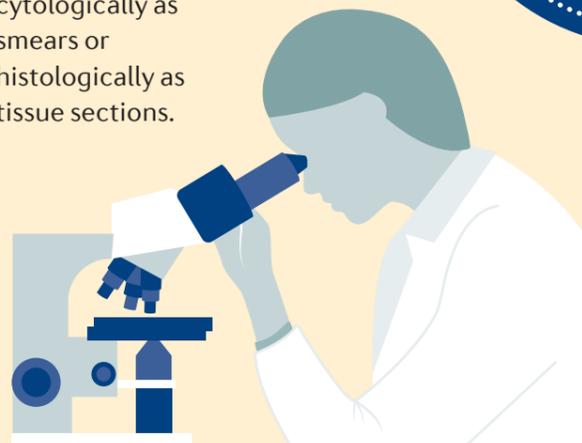


For the Primer, visit [doi:10.1038/nrdp.2016.22](https://doi.org/10.1038/nrdp.2016.22)

→ Pancreatic cancer is currently the fourth highest cause of cancer-related deaths in developed countries. The majority of malignant neoplasms of the pancreas are adenocarcinomas, which accounted for >300,000 deaths globally in 2015 alone.

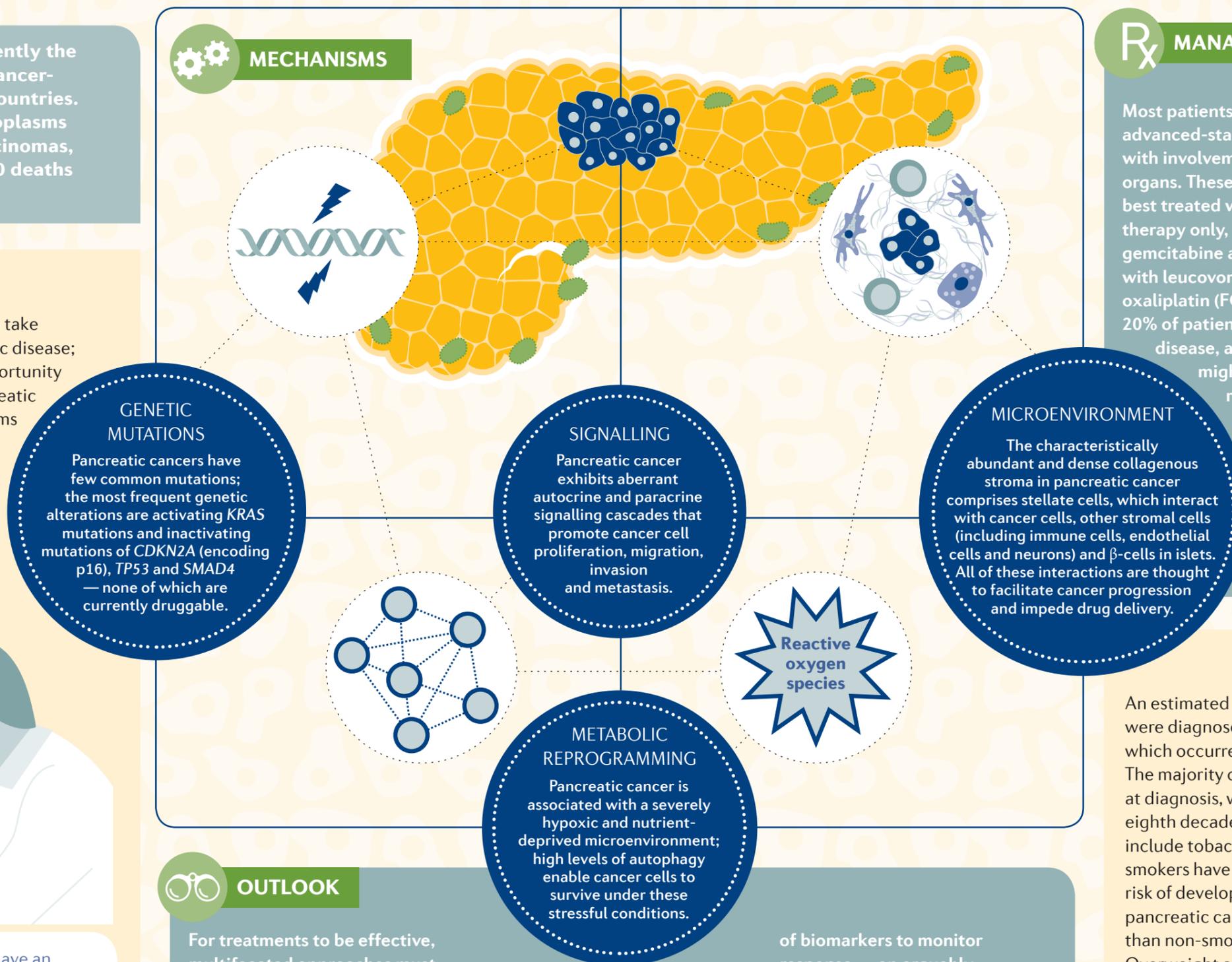
### DIAGNOSIS

Neoplastic cells in the pancreas can take >10 years to develop into metastatic disease; thus, there is a large window of opportunity for early detection. However, pancreatic cancer does not have overt symptoms and lacks reliable biomarkers for detection, resulting in the majority of patients being diagnosed with advanced-stage disease. A diagnosis can only be confirmed with pathological analysis of pancreatic tissue samples, which can be conducted cytologically as smears or histologically as tissue sections.



Some individuals who have an increased risk of developing pancreatic cancer might benefit from screening, for example, those with a positive family history or with genetic conditions such as Peutz–Jeghers syndrome.

### MECHANISMS



### OUTLOOK

For treatments to be effective, multifaceted approaches must be developed that not only target cancer cells but also reprogramme the cancer stroma. Achieving such a goal will require detailed knowledge of

the molecular underpinnings of individual tumours, development of drugs against rational targets, assessment of new therapies in trials and development

of biomarkers to monitor response — an arguably enormous challenge. However, progress is being made and innovative strategies, including immunotherapies, are currently in clinical trials.

### Rx MANAGEMENT

Most patients present with advanced-stage disease with involvement of distant organs. These patients are best treated with palliative therapy only, including chemotherapy with gemcitabine alone or with nab-paclitaxel, or with leucovorin, 5-fluorouracil, irinotecan and oxaliplatin (FOLFIRINOX). Fewer than 20% of patients have surgically resectable disease, although neoadjuvant therapies might shift tumours towards resectability. Surgery alone is not sufficient to achieve long-term survival, but adjuvant therapy with either gemcitabine or 5-fluorouracil and leucovorin has demonstrated considerable improvements in overall survival.

! Despite best efforts, >90% of patients will relapse and ultimately die of their disease.

### EPIDEMIOLOGY

An estimated 367,000 cases of pancreatic cancer were diagnosed worldwide in 2015, >50% of which occurred in high-income countries. The majority of patients are >50 years of age at diagnosis, with most being in their seventh or eighth decade of life. Preventable risk factors include tobacco smoking; smokers have a 2–3-fold higher risk of developing pancreatic cancer than non-smokers. Overweight and obesity, low physical activity and diabetes mellitus are also associated with pancreatic cancer.

