The NETwork! Registry: Preliminary data suggests increasing incidence in a national study of neuroendocrine cancer in New Zealand (NZ)

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Background:

The incidence, treatment and survival from neuroendocrine tumours (NETs) in NZ has not previously been examined. Internationally, epidemiological descriptions of NETs are derived from institutional series or regional registries. In NZ there is currently a limited centralised record of NETs since historically many have not been recorded in the National Cancer Registry. We aimed to address this by compiling a national database of patients with NETs. We report initial data from a retrospective study, which includes every NET diagnosed in NZ over a 5-year period.

Aims:

1. To identify all patients diagnosed with NETs in NZ. This was done in two groups; an in-depth picture of all NETs diagnosed in NZ between 2008 and 2012 (described in this poster) and a longer term view of NETs in the Auckland region diagnosed between 1995 and 2012.
2. To provide a definitive description of NET epidemiology and outcomes over this time period.

Methods:

Our primary data source was the New Zealand Cancer Registry searched using ICD-03 codes. Secondary data was obtained from searches of both public and private pathology records in every district health board (n=20). Clinical data on each case was collected from inspection of individual medical records. Pulmonary small cell carcinoma was excluded from the study. Ethical approval for this study was obtained via HDEC Northern A Ethics Committee (ref 12/NTA/60).

In total, we collected information on 3334 patients, including presentation, tumour characteristics, investigation, treatment and outcome, collected by a team of research nurses and healthcare professionals who entered data via a remote desktop using MS Access for the user interface and SQL database for data storage. The data was secured using a double-password entry system; a University of Auckland network login and a database login. Data was entered according to a centralized protocol and data dictionary.

Classification of NETs was defined as per WHO 2010 nomenclature. Neuroendocrine tumours in the analysis included gastroenteropancreatic (GEP) NETs, bronchopulmonary carcinoids and neuroendocrine carcinoma, extrapulmonary small cell carcinoma, large cell carcinoma, medullary thyroid carcinoma, Merkel cell carcinoma, paraganglioma and phaechromocytoma and NETs of other primary sites such as gynaecological and genitourinary.

Age adjusted incidence rates were calculated using Statistics New Zealand summary data for the total NZ population during each of the five years 2008-2012 (1), these were adjusted against the WHO age distribution of a standard population (2001).

Figure 1. Age adjusted incidence of NETs

1736 patients were diagnosed with NET between 2008 and 2012, giving a crude incidence rate of 7.6 per 100,000 in 2008 steadily increasing to 8.6 per 100,000 in 2012. When adjusted for age, incidence rates rise from 5.7 per 100,000 in 2008 to 6.2 per 100,000 in 2012, a 9% increase in incidence over the 5 year period (Fig 1). Age adjusted incidence is comparable to incidence found in studies overseas(2).

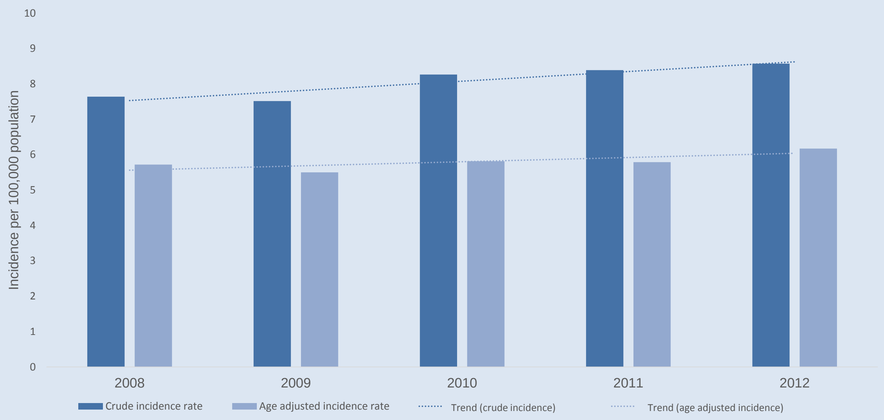

Figure 2. Spread of disease at diagnosis

A large proportion of patients (47%) had either lymph node or distant metastases diagnosed from radiological staging at diagnosis. Extrapolation to the Australian population suggests over 2000 new cases per year, with over 900 metastatic at diagnosis.
It should be noted that of the 1736 patients analysed, 324 patients did not have radiological staging completed either at diagnosis or within 12 months post diagnosis.

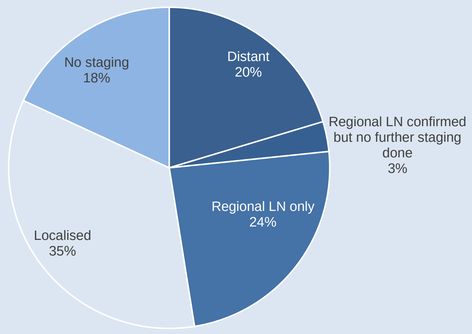

Figure 3. Primary site of NETs diagnosed 2008-2012

In total, gastroenteropancreatic NETs made up 49% of all NETs reported. Other common primary sites include lung (12%) and skin (11%). The primary site was unable to be identified in many cases (11%). The most common GEP NETs were jejunal / illeal (12%), appendical (11%) and pancreatic (7%).

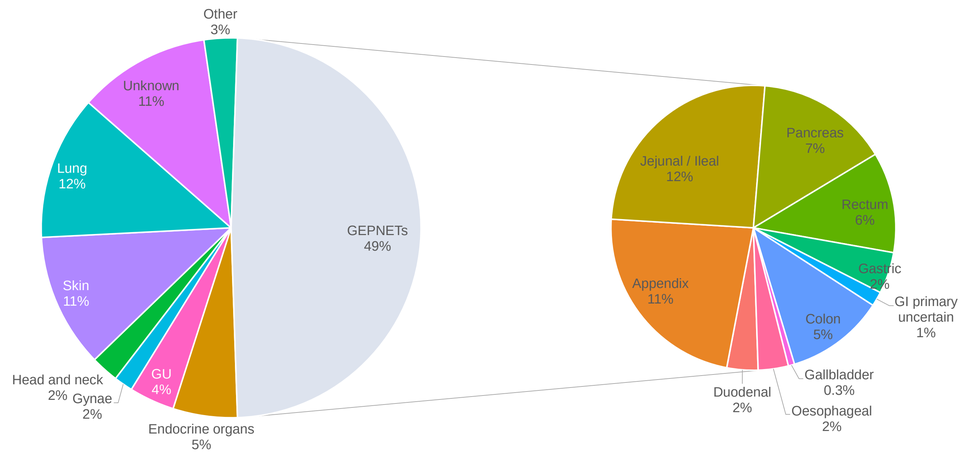

Figure 4. Incidence of NETs by ethnicity

There appears an apparently much lower rate of NETs in people of Asian ethnicity which warrants further investigation

Figure 5. Age at diagnosis of NETs 2008-2012

The median age of diagnosis of NETs varies considerably with primary site, with appendical NETs more common in younger patients with average age of diagnosis 35 years, whilst the median age of diagnosis for skin NETs (Merkel Cell Carcinomas) was 80 years. This suggests a diverse family of tumours with different aetiologies in different organ sites.

Figure 6. Survival of patients diagnosed with NETs 2008-2012

When reviewing mortality from all causes (not disease specific), the survival rates for patients with NETs vary considerably according to primary site of diagnosis. Overall, survival of NETs at 5 years post diagnosis is around 60%.

Conclusions:

- **The burden of neuroendocrine cancer is greater than previously perceived with a rising incidence and a high proportion of metastatic cases at diagnosis.**
- **NETs of different organs have distinct variation in incidence and survival. This stresses the importance of individualized multidisciplinary case management.**
- **The incidence of NETs is rising in New Zealand. This rise is evident over the relatively short time period of 5 years.**
- **We believe this is the first analysis of NET incidence conducted on a complete national population, and therefore offers a level of accuracy not previously available.**

The incidence of NETs is higher than the incidence of ovarian, stomach, cervical or oesophageal cancer(3). Our data also shows that NETs arising from different anatomical sites behave quite differently in terms of age at diagnosis and survival. In addition there are also wide variations between individual patients when comparing age of diagnosis and survival. These results serve as a reminder that NETs are not all the same but are a conglomeration of different disease processes, and therefore require organ specific management. The lower incidence of NETs recorded in patients of Asian ethnicity is notable, and warrants further investigation as to the reasons behind this.

The Register is an extremely powerful tool which can be used to identify patients and to link their clinical information with tissue samples for genomic analysis annotated with the patients' clinical outcome. The collection of this information has taken over three years; identifying patients from hospital pathology records as well as the NZCR revealed a much greater number of patients diagnosed than we had anticipated, probably because some NETs were historically categorized as non-malignant and hence were not reported to the National Cancer Registry. This thorough examination of an entire population has resulted in a resource that we hope will be used to progress many more projects investigating NET subgroups and populations, which will guide healthcare funding and delivery for people with NETs.

References:

1. Statistics New Zealand Census Data 2013 / 2006
2. Dasart, A. et a. Trends in the Incidence, Prevalence and Survival Outcomes in Patients with Neuroendocrine Tumours in the United States. JAMA Oncology, April 2017
3. New Zealand Ministry of Health Cancer: New registrations and deaths 2013