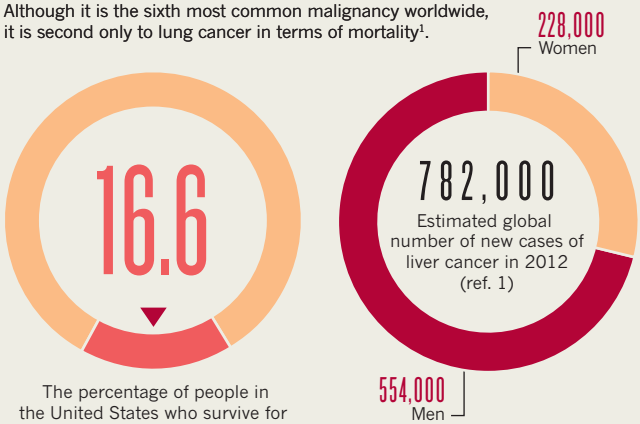
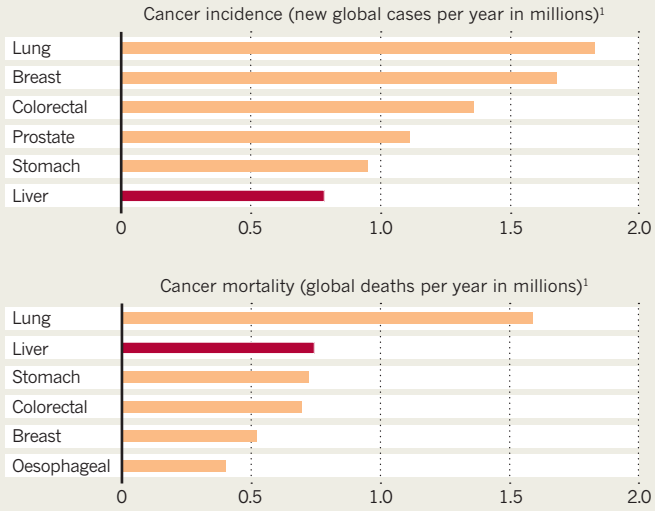
A PREVENTABLE CANCER

Liver cancer is difficult to treat, and lethal if not caught early. But its most common causes, such as hepatitis viruses and obesity, can be prevented. By **Lucas Laursen**.

OUT OF PROPORTION

Not only does liver cancer strike more men than women, it also causes a disproportionate number of cancer-related deaths. Although it is the sixth most common malignancy worldwide, it is second only to lung cancer in terms of mortality[1].

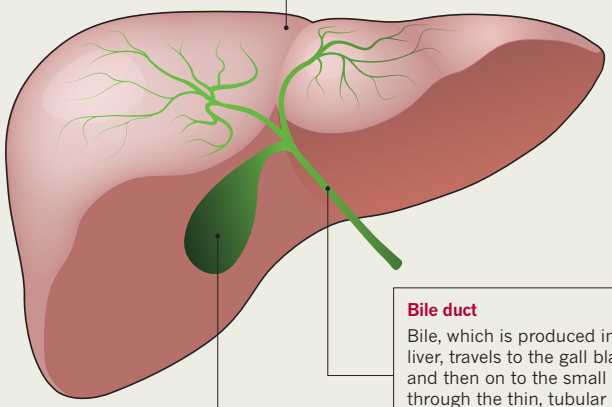




DOMINANT SUBTYPE

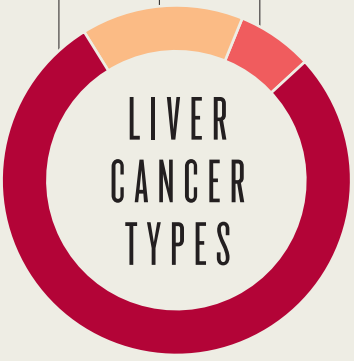
Liver cancer has several subtypes, but one — hepatocellular carcinoma (HCC) — is by far the most common worldwide. In some countries, the proportion of subtypes differs as a result of different risk factors.

Liver
The liver contributes to a wide range of functions, including digestion, detoxification and metabolism. It is also the only internal human organ that can regenerate: as little as 25% of its original tissue is necessary to restore the liver to its original size. HCC is named after the cells in which it develops, the hepatocytes.



Bile duct
Bile, which is produced in the liver, travels to the gall bladder and then on to the small intestine through the thin, tubular bile duct. Bile-duct cancer, also known as cholangiocarcinoma, is less common than disease that starts in the lobes of the liver itself.

Gall bladder
Bile acids, which are used in digestion, are stored in the gall bladder and released into the small intestine on ingestion of fatty foods. Certain bacteria in the gut convert bile acids into toxic chemicals that might contribute to liver cancer.



~78% **HCC**
HCC accounts for the overwhelming majority of liver cancers[3]. It is the disease addressed by this Outlook, as well as by most liver-cancer research.

~15% **Bile-duct cancer**
Bile-duct cancer is more common than HCC in some Asian countries, but it makes up a relatively small number of liver-cancer cases worldwide[4].

~7% **Hepatoblastoma and various liver sarcomas and carcinomas**
These include most cases of paediatric liver cancer, which has increased in incidence in recent years but is still a rare disease.

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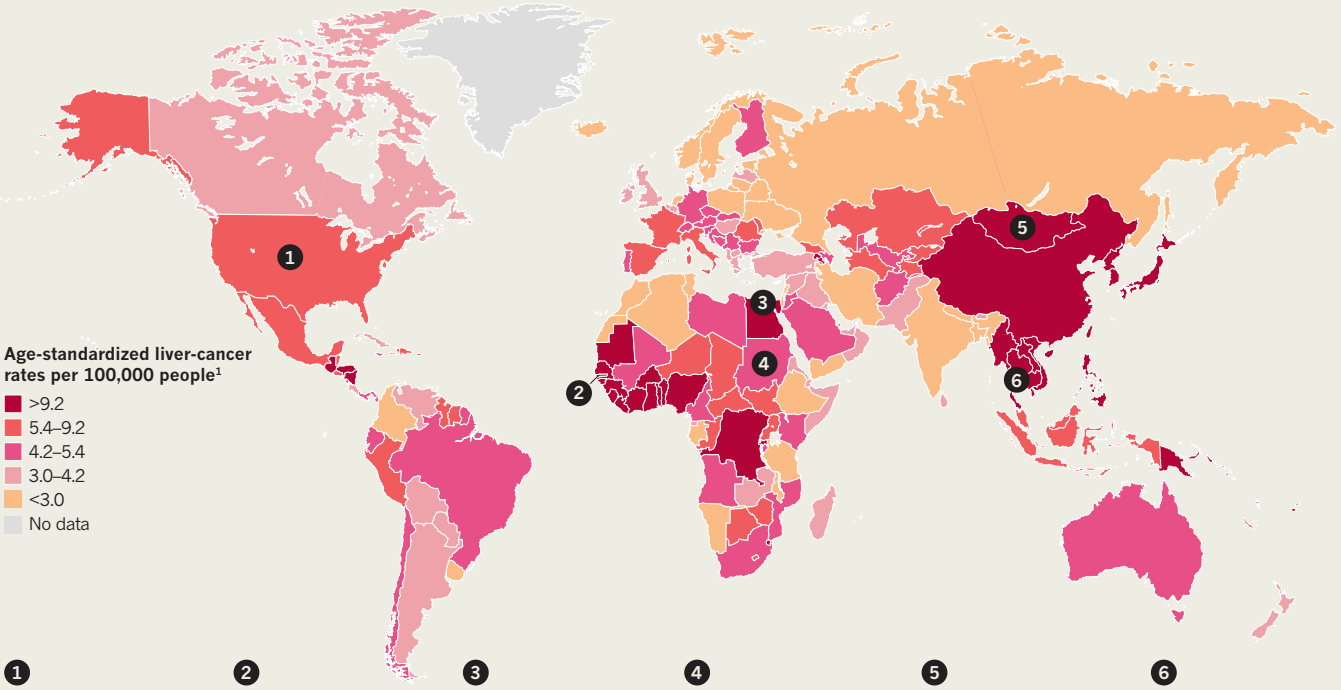
RISK ASSESSMENT

Liver-cancer rates vary widely between countries, with the highest rates occurring in Africa and east Asia. The disease is nearly always preceded by chronic liver damage, most commonly caused by hepatitis B. Highlighted below are other common causes in selected countries.



1 UNITED STATES

Poor diet, low activity levels and genetics all contribute to high rates of obesity and fatty liver disease in the United States. Liver cancer is 17–18% likelier among overweight people and 83–89% likelier among obese people[5,6].

2 GAMBIA

The hepatitis B virus (HBV) causes around half of all cases of liver cancer worldwide[8]. Gambia once had one of the world's highest rates of HBV infection, but a vaccination programme started in 1990 has begun to have an effect[9].

3 EGYPT

The hepatitis C virus (HCV) is responsible for about 15% of all global liver-cancer cases[8], and Egypt has the world's highest rate of HCV[11].

4 SUDAN

Aflatoxin fungi, found on crops such as maize (corn) and peanuts, might cause up to 28% of liver cancers worldwide[12]. Sudan has unusually high crop concentrations of aflatoxin, which has synergistic effects with HBV and HCV.

5 MONGOLIA

Mongolia has the world's highest incidence of liver cancer, at 78 cases per 100,000 residents[1]. It has unusually high rates of alcohol abuse and infection with HBV and HCV.

6 THAILAND

Eating raw fish infested with a parasitic flatworm called a liver fluke can cause bile-duct cancer. The liver fluke is common in Thailand, one of the few countries where bile-duct cancers are more common than HCC.

2009
First year since 1969 that HCC rates in the United States did not rise[7]

95
Percentage of adults in Gambia who have been exposed to HBV (upper estimate)[10]

14.7
Percentage of people in Egypt who are infected with HCV[11]

60
Percentage of liver-cancer cases in Sudan (before the country split) that could be due to aflatoxin[13]

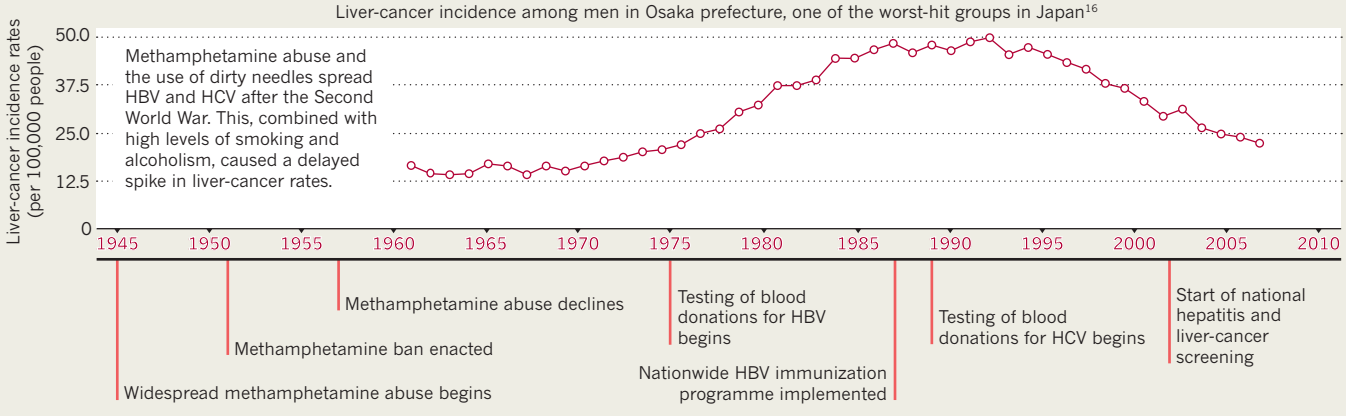
×8
Difference between liver-cancer incidence in Mongolia and the global average[1]

89
Percentage of liver-cancer cases caused by liver flukes in Khon Kaen, Thailand[14]

A SUCCESS STORY

Liver disease takes decades to progress to cancer, which makes prevention research difficult. In Japan, a 30-year gap separated the peak of hepatitis infections (both HBV and HCV) and the resulting rise in liver cancer[15]. But public-health efforts on multiple fronts are bringing liver-cancer rates back down.

Liver-cancer incidence among men in Osaka prefecture, one of the worst-hit groups in Japan[16]



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