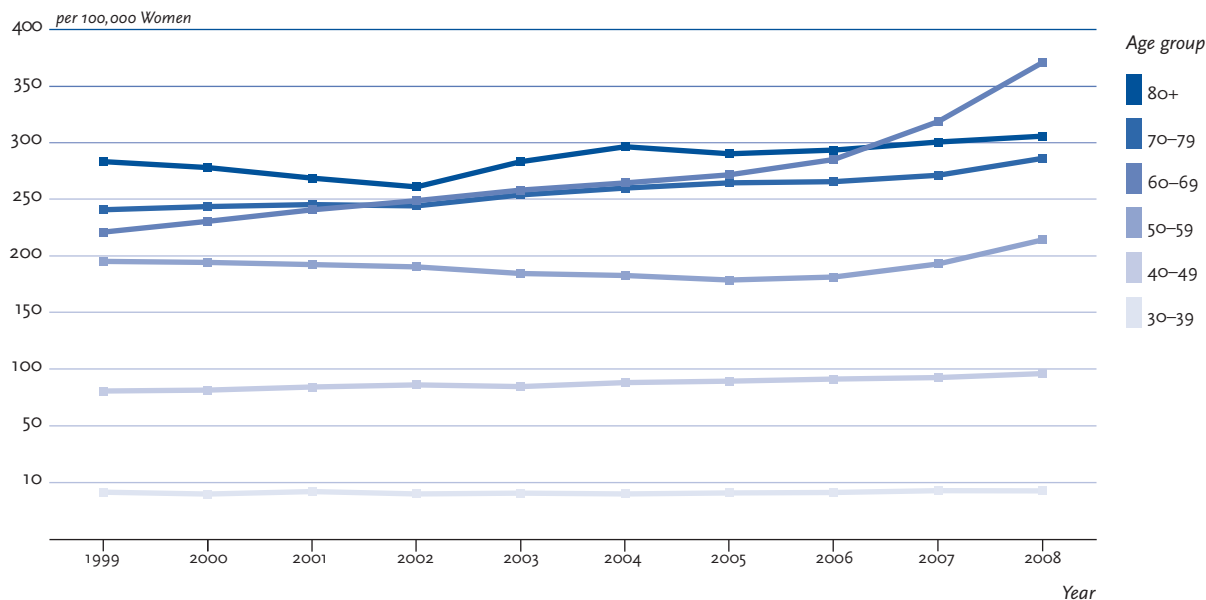
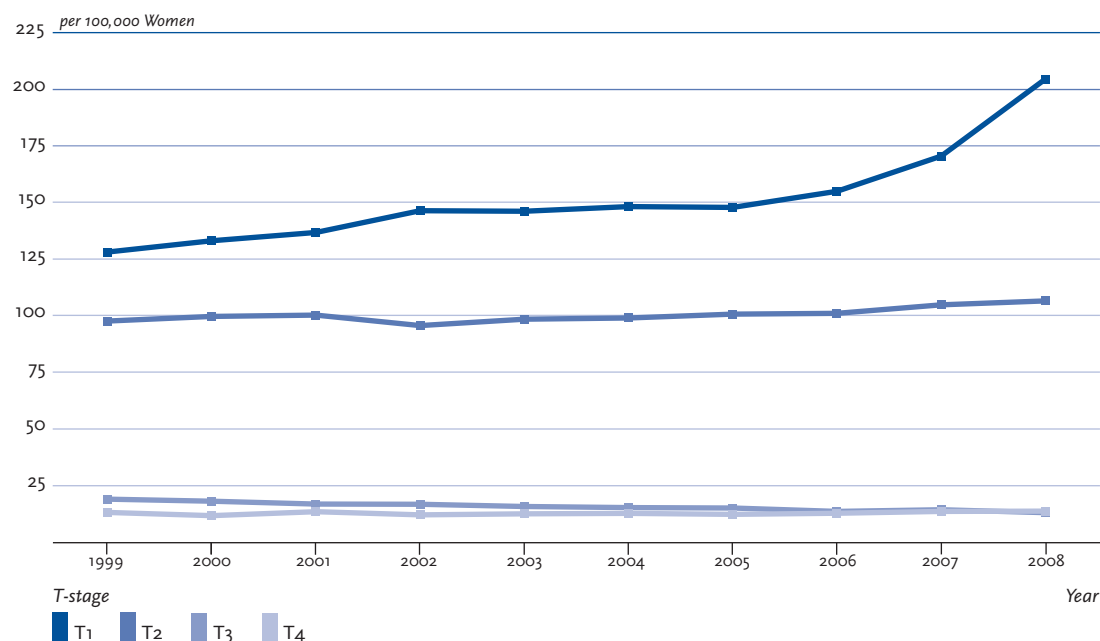


Figure 8**Breast cancer incidence (ICD-10: C50) by tumour size (T-stages) for women in Germany aged 50 to 69 years, from 1999-2008**

Source: ZfKD



Synopsis

Early cancer detection produces opportunities (reduced mortality rates, partially reduced incidence rates) as well as certain risks («over-diagnosis», «over-therapy»). If diagnosed in time, the chances of success of the therapies prescribed for the cancer types discussed here, and therefore the chances of survival of the affected patients, can be very high.

The anxiety caused by a false suspicion or premature diagnosis, however, and the potential consequences of what may in some cases be a superfluous therapy, can impair the patients' quality of life.

Against this background, the methodical further development of early detection services on the one hand and the appropriate handling of available measures on the other are of key importance in the field of health policy.

Accordingly, more focus on European guidelines is the current goal within the scope of the National Cancer Plan (BMG 2012), which should result in the medium term in a higher level of organisation of the early detection of cervical and colorectal cancer in Germany.

It is planned to implement this in systematically organised, quality assured screening programmes. The provision of better information to insured persons regarding the benefits and risks of early cancer detection, as well as regular invitation letters to improve participation rates, should strengthen early detection.

In the long term, the concept of risk-adapted early detection is being considered for several cancer types (e. g. colorectal and prostate cancer) in order to identify persons with a considerably higher risk on the basis of certain risk

indicators (e. g. family history) and offer them suitable early cancer detection measures (BMG 2012). More research is required here at the moment, however.

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Imprint

GBE kompakt

Publisher

Robert Koch Institute
Nordufer 20
13353 Berlin

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Citation Format

Kraywinkel K, Bertz J, Laudi A, Wolf U (2012)
Epidemiology and Early Diagnosis of
Common Cancers in Germany.
Published by Robert Koch Institute Berlin,
GBE kompakt 3(4)
www.rki.de/gbe-kompakt (last revised: 25.10.2012)

ISSN 2191-4974

The Robert Koch Institute is a federal institute within the
portfolio of the Federal Ministry of Health