

UNITED EUROPEAN
GASTROENTEROLOGY

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Pancreatic Cancer Across Europe

Taking a united stand



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“

Pancreatic cancer has a lower survival rate than any other cancer in Europe. Improvements in patient outcomes have largely stood still for the past forty years, which is in contrast to the progression in survival rates we have witnessed with many other cancers.

The number of deaths from pancreatic cancer has almost doubled in the past three decades and it now claims the lives of over 90,000 EU citizens every year. Forecasts predict that this dreadful disease shows no sign of relenting either, with the number of cases and deaths both estimated to increase by 40% by 2035. Public awareness of this disease, including its symptoms which are often hard to identify, is alarmingly low and the majority of patients have little or no hope of longer survival at the point of diagnosis.

Despite appalling patient outcomes, pancreatic cancer receives less than 2% of overall cancer research funding across Europe. This must change and harmonized efforts are needed now more than ever from both an EU and member state level.

The European Parliament Interest Group on Digestive Health welcomes and supports participation from medical, patient and other communities that will help to turn the tide for pancreatic cancer. With increased research, we can enhance our understanding of this complex disease, identify the correct tools to achieve earlier diagnosis and, ultimately, save more lives. It's time for the EU to take a stand and fight the world's toughest cancer.

”

MEP Pavel Poc
Chair – European Parliament Interest Group on Digestive Health

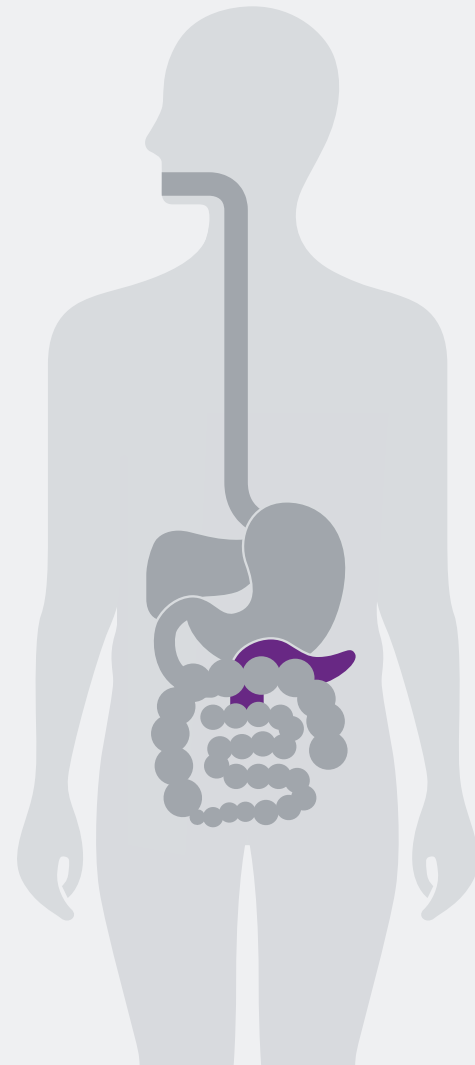
INTRODUCTION

Pancreatic cancer has the lowest survival rate of all cancers in Europe.¹ Responsible for over 95,000 EU deaths every year,² life expectancy at the time of diagnosis is just 4.6 months.³ Recent estimates have indicated that the number of deaths from pancreatic cancer overtook breast cancer mortality rates across the EU in 2017, meaning that the disease is now the EU's third leading cause of cancer-related death, behind lung and colorectal cancer.⁴

Pancreatic cancer ranks seventh in terms of incidence rates, with 100,000 new cases every year,⁵ affecting almost as many people as liver and oesophageal cancer combined. Risk factors associated with pancreatic cancer include smoking, chronic pancreatitis, diabetes, obesity and a family history of the disease, whilst incidence rates increase with age.

Pancreatic cancer occurs when malignant cells begin to form and multiply in the tissues of the pancreas – an organ found behind the stomach. Often referred to as the 'silent killer', symptoms can be hard to identify, thus making it difficult to diagnose the disease early, which is essential for potential life-saving surgery.

By harnessing the expertise and opinions of leading pancreatic cancer specialists, stakeholder organisations, patient groups and policymakers, this report highlights the serious impact of pancreatic cancer throughout Europe, the issues facing clinicians and patients, and how, collectively, we can improve patient outcomes for this appalling disease.



PANCREATIC CANCER: THE FACTS



There has been little improvement in patient outcomes over the last four decades. Action is urgently needed at the highest level, so it is time for the EU and its Member States to support those affected by pancreatic cancer.

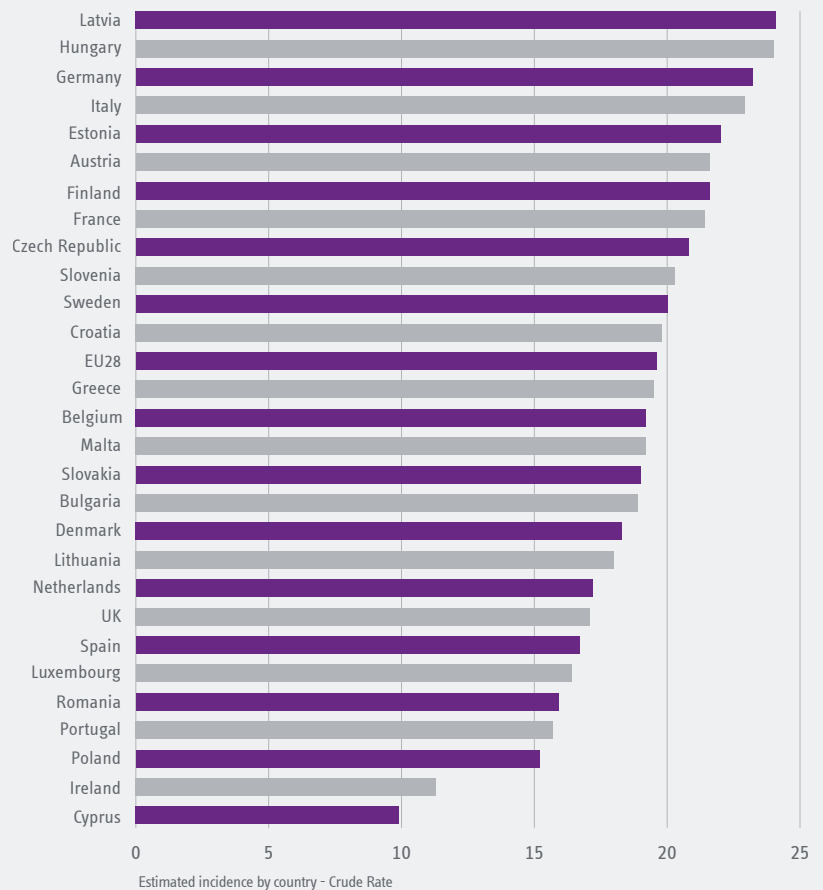


The fact that pancreatic cancer is the EU's third biggest cancer killer, despite being the seventh most common cancer, highlights the extremely poor outlook for patients. We urgently need more research, more awareness and a policy that supports quick diagnosis and treatment.



Matthias Löhr
Secretary, European Pancreatic Club (EPC)

Pancreatic Cancer incidence rates, EU countries⁶

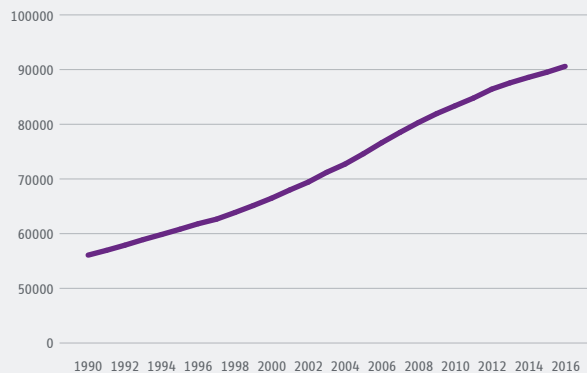


PANCREATIC CANCER: THE FACTS

Just 3% of patients diagnosed with pancreatic cancer survive for five years and it is the only cancer that has seen no improvement in survival in forty years.⁷

Across Europe, the number of pancreatic cancer mortalities has steadily risen over the past few decades. In the EU between 1992 and 2016, the number of pancreatic cancer deaths increased 62%, rising from 56,072 deaths in 1992 to 90,591 deaths by 2016.⁸

Pancreatic Cancer EU-28 Deaths - 1990-2016⁹

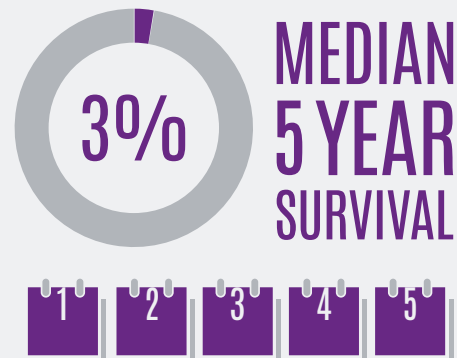


Though understanding of the molecular mechanisms leading to pancreatic cancer has been improved, the majority of affected patients are still being diagnosed at an advanced stage, and, with pancreatic tumours highly resistant to chemotherapy and radiation and surgery rarely an effective option, it is no wonder that the 5-year survival rates are so low.



Guilherme Macedo

Executive Committee Member, World Gastroenterology Organisation (WGO)



PANCREATIC CANCER: THE FACTS

Between 1990 and 2016, the increase in pancreatic cancer death rates has been the highest of Europe's five biggest cancer killers.¹⁰

Death rates (per 100,000) for the top five biggest cancer killers in the EU (1990-2016)¹⁰

Cancer site	1990 death rate	2016 death rate	% change between 1990 and 2016	
Breast cancer	14.82	11.11	-25%	▼
Tracheal, bronchial, and lung cancer	37.77	30.30	-20%	▼
Colorectal cancer	21.80	18.72	-14%	▼
Prostate cancer	8.74	8.83	+1%	▲
Pancreatic cancer	9.30	9.72	+5%	▲

PANCREATIC CANCER: SYMPTOMS

Pancreatic cancer presents vague early symptoms, often making the disease difficult to recognise and diagnose at an early stage.

The symptoms of pancreatic cancer, which are often also associated with other conditions, can include the following:



Jaundice
(yellowing of skin and eyes)



Nausea



Abdominal and back pain



A change in bowel habits



Unexplained weight loss



New onset diabetes



Depression



Loss of appetite



We have seen success in the past when symptom awareness and early diagnosis have brought down a deadly killer. We all need to work together to achieve this for pancreatic cancer.



Jola Gore Booth
Founder and CEO, Digestive Cancers Europe (DiCE)



There is a lack of targeted initiatives devoted to pancreatic cancer, and only some countries are using cancer registries to collect data on pancreatic cancer. Through joint actions, the European Cancer Patient Coalition is part of a dedicated mission to identify opportunities for improving detection, diagnosis and access to clinical expertise for every European affected by pancreatic cancer.



Francesco de Lorenzo
President, European Cancer Patient Coalition (ECPC)

PANCREATIC CANCER: RISK FACTORS

Whilst further research is required to help our understanding of the causes of pancreatic cancer, there are a number of risk factors that have been shown to increase the chances of developing the disease. It's important to note that people can also develop pancreatic cancer if they don't have any of the risk factors. It is estimated that two-thirds of the major risk factors associated with pancreatic cancer are potentially modifiable, providing an opportunity for preventing the disease.¹¹



Smoking is related to 20% of all pancreatic cancer cases and causes a 75% increase in the risk of pancreatic cancer compared to non-smokers.¹² Risk increases with the number of cigarettes smoked and the duration of smoking.¹³



Whilst there is an increased risk of pancreatic cancer in patients with long-standing diabetes, recent-onset diabetes is frequently associated with pancreatic malignancy.¹⁸ Individuals who have been diagnosed with type 2 diabetes within 4 years have a 50% higher risk of developing pancreatic cancer, in comparison to individuals who have had diabetes for 5 years or more.¹⁹



Obesity contributes to poorer prognosis and survival rates compared to non-obese patients.¹⁴ Compared to individuals with a healthy body mass index (BMI), obese patients are found to have a 47% higher risk of pancreatic cancer.¹⁵



Patients with chronic pancreatitis, especially those who have hereditary pancreatitis, have an increased risk of developing pancreatic cancer. Approximately 4% of patients with chronic pancreatitis will develop pancreatic cancer.²⁰



Pancreatic cancer risk increases 2-3 times if an individual's parents, sibling or child has had the disease.¹⁶ It is thought that up to 10% of pancreatic cancer cases are linked to genetic conditions.¹⁷



Whilst further research is required, there is accumulating evidence demonstrating that heavy alcohol consumption (four or more drinks per day) is associated with pancreatic cancer.²¹



We need to take the opportunity to improve awareness of these modifiable risk factors relating to lifestyle, as well as the symptoms, to facilitate earlier diagnosis and provide patients with the best possible chances of successful treatment.



Johanna Laukkarinen

Pancreatic cancer expert, Tampere University Hospital, Finland

PANCREATIC CANCER: DIAGNOSIS AND TREATMENT

Current screening for pancreatic cancer

The extremely poor outlook for pancreatic cancer emphasises the requirement for novel strategies to aid earlier diagnosis. Research has indicated that the disease can be present in the body for many years before patients fall ill,²² providing a critical opportunity for early detection.

Despite the severity of the disease, population-based screening for pancreatic cancer is not currently plausible. The heterogeneity of the disease makes screening for early diagnosis a significant challenge.

Genetic screening is currently available and certain genetic mutations and risk factors have been detected, but as only 5-10% of pancreatic cancer cases are explained by inherited mutations, this is only relevant for a specific sub-group of patients. We therefore need to find other means of detecting pancreatic cancer early.



**SCREENING FOR EARLY PANCREATIC
CANCER DIAGNOSIS PRESENTS A
SIGNIFICANT CHALLENGE**



The main reason for slow progress in improving pancreatic cancer mortality rates is down to the complex nature of the disease. Pancreatic cancer is asymptomatic and for those who do present with symptoms, the disease is usually at an advanced stage and too late to treat successfully.



Johanna Laukkarinen

Pancreatic cancer expert, Tampere University Hospital, Finland

For more patients to benefit from advanced treatments, earlier detection of those at high-risk is essential. A recent consensus from the International Cancer of the Pancreas Screening Consortium Summit agreed that screening is recommended for high risk individuals, including those with close relatives to a pancreatic cancer patient and those with BRCA2 and hereditary non-polyposis colorectal cancer mutation carriers.²³

Decisions are still needed, however, to agree the specific screening methods, surveillance and management of high risk individuals.

Sorin Barbu, Professor of Surgery at the Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania, explains “Today, at the time of diagnosis, only 20% of pancreatic cancer patients are suitable for resection and able to have multidisciplinary treatment. From this 20%, only 20% reach five-year survival. We need more efficient screening methods to increase the initial 20% receiving multidisciplinary treatment.”

PANCREATIC CANCER: DIAGNOSIS AND TREATMENT

Currently, there is also concern over the precision and provision of endoscopic ultrasounds for pancreatic cancer detection. The training needed to reach the level of excellence to detect genetic markers and tumour biology is extremely long and accuracy can be compromised. “We need to urgently refine these techniques for more accurate results.” Johanna Laukkarinen states.

Surgical and treatment challenges

By 2035, the number of cases of pancreatic cancer is predicted to rise by almost 40%²⁴ so as well as difficulties in achieving early diagnosis, the complexities of pancreatic cancer tumour growth also pose significant surgical and treatment challenges.

As a result, resection - which is the performance of surgery to remove the organ - is currently the only curative approach for pancreatic cancer, but this is only curative in the minority of cases. Resections often require a complex operation which involves vascular resection and reconstruction.

As well as surgical complications, the specific properties of the tumour microenvironment can affect treatment success and pancreatic cancer tumours are notoriously resistant to both chemotherapies and emerging immunotherapies.²⁵ This is because the tumour’s density can prevent the penetration of therapeutic agents.



Very few diseases have as high a metastatic rate, where the cancer has spread from the primary site, as pancreatic cancer, with 80% of cases already being metastatic.



Thomas Seufferlein

Pancreatic cancer expert, University of Ulm, Germany



PANCREATIC CANCER TUMOURS ARE NOTORIOUSLY RESISTANT TO BOTH CHEMOTHERAPIES AND EMERGING IMMUNOTHERAPIES

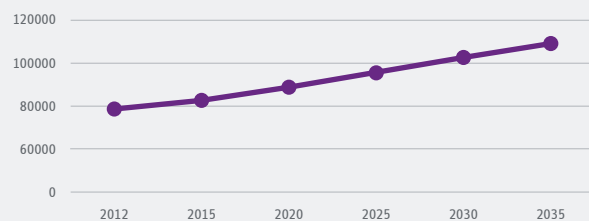
PANCREATIC CANCER: DIAGNOSIS AND TREATMENT

Turning the tide

Despite the diagnostic and treatment challenges, the tide is at last beginning to turn. Significant strides are being made with new treatment regimens and in the understanding of the different genetic mutations involved within pancreatic cancer subgroups, as well as the impact of the microbiome on pancreatic cancer.

With promising recent advances in immunotherapy and neoadjuvant therapy, resulting in more successful resections and targeted treatments, coordinated efforts are needed now to facilitate and accelerate these advances and improve survival rates.

Estimated number of pancreatic cancer deaths in EU²⁵



Thomas Seufferlein adds, “Although pancreatic cancer is a highly diverse disease, we can now identify specific pancreatic cancer subgroups with certain molecular features. Identifying these groups is an exciting step forward and will enable us to substantially improve prognosis and offer a potential lifeline to pancreatic cancer patients.”

Pancreatic cancer and the microbiome



Research looking at the impact of the microbiome on pancreatic cancer is a particularly exciting new area, as the pancreas was previously thought of as a sterile organ.



Thomas Seufferlein

Pancreatic cancer expert, University of Ulm, Germany

The microbial population of the cancerous pancreas has been found to be approximately 1,000 larger than that of a non-cancerous pancreas.²⁶ Research has shown that removing bacteria from the gut and pancreas slowed cancer growth and reprogrammed immune cells to react against cancer cells. These findings are significant and could be practice-changing as the removal of certain bacterial species could enhance the efficacy of chemotherapy or immunotherapy and there is the potential for increasing patients’ good bacteria in order to slow tumour growth or decrease pancreatic cancer risk.²⁷

PANCREATIC CANCER: DIAGNOSIS AND TREATMENT

“Such research will also improve our understanding of the micro-environment in a metastatic setting and how the tumour responds to its environment” comments Thomas Seufferlein. “This will inform the development of treatments which can inhibit tumour growth, change metastatic behaviour and ultimately alter disease progression. We should have new, important data within the next five years and, hopefully, find that targeting the microbiome as well as tumour cells will significantly improve treatment outcomes.”

Molecular markers of pancreatic cancer subgroups



Looking ahead, it is also important to maximise what we already know about the different subgroups of patients, including which groups are benefitting most from what treatment, as this will help to inform treatment pathways.



Thomas Seufferlein

Pancreatic cancer expert, University of Ulm, Germany

Recent research has found that T-cell immunity has been linked to the unprecedented long-term survival of a small group of patients with pancreatic cancer. T-cells, a type of white blood cell, help to fight disease and infection and play

a vital role in cell-mediated immunity. New research now focuses on identifying which particular molecules are capable of stimulating an immune response and this will potentially aid the development and application of future immunotherapies for the benefit of patients.²⁸

Greater understanding of the role of the microbiome, both as biomarkers of increased risk for pancreatic cancer, as well as potential therapeutic targets and cancer immunotherapy, brings the promise of personalised medicine ever closer and the hope of improved treatment outcomes in the future.

Neoadjuvant therapy for earlier treatment

As pancreatic cancer is increasingly recognised as a systemic disease with micro-metastases at the time of diagnosis, multimodality therapy, which involves a combination of treatments rather than resection alone, is now considered to be the treatment of choice.²⁹

Neoadjuvant therapy - treatment given as a first step to shrink tumours before surgery - is being heralded as the preferred treatment as it can treat the disease earlier, when micro-metastases are just becoming established. Neoadjuvant therapy can downsize large tumours, allowing for clearer resection and improved survival rates as a result.³⁰ Further research, however, is urgently needed to improve the precision of staging tools, to verify the preferred regimen of treatment and reduce the toxicity of the neoadjuvant therapy to enable it to reach its full potential in improving survival rates.

FUNDING

As well as diagnostic and treatment challenges associated with the complexity of the disease, limited funds for research into pancreatic cancer has also contributed to the lack of improvement in patient outcomes. “Many countries are cutting resources for pancreatic cancer, whilst other cancers are still receiving funding” points out Johanna Laukkarinen.

Despite being Europe’s third biggest cancer killer, research on pancreatic cancer receives less than 2% of all cancer research funding in Europe.³² This needs to change and coordinated efforts are now vital at an EU and member state level, to accelerate advances and reduce the high mortality burden throughout the continent. “Policy makers must produce a targeted EU funding policy for pancreatic cancer” states Dr Barbu.



Considerable research has been done to identify different mutations involved within pancreatic cancer subgroups. However, given that these subgroups are small, the research involved is expensive as so many patients need to be screened in order to identify the few that have respective alterations in their cancer. Screening for these subgroups is also not reimbursed and this is impeding implementation into clinical practice and impacting treatment outcomes.



Pancreatic cancer has been chronically underfunded for decades. As the third leading cause of cancer death in Europe, attention must urgently be focussed on the provision of increased and significant funding for pancreatic cancer research at both the EU and Member State levels.



Ali Stunt
Board Member, Pancreatic Cancer Europe (PCE)

FUNDING



We have to prioritise earlier diagnosis for pancreatic cancer patients, especially in people with an enhanced risk, as this is the main reason for the lack of improvement in patient outcomes in recent decades. Increasing research funding will provide a significant change to reversing this dreadful outlook.



Evelien Dekker

Gastrointestinal cancer expert, University of Amsterdam's Faculty of Medicine, The Netherlands



We must join forces to increase the pace at which we improve our responses to pancreatic cancer. We all have our part to play in reversing the neglected status of pancreatic cancer and improving the lives of our patients.



Philip Poortmans

President, European CanCER Organisation (ECCO)

In order to improve long-term outcomes for pancreatic cancer patients, it is essential that patients have access to a range of new treatment options. More real-world survival time data is needed in order to efficiently analyse the European pancreatic cancer burden on individuals and health systems. This will help to evaluate the direct and indirect costs of the disease as well as assess the extent of the unmet needs, allowing for more accurate budgeting and planning provision of care at national and regional levels.

Johanna Laukkarinen adds “Another important focus of the future is to enable the centralisation of care for pancreatic cancer. A new healthcare law is already in place in Finland to ensure that pancreatic cancer patients only receive surgery at the five main specialised university hospitals. This is a significant step forward but needs to be replicated across Europe to ensure that all patients receive the best possible care in high-volume centres of excellence.”



TRANSFORMING PANCREATIC CANCER BY 2035

UEG and its partners are calling for united efforts at the highest level, focusing on the following key initiatives:



Awareness

To improve symptom and risk factor awareness in order to provide the earliest possible diagnosis and to enable high-risk patients to modify lifestyle-related risk factors



Standard of Care

To deliver a pan-European standard of care, including the provision of treatment at centres of excellence and the implementation of comprehensive quality of life data from broader EU registries



EU & Member State Funding

To ensure pancreatic cancer is regarded with the same urgency as other cancers and funding is increased for research and diagnostics



Research

To increase research into diagnostic and treatment areas, including molecular markers, multimodal treatment regimes and tumour microenvironments



Europe-wide Biobanks

To facilitate improved diagnostics, improving the understanding of tumour biology and aiding the development of more precise treatment regimens for patients



Surveillance

To develop a consensus on screening methods and surveillance (particularly of higher risk patients) and address the management and funding of screening to ensure earlier diagnosis and treatment

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If we are to take a stand against the continent's deadliest cancer, we must address the insufficient research funding; that is where the European Union can lead the way. This report enables us to understand where funding needs to be targeted, helping us to call for a greater focus on the key developments needed to turn the tide of this merciless killer. Whilst medical and scientific innovations have positively changed the prospects for many cancer patients, those diagnosed with pancreatic cancer have not been blessed with much clinically meaningful progress.

To deliver earlier diagnoses and improved treatments we need to engage now in more basic as well as applied research to see real progress for our patients in the years to come.

//**Markus Peck**

UEG Public Affairs Committee

Chairman at the Department of Internal Medicine and Gastroenterology (IMuG) at Klinikum Klagenfurt am Wörthersee in Klagenfurt, Austria

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