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European Cancer Organisation Essential Requirements for Quality Cancer Care (ERQCC): Pancreatic Cancer

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Abbreviations

CHAFEA	Consumers, Health, Agriculture and Food Executive Agency
EU	European Union
iPAAC	Innovative Partnership for Action Against Cancer

1 Executive summary: the need for quality frameworks

There has been a growing emphasis on driving up quality in cancer organisations given variations in outcomes in Europe. The European Cancer Concord (ECC), a partnership of patients, advocates and cancer professionals, recognised major disparities in the quality of cancer management and in the degree of funding in Europe in its European Cancer Patient's Bill of Rights, a patient charter that underpins equitable access to optimal cancer control, cancer care and research for Europe's citizens.[1]

This followed an assessment of the quality of cancer care in Europe as part of the first EU Joint Action on Cancer, the European Partnership for Action Against Cancer (EPAAC, http://www.epaac.eu), which reported that there are important variations in service delivery between and within countries, with repercussions in quality of care. Factors such as waiting times and provision of optimal treatment can explain about a third of the differences in cancer survival among countries, while lack of a national cancer plan that promotes clinical guidelines, professional training and quality control measures, may be responsible for a quarter of the survival differences.

The EU Joint Action on Cancer Control (CANCON), which replaced EPAAC from 2014, also focused on quality of cancer care and in 2017 published the *European Guide on Quality Improvement in Comprehensive Cancer Control.*[2] This recognised that many cancer patients are treated in general hospitals and not in comprehensive cancer centres (CCCs), and explored a model of 'comprehensive cancer care networks' that can integrate expertise under a single governance structure.

Further, research shows that care provided by multidisciplinary teams (MDTs) results in better clinical and organisational outcomes for patients[3] and are the core component in cancer care.[4]

Countries have been concentrating expertise for certain tumour types in such networks and in dedicated centres, or units, such as those for childhood and rare cancers, and all CCCs have teams for the main cancer types. However, for common adult tumours, at the European level there has been widespread effort to establish universal, dedicated units only for breast cancer, following several European declarations that set a target at the year 2016 for care of all patients with breast cancer to be delivered in specialist multidisciplinary centres. While this target was not met,[5] the view of the ERQCC expert group is that healthcare organisations must adopt the principles of such dedicated care for all tumour types.

1.1 Pancreatic cancer

The pancreas has long been a focus for specialists (for example, the European Pancreatic Club, https://www.europeanpancreaticclub.org, was founded in 1965), and there are now a number of European and national clinical guidelines for pancreatic cancer in particular. Several countries have also established requirements for MDTs and centralisation of expertise for pancreatic cancer care.

The latest European Commission initiative, Innovative Partnership for Action Against Cancer (iPAAC), has included pancreatic cancer as a neglected cancer in a work package on challenges in cancer care; carried out a systematic literature review on centralisation of pancreatic cancer care; and developed a standard and indicators for pancreatic and colorectal cancer care networks (these are due for publication in 2021).

iPAAC has also issued the Bratislava Statement on recommendations for improving pancreatic cancer care,[6] which includes implementing policies that promote specialisation and put expert MDTs at the centre of the decision-making process, and identifying reference centres and building on efficient models of centralised care. Following the statement, a report that describes the advantages of multidisciplinary reference centres has been published.[7]

This ERQCC paper complements iPAAC's initiatives in the wider context taken by the ERQCC project in setting out the challenges in pancreatic cancer care and the details of the expert MDT.

2 Figures and tables

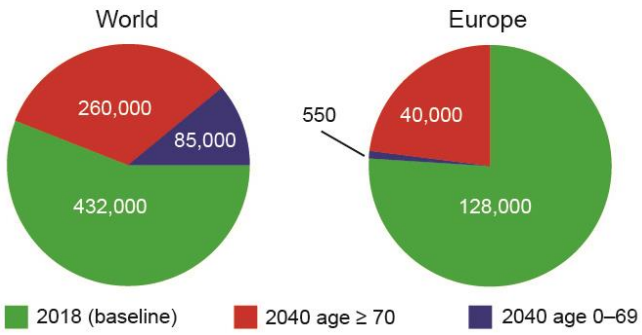

Figure 1. Mortality projection of pancreatic cancer for both sexes from 2018 (baseline estimates) to additional cases estimated by 2040 indicating burden of older age. Incidence projection figures are similar. Source: Global Cancer Observatory, International Agency for Research on Cancer. https://gco.iarc.fr

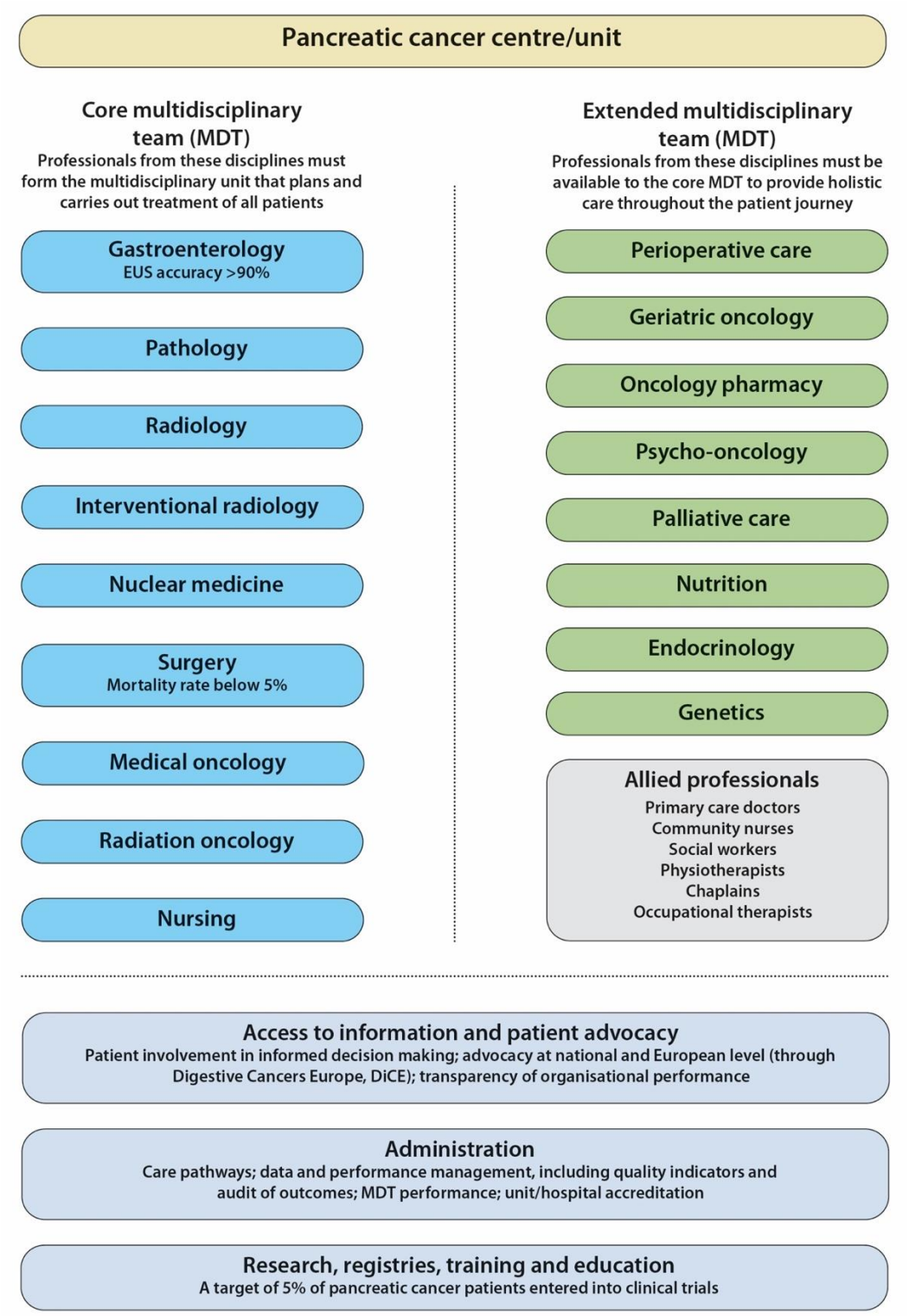

Figure 2. Schematic of MDT

3 Pancreatic cancer: key facts and challenges

3.1 Key facts

3.1.1 Epidemiology

- By far the most common type of pancreatic cancer, about 95% of cases, is adenocarcinoma. This arises in the exocrine cells, which make up the majority of the organ and is the main focus of this ERQCC paper. There are less common variants of exocrine cancer, including acinar cell carcinoma, adenosquamous, squamous cell, signet ring cell, undifferentiated carcinomas, and undifferentiated carcinomas with giant cells. Pancreatic cancer can also arise in endocrine cells (about 5% of cases) – the way neuroendocrine pancreatic neoplasm is diagnosed and treated by the MDT is covered briefly in section 5.
- Pancreatic cancer is estimated to be the 8th most common cancer in Europe with about 102,000 new cases diagnosed in 2018 at a rate of 18.8 per 100,000 (new European age standardised rate, European Union (EU) 28 + European Free Trade Association (EFTA) countries).[8] Despite the relatively low incidence, pancreatic cancer is the 5th leading cause of cancer-related deaths and, in contrast to other tumour types, no significant reduction in mortality rates has been recorded in recent years. About 97,800 people were estimated to have died in 2018 at a rate of 17.9 per 100,000.[8] Countries with the highest estimated incidence were in eastern Europe – Hungary (24.2), Latvia and Slovakia; the lowest in Iceland (12.1), Cyprus and Portugal. However, Iceland had the highest estimated mortality (22.3) followed by Hungary and Finland, while the lowest mortality was estimated in Portugal (13.7), Spain and Ireland.[8] Overall, pancreatic cancer has accounted for 7.4% of all deaths from cancer in Europe.[9]
- Both incidence and mortality have been estimated to be higher in males (21.5 and 20.7 per 100,000, EU + EFTA) than in females (16.4 and 15.4).[8] In males, pancreatic cancer has accounted for 3.3% of new cancer diagnoses and 6% of cancer-related deaths. In females these figures were 3.5% and 7.4%.[9] Projections of incidence and mortality show major increases globally, especially in those aged ≥ 70; in Europe, the older age group is projected to account for the great majority of increased incidence and mortality (Figure 1).

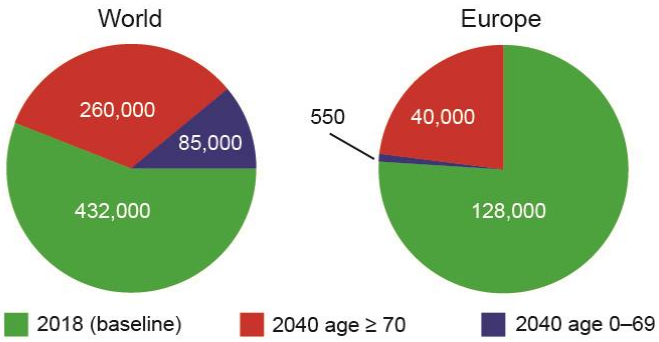

Figure 1. Mortality projection of pancreatic cancer for both sexes from 2018 (baseline estimates) to additional cases estimated by 2040 indicating burden of older age. Incidence projection figures are similar. Source: Global Cancer Observatory, International Agency for Research on Cancer. https://gco.iarc.fr

- Survival for patients with pancreatic cancer is low. Age-standardised 1-, 3- and 5-year relative survival rates in Europe between 2000 and 2007 in the EUROCARE-5 study (the most recent in this series) were 26%, 9.3% and 6.9% with no trend toward better outcomes.[10] Survival has varied between 5% in Ireland/UK and 8% in southern Europe; the highest rates were 11% in Belgium and Italy. It is reported to be the only cancer that has seen no improvement in survival in 40 years;[11] a systematic review published in 2015 found real-world median survival time in Europe was less than 5 months and less than 10% of patients survived beyond 5 years.[12]
- Given present lack of improvement, pancreatic cancer is predicted to become the third leading cause of cancer-related deaths in the EU countries by 2025 after lung and colorectal cancers.[13] It has been projected to be the second cause of cancer death in the US by 2030.[14]

3.1.2 Risk factors

- While the mechanisms underlying the development of pancreatic cancer are largely unknown, a number of risk factors have been identified. The most important are older age, obesity, smoking, alcohol abuse, diabetes mellitus, chronic pancreatitis intraductal papillary mucinous neoplasm, and environmental exposure to certain chemicals. Less clear are risk factors that have been suggested by some studies including type of diet, coffee, lack of physical inactivity, periodontal disease, *Helicobacter pylori* infection, ulcerative colitis, chronic hepatitis B and hepatitis C infection, and cirrhosis.[15]
- In addition, although pancreatic cancer is not explicitly caused by certain genes, about 10% of pancreatic cancers arise in higher risk families.[16] Some are diagnosed within the context of genetic syndromes such as:
  - Hereditary breast/ovarian cancer syndrome (caused by alterations of *BRCA1, BRCA2, PALB2*)
  - Lynch syndrome (caused by alterations of *MLH1*, *MSH2*, *MSH6*, *PMS2*).

- Familial atypical multiple mole melanoma syndrome (caused by alterations of *CDKN2A)*
- Hereditary pancreatitis (caused by alterations of *PRSS1*, *SPINK1*0)
- Peutz-Jeghers syndrome (caused by alterations of *STK11*)
- Cystic fibrosis (caused by alterations of *CFTR*).

3.1.3 Diagnosis and treatment summary

The key European clinical guidelines for pancreatic cancer are from the European Society of Medical Oncology (ESMO).[17] *Recent reviews cover standards of care and other guidelines.*[18,19]

- Common signs and symptoms of pancreatic cancer include abdominal pain often radiating to the back, painless jaundice, decreased appetite, weight loss, nausea, steatorrhoea (fat in faeces), asthenia (lack of energy), and new-onset diabetes. Generally, these signs and symptoms do not accompany the early phase of tumour growth but manifest when the tumour is too advanced for potentially curative surgical treatment.[20]
- Recommended diagnostic and staging tests for pancreatic cancer include pancreatic protocol computed tomography (CT) scan (or magnetic resonance imaging, MRI, with diffusion-weighted and cholangiopancreatography sequences, but is less used owing to cost and availability, and must be supplemented by chest CT). Endoscopic ultrasound (EUS)-guided fine-needle aspiration/biopsy (FNAB) is generally used for cytological/histological confirmation, which is needed especially before medical treatment in patients who are not candidates for upfront curative surgery. Endoscopic retrograde cholangio-pancreatography (ERCP) is the procedure of choice for insertion of biliary stents in patients with obstructive jaundice. Nuclear medicine – ^{18}F-FDG positron emission tomography (PET) – is used in selected staging cases.
- Only 10–20% of patients present with a tumour that is localised to the pancreas and is potentially amenable to surgical resection (the most common procedure is pancreaticoduodenectomy, also known as Whipple's procedure).[21] Depending on the degree of involvement of the surrounding vessels, these tumours are divided into resectable and borderline resectable. While upfront surgery followed by adjuvant chemotherapy is a common approach for these patients,[22,23] routine practice and investigational clinical trials are including pre-operative treatments (induction chemotherapy and/or chemoradiotherapy) followed by surgery in borderline resectable patients to facilitate resection, reduce the risk of positive margins and improve survival.[24,25] Latest guidelines from the Japan Pancreas Society recommend induction chemotherapy even in resectable tumours.[26]
- The vast majority of pancreatic cancer patients present with inoperable locally advanced or metastatic tumours (approximately 80-90% of cases), for whom standard treatment is systemic chemotherapy. Chemoradiotherapy is an option for patients with controlled disease after induction chemotherapy.[27,28] While palliation is generally the aim of treatment, a minority of patients with initially inoperable locally advanced tumours may benefit from treatment-induced downstaging and become candidates for a potentially curative surgical approach.[29]

3.2 Challenges in pancreatic cancer care

3.2.1 Prevention and detection

- There are no ways to reduce pancreatic cancer risk other than reducing lifestyle factors such as smoking, alcohol and obesity, and also exposure to certain chemicals. The European Prospective Investigation into Cancer and Nutrition (EPIC) study has reported that a healthy lifestyle was inversely associated with pancreatic cancer risk, and that public health measures targeting compliance with healthy lifestyles may have an impact on incidence of pancreatic cancer.[30]
- There is no routine screening for pancreatic cancer, and no evidence of benefit for screening high-risk groups. People who may be at higher risk can be referred for advice and genetic testing (see genetics, sections 3.2.5, 4.5.8).
- Early detection of pancreatic cancer is the overriding challenge for improving outcomes but primary care professionals may see only a few cases of pancreatic cancer in their careers. While obstructive jaundice is a symptom that is a clear 'red flag' for referral, other symptoms such as pain or weight loss are vague and it remains a challenge to know when to refer and how to improve diagnostic pathways.[31]
- The challenge for early detection is highlighted by emergency presentation, which is common in some countries and is a major factor in worse outcomes. For example, in England 46% of nearly 84,000 cases in the years 2006 to 2016 were diagnosed following an emergency.[32]

3.2.2 Diagnosis and staging

- Establishing the correct diagnosis can be difficult and requires an expert team comprising professionals in gastroenterology, radiology, nuclear medicine and pathology, and state-of-the-art equipment.[33] The diagnostic yield of EUS-guided FNAB can be sub-optimal; inconclusive pathology reports are not uncommon and repeat biopsy may be required.[34] High-quality imaging is central to staging.[35]
- Deciding if a patient is eligible for surgery in borderline cases can be difficult and consensus is subject to research.[36] Better patient selection for surgery is an ongoing aim; accuracy of staging is needed also for decisions about therapies used to downsize tumours before possibly surgery, adding to the importance of the MDT during the diagnostic process. The challenge is to avoid futile surgery but not overstage patients who could be offered potentially curative treatment. Interpretation of surgical eligibility and a significant number of therapeutic recommendations may be changed when patients are referred to a specialist MDT (see also section 4.2). But there is evidence from a study of several centres in Europe that there can be 'concerning' disagreements on curative or palliative strategies.[37]

3.2.3 Treatment and outcomes

- Treatment for pancreatic cancer is multimodal and highly specialised and must be carried out by the MDT advocated in this ERQCC paper. There is evidence that treatment of patients in a centralised and specialised clinical setting that applies the latest guidelines is associated with better outcomes (although much of the literature focuses only on surgical

volumes and outcomes – see also section 4.2), but there are many patients not receiving such care. For example, a review found that most European countries have failed to establish centralisation of pancreatic surgery in high-volume centres;[38] in the US, adherence to National Comprehensive Cancer Network guidelines improves survival, but compliance nationwide is low, especially for patients treated outside academic centres.[39]

- Many patients diagnosed with advanced disease require immediate supportive care for symptoms including pain, digestive obstruction, nutritional-based weight loss and cachexia (cancer-induced wasting), and depression and distress after diagnosis. Opportunities to provide supportive care before any cancer-directed treatment is started are often overlooked.[40]
- Surgery can be highly demanding with significant morbidity and some mortality, although the approach and quality of surgery has improved greatly in recent years.[41] Surgery requires not only highly experienced surgeons but an expert team of other professionals and high-quality facilities including intensive care to manage perioperative and post-operative care and complications, and to promote optimal recovery. There has been an encouraging advance in adjuvant therapy (medical treatment after surgery) that has extended median survival to 54.4 months in a clinical trial.[42]
- For the great majority of patients not eligible for radical surgery the MDT must offer a range of high-quality multidisciplinary treatments and care. Medical oncologists (clinical oncologists in some countries) are pivotal to providing cancer-directed therapy that meets clinical guidelines and emerging evidence from clinical trials (including for patients eligible for surgery) that are critical to improving survival and quality of life. Patients are sometimes still treated by oncologists without expert knowledge, outside of high-volume centres.
- Overtreatment and undertreatment are significant issues in pancreatic cancer. Owing to its seriousness, unwarranted surgery may be carried out that does not improve survival and deceases remaining quality of life, and chemotherapy may also be given without due attention to indication. Conversely, surgery and chemotherapy rates differ widely among countries and regions, suggesting that significant numbers of patients are not receiving appropriate curative and supportive treatments. In particular, the proportion of patients who undergo surgery (resection rate), while generally low, also varies greatly in Europe. The reasons for variations require further studies.[43]
- A large number of pancreatic cancer patients receive no cancer-directed therapy at all, although some may decline chemotherapy. A study in Ontario, Canada, found that a considerable proportion of patients with noncurable pancreatic cancer did not have a specialised cancer consultation and most did not receive cancer-directed therapy.[44] Another study from Canada found that a significant proportion of patients with advanced pancreatic cancer were never referred to a cancer centre.[45] A report from the Netherlands found many patients did not receive cancer treatment, although patient choice was the main reason.[46]

3.2.4 Survivorship and palliative care

- Patients who have undergone treatment, both primary surgery and supportive/palliative, are likely to have a wide range of physical and psychological needs that may be overlooked or underprovided, especially where lack of integration between primary/community and acute sectors is poor. An overarching challenge for all members of an MDT is to maintain quality of life.[47] Integrating psychosocial and psycho-oncology services and promoting

excellence in communications skills among MDT members are crucial for pancreatic cancer patients.

- A great majority of pancreatic cancer patients will require high-quality palliative care, which may not be available at all locations. Symptoms caused by pancreatic cancer and its treatments can be debilitating and profoundly distressing, such as cachexia.[48] Pain affects about 80% of patients.[49] Studies have shown benefits of early introduction of palliative care, not just for patients but also for carers and healthcare systems, especially in lung cancer.[50] Studies have now also shown the benefits of early palliative care for non-colorectal gastrointestinal cancers including pancreatic (see also palliative care in the extended MDT, section 4.5.5).[51]

3.2.5 Genetics and screening/surveillance

- The genetic contribution to pancreatic cancer is important but currently genetic screening is likely to be offered only to patients with a family history of the disease, which misses about 90% of patients. Family members of patients could be offered investigations to further assess their risk,[52] but the accuracy of procedures and agreement on which patients to include is challenging,[53] as is the selection of test types and their timing.
- Clinical geneticists and genetic counsellors are under-resourced and demand for more testing is likely to place pressure on health systems. There is also a growing number of unregulated consumer tests that will further exacerbate pressure.[54]

3.2.6 Inequalities

- Variation in treatment for pancreatic cancer in Europe indicates that there may be inequalities in access to high-quality care at a population level, although comparisons are hard to make owing to widely varying incidence and quality of registry information. What is certain is that as with other cancers, some countries in eastern Europe lack access to drugs, equipment and new techniques that may be critical to improving care, as documented by ESMO and ESTRO for medical therapies and radiation oncology;[55,56,57] access to certain drugs is also limited in other countries such as England.
- A report by Pancreatic Cancer Europe noted differences in incidence and survival rates across Europe but also highlighted disparities in public health measures that reduce risk; access to specialised treatment; data collection; research; and priority in national cancer plans (only 5 countries – France, Ireland, Luxembourg, Romania and Spain – had specific pancreatic cancer actions).[58]
- Pancreatic cancer is most common in older adults aged over 65, who comprise about two-thirds of cases, and about half of cases are in those aged 70 and over, meaning that there is a substantial challenge in care for older groups. Treatment decisions are more complex because of the scarcity of data from large randomised studies in older patients and the heterogeneity of this population concerning functional status, comorbidity and polypharmacy. Not age, but comorbidity, life expectancy, and patient preferences should be decisive factors when offering treatment; evidence suggests that older patients who receive treatment have improved survival outcomes (see section 4.5.2, geriatric oncology).[59]

- Some studies indicate that people with low socioeconomic status (SES) are less likely to receive surgery, chemotherapy and radiotherapy, and have higher mortality rates that those with higher SES. A study in the Netherlands found that those with higher SES were more likely to be treated in high-volume university hospitals.[60]

3.2.7 Research

- Pancreatic cancer is a complex and heterogenous disease with the current overarching challenge of little progress in improving cure and survival rates. The range of particular research challenges is wide,[61,62] extending from prevention, early detection,[63] risk stratification and early diagnosis, to new localised techniques and multimodal treatment based on better understanding of the biology,[64] to improving quality of life. Finding new medical therapies has been particularly challenging. Research into the increased use of supportive care is important given the high mortality of pancreatic cancer.[18]
- Funding for pancreatic cancer research has lagged behind other cancers in many countries, and in Europe has received less than 2% of all cancer research funding.[65]
- It is important that centres treating pancreatic cancer aim to participate in clinical trials as this may be associated with better implementation of the standard of care.

3.2.8 Cancer registration and data availability

- Cancer registration practice, coverage and quality are highly unequal across Europe.[66] Consequently, basic epidemiological data on incidence, mortality and survival are not uniformly available for all countries. Also, only a minority of cancer registries can provide sufficient data for the calculation of parameters necessary for the assessment of outcomes and quality of care.[67]
- Only a few countries have established clinical registries capable of benchmarking pancreatic cancer care and there is little historical pan-European cooperation on establishing comparable indicators. There are recent initiatives that are aiming to fill this gap from Pancreatic Cancer Europe and EURECCA (European Registration of Cancer Care).

4 Organisation of care

4.1 Care pathways and timelines

- Care for people with pancreatic cancer must be organised in pathways that cover the patient's journey from their point of view in healthcare system models that optimise care of pancreatic cancer and follow current national and European evidence-based clinical practice guidelines on diagnosis, treatment and follow-up. The European Pathway Association defines a care pathway as 'a complex intervention for the mutual decision making and organisation of care processes for a well-defined group of patients during a

well-defined period'. This broad definition covers terms such as clinical, critical, integrated, patient pathways that are also often used. See http://e-p-a.org/care-pathways and also the WHO framework on integrated people-centred health services, https://bit.ly/2VSN3vk.

- Examples of pancreatic cancer care pathways are from the National Institute for Health and Care Excellence (NICE)[68] and Cancer Council Victoria, Australia.[69] Integrated care plans (ICPs) have been proposed as a way to improve patient-oriented quality in complex diagnosis and treatment care pathways. They are described as structured multidisciplinary care plans for a specific clinical condition, and describe the tasks to be carried out together with their timing and sequence and the disciplines involved in completing the task.
- Delays in starting surgical treatment must be minimised but can be challenging as high-volume centres can have extensive waiting lists. In particular, surgery should not be delayed for tumours < 20 mm as this may negatively affect prognosis.[70] The confounding effect of clinical stage with waiting time should be taken into account in centralisation policy.[71]
- With emergency presentation being a major problem in pancreatic cancer, there must be pathways to ensure patients are seen in specialist units as soon as possible.
- After a diagnosis, it must be clear to the patient which professional is responsible for each step in the treatment pathway and who is following the patient during the journey (usually called a case manager or patient navigator). In some countries, case managers during the main stages of treatment are cancer nurses.
- Follow-up, support and care for long-term survivorship, and palliative care, must be part of a care pathway.

4.2 Pancreatic cancer units/centres and MDTs

- Pancreatic cancer diagnosis and treatment must be managed by a core and extended MDT described below, at a pancreatic cancer unit or centre. Pancreatic cancer is often located in a hepatobiliary and pancreatic MDT (HPB MDT) that treats disease of the liver, biliary tree and pancreas, or in a broader gastrointestinal unit. The ERQCC expert group considers that optimal care is delivered when all members of the core MDT work in a single unit or centre, but it is recognised that some members may be based at nearby or other locations, which may have part of the expertise necessary (such as radiation oncology) and that some patients will not live near specialist units, in which case there must be a structure in place to enable discussion of patient management in weekly teleconferences with an expert centre.
- In its most recent guideline on pancreatic cancer, NICE recommended that all people with a suspected or confirmed diagnosis should have their management determined by a specialist MDT.[72] It recognised that people may prefer to be treated at local hospitals, especially if their disease is advanced with a poor outlook, but when patients do choose such care the overriding consideration is that the management protocol is set by a specialist centre. NICE looked for evidence for referral to specialist MDTs according to survival outcomes, proportion of people receiving chemotherapy, entry into clinical trials, resection rates, post-operative mortality, patient satisfaction and quality of life, but no studies met its criteria. However, its expert committee agreed that making this recommendation would help to standardise quality of care, and the involvement of specialists should help to improve patient outcomes.

- Of the available evidence, there is a significant number of studies on the centralisation of pancreatic cancer surgery in specialised high-volume centres, most recently described by iPAAC in its systematic literature review (forthcoming). In Europe there are two main strategies that have led to centralisation – designation of certain hospitals or cancer centres as only those able to perform surgery, or setting a minimum volume of surgeries that a centre must perform, the latter enforced by law in some countries. The volume varies considerably (and there is also variation in the criteria that health systems use to establish a minimum): 10 in Germany, Belgium, Norway, and Austria; 11 in Spain; 20 in Canada, the United States, the Netherlands, and Switzerland; 30 in France; up to 50–100 in Italy; 80 in the United Kingdom, and more than 100 in Denmark (Denmark has taken radical steps to consolidate its surgical centres in recent years, in particular for lung cancer; Finland has likewise mandated that surgery is only carried out in 5 university hospitals). Note that some figures are for all pancreatic disease, not just cancer.
- Among the studies linking volume to outcomes:
  - The Dutch Pancreatic Cancer Group found significant advantages in centres performing 40 or more pancreatoduodenectomies;[73] in England it has been reported that mortality after resections for oesophageal, gastric and pancreatic cancer falls as surgeon volume rises up to 30 cases;[74] an up to date review that summarises data on the effect of centralisation on mortality, complications, hospital facilities used, and costs of pancreatic surgery has found beneficial effects associated especially with better short-term prognosis;[75] one recent study on centralisation with specialist surgeons found a significant decrease in complications, less time in surgery and subsequently less need for intensive care and better recovery[76]
  - However, it is not the occurrence of complications after surgery but treatment of complications that may drive differences in mortality, with evidence that higher volume centres perform better in so-called 'failure to rescue'[77]
  - Major complications though may be significantly associated with higher costs, which centralisation of care may reduce.[78,79]
- Other evidence in favour of MDTs shows that for gastrointestinal malignancies and, specifically for pancreatic cancer, a significant number of therapeutic recommendations may be changed following referral to expert centres; up to 25% of cases in a study of a single day multidisciplinary clinic,[80] about 20% in a review of referrals to gastrointestinal MDTs,[81] and a significant number according to a systematic review.[82] Centralisation and MDT working in Denmark has increased patient flow, improved quality of decision-making and offered more patients surgical treatment without increasing morbidity or mortality.[83]
- While it is recognised that centralisation of surgery has an impact on the quality of the MDT, there are few studies that have examined the effects on care of the great majority of patients, who do not undergo surgery, for the essential multidisciplinary care they must receive as detailed in this ERQCC paper. This is a common issue in cancer care but is increasingly recognised by some national authorities such as the German Cancer Society, which now includes audits of quality indicators and targets for advanced and metastatic disease treatments and care, and which also includes psychosocial care (see section 6.2.4).
- Several national health systems have also set mandatory requirements for a pancreatic cancer MDT, among them:
  - SONCOS in the Netherlands. The MDT is similar to the one set out in this ERQCC paper and specifies that there must be at least 2 certified surgeons and at least 2

gastroenterologists with experience in interventional endoscopies, and also builds on a set of requirements for the SONCOS colorectal MDT[84]

- Belgium – specifies criteria for pancreatic cancer reference centres, which must include at least 2 surgeons, 2 radiologists, 2 gastroenterologists, a clinical nurse specialist, a nutritionist and a psychologist. There must be at least 3 specialists with proven experience based on academic and symposium work, and knowledge of guidelines. There is also a volume requirement of at least 40 for all cases.[85] Belgium has also reviewed the effects of high vs low volume centres for pancreatic and oesophageal surgery, with the authors making a 'plea for centralisation'.[86]

- Concerning a minimum number of pancreatic resections that needs to be performed for high-quality care, the ERQCC expert group notes that this is still debated, as there is high variability of data reported in the literature. The mortality rate following pancreaticoduodenectomy in high-volume centres is between 2% and 5% but studies have reported only the association between the number of performed procedures and mortality risk without weighting the preoperative risk of surgical complications. For this reason, the ERQCC expert group considers that a mortality rate below 5% (and 2% for low risk cases), rather than a minimum number of surgical procedures per year, are essential requirements. This is also supported by iPAAC in its work on pancreatic cancer standards, and does not conflict with these detailed standards and with other indicators developed by the German Cancer Society and others. A supporting study in Italy on pancreatic surgery found that although many hospitals had low volume that was associated with high mortality, applying minimum volume thresholds of 10 or 25 resections a year would still give a mortality rate higher than 5% in a substantial number of hospitals and more than 10% in some.[87] The authors report that without considering a mortality threshold, hospital selection based only on surgical volume could prove inadequate. While both volume and mortality thresholds should be implemented in centralisation models, the ERQCC expert group considers that volume is a factor for healthcare systems to determine.
- The ERQCC expert group recognises that some countries specify more than one specialist (such as at least 2 gastroenterologists and surgeons) for centres but considers that it is not possible to set such criteria for all of Europe. Nevertheless, all functions of the core and extended MDT must be in place according to local organisation.

4.3 The MDT for pancreatic cancer

Treatment strategies for all pancreatic cancer patients must be decided on, planned and delivered as a result of consensus among a core MDT that comprises the most appropriate members for the particular diagnosis and stage of cancer, patient characteristics and preferences, and with input from an extended community of professionals (Figure 2). The heart of this decision-making process is normally a weekly or more frequent MDT meeting where all cases are discussed with the objective of following the recommendations from clinical guidelines and, when indicated, balancing these with the needs of the individual pancreatic cancer patient.

To properly treat and care for patients with pancreatic cancer, it is essential that the core MDT comprises health professionals from the following disciplines:

- Gastroenterology
- Pathology
- Radiology
- Interventional radiology
- Nuclear medicine
- Surgery
- Medical oncology
- Radiation oncology
- Nursing.

According to the case, this core MDT meets to discuss:

- All patients with a suspected, but not yet confirmed (in view of failure of prior diagnostic tests) diagnosis of pancreatic cancer to decide on further diagnostic approaches to confirm or rule out pancreatic cancer
- All new patients after diagnosis and staging to decide on an optimal treatment plan, curative or palliative
- All patients after major treatment to decide on further treatment (such as adjuvant chemotherapy)
- All patients for whom changes to treatment programmes are indicated and have multidisciplinary relevance and/or may require deviations from clinical practice guidelines.

The core MDT must be supported by a team of healthcare professionals from other disciplines (the extended MDT) who do not need to attend every MDT meeting but must be available to provide their expert input and contribute to the MDT decisions whenever required. The extended MDT must include health professionals from the following disciplines:

- Perioperative care
- Geriatric oncology
- Oncology pharmacy
- Psycho-oncology
- Palliative care
- Nutrition
- Endocrinology
- Genetics.

The expert group also recognises the contributions of department heads, data managers, documentation specialists, patient representatives, carers, clinical trials coordinators and others (see also ‘Other essential requirements’, section 6).

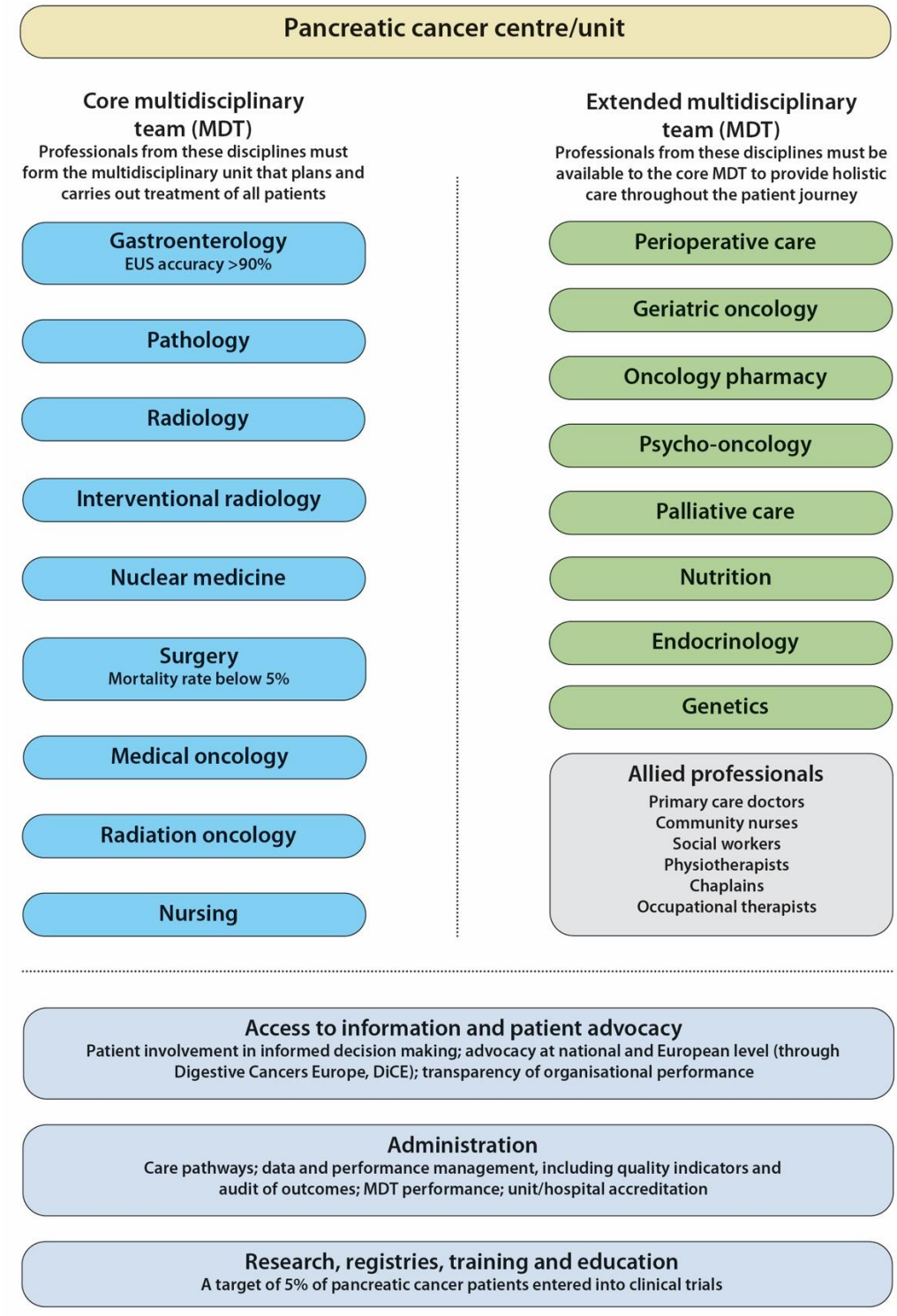

Figure 2. Schematic of MDT

4.4 Disciplines in the core MDT

General statement: Core MDT members must have excellent communications skills to engage patients and their family and carers in the benefits and risks of treatments, and availability of support, to ensure that options are explained to, and are appropriate for, the patient, and are not unduly influenced by age but more by medical fitness and choice.

4.4.1 Gastroenterology

Gastroenterologists specialise in diseases and conditions of the gastrointestinal (GI) tract and can be involved with the entire patient pathway for pancreatic cancer, from diagnosis to treatment and supportive/palliative care. They are often the professionals who first see patients with suspected cancer and are expert in the use of diagnostic techniques, in particular endoscopy and interventional procedures such as ERCP and EUS.

EUS with FNAB is essential to establish a proper diagnosis, especially in patients with borderline resectable or locally advanced disease who are not suitable for upfront surgery but are candidates for chemotherapy and/or radiotherapy.[88] Therefore, EUS with FNAB must be promptly offered to guarantee high sensitivity and specificity rates. In this setting, an on-site evaluation of EUS-guided tissue acquisition by a cytopathologist may allow a real-time evaluation of sample adequacy and diagnostic yield.

In some countries gastroenterologists are certified to deliver medical therapies, and there is crossover also with other disciplines depending on training and interests, in particular interventional radiology, surgery and genetics.

Essential requirements: gastroenterology

- There must be at least 1 gastroenterologist in the MDT with specialist knowledge of pancreatic cancer.
- Gastroenterologists must have expertise in performing EUS with FNAB with an accuracy of more than 90%.[89]
- Gastroenterologists must have expertise in performing EUS-guided celiac plexus neurolysis in patients with chronic abdominal pain that is not controlled by medical therapy.
- Gastroenterologists must have expertise in performing ERCP and biliary duct stenting in patients with jaundice.
- Gastroenterologists must have expertise in performing endoscopic drainage of postoperative intra-abdominal collections that cannot be approached percutaneously.

4.4.2 Pathology

Histologic confirmation is required to establish the diagnosis of pancreatic cancer because of the broad spectrum of neoplasms occurring in the pancreas and because some forms of pancreatitis can create difficulties regarding differential diagnosis from cancer in imaging studies. Tissue diagnosis is necessary especially for patients with unresectable tumours,

patients with suspected metastatic disease, and patients who are unable to undergo upfront surgery and are considered for neoadjuvant therapy.

Pathologists conduct detailed studies of tumours based on the samples (biopsy and resection) and prepare a pathology report for discussion at MDT meetings.

Essential requirements: pathology

- Pathologists must have expertise in reporting diagnostic biopsies and surgical specimens of pancreatic cancer.
- A cytopathologist must be present during EUS with FNAB to determine whether additional sampling is required.[90]
- Pathologists must be aware of all recently published guidelines and reviews on pathological reporting on pancreatic neoplasms, and their pathology reports must contain all necessary list of items as recommended by professional organisations.[91,92] The use of structured (or synoptic) reports must be encouraged.
- With the increasing importance of molecular data in therapeutic decisions, access to an accredited molecular pathology laboratory must be guaranteed, although it may not be on site.

4.4.3 Radiology

Radiology plays a critical role in the diagnosis, staging and follow-up of pancreatic cancer. Key contributions of radiology to the management of patients include:

- Establishing a differential diagnosis between pancreatic cystic lesions and pancreatic tumours, or between adenocarcinoma and neuroendocrine pancreatic neoplasms (see section 5)
- Providing a detailed characterisation of the anatomical relationship between pancreatic tumours and the surrounding vessels to define the resectability status of patients with nonmetastatic disease
- Assessing response to medical treatments in both early stage and advanced settings.

Radiologists guide other MDT members on the most appropriate imaging test to use depending on the clinical scenario.

Essential requirements: radiology

- Radiologists must have expertise in gastrointestinal imaging and knowledge of the treatment options for pancreatic cancer, and be aware of the criteria for surgical eligibility according to guidelines.
- As initial staging of pancreatic cancer is based mainly on CT findings, radiologists must have knowledge of state-of-the-art CT protocols.[93] They must know how to adapt the technique depending on the clinical scenario: assessment of primary tumour, local resectability, and of metastatic disease, especially in the liver.[94] Expertise in liver MR

imaging, with the use of hepato-specific contrast agents, is also essential, as it may be necessary to characterise focal liver lesions identified at CT and to spare surgery for patients who are not resectable due to the presence of liver metastases.[95,96,97,98] Where available, expertise in liver contrast-enhanced ultrasound (CEUS) may aid in focal liver lesion characterisation.

- Radiologists assessing the response to treatment of pancreatic cancer must be made aware of ongoing systemic therapy and of local therapies, if performed, such as radiotherapy. They must be aware of how to assess response after neoadjuvant cancer therapy.[93] When evaluating the results of chemotherapy, radiologists must use the RECIST 1.1 criteria.
- State-of-the-art imaging equipment must be available: multidetector CT (MDCT), possibly with dual-energy capabilities,[99] and high-field MR possibly with liver-specific contrast agents.[100]
- Radiologists must know when to refer a patient to nuclear medicine for PET-CT. Collaboration is fundamental to allow joint patient management, reading and reporting.

4.4.4 Interventional radiology

Interventional radiologists are most usually involved in diagnostic work-up, providing percutaneous image guided pancreatic core biopsy when it is not possible during endoscopy or when previous endoscopic attempts provided uninformative tissue material. In advanced stages, image guided biopsy can be indicated for metastatic disease (liver, lung, lymph node).

ERCP is the standard approach for patients with jaundice (see gastroenterology, section 4.4.1) but percutaneous biliary drainage may be carried out by interventional radiologists when ERCP is not feasible.

Because of the very high rate of perioperative complications/morbidity after Whipple resection, percutaneous minimally invasive management of clinical conditions is mandatory for patient survival. Percutaneous drainage of fluid collections, and percutaneous biliary drainage in bile leakage through the anastomoses, are procedures performed by interventional radiologists. Post-surgical bleeding is another complication of pancreatic resection and arterial embolisation is a typical interventional radiology procedure for controlling bleeding.[101]

A possible delayed complication of Whipple is stenosis of hepatico-jejunal anastomoses, which may require bile dilation by interventional radiologists.

Essential requirements: interventional radiology

- An interventional radiologist with pancreatic cancer experience must be part of the core MDT.
- An interventional radiology service must be available at all times and must include dedicated facilities such as an angio suite for biliary drainage and angiography, and ultrasound and CT for percutaneous procedures.

- An interventional radiologist must be available for the palliation of jaundice after unsuccessful ERCP attempts or when ERCP is not technically feasible.
- An interventional radiologist must be available at all times to the surgical team.

4.4.5 Nuclear medicine

Current nuclear medicine techniques in pancreatic cancer are ^{18}F-FDG PET/CT or ^{18}F-FDG PET/MRI. There is evidence of diagnostic accuracy of ^{18}F-FDG PET hybrid imaging techniques in selected clinical oncological indications.[102] According to clinical guidelines, ^{18}F-FDG PET may provide important additional information for staging, restaging and follow-up of pancreatic cancer for:

- Initial staging of high-risk patients to detect extra-pancreatic metastases[103,104]
- Detection of recurrent pancreatic cancer.[105]

Essential requirements: nuclear medicine

- ^{18}F-FDG PET/CT or ^{18}F-FDG PET/MRI must be available and must be managed by nuclear medicine physicians with the appropriate expertise.
- Nuclear medicine personnel must be able to perform daily verification protocols and to react accordingly. Quality-assurance protocols must be in place. An option for ensuring the high quality of PET/CT scanners is provided by the European Association of Nuclear Medicine (EANM) through EARL accreditation.

4.4.6 Surgery

Surgery for pancreatic cancer is the primary treatment with curative intent and is usually combined with medical therapies. Only 10-20% of patients have resectable, early-stage, pancreatic cancer amenable to potentially curative surgery. Pancreatic resections are demanding operations and are often associated with a high-risk of complications and mortality, although perioperative mortality is low in high-volume settings, as detailed in section 4.2.[106]

Each case of localised, resectable pancreatic cancer must be carefully discussed by the MDT. The experience of the surgical team is crucial for improving surgical and oncological outcomes and for the application of new techniques such as minimally invasive surgery.[107] The main surgical aim is to achieve R0 resection (negative margins).

The role of surgeons is to:

- Perform radical resection
- Perform palliative surgery (double by-pass hepatico-jejunostomy and gastro-jejunostomy) when palliative endoscopy stenting fails (endoscopy is preferred, because it offers rapid recovery and rapid starting of chemotherapy)

- Take part in perioperative care: assisting in preparation of patients (accounting for co-morbidities, nutrition etc.) and early diagnosis and treatment of postoperative complications, avoiding 'failure-to-rescue'.

Essential requirements: surgery

- Surgery must be performed in a centre with significant expertise in pancreatic surgery. The centre must have a mortality rate between 2% (low risk cases) and 5% (other cases) for radical pancreatic surgery.
- The pancreatic surgery team must be able to perform major vascular and visceral resection and have an expertise in minimally invasive procedures (distal pancreatectomy). Competences may involve collaboration with other surgical specialists, such as for vascular resection.
- The surgical team must be able to handle major complications, coordinating specialists such as anaesthesiologists and interventional radiologists.
- There must be a perioperative care programme that includes anaesthesiologists, intensivists, nurses, psychologists and nutritionists and there must be an intensive care unit.
- Audit of morbidity and mortality must be carried out and presented at MDT meetings at least every 6 months. Apart from surgical-related mortality, a registry must also record typical complications such as postoperative pancreatic fistula (POPF), postoperative pancreatic haemorrhage (PPH), delayed gastric emptying (DGE) syndrome, biliary leakage and reoperations.
- Pancreatic surgeons must participate in clinical trials wherever possible.

4.4.7 Medical oncology

Medical oncologists (clinical oncologists in some countries) play a key role in the management of pancreatic cancer patients given that many will receive medical therapy. Systemic chemotherapy is a standard treatment for patients with resected pancreatic cancer (i.e. adjuvant chemotherapy)[22,23,108] and for those with unresectable locally-advanced or metastatic disease (i.e. palliative chemotherapy).[27,28,109] There is increased consideration in routine practice and clinical trials for chemotherapy before surgical resection of borderline and immediately resectable tumours (i.e. neoadjuvant chemotherapy).[25]

A majority of patients present with advanced stage disease and pre-existing comorbidities, and most require medical treatment that is both cancer specific and able to control cancer-related symptoms.

On the basis of the MDT's determination of the patient's suitability for surgery, the medical oncologist's role includes:

- For patients with resectable or borderline resectable disease, determining indications for adjuvant or neoadjuvant chemotherapy, respectively, on the basis of imaging (for

neoadjuvant therapy), pathological staging, the patient's medical conditions, and surgical procedure
- Planning medical treatments for inoperable locally advanced and metastatic disease, defining the type and timing of chemotherapy, scheduling radiological re-evaluations and establishing the therapeutic strategy according to response and the patient's tolerance of treatment.

Medical oncologists also participate in supportive care to minimise cancer-related symptoms (including jaundice, pain, nausea and vomiting, lack of appetite, fatigue) and effect of treatment-related toxicities).

Essential requirements: medical oncology

- Medical oncologists must have in-depth knowledge of the behaviour and natural history of pancreatic cancer and thorough understanding of the differences (in terms of efficacy, toxicity and interaction with other treatments or comorbidities) between the available cytotoxic agents.
- Medical oncologists must assess patient suitability for systemic chemotherapy and select the most appropriate chemotherapy regimen (either in the curative or palliative setting) based on patient clinical conditions, comorbidities, concomitant medications, preferences and expectations, tumour-related characteristics and treatment intent. They must take account of the frequent debilitating symptoms and complications in pancreatic cancer that can affect performance status and suitability for treatments, and must discuss with patients the goals of systemic chemotherapy, and provide an overview of expected benefits and potential chemotherapy related toxicities.
- Medical oncologists must help to coordinate all other aspects of patient care including clinical and molecular diagnostic testing, screening for familiar susceptibility and genetic syndromes, and delivery of multimodal treatments (such as combination of chemotherapy, surgery and/or radiotherapy). They must implement appropriate supportive and palliative care, including early referral to specialist palliative care.
- Medical oncologists must participate in clinical trials wherever possible.

4.4.8 Radiation oncology

While pancreatic cancer is generally considered as a systemic disease, radiotherapy plays an important role in the management of patients. It is often used for borderline resectable and locally advanced tumours following induction chemotherapy, after which the MDT should evaluate secondary resectability.[110,111] Conventionally fractionated radiotherapy is predominantly administered with simultaneous chemotherapy which is fluoropyrimidine-based (infusional or oral) or gemcitabine. Stereotactic body radiotherapy (SBRT) is becoming an alternative to long-course chemoradiotherapy in the neoadjuvant setting and for the treatment of unresectable locally advanced or locally recurrent tumours. Radiotherapy can also help to control palliative symptoms such as pain.[112]

Radiation oncologists (clinical oncologists in some countries) are responsible for patients' ongoing care and wellbeing according to these clinical situations. Also, they must be able to

identify tumour- and treatment-related complications and manage these according to best practice in conjunction with other MDT members.

Essential requirements: radiation oncology

- Radiation oncologists treating pancreatic cancer must know the indications for radiotherapy, and its optimal sequencing with other treatment modalities, especially in the setting of non-metastatic disease.[17,113] They must know the latest technical developments in treatment simulation, planning and delivery, and the optimal dosing and fractionation based on the clinical scenario.[114]
- Intensity modulated radiotherapy (IMRT) must be regarded as standard practice and SBRT must be offered as a routine option in pancreatic cancer centres.
- Image-guided delivery techniques (image-guided radiotherapy, IGRT) before every fraction must be regarded as standard practice in both conventionally fractionated and hypofractionated regimens.
- State of the art planning and delivery procedures (such as intravenous contrast-enhanced simulation CT, 4-D CT scans, use of fiducial markers, and maximal sparing of sensitive bowel structures such as duodenum) must be in place for every patient who is a candidate for radiotherapy with curative intent.
- ^{18}F-FDG PET/CT imaging must be available for radiotherapy planning especially in locally recurrent disease and must be delivered by a nuclear medicine professional.
- For palliative indications, taking into account the clinical deterioration occurring in most patients, rapid access to radiotherapy must be guaranteed. Time-to-treatment must be tracked as an indicator.
- Radiation oncologists must be able to identify tumour- and treatment-related complications and manage these according to best practice in conjunction with other MDT members.

4.4.9 Nursing

Specialist cancer nurses provide information, care and support to patients and their families throughout the patient pathway. Nurses are a key contact for patients, coordinating personalised information to facilitate informed decision-making for treatment options, undertaking holistic needs assessments, helping to manage symptoms, and developing patient empowerment and respecting the decisions of patients.

Nurses play a vital role in caring for pancreatic cancer patients given that most will have advanced disease and it is essential that patients have support to manage the symptoms of the disease and treatment side-effects with a view to maximising quality of life. Pancreatic cancer patients have been described as a ‘nursing population’ given the many needs – physical, psychological, spiritual and existential – that nurses can attend to,[115] which may include helping to introduce early palliative care.[116]

Due to the increasing complexity of care, cancer nursing is carried out by advanced nurse practitioners in some countries. Their roles include delivering systemic treatments, assessing

treatment-related toxicities and advising on their management, providing survivorship care, and organising surveillance on consequences of treatment.

The ERQCC group recognises the contribution of the European Oncology Nursing Society (EONS) and its Recognising European Cancer Nursing (RECaN) project (https://www.cancernurse.eu/research/recan.html), and the EONS Cancer Nursing Education Framework.[117]

Essential requirements: nursing

- Nurses must have training in pancreatic cancer and implications for care, including the side-effects of chemotherapy and the supportive and palliative care needs of surgical and non-surgical patients throughout the care journey.
- Nurses must conduct holistic assessments to ensure safe, personalised and age-appropriate nursing care, and provide patient information and support to promote self-efficacy throughout the patient journey and must promote a culture of shared decision-making. They must provide information and education to the patient and family/carers and be the point of contact for them where they act as case managers.
- Nurses must ensure systematic screening throughout the disease trajectory to uncover physical symptoms such as pain, psychosocial distress, impairment of physical functioning, malnutrition and frailty. Validated instruments (e.g. distress thermometer) must be used where appropriate.
- When performing roles such as case manager or nurse navigator, nurses must help to coordinate care with healthcare professionals within and outside the core MDT, including with nutritionists, psycho-oncologists, home care services and palliative care services.

4.5 Disciplines in the extended MDT

4.5.1 Perioperative care

Anaesthesiologists and intensive care specialists have key roles in the management of patients undergoing surgery for pancreatic cancer. These include:

- Surgical risk assessment
- Preoperative optimisation of co-existing medical conditions
- Perioperative clinical pathway management (including intraoperative care)
- Postoperative management and management of complications in intensive care facilities
- Acute and chronic pain management.

Enhanced recovery after surgery (ERAS) recommendations for pancreatic cancer have been published.[118]

Other specialists involved in perioperative care include nurses, interventional radiologists, nutritionists and oncology pharmacists.

Essential requirements: perioperative care

- Patients undergoing pancreatic cancer surgery must have appropriate assessment led by anaesthesiologists and other perioperative specialists in partnership with surgeons.
- Surgical centres must have the necessary anaesthetic and intensive care expertise and infrastructure to manage elective pancreatic cancer surgery and provide the often complex support for postoperative complications in high-risk patients.
- Centres must consider the ERAS recommendations for all patients undergoing surgery.

4.5.2 Geriatric oncology

Half of pancreatic cancer patients are aged 70 or older,[119] and by 2030 it is expected that about 70% of pancreatic cancer will be diagnosed in older adults. Age by itself is not a selection criterion for surgery,[120] chemotherapy[121] or radiotherapy[122] in pancreatic cancer. Supportive care (nutrition and adapted physical activity, treatment of pain and anxiety/depression) holds a major place in pancreatic cancer management, particularly in older patients.

Older patients are a heterogeneous group in terms of medical, psychosocial and functional status, and vulnerabilities, all factors with an impact on survival and treatment toxicity. Cognitive impairment affects all aspects of treatment – ability to consent, compliance with treatment, and risk of delirium.

The MDT must have access to health professionals with experience of cancer in geriatric patients to offer personalised treatment accordingly. They may be geriatricians or geriatric oncologists (most often medical oncologists with a geriatric speciality, which is a growing field), and others including nurses and psychologists. The International Society of Geriatric Oncology (SIOG) admits a broad range of professionals to membership. Their role is to:

- Ensure that older patients are screened for frailty
- Coordinate recommendations with other specialists when personalised treatment is required for older patients.

Essential requirements: geriatric oncology

- All older patients (≥ 70) must be screened with a quick, simple frailty screening tool, such as the adapted Geriatric-8 (G8) screening tool. [123,124]
- Frail patients, as suggested by the screening tool, must undergo a full geriatric assessment as this can lead to a change in clinical decisions in up to 40% of cases.[125,126] The assessment can be based on self-report combined with objective assessments that can be performed by a specialist nurse in collaboration with a physician (geriatrician/specialist in internal medicine).
- For frail and disabled patients, a geriatrician or specialist nurse must be present in the MDT meeting to discuss treatment options aligned with the patient's goals of care.

- Cognitive impairment affects all aspects of treatment and screening using tools such as Mini-Cog[127] is essential. A geriatrician or a geriatric psychiatrist or neurologist would preferably be involved with impaired patients.
- In the perioperative setting, older patients must be assessed for the risk of post-operative delirium using tools such as the Delirium Prediction Score.[128] Algorithms may be of interest to evaluate the risk of post-operative morbidity and mortality (e.g. http://www.riskcalculator.facs.org).
- Oncologists and geriatricians must ensure the early integration of palliative care plans and geriatric interventions where appropriate.

4.5.3 Oncology pharmacy

The complexity and high toxicity profile of chemotherapy regimens combined with the frequent frailty of patients in pancreatic cancer makes optimisation of pharmacotherapy a necessity. The main focus of the oncology pharmacists' work is the drug-related needs of the individual patient. Individual drug therapy should be effective, safe and suitable for the patient to assure good tolerability and consequently have positive impact on treatment outcomes.

The role of the oncology pharmacist is to:

- Liaise with the medical oncologist/clinical oncologist to discuss cancer specific treatments, including interactions with other treatments, to help ensure effective, safe and cost-effective pancreatic cancer treatment
- Counsel patients about their drug treatment
- Supervise the preparation of oncology drugs.

Essential requirements: oncology pharmacy

- Oncology pharmacists must have experience with antineoplastic treatments and supportive care; interactions between drugs; drug dose adjustments based on age, liver and kidney function, and toxicity profile; utilisation and monitoring of pharmacotherapy; patient counselling and pharmacovigilance; and knowledge of complementary and alternative medicines.
- Oncology pharmacists must have experience with parenteral and enteral feeding support for post-surgical patients, and also with pancreatic enzyme replacement therapy.
- Oncology pharmacists must comply with the European Quality Standard for the Oncology Pharmacy Service (QuapoS).[129] Oncology drugs must be prepared in the pharmacy and dispensing must take place under the supervision of the oncology pharmacist.
- Oncology pharmacists must provide personalised information for patients on their drug therapy to support adherence and monitor side-effects.
- Oncology pharmacists must work with medical oncologists on clinical cancer trials.

4.5.4 Psycho-oncology

Many pancreatic cancer patients report clinically significant distress that can continue throughout the patient pathway. Common reactions include excessive worry and rumination,

difficulty concentrating, insomnia, increased use of alcohol and other drugs, social withdrawal and somatic complaints. Depression has been reported to be more common in pancreatic cancer patients than in other malignancies[130] and has been associated with pancreatic cancer even prior to diagnosis.[131]

Psycho-oncology services are most usually led by a clinical psychologist supported by psychotherapists, counsellors, nurses, psychiatrists and social workers, and are also integrated with palliative care. The International Psycho-Oncology Society (IPOS) admits members from a broad range of professions with experience and training in clinical psycho-oncology. Their role is to:

- Ensure that psychosocial distress, depression and other psychological disorders and psychosocial needs are identified by screening throughout the disease continuum, and are considered by the MDT in its decision making
- Promote effective communication between patients, family members and healthcare professionals
- Support patients and family members in coping with multifaceted disease effects.

A recent paper shows how psycho-oncology services can be integrated into a same-day multidisciplinary pancreatic cancer clinic.[132]

Essential requirements: psycho-oncology

- Psychosocial care must be provided at all stages of the disease and its treatment for patients and their partners and families and must be present to ensure comprehensive cancer care.
- Patients must have access to a self-administered psychological assessment tool (e.g. distress thermometer). Scores below a certain level must be routinely managed by the primary care team; above that level there must be further clinical interviewing and screening for anxiety and depression, and referral to the most appropriate professional, such as a mental health physician.
- It is imperative that the MDT members treating pancreatic cancer patients have communication skills to deliver bad news and discuss prognosis with patients and their families.
- Psychosocial interventions must be based on clinical practice guidelines such as the NCCN Guidelines for Distress Management (https://www.nccn.org/professionals/physician_gls/default.aspx).

4.5.5 Palliative care

Palliative care, as defined by the World Health Organization, applies not only at end of life, but throughout cancer care (http://www.who.int/cancer/palliative/definition). Palliative care means patient and family centred care that enhances quality of life by preventing and treating physical, psychosocial and spiritual suffering.[133,134]

Supportive care is often used as an alternative term that conveys less stigma about advanced cancer (and can lead to better take-up of interventions),[135] but is most accurately 'the prevention and management of the adverse effects of cancer and its treatment', as defined by the Multinational Association for Supportive Care in Cancer (MASCC, https://www.mascc.org). In recent years, supportive/palliative provision has become increasingly integrated and important in meeting major unmet needs, and ESMO has proposed the use of the term 'patient-centred care' to encompass both supportive and palliative care.[136]

Best supportive care includes non-specific treatment of fatigue, pain, anxiety and depression, chemotherapy related toxicities, and thromboembolic disease treatment and prevention in high-risk patients.[18,137] Nutrition (see 3.5.6) and physical activity interventions are also receiving attention.

Early palliative care for pancreatic cancer patients with metastatic or locally advanced inoperable pancreatic cancer has a positive impact on clinical outcomes, quality-of-care outcomes, and costs, as well as having a significant impact on some indicators for end of life treatment aggressiveness, suggesting that quality of care is improved.[138,139,140,141] A higher number of palliative care consultations are associated with less aggressive end of life care.

It is fundamental for pancreatic cancer patients to receive honest communication, advance care planning and help to meet unmet physical, informational, psychological and spiritual needs, and help with existential distress.

Palliative care includes palliative and supportive care provided by oncology professionals in the MDT and other clinicians who are responsible for cancer care, and specialised care provided by a multidisciplinary palliative care team.[142,143]

Essential requirements: palliative care

- The MDT must offer optimal supportive and palliative care at the earliest opportunity and as proposed by the palliative care team. Specialist palliative care especially must be available to patients with advanced pancreatic cancer from the initial MDT meeting, irrespective of the cancer-specific treatment plan, and must continue during the course of the illness.
- The palliative care team must include palliative care physicians and specialist nurses, working with an extended team of social workers, chaplains, psychotherapists, physiotherapists, occupational therapists, nutritionists, pain specialists and psycho-oncologists.

- The palliative care team must possess communication and ethical skills for discussing bad news and end of life care that respect patient autonomy and support decision making, coping with change and quality of life.
- The palliative care team must have good knowledge of cancer disease and cancer treatments, and therapies for treating pain, anorexia, fatigue, depression etc.
- The palliative care team must have experience of taking care of frail older patients and their families.
- To ensure continuity of care at home, the palliative care team must work with community/primary care providers.
- Palliative care specialists, oncologists and healthcare providers must recognise the objectives of the European Association for Palliative Care (https://www.eapcnet.eu) and aspire to meet the standards of ESMO Designated Centres of Integrated Oncology & Palliative Care (https://bit.ly/3qJtl3w).

4.5.6 Nutrition

Nutritional problems are frequent in patients with pancreatic cancer; malnutrition is associated with reduced survival, lower quality of life and higher risk of treatment complications, therefore requiring early screening and intervention to optimise therapy. Many patients present with significant weight loss and cancer-induced cachexia and anorexia, while treatments, especially surgery, can induce several impacts on nutrition status, including pancreatic enzyme insufficiency, micronutrient deficiencies, diabetes, fatty liver, and metabolic bone disease.[144]

A nutritionist or dietitian is an essential member of the extended MDT to manage nutritional interventions, as set out in guidelines.[145,146] This includes pre- and perioperative nutritional care for patients undergoing pancreatic cancer surgery.[147]

Essential requirements: nutrition

- Nutritionists must carry out systematic nutrition screening at the time of diagnosis of pancreatic cancer, including assessment of body composition (fat free mass, visceral fat), dietary intake and physical activity.
- Nutritionists must prepare an intervention plan (for inadequate food intake, oral nutritional supplements, enteral or parenteral nutrition should be used).
- Nutritionists must be part of the perioperative surgical team.
- Nutritionists must have expertise in pancreatic enzymatic replacement therapy.
- Nutritionists must support the tolerability of therapeutic measures.
- Counselling with good communication skills is necessary to ensure compliance with plans.
- Regular follow-up of body weight and body mass index (BMI) must be carried out.

4.5.7 Endocrinology

Endocrinologists play a major role in the MDT for neuroendocrine neoplasm (section 5) but also have an important role in the care of patients with exocrine pancreatic cancer owing to a high prevalence of diabetes among patients. An endocrinologist specialising in diabetes may also be called a diabetologist, reflecting the importance of diabetes as a metabolic disorder.

Diabetes is a risk factor for pancreatic cancer, but pancreatic cancer can also cause diabetes, as can surgery for pancreatic cancer. Diabetes secondary to diseases of the pancreas is termed type 3c and about 8% of cases are estimated to occur in people with pancreatic cancer. There are also associations with pre-existing diabetes and poorer survival in pancreatic cancer patients, and risk of complications after surgery.[148]

A primary goal of treatment is to prevent short-term metabolic complications that can lead to morbidity and delay cancer-related treatment.[148] Many patients also develop diabetes after surgery or have worsening of glycaemic control during chemotherapy owing to antiemetic steroids (although some may have improved control). Follow-up management of diabetes in patients who have undergone surgery may be necessary.

The relationship between diabetes and pancreatic cancer is complex and there may be important implications for prevention of the disease.[149] Much is unknown about the relationship and large-scale research projects and registries such as the European Prospective Investigation into Cancer and Nutrition (EPIC) must be supported.

Essential requirements: endocrinology

- An endocrinologist (or diabetologist) with knowledge of treating diabetes in pancreatic cancer patients must be part of the extended MDT.
- Endocrinologists must manage diabetes and complications in accordance with patient treatment and care plans.
- Endocrinologists must care for patients who undergo curative surgery and have life-lasting diabetes.
- Endocrinologists must consider contributing to research on links between diabetes and pancreatic cancer in prevention and treatment.
- Endocrinologists must participate in early differential diagnosis between exocrine and endocrine tumours (see section 5).

4.5.8 Genetics

Given that hereditary syndromes are involved in about 10% of pancreatic cancer cases it is important that genetic assessment is a routine part of the pancreatic cancer service. Genetic risk assessment must be carried out at the initial consultation at the centre and reassessed periodically. This may be carried out by a gastroenterologist, medical oncologist or surgeon, or other MDT members who may include a clinical geneticist, and supported by genetic counsellors.

The genetic risk assessment identifies individuals with pancreatic cancer who are at increased risk of additional primary cancers, which can affect treatment plans, screening practices, and prevention options for both cancer patients and their at-risk relatives. The American Society of Clinical Oncology (ASCO) recommends that the minimum family history for patients with cancer includes first- and second-degree relatives.

Reassessment should include any new family history information from the patient and clinician re-evaluation of family history in light of new medical information and medical advances. Reassessment is important because cancer family histories change significantly over time. Germline genetic testing should then be performed in the context of appropriate pre- and post-genetic counselling.

NICE currently recommends surveillance for pancreatic cancer of people with hereditary pancreatitis and a *PRSS1* mutation; *BRCA1*, *BRCA2*, *PALB2*, or *CDKN2A* (p16) mutations, and one or more first-degree relatives with pancreatic cancer; and Peutz-Jeghers syndrome.[72] It further says that surveillance should be considered for people with 2 or more first-degree relatives with pancreatic cancer, across 2 or more generations; and people with Lynch syndrome (mismatch repair gene [*MLH1*, *MSH2*, *MSH6*, or *PMS2*] mutations) and any first-degree relatives with pancreatic cancer.

Essential requirements: genetics

- All pancreatic cancer patients must have an initial genetic assessment carried out by an appropriately trained member of the MDT or by a clinical genetics service allied to the MDT. The assessment must include at-risk relatives.
- Genetic risk reassessment must be carried out for both patients and at-risk relatives to capture changes in family history.
- Genetic counselling and germline testing must be available to patients and families.
- Surveillance of people with certain syndromes and relations with pancreatic cancer must be considered in line with current recommendations.

5 Pancreatic neuroendocrine neoplasm

This section covers briefly the requirements for the MDT when treating patients with neuroendocrine neoplasm and is not intended to be comprehensive. Key references: ESMO's clinical practice guidelines on gastroenteropancreatic neuroendocrine neoplasms[150] and European Neuroendocrine Tumor Society (ENETS) consensus guidelines (https://www.enets.org/basics.119.html).

Pancreatic neuroendocrine neoplasm requires the same core and extended MDT members as for the much more common exocrine pancreatic cancer, but there are major differences in the specialist knowledge and skills required. Also commonly called pancreatic neuroendocrine tumours (PanNETs), these cancers comprise 2 main groups – functional, which make excess hormones (hypersecretion) and can cause a wide variety of symptoms, and non-functional, which do not produce hypersecretion. Incidence of PanNETs has increased in recent years owing mostly to incidental findings from imaging. Understanding of the biology of PanNETs has increased substantially in recent years.[151]

Diagnosis: a key challenge is an early differential diagnosis between exocrine and endocrine tumours. The MDT must have these skills:

- Radiology – an expert radiologist using CT and MRI can suspect endocrine differentiation on appearance of the lesion and contrast enhancement distribution in primary tumour and metastatic sites in both functioning and non-functioning PanNETs
- Nuclear medicine – may indicate endocrine differentiation for primary tumours and metastatic sites, and provide information for staging. The preferred technique is somatostatin receptor imaging preferably with PET ^{68}Ga-DOTA peptides
- Gastroenterology/pathology – whenever possible an EUS guided fine needle biopsy must be performed to reach a pathological diagnosis including, at least, immunohistochemistry staining for chromogranin A, synaptophysin and Ki-67
- Genetics/endocrinology – accurate familial history may help suspect PanNETs associated with multi-endocrine genetic syndromes (*MEN1*, *NF1*, *VHL* etc.). Apart from genetic association, evaluation of any endocrine secretory pattern (insulin, glucagon, GHRH) must be carried out depending on the clinical suspect in functional tumours.

Treatment: decision making must be based on key features such as proliferative activity, hormonal hypersecretions, somatostatin receptor expression, tumour growth rate and extent of the disease. The main MDT members who carry out treatment are surgeons, medical oncologists, endocrinologists and nuclear medicine specialists.

- *Local/localregional disease:* when feasible, surgery is the main treatment; some researchers have suggested watchful waiting for non-functional ≤ 2 cm tumours and confirmatory clinical trials are ongoing. Functional tumours require medical therapy according to the type of hypersecretion. An alternative to pancreatectomy in selected cases is enucleation, where just the tumour is removed.
- *Advanced/metastatic disease:* in selected cases with liver disease, surgery may be performed on the primary tumour and metastases; liver transplantation is a rare option in inoperable cases. Medical therapies based on phase III trials include somatostatin analogues and the targeted therapies, everolimus and sunitinib. Evidence from older phase II trials include chemotherapy with agents such as temozolomide and streptozotocin. Peptide receptor radionuclide therapy (PRRT) may also be an option.

Supportive care for patients is important but said to be often forgotten.[152] Care may include management of clinical syndromes, debaulking surgery, and as with most cancers, psychosocial support, expert nursing, nutritional support and pain management. Follow-up must include clinical symptom monitoring and imaging.

See also section 6.1 for details of patient organisations. There are specialist neuroendocrine centres in Europe, many of which have been certified by ENETS as centres of excellence (https://www.enets.org/coe_map.html).

6 Other essential requirements

6.1 Patient involvement, access to information and transparency

- Patients must be involved in every step of the decision-making process. Their satisfaction with their care must be assessed throughout the patient care pathway. Patients and their families and carers must be offered relevant, objective and understandable information, which may include decision support aids, to help them appreciate the process that will be followed with their treatment from the point of diagnosis. They must be supported and encouraged to engage with their health team to ask questions and obtain feedback on their treatment wherever possible.
- It is also essential that pancreatic cancer patient support and advocacy organisations are involved whenever relevant throughout the patient pathway. These groups work to:
  - Improve patients' knowledge and ability to take decisions
  - Secure access to innovative therapies and improve quality of treatment
  - Support pancreatic cancer research, such as by being involved in the better design of clinical trials
  - Advocate at European and national health policy level.
- The main pan-European advocacy group is Digestive Cancers Europe (DiCE) (https://digestivecancers.eu), which has expanded its remit from colorectal cancer (as EuropaColon) to other cancers of the digestive tract. The World Pancreatic Cancer Coalition includes DiCE among its members, and both agencies include a number of national groups in Europe such as Fondation A.R.CA.D (Aide et Recherche en Cancérologie Digestive, France, www.fondationarcad.org), Arbeitskreis der Pankreatektomierten (AdP, Germany, https://www.bauchspeicheldruese-pankreas-selbsthilfe.de) and Pancreatic Cancer UK (https://www.pancreaticcancer.org.uk).
- Pancreatic Cancer Europe (https://www.pancreaticcancereurope.eu) is a multistakeholder platform that aims to bring together academics, physicians, politicians, patient groups, journalists and industry. It has developed a 'heatmap' that shows the profile of pancreatic cancer in Europe, including public campaigns, research programmes, registries and clinical guides. It produced a manifesto for the 2019 European elections and the inequality report noted in section 3.2.6.[58]
- The International Neuroendocrine Cancer Alliance (INCA) is an umbrella organisation representing 26 patient advocacy and research groups (https://incalliance.org). European members include Association des Patients porteurs de Tumeurs Endocrines Diverses (APTED), France (http://apted.fr), Netzwerk Neuroendokrine Tumoren in Germany (http://www.netzwerk-net.de), and Neuroendocrine Cancer UK (http://www.netpatientfoundation.org).
- Conclusions on each MDT case discussion must be made available to patients and their primary care physician, who must also be informed on all aspects of care such as treatments given, side-effects experienced, and participation in clinical trials.
- Advice on seeking second opinions must be supported.
- Cancer healthcare providers must publish on a website, or make available to patients on request, data on centre/unit performance, including:
  - Information services
  - The personnel in the MDT and their responsibilities

  - Waiting times to first appointment
  - Pathways of cancer care
  - Numbers of patients and treatments available at the centre
  - Number of operated patients at the centre (per procedure)
  - Clinical trials.
- In some countries or centres it may be appropriate to publish:
  - Clinical outcomes such as mortality rates after surgery
  - Patient reported outcomes
  - Incidents/adverse events.

6.2 Performance and quality

6.2.1 Audit and indicators

The pancreatic cancer centre must develop:

- Performance measurement metrics/quality indicators and audits based on the essential requirements in this paper and on clinical guidelines
- Operational policies to ensure the full benefits of a coordinated clinical pathway based on published guidelines
- Accountability within the governance processes in individual institutions
- Systems to ensure safe and high-quality patient care and experience throughout the clinical pathway
- Effective data management and reporting systems
- Engagement with patients, their carers and support groups to ensure reporting of patient outcomes and experience.

This includes national audits and indicators in some countries that may be mandatory (see examples in 6.2.4 below). The expert group considers there is an urgent requirement for consistent collection of a minimum set of structure, process and outcomes measures for all centres, and endorses the indicator set that will be published by iPAAC. These indicators will include the following and should be considered as a minimum requirement:

- Pretherapeutic patients discussed by the MDT
- Postoperative patients discussed by the MDT
- Endoscopic complications
- Patients eligible for adjuvant chemotherapy
- Patients who should receive palliative chemotherapy
- Surgery rates for early and advanced stages
- Clear margins after surgery
- Lymph node examination after surgery
- Complete pathology reports after surgery
- Revision surgeries
- Postoperative wound infections

- 30 day mortality after surgery
- Counselling.

Other common indicators are:

- Proportion of patients according to clinical stage at time of diagnosis
- Proportion of patients receiving treatment with curative and palliative intent
- 1, 3 and 5 year overall survival rates
- Adherence to MDT recommendations.

6.2.2 MDT performance

- All MDT decisions must be documented in an understandable manner, and must become part of patient records. Decisions taken during MDT meetings must be monitored, and deviations reported back to the MDT. It is essential that all relevant patient data, such as pathology reports and imaging scans, meet quality standards and are available at the time of the MDT meeting, and that the MDT is aware of patient preferences, comorbidities and clinical conditions.
- The core and extended MDTs must meet at least twice a year to review the activity of the previous period based on the audited metrics, discuss changes in protocols and procedures, and improve the performance of the unit/centre. MDT performance must be quality assured both internally and by external review with demonstration of cost-effectives of quality improvements, and MDT guidance must be promoted nationally and written into national cancer plans.
- The ERQCC expert group strongly recommends that further attention must be given to measures of patients reported outcomes, not only to agree which tools should be used, but also to use them more systematically as part of discussions and evaluation within the MDT.

6.2.3 Accreditation

The ERQCC expert group strongly recommends participation in national or international accreditation programmes,[153] e.g. Organisation of European Cancer Institutes (OECI) accreditation (http://oeci.selfassessment.nu/cms), and the German Cancer Society certification system for cancer centres, which is offered to centres outside Germany (http://www.ecc-cert.org).

6.2.4 National/international quality and audit examples

- The Dutch Pancreatic Cancer Audit is mandatory in all 18 centres in the Netherlands that carry out pancreatic surgery, with data collection starting in 2013. All patients undergoing surgical exploration for a suspected pancreatic or periampullary tumour are included, as

mandated by the Dutch Healthcare Inspectorate. The audit includes 16 indicators and 20 case-mix factors identified in a literature search that included 16 randomised controlled trials. Morbidity, mortality, and length of stay have been analysed of all pancreatic resections registered during the first 2 audit years, and it was reported that outcomes were good compared with other nationwide registries.[154] However, there has been little improvement in meeting other quality indicators in a multidisciplinary guideline in the Netherlands in recent years (including discussion in MDT meetings and use of chemotherapy).[155]

- NICE has published a quality standard for pancreatic cancer that includes statements on establishing specialist MDTs, staging, surgery, enzyme replacement therapy and addressing the psychological needs of patients.[156] It is based on NICE's recommendations for diagnosing and treating pancreatic cancer.
- The German Cancer Society produces reports on certified cancer centres in Germany and neighbouring countries that are part of the scheme. For pancreatic cancer, there were 106 certified centres in the 2018 audit year (2017 indicator year), a rapid increase from just 42 in the first report in 2013, and primary cases seen increased to more than 5,000 at these centres from about 1,800 during this period. Neuroendocrine neoplasms were added in the 2017 indicator year. The indicators are comprehensive, and include pre- and post-operative care presentation, lymph node examination, endoscopy complications, revision surgeries, post-operative wound infections, adjuvant and palliative chemotherapy, psycho-oncological and social services counselling, and participation in research.[157]
- Since 2012, Sweden has published annual reports on the Swedish National Pancreatic and Periampullary Cancer Registry to stimulate multidisciplinary and equality in care. Indicators include patients discussed by a MDT, patient reported outcomes and palliative care. See https://bit.ly/3gfZ6fs. A paper reports that the registry shows that Sweden is meeting international standards and has encouraged better collaboration and openness among surgeons.[158]
- The Danish Pancreatic Cancer Database aims to prospectively describe the epidemiology, diagnostic workup, histological or cytological diagnosis, treatment and outcome of patients in Denmark.[159]
- A group in Australia conducted a Delphi survey among pancreatic cancer experts and identified quality indicators in 5 areas: diagnosis and staging, surgery, other treatment, patient management and outcomes.[160] From 113 potential quality indicators, 34 indicators met the inclusion criteria and 27 (7 diagnosis and staging, 5 surgical, 4 other treatment, 5 patient management, 6 outcome) were included in the final set, which can be applied as a tool for internal quality improvement, comparative quality reporting, public reporting and research in care.
- A multicenter study analysed patients undergoing surgery in 23 international expert centres and proposed outcome benchmarks that may provide comparisons between patient cohorts, centres, countries, and surgical techniques.[161]
- The German Society for General and Visceral Surgery (DGAV) has established a national registry for quality control, risk assessment and outcomes research in pancreatic surgery in Germany (DGAV SuDoQ|Pancreas).[162] It has been used, for example, to examine the impact of preoperative biliary stenting, a controversial procedure.[163]
- A group in Germany has created an evidence map of pancreatic surgery, recognising that it is a large and complex field of research. It aims to create a systematic and living evidence map of surgery (https://www.evidencemap.surgery).[164]

- The European Consortium of Minimally Invasive Pancreatic Surgery (E-MIPS) is setting up a European registry on MIPS with the European-African Hepato-Pancreato-Biliary Association (E-AHPBA).[165]
- Two projects in England are a 'bridging' clinic that offers supportive care between diagnosis and main treatments,[40] and a nurse-led, rapid-access pathway for diagnosing pancreatic cancer.[166]

6.3 Education and training

- It is essential that each pancreatic cancer centre provides professional clinical and scientific education on the disease and that at least one person is responsible for this programme. Healthcare professionals working in pancreatic cancer must also receive training in psychosocial oncology, palliative care, rehabilitation and communication skills. Such training must also be incorporated into specialist postgraduate and undergraduate curriculums for physicians, nurses and other professionals.
- Expert training and accreditation in procedures including endoscopy and surgery are vital to give professionals the skills and confidence to carry out complex operations and improve patient care. There is a need for more accreditation centres and training programmes in Europe and globally.
- An expert group on cancer control at the European Commission has endorsed a recommendation for multidisciplinary training of cancer specialists to improve the value of MDTs and patient care.[167]
- The ERQCC expert group highlights the importance of European training standards in medical oncology, available from ESMO and the European Union of Medical Specialists (UEMS).

6.4 Clinical research and registries

- Centres treating pancreatic cancer must have clinical research programmes (either their own research or as a participant in programmes led by other centres). The research portfolio should have both interventional and non-interventional projects and include academic research. The MDT must assess all new patients for eligibility to take part in academic and industry sponsored clinical trials at the centre or in research networks.
- The German Cancer Society specifies a minimum accrual rate for clinical trials of 5% and the OECI requirement for CCCs is >10%. The ERQCC expert group considers that the 5% target is an important recommendation for all pancreatic cancer units.
- Collaboration with European academic networks is strongly recommended – see the European Study Group for Pancreatic Cancer (ESPAC), International Study Group of Pancreatic Surgery (ISGPS), gastrointestinal cancer group of the European Organisation for Research and Treatment of Cancer (EORTC – http://www.eortc.org), and the European Clinical Research Infrastructure Network (ECRIN – http://www.ecrin.org). Correlative biomarker research is a crucial part of all phases of clinical studies, and requires close cooperation with biobanks such as in EORTC's SPECTA programme (http://www.eortc.org/specta).
- In countries where clinical trials are less available, centres treating pancreatic cancer should engage with policymakers to investigate referring patients to other countries (as

proposed with European Reference Networks) and should be prepared to participate in clinical trials from an organisational standpoint. Researchers at other centres should be considered as part of the extended MDT for at least annual discussion of clinical trial participation. Generally, pan-European action should be taken to increase participation of pancreatic cancer patients in clinical trials (both industry-sponsored and academic), and internet access to local clinical trial databases should be developed.

- Older adults are currently underrepresented in pancreatic cancer clinical trials.[168] Inclusion of older patients in clinical trials and proper assessment (e.g. G-CODE)[169] must be encouraged.
- Cancer control plans must include high-quality cancer population and specialist registries to inform clinical research and to improve the quality of care. A population example is Nordcan (http://www-dep.iarc.fr/NORDCAN), which includes pancreatic cancer in 50 cancer types in the Nordic countries. Pancreatic cancer examples (apart from surgical examples noted in section 6.2.4) include:
  - PancreOS – a proposed project, supported by Pancreatic Cancer Europe, to develop a pan-European hospital-based registry. A European Parliament event on 18 November 2020 set out the challenges of this project (see https://youtu.be/nq-sgO3tO6g)
  - European Registry of Hereditary Pancreatitis and Familial Pancreatic Cancer (EUROPAC) – a collaborative study involving pancreas specialists from around Europe. https://bit.ly/2n4ssq4
  - TPK – a pancreatic tumour registry in Germany from which a variety of studies have been published, such as on nutrition in patients with advanced disease, patient reported outcomes, and treatments. See the publications list at https://www.iomedico.com
  - Precision-Panc – a research platform founded in 2017 in the UK that is networking hospitals treating pancreatic cancer to research treatments for patients not eligible for surgery. https://www.precisionpanc.org

7 Conclusion

Taken together, the information presented in this paper provides a description of organisational requirements for establishing a high-quality pancreatic cancer service. The ERQCC expert group is aware that it is not possible to propose a 'one size fits all' system for all countries, but urges that access to MDTs and specialised treatments is guaranteed to all patients with pancreatic cancer.

[1] Højgaard, L., Löwenberg, B., Selby, P., Lawler, M., Banks, I., Law, K., et al., 2017. The European Cancer Patient's Bill of Rights, update and implementation 2016. ESMO Open 1 (6), e000127. https://doi.org/10.1136/esmoopen-2016-000127.

[2] Albreht, T., Kiasuma, R., Van den Bulcke, M., 2017. Cancon Guide – Improving cancer control coordination. https://cancercontrol.eu/archived/cancercontrol.eu/guide-landing-page/index.html.

[3] Prades, J., Remue, E., van Hoof, E., Borràs, J.M., 2015. Is it worth re-organising cancer services on the basis of multidisciplinary teams (MDTs)? A systematic review of the objectives and organisation of MDTs and their impact on patient outcomes. Health Policy 119 (4), 464–474. http://dx.doi.org/10.1016/j.healthpol.2014.09.006.

[4] Borràs, J.M., Albreht, T., Audisio, R., Briers, E., Casali, P., Esperou, H., et al., 2014. Policy statement on multidisciplinary cancer care. Eur. J. Cancer 50 (3), 475–480. https://doi.org/10.1016/j.ejca.2013.11.012.

[5] Cardoso, F., Cataliotti, L., Costa, A., Knox, S., Marotti, L., Rutgers, E., et al., 2017. European Breast Cancer Conference manifesto on breast centres/units. Eur. J. Cancer 72, 244–250. http://dx.doi.org/10.1016/j.ejca.2016.10.023.

[6] Borràs, J.M., Prades, J., Coll, C., 2020. Consensus recommendations for pancreatic cancer care: the Bratislava statement. https://bit.ly/3lM1jR2.

[7] Borràs, J.M., Prades, J., Coll, C., 2020. Report with recommendations for improving access to expert clinicians in reference hospitals concerning patients' diagnosis and treatment of pancreatic cancer, and its potential impact on outcomes. https://bit.ly/311dPEQ.

[8] European Cancer Information System. https://ecis.jrc.ec.europa.eu/index.php.

[9] Ferlay, J., Colombet, M., Soerjomataram, I., Dyba, T., Randi, G., Bettio, M., et al., 2018. Cancer incidence and mortality patterns in Europe: estimates for 40 countries and 25 major cancers in 2018. Eur. J. Cancer 103, 356–387. https://doi.org/10.1016/j.ejca.2018.07.005.

[10] Lepage, C., Capocaccia, R., Hackl, M., Lemmens, V., Molina, E., Pierannunzio, D., et al., 2015. Survival in patients with primary liver cancer, gallbladder and extrahepatic biliary tract cancer and pancreatic cancer in Europe 1999-2007: results of EUROCARE-5. Eur. J. Cancer 51 (15), 2169–2178. https://doi.org/10.1016/j.ejca.2015.07.034.

[11] United European Gastroenterology, 2019. Pancreatic cancer across Europe. Taking a united stand. https://bit.ly/39JU9KO.

[12] Carrato, A., Falcone, A., Ducreux, M., Valle, J.W., Parnaby, A., Djazouli, K., et al., 2015. A systematic review of the burden of pancreatic cancer in Europe: real-world impact on survival, quality of life and costs. J. Gastrointest. Cancer 46 (3), 201–211. https://doi.org/10.1007/s12029-015-9724-1.

[13] Ferlay, J., Partensky, C., Bray, F., 2016. More deaths from pancreatic cancer than breast cancer in the EU by 2017. Acta Oncol. 55 (9–10), 1158–1160. https://doi.org/10.1080/0284186X.2016.1197419.

[14] Rahib, L., Smith, B.D., Aizenberg, R., Rosenzweig, A.B., Fleshman, J.M., Matrisian, L.M., 2014. Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. Cancer Res. 74 (11), 2913–2921. https://doi.org/10.1158/0008-5472.CAN-14-0155.

[15] McGuigan, A., Kelly, P., Turkington, R.C., Jones, C., Coleman, H.G., McCain, R.S., 2018. Pancreatic cancer: a review of clinical diagnosis, epidemiology, treatment and outcomes. World J. Gastroenterol. 24 (43), 4846–4861. https://doi.org/10.3748/wjg.v24.i43.4846.

[16] Permuth-Wey, J., Egan, K.M., 2009. Family history is a significant risk factor for pancreatic cancer: results from a systematic review and meta-analysis. Fam. Cancer. 8 (2), 109–117. https://doi.org/10.1007/s10689-008-9214-8.

[17] Ducreux, M., Cuhna, A.S., Caramella, C., Hollebecque, A., Burtin, P., Goéré, D., et al., 2015. Cancer of the pancreas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann. Oncol. 26 Suppl 5, v56–68. https://doi.org/10.1093/annonc/mdv295.

[18] Grossberg, A.J., Chu, L.C., Deig, C.R., Fishman, E.K., Hwang, W.L., Maitra, A., et al., 2020. Multidisciplinary standards of care and recent progress in pancreatic ductal adenocarcinoma. CA Cancer J. Clin. 70, 375–403. https://doi.org/10.3322/caac.21626.

[19] Taieb J, Abdallah R., 2020. How I treat pancreatic cancer. ESMO Open 4 (Suppl 2), e000818. https://doi.org/10.1136/esmoopen-2020-000818.

[20] Hidalgo, M., 2010. Pancreatic cancer. N. Engl. J. Med. 362 (17), 1605–1617. https://doi.org/10.1056/NEJMra0901557.

[21] Willett, C.G., Czito, B.G., Bendell, J.C., Ryan, D.P., 2005. Locally advanced pancreatic cancer. J. Clin. Oncol. 23 (20), 4538–4544. https://doi.org/10.1200/JCO.2005.23.911.

22 Neoptolemos, J.P., Palmer, D.H., Ghaneh, P., Psarelli, E.E., Valle, J.W., Halloran, C.M., et al., 2017. Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomised, phase 3 trial. Lancet 389 (10073), 1011–1024. https://doi.org/10.1016/S0140-6736(16)32409-6.

[23] Conroy, T., Hammel, P., Hebbar, M., Ben Abdelghani, M., Wei, A.C., Raoul, J.L., et al., 2018. FOLFIRINOX or gemcitabine as adjuvant therapy for pancreatic cancer. N. Engl. J. Med. 379 (25), 2395–2406. https://doi.org/10.1056/NEJMoa1809775.

[24] Murphy, J.E., Wo, J.Y., Ryan, D.P., Jiang, W., Yeap, B.Y., Drapek, L.C., et al., 2018. Total neoadjuvant therapy with FOLFIRINOX followed by individualized chemoradiotherapy for borderline resectable pancreatic adenocarcinoma: a phase 2 clinical trial. JAMA Oncol. 4 (7), 963–969. https://doi.org/10.1001/jamaoncol.2018.0329.

[25] Janssen, Q.P., Buettner, S., Suker, M., Beumer, B.R., Addeo, P., Bachellier, P., et al., 2019. Neoadjuvant FOLFIRINOX in patients with borderline resectable pancreatic cancer: a systematic review and patient-level meta-analysis. J. Natl. Cancer Inst. 111 (8), 782–794. https://doi.org/10.1093/jnci/djz073.

[26] Okusaka, T., Nakamura, M., Yoshida, M., Kitano, M., Uesaka, K., Ito, Y., et al., 2020. Clinical practice guidelines for pancreatic cancer 2019 from the Japan Pancreas Society: a synopsis. Pancreas 49 (3), 326–335. https://doi.org/10.1097/mpa.0000000000001513.

[27] Conroy, T., Desseigne, F., Ychou, M., Bouché, O., Guimbaud, R., Bécouarn, Y., et al., 2011. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. N. Engl. J. Med. 364 (19), 1817–1825. https://doi.org/10.1056/NEJMoa1011923.

[28] Von Hoff, D.D., Ervin, T., Arena, F.P., Chiorean, E.G., Infante, J., Moore, M., et al., 2013. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. N. Engl. J. Med. 369 (18), 1691–1703. https://doi.org/10.1056/NEJMoa1304369.

[29] Suker, M., Beumer, B.R., Sadot, E., Marthey, L., Faris, J.E., Mellon, E.A., et al., 2016. FOLFIRINOX for locally advanced pancreatic cancer: a systematic review and patient-level meta-analysis. Lancet Oncol. 17 (6), 801–810. https://doi.org/10.1016/S1470-2045(16)00172-8.

30 Naudin, S., Viallon, V., Hashim, D., Freisling, H., Jenab, M., Weiderpass, E., et al., 2019. Healthy lifestyle and the risk of pancreatic cancer in the EPIC study. Eur. J. Epidemiol. 35, 975–986. https://doi.org/10.1007/s10654-019-00559-6.

[31] Schmidt-Hansen, M., Berendse, S., Hamilton, W., 2016. Symptoms of pancreatic cancer in primary care: a systematic review. Pancreas 45 (6), 814–818. https://doi.org/10.1097/MPA.0000000000000527.

[32] National Cancer Registration and Analysis Service, 2017. Routes to diagnosis 2006-2015. http://www.ncin.org.uk/publications/routes_to_diagnosis.

[33] Zhang, L., Sanagapalli, S., Stoita, A., 2018. Challenges in diagnosis of pancreatic cancer. World J. Gastroenterol. 24 (19), 2047–2060. https://dx.doi.org/10.3748%2Fwjg.v24.i19.2047.

[34] Eloubeidi, M.A., Jhala, D., Chhieng, D.C., Chen, V.K., Eltoum, I., Vickers, S., et al., 2003. Yield of endoscopic ultrasound-guided fine-needle aspiration biopsy in patients with suspected pancreatic carcinoma. Cancer 99 (5), 285–292. https://doi.org/10.1002/cncr.11643.

[35] Soloff, E.V., Zaheer, A., Meier, J., Zins, M., Tamm, E.P., 2018. Staging of pancreatic cancer: resectable, borderline resectable, and unresectable disease. Abdom. Radiol. (NY) 43 (2), 301–313. https://doi.org/10.1007/s00261-017-1410-2.

[36] Isaji , S., Mizuno, S., Windsor, J.A., Bassi, C., Fernández-Del Castillo, C., Hackert, T., et al., 2018. International consensus on definition and criteria of borderline resectable pancreatic ductal adenocarcinoma 2017. Pancreatology 18 (1), 2–11. https://doi.org/10.1016/j.pan.2017.11.011.

[37] Kirkegård, J., Aahlin, E.K., Al-Saiddi, M., Bratlie, S.O., Coolsen, M., de Haas, R.J., et al., 2019. Multicentre study of multidisciplinary team assessment of pancreatic cancer resectability and treatment allocation. Br. J. Surg. 106 (6), 756–764. https://doi.org/10.1002/bjs.11093.

[38] Polonski, A., Izbicki, J.R., Uzunoglu, F.G., 2019. Centralization of pancreatic surgery in Europe. J. Gastrointest. Surg. 23 (10), 2081–2092. https://doi.org/10.1007/s11605-019-04215-y.

[39] Jaap, K., Fluck, M., Hunsinger, M., Wild, J., Arora, T., Shabahang, M., et al., 2018. Analyzing the impact of compliance with national guidelines for pancreatic cancer care using the National Cancer Database. J. Gastrointest. Surg. 22 (8), 1358–1364. https://doi.org/10.1007/s11605-018-3742-9.

[40] Sreedharan, L., Kumar, B., Jewell, A., Banim, P., Koulouris, A., Hart, A.R., 2019. Bridging clinic: the initial medical management of patients with newly diagnosed pancreatic cancer. Frontline Gastroenterol. 10 (3), 261–268. https://doi.org/10.1136/flgastro-2018-101002.

[41] Weniger, M., Miksch, R.C., Maisonneuve, P., Werner, J., D'Haese, J.G., 2020. Improvement of survival after surgical resection of pancreatic cancer independent of adjuvant chemotherapy in the past two decades – a meta-regression. Eur. J. Surg. Oncol. 46 (8), 1516–1523. https://doi.org/10.1016/j.ejso.2020.02.016.

[42] Klaiber, U., Hackert, T., Neoptolemos, J.P., 2019. Adjuvant treatment for pancreatic cancer. Transl. Gastroenterol. Hepatol. 4, 27. https://doi.org/10.21037/tgh.2019.04.04.

[43] Huang, L., Jansen, L., Balavarca, Y., Molina-Montes, E., Babaei, M., van der Geest, L., et al., 2019. Resection of pancreatic cancer in Europe and USA: an international large-scale study highlighting large variations. Gut 68 (1), 130–139. 10.1136/gutjnl-2017-314828.

44 Mavros, M.N., Coburn, N.G., Davis, L.E., Mahar, A.L., Liu, Y., Beyfuss, K., et al., 2019. Low rates of specialized cancer consultation and cancer-directed therapy for noncurable pancreatic adenocarcinoma: a population-based analysis. CMAJ 191 (21), E574–E580. https://doi.org/10.1503/cmaj.190211.

[45] Abdel-Rahman, O., Xu, Y., Tang, P.A., Lee-Ying, R.M., Cheung, W.Y., 2018. A real-world, population-based study of patterns of referral, treatment, and outcomes for advanced pancreatic cancer. Cancer Med. 7 (12), 6385–6392. https://doi.org/10.1002/cam4.1841.

[46] Zijlstra, M., van der Geest, L.G.M., van Laarhoven, H.W.M., Lemmens, V.E.P.P., van de Poll-Franse, L.V., Raijmakers, N.J.H., 2018. Patient characteristics and treatment considerations in pancreatic cancer: a population based study in the Netherlands. Acta Oncol. 57 (9), 1185–1191. https://doi.org/10.1080/0284186X.2018.1470330.

[47] Scott, E., Jewell, A., 2019. Supportive care needs of people with pancreatic cancer: a literature review. Cancer Nurs. Pract. 10 January. https://doi.org/10.7748/cnp.2019.e1566.

[48] Mueller, T.C., Burmeister, M.A., Bachmann, J., Martignoni, M.E., 2014. Cachexia and pancreatic cancer: are there treatment options? World J. Gastroenterol. 20 (28), 9361–9373. https://doi.org/10.3748/wjg.v20.i28.9361.

[49] Koulouris, A.I., Banim, P., Hart, A.R., 2017. Pain in patients with pancreatic cancer: prevalence, mechanisms, management and future developments. Dig. Dis. Sci. 62 (4), 861–870. https://doi.org/10.1007/s10620-017-4488-z.

[50] Bhattacharya, P., Dessain, S.K., Evans, T.L., 2018. Palliative care in lung cancer: when to start. Curr. Oncol. Rep. 20 (11), 90. https://doi.org/10.1007/s11912-018-0731-9.

[51] Temel, J.S., Greer, J.A., El-Jawahri, A., Pirl, W.F., Park, E.R., Jackson, V.A., et al., 2017. Effects of early integrated palliative care in patients with lung and GI cancer: a randomized clinical trial. J. Clin. Oncol. 35 (8), 834–841. 10.1200/JCO.2016.70.5046.

[52] Hu, C., Hart, S.N., Polley, E.C., Gnanaolivu, R., Shimelis, H., Lee, K.Y., et al., Association between inherited germline mutations in cancer predisposition genes and risk of pancreatic cancer. JAMA 319 (23), 2401–2409. https://doi.org/10.1001/jama.2018.6228.

[53] Lorenzo, D., Rebours, V., Maire, F., Palazzo, M., Gonzalez, J.M., Vullierme, M.P., et al., 2019. Role of endoscopic ultrasound in the screening and follow-up of high-risk individuals for familial pancreatic cancer. World J. Gastroenterol. 25 (34), 5082–5096. https://doi.org/10.3748/wjg.v25.i34.5082.

[54] Rutgers, E., Balmana, J., Beishon, M., Benn, K., Evans, D.G., Mansel, R., et al., 2019. European Breast Cancer Council manifesto 2018: genetic risk prediction testing in breast cancer. Eur. J. Cancer 106, 45–53. https://doi.org/10.1016/j.ejca.2018.09.019.

[55] Cherny, N., Sullivan, R., Torode, J., Saar, M., Eniu, A., 2016. ESMO European Consortium Study on the availability, out-of-pocket costs and accessibility of antineoplastic medicines in Europe. Ann. Oncol. 27 (8), 1423–1443. https://doi.org/10.1093/annonc/mdw213.

[56] Lievens, Y., Borràs, J.M., Grau, C., 2020. Provision and use of radiotherapy in Europe. Mol. Oncol. 14 (7), 1461–1469. https://doi.org/10.1002/1878-0261.12690.

[57] Grau, C., Defourny, N., Malicki, J., Dunscombe, P., Borras, J.M., Coffey, M., et al., 2014. Radiotherapy equipment and departments in the European countries: final results from the ESTRO-HERO survey. Radiother. Oncol. 112 (2), 155–164. https://doi.org/10.1016/j.radonc.2014.08.029.

[58] Pancreatic Cancer Europe, 2018. Pancreatic cancer inequality report. https://bit.ly/2JTbOFi.

[59] Xie, H., Liu, J., Yin, J., Ogden, J.R., Mahipal, A., McWilliams, R.R., et al., 2020. Role of surgery and perioperative therapy in older patients with resectable pancreatic ductal adenocarcinoma. Oncologist 25 (11), e1681–e1690. https://doi.org/10.1634/theoncologist.2020-0086.

[60] van Roest, M.H., van der Aa, M.A., van der Geest, L.G., de Jong, K.P., 2016. The impact of socioeconomic status, surgical resection and type of hospital on survival in patients with pancreatic cancer. A population-based study in the Netherlands. PLoS One 11 (11), e0166449. https://doi.org/10.1371/journal.pone.0166449.

[61] Pancreatic Cancer Europe, 2017. Pancreatic cancer research in Europe. Multistakeholder brainstorming meeting. 12 April. https://bit.ly/37L81BV.

[62] Zhu, H., Li, T., Du, Y., Li, M., 2018. Pancreatic cancer: challenges and opportunities. BMC Med. *1*6, 214. https://doi.org/10.1186/s12916-018-1215-3.

[63] Singhi, A.D., Koay, E.J., Chari, S.T., Maitra, A., 2019. Early detection of pancreatic cancer: opportunities and challenges. Gastroenterology 156 (7), 2024–2040. https://doi.org/10.1053/j.gastro.2019.01.259.

[64] Orth, M., Metzger, P., Gerum, S., Mayerle, J., Schneider, G., Belka, C., et al., 2019. Pancreatic ductal adenocarcinoma: biological hallmarks, current status, and future perspectives of combined modality treatment approaches. Radiat. Oncol. 14 (1), 141. https://doi.org/10.1186/s13014-019-1345-6.

65 United European Gastroenterology, 2018. Pancreatic cancer death rates rising across Europe, report reveals. Press release, 15 November. https://bit.ly/33RWUGa.

[66] Forsea, A.M., 2016. Cancer registries in Europe – going forward is the only option. Ecancermedicalscience 10, 641. https://doi.org/10.3332/ecancer.2016.641.

[67] Siesling, S., Louwman, W.J., Kwast, A., van den Hurk, C., O'Callaghan. M., Rosso, S., et al., 2015. Uses of cancer registries for public health and clinical research in Europe: Results of the European Network of Cancer Registries survey among 161 population-based cancer registries during 2010-2012. Eur. J. Cancer 51 (9), 1039–1049. https://doi.org/10.1016/j.ejca.2014.07.016.

[68] National Institute for Health and Care Excellence. Pancreatic cancer overview. https://pathways.nice.org.uk/pathways/pancreatic-cancer.

[69] Cancer Council Victoria, 2016. Optimal care pathway for people with pancreatic cancer. https://bit.ly/33R0Tmt.

[70] Marchegiani, G., Andrianello, S., Perri, G., Secchettin, E., Maggino, L., Malleo, G., et al., 2018. Does the surgical waiting list affect pathological and survival outcome in resectable pancreatic ductal adenocarcinoma? HPB (Oxford) 20 (5), 411–417. https://doi.org/10.1016/j.hpb.2017.10.017.

[71] Seo, H.K., Hwang, D.W., Park, S.Y., Park, Y., Lee, S.J., Lee, J.H., et al., 2018. The survival impact of surgical waiting time in patients with resectable pancreatic head cancer. Ann. Hepatobiliary Pancreat. Surg. 22 (4), 405–411. https://doi.org/10.14701/ahbps.2018.22.4.405.

[72] National Institute for Health and Care Excellence, 2018. Pancreatic cancer in adults: diagnosis and management. NICE guideline [NG85]. https://www.nice.org.uk/guidance/ng85.

[73] van der Geest, L.G., van Rijssen, L.B., Molenaar, I.Q., de Hingh, I.H., Groot Koerkamp, B., Busch, O.R., et al., 2016. Volume-outcome relationships in pancreatoduodenectomy for cancer. HPB (Oxford) 18 (4), 317–324.

[74] Mamidanna, R., Ni, Z., Anderson, O., Spiegelhalter, S.D., Bottle, A., Aylin, P., Faiz, O., et al., 2016. Surgeon volume and cancer esophagectomy, gastrectomy, and pancreatectomy: a population-based study in England. Ann. Surg. 263 (4), 727–732. https://doi.org/10.1097/SLA.0000000000001490.

[75] Ahola, R., Sand, J., Laukkarinen, J., 2020. Centralization of pancreatic surgery improves results: review. Scand. J. Surg. 109 (1), 4–10. https://doi.org/10.1177/1457496919900411.

[76] Faraj, W., Mukherji, D., Zaghal, A.M., Nassar, H., Mokadem, F.H., Jabbour, S., et al., 2019. Perioperative management of pancreaticoduodenectomy: avoiding admission to the intensive care unit. Gastrointest. Tumors 6 (3-4), 108–115. https://doi.org/10.1159/000502887.

[77] van Rijssen, L.B., Zwart, M.J., van Dieren, S., de Rooij, T., Bonsing, B.A., Bosscha K., et al., 2018. Variation in hospital mortality after pancreatoduodenectomy is related to failure to rescue rather than major complications: a nationwide audit. HPB (Oxford) 20 (8), 759–767. https://doi.org/10.1016/j.hpb.2018.02.640.

[78] Enestvedt, C.K., Diggs, B.S., Cassera, M.A., Hammill, C., Hansen, P.D., Wolf, R.F., 2012. Complications nearly double the cost of care after pancreaticoduodenectomy. Am. J. Surg. 204 (3), 332–338. https://doi.org/10.1016/j.amjsurg.2011.10.019.

[79] Williamsson, C., Ansari, D., Andersson, R., Tingstedt, B., 2017. Postoperative pancreatic fistula-impact on outcome, hospital cost and effects of centralization. HPB (Oxford) 19 (5), 436–442. https://doi.org/10.1016/j.hpb.2017.01.004.

[80] Pawlik, T.M., Laheru, D., Hruban, R.H., Coleman, J., Wolfgang, C.L., Campbell, K., et al., 2008. Evaluating the impact of a single-day multidisciplinary clinic on the management of pancreatic cancer. Ann. Surg. Oncol. 15 (8), 2081–2088. https://doi.org/10.1245/s10434-008-9929-7.

[81] Basta, Y.L., Baur, O.L., van Dieren, S., Klinkenbijl, J.H., Fockens, P., Tytgat, K.M., 2016. Is there a benefit of multidisciplinary cancer team meetings for patients with gastrointestinal malignancies? Ann. Surg. Oncol. 23 (8), 2430–2437. 10.1245/s10434-016-5178-3.

[82] Basta, Y.L., Bolle, S., Fockens, P., Tytgat, K.M.A.J., 2017. The value of multidisciplinary team meetings for patients with gastrointestinal malignancies: a systematic review. Ann. Surg. Oncol. 24 (9), 2669–2678. 10.1245/s10434-017-5833-3.

[83] Hansen, M.F.C., Storkholm, J.H., Hansen, C.P., 2020. The results of pancreatic operations after the implementation of multidisciplinary team conference (MDT): a quality improvement study. Int. J. Surg. 77, 105–110. https://doi.org/10.1016/j.ijsu.2020.03.045.

[84] SONCOS, 2017. Standardisation of Multidisciplinary Care in the Netherlands. SONCOS Standardisation Report 5. https://bit.ly/33RXdki.

[85] Belgian Health Care Knowledge Centre, 2014. Cancers of the pancreas. Preferred model of care and criteria for reference centres. KCE report 219 addendum. https://bit.ly/2W6Rbry.

[86] De Schutter, H., Silversmit, G., Haustermans, K., Van Eycken, L., 2018. Relation between center volumes for pancreatic and esophageal cancer surgeries and outcome in Belgium: a plea for centralization. Ann. Oncol. 29 Suppl 8, viii562. https://doi.org/10.1093/annonc/mdy297.001.

[87] Balzano, G., Guarneri, G., Pecorelli, N., Paiella, S., Rancoita, P.M.V., Bassi, C., et al., 2020. Modelling centralization of pancreatic surgery in a nationwide analysis. Br. J. Surg. 107 (11), 1510–1519. https://doi.org/10.1002/bjs.11716.

[88] Polkowski, M., Jenssen, C., Kaye, P., Carrara, S., Deprez, P., Gines, A., et al., 2017. Technical aspects of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline – March 2017. Endoscopy 49 (10), 989–1006. https://doi.org/10.1055/s-0043-119219.

[89] Banafea, O., Mghanga, F.P., Zhao, J., Zhao, R., Zhu, L., 2016. Endoscopic ultrasonography with fine-needle aspiration for histological diagnosis of solid pancreatic masses: a meta-analysis of diagnostic accuracy studies. BMC Gastroenterol. 16 (1), 108. https://doi.org/10.1186/s12876-016-0519-z.

[90] Hébert-Magee, S., Bae, S., Varadarajulu, S., Ramesh, J., Frost, A.R., Eloubeidi, M.A., et al., 2013. The presence of a cytopathologist increases the diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration cytology for pancreatic adenocarcinoma: a meta-analysis. Cytopathology 24 (3), 159–171. https://doi.org/10.1111/cyt.12071.

[91] Pitman, M.B., Layfield, L.J., 2014. Guidelines for pancreaticobiliary cytology from the Papanicolaou Society of Cytopathology: a review. Cancer Cytopathol. 122 (6), 399–411. https://doi.org/10.1002/cncy.21427.

[92] Kakar, S., Shi, C., Adsay, N.V., Fitzgibbons, P., Frankel, W.L., Klimstra, D.S., et al., 2017. Protocol for the examination of specimens from patients with carcinoma of the pancreas. College of American Pathologists. https://capatholo.gy/3mVMjBm.

[93] Zins, M., Matos, C., Cassinotto, C., 2018. Pancreatic adenocarcinoma staging in the era of preoperative chemotherapy and radiation therapy. Radiology 287 (2), 374–390. https://doi.org/10.1148/radiol.2018171670.

[94] Brennan, D.D., Zamboni, G.A., Raptopoulos, V.D., Kruskal, J.B., 2007. Comprehensive preoperative assessment of pancreatic adenocarcinoma with 64-section volumetric CT. Radiographics 27 (6), 1653–1666. https://doi.org/10.1148/rg.276075034.

[95] Bowman, A.W., Bolan, C.W., 2019. MRI evaluation of pancreatic ductal adenocarcinoma: diagnosis, mimics, and staging. Abdom. Radiol. (NY) 44 (3), 936–949. https://doi.org/10.1007/s00261-018-1686-x.

[96] Kim, H.J., Park, M.S., Lee, J.Y., Han, K., Chung, Y.E., Choi, J.Y. et al., 2019. Incremental role of pancreatic magnetic resonance imaging after staging computed tomography to evaluate patients with pancreatic ductal adenocarcinoma. Cancer Res. Treat. 51 (1), 24–33. https://doi.org/10.4143/crt.2017.404.

[97] Marion-Audibert, A.M., Vullierme, M.P., Ronot, M., Mabrut, J.Y., Sauvanet, A., Zins, M. et al., 2018. Routine MRI with DWI sequences to detect liver metastases in patients with potentially resectable pancreatic ductal carcinoma and normal liver CT: a prospective multicenter study. AJR Am. J. Roentgenol. 211 (5), W217–W225. https://doi.org/10.2214/AJR.18.19640.

[98] Ito, T., Sugiura, T., Okamura, Y., Yamamoto, Y., Ashida, R., Aramaki, T, et al. 2017. The diagnostic advantage of EOB-MR imaging over CT in the detection of liver metastasis in patients with potentially resectable pancreatic cancer. Pancreatology 17 (3), 451–456. https://doi.org/10.1016/j.pan.2017.03.001.

[99] Marin, D., Nelson, R.C., Barnhart, H., Schindera, S.T., Ho, L.M., Jaffe, T.A. et al., 2010. Detection of pancreatic tumors, image quality, and radiation dose during the pancreatic parenchymal phase: effect of a low-tube-voltage, high-tube-current CT technique – preliminary results. Radiology 256 (2), 450–459. https://doi.org/10.1148/radiol.10091819.

[100] Jha, P., Yeh, B.M., Zagoria, R., Collisson, E., Wang, Z.J., 2018. The role of MR imaging in pancreatic cancer. Magn. Reson. Imaging Clin. N. Am. 26 (3), 363–373. https://doi.org/10.1016/j.mric.2018.03.004.

[101] Khalsa, B.S., Imagawa, D.K., Chen, J.I., Dermirjian, A.N., Yim, D.B., Findeiss, L.K., 2015. Evolution in the treatment of delayed postpancreatectomy hemorrhage: surgery to interventional radiology. Pancreas 44 (6), 953–958. https://doi.org/10.1097/mpa.0000000000000347.

[102] Boellaard, R., Delgado-Bolton, R., Oyen, W.J., Giammarile, F., Tatsch, K., Eschner, W., et al., 2015. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. Eur. J. Nucl. Med. Mol. Imaging 42 (2), 328–354. https://doi.org/10.1007/s00259-014-2961-x.

[103] National Comprehensive Cancer Network (NCCN). NCCN Guidelines for Pancreatic Adenocarcinoma. https://www.nccn.org/professionals/physician_gls/default.aspx.

[104] Qayyum, A., Tamm, E.P., Kamel, I.R., Allen, P.J., Arif-Tiwari, H., Chernyak, V., et al., 2017. ACR Appropriateness Criteria staging of pancreatic ductal adenocarcinoma. J. Am. Coll. Radiol. 14 (11S), S560–S569. https://doi.org/10.1016/j.jacr.2017.08.050.

[105] Daamen, L.A., Groot, V.P., Goense, L., Wessels, F.J., Borel Rinkes, I.H., Intven, M.P.W., et al., 2018. The diagnostic performance of CT versus FDG PET-CT for the detection of recurrent pancreatic cancer: a systematic review and meta-analysis. Eur. J. Radiol. 106, 128–136. 10.1016/j.ejrad.2018.07.010.

[106] Clancy, T.E., 2015. Surgery for pancreatic cancer. Hematol. Oncol. Clin. North Am. 29 (4), 701–716. https://doi.org/10.1016/j.hoc.2015.04.001.

[107] Maggino, L., Vollmer, C.M. Jr, 2017. Recent advances in pancreatic cancer surgery. Curr. Treat. Options Gastroenterol. 15 (4), 520–537. https://doi.org/10.1007/s11938-017-0150-2.

[108] Oettle, H., Neuhaus, P., Hochhaus, A., Hartmann, J.T., Gellert, K., Ridwelski, K., et al., 2013. Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial. JAMA 310 (14), 1473–1481. https://doi.org/10.1001/jama.2013.279201.

[109] Burris, H.A. 3rd, Moore, M.J., Andersen, J., Green, M.R., Rothenberg, M.L., Modiano, M.R., et al., 1997. Improvements in survival and clinical benefit with gemcitabine as first-line therapy for patients with advanced pancreas cancer: a randomized trial. J. Clin. Oncol. 15 (6), 2403–2413. https://doi.org/10.1200/jco.1997.15.6.2403.

[110] Huguet, F., André, T., Hammel, P., Artru, P., Balosso, J., Selle, F.,et al., 2007. Impact of chemoradiotherapy after disease control with chemotherapy in locally advanced pancreatic adenocarcinoma in GERCOR phase II and III studies. J. Clin. Oncol. 25 (3), 326–331. https://doi.org/10.1200/jco.2006.07.5663.

[111] Versteijne, E., Suker, M., Groothuis, K., Akkermans-Vogelaar, J.M., Besselink, M.G., Bonsing, B.A., et al., 2020. Preoperative chemoradiotherapy versus immediate surgery for resectable and borderline resectable pancreatic cancer: results of the Dutch randomized phase III PREOPANC trial. J. Clin. Oncol. 38 (16), 1763–1773. https://doi.org/10.1200/jco.19.02274.

[112] Rwigema, J.C., Parikh, S.D., Heron, D.E., Howell, M., Zeh, H., Moser, A.J., et al., 2011. Stereotactic body radiotherapy in the treatment of advanced adenocarcinoma of the pancreas. Am. J. Clin. Oncol. 34 (1), 63–69. https://doi.org/10.1097/coc.0b013e3181d270b4.

[113] Palta, M., Godfrey, D., Goodman, K.A., Hoffe, S., Dawson, L.A., Dessert, D., et al., 2019. Radiation therapy for pancreatic cancer: executive summary of an ASTRO clinical practice guideline. Pract. Radiat. Oncol. 9 (5), 322–332. https://doi.org/10.1016/j.prro.2019.06.016.

[114] Brunner, T.B., Haustermans, K., Huguet, F., Morganti, A.G., Mukherjee, S., Belka, C., et al., 2020. ESTRO ACROP guidelines for target volume definition in pancreatic cancer. Radiother. Oncol. 154, 60–69. https://doi.org/10.1016/j.radonc.2020.07.052.

[115] Green, L.M., 2015. Meeting the complex needs of patients with pancreatic cancer. Oncol. Nurs. News 10 April. https://bit.ly/3aPprgL.

[116] Mohammed, S., Savage, P., Kevork, N., Swami, N., Rodin, G., Zimmermann, C., 2020. 'I'm going to push this door open. You can close it': a qualitative study of the brokering work of oncology clinic nurses in introducing early palliative care. Palliat. Med. 34 (2), 209–218. https://doi.org/10.1177/0269216319883980.

[117] European Oncology Nursing Society (EONS), 2018. EONS Cancer Nursing Education Framework. https://bit.ly/33QHhPF.

[118] Lassen, K., Coolsen, M.M., Slim, K., Carli, F., de Aguilar-Nascimento, J.E., Schäfer, M., et al., 2012. Guidelines for perioperative care for pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS) Society recommendations. Clin. Nutr. 31 (6), 817–830. https://doi.org/10.1016/j.clnu.2012.08.011.

[119] Bouvier, A.M., Uhry, Z., Jooste, V., Drouillard, A., Remontet, L., Launoy, G., et al., 2017. Focus on an unusual rise in pancreatic cancer incidence in France. Int. J. Epidemiol. 46 (6), 1764–1772. https://doi.org/10.1093/ije/dyx088.

[120] Turrini, O., Paye, F., Bachellier, P., Sauvanet, A., Sa Cunha, A., Le Treut, Y.P., et al., 2013. Pancreatectomy for adenocarcinoma in elderly patients: postoperative outcomes and long term results: a study of the French Surgical Association. Eur. J. Surg. Oncol. 39 (2), 171–178. https://doi.org/10.1016/j.ejso.2012.08.017.

[121] Macchini, M., Chiaravalli, M., Zanon, S., Peretti, U., Mazza, E., Gianni, L., et al., 2018. Chemotherapy in elderly patients with pancreatic cancer: efficacy, feasibility and future perspectives. Cancer Treat. Rev. 72, 1–6. https://doi.org/10.1016/j.ctrv.2018.10.013.

[122] Ciabatti, S., Cammelli, S., Frakulli, R., Arcelli, A., Macchia, G., Deodato, F., et al., 2019. Radiotherapy of pancreatic cancer in older patients: a systematic review. J. Geriatr. Oncol. 10 (4), 534–539. https://doi.org/10.1016/j.jgo.2018.09.007.

[123] Petit-Monéger, A., Rainfray, M., Soubeyran, P., Bellera, C.A., Mathoulin-Pélissier, S., 2016. Detection of frailty in elderly cancer patients: improvement of the G8 screening test. J. Geriatr. Oncol. 7 (2), 99–107. https://doi.org/10.1016/j.jgo.2016.01.004.

[124] Martinez-Tapia, C., Paillaud, E., Liuu, E., Tournigand, C., Ibrahim, R., Fossey-Diaz, V., et al., 2017. Prognostic value of the G8 and modified-G8 screening tools for multidimensional health problems in older patients with cancer. Eur. J. Cancer 83, 211–219. https://doi.org/10.1016/j.ejca.2017.06.027.

[125] Hamaker, M.E., Te Molder, M., Thielen, N., van Munster, B.C., Schiphorst, A.H., van Huis, L.H., 2018. The effect of a geriatric evaluation on treatment decisions and outcome for older cancer patients – a systematic review. J. Geriatr. Oncol. 9 (5), 430–440. https://doi.org/10.1016/j.jgo.2018.03.014.

[126] Wildiers, H., Heeren, P., Puts, M., Topinkova, E., Janssen-Heijnen, M.L., Extermann, M., et al., 2014. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. J. Clin. Oncol. 32 (24), 2595–2603. https://doi.org/10.1200/JCO.2013.54.8347.

[127] Borson, S., Scanlan, J.M., Chen, P., Ganguli, M., 2003. The Mini-Cog as a screen for dementia: validation in a population-based sample. J. Am. Geriatr. Soc. 51 (10), 1451–1454. http://dx.doi.org/10.1046/j.1532-5415.2003.51465.x.

[128] Kim, M.Y., Park, U.J., Kim, H.T., Cho, W.H., 2016. DELirium prediction based on hospital information (Delphi) in general surgery patients. Medicine (Baltimore) 95 (12), e3072. https://doi.org/10.1097/MD.0000000000003072.

[129] European Society of Oncology Pharmacy, 2018. Quality Standard for the Oncology Pharmacy Service (QuapoS 6). https://esop.li/quapos.

[130] Brintzenhofe-Szoc, K.M., Levin, T.T., Li, Y., Kissane, D.W., Zabora, J.R., 2009. Mixed anxiety/depression symptoms in a large cancer cohort: prevalence by cancer type. Psychosomatics 50 (4), 383–391. https://doi.org/10.1176/appi.psy.50.4.383.

[131] Holland, J.C., Korzun, A.H., Tross, S., Silberfarb, P., Perry, M., Comis, R., et al., 1986. Comparative psychological disturbance in patients with pancreatic and gastric cancer. Am. J. Psychiatry 143 (8), 982–986. https://doi.org/10.1176/ajp.143.8.982.

[132] Warner-Cohen, J., Polokowski, A.R., Pinto, D., Zavadsky, T., Beyer, K, Saif, M.W., et al., 2020. Increasing access to multidisciplinary care in pancreatic cancer. Psychooncology Jul 20. https://doi.org/10.1002/pon.5493.

- [133] Haun, M.W., Estel, S., Rücker, G., Friederich, H.C., Villalobos, M., Thomas, M., et al., 2017. Early palliative care for adults with advanced cancer. Cochrane Database Syst. Rev. 12 (6), CD011129. https://doi.org/10.1002/14651858.CD011129.pub2.
- [134] Kavalieratos, D., Corbelli, J., Zhang, D., Dionne-Odom, J.N., Ernecoff, N.C., Hanmer, J., et al., 2016. Association between palliative care and patient and caregiver outcomes: a systematic review and meta-analysis. JAMA 316 (20), 2104–2114. https://doi.org/10.1001/jama.2016.16840.

[135] Aapro, M.S., 2012. Supportive care and palliative care: a time for unity in diversity. Ann Oncol. 23 (8), 1932–1934. https://doi.org/10.1093/annonc/mds239.

[136] Jordan, K., Aapro, M., Kaasa, S., Ripamonti, C.I., Scotté, F., Strasser, F., et al., 2018. European Society for Medical Oncology (ESMO) position paper on supportive and palliative care. Ann. Oncol. 29 (1), 36–43. https://doi.org/10.1093/annonc/mdx757.

[137] Védie, A.L., Neuzillet, C., 2019. Pancreatic cancer: best supportive care. Presse Med. 48 (3 Pt 2), e175e185. https://doi.org/10.1016/j.lpm.2019.02.032.

[138] Jang, R.W., Krzyzanowska, M.K., Zimmermann, C., Taback, N., Alibhai, S.M., 2015. Palliative care and the aggressiveness of end-of-life care in patients with advanced pancreatic cancer. J. Natl. Cancer Inst. 107 (3). https://doi.org/10.1093/jnci/dju424.

[139] Maltoni, M., Scarpi, E., Dall'Agata, M., Zagonel, V., Bertè, R., Ferrari, D., et al., 2016. Systematic versus on-demand early palliative care: results from a multicentre, randomised clinical trial. Eur. J. Cancer 65, 61–68. https://doi.org/10.1016/j.ejca.2016.06.007.

[140] Maltoni, M., Scarpi, E., Dall'Agata, M., Schiavon, S., Biasini, C., Codecà, C., et al., 2016. Systematic versus on-demand early palliative care: a randomised clinical trial assessing quality of care and treatment aggressiveness near the end of life. Eur. J. Cancer 69, 110–118. https://doi.org/10.1016/j.ejca.2016.10.004.

[141] Udelsman, B.V., Lilley, E.J., Qadan, M., Chang, D.C., Lillemoe, K.D., Lindvall, C., et al., 2019. Deficits in the palliative care process measures in patients with advanced pancreatic cancer undergoing operative and invasive nonoperative palliative procedures. Ann. Surg. Oncol. 26 (13), 4204–4212. https://doi.org/10.1245/s10434-019-07757-2.

- [142] Ferrell, B.R., Temel, J.S., Temin, S., Alesi, E.R., Balboni, T.A., Basch, E.M., et al., 2017. Integration of palliative care into standard oncology care: American Society of Clinical Oncology Clinical Practice Guideline Update. J. Clin. Oncol. 35 (1), 96–112. https://doi.org/10.1200/JCO.2016.70.1474.

[143] Quill, T.E., Abernethy, A.P., 2013. Generalist plus specialist palliative care – creating a more sustainable model. N. Engl. J. Med. 368 (13), 1173–1175. https://doi.org/10.1056/NEJMp1215620.

[144] Gilliland, T.M., Villafane-Ferriol, N., Shah, K.P., Shah, R.M., Tran Cao, H.S., Massarweh, N.N., et al., 2017. Nutritional and metabolic derangements in pancreatic cancer and pancreatic resection. Nutrients 9 (3), 243. https://doi.org/10.3390/nu9030243.

[145] Weimann, A., Braga, M., Carli, F., Higashiguchi, T., Hübner, M., Klek, S., et al. 2017. ESPEN guideline: clinical nutrition in surgery. Clin. Nutr. 36 (3), 623–650, https://doi.org/10.1016/j.clnu.2017.02.013.

[146] Arends, J., Bachmann, P., Baracos, V., Barthelemy, N., Bertz, H., Bozzetti, F., et al., 2017. ESPEN guidelines on nutrition in cancer patients. Clin. Nutr. 36 (1), 11–48, https://doi.org/10.1016/j.clnu.2016.07.015.

[147] Afaneh, C., Gerszberg, D., Slattery, E., Seres, D.S., Chabot, J.A., Kluger, M.D., 2015. Pancreatic cancer surgery and nutrition management: a review of the current literature. Hepatobiliary Surg. Nutr. 4 (1), 59–71. https://doi.org/10.3978/j.issn.2304-3881.2014.08.07.

[148] Hart, P.A., Bellin, M.D., Andersen, D.K., Bradley, D., Cruz-Monserrate, Z., Forsmark, C.E., et al., 2016. Type 3c (pancreatogenic) diabetes mellitus secondary to chronic pancreatitis and pancreatic cancer. Lancet Gastroenterol. Hepatol. 1 (3), 226–237. https://doi.org/10.1016/s2468-1253(16)30106-6.

[149] Andersen, D.K., Korc, M., Petersen, G.M., Eibl, G., Li, D., Rickels, M.R., et al., 2017. Diabetes, pancreatogenic diabetes, and pancreatic cancer. Diabetes 66 (5), 1103–1110. https://doi.org/10.2337/db16-1477.

[150] Pavel, M., Öberg, K., Falconi, M., Krenning, E.P., Sundin, A., Perren, A., et al., 2020. Gastroenteropancreatic neuroendocrine neoplasms: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann. Oncol. 31 (7), 844–860. https://doi.org/10.1016/j.annonc.2020.03.304.

[151] Buicko, J.L., Finnerty, B.M., Zhang, T., Kim, B.J., Fahey, T.J. 3rd, Nancy Du, Y.C., 2019. Insights into the biology and treatment strategies of pancreatic neuroendocrine tumors. Ann. Pancreat. Cancer 2, 12. https://doi.org/10.21037/apc.2019.06.02.

[152] Jin, X.F., Spampatti, M.P., Spitzweg, C., Auernhammer, C.J., 2018. Supportive therapy in gastroenteropancreatic neuroendocrine tumors: often forgotten but important. Rev. Endocr. Metab. Disord. 19 (2), 145–158. https://doi.org/10.1007/s11154-018-9443-6.

[153] Wind, A., Rajan, A., van Harten, W.H., 2016. Quality assessments for cancer centers in the European Union. BMC Health Serv. Res. 16, 474. https://doi.org/10.1186/s12913-016-1738-2.

[154] van Rijssen, L.B., Koerkamp, B.G., Zwart, M.J., Bonsing, B.A., Bosscha, K., van Dam, R.M., et al., 2017. Nationwide prospective audit of pancreatic surgery: design, accuracy, and outcomes of the Dutch Pancreatic Cancer Audit. HPB (Oxford) 19 (10), 919–926. https://doi.org/10.1016/j.hpb.2017.06.010.

[155] Mackay, T.M., Latenstein, A.E.J., Bonsing, B.A., Bruno, M.J., van Eijck, C.H.J., Groot Koerkamp, B., et al., 2020. Nationwide compliance with a multidisciplinary guideline on pancreatic cancer during 6-year follow-up. Pancreatology 20 (8), 1723–1731. https://doi.org/10.1016/j.pan.2020.10.032.

[156] National Institute for Health and Care Excellence, 2018. Pancreatic cancer. Quality standard [QS177]. https://www.nice.org.uk/guidance/qs177.

[157] German Cancer Society (DKG). Annual report 2019 of the certified pancreatic cancer centres. Audit year 2018/Indicator year 2017. https://ecc-cert.org/annual-reports.

[158] Tingstedt, B., Andersson, B., Jönsson, C., Formichov, V., Bratlie, S.O., Öhman, M., et al., 2019. First results from the Swedish National Pancreatic and Periampullary Cancer Registry. HPB (Oxford) 21 (1), 34–42. https://doi.org/10.1016/j.hpb.2018.06.1811.

[159] Fristrup, C., Detlefsen, S., Hansen, C.P., Ladekarl, M., 2016. Danish Pancreatic Cancer Database. *Clin. Epidemiol*. 8, 645–648. https://doi.org/10.2147/clep.s99471.

[160] Maharaj, A.D., Ioannou, L., Croagh, D., Zalcberg, J., Neale, R.E., Goldstein, D., et al., 2019. Monitoring quality of care for patients with pancreatic cancer: a modified Delphi consensus. HPB (Oxford) 21 (4), 444–455. https://doi.org/10.1016/j.hpb.2018.08.016.

[161] Sánchez-Velázquez, P., Muller, X., Malleo, G., Park, J.S., Hwang, H.K., Napoli, N., et al., 2019. Benchmarks in pancreatic surgery: a novel tool for unbiased outcome comparisons. Ann. Surg. 270 (2), 211–218. https://doi.org/10.1097/SLA.0000000000003223.

[162] Wellner, U.F., Klinger, C., Lehmann, K., Buhr, H., Neugebauer, E., Keck, T., 2107. The pancreatic surgery registry (StuDoQ|Pancreas) of the German Society for General and Visceral Surgery (DGAV) – presentation and systematic quality evaluation. Trials 18 (1), 163. https://doi.org/10.1186/s13063-017-1911-x.

[163] Bolm, L., Petrova, E., Woehrmann, L., Werner, J., Uhl, W., Nuessler, N., et al., 2019. The impact of preoperative biliary stenting in pancreatic cancer: a case-matched study from the German nationwide pancreatic surgery registry (DGAV StuDoQ|Pancreas). Pancreatology 19 (7), 985–993. https://doi.org/10.1016/j.pan.2019.09.007.

[164] Probst, P., Hüttner, F.J., Meydan, Ö., Kalkum, E., Kretschmer, R., Jensen, K., et al., 2019. Evidence map of pancreatic surgery: protocol for a living systematic review and meta-analysis. BMJ Open 9 (9), e032353. https://doi.org/10.1136/bmjopen-2019-032353.

[165] van der Heijde, N., Vissers, F.L., Boggi, U., Dokmak, S., Edwin, B., Hackert, T., et al., 2020. Designing the European registry on minimally invasive pancreatic surgery: a pan-European survey. HPB (Oxford) Sep 12, S1365-182X(20)31128-X. https://doi.org/10.1016/j.hpb.2020.08.015.

[166] Stevenson-Hornby, V., 2018. A rapid-access diagnostic pathway in suspected pancreatic cancer. Nurs. Times 114 (12), 34–35. https://bit.ly/37H7EIn.

[167] Benstead, K., Turhal, N.S., O'Higgins, N., Wyld, L., Czarnecka-Operacz, M., Gollnick, H., et al., 2017. Multidisciplinary training of cancer specialists in Europe. Eur. J. Cancer 83, 1–8. https://doi.org/10.1016/j.ejca.2017.05.043.

[168] White, M.N., Dotan, E., Catalano, P.J., Cardin, D.B., Berlin, J.D., 2019. Advanced pancreatic cancer clinical trials: the continued underrepresentation of older patients. J. Geriatr. Oncol. 10 (4), 540–546. https://doi.org/10.1016/j.jgo.2018.11.001.

[169] Paillaud, E., Soubeyran, P., Caillet, P., Cudennec, T., Brain, E., Terret, C., et al., 2018. Multidisciplinary development of the Geriatric Core Dataset for clinical research in older patients with cancer: a French initiative with international survey. Eur. J. Cancer 103, 61–68. https://doi.org/10.1016/j.ejca.2018.07.137.