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Global Challenges in Access to Diagnostics and Treatment for Neuroendocrine Tumor (NET) Patients

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Abstract

SCAN, an online survey, measured access to diagnosis, treatments and monitoring of neuroendocrine tumor (NET) patients globally. Between September and November 2019, NET patients and healthcare professionals (HCPs) completed an online, semi-standardized survey with 54 patient questions and 33 HCP questions. A total of 2359 patients with NET and 436 HCPs responded. Misdiagnosis was common (44% [1043/2359]). Mean time to diagnosis was 4.8 years (standard deviation [SD], 6.2). Compared with global figures (60% [1407/2359]), the availability of ^{68}Ga-DOTA positron emission tomography (PET)/computed tomography (CT) was significantly lower in Asia (45% [126/280]) and higher in Oceania (86% [171/200]). HCPs reported that ^{68}Ga-DOTA PET/CT was free/affordable to fewer patients in Emerging and Developing Economies (EDE) than Advanced Economies (AE; 17% [26/150] and 59% [84/142], respectively). Compared with global data (52% [1234/2359]), patient-reported availability of peptide receptor radionuclide therapy (PRRT) was significantly lower in Asia (31% [88/280]) and higher in Oceania (61% [122/200]). Significant differences were observed in average annual NET specialist costs between AE and EDE ($1081 and $2915, respectively). Compared with AE, patients in EDE travelled farther for NET specialists (1032 [SD, 1578] and 181 [SD, 496] km, respectively). Patients and HCPs both recommended referral to HCPs that were more knowledgeable in the field of NETs and had better access to NET experts/specialist centers. National care pathways, enhancing HCP NET knowledge and ensuring effective diagnostics and access to appropriate treatments are crucial to improving patient survival and NET care worldwide.

KEY WORDS

Neuroendocrine tumor, access to diagnostics, global challenges, patient survey, healthcare provider survey

WHAT'S NEW/NOVELTY AND IMPACT OF THE WORK

Access to diagnosis and treatment in NETs varies Worldwide due to inconsistent availability of diagnostic facilities/techniques, affordability, diagnosis waiting time and misdiagnosis. This study surveyed 2359 patients and 436 healthcare providers and revealed problematic access to NET diagnostic facilities and treatment in developing economies than advanced economies with higher costs. The findings are important for guiding improved provision of diagnostic and care pathways for NET in differing World regions and potentially optimizing treatment and survival.

INTRODUCTION

Neuroendocrine tumors (NETs) are rare neoplasms arising from neuroendocrine cells.[1] Extensive presence of these specialized cells in the body allows NETs to develop in many organ systems, primarily including the gastrointestinal tract, pancreas and lung.[1,2] The body-wide presentation, diverse symptoms and rarity of NETs make timely diagnosis and management challenging.[1,3] Reported incidence of NETs varies greatly, likely owing to underreporting and varying nomenclature/classifications.[4] Recent data suggest an incidence of 6.98/100,000 in the US[5] and 8.6/100,000 in the UK.[6] Incidence rates are increasing, possibly due to improved awareness of NET and diagnostic tools.[5,6]

The International Neuroendocrine Cancer Alliance (INCA) is a global, non-profit organization, comprising 29 patient advocacy and research groups from 25 countries. The INCA undertook international NET surveys in 2014[7] and 2017,[8] which identified considerable patient-reported burden relating to symptoms and healthcare resource use, plus significant unmet needs. In 2019, the INCA launched SCAN (Survey of Challenges in Access to Diagnostics and Treatment for Neuroendocrine Tumor Patients), to globally assess current provision of NET diagnostics, treatment and care in terms of awareness, availability, affordability and quality. It also aimed to provide information in four areas:

Time to diagnosis; awareness and information spread; access to optimal NET healthcare; adequacy of healthcare systems to NET patient needs.

MATERIALS AND METHODS

2.1 Survey methods

Between September and November 2019, NET patients, their family/caregivers and healthcare professionals (HCPs) voluntarily completed an online, semi-standardized survey. The patient survey included 54 questions (46 closed; eight open-ended), while the HCP survey contained 33 questions (26 closed; seven open-ended), with most being cross-comparable (Supplementary Appendix). Completion of every question was not compulsory; results were based on total responses per question. The survey was freely available in 14 languages. Dissemination was via NET patient groups, medical societies and social media. Participation was not limited to patients or HCPs associated with expert NET centers. No formal matching of patients with their HCPs occurred. The survey tool used checked the IP addresses of respondents and automatically excluded the submission of multiple answers from a single IP address. Also, SPSS was used to control for identical answers from the same IP address to avoid repetition. NET-related expenses were calculated as the average annual out-of-pocket expenses from household income. Patient unit costs were calculated as the annual reported cost per intervention divided by the frequency of the intervention in those reporting a cost, converted to 2020 US dollars. Healthcare quality was rated on a 5-point Likert scale (1=poor to 5=excellent). Responses were anonymous; thus, ethical approval was not required.

2.2 Statistical analysis

Descriptive statistics, including means, standard deviations (SD) and percentages were used to summarize survey responses. Analyses were performed using SPSS 15.0 for Windows and Microsoft Excel. Chi-squared and t-tests were used, as appropriate, to assess differences between groups. A P-

value of less than 0.05 was accepted as statistically significant. Advanced Economies (AE) and Emerging and Developing Economies (EDE) were classified as per the International Monetary Fund.[9]

3. RESULTS

3.1 Respondent characteristics

A total of 2359 NET patients (376 [16%] questionnaires were completed by their family/caregivers; Table 1 and S1) and 436 HCPs (Table S2) completed the questionnaire. Most patients were European (47% [1102/2359]) or North American (NA, 31% [727/2359]), and the gastrointestinal tract/pancreas were the most common primary sites (71% [1408/1983]). HCPs chiefly worked in Asia (42% [184/436]) or Europe (34% [149/436]) and were primarily medical oncologists (25% [108/436]; Table S3). Patients were predominantly from AE (88% [2076/2359]), whereas HCPs were evenly distributed across economies (AE, 51% [221/436]).

3.2 Neuroendocrine tumor healthcare

Globally, patients rated NET healthcare quality as 3.5 on a 5-point Likert scale. In comparison, significantly higher scores were reported by patients in Europe (3.6) and Oceania (3.8), and significantly lower scores by patients in Asia (2.6). Compared with global data (3.3), HCPs rated care higher in Europe (3.6), NA (3.9) and Oceania (4.0), and lower in Asia (2.8). Patient and HCP scores were aligned across continents.

Almost half the patients (49% [1149/2359]) and HCPs (52% [228/436]) reported NET state healthcare coverage, most commonly in Europe (64% [709/1102] and 63% [94/149], respectively; Table S4). In AE, 0–10% of annual household income was frequently used for NET-related expenses (41% [860/2076]). In EDE, almost half (47% [134/283]) the patients reported that ≥31% of annual income

contributed to NET expenses. No statistically significant differences in average annual patient out-of-pocket costs were observed between EDE ($13024; N=199) and AE ($3932; N=1145).

3.3 Early diagnosis

Globally, almost half (44% [1043/2359]) the patients were initially misdiagnosed. Of these, less than one-fifth (19% [195/1042]) received a NET diagnosis within one year of developing their first symptom. A total of 26% (606/2359) were incidentally diagnosed with NETs during testing for another condition. Globally, mean time to diagnosis for misdiagnosed patients was 4.8 (SD, 6.2) years. In comparison, there was considerable variation between continents (Asia 2.3, Europe 4.0, NA 6.4 years), although no significant difference was observed for Oceania (4.8 years). At diagnosis, 24% (554/2359) of patients reported having stage IV NETs, 15% (349/2359) stage 0-1 and 17% (401/2359) stage II or III. A total of 45% (1055/2359) did not know or were not told their tumor stage, although half (50% [523/1055]) of these tumors were described as having spread.

Time to diagnosis (TTD) can be simply time from the first noticed symptoms (can even be vague symptoms for non-functional NET leading to seeking medical advice) up to final diagnosis. It is true, however, that incidental diagnoses still cannot be included.

Diagnostics that led to the initial NET diagnosis were most commonly suggested by gastroenterologists (26% [435/1670]) and general practitioners (GPs; 20% [334/1670]) according to gastroenteropancreatic-NET patients; by pulmonologists (26% [60/234]) and surgeons (14% [32/234]) according to lung NET patients; and by endocrinologists (33% [35/106]) according to genetic/inherited NET patients. Globally, 60% (1407/2359) of patients reported that ^{68}Ga-DOTA positron emission tomography (PET)/computed tomography (CT) was available as a diagnostic tool (Figure 1). In comparison, according to patients, the availability of this scan was significantly lower in Asia and Europe (45% [126/280] and 51% [561/1102], respectively) and greater in NA and Oceania (73%

[529/727] and 86% [171/200], respectively). Although not statistically significant, a greater number of HCPs reported that ^{68}Ga-DOTA PET/CT was available as a diagnostic tool (Global 71% [310/436], Asia 68% [125/184], Europe 70% [105/149], NA 77% [54/70], Oceania 88% [15/17]).

Access to serum Chromogranin A (CgA) as a diagnostic tool varied considerably between continents. Compared with global data (58% [1377/2359]), a significantly higher proportion of patients in NA (70% [507/727]) and Oceania (71% [142/200]) reported that they had access to CgA compared with Europe (57% [630/1102]), and fewer in Asia (26% [73/280]). There was a significant difference in access to CgA reported by HCPs globally (72% [314/436]) and those in Europe (84% [125/149]; P=0.004), NA (86% [60/70]; P=0.015), Oceania (88% [15/17]) and Asia (55% [102/184]). The diagnostic tool availability reported by patients followed a similar trend across continents.

HCPs reported that CT was free/affordable for approximately three-quarters of patients in AE and EDE (79% [124/156] and 76% [110/145], respectively). Biopsy and CgA were free/affordable for a high proportion of AE patients (79% [126/159] and 76% [116/152], respectively), but lesser in EDE (54% [91/170] and 67% [89/132], respectively). Fewer patients reported ^{68}Ga-DOTA PET/CT as free/affordable (AE, 59% [84/142]; EDE, 17% [26/150]).

3.4 Awareness of diagnostic, treatment and monitoring tools

Globally, for both patients and HCPs, biopsy and CT were the most well-known diagnostic tools (biopsy, 81% [1917/2359] and 94% [411/436], respectively; CT, 79% [1874/2359] and 86% [376/436], respectively) and the most widely available (biopsy, 79% [1872/2359] and 94% [408/436], respectively; CT, 78% [1837/2359] and 85% [370/436], respectively). However, a sizeable proportion of patients and HCPs were unaware of ^{68}Ga-DOTA PET/CT (33% [785/2359] and 19% [83/436]), respectively) or CgA (38% [908/2359] and 21% [92/436], respectively) as diagnostic tools.

Surgery was the most well-known treatment (patients, 84% [1983/2359]; HCPs, 90% [392/436]). Overall, HCPs were aware of somatostatin analogs (SSAs; 89% [387/436]) and peptide receptor radionuclide therapy (PRRT; 77% [336/436]), but patient awareness of these was more limited (SSAs 68% [1599/2359], PRRT 64% [1520/2359]). Monitoring using conventional imaging was well-recognized across continents (patients 85% [2007/2359], HCPs 91% [396/436]). However, fewer patients and HCPs were aware of CgA monitoring (66% [1550/2359] and 76% [331/436], respectively) and ^{68}Ga-DOTA PET/CT monitoring (68% [1603/2359] and 74% [323/436], respectively).

Further to PRRT, its rollout across NA has increased significantly in recent years compared to Europe, and rollout varies significantly between countries, as reflected in the differences in awareness between HCP's and patients and between both regions. HCPs are potentially more aware of PRRT than patients possibly because of limited knowledge of treatment options and medical terminology amongst a heterogeneous patient group surveyed. Conversely, most HCPs regularly seeing NETs are at least broadly familiar with their management. Participants from NA may have been largely more well informed and involved patients.

3.5 Awareness of NET Clinical Trials

A higher proportion of patients were unaware of NET trials compared with HCPs (28% [659/2359] vs. 16% [68/436]; P<0.001). Patient understanding as to the purpose of clinical trials varied from poor/fair (22% [524/2359]), to good (24% [561/2359]), to very good/excellent (39% [920/2359]; 15% [354/2359]) were uncertain. Only 17% (403/2359) of patients had participated in NET trials, while 79% (1861/2359) desired more information and 67% (1586/2359) wanted to participate in trials if eligible.

3.6 Access to treatments and care

The majority (80% [1893/2359]) of patients reported that surgery was widely available. Compared with global data, significantly fewer patients from Asia (P<0.001) and more from Europe (P=0.002)

reported that SSAs were widely available (Figure 2). Similarly, significant differences were reported by patients regarding PRRT availability. Compared with global figures, HCPs reported no significant differences in SSA or PRRT availability, except for PRRT in NA (64 vs. 80%; P=0.007).

HCPs reported that surgery, SSAs and PRRT were free/affordable to a higher proportion of AE patients compared with EDE patients (P<0.001 for all; Figure 3). Statistically significant differences regarding unit costs for interventions were also observed between AE and EDE patients, although sample sizes were small. More details are provided in Table S5, available in the Supplementary Appendix.

Monitoring using conventional imaging was widely available (patients 82% [1941/2359], HCPs 90% [394/436]). Globally, 60% (1416/2359) of patients reported that ^{68}Ga-DOTA PET/CT monitoring was available. In comparison, significant differences were observed for Asia (43% [120/280]), Europe (55% [609/1102]), NA (68% [493/727]) and Oceania (86% [171/200]). Similar findings were reported by HCPs.

Globally, CgA monitoring was available to 62% (1460/2359) of patients. In comparison, significant differences were observed for Asia (29% [80/280]), NA (70% [510/727]) and Oceania (76% [151/200]). Globally, HCPs reported that 71% of patients had access to CgA monitoring. In comparison, significant differences were observed for patients in Asia (55% [101/184]), Europe (82% [122/149]) and NA (83% [58/70]).

According to HCPs, significantly more AE patients could afford conventional imaging (78% [143/183] vs. 68% [103/152]) and CgA monitoring (74% [127/171] vs. 63% [75/119]) compared with EDE patients. Similar results were reported for ^{68}Ga-DOTA PET/CT monitoring (AE, 61% [96/158] vs. EDE, 22% [16/120]). Patient unit cost of monitoring tools was similar for AE and EDE: Conventional imaging in

AE was $504 (N=343) vs. $669 in EDE (N=108); CgA was $209 in AE (N=181) vs. $586 in EDE (N=46); ^{68}Ga-DOTA PET/CT was $1056 in AE [N=114] vs. $1251 in EDE (N=41).

3.7 Neuroendocrine tumor specialists

Globally, 53% (1255/2359) of patients visited a NET specialist within the preceding 12 months (Table 2). The number of specialist visits within the last year were significantly higher in AE than EDE (55% [1143/2076] vs. 40% [112/283]). Average annual specialist costs were significantly lower in AE ($1081) than EDE ($2915). Patients traveled further to see NET specialists in EDE (1032 km [SD 1578]) than AE (181 km [SD 496]).

A quarter of patients (25% [594/2359]) and approximately a third of HCPs (37% [161/436]) reported poor access to reliable NET information. Another key issue for patients was the lack of experts providing first or second opinions (23% [550/2359]). HCPs were most concerned with slow documentation processing between experts/institutions (33% [143/436]). Top recommendations by patients and HCPs were to have more HCPs knowledgeable in NETs (62% [1470/2359] and 50% [217/436], respectively) and better NET specialist/center access (53% [1244/2359] and 63% [275/436], respectively). Patients also recommended availability of a wider range of treatments (34% [806/2359]), while HCPs recommended more information and opportunities relating to NET trials (43% [187/436]).

4 DISCUSSION

4.1 Summary of findings and comparisons with previous surveys

SCAN provided an extensive representation of current NET care, identified important challenges and specified recommendations on improving quality of care. Globally, NET care was shown to require improvement, particularly in Asia and EDE. Delayed diagnosis remains a major issue. Although SCAN

results showed improved access to specialized diagnostics, time from first symptoms to correct diagnosis was still poor (mean 4.8 years) and this major unmet need has not improved from the INCA NET survey conducted in 2014 (4.3 mean years)[7] and the NET Patient Foundation survey in 2018 (4.5 median years).[10] Access to ^{68}Ga-DOTA PET/CT has improved. Compared with the INCA NET survey in 2017,[8] fewer patients and HCPs reported that ^{68}Ga-DOTA PET/CT was unavailable (40 vs. 71% and 29 vs. 38%, respectively). Availability of PRRT reported by patients was similar to the 2017 survey, although a higher proportion of HCPs reported that PRRT was unavailable compared with SCAN (43 vs. 37%).[8] Despite some improvements, SCAN highlighted that global availability and affordability of specialized tools remains poor and a critical area to advance.

4.2 Factors affecting neuroendocrine tumor diagnosis

Time to diagnosis remains considerable, partly owing to the non-specific symptoms of NETs,[11] but also the sparsity and inaccessibility of HCPs that are knowledgeable in NETs.[12,13] Better access to NET experts was previously highlighted as a major unmet need[7,14] and continues to exist. Singh[7] reported an average distance to NET specialists of 182 km compared with 255 km in SCAN, reflecting deteriorating accessibility; however, there were less African and Asian patients in that survey than in SCAN (5 vs. 13%). Along with NET specialists, SCAN found other HCPs, namely GPs, play critical roles in NET care, highlighting that improvement of awareness and education of all HCPs is crucial to achieving early diagnosis.

Poor access to diagnostics in EDE supports economic disparities highlighted by Hallet[15] who assessed NET patient care across economic groups. Although statistically non-significant due to small samples, low socioeconomic status (SES) patients underwent fewer nuclear medicine diagnostics than high SES patients.[15] Low SES was also associated with worse overall survival (hazard ratio, 1.2; 95% confidence interval, 1.1–1.3) partly due to increased likelihood of metastatic recurrence (41 vs. 38%).[15] Hallet also

found low SES to be an independent predictor of worse overall survival for NET patients.[16] The inaccessibility of treatments and monitoring tools in EDE highlighted by SCAN means patients may lack continuous treatment and follow-up, with consequent inferior survival of low SES patients.

SCAN identified poor patient awareness of diagnostics, treatments and clinical trials, likely due to poor access to NET information, highlighted by previous surveys.[7,8,17] Leyden[8] reported less than one-quarter of patient informational needs were fully met. Patients believed GPs lacked NET knowledge and struggled to obtain information from HCPs not specialized in NETs.[17] Obfuscation surrounds NET terminology, and patients report perplexity about NET terms.[18,19] A recent trial, in which 55% of patients sought more information at baseline, found that a web-based, personalized information system did not improve patients' satisfaction with information received.[20] These findings highlight the inadequate improvement in dissemination of information. Provision of understandable information must increase to improve patient experiences, ideally through direct contact with HCPs and NET patient associations.

4. 3 Study limitations

SCAN represents the biggest global compendium of NET data extant and assessed patient and HCP perspectives regarding NET care. Almost 3000 patients and HCPs responded; however, caution is needed when interpreting results for Africa and South America due to small sample sizes. Voluntary response sampling allowed for efficient data collection, but potentially resulted in group numbers and demographic and geographic imbalances. For example, many respondents were well-educated and of higher income, and the use of an online survey tool might have created difficulties for some patients. HCPs were from a wide variety of specialties and approximately one-fifth of HCPs reported no experience in diagnosing and treating NETs. Concerning time to diagnosis, the fact that incidental diagnoses cannot be included is a limitation.

The methodology used did not appear to impact the age profile of the sample with the age distribution being similar to that of other registries.[5,21,22] Voluntary sampling may also introduce bias by reflecting highly engaged respondents. Due to the relatively small number of respondents from certain regions, there are clear discrepancies between Asia and Europe/NA/Oceania and between EDE and AE, in favor of Eu/NA/Oc and AE, respectively. Also, the completion of every question was not compulsory, and so the number of respondent per single question is unknown, which is a potential limitation. However, these demographic features do not appear to have a significant impact on the explorative data results, such as, NET type, tool usage, diagnosticians used, issues and recommendations. Therefore, despite limitations and demographic biases, SCAN provides robust NET data that are aligned across NET types and continents, and highlights continued unmet needs alongside invaluable recommendations from patients and HCPs for improving NET healthcare.

4.4 Conclusion

Development of national care pathways, mandatory expert center referral, and support for resource capability ensuring effective diagnostics and access to appropriate treatments for all patients are critical to achieving earlier diagnosis and optimal NET care. Tackling accessibility and affordability issues, especially in EDE, is key to minimizing care access disparities between SES groups. Raising awareness amongst GPs and other HCPs that NETs tend to present late with non-specific symptoms that may be attributed to an alternative diagnosis is also imperative to further improve NET care. SCAN contributes to positioning NET research on an equal footing with other cancers of similar prevalence and the results are crucial to improving patient survival and NET care worldwide.

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CONFLICT OF INTEREST

Marianne Pavel has received consultancy fees from Ipsen, AAA, Hutchmed and honoraria for presentations from Ipsen, AAA, Boehringer Ingelheim, Riemser and Lilly. Teodora Kolarova has received institutional grants from AAA, Ipsen, ITM, Novartis and Camurus as part of INCA. Simron Singh has received institutional grant funding from AAA/Novartis and honorarium from Ipsen, AAA/Novartis. Simone Leyden has received consultancy fees from ITM and is an employee of Telix. None of the other authors have any conflicts.

DATA AVAILABILITY STATEMENT

SCAN data are available from the corresponding author upon request.

ETHICS STATEMENT

Responses were anonymous, thus ethical approval was not required

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Table 1: Summary of NET patient sociodemographics and clinical characteristics

	Patients* n, (%) (N=2359)
Sociodemographics and clinical characteristics	
Region (n, %)	
Africa	16 (1)
Asia	280 (12)
Europe	1102 (47)
North America	727 (31)
South America	34 (1)
Oceania	200 (8)
Economy (n, %)	
Advanced	2076 (88)
Emerging and developing	283 (12)
NET Type (n, %)**	
Gastroenteropancreatic	1408 (71)
Genetic/inherited	91 (4)
Lung	198 (10)
Paraganglioma/ Pheochromocytoma	61 (3)
NET of unknown origin	131 (7)

Other	54 (3)
Don't know	40 (2)
Age, mean (SD) years	13 (56)
Age (n, %)	
0-49	662 (28)
50-59	686 (29)
60-69	669 (28)
≥70	342 (15)
Female, %	1486 (63)
Age at diagnosis, mean (SD) years	51 (13)
Years with diagnosis, mean (SD) years	5 (6)
Education (n, %)	
Primary or lower	66 (3)
Secondary	275 (12)
College, non-university high school	747 (32)
University or higher	1205 (51)
Prefer not to say	66 (3)
Income level (n, %)	
Low	420 (18)
Average	1324 (56)

High	482 (20)
Cannot say	133 (6)

*16% of NET patients were caregivers; **NET type only reported for 1983 patients; NET: neuroendocrine tumor; SD: standard deviation

Table 2: Access to a NET specialist

	Awareness, % (n)	Consulted with NET specialist in last year, % (n)	Average annual frequency of consulting with a NET specialist, mean (SD)	Average distance, mean km (SD)	Average yearly costs for NET specialist, mean USD (SD)
Global	73 (1724/2359)	53 (1255/2359)	5 (12) [N=1135]	255 (706) [N=1154]	1485 (8524) [N=313]
Africa	19 (3/16)	19 (3/16)	5 (6) [N=3]	1900 (2693) [N=3]	-
Asia	58 (162/280)	43 (120/280)	8 (25) [N=90]	823 (1341) [N=107]	4565 (17417) [N=71]
Europe	79 (874/1102)	61 (668/1102)	4 (12) [N=606]	127 (504) [N=627]	378 (1190) [N=101]
North America	72 (523/727)	48 (350/727)	4 (5) [N=330]	349 (693) [N=310]	819 (1925) [N=110]
South America	44 (15/34)	26 (9/34)	4 (4) [N=7]	319 (334) [N=7]	264 (60) [N=6]
Oceania	74 (147/200)	53 (105/200)	6 (13) [N=99]	112 (200) [N=100]	456 (494) [N=24]
AE	76 (1576/2076)	55 (1143/2076)	4 (10) [N=1050]	181 (496) [N=1053]	1081 (4651) [N=244]

EDE	52 (148/283)	40 (112/283)	10 (30) [N=85]	1032 (1578) [N=101]	2915 (15918) [N=69]

AE: advanced economies; EDE: emerging and developing economies; SD: standard deviation; km; kilometers; NET: neuroendocrine tumor; USD: United States dollars.

FIGURE 1: Availability of specialized diagnostic tools

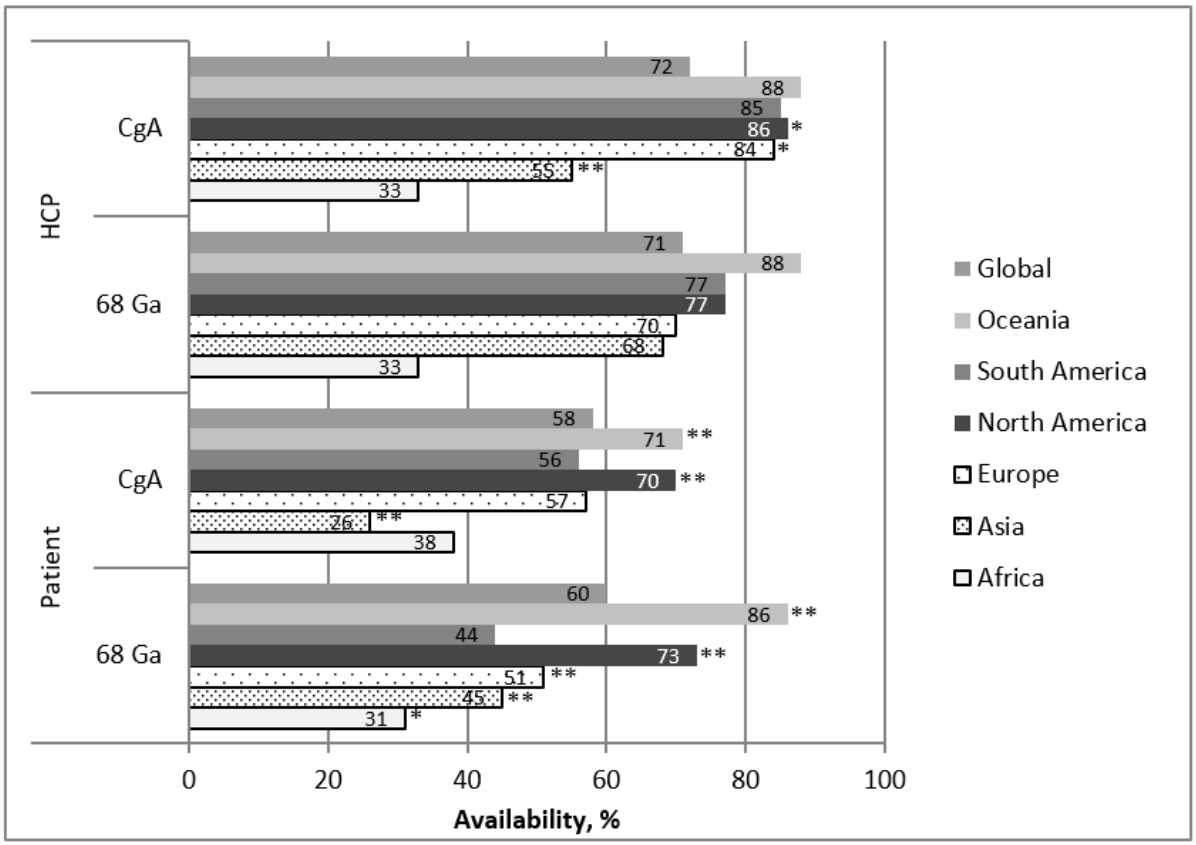

Figure 1 legend: Africa: Patients (N=16), HCPs (N=3); Asia: Patients (N=280), HCPs (N=184); Europe: Patients (N=1102), HCPs (N=149); North America: Patients (N=727), HCPs (N=70); South America: Patients (N=34), HCPs (N=13); Oceania: Patients (N=200), HCPs (N=17); Global: Patients (N=2359), HCPs (N=436). *P<0.05 and **P<0.001 for continent vs. global comparisons. CgA, chromogranin A; FDG-PET, fluorodeoxyglucose-positron emission tomography; HCP, healthcare professional; ^{68}Ga, ^{68}Ga-DOTA positron emission tomography/computed tomography.

FIGURE 2: Availability of specialized treatment

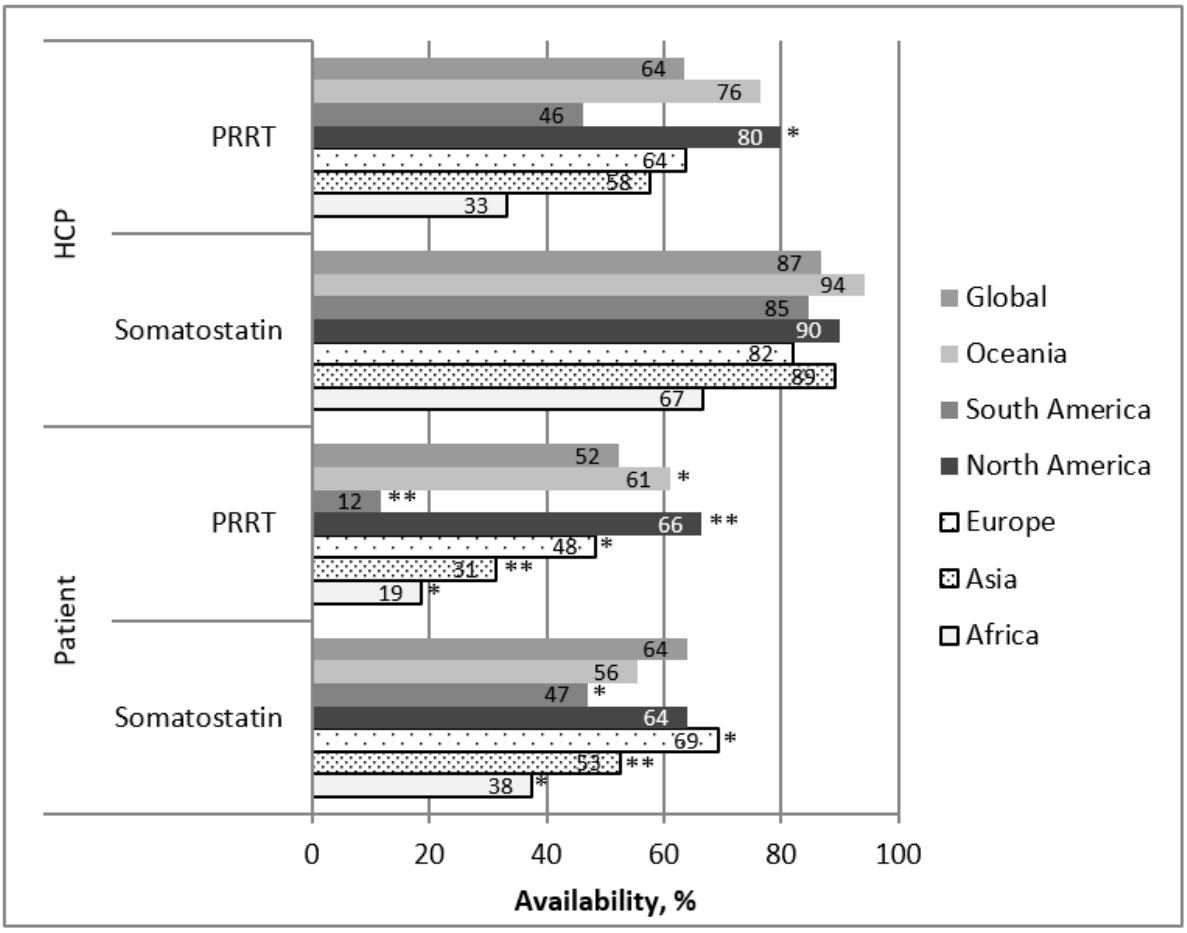

Figure 2 legend: Africa: patients (N=16), HCPs (N=3); Asia: Patients (N=280), HCPs (N=184); Europe: Patients (N=1102), HCPs (N=149); North America: Patients (N=727), HCPs (N=70); South America: Patients (N=34), HCPs (N=13); Oceania: Patients (N=200), HCPs (N=17); Global: Patients (N=2359), HCPs (N=436). *P<0.05 and **P<0.001 for continent vs. global comparisons. HCP, healthcare professional; PRRT, peptide receptor radionuclide therapy.

FIGURE 3: Healthcare professionals rated affordability and mean neuroendocrine tumor patient unit costs of the top five most frequently received treatments

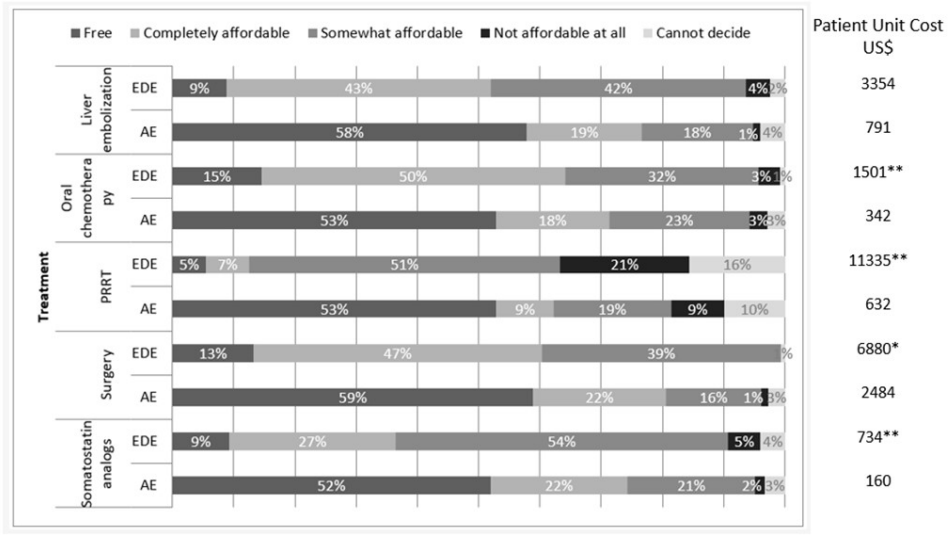

Figure 3 legend: Somatostatin analog: HCP AE (N=183), EDE (N=151), Patient AE (N=299), EDE (N=52); Surgery: HCP AE (N=180), EDE (N=151), Patient AE (N=90), EDE (N=31); PRRT: HCP AE (N=172), EDE (N=128), Patient AE (N=40), EDE (N=10); Oral chemotherapy: HCP AE (N=174), EDE (N=117), Patient AE (N=47), EDE (N=21); Liver embolization: HCP AE (N=171), EDE (N=125), Patient AE (N=11), EDE (N=16). *P<0.05 and **P<0.001 for AE vs. EDE Patient unit cost comparisons. AE, advanced economies; EDE, emerging and developing economies; HCP, healthcare professional; PRRT, peptide receptor radionuclide therapy