3.6 Liver

Epidemiology
Liver cancer is relatively uncommon, but in view of its poor prognosis it ranks among the ten most frequent causes of death due to cancer for both men and women. There are approximately 8,600 new cases in Germany every year, and roughly the same number of deaths. The median age at diagnosis is 71 years for men and 74 years for women. Only about 4% of cases are diagnosed before 45 years of age. One in 84 men and one in 200 women in Germany develop a malignant liver tumour in the course of their life.

Some 66% of malignant tumours develop from liver cells (hepatocellular carcinoma), and almost 21% from cells in the intrahepatic bile ducts (cholangiocarcinoma). This proportion is significantly higher for women.

Since 1980, the mortality rate for men has risen steadily by a total of 52%, even after age-standardisation, while it has remained more or less unchanged for women in the same period. The increased mortality rate in men was independent of the histology of the tumour. The age-standardised incidence rate for liver cancer in men has increased by about 20% since 1999.

Currently, incidence and mortality rates in the north-western federal states are somewhat lower than in the rest of Germany. In an international comparison, the highest incidence and mortality rates are to be observed in France and in The United States.

In Germany, the relative 5-year-survival rates for women and for men are around 15%.

Risk factors and early detection
Cirrhosis of the liver is the most important risk factor for liver cancer. In Germany, the most common causes for the development of cirrhosis of the liver are high alcohol consumption levels and/or chronic hepatitis C virus infection. Non-alcoholic fatty liver disease also increases the risk of liver cancer. These may, for example, occur as a consequence of diabetes mellitus and/or due to metabolic syndrome. In turn, the trigger for metabolic syndrome is very often obesity.

A chronic infection with the hepatitis B virus, even without cirrhosis of the liver, is also a risk factor for liver cancer. Tobacco consumption is associated with an increased risk, as well. Besides, contamination of food with Aflatoxin B1 (mould fungus poisoning) increases the risk of liver cancer. Finally, hereditary metabolic diseases such as haemochromatosis can also increase this risk.

Early detection examinations for the general population are not included in the statutory health insurance screening programmes. It is recommended that regular ultrasound check-ups be offered to all patients with cirrhosis of the liver, chronic hepatitis B or C infections, or with fatty liver disease. Blood tests (for alpha-fetoprotein) are only of minor relevance.
Figure 3.6.1a
Age-standardised incidence and mortality rates, by sex, ICD-10 C22, Germany 1999–2012
per 100,000 (European standard)

Figure 3.6.1b
Absolute numbers of incident cases and deaths, by sex, ICD-10 C22, Germany 1999–2012

Figure 3.6.2
Age-specific incidence rates by sex, ICD-10 C22, Germany 2011–2012
per 100,000
### Table 3.6.2
Cancer incidence and mortality risks in Germany by age and sex, ICD-10 C22, database 2012

<table>
<thead>
<tr>
<th>Age</th>
<th>Risk of developing cancer</th>
<th>Mortality risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>in the next ten years</td>
<td>ever</td>
</tr>
<tr>
<td>Men aged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35 years</td>
<td>&lt;0.1% (1 in 7,900)</td>
<td>1.2% (1 in 87)</td>
</tr>
<tr>
<td>45 years</td>
<td>0.1% (1 in 1,600)</td>
<td>1.2% (1 in 87)</td>
</tr>
<tr>
<td>55 years</td>
<td>0.2% (1 in 430)</td>
<td>1.2% (1 in 87)</td>
</tr>
<tr>
<td>65 years</td>
<td>0.5% (1 in 210)</td>
<td>1.1% (1 in 94)</td>
</tr>
<tr>
<td>75 years</td>
<td>0.5% (1 in 190)</td>
<td>0.7% (1 in 140)</td>
</tr>
<tr>
<td>Lifetime risk</td>
<td>1.2% (1 in 84)</td>
<td>1.1% (1 in 95)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Women aged</th>
<th>in the next ten years</th>
<th>ever</th>
<th>in the next ten years</th>
<th>ever</th>
</tr>
</thead>
<tbody>
<tr>
<td>35 years</td>
<td>&lt;0.1% (1 in 10,400)</td>
<td>0.5% (1 in 200)</td>
<td>&lt;0.1% (1 in 16,600)</td>
<td>0.5% (1 in 190)</td>
</tr>
<tr>
<td>45 years</td>
<td>&lt;0.1% (1 in 3,900)</td>
<td>0.5% (1 in 200)</td>
<td>&lt;0.1% (1 in 5,600)</td>
<td>0.5% (1 in 200)</td>
</tr>
<tr>
<td>55 years</td>
<td>0.1% (1 in 1,400)</td>
<td>0.5% (1 in 210)</td>
<td>0.1% (1 in 1,800)</td>
<td>0.5% (1 in 200)</td>
</tr>
<tr>
<td>65 years</td>
<td>0.1% (1 in 740)</td>
<td>0.4% (1 in 230)</td>
<td>0.1% (1 in 780)</td>
<td>0.5% (1 in 210)</td>
</tr>
<tr>
<td>75 years</td>
<td>0.2% (1 in 480)</td>
<td>0.3% (1 in 300)</td>
<td>0.2% (1 in 430)</td>
<td>0.4% (1 in 250)</td>
</tr>
<tr>
<td>Lifetime risk</td>
<td>0.5% (1 in 200)</td>
<td></td>
<td>0.5% (1 in 190)</td>
<td></td>
</tr>
</tbody>
</table>

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**Figure 3.6.3**

Distribution of T-stages at first diagnosis by sex

*Not presented due to the large proportion of missing data.*

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**Figure 3.6.4a**

Absolute survival rates up to 10 years after first diagnosis, by sex, ICD-10 C22, Germany 2011–2012

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**Figure 3.6.4b**

Relative survival rates up to 10 years after first diagnosis, by sex, ICD-10 C22, Germany 2011–2012
Figure 3.6.5
Registered age-standardised incidence and mortality rates in German federal states, by sex, ICD-10 C22, 2011–2012
per 100,000 (European standard)

Figure 3.6.6
International comparison of age-standardised incidence and mortality rates, by sex, ICD-10 C22, 2011–2012 or latest available year (details and sources, see appendix)
per 100,000 (European standard)
### 3.7 Gall bladder and biliary tract

#### Epidemiology

In Germany, about 4,950 new cases of malignant tumours of the gall bladder (approx. 37 %) and of the biliary tract outside the liver (63 %) were diagnosed in 2012. Women develop gall bladder carcinomas more frequently, whereas tumours in the extra hepatic biliary tracts are diagnosed more frequently in men. Histologically, the majority of these are adenocarcinomas. Other histological variants such as squamous-cell carcinomas or hybrid forms are rare. As with liver cancer, the risk of developing this type increases steadily with age. The lifetime risk is about 0.6 % for women and 0.5 % for men.

Since 1999 the age-standardised incidence rate in Germany has declined for women (especially for gall bladder carcinomas) and remained largely unchanged for men. However, because of demographic changes the absolute number of new cases has increased slightly among men. The age-standardised mortality rates for the same period have decreased constantly in both genders.

The survival prospects with malignant tumours of the gall bladder and biliary tract are generally poor, yet better than for liver cancer. The relative 5-year survival rate for women is 15 % and 21 % for men. Details with regard to tumour stage at point of diagnosis exist for approximately 60 % of gall bladder cases registered, most of which were diagnosed in stage T2 and T3.

#### Risk factors and early detection

The triggers for carcinomas of the gall bladder and biliary tract are not absolutely clear. Overweight is considered to be a risk factor for both. The presence of gallstones can be a risk for gall bladder carcinomas. In the current scientific debate, chronic inflammatory diseases of the biliary tract, such as primary sclerosing cholangitis (PSC), choledochal cysts, the inflammatory bowel disease ulcerative colitis, liver diseases as a result of the high consumption of alcohol, hepatitis-C virus infection, and HIV infection, Diabetes and smoking are all deemed to be possible risk factors. A further risk factor, especially in Asia, is an infection with the parasitic liver flukes Clonorchis sinensis or Opisthorchis viverrini.

Various markers are being tested for their suitability for early detection among persons at risk, however, without any practical consequences. There is no screening programme on offer for the general population. Often, however, early stage diagnosis is made upon removing the gall bladder for other reasons.