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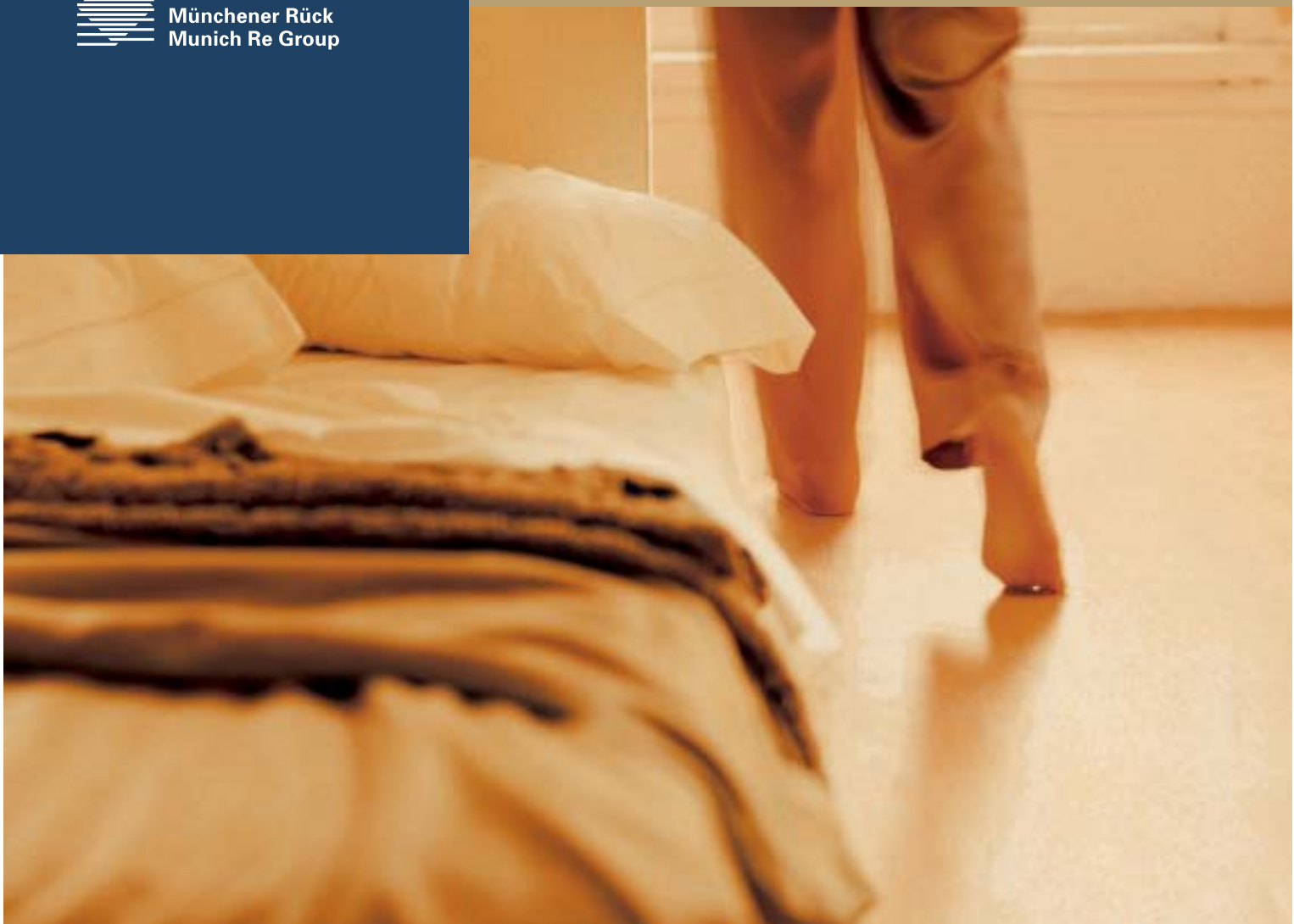
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Münchener Rück  
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Restless legs syndrome – Walking around alleviates the complaint.



# Impairment

## Restless legs – The pain that waits until evening falls

Night walkers are people who suffer from restless legs syndrome (RLS) – the name of which accurately describes the main symptom. They suffer from a combination of pain, sensation of heat and jitteriness, resulting in an inability to rest their legs in the evenings.

The greatest torture begins during the night. Unnerved, sufferers are forced to leave their beds and – driven by the restlessness – pace the floor like caged tigers. The anguish often abates after a few hours, but some cases do not find rest before the break of day.

### A common but not well-known affliction

Restless legs syndrome is a common disease. This condition affects 2–10% of the population, women twice as often as men. The symptoms may start at any age and are often misinterpreted: in young people as “growth pains” or even hyperactivity disorder (hyperkinetic syndrome). Only a few patients report cure or symptom-free remission sustained over several months. Quite the opposite, in fact, as two-thirds of sufferers find that the symptoms even increase in intensity with time, spreading to other parts of the body and eventually affecting the arms and hands as well.

Experts suspect that the cause is an hereditary disorder of cerebral metabolism. In at least half the cases, other family members have similar symptoms or at least sleep disturbances. Women often mention a family history of vein problems.

### Diagnostic criteria for restless legs syndrome

- Sensory symptoms
  - Prickling, creeping, itching, pulling
- Compelling urge to move
  - Restlessness, pacing the floor, massaging the legs
- Symptoms occurring at rest
  - Temporary relief of symptoms with active movement
- Symptoms worse in the evening or at night

It is important to distinguish secondary forms of the condition, for which the prognosis is quite different. Secondary RLS means that the problem has been triggered by an underlying disease; typical causes are kidney diseases, diabetes mellitus, rheumatic arthritis and iron deficiency. Symptoms may arise for the first time during pregnancy but they usually disappear after the baby is born.

### Treatment and occupational disability

The distinction between restless legs and polyneuropathy, such as is seen in alcoholism, liver diseases and vitamin deficiency, is important for the prognosis. The main criteria distinguishing this syndrome from other paraesthesia are the time of day when symptoms occur and their relief with activity. In RLS, patients have a compelling urge to get up and move around. This compulsion to move the legs simply cannot be ignored and the urge is ultimately irresistible.

At least 1% of patients have such severe symptoms that medication is necessary. Since the 1980s, various medicines have been used which have an effect on dopamine metabolism. These are often medicines that have proved of value in the treatment of Parkinson's disease. Although this does not indicate an increased risk of developing Parkinson's, the medicines themselves may be problematic because of their side effects – especially in relation to being able to work. This also applies to the use of benzodiazepines (e.g. Valium® and related drugs) and morphine-like medicines.

Over and above the subjective feelings, having a good night's sleep and waking refreshed are the basics of good performance and the ability to cope with stress at work. An intact sleeping/waking biorhythm is therefore essential and non-refreshing sleep represents an important sociomedical problem.

The increased accident risk associated with sleep disorders that give rise to symptoms of daytime sleepiness not only limits the ability to drive safely but also reduces workplace performance. In some cases, certain sleep disorders may precede occupational disability, as tiredness at work not only affects the individual but may also endanger others.

## Risk assessment of restless legs syndrome

### Documentation for risk assessment

- Report on the course of the disease from the attending physician; results of any diagnostic investigations that have been carried out
- Information on current treatment

### Secondary restless legs syndrome

The risk is determined on the basis of the underlying disease, e.g. renal failure, diabetes, etc.

### Primary restless legs syndrome

#### Life

Normal risk

#### Disability

With a stable long-term course and without previous occupational disability, the morbidity risk is only mildly increased. There is a high morbidity risk if medication was started, or it came to occupational disability.

#### Health

Medium to large increase in risk. The risk is clearly increased if medication is already being taken. In severe cases: Decline.

# Non-alcoholic steatohepatitis (NASH) – Non-drinkers can get a fatty liver too

It is difficult to give a prognosis for fatty liver. That is to say, it is easy only when it is due to alcohol-induced liver damage. If our client categorically denies the consumption of any alcohol, the risk is more difficult to assess.

Fatty liver is the most common form of hepatic change in the western world. The first signs are often raised values in liver function tests, and then an ultrasound scan is carried out to investigate. If the echo density is increased in comparison with that of the renal tissue, a diagnosis of steatohepatitis is likely. At the beginning of the 1980s, it was found that the livers of obese patients may change in the same way as those of alcoholics.

## From NAFL to NASH

The term non-alcoholic fatty liver disease (NAFL) describes a great many different fatty changes in the liver, of various degrees of severity. At one end of the scale is the basically benign non-alcoholic fatty liver; at the other end is non-alcoholic steatohepatitis (NASH). In contrast to NAFL, the levels of liver enzymes (transaminases) measured in the blood are raised in NASH.

When non-alcoholic changes were first reported over 20 years ago, there was a great deal of scepticism. Steatohepatitis was too closely linked with alcohol in the general mind. And it was completely unclear how often non-alcoholic steatohepatitis occurred. At the time, it was thought that it could only be in isolated cases. Since then, NASH has become recognised as one of the most common liver diseases in the western world: 3% of the population are affected.

## Fatty changes in the liver: causes and consequences

Fatty changes in the liver are due to two factors: obesity and alcohol. And whichever the cause, the worst-case scenario is inflammation (hepatitis) in the fatty liver leading to fibrosis, cirrhosis or cancer of the liver (hepatocellular carcinoma).

Medicines are also frequent causes of non-alcoholic steatohepatitis. In particular, long-term treatment with cortisone (steroids) needs to be mentioned in this respect.

Insulin resistance plays a central role in the development of non-alcoholic fatty liver disease. Elevated levels of free fatty acids in the blood overwhelm the metabolic processes in the liver. The free fatty acids are then deposited in the liver and at first give rise to harmless fatty changes. Those affected are frequently persons with type 2 diabetes and clearly overweight.

It is still unclear why, in some patients, benign fatty changes do not remain as such but rather progress to an unfavourable steatohepatitis. The most popular explanation today is the "two-hit hypothesis". Fat deposition in the liver is the first "hit" which increases the sensitivity of the organ to other hitherto unidentified mechanisms which provide the second injurious and decisive "hit".

## Non-alcoholic steatohepatitis (NASH)

Healthy liver



Fatty liver



Increased fat deposition and enlargement of the liver



Liver fibrosis



Scarring and increased damage to liver cells



Cirrhosis



The scarred tissue damages the structure of the liver, preventing the flow of blood through the organ.

NASH covers a broad spectrum, from asymptomatic changes in the case of fatty liver to cirrhosis of the liver.

### Non-alcoholic steatohepatitis (NASH) – Associated conditions

- Metabolic syndrome (obesity, diabetes mellitus, hyperlipidaemia, hypertension)
- Rapid loss of weight following gastrointestinal operations (extensive resection of the small intestine, gastroplasty, intestinal bypass)
- Medicines (steroids [cortisone], amiodarone, etc.)
- Inborn metabolic disorders (e.g. iron overload in haemochromatosis)

### Prognostically unfavourable factors for fatty liver

- Age > 45 years
- Diabetes mellitus
- AST > ALT
- Histological “progressive form”
- Signs of liver fibrosis

### Those affected are often symptom-free

NASH has a broad spectrum of disease: from asymptomatic changes to cirrhosis of the liver. Most of those affected have no other problems with the liver. Older, very obese persons have the highest risk of developing fibrosis of the liver. This may result in cirrhosis of the liver or even cancer. It is estimated that up to 70% of all cases of cirrhosis of the liver with no clear underlying cause (cryptogenic) have probably developed from non-alcoholic steatohepatitis. In other words, alcohol is not necessarily to blame in all unclear cases.

There is no confirmatory test for NASH; this is purely a diagnosis of exclusion. For the clinical physician three things are crucial: the exclusion of excessive alcohol consumption; the exclusion of other liver diseases such as infections due to hepatitis B and C; and typical findings in the liver biopsy.

It is very difficult to rule out alcohol misuse for certain. The generally-accepted threshold for the toxic effects of alcohol is drinking 30 g/day, which is equivalent to about two glasses of wine. The prerequisite for a diagnosis of NASH is a maximum alcohol intake < 20 g/day. In addition, carbohydrate deficient transferrin (CDT) is determined and the result must, of course, lie within the normal range. If the AST/ALT ratio is < 1, this is further evidence that alcohol consumption is not the cause.

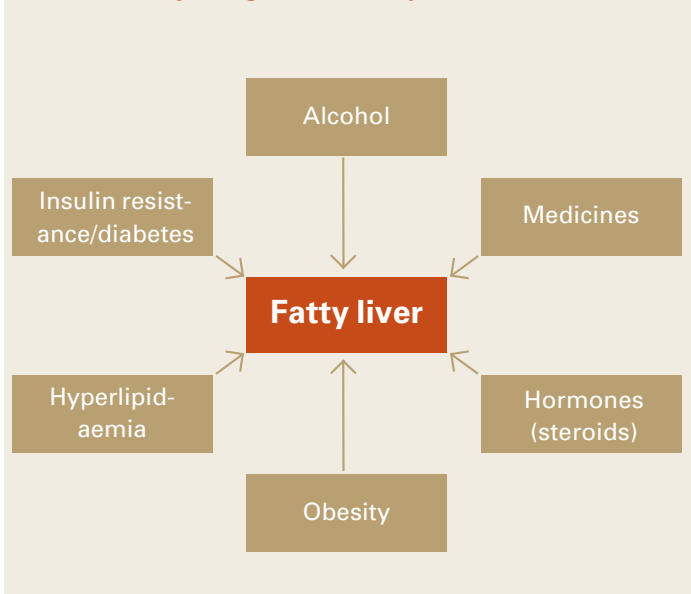
### Risk assessment

Rating of raised liver function tests poses difficult questions: is too much alcohol the cause? Is there an underlying infectious disease? What is the future course of the disease? What can still be accepted and what is too much?

With increasing knowledge of NASH, we see in fact more lives in which an optimal review of the steatohepatitis symptom complex has already been carried out. As the consumption of alcohol has then been sufficiently well excluded, and the prognosis of NASH per se is benign, such cases can also be rated more favourably even with really high levels of liver enzymes and fatty liver on sonography. However, caution should still be exercised if there are any prognostically unfavourable factors with the fatty liver. If the medical reports indicate a diagnosis of NASH, we always recommend referral to the medical officer – especially if there are any doubts whether the case has been fully reviewed or if there is still a possibility of infectious disease, autoimmune disease or an inborn metabolic disorder. Rating of the underlying disease would then, of course, be necessary.

Distinguishing non-alcoholic hepatitis from alcoholic hepatitis is not important just because of the immediate toxic effects of alcohol but also because the assumption or exclusion of an excessive alcohol intake has far-reaching implications. Besides the direct effects on health, these range through addiction to a much more complex concept of damage. More accidental injuries, problems and days absent from work, as well as breakdowns within the family and circle of friends, lead to immense social costs. For life insurance, this means that, in addition to the higher medical risk, there is a clearly increased subjective risk – characterised by failure to pay premiums, increased lapse risk and non-disclosure violations.

### Multifactorial pathogenesis of fatty liver



## Kidney and liver – Risk assessment of organ donors

Organ transplantation in patients with end-stage kidney and liver disease has become well established. After a transplant, the patients mostly live longer and better. Donor organs are, however, in short supply, as the waiting lists at transplant centres show.

There has been a chronic lack of organs for years. The situation will only ease if living donation increases as an alternative to organ donation by people who have died. One of the two kidneys, or part of the liver, pancreas or lungs, can be taken from living donors. The donor is usually a close relative, but a spouse, partner or long-standing friend may also be considered. The great advantage of living organ transplantation is that the surgery can be planned and the recipient's waiting time for the organ is reduced. Statistics on living organ transplantation show better long-term survival than after transplantation of cadaveric organs. In the USA today the majority of the kidneys transplanted come from living donors.

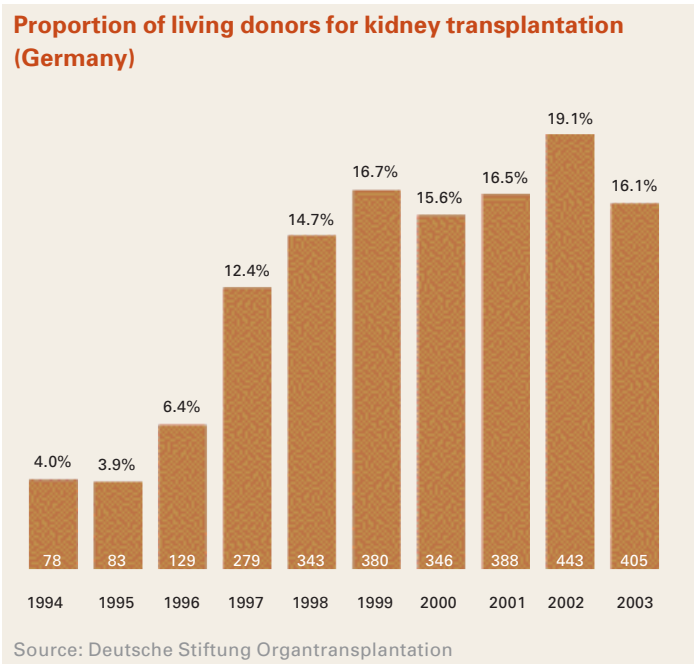
The disadvantages of living organ donation fall on the donor, since he or she, as a healthy person, has to undergo a major operation.

### Risk of living liver donation

Since it was first introduced in 1989, living liver donation has become established as the standard method in children. In contrast, it is not yet a routine procedure in adults. With living liver donation, the right lobe of the liver is removed from the donor and transferred to the recipient.

The amount of liver tissue which a patient needs in the transplant must not be less than a critical quantity, equivalent to 1% of the body weight. A man weighing 70 kilograms must therefore receive 700 g of liver tissue from the donor. For this reason the left (and smaller) lobe is sufficient only for very small recipients.

Living liver donation means a major operation for the donor. Even though complications have occurred only rarely to date, deaths have been reported. According to the official European statistics, the procedure has a fatal outcome in about 1% of living donors. Only the first six months following surgery are critical and if the donation goes as planned, the donor's liver function is not impaired afterwards. The liver regenerates and is able to regain practically the size of the original organ. A retrospective analysis of liver donors in Japan showed that some 12% of donors had complications after surgery. Data were analysed from 1841 donors, who had donated part of their liver between 1989 and 2002; 228 donors suffered complications, mainly biliary fistulae or persistent hepatic dysfunction. In the period studied, no donor died as a result of the operation.





### Risk of living kidney donation

Living kidney donors have been observed after surgery for more than 20 years. The most relevant finding is that life expectancy is not reduced after a kidney has been removed. The remaining kidney has sufficient reserves to allow the donor to lead a completely normal life after the operation.

The only thing that is still unclear is whether donating a kidney can induce high blood pressure. There are no unequivocal figures on this, but generally the renal function of a donor is described as stable. The loss of the remaining kidney – the donor no longer has any reserve – because of cancer or injury is unlikely but, of course, always possible.

For both operations: the surgical incision severs superficial nerves, resulting in “furry” areas of skin which can be a nuisance. In addition, an incisional hernia is possible but this is usually harmless.

**Living kidney donations are on the increase for a variety of reasons: shortage of cadaveric organs, more successful outlook with transplantations following a living organ donation, and the growing willingness to donate organs among relatives and close friends.**

## Risk assessment of living donors

Post-operatively a surgical progress report is required.  
Were there any complications? How is the kidney and liver function? Is there occupational disability?

### Kidney donors

#### – Pre-operative and post-operative (six months after the operation)

##### Life

Standard risk

##### Disability

Standard with additional agreement: "In establishing the existence and degree of any disability not arising directly or indirectly from donation of the (indicate left or right) kidney, the absence of this kidney will not be taken into account."

##### Health

Postpone for six months after the operation; as a rule, acceptance with standard terms thereafter; possible slight short-term risk loading because of the expected increased costs of follow-up examinations

### Liver donors

#### – Pre-operative

##### Life and disability

Postpone for six months after the operation

#### – Post-operative (six months after the operation)

##### Life

Borderline standard risk

##### Disability

Normal with exclusion clause "No claim shall be admitted in respect of any disease, disability, disorder, injury, any operation, or treatment, whether directly or indirectly caused by liver donor"

##### Health

Postpone for six months after the operation; as a rule, acceptance with standard terms thereafter; possible slight short-term risk loading because of the expected increased costs of follow-up examinations

## Attention deficit hyperactivity disorder (ADHD) – A hard lot for fidgets

Inattentive, hyperactive children, unable to concentrate, can exasperate even the most patient parents. Attention deficit hyperactivity disorder (ADHD) therefore often features as a condition purely affecting children. But fidgety children grow up to be adults – they learn an occupation and start a family. And want insurance.

“Today, will you please sit still at table?” But fidgets don’t listen to what their fathers tell them; they wriggle and jiggle around, kick their feet and rock back and forth on their chairs until “That’s getting on my nerves”. The story of “Zappel-Philipp” (“Fidgety Philip”) which appeared in 1846 in the second edition of “Struwwelpeter”, the German book of cautionary tales for children, was a classic description of hyperactivity in children.

ADHD is common; 3–6% of the population may be affected by it. The disorder is diagnosed four times more commonly in boys as in girls. And the number of children it affects is increasing. A distinct ADHD trend can be seen. That is not to say that ADHD is being diagnosed too readily – the condition was previously identified too rarely and was often attributed to an isolated learning disorder. In girls, the disorder is possibly still too often overlooked, as they show less aggressive behaviour.

A considerable number of these teachers’ nightmares carry the condition with them into adulthood. At least 30% of those affected still meet the diagnostic criteria as adults. Even though Albert Einstein, Winston Churchill and Dustin Hoffman are often mentioned as having led successful lives despite hyperactivity, they also suffered. The disorder has lifelong effects in a large proportion of patients, both in their professional and private lives.

Designation and classification of the syndrome are still not uniform and make it more difficult to understand. However, there is consensus on three main characteristics that always occur in association with ADHD:

- Attention: The children are easily distracted, lack concentration, and their attention span is short. They appear not to listen, forget things and have no perseverance.
- Impulsiveness: These children do things without thinking, are unable to wait their turn in the queue, interrupt and frequently disturb others and have little tolerance of frustration. They are disorganised and untidy, have volatile moods, over-react and take offence easily.
- Activity: The children are constantly in motion, as if driven by an inner motor, fidget, are restless, overactive, and only with great difficulty able to keep quiet and play peacefully.

Despite the wide range of symptoms, the causes of ADHD are quite well known. Today it is thought to be predominantly an hereditary disorder; smoking in pregnancy is an additional risk factor.

**The symptoms change as people grow older. Chaotic thinking structures are often reflected in the immediate environment of the person affected.**

### Disorder and chaos: The adult with ADHD

The life of adults with ADHD is beset with risk in many forms. All their lives they will have an increased frequency of accidents and injuries. In addition, they underestimate dangers – hazardous motorcycle riding and car driving are the results. And not least, they create dangerous situations, especially in sport.

The lingering impulsiveness is no longer seen in the kindergarten class but in the workplace and partnerships; these adults often lose their jobs and change their partners frequently. Their homes are chaotic; their desks are piled with papers in disarray. Work is started but rarely finished. Social conflicts are inevitable.

These conflicts do not always end harmlessly. There are often outbreaks of rage and loss of control. Because of frustration, which may persist for years, an increased tendency to violence may develop. Emotional disturbances often arise, especially “feeling down”. They are dissatisfied, apathetic, always bored, indifferent and unhappy. The affected person tries to counteract this constant ill humour with dangerous activities and self-treatment: alcohol, recreational drugs and especially smoking. Treatment of these addictions is difficult and often futile.



### The jungle of terms

<b>ADHD</b>	Attention deficit hyperactivity disorder
<b>ADD</b>	Attention deficit disorder (without hyperactivity); commonly-used term for attention disorders in the USA and by the World Health Organization (WHO)
<b>HKS</b>	Hyperkinetic syndrome; synonym for ADHD
<b>MBD</b>	Minimal brain dysfunction; formerly the most commonly-used term and an umbrella for conditions that are difficult to classify (motor development with coordination problems, behavioural problems, restlessness, etc.)

### Therapy and prognosis

The probability that people “grow out” of this problem is very low. In favourable cases, those affected acquire greater competence in problem management and look for work that is tailored to their particular abilities and deficiencies (e.g. in computers, the hotel and catering industry, acting). The symptoms of ADHD may only come to the fore when compensatory abilities are exhausted – in times of crisis or when great demands are made on the person. For this reason, it may be a long time before ADHD manifests as a relevant disorder. As a rule, it can be seen in retrospect that the problems have been there since childhood.

As ADHD is probably caused by a metabolic disorder, most specialists today agree that primary treatment requires medication. Ritalin® is the medicine frequently used for the treatment of ADHD in children. Hyperactivity and impulsiveness are reduced and the concentration span prolonged in more than 70% of cases. The effects last only as long as the medicine is taken. Other therapy is required in addition to the medication. Depending on the age of the patient, the following measures may be considered: behavioural therapy such as learning new behavioural strategies, regular sporting activities and psychotherapy.

In adulthood, a combination of psychotherapy and sociotherapy together with medication seems to have the best chances of success. Sociotherapy is the coordination of prescribed treatment and the guidance and motivation of the person affected. Amongst other drugs, psychostimulants and antidepressants may be used.

As there is a lack of experience and prognostic criteria for ADHD, risk assessment is not easy. Risk assessors have been confronted with this diagnosis only in recent years. A non-uniform nomenclature and the numerous comorbidities make it even more difficult. Drug and alcohol addiction in particular carry a very unfavourable prognosis.

# Risk assessment of attention deficit hyperactivity disorder in adults

## Documentation for risk assessment

- Report on the course of the disorder from the attending physician (usually a paediatrician, psychiatrist or neurologist); therapy reports, etc.
- Up-to-date report from the family doctor; information about current medication, addictions; job history

## Extent of the disorder

Because of the great variability in the course of this disorder, the documents should be sufficiently meaningful to allow at least a rough estimate of the severity of the condition, and they should also cover a sufficiently long period of at least several years.

- Mild: The school performance was only slightly or moderately reduced and social adjustment has been achieved, even if delayed. The prognosis is good if the disorder is diagnosed early and treated. The affected person has a stable job.
- Severe: Signs are episodes of rage, drug misuse and dependency, paired with low intelligence quotient, unfavourable social milieu (severe adjustment problems with the parents) and additional problems such as violent behaviour, running away, anxiety, depression, suicidal thoughts, frequent accidents, frequent delinquencies and being put in a home. In addition, problems can be seen in more than two areas (e.g. in the workplace and at home).
- Additional rating of comorbidity:
  - Affective disorders (depression or mania)
  - Anxiety disorders
  - Tics, including Tourette syndrome
  - Sleep disturbances
  - Drug and alcohol addiction

## Life

- Mild cases: Borderline risk
- Severe cases: Higher risk, slight extramortality
- With evidence of addiction: Decline

## Accidental death/disability benefit

- Mild cases: Borderline to mildly elevated risk
- Severe cases: Decline

## Disability

- Mild cases: Slight to moderate extramorbidity
- Severe cases or with evidence of addiction: Decline

## Health

- In general: Decline

# Diagnostics

## CDT – A test to detect alcoholism

Chronic alcohol misuse is the main cause of liver disease. Costs arising from alcohol abuse are enormous, greater even than those of tobacco or illegal drugs. And not only is there damage to the liver to consider, the costs of road traffic accidents or early occupational disability are also huge.

Excessive alcohol consumption probably leads to an early death. It is estimated that the mortality rate of alcoholics is ten times that of normal.

### **Illness due to alcohol**

Alcohol-related mortality has numerous causes. Besides death from alcohol-induced cirrhosis of the liver, a great many other deaths can be attributed to alcohol.

Basically, two groups of conditions can be distinguished:

#### Classic alcohol-related diseases which are in all probability due to alcohol consumption:

- Alcoholic psychoses
- Alcoholic fatty liver
- Alcoholic hepatitis
- Alcoholic cirrhosis of the liver
- Alcoholic polyneuropathy

#### Diseases to which alcohol consumption makes a contribution:

- Cancer of the upper digestive tract (mouth, pharynx, oesophagus)
- Cancer of the stomach
- Liver cancer
- Cancer of the pancreas
- Heart disease (e.g. heart failure)
- Circulation disorders (e.g. high blood pressure)

In addition to the above, there is a certain mortality from accidents – about every sixth road traffic fatality is the result of an accident in which alcohol was involved.

### **Alcohol markers MCV and GGT**

It is virtually impossible to assess accurately how much alcohol someone really drinks. Questionnaires tend to be useless in this respect as the information people give on their alcohol intake is unreliable. It is therefore often recommended that alcohol markers are determined to detect excessive alcohol consumption. These alcohol markers are MCV and GGT.

### MCV (mean corpuscular volume)

The MCV indicates the size of the red blood cells. Not all blood cells are the same size, so the result is given as the mean volume, i.e. the average size is calculated.

The MCV starts to increase only after prolonged alcohol consumption. Return of the MCV to normal following alcohol abuse is not to be expected before 3-4 months' abstinence.

The MCV is increased in:

- Vitamin B12 deficiency (pernicious anaemia, malabsorption)
- Folic acid deficiency, pregnancy
- Cirrhosis of the liver, alcohol abuse

and decreased in:

- Iron deficiency anaemia
- Thalassaemia minor

### GGT: Gamma-GT (gamma-glutamyl transferase, gamma-glutamyl transpeptidase)

GGT in the blood is a sensitive indicator of liver and biliary tract disease as well as of alcoholism. Alcoholic liver damage and biliary tract obstruction in particular raise GGT levels. Practically all the GGT measured in the blood comes from the liver, especially from the small biliary ducts where particularly high GGT activity is to be found. Raised GGT:

- If the values of other liver function tests (AST, ALT, cholinesterase [CHE]) are raised besides GGT, there is probably disease of the liver or biliary tract.
- A very large increase, to values that are 10 to 30 times normal, indicates an obstruction of the bile flow in the biliary tract.
- If GGT is raised in isolation and the other liver function tests (AST, ALT, CHE) are normal, then the liver may be diseased. This is often the case with the long-term use of certain medicines, such as for epilepsy, with alcohol misuse and fatty liver, more rarely with cancer in the liver or with long-standing congestion in the liver due to poor blood flow because of heart failure. Mildly elevated values are seen in a large number of hospital patients and no specific cause is usually found for this.

### FAQs about GGT

#### What is the typical constellation associated with elevated GGT values when alcohol is the cause?

It is typical to find an isolated elevation of GGT with normal or nearly normal results of other liver function tests. 30–50% of all the elevated GGT concentrations measured are due to alcohol.

#### Is the liver always damaged if GGT is elevated?

GGT may also be elevated without liver damage. If the ALT and AST levels are also raised, however, damage to the liver has very likely occurred.

#### One over the eight – Are GGT levels raised then?

A one-off excess of alcohol does not raise the concentration of GGT. There must have been an increased alcohol intake over a long period. Only when the liver has previously been damaged can a single binge elevate GGT levels.

#### Does the GGT go back to normal when the days of heavy drinking are over?

Depending on how high the initial value is, it may take 2–3 months for GGT to return to the normal range. As a rule of thumb: the GGT falls to half of the initial value if no more alcohol is being drunk. If the GGT does not return to normal, however, it must be assumed that the liver is severely damaged, e.g. by alcoholic hepatitis or cirrhosis of the liver.

### Review of MCV and GGT

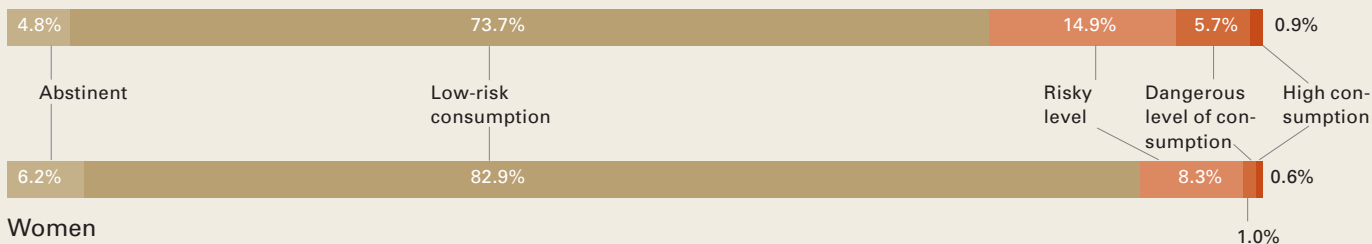
Although MCV and GGT are traditionally regarded as the markers of chronic alcohol misuse, they are actually of limited value for this purpose. Neither test is reliable in detecting chronic alcohol consumption. This can be seen in the following consideration of sensitivity and specificity, the two most important parameters for evaluating the performance of a test.

The sensitivity is the probability of the test finding disease among those who have the disease or the proportion of people with disease who have a positive test result. Data on the sensitivity of MCV and GGT in recognising chronic alcohol misuse vary considerably and lie between 25% and 75%. In other words, in the worst case, only 25 out of every 100 alcoholics would be conspicuous by a raised GGT.

And a look at the specificity of MCV and GGT testing for alcohol misuse is not much help here either. The specificity describes the probability of the test finding no disease

## Drinking: Men and women are unequal

### Men



Source: Representative survey on the use of psycho-active substances by adults in Germany in 2000. Sucht 2001

among those who do not have the disease or the proportion of individuals without the disease correctly identified by the test method, i.e. with a true negative result. A test with a high specificity is useful to rule out a particular disease. The specificities of GGT and MCV are quite low, however, so that non-alcoholic liver diseases, various medicines, and metabolic disorders can give rise to pathological values.

The poor performance of both tests is partly due to the fact that these two alcohol markers are, strictly speaking, not related to increased alcohol consumption per se, but rather indicate organ damage induced by alcohol. And the frequency and extent of the different forms of organ damage are obviously very variable.

### The alcohol marker CDT

CDTs (carbohydrate-deficient transferrins) are derivatives of the iron transport protein transferrin. After chronic alcohol consumption, defective transferrin molecules are formed. The percentage of CDT in the total transferrins is determined in the laboratory. If it is greater than 6%, this is a clear indication of chronic alcohol misuse. This value is attained by drinking more than 60 g alcohol per day, equivalent to about 1.5 litres of beer or 0.7 litres of wine.

CDT may be raised for the following reasons:

- Chronic alcoholism
- Genetic transferrin variants (1%)
- Pregnancy
- Hepatic causes
  - primary biliary cirrhosis
  - chronic hepatitis
  - primary hepatocellular carcinoma

### CDT is more specific than the traditional alcohol markers

In contrast to the classic laboratory markers used to date (GGT and MCV), CDT is highly specific for chronic alcohol consumption. Apart from chronic alcoholism, there are very few reasons for an elevated CDT concentration. Of these, only pregnancy and genetic transferrin variants are harmless.

### CDT is the body's memory of alcohol

This test does not react to short-term alcohol loads. Values start to rise when more than 60 g alcohol/day has been consumed over a period of at least 14 days. CDT is an alcohol marker which is not affected by every now and then partying but registers exactly when it is no longer a question of just the occasional drink. It likewise requires 14 days' abstinence from alcohol before values return to normal.

### CDT is an independent marker of alcohol misuse

In contrast to the transaminases (GGT, ALT), CDT concentrations rise in chronic alcohol misuse independently of the liver damage. More CDT is produced even before alcoholism has led to liver damage and changes in the other blood tests.

### CDT in risk assessment

#### Screening for alcohol misuse

With all its inherent dangers, it would stand to reason that applicants should be screened for alcoholism with the help of a CDT test. Whether this is meaningful or not can be seen from closer consideration of the positive predictive value (PPV) of the test and our insured population. The PPV tells us how high the probability is that an applicant with a pathological CDT result really does drink excessive amounts of alcohol. We use Bayes' formula to calculate the

### How useful is a test?

It is not possible to evaluate the validity of a test without knowing a few important statistical terms. Sensitivity and specificity are often wrongly considered in isolation: this is like wanting to evaluate how well a car will accelerate up a hill using information about its horsepower but without knowing the weight of the car or the gradient of the road.

In risk assessment, therefore, we are above all interested in a test that gives reliable answers to the following two questions:

- If an applicant has a positive test result, what is the probability that he/she really has the disease? (positive predictive value)
- If an applicant has a negative test result, what is the probability that he/she really does not have the disease? (negative predictive value)

The predictive value therefore gives the probability of having the disease. In contrast, the sensitivity gives the probability that a person with the disease will be detected with the help of the test. It is important to note that the probability of a true positive test result increases with the prevalence of the disease under investigation. Prevalence is taken to mean the frequency of a disease in a specific group of people or population.

#### Example of a laboratory test

A laboratory test to detect a disease suffered by 6% of a specific population (= prevalence) has the following performance characteristics:

If a person has the disease, the test will show this with a probability of 96% (sensitivity). If a person does not have the disease, there is a 16% chance of having a (false) positive result, the specificity is 84%.

Prevalence = 6%  
Sensitivity = 96%  
Specificity = 100% – 16% = 84%

#### Calculation of positive/negative predictive values: Bayes' formula

$$PPV = \frac{\text{Sensitivity} * \text{Prevalence}}{\text{Sensitivity} * \text{Prevalence} + (1 - \text{Specificity}) * (1 - \text{Prevalence})}$$

$$NPV = \frac{\text{Specificity} * (1 - \text{Prevalence})}{\text{Specificity} * (1 - \text{Prevalence}) + (1 - \text{Sensitivity}) * \text{Prevalence}}$$

In this case, the positive predictive value is 27.7% and the negative predictive value 99.7%. This can be interpreted as follows: despite an applicant's laboratory test result being positive, the probability that he/she is really suffering from the disease is still only 27.7%. Put another way: out of 100 applicants with a positive pathological finding, only 27 actually have the disease.

A negative result, however, is correct in 99.7% of cases. This test is therefore extremely suitable to reliably exclude a disease. On the other hand, it makes a very poor screening test, as too many healthy applicants are characterised as having the disease.

PPV. This takes into account the test parameters of sensitivity and specificity as well as the prevalence (i.e. the frequency of all cases of a particular disease in a given population at the time of investigation).

Data on the prevalence of dangerous alcohol consumption vary considerably from country to country. In our considerations, we assume a prevalence of dangerous alcohol consumption in the general population of approximately 4%. The prevalence within applicants for insurance products may be lower, however, as one of the effects of alcoholism is a disregard of self-interest and limited awareness of responsibility. In our sample calculation, we are therefore assuming in our application portfolio a prevalence half that of the general population as a whole.

#### The results

Here, the positive predictive value is only 41.7%. For every 1,000 applicants tested, we would find just 33 (3.36%) with a positive test result. But only 14 of these really have an alcohol problem – 19 people would be unjustly classified as alcoholics. And after the test it still remains unclear which of these 33 positives really do consume too much alcohol. The result is sure to engender further work and unpleasant correspondence between client and underwriter.

### CDT as confirmatory test with raised GGT

We often find elevated GGT values in medical reports without any further indication as to the cause. For the applicant population with this constellation, it has to be assumed that there is a higher prevalence of alcohol misuse. We therefore now increase the prevalence to 10%. In this case, we are more interested in the negative predictive value (NPV). To be more precise: how definitely can alcoholism be ruled out by a negative test result? Here, the negative predictive value is 96.7%: Of 100 persons with a negative test result, 96 really do not drink too much alcohol.

### Summary

CDT is not a suitable screening test for alcohol misuse in risk assessment. The number of false positive results would lead to too much unedifying extra work and the annoyance of applicants.

However, the test is still useful in risk assessment to rule out alcoholism in situations where there is an elevated a priori probability. This applies particularly to applicants who have a past history of alcoholism and elevated liver function tests.

### Cost-benefit considerations in medical risk assessment

The costs and efforts required to obtain firm diagnostic evidence depend considerably on the population in which the investigation or test is being carried out. If one wants to determine the usefulness of a diagnostic test, the representative number of persons that have a specific characteristic, for example, a disease (the prevalence) has a direct influence on the result. This has far-reaching implications.

For example: the reliability of one and the same diagnostic tool may be very different for a population of hospital patients and for a population of insured persons, as there are more sick persons in a hospital population than in an insured population. For this reason, well established clinical investigations do not automatically help in risk assessment. The frequency and quality of the test should not be the decisive characteristics. Risk assessment is usually done in a low-risk area: the conditions to be diagnosed are less common here than in all areas of healthcare. Diseases already considered to be rare are even rarer here. Antiselection may, however, lead to the prevalence clearly deviating from that in a normal population. This is particularly striking in, for example, special types of cover in life, health and personal accident insurance. One example: a disability product with benefit to be paid exclusively in the case of disability due to multiple sclerosis (MS), leads to an antiselective appeal for patients with MS, i.e. the number of MS patients in the application portfolio increases. With cover for death, many risk factors are considered to be much less threatening in the applicant's self-perception (e.g. cholesterol and overweight). These risk factors therefore have a much smaller antiselective potential.

In the long run, the crucial issues are how much additional information can be gained through the test ("attribution ratio") and how this affects the course of the portfolio ("impact factor").

#### Example: "Attribution ratio"

An applicant admits that he has been on antiretroviral therapy for an HIV infection for several years. In this case a recent HIV antibody test brings no additional information. The results will not affect the rating decision. The test is therefore – irrespective of the insurance sum – superfluous and too expensive even if it delivers good test parameters. In another case, though, a great deal of information may be gained from a laboratory test – for instance if the applicant states that he has had infectious hepatitis some years previously. But which type of hepatitis? Hepatitis A, B or C? A blood test can give a definite answer and make it very much easier to estimate the prognosis.

#### Example: "Impact factor"

Here the crucial question is what proportion of the affected persons in the portfolio will claim (through death, occupational disability, etc.)? At what point in time will this happen? At the beginning or at the end of the contractual period? Do the affected persons possibly drop out of the portfolio for other reasons (unemployment, cancellation risk) and how long will it probably be until this happens?

Medical investigations for life insurance have now come to represent a thoroughly significant proportion of total new business costs. The selection of medical investigations for risk assessment is therefore of growing importance.

## A case in practice – ADHS

**C**

### Case report

**17-year-old man about to start training as a programmer**

**Cover:**

**Life, disability and accidental disability benefit**

Diagnosed with attention deficit hyperactivity disorder at the age of 7 years. Treated with Ritalin® since then. Was able to finish school without any delays. For the last month the applicant has been making a trial withdrawal of Ritalin. The medical report is positive: "This athletic young man has only mild ADHD and the course of the disease is favourable."

**R**

### Our rating

Life: Borderline risk

TPD own: Postpone for two years after completion of professional training

TPD any: +25 %

Accidental disability benefit: +50 %

**C**

### Commentary

ADHD leads to reduced performance in school and the workplace as well as disorders in the social context. Clinical observational studies have shown that those affected much more often have to leave school early and therefore without leaving qualifications. They often do not have a career that corresponds to their abilities, have to take more time off work and finally change jobs for health reasons.

People with ADHD are more often affected by early pregnancy and sexually transmitted diseases. All kinds of misfortunes befall them on a daily basis when driving and in everyday life and they are exposed to a higher risk of accidents.

In order to rate ADHD, it is important to determine the severity of the impairment. The case presented here is one of a mild attention deficit hyperactivity disorder. The prognosis is favourable. The condition was diagnosed early and treated, the applicant was able to finish school and so far there are no noticeable social problems.

It cannot yet be assessed whether the young man is suitable for his chosen career. The occupational morbidity risk (own profession) therefore has to be deferred for as long as it takes to be sure about the appropriateness of the career. As a rule, this is the case some years after the end of the training period. But even then, the risk has to be assessed cautiously. In any case, the following should be well documented: how is treatment going? Have there been any accidents or time off work? The risk of total and permanent disability (any profession) is slightly increased and can already be estimated with sufficient certainty.

## Chance findings

### Colonic diverticula – When the intestine starts to get old

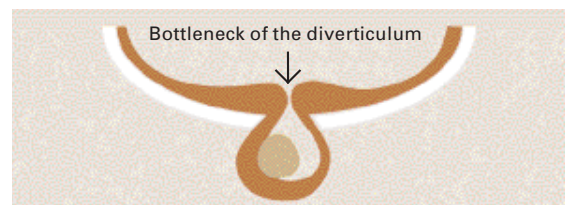
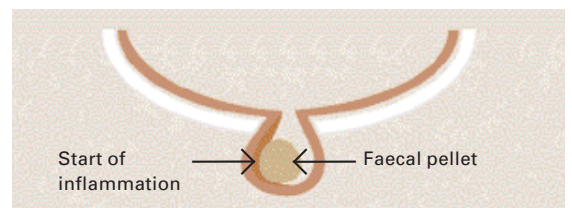
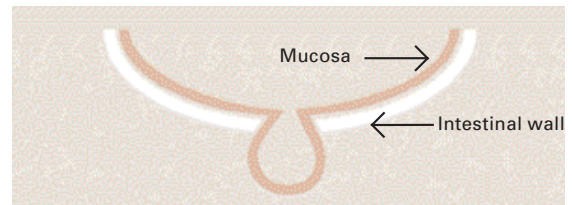
Although diverticula of the large intestine give no cause for concern to most patients, they make the risk assessor uneasy. However, three-quarters of all people with diverticulosis (diverticular disease) remain symptom-free for their entire lives and the chances of complications are slight.

Diverticula of the large intestine are pouches of the intestinal lining (mucosa) protruding through gaps in the intestinal wall musculature. Diverticulosis is the most common intestinal disease in the western world, so that it really can be considered a disease of civilisation. In contrast, the condition is rarely seen in countries where the diet still has a high fibre content.

The intestinal protrusions form primarily through certain weakened areas in the gut wall. They are often to be found around the entry portals of the blood vessels, where the intestinal structure is weaker. The segment of the large intestine most commonly involved is the sigmoid colon in the left lower abdomen. Diverticula probably form because of increased pressure in the intestine, when straining at stool, for example.

The size and number of diverticula increase with age: fewer than 10% of people below the age of 40 years have diverticulosis, while more than 40% of the over-70s are affected.

#### Colonic diverticulosis



**Diverticula of the large intestine are pouches of the intestinal lining (mucosa) protruding through gaps in the intestinal wall musculature. The most common complication is inflammation of the protruded gut wall: diverticulitis.**

### The prognosis is good

80% of all people with diverticulosis remain free of symptoms for their entire lives. Diverticula cause problems only when complications arise. The most common complication is inflammation of the protruded gut wall: diverticulitis. Very rarely, there may be bleeding from diverticula but this stops spontaneously in more than 80% of cases.

Diverticulitis is not pleasant. It causes pain on the left side of the middle and lower abdomen. At the same time, the abdomen may be greatly distended and sometimes the inflamed intestine may be palpated as a thickened “roll” that is painful when pressed. Perforation of the inflamed diverticulum is a serious complication. When, as is often the case, another abdominal organ overlies the focus of inflammation, the perforation is said to be “covered”. This means that pus and faecal residues are not emptied into the abdominal cavity but form an abscess. Resulting infection of the peritoneum (peritonitis) is life-threatening and requires prompt surgical treatment.

Fistulas may develop following diverticulitis; they may lead to another part of the intestine, the vagina or the bladder. With recurrent inflammation, the resulting scar tissue progressively narrows the intestine. This constriction does not regress spontaneously and often leads to intestinal obstruction.

### Treatment

Asymptomatic small bowel diverticula discovered purely by chance are not treated. It is advisable, however, to add more roughage (fibre) to the diet in the form of whole grain products, salad, fruit and vegetables.

If inflammation occurs repeatedly, it may be necessary to remove that section of the large bowel affected by diverticulosis.

## Risk assessment of colonic diverticulosis

### Documentation for risk assessment

- Information on the course of the disease to date from the person applying for insurance cover
- A medical report is necessary if the course is complicated

### Favourable factors

- No symptoms
- Chance finding

### Unfavourable factors

- Recurrent symptoms
- Surgical clearance planned in the near future or symptoms persisting after operation
- Intestinal abscess or fistula formation
- Intestinal stenosis (narrowing of the gut lumen)

### Life

- Borderline standard risk if asymptomatic or operated on and fully cured
- Slight extramortality with recurrent diverticulitis. The risk should be postponed if surgical clearance is planned.

### Disability

- Asymptomatic diverticula: borderline standard risk
- Single episode of diverticulitis: slight extramorbidity
- Recurrent diverticulitis: moderate extramorbidity
- Operated on and fully cured: standard risk again

### Health

Slight to moderate loading, depending on the course of the disease to date. If an operation is planned in the near future, the risk should be postponed until complete recovery.

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Münchener Rückversicherungs-Gesellschaft  
Königinstrasse 107  
80802 München  
Germany

Tel.: +49 (0) 89/38 91-0

Fax: +49 (0) 89/38 90 56

<http://www.munichre.com>

**Responsible for content**

Life

**Person to contact**

Dr. Alfred Beil

Tel.: +49 (0) 89/38 91-95 68

Fax: +49 (0) 89/38 91-7 95 68

E-mail: [abeil@munichre.com](mailto:abeil@munichre.com)

**Printed by**

WKD-Offsetdruck GmbH  
Oskar-Messter-Strasse 16  
85737 Ismaning, Germany

**Picture credits**

Cover: Botanica/Mauritius Images

Inside cover: Botanica/Mauritius Images

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Münchener Rückversicherungs-Gesellschaft  
Königinstrasse 107  
80802 München  
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Order number 302-04445