

Neuroendocrine cancer: an ideal patient care pathway

Addressing inequities in diagnosis, care and support



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The
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Partnership

Contents

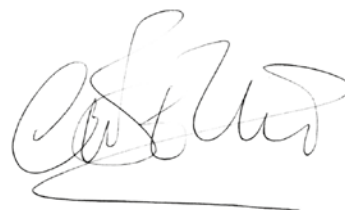
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Foreword

Neuroendocrine cancers, medically known and referred to in this report as neuroendocrine neoplasms (NENs), are a diverse group of cancers that are increasing in incidence. In 2018, the incidence of NENs in England was 8.61 per 100,000 people, a marked increase from 2.35 per 100,000 in 1995. Prevalence has also risen; NENs as a group have become the tenth most prevalent cancer in England. We therefore urgently need to address the persistent challenges and inequities in NEN diagnosis and disease management, and rethink how care is optimally provided.

The development of a patient care pathway for neuroendocrine cancer has been the culmination of over two decades of work from Neuroendocrine Cancer UK to raise awareness of NENs and provide support and guidance for patients. The pathway has been designed in close collaboration with a multidisciplinary advisory group and ultimately aims to address the significant inequities and care delays experienced by people living with NENs. The pathway and associated report provide clear evidence and recommendations to decision-makers on areas for improvement to reduce the burden of these cancers in England. We hope that it serves as a catalyst for healthcare providers and policymakers to begin making change. We also hope that it is an empowering tool for all people living with this disease, supporting them to seek the right care, in the right place, at the right time.

Effective integration of this pathway within NHS England is a key priority and will help us achieve optimal care provision for all people with NENs within the existing expert multidisciplinary teams across the UK. This pathway aligns with the NHS Long Term Plan's goals, including addressing unmet patient need, tackling local variation in patient care and outcomes, and ensuring faster cancer diagnosis. Application will therefore not only change lives for people diagnosed with a NEN, but also support the NHS more widely.



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Executive summary

As a group, neuroendocrine neoplasms (NENs) are the tenth most prevalent cancer in England,¹ and their diverse presentation makes diagnosis and management complex.^{1,2} Providing care for people with NENs is further challenged by low disease awareness, missed detection opportunities, delays in diagnosis, barriers in access to appropriate treatments and, crucially, the absence of a national care pathway.

Having a standardised patient care pathway is essential to support progress towards optimal care provision for people with NENs in England.

The pathway presented in this report outlines the ideal patient journey from point of suspicion to follow-up care. People with NENs, however, face a number of barriers and inequities along this pathway; support from all relevant stakeholders is needed to help overcome them at each stage, with the following policy actions recommended:

1

Point of suspicion

- Continue to support and roll out initiatives (such as Cancer Research UK's 'Talk Cancer' training programme) to increase awareness of symptoms for NENs
- Reference the patient care pathway for neuroendocrine cancer in relevant disease-specific and non-specific symptoms pathways, and include NENs in the National Institute for Health and Care Excellence (NICE) guideline for suspected cancer

2

Testing, diagnosis and grading

- Ensure Cancer Alliances' and Integrated Care Systems' (ICSs) NENs diagnostic practice aligns with the core principles of the NHS Faster Diagnosis Framework
- Invest in infrastructure to support diagnosis of rare cancers and establish a more even distribution of specialist services (e.g. positron emission tomography (PET) scans)
- Continue to support and develop work facilitating early integration of genetic and genomic advances into diagnostic pathways

3

Referral to a specialist multidisciplinary team and treatment

- Roll out the patient care pathway for neuroendocrine cancer across ICSs and Cancer Alliances in England
- Support and expand existing training programmes to inform healthcare professionals about NENs (e.g. the ‘NETs for Newcomers’ course run by the UK and Ireland Neuroendocrine Tumour Society (UKINETS))
- Accelerate academic and clinical research into the optimal types and order of treatments for different NENs

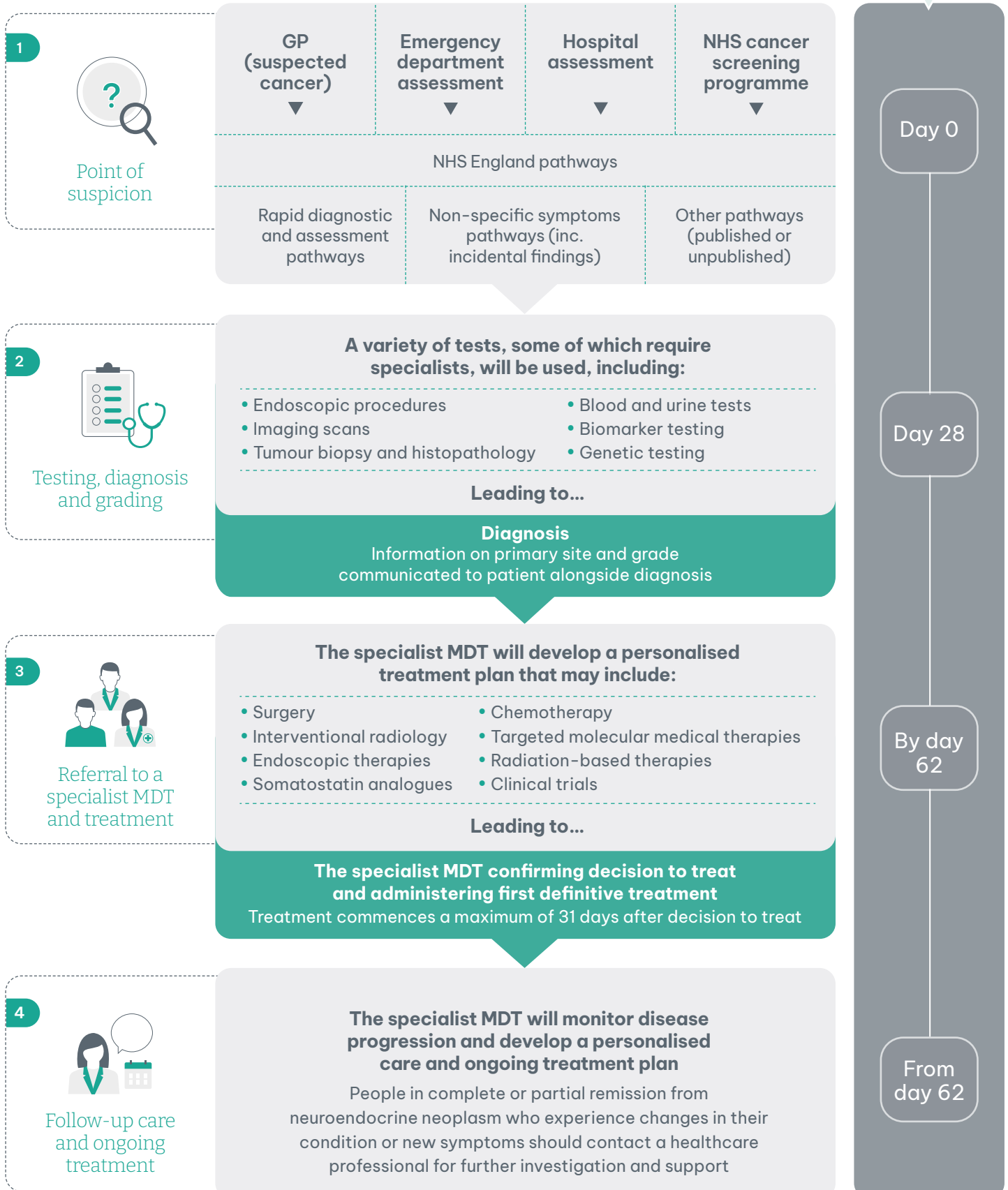
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Follow-up care and ongoing treatment

- Apply lessons learnt from the implementation of NHS personalised stratified follow-up pathways to follow-up care for people with NENs
- Further develop existing initiatives and novel interventions (e.g. free disease-appropriate counselling services, such as Neuroendocrine Cancer UK’s free counselling and psychotherapy services) that support accessible and holistic follow-up care for all people diagnosed with a NEN

Patient care pathway for neuroendocrine cancer

HOW LONG should I expect each stage to take according to NHS England guidelines?



Introduction

Neuroendocrine neoplasms (NENs) are a diverse group of rare cancers arising in neuroendocrine cells.^{3,4} These cells are present throughout the body,³ so NENs can occur in the lungs, gastrointestinal tract, female reproductive system, prostate, testicles, thyroid and elsewhere.⁵ As neuroendocrine cells help regulate how these body systems function, the symptoms experienced and care required by people living with NENs are hugely varied.⁶ This diversity contributes to the lack of knowledge and understanding of NENs among some healthcare professionals, people diagnosed with NENs and the general public.^{7,8} Consensus on the distinction between types of NENs and terminology used would help facilitate discussion (*Box 1*).⁷

BOX 1. Types of neuroendocrine neoplasms

NENs can be classified as either:⁴

- well-differentiated neuroendocrine tumours (NETs)*
- poorly differentiated neuroendocrine carcinomas (NECs).

*Note: some site-specific NETs may be referred to as carcinoid tumours.⁹

Differentiation refers to the development, appearance and organisation of tumour cells.¹⁰ Poorly differentiated NECs have cells and tissue structures that are very abnormal and not arranged in the usual way.¹⁰ Well-differentiated tumours, NETs, are very similar in characteristics and organisation to normal tissues and they can be mistaken for benign tumours.¹⁰

NENs may be described as functional (if the person experiences hormone-related symptoms) or non-functional (if they do not).¹¹

Some people with NENs may experience carcinoid syndrome: a collection of symptoms caused by excessive hormone release.¹² Furthermore, some NENs have been viewed as benign rather than malignant because they do not progress as obviously as other site-specific cancers.^{8,13}

Such variance and unusual behaviour can cause confusion among healthcare professionals and people with NENs alike,⁸ resulting in misunderstandings and potential minimising of the serious implications of a NEN diagnosis.^{8,14,15}

Whatever their subtype, all NENs are cancers and, as such, they warrant prompt, accurate diagnosis, as well as disease-specific specialist care and treatment.^{8,14,15}

The increasing burden of NENs is placing new challenges on the NHS. The incidence of NENs is rising in England,¹ necessitating prompt investment to accommodate increased demand and reduce unnecessary delays in care. Studies have shown that the majority of people with NENs are diagnosed with advanced cancer, necessitating urgent, accurate diagnostic assessments and increased healthcare requirements.¹⁶⁻¹⁸ Long delays to diagnosis and poor access to specialist care can result in significant anxiety, poorer quality of life and threat to survival.¹⁹⁻²² Such barriers to care and pre-existing inequities have been accentuated by the COVID-19 pandemic.²³⁻²⁵

Physical and psychosocial needs of people living with NENs in England remain unmet. Emotional and quality-of-life consequences are often overlooked due to the urgent clinical decision-making required, as well as the overarching lack of information around available resources and support for people diagnosed with NENs.^{8 15 26} Increasing awareness and provision of clear, high-quality information on NENs will enable healthcare professionals to support emotional wellbeing and improve the quality of life of people with NENs more effectively.^{7 19 21 22 27}

Neuroendocrine Cancer UK has developed this patient care pathway to demonstrate the ideal care provision for people with NENs in England and address existing barriers. A cancer pathway is defined as ‘the patient’s journey from the initial suspicion of cancer through clinical investigations, patient diagnosis and treatment’.²⁸ Pathways can improve clinical and quality-of-life outcomes,^{15 29} as well as streamlining resource allocation and reducing the economic burden on the health system. This report embodies these aims and goes further to outline the follow-up care expectations and barriers for people living with NENs. It is also a first in bringing together national expertise to create a dedicated patient care pathway for people living with NENs in England;^{7 30} specific aspects may also be relevant to the rest of the UK and beyond.

We hope this pathway can provide support and information to anyone with a NEN diagnosis. Everyone living with NENs in England has a different experience of NHS care, even if the primary site and type of NEN are the same.^{1 8 14 15} The pathway presented in this report is applicable to all NEN types, with a primary focus on NENs of the respiratory (lung) and gastrointestinal tract (gastroenteropancreatic or GEP-NENs), as these are the most common subtypes reported.¹¹⁷ The pathway is not intended to be a prescriptive plan of care; rather, it is meant as a practical tool to inform and empower. By signposting to informational resources and guidelines, the pathway aims to improve knowledge and awareness of care available for NENs, reduce variability in access to essential specialist services, and support healthcare professionals with clinical decision-making.



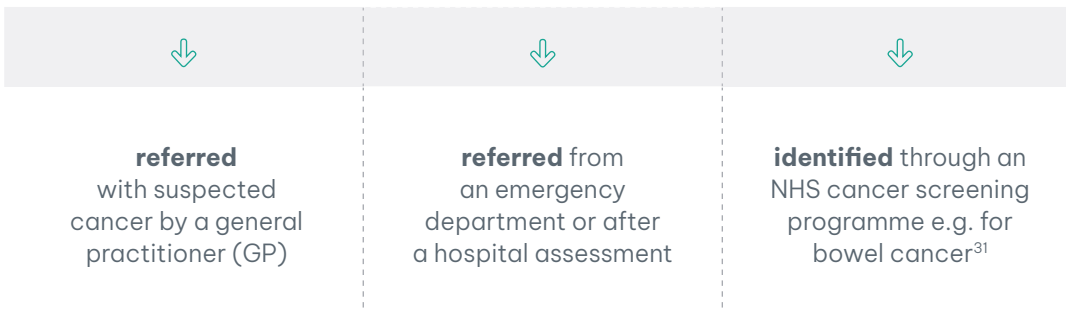
Point of suspicion

1.1 What does point of suspicion involve?

NHS TIME FRAMES

Point of suspicion is day 0 and marks a person's entry into the patient care pathway for neuroendocrine cancer. All time frames are counted from this date.

The point of suspicion is when a healthcare professional refers a person with a possible cancer for investigation.²⁸ There are many ways this could happen. For example, a person could be:²⁸



Following the point of suspicion, people will ideally be urgently referred and begin following a care pathway, such as the NHS England rapid diagnostic and assessment pathways for colorectal, lung, oesophago-gastric or prostate cancers,³²⁻³⁵ the Oxford Suspected CANcer (SCAN) diagnostic pathway,³⁶ or regional pathways for non-specific symptoms.³⁷⁻⁴⁰

Point of suspicion

What does this mean for people with GEP-NENs and lung NENs?

GEP-NENs	Lung NENs
<p>Many people eventually diagnosed with GEP-NENs are originally referred with suspected cancer by their GPs, after presenting with acute abdominal pain or other symptoms.¹⁴</p> <p>Most GEP-NENs are non-functioning, so if symptoms occur, they are related to the size or location of the cancer in the gastrointestinal tract and may include back pain, fatigue, abdominal pain, altered bowel habits, nausea and weight loss.^{11,13} These symptoms may fit with criteria for referral via the NHS England rapid diagnostic and assessment pathways for colorectal or oesophago-gastric cancers^{33,35} and the UK bowel cancer screening programme.³¹ Many occur late in the disease trajectory, meaning that a person's condition may be more easily confused with common site-specific cancers.^{5,13}</p> <p>However, if a GEP-NEN is functional, the symptoms may be atypical, occurring as a result of the overproduction of specific hormones.¹¹ For example, a functional pancreatic NEN can overproduce hormones such as insulin, gastrin and glucagon, and the symptoms might mimic those of other conditions (e.g. diabetes) and include dizziness, sweating and hunger.^{11,13} On the other hand, a small bowel NEN would overproduce histamine and serotonin, among other hormones, causing symptoms of carcinoid syndrome, such as flushing, wheezing and diarrhoea.^{41,42}</p>	<p>The point of suspicion for people eventually diagnosed with lung NENs is typically the NHS England rapid diagnostic and assessment pathway for lung cancer,³² with many individuals originally referred by their GP.⁴³</p> <p>The Targeted Lung Health Check programme currently rolling out free lung checks for eligible people aged 55–75 years in some regions of the UK may also help to detect NENs, but it is focused on those with a history of smoking.⁴⁴ There is currently no national level screening programme for lung cancer in the UK.⁴⁵ However, the recent UK National Screening Committee recommendation for targeted lung cancer screening across the UK⁴⁶ could mark a significant milestone in assisting earlier diagnosis of lung NENs.</p> <p>If symptoms are present, they may be similar to those of other lung conditions and cancers (e.g. persistent cough, recurring chest infections and/or worsening breathlessness) or allergy.⁴⁷</p>

1.2 Barriers to care

Simply getting to the point of suspicion is a significant milestone, given the often non-specific symptoms of NENs. Many people are asymptomatic before being diagnosed with a NEN, and where symptoms do occur, the most frequent are non-specific, for example pain, fatigue, diarrhoea, flushing and/or nausea.^{13 14 48} Symptoms may also mimic those of more common conditions (e.g. irritable bowel syndrome) or experiences (e.g. menopause), which may lead to a different pathway of care and postponement of an accurate diagnosis.^{8 19 26 48 49} Owing to the many and significant delays leading up to the point of suspicion, the majority of NENs are advanced at the time of diagnosis.^{16 17} Many initiatives have begun to increase awareness of signs and symptoms of a wide range of cancers,⁵⁰⁻⁵⁴ but more work is needed.

Low awareness, fear, or dismissal of symptoms can lead to delays in diagnosis. Some people may not associate non-specific symptoms with potential cancer, and a widespread lack of understanding of NEN symptoms prevents timely cancer suspicion.¹⁴ Others may trivialise their symptoms to reduce worry,^{14 48} which could lead to a reluctance to visit a doctor and significant diagnostic delays.^{14 43}

Low recognition of NEN symptoms by healthcare professionals may also delay referrals for diagnostic tests. Many symptoms associated with NENs do not necessarily qualify for a rapid referral in the current National Institute for Health and Care Excellence (NICE) guideline for suspected cancer pathway⁵⁵ and are often confused with those of other conditions.^{8 19 26 48 49} A separate but linked issue is that the guideline does not acknowledge NENs as a possible cancer for any of the non-specific features of cancer listed, many of which can be attributed to NENs.⁵⁵ Therefore, GPs face a significant challenge differentiating a potential malignancy from other benign diseases, especially when a person has non-specific symptoms.¹⁵ As the majority of people with cancer are referred through their GP,⁴³ this can cause significant delays; in the UK, individuals visit their GPs an average of 11 times before receiving a diagnosis of NEN.⁴⁸ To prevent such delays, it is essential that NENs are recognised in the NICE guideline for suspected cancer, with the diagnostic process further supported by formalised non-specific symptoms referral pathways.^{8 56} Significant progress has been made over recent years to increase coverage of these services across the country and ensure appropriate local infrastructure is in place for effective referral and care, but more work is needed.^{8 56}

Limited availability of formal education programmes for healthcare professionals further adversely affects the potential for an early, quick and accurate diagnosis. For example, given the most common types of NENs and symptoms reported, onward referrals tend to be directed towards gastroenterology departments. However, few UK gastroenterologists have received specialist training in NENs and are able to diagnose them rapidly.¹⁹ It is only with increased awareness and education of a variety of specialties that we will start to see a reduction in diagnosis times and more active use of the expert guidelines⁵⁷⁻⁶⁰ available for the care of people with NENs.

1.3 Addressing these barriers

Tackling poor awareness and fear of symptoms is challenging, but thoughtful intervention can make a difference. Several initiatives have been introduced across the UK with the aim of raising public and practitioner awareness of signs and symptoms of cancer. These include the Be Clear on Cancer programme originally launched by Public Health England,⁵⁰ Health Education England's e-learning for healthcare programmes,⁶¹ Cancer Research UK's 'Talk Cancer' training programme,⁵¹ and many regional initiatives.⁵²⁻⁵⁴ We need concerted action to improve the awareness of non-specific, rare and less common cancer symptoms for NENs and many other rare or less common cancers.^{8,43,56}

The recently published formal classification of NENs will begin to address the challenges posed by the complex presentation of this diverse cancer. In 2018, the International Agency for Research on Cancer (IARC) and the World Health Organization (WHO) proposed the most comprehensive, evidence-based consensus for the classification of NENs.^{4,62} Crucially, it recognises the key differences between NETs and NECs, including the different symptoms experienced,⁶² helping healthcare professionals be better informed and able to suspect NENs, where appropriate.

Inclusion of NENs in clear, evidence-based cancer referral pathways will help streamline the process to and from the point of suspicion. An awareness of the variety of pathways available to support individuals with a potential NEN diagnosis will ensure efficient referral to specialist care.^{43,63} To support this, the patient care pathway for neuroendocrine cancer provides information on the most common points of suspicion for people with NENs, including which existing pathways might feed into the NEN pathway, e.g. non-specific symptoms pathways. The number of non-specific symptoms pathways has increased dramatically in recent years, under the leadership of local Cancer Alliances.^{56,64} This means a number of patients are now being cared for appropriately who might otherwise have

been referred to an unsuitable cancer pathway or through emergency care, where projected outcomes are likely to be much worse.^{56 64} The recognition of NENs in the latest NICE guidelines for suspected cancer⁵⁵ will accelerate these positive outcomes and increase awareness of NENs among the healthcare community.



Point of suspicion: policy recommendations

- > Continue to support and roll out initiatives (such as Cancer Research UK's 'Talk Cancer' training programme) to increase awareness of symptoms for NENs
- > Reference the patient care pathway for neuroendocrine cancer in relevant disease-specific and non-specific symptoms pathways, and include NENs in the NICE guideline for suspected cancer

2



Testing, diagnosis and grading

2.1 What do testing, diagnosis and grading involve?

NHS TIME FRAMES

According to the NHS England Faster Diagnosis Standard, all people in England should either have a diagnosis or have cancer ruled out within 28 days of being referred by their GP or by the National Screening Service for suspected cancer.⁶⁵

A significant number of tests and investigations are available to accurately diagnose and grade NENs. Multiple tests are needed to confirm a diagnosis.⁶⁶ A combination of the following may be used based on an individual's symptoms and medical history:⁶⁶

endoscopic procedures to inspect the internal state of organs e.g. gastrointestinal tract	imaging scans , such as <u>positron emission tomography (PET)</u> , <u>computerised tomography (CT)</u> and/or <u>magnetic resonance imaging (MRI)</u> to identify the presence of tumours and determine the extent of disease	tumour biopsy and histopathology to investigate abnormalities of suspected tumours	blood and urine tests to inspect levels of various clinical markers	biomarker testing (which can be done as part of blood and urine tests) to assess levels of specific <u>biological markers</u> or indicators, such as hormones	genetic testing as there are several <u>germline mutations</u> associated with increased likelihood of certain types of NEN. ^{62 67-69}

Findings are used to identify primary tumours, determine the grade of cancer (*Box 2*) and ultimately inform treatment decisions.⁶⁶ The stage, or extent to which the cancer has spread, is often ascertained through imaging scans;^{66 70} however, there is currently no standardised approach to staging for people

with NENs.⁷¹ A NEN diagnosis and grading is often confirmed by a biopsy and histological analysis.^{19 66 72}

BOX 2. Grades of NENs

Grading of NENs refers to the number of active cells within the cancer, which provides an indication of prognosis and likelihood of the cancer spreading (metastasis). Therefore, it is crucial in determining the type and urgency of treatment required.¹⁰

The IARC/WHO classification of NENs outlines that the grade is determined by the NEN type:^{4 62 73}

- NETs are well differentiated and can be grade 1, 2 or 3
- NECs are poorly differentiated and are grade 3.

The higher the grade, the faster the cancerous cells replicate; they can appear more abnormal when compared with normal cells, and starting treatment is more urgent.^{4 10 62}

Owing to their rarity and diversity, NENs will often not be the first cancer suspected. Incidental diagnosis of NENs,^{74 75} and cancer more broadly, is not uncommon; 4% of people with cancer in England are diagnosed incidentally.⁷⁶ Therefore, an awareness of NENs among all healthcare professionals is paramount for early detection and accurate diagnosis, which form key components of the NHS Long Term Plan.³⁷

Testing, diagnosis and grading

What does this mean for people with GEP-NENs and lung NENs?

GEP-NENs	Lung NENs
<p>GEP-NENs arise anywhere within the gastrointestinal tract, including in the pancreas; collectively, they are the most common NENs diagnosed in England.^{17 48}</p> <p>The diagnostic tests used for people with a suspected GEP-NEN are numerous:⁶⁶ biomarker testing is particularly common,⁷⁰ and appropriate <u>nuclear medicine</u> imaging is the most sensitive (e.g. <u>Gallium-68</u> PET scans).^{77 78}</p> <p>GEP-NENs are separated into NENs with a primary site of the gut and those with a primary site of the pancreas, and from there subtyped and graded into NETs (grades 1-3), and small-cell type and large-cell type NECs (grade 3).⁴ It is important that the grades of a GEP-NEN are distinguished, as the prognosis and treatment strategies can differ dramatically, especially for high-grade pancreatic NETs and NECs.⁷⁹</p>	<p>Lung NENs are the second most common NENs diagnosed in England.^{117 48} A variety of diagnostic methods are used to determine a lung NEN, including blood tests, urine tests and scans (e.g. PET).⁶⁶</p> <p>Lung NETs are divided into typical carcinoids and atypical carcinoids.^{4 47 80} Lung NECs are divided into small-cell lung carcinoma and large-cell NEC.^{4 47 80}</p>

2.2 Barriers to care

The diversity of NENs causes significant challenges at the point of diagnosis, including choosing the right diagnostic tests. NENs are often misdiagnosed, and diagnosis is frequently delayed.^{14 17 48} For example, the results of a recent survey of more than 300 people with NETs in the UK found a median time of 53.8 months from first symptom to diagnosis.⁴⁸ Delays are influenced by the complexity of NEN presentation and significant number of possible primary sites.¹⁷ People with NENs may also experience symptoms related to excessive hormone release, which further challenges the diagnostic process.^{12 72} As a result, choosing the most appropriate diagnostic tests is difficult, and administration of a variety of tests can cause undue delays to diagnosis.

Limited access to diagnostic tools and specialists, especially in certain regions, compounds these delays. There is no single test that can confirm a diagnosis of NEN – even histology may be open to misinterpretation.⁸¹ Currently, there is an uneven distribution of NEN diagnostic services across England,¹⁴ in particular imaging and scanning facilities.⁸² Healthcare workforce restrictions⁸³ may exacerbate inequities in diagnosis, including a limited number of radiologists available to support diagnosis.⁸⁴ This particularly impacts the availability of PET scanning with Gallium-68 across the country, and the centres with this specific imaging capability are not necessarily those with a specialist NEN service.^{21 85} Effective communication of test results among healthcare professionals is crucial to avoid people getting ‘stuck’ at this point of the pathway.²⁶ We need data-driven decision-making, improved management of specialist provision and advancement of information technology systems to achieve faster diagnosis.²⁶

Not all NENs are accurately graded, preventing a full analysis of incidence and prevalence. Any NENs classification system is challenging, owing to the variety of presentations and sites where the cancer could occur.^{17 71} Accurate grading is also dependent on the experience and expertise of the healthcare professional reviewing the histology and their access to peer review.^{4 26} However, given the impact that accurate grading can have on treatment decision-making and prognosis, it is essential that every person with a NEN diagnosis receives expert confirmation and a tailored treatment plan appropriate for them.

2.3 Addressing these barriers

The realisation of core NHS ambitions to improve cancer care in England will help address diagnostic challenges caused by the diversity and complexity of NENs. The variety, rarity and increasing incidence of NENs¹ demands a proactive and systematic approach to care delivery. Several valuable initiatives support this and aim to increase the speed of diagnosis of cancer across the country. These include:

- the NHS Long Term Plan³⁷ and subsequent implementation of the NHS England Faster Diagnosis Standard, both of which advocate for all cancers, including NENs, to be diagnosed or ruled out as quickly as possible^{37 65}
- the NHS Faster Diagnosis Framework,⁶⁴ which includes the roll-out of non-specific symptoms pathways in England and the NHS England timed rapid diagnostic and assessment pathways for colorectal, lung, prostate and oesophago-gastric cancers³²⁻³⁵
- the Cancer Research UK Early Diagnosis Initiative.⁸⁶

The patient care pathway for neuroendocrine cancer aligns with not only the Cancer Research UK Early Diagnosis Initiative,⁸⁶ but also the NHS Faster Diagnosis Framework's core principles of early identification, broad assessment of symptoms, coordinated testing, timely diagnosis and appropriate onward referral, all of which are underpinned by excellent patient coordination and support.⁶⁴ To further enact these plans and diagnose rare cancers early and accurately, more healthcare professionals need to receive appropriate training.

Comprehensive testing, diagnosis and grading of NENs can only be achieved by increasing access to diagnostic tools and specialists for people living with NENs. Improvements in diagnosis and screening services for other cancers would likely improve the timeliness of NEN diagnosis and could be undertaken through systematic implementation of the NHS England timed rapid diagnostic and assessment pathways.³²⁻³⁵ A more even distribution of specialist diagnostic services (e.g. PET scans) in England is also needed to ensure equitable access across the country.¹⁴ This will reduce waiting times and unacceptable variations in access to services.^{48 87}

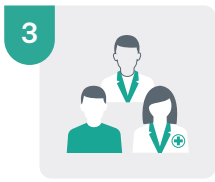
Personalisation of testing and integration of innovative diagnostic methods will help establish a more widespread consensus on NEN classification. Ongoing refinement of NEN classification is to be expected as knowledge increases.⁸⁸ Therefore, it is important that guidance, pathways and healthcare professionals remain updated. For example, over the past two decades, the number of biomarkers and genetic elements associated

with NENs has increased.⁸⁹ In recognition of this, in 2021, Neuroendocrine Cancer UK became a member of Genetic Alliance UK, a charity working to improve the lives of people affected by all types of genetic conditions.⁹⁰ However, systematic integration of genetic screening for germline mutations associated with NENs in healthcare is limited⁶⁸ despite 10–30% of NENs of the pancreas occurring as a result of a genetic predisposition.^{11 91} Current regional and national genomics research projects are underway to further develop our understanding of NENs.⁴⁹ Greater application of these technologies during the testing, diagnosis and grading stages could help speed up diagnosis, streamline therapeutic decision-making and support management of any affected family members.



Testing, diagnosis and grading: policy recommendations

- > Ensure Cancer Alliances' and Integrated Care Systems' NENs diagnostic practice aligns with the core principles of the NHS Faster Diagnosis Framework
- > Invest in infrastructure to support diagnosis of rare cancers and establish a more even distribution of specialist services (e.g. PET scans)
- > Continue to support and develop work facilitating early integration of genetic and genomic advances into diagnostic pathways



Referral to a specialist multidisciplinary team and treatment

NHS TIME FRAMES

According to the NHS Constitution for England, people with suspected cancer of any type should experience:⁹²

- a maximum 62-day wait from urgent referral for suspected cancer or from an NHS cancer screening service to first treatment
- a maximum 31-day wait between decision to treat and first definitive treatment

3.1 What does referral to a specialist multidisciplinary team involve?

Referral to a specialist, disease-specific multidisciplinary team (MDT) is the gold standard of care for all people with a cancer diagnosis, including those with a NEN.^{19 93} MDTs facilitate a holistic, personalised approach to determining an effective disease management strategy.^{7 19 93 94} Depending on the complexity of their disease, people may be referred to an MDT for discussion prior to diagnosis and determination of cancer spread. Alternatively, they may be referred once a diagnosis is established, to confirm staging and grading, and determine the treatment plan.²⁶ Standards of care are recommended to help support and streamline MDT working by establishing a consensus on the treatment or care that a person should receive, using recognised international, national, regional or local guidelines.⁹⁵

A variety of MDTs care for people with NENs across England. The MDT may be a regional or larger team within a specialist NET centre,⁵⁷ or a team from one of the 11 European Neuroendocrine Tumor Society (ENETS) Centers of Excellence in England.⁹⁶ Even though the exact make-up of an MDT may vary, it is important that they include disease-specific expertise; ENETS Centers of Excellence criteria indicate that an MDT for NENs should involve the following core, NEN-experienced partners (defined in the [glossary](#)):^{13 93 97}

- site-specific surgeons
- site-specific specialists (e.g. gastroenterologists, endocrinologists)
- medical and clinical oncologists
- nuclear medicine physicians
- radiologists
- histopathologists
- specialist nurses (including cancer clinical nurse specialists and advanced nurse practitioners)
- MDT coordinators.

A variety of other healthcare professionals are not core members of the MDT, based on the ENETS criteria,⁹⁷ but do play vital roles in NENs care. These include GPs, primary care staff, allied health professionals and others.

3.2 What does treatment involve?

In accordance with the large number of NEN types and subtypes, there are many diverse NEN treatments. Treatment is determined by the tumour's primary site and grade,^{59 60} disease progression, and the individual's overall health and quality of life.⁹⁸ While there are many types of therapies for NENs – which people may receive at different points in their treatment – not all treatments are suitable for all types of NENs, and some may not be licensed/approved, even if they may be clinically appropriate:⁹⁸

SURGERY

currently offers a potential cure for some people with certain types of NENs. The types of surgery vary depending on the grade and primary site of NEN, and the overall health of and risks for the person. Where surgery may not be curative, it can play a life-extending and/or symptom-alleviating role by preventing other complications associated with NENs e.g. bowel obstruction.⁹⁹

INTERVENTIONAL RADIOLOGY

encompasses imaging techniques, such as MRI and CT scans, to precisely target therapies and minimise impact on the rest of the body. Examples of interventional radiology therapies include tumour ablative therapy and embolisation.

ENDOSCOPIC THERAPIES

use an endoscope to deliver treatments to specific parts of an organ, usually within the gastrointestinal tract or lung.¹⁰⁰ This is sometimes an alternative to surgery in early-stage NETs.¹⁰⁰

SOMATOSTATIN ANALOGUES (SSA)

are medications that can slow the growth rate of well-differentiated NETs and reduce the hormone-related symptoms of functional NENs, such as flushing and diarrhoea. By reducing hormone levels, SSAs may effectively reduce the severity of the symptoms experienced.

CHEMOTHERAPY

is often the first-line therapy for people with a high-grade NEN, as it could stop or slow some cancer cells from reproducing or growing.

TARGETED MOLECULAR MEDICAL THERAPIES

are used to treat well-differentiated NETs only and work by interfering with specific molecules that are involved in the growth, progression and spread of cancer.¹⁰¹ In contrast to chemotherapies, which act on all rapidly dividing normal and cancerous cells, targeted therapies act on specific biological structures that are associated with cancer.¹⁰¹

- > Targeted molecular medical therapies include hormone therapies, gene expression modulators and immunotherapies.¹⁰¹

RADIATION-BASED THERAPIES

use high or concentrated doses of radiation to try to destroy cancer cells and shrink tumours, with various levels of targeting. Examples include:

- > external beam radiotherapy, which uses an external source of radiation pointed at a particular part of the body to target cancer cells¹⁰²
- > internal radiation therapy, which involves inserting radioactive material inside the body to destroy cancer cells and provide effective treatment¹⁰³
- > targeted molecular radiation therapy, e.g. radioligand therapy, which delivers radiation specifically directed to proteins or other structures that are present on the surface of cancer cells to try to destroy them.¹⁰⁴

Clinical trials are often a means of treating people with NENs, and, at any one time, a number of clinical trials may be underway.⁹⁸ Clinical trials looking at the use of immunotherapy and/or gene therapy in NENs are currently ongoing or planned.^{105 106}

Treating the symptoms of cancer – and managing the side effects of treatments – is an important aspect of care along the whole pathway, not just as part of end-of-life care. The immediate care required by all people diagnosed with NENs, as well as the lifelong care needed for the majority, involves using medications and other forms of therapy with the aim of treating symptoms, managing side effects and ultimately improving quality of life.¹⁰⁷

Referral to MDT and treatment

What does this mean for people with GEP-NENs and lung NENs?

GEP-NENs	Lung NENs
<p>Healthcare professionals involved in the core MDT and extended care team for people diagnosed with GEP-NENs include site-specific specialists, such as gastroenterologists, <u>hepatopancreaticobiliary</u> surgeons, histopathologists, oncologists, nuclear medicine physicians, endocrinologists, cancer nurse specialists and geneticists.¹⁰⁸⁻¹¹⁰</p> <p>Although there are a variety of treatment options available,^{18 111} the majority of people with GEP-NENs are diagnosed with metastatic disease.¹³ People with GEP-NET may require long-term systemic anti-tumour-growth medication and/or hormone-related symptom relief.^{13 18 111} Treatments include many of those listed above, either alone or in combination.¹⁸ Combining therapies is complex and requires extra care and support from the MDT. <u>Chemotherapy</u> is the main first-line treatment for primary GEP-NEC and may provide symptom relief for those with metastatic disease.¹⁰¹</p>	<p>Healthcare professionals involved in the core MDT and extended care team for people diagnosed with lung NENs include site-specific specialists, such as respiratory physicians, thoracic surgeons and lung oncologists as well as nuclear medicine physicians and lung cancer nurse specialists.^{108 109 112-114}</p> <p>Surgery is the first choice for early-stage disease, while SSAs, targeted molecular medical therapies and/or interventional radiology are the most common treatments for metastatic lung NETs.¹¹⁴⁻¹¹⁷ Chemotherapy is predominantly used to treat lung NECs.¹⁰¹</p> <p>However, there is a lack of consensus between lung NEN management guidelines regarding optimal treatment approaches,^{115 118} meaning care and sequence of treatments can vary between different centres and specialists.</p>

3.3 Barriers to care

Despite the acknowledged value of multidisciplinary care for people with NENs, access to care can be challenging. In England and across the UK, there is limited access to multidisciplinary care for people living with NENs, and the complexity in reaching it places a substantial and unnecessary burden on the health system.^{14 16} Many people have reported waiting a long time for specialist care and experiencing a lack of urgency and concern from healthcare professionals regarding their condition and need for referral.^{8 14} The majority of people with NENs will be referred by GPs or emergency department staff, who may not be aware of existing local MDTs for NENs or ENETS Centers of Excellence, which may delay timely and appropriate referral.^{8 14 96} Even if the referring professional is aware, referral may be delayed by misunderstandings around the funding of specialist care, the timing or appropriateness of referral, the referral process itself, and/or concerns around geographical distances.^{8 14 93} Such complex service provision, in addition to delayed diagnosis and difficulty understanding the biological intricacy of NENs, can negatively impact not only prognosis but also the mental health of people with NENs, resulting in feelings of confusion and isolation.^{8 15}

The location and make-up of MDTs, and thus access to specialist care, may vary considerably. ENETS Centers of Excellence are accredited and certified NHS facilities that can deliver the highest-quality care to people living with NENs.¹¹⁹ However, their geographical distribution across England is uneven.⁹⁶ This can result in limited access to this care and significant travel or personal costs for people who do not live near them, compounding difficulties for those with advanced or highly complex NENs and/or those facing social disadvantage.^{18 26 30 49 82 120} Limited access to specialists has been widely reported by people with suspected or diagnosed NENs.^{7 14} These specialists include site-specific professionals, as well as those primarily involved in ongoing care after diagnosis, such as clinical nurse specialists^{8 121} and specialists in mental health⁷ and nutrition.¹²²⁻¹²⁵

The types of treatment available may also vary between centres.

Concerns over equitable access to radioligand therapy in England are well documented.^{85 120 126-129} Despite radioligand therapy being approved by NICE and funded by NHS England for certain NEN subtypes,¹³⁰ not all people who are eligible for treatment receive it, due largely to a lack of trained staff and facilities, but also to a lack of or late referral.^{126 127} By contrast, many chemotherapy regimens used in NEN treatment are often more available, but some may require an overnight stay in hospital or outpatient care, meaning treatment could be delayed or a referral made to a centre farther from where a person lives.¹³¹ Inequities in treatment access for people living with NENs

also apply to clinical trials. Individuals must be referred by their MDT and meet the eligibility criteria for a given clinical trial.¹³² If their MDT is unaware of the trials available for their type of NEN, they may miss out on potentially beneficial treatment.²¹

These challenges are compounded by the absence of specialised commissioning for NENs. Even though NENs are a group of individually rare cancers (by incidence), there is no commissioning of specialised services.⁸² The absence of a commissioned, dedicated service for NENs has contributed to geographical differences in care provision and an uneven distribution of available specialists and treatment.¹⁴

3.4 Addressing these barriers

The patient care pathway for neuroendocrine cancer helps make access to MDTs more straightforward for people diagnosed with NENs. The patient care pathway, which forms the first national care pathway for people living with NENs in England, outlines a variety of referral mechanisms, diagnostic methods and treatment types for this diverse and complex condition. It can be used to increase healthcare professionals' awareness of the multidisciplinary care required for NENs and begin to address the significant unmet need in access.^{7 16 133} This will support more urgent referral and onward care, ultimately reducing the substantial burden that challenges in access to MDT management place on the health system.^{8 14}

The need for more equitable access to high-quality, specialised and coordinated multidisciplinary care is well recognised and is starting to be addressed. There are acknowledged issues in the availability of NHS staff,⁸³ including cancer care specialists, and these issues are amplified for rare conditions such as NENs.^{43 83} The recent transition of NHS Clinical Commissioning Groups to Integrated Care Systems (ICSs) in England¹³⁴ provides a great opportunity for accelerated change in MDT coordination and management.^{8 26 49 82} Under this new system, the various specialists and healthcare professionals required to provide appropriate and effective care for people with NENs are more likely to work together frequently.¹³⁴ Given this work is already underway, ICSs, Cancer Alliances and other NHS bodies should work collaboratively to adopt the patient care pathway for neuroendocrine cancer and ensure equitable access to diagnostics, multidisciplinary care and treatment across the country. Effective communication and collaboration at all levels will be vital to ensure this is a success.^{135 136} Failure to address these issues will perpetuate suboptimal and highly variable clinical outcomes and patient experiences, devastatingly so for those with advanced or complex disease presentation

and/or disease trajectory. Progress is being made – for example, in the past two years, a national trial pilot programme for liver transplantation has begun for people with NET liver metastases in the UK and Ireland.¹³⁷

Improving national education of healthcare professionals in NENs will increase access to specialist care across the country. To this end, since 2018, the UK and Ireland Neuroendocrine Tumour Society (UKINETS) has collaborated with other professional societies to host an annual ‘NETs for Newcomers’ course to train healthcare professionals in the diagnosis, investigation and management of people with NENs.¹³⁸ Neuroendocrine Cancer UK has developed a Neuroendocrine Cancer Nurse competency framework, which is accredited by the Royal College of Nursing. This framework aims to increase the awareness, confidence, skills and knowledge of specialist nurses to promote and enhance appropriate care for those diagnosed with neuroendocrine cancer.¹²¹ Supporting and expanding initiatives such as these will ensure healthcare professionals are better informed about NENs and able to provide more optimal care.

There are still many changes required to improve equitable access to treatment and inclusion in clinical trials. Although the transition to ICSs is helpful, future improvements must also address the lack of literature on the optimal types and order of treatments for different NENs, as well as the need for personalised treatment and support.^{18 111} For example, there have been many calls to secure appropriate funding for equitable availability of radioligand therapy in the UK.^{85 128 129 139} There is also a growing consensus on the need for nutritional support throughout the care pathway,^{123 124} clearer communication,²² and expansion of the eligibility criteria for clinical trials.^{21 132} The last will promote appropriate onward referral, supported by the NHS ambition to better embed clinical research delivery in the health systems of all devolved UK nations.¹⁴⁰

Roll-out of the patient care pathway for neuroendocrine cancer within ICSs and Cancer Alliances would also begin to remedy the lack of specialised commissioning for NENs. The patient care pathway for neuroendocrine cancer highlights the importance of disease-specific specialist MDT involvement and aims to raise awareness of the variety of available and potential treatments for NENs. The pathway also underlines the need for well-organised NEN services and clear future policy priorities. Therefore, integration of the pathway within ICS and Cancer Alliance operations would provide clarity on the diagnostic process and tests required. In the absence of specialised commissioning, this would have a notable effect on addressing and rebalancing the current unmet needs of people with NENs and the inequities in care they experience.



Referral to a specialist multidisciplinary team and treatment: policy recommendations

- > Roll out the patient care pathway for neuroendocrine cancer across ICSs and Cancer Alliances in England
- > Support and expand existing training programmes to inform healthcare professionals about NENs (e.g. the 'NETs for Newcomers' course run by UKINETS)
- > Accelerate academic and clinical research into the optimal types and order of treatments for different NENs



Follow-up care and ongoing treatment

4.1 What do follow-up care and ongoing treatment involve?

NHS TIME FRAMES

According to the NHS Constitution for England, people in England should have a maximum 31-day wait from the decision to treat for subsequent treatments (i.e. after their first definitive treatment) if the treatment is surgery, a course of radiotherapy or anti-cancer medication.⁹²

Follow-up care and ongoing treatment are highly personalised to each individual's specific needs. After the initial treatment course finishes, people should have regular appointments with their doctor or specialist nurse to assess any changes in health or wellbeing.⁴⁹ Expert, evidence-based clinical site- and grade-specific guidelines have been published to indicate the recommended type and interval of follow-up investigations and clinical review. These guidelines are regularly reviewed and updated to reflect advances in knowledge regarding disease, diagnostic techniques and treatments.⁵⁷⁻⁶⁰

For many people with a NEN diagnosis, follow-up care is lifelong and should ideally take place in specialist NEN centres, with access to an MDT. On advice from specialist centres, some follow-up may occur in local hospitals, with referral back to the centre if the person's condition changes.⁵⁸ People may undergo tests to address any concerns early or establish whether further rounds of treatment are needed.¹⁴¹ Many aspects of a person's condition can inform their follow-up, including organs affected, NEN grade, how much the cancer has spread, excess hormone release, treatment effects and response, ongoing results and medical history.⁵⁸ The frequency of follow-up should be clinically dictated and include those with high-grade tumours, complex or persistent symptoms, complications of diagnosis and/or high burden of disease.⁵⁸ In addition to the physiological and practical challenges of living with NENs, the psychological burden is likely to be significant.^{8 14 15 142 143} Mental health support should not only be systemically

available for all people diagnosed with NENs, from the point of diagnosis, but also be offered to families and carers.^{15 20}

Follow-up care and ongoing treatment

What does this mean for people with GEP-NENs and lung NENs?

GEP-NENs	Lung NENs
<p>Guidelines note that follow-up should be lifelong for most people with GEP-NENs.^{58 59} The frequency of appointments may vary based on clinical symptoms and test results, including biomarker levels and imaging results.^{58 59} It can vary from every 2–3 months for people with grade 3 stomach NENs to every 6–12 months for many grade 1 GEP-NENs.⁵⁸ Only people with small, localised grade 1 GEP-NETs that have been completely removed surgically and have no concerning histological or clinical features may be exempt from long-term follow-up.⁵⁸</p>	<p>The ENETS 2017 consensus guidelines note that follow-up should be lifelong for most people with lung NENs.⁵⁸ The frequency of appointments will range from every 2–3 months for people with poorly differentiated large-cell NECs to every 6–12 months for people with lung NETs after surgery.⁵⁸</p> <p>Various imaging techniques can be used during follow-up for people with lung NENs, including CT scans, chest X-rays and PET scans.¹⁴⁴ Guidelines note that follow-up for these cancers should be lifelong because recurrences are very common.⁶⁰</p>

4.2 Barriers to care

The main barriers to multidisciplinary care along the entire patient pathway for people living with NENs also impact follow-up care and ongoing treatment. Establishing a timely and accurate diagnosis and ensuring specialist MDT management of a person’s NEN creates an essential foundation for follow-up care. However, as the capacity of healthcare facilities to provide ongoing specialist NEN care is hugely varied across the country – largely due to differences in funding, resource availability, healthcare professionals’ interest in and knowledge of NENs, and numbers of adequately trained personnel – people often experience a different frequency and quality of follow-up care, even if they have similar types of NEN.^{14 20 49 56 82} Some of these issues are compounded by poor communication within MDTs and between healthcare professionals and patients.²⁶ For example, people may not know to whom they should highlight changes in their condition post-treatment, which may lead to delayed or poorly personalised care.^{15 20 29 56} Clear points of contact for patients and effective communication channels between healthcare professionals must be a priority.^{15 29 56}

Lifelong follow-up care is recommended for almost all NENs, but this is not consistently provided. Despite the long-term need for monitoring and treatment,⁵⁸ there is a lack of consensus on the best approach to follow-up care among healthcare professionals.⁴⁹ This is acknowledged by European clinical practice guidelines for NENs, which state that standardised follow-up regimens do not yet exist for people living with NENs.⁵⁸⁻⁶⁰ Decisions are therefore based on a clinician's evaluation of the person's specific symptoms and the outcomes of ongoing testing,⁵⁸⁻⁶⁰ which can result in suboptimal follow-up, with important treatment possibly delayed.⁴⁹ As the quality and capacity of multidisciplinary care varies across the country,^{21 26 49 93} follow-up procedures also differ.^{15 49}

Disparities in care on an individual level are felt most keenly during follow-up, as treatment and care for people living with NENs become increasingly personalised. Language, literacy, financial and cultural barriers limit accessibility of available information and support for patients, which can have a negative effect on their care-seeking behaviours.⁸ Such inequalities have a negative impact on mental health and, ultimately, outcomes, underlining the importance of education on the value of follow-up to patients.⁸

All of the challenges faced by people living with NENs have been exacerbated by the COVID-19 pandemic. The negative impact the pandemic has had on the mental health of people living with NENs is well documented.^{8 15 23-25 145 146} A 2020 survey of experiences during the pandemic found that people undergoing longer-term follow-up for NENs felt a greater reluctance to seek out care than before the pandemic. They also experienced greater anxiety and decreased psychosocial wellbeing.¹⁴⁵

4.3 Addressing these barriers

Health system infrastructure is desperately needed to provide consistent and long-term care for people with NENs. As the prevalence of NENs is increasing in England,¹ high-quality follow-up care is of vital importance. This is recognised by the patient care pathway for neuroendocrine cancer as a defined stage in the care of people diagnosed with NENs. Seeing as the condition is lifelong for most, systematic planning among MDTs for long-term management is crucial.⁵⁸ Experts have begun compiling and analysing a wealth of patient data through the ENETS database¹⁴⁷ to ensure future follow-up guidelines are better informed.⁴⁹ The data will also support NHS England's implementation of the NHS personalised stratified follow-up pathways,³⁷ which aim to streamline follow-up cancer care, depending on the types and levels of resources needed to meet patients' needs.^{148 149}

It is hoped that this initiative will improve the experiences and quality of life of people with NENs following cancer treatment, as well as making services more efficient and cost-effective.^{148 149} This pathway is currently being streamlined to breast, prostate and colorectal cancers; less common cancers, such as NENs, are unlikely to be explicitly prioritised.¹⁴⁹ However, lessons learnt may be used to model follow-up care for people with NENs in England and further develop this patient care pathway.

Significant efforts from the NHS and patient organisations must continue to be made to ensure accessible and holistic follow-up care, recognising the additional burden caused by the COVID-19 pandemic. In addition to clinical needs, addressing the financial, language, cultural and literacy barriers faced by many, as well as overall quality-of-life management, is of great importance,⁸ as the majority of people are diagnosed with advanced NENs¹⁶⁻¹⁸ and treatment is lifelong.⁵⁸ Neuroendocrine Cancer UK provides a wealth of support to people undergoing follow-up care for NENs, including patient education events, practical advice, expert-endorsed information about NENs, and signposting to support groups.¹⁴² These groups aim to address the mental health challenges often experienced by people with NENs during follow-up.^{8 15 23-25 145 146} Neuroendocrine Cancer UK and many other organisations in England, such as Maggie's Centres, also provide free counselling and psychotherapy services to help people with NENs talk through anything concerning them, including tests, treatments, MDT care, finances and relationships.^{150 151} Increasing the number and scope of services such as these will go further to help address the inequities in care that exist for people with NENs in England⁷ and support the ambitions of the NHS Long Term Plan, which calls for greater access to health and wellbeing support for all people with cancer.³⁷



Follow-up care and ongoing treatment: policy recommendations

- > Apply lessons learnt from the implementation of NHS personalised stratified follow-up pathways to follow-up care for people with NENs
- > Further develop existing initiatives and novel interventions (e.g. free disease-appropriate counselling services, such as Neuroendocrine Cancer UK's free counselling and psychotherapy services) that support accessible and holistic follow-up care for all people diagnosed with a NEN

Implementing the patient care pathway for neuroendocrine cancer

All people with NENs should be able to receive efficient, effective and personalised care, regardless of where they live. Many factors must be taken into consideration to address the barriers to optimal NEN care provision and integrate the patient care pathway for neuroendocrine cancer into the health system in England. The NHS Long Term Plan underlines the importance of holistic needs assessments and care plans, assignment of a clinical nurse specialist, and health and wellbeing support for effective, personalised care.³⁷ We hope that implementation of the pathway will reinforce the need for these aspects of care and contribute to the wider efforts across the NHS to spread effective service models, standardise diagnostic and treatment approaches and ensure optimal use of existing resources and expertise, all of which will work to reduce the inequities faced by those living with NENs. Clinical and institutional leaders must ensure this pathway not only benefits the patient experience but also encourages system-level improvements from the point of suspicion to treatment and follow-up care. The patient care pathway for neuroendocrine cancer alone cannot address all of the issues highlighted in this report. However, it can provide a framework for improving earlier access to specialist management and more appropriate onward care.

‘There is a lot of work being done across NHS England to improve earlier diagnosis and high-quality multidisciplinary care of a range of diseases, and we want to ensure NENs are recognised in this work.’

CATHERINE BOUVIER ELLIS, Neuroendocrine Cancer UK¹⁵²

We call on all stakeholders involved in planning and delivering care for people living with NENs to apply this pathway and address the barriers that exist at each stage. By clarifying what optimal care for NENs should look like, we hope to directly help people diagnosed with NENs, their families and carers, and the healthcare professionals responsible for their care. By suggesting ways to address the main barriers faced at each stage

of the pathway, we can ensure individuals receive a timely and accurate diagnosis. We can also drive improvements in outcomes, reduce delays in treatment, further support specialist MDTs and begin to tackle the numerous inequities in care provision across England. Not only will this improve the experience of people with NENs, but it will also optimise current infrastructure and resources, which will, in turn, go some way towards lessening the social and economic burden on the health system.

Glossary

Ablative therapy: the removal or destruction of a body part or tissue or its function, which may be performed via surgery, hormones, medications, radiofrequency, heat or other methods.¹⁵³

Advanced cancer: cancer that has spread to other parts of the body and is not possible to cure; also known as metastatic or secondary cancer.¹⁵⁴

Allied health professionals: professionals who provide holistic care at all stages of the patient journey post-diagnosis.¹⁵⁵ In NENs, the most common roles include physiotherapists, radiographers, occupational therapists and dietitians (monitoring nutrition among people with NENs is crucial in determining the most appropriate support and treatments).¹²²

Benign: a non-cancerous condition, tumour or growth that does not pose a threat to life.¹⁵⁶

Biological marker: a substance, physiological characteristic, gene etc. that indicates, or may indicate, the presence of disease, abnormal physiology or a psychological condition.¹⁵⁷

Biopsy: a procedure that involves taking a small sample of tissue from the person for examination under a microscope.¹⁵⁸

Carcinoid syndrome: a collection of symptoms caused by excessive hormone release from certain neuroendocrine tumours.¹²

Carcinoid tumour: an old term for slow-growing cancerous tumours usually found in the gastrointestinal system, and sometimes in the lungs or other sites; they may spread to the liver or other parts of the body, and secrete substances (e.g. hormones), causing carcinoid syndrome.⁹

Carcinoma: any tumour that grows in an uncontrolled way and is derived from cells that cover the internal or external surfaces of the body.¹⁵⁷

Chemotherapy: the treatment of disease, especially cancer, using chemical agents.¹⁵⁷

Clinical oncologists: doctors who assess, treat and manage people with cancer using a combination of chemotherapy and radiotherapy;¹⁵⁹ they are often involved in treating people diagnosed with NENs.⁹³

Clinical trial: a programme in which the safety and/or effectiveness of a diagnosis or treatment is assessed for research purposes.¹⁶⁰

Computerised tomography (CT): a type of scan that uses X-rays and a computer to create detailed images of the inside of the body.¹⁶¹

Embolisation: a minimally invasive procedure performed by interventional radiologists in which the blood supply to masses (tumours, growths etc.) or vessels is cut off, relieving symptoms caused by those masses or vessels.¹⁶²

Endoscope: a long, thin medical device that is used to examine the hollow organs of the body e.g. the digestive system.¹⁰⁰

Endoscopic procedure: a medical technique where the inside of the body is examined internally using an endoscope.¹⁶³

External beam radiotherapy: the most frequently used form of radiotherapy, where an external source of radiation is pointed at a particular part of the body.¹⁰²

First-line therapy: the first treatment given for a disease.¹⁶⁴

Follow-up: a routine examination of a person at various intervals after medical or surgical treatment.¹⁵⁷

Gallium-68: a radioactive element that is often used in conjunction with PET to image tumours, including neuroendocrine tumours and metastases.¹⁶⁵

Gastroenterology: the branch of medical science concerned with diseases of the stomach and intestines.¹⁵⁷

Gene therapy: the replacement or alteration of certain genes to prevent the occurrence of inherited diseases.¹⁵⁷

Germline mutation: a gene change in a body's reproductive cell (egg or sperm) that is passed on from parents to offspring.¹⁶⁶

Hepatopancreaticobiliary: in relation to the liver, biliary system and pancreas.¹⁶⁷

Histology: the study of the tissues of an organism.¹⁵⁷

Histopathologists: medical doctors who study organ and tissue biopsies and perform genetic analyses to help establish a diagnosis and inform treatment plans.¹⁶⁸

Immunotherapy: a type of treatment that involves taking medicines that encourage the immune system to fight cancer, infections and other diseases.¹⁶⁹

Internal radiation therapy: treatment with a radioactive material that is put inside the body to try to destroy cancer cells.¹⁰³

Magnetic resonance imaging (MRI): a type of scan that is often used to diagnose health conditions that affect organs, tissues and bone.¹⁷⁰

Malignant: a term used to describe cancer; malignant cells grow in an uncontrolled way and can invade nearby tissues and spread to other parts of the body.¹⁷¹

Medical oncologists: doctors who assess, treat and manage people with cancer using non-radiological treatments only;^{159 172} they are often involved in treating people diagnosed with NENs.⁹³

Metastasis: the spread of cancer to parts of the body other than the site of origin.¹⁷³

Multidisciplinary team (MDT): a team made up of disease-specific experts from different specialties, with a designated lead clinician.⁹³

Multidisciplinary team coordinators: professionals responsible for managing all patient information, documenting the person's progress against the NHS time frames for care, and ensuring relevant appointments are scheduled and all discussions are recorded to enable key decisions to be made efficiently.^{174 175}

Neoplasm: any abnormal new growth of tissue.¹⁵⁷

Nuclear medicine: the use of radioactive substances to examine, diagnose and treat people with life-threatening or chronic conditions.¹⁷⁶

Nuclear medicine physicians: medical doctors who use radioactive substances to examine, help to diagnose and treat people with conditions such as NENs.¹⁷⁶

Positron emission tomography (PET): a type of scan that produces three-dimensional, colour images that show how tissues work.¹⁷⁷

Primary care staff: healthcare professionals (e.g. GPs) who provide the first point of contact in the health and care system for most people, as well as playing a pivotal role in follow-up care.^{58 178} The majority of people eventually diagnosed with NENs are originally referred with suspected cancer by their GP.^{14 43}

Primary site: the place in the body where a cancer starts; also known as primary cancer.¹⁷⁹

Primary tumour: the original, or first, tumour in the body.¹⁸⁰

Radioligand therapy: a treatment that delivers radiation specifically targeted to proteins or other structures present on cancer cells.¹⁰⁴

Radiologists: doctors who specialise in medical imaging, which plays an indispensable role in NEN diagnosis, prognosis, treatment and management.⁸⁷

Radiotherapy: the treatment of disease, especially cancer, by means of internal or external radiation exposure.¹⁵⁷

Site-specific specialists: medical doctors, such as gastroenterologists and endocrinologists, who use expert knowledge to help manage symptoms, establish an accurate and timely diagnosis, and guide treatment plans.^{93 97}

Specialised services: NHS England services that support people with a range of rare and complex conditions; they often involve treatments provided to people with rare cancers, genetic disorders or complex medical or surgical conditions.¹⁸¹

Specialist nurses: healthcare professionals who provide direct, specialist care to individuals¹⁸² and liaise with other members of the multidisciplinary team; specialist nurses involved in the care of people with NENs will often have additional experience, expertise and training in NENs, oncology or endocrinology.¹⁸²

Surgeon: a medical professional trained to perform surgical operations.¹⁵⁷ As surgery is often the first treatment for many people diagnosed with NENs, surgeons are an integral part of the multidisciplinary team.⁹⁹

Targeted molecular medical therapies: therapies that act on specific biological structures associated with cancer to slow disease growth, progression and spread.¹⁰¹

Tumour: an abnormal mass of tissue that results when cells divide more than they usually would or do not die when they usually would.¹⁸³

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About

➔ Neuroendocrine Cancer UK

Neuroendocrine Cancer UK is a UK-wide charity solely dedicated to providing support and information to those affected by neuroendocrine cancer.

<https://www.neuroendocrinecancer.org.uk/>

➔ The Health Policy Partnership

The Health Policy Partnership is an independent research organisation, working with partners across the health spectrum to drive the policy and system changes that will improve people's health.

<https://www.healthpolicypartnership.com/>

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