



Epidemiologia dei Tumori Neuroendocrini

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AZIENDA OSPEDALIERA DI RILIEVO NAZIONALE
NAPOLI



OSPEDALE SACRO CUORE DI GESÙ
FATEBENEFRAELLI
U.O. DI ONCOLOGIA

Andamento epidemiologico negli anni

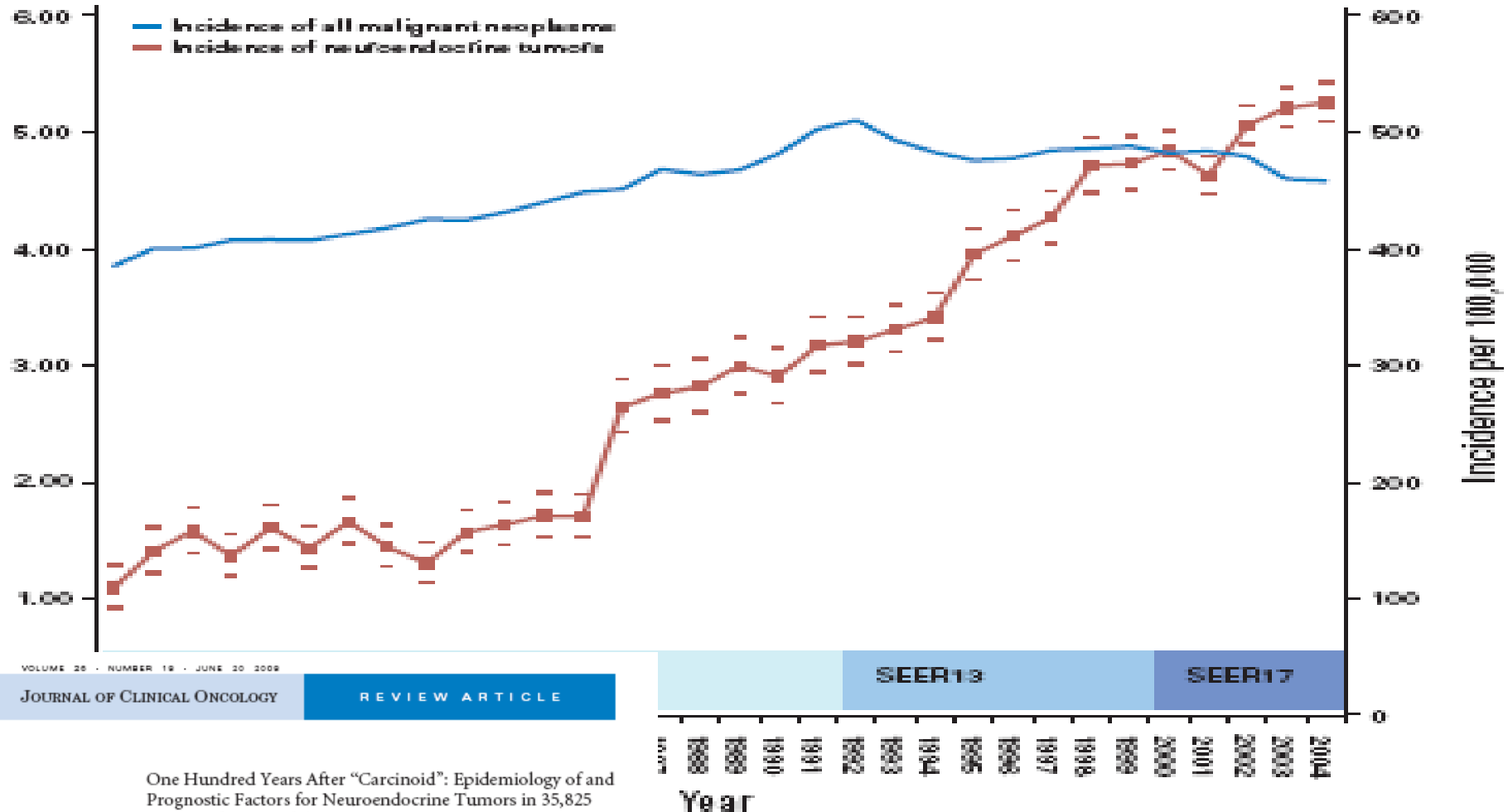
Storia clinica dei NETs

Indagine epidemiologica Cardarelli





NET incidence is increasing dramatically



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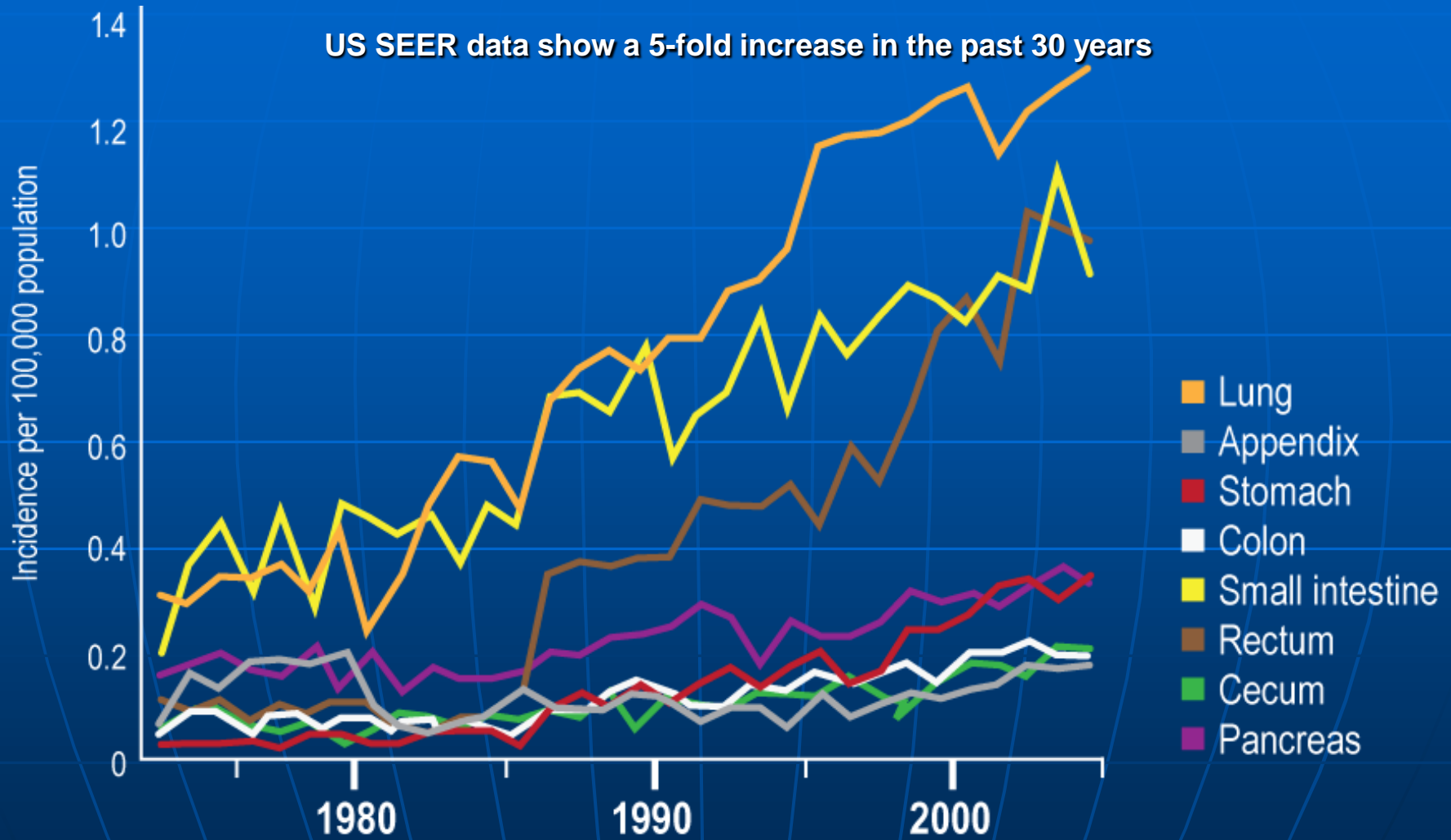
REVIEW ARTICLE

One Hundred Years After "Carcinoid": Epidemiology of and Prognostic Factors for Neuroendocrine Tumors in 35,825 Cases in the United States

James C. Yao, Manal Hassan, Alexandria Phan, Cecile Dugohoy, Colleen Leary, Joanne E. Mara, Eddie E. Abdalla, Jason B. Fleming, Jean-Nicolas Vauthey, Afif Rashid, and Douglas B. Evans



NET Incidence is increasing dramatically





Overview of Neuroendocrine Tumors (NETs)

NETs are sometimes called carcinoid tumors

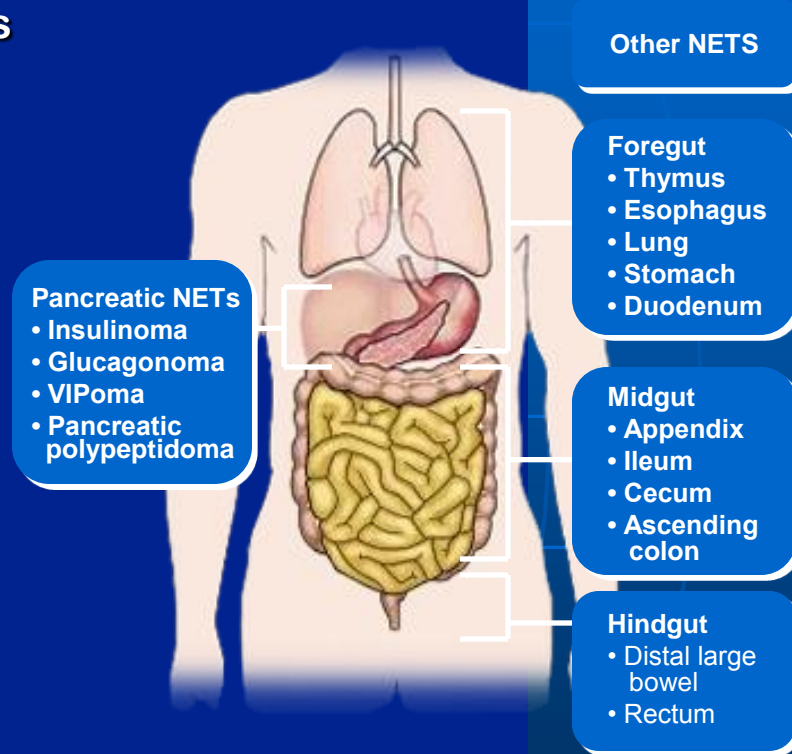
May be undetected for years without obvious signs or symptoms

NETs can be characterized by their ability to produce peptides that lead to their syndromes

Can be symptomatic and asymptomatic

NETs are generally classified as foregut, midgut, or hindgut depending on their embryonic origin

- Foregut tumors develop in the respiratory tract, thymus, stomach, duodenum, and pancreas
- Midgut tumors develop in the small bowel, appendix, and ascending colon
- Hindgut tumors develop in the transverse colon, descending colon, or rectum





Differenze tra NET GI e NET pancreatici

Table 5 Survival of patients

	3 years survival rate (%)	5 years survival rate (%)	p (log-rank test)
Age at diagnosis			
> 50 years	74.7	73.3	0.03
≤ 50 years	89.4	85.3	
Primary tumor site			
PETs	71.3	62	0.0001
GI carcnooids	89.9	89.9	

Endocrine-Related Cancer (2005) 12 1083–1092

Prognostic factors and survival in endocrine tumor patients: comparison between gastrointestinal and pancreatic localization

Francesco Panzuto¹, Silvia Nasoni¹, Massimo Falconi⁴, Vito Domenico Corleto¹,
Gabriele Capurso¹, Sara Cassetta¹, Michela Di Fonzo¹, Valentina Tornatore¹,
Massimo Milione^{1,5}, Stefano Angeletti¹, Maria Sofia Cattaruzza²,
Vincenzo Ziparo³, Cesare Bordi⁵, Paolo Pederzoli⁴ and Gianfranco Delle Fave¹

	Overall <i>n</i> (%)	Pancreas <i>n</i> (%)	GI tract <i>n</i> (%)
Disease staging [<i>n</i> = 154]			
Group I	55 (35.7)	20 (36.4)	28 (50.9)
Group II	18 (11.7)	6 (33.3)	12 (66.7)
Group III	61 (39.6)	28 (45.9)	26 (42.6)
Group IV	20 (13)	11 (55)	7 (35)
Differentiation of tumor cells [<i>n</i> = 125]			
Good	112 (89.6)	49 (43.7)	56 (50)
Poor	13 (10.4)	9 (69.3)*	3 (23)
Ki67 [<i>n</i> = 96]			
≤ 2%	58 (60.4)	22 (37.9)	30 (51.7)
>2%	38 (39.6)	27 (71)†	9 (23.7)
Primary tumor size [<i>n</i> = 129]			
≤ 3 cm	65 (50.4)	17 (26.2)†	48 (73.8)
>3 cm	64 (49.6)	46 (71.9)†	18 (28.1)
SRS [<i>n</i> = 105]			
Positive	97 (92.4)	51 (52.6)	38 (39.2)
Negative	8 (7.6)	6 (75)	2 (25)

Differenze tra NET GI e NET pancreatici

Endocrine-Related Cancer (2005) 12 1083–1092

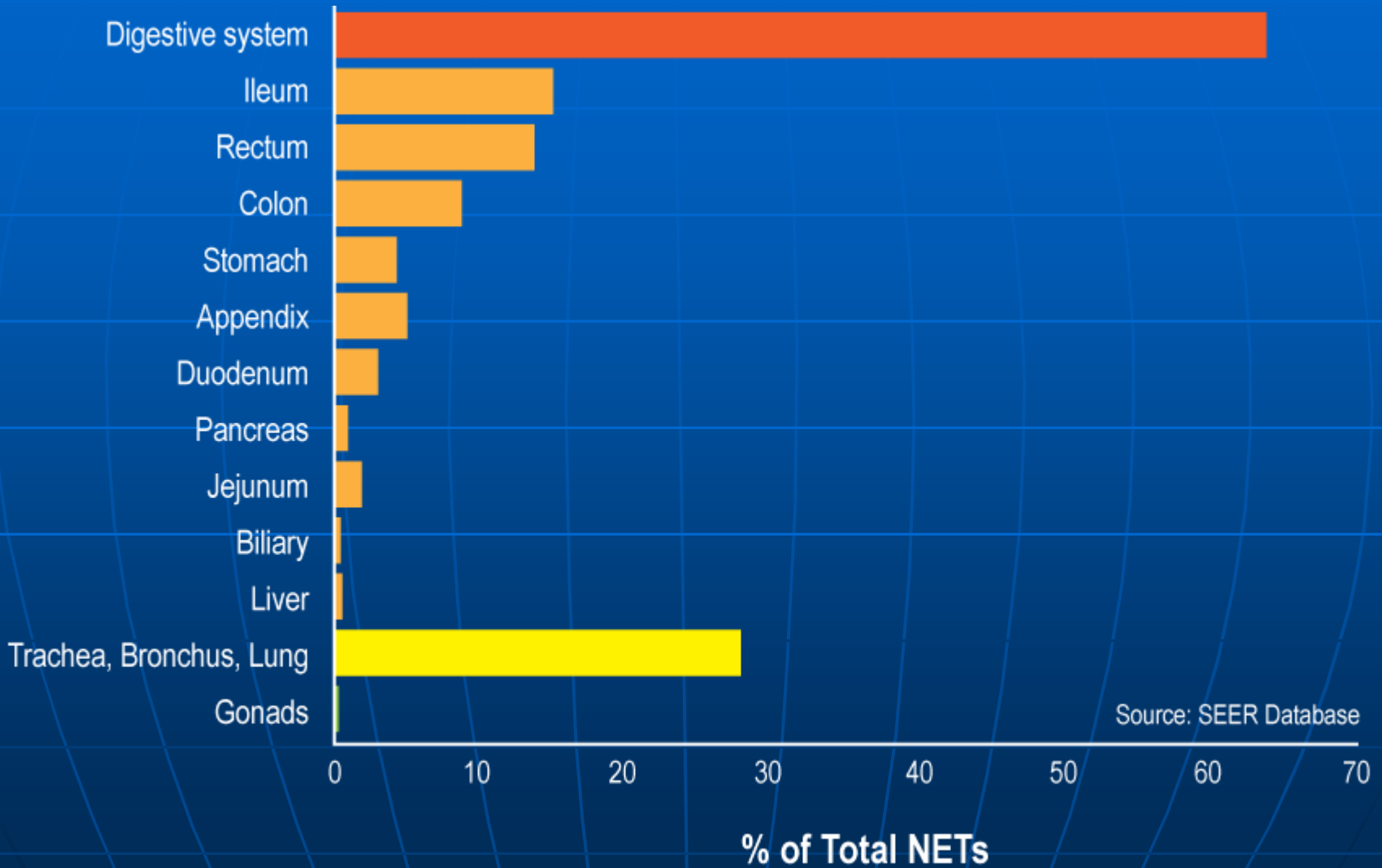
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F. Riccardi, Gruppo NET Cardarelli

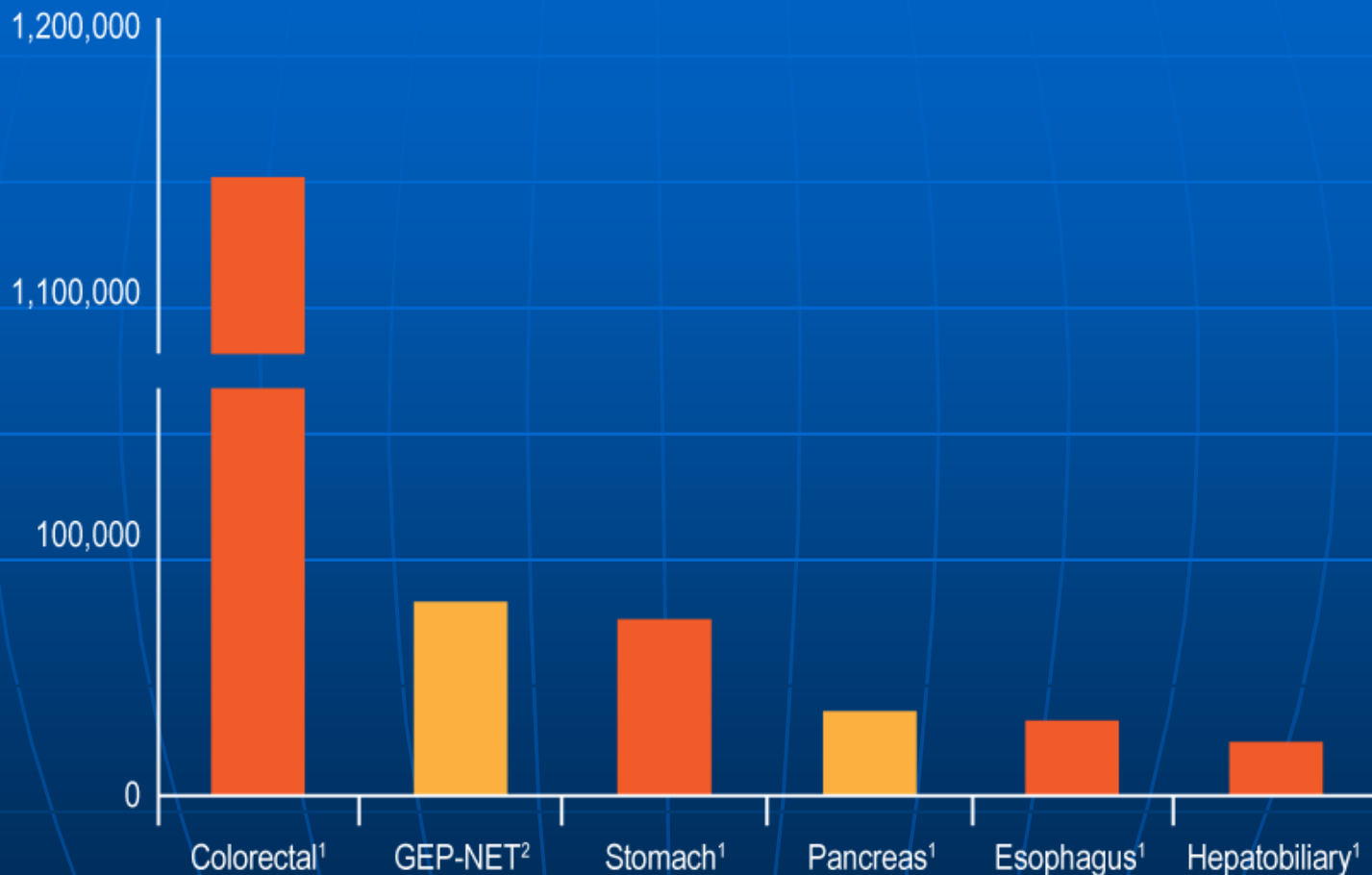


GEP-NETs are the most prevalent NETs





NETs are the second most prevalent type of GI malignancy



Prevalence in SEER Database



il ruolo “primario” dell’Anatomo Patologo

Aspetti fondamentali

- standardizzazione delle procedure istologiche*
- criteri classificativi omogenei (WHO)*
- revisione della diagnosi istologica*
- differenziazione neuroendocrina (CGA, SIN)*
- indice proliferativo (Ki-67 score, se polmone conta mitotica)*

Aspetti da sviluppare

- *Uniformare la terminologia relativa alle classificazioni esistenti*
- *Individuare fattori prognostici indipendenti*
- *Individuare fattori predittivi della risposta*



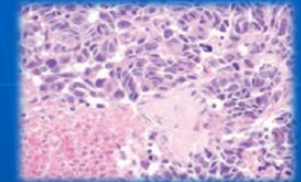
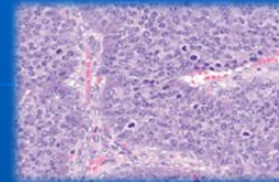
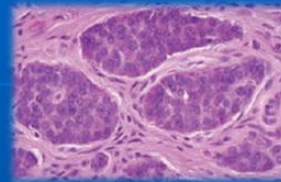


WHO Classification Groups NETs by Diagnostic Factors

Prognosis of Patients With NETs

Good

Poor



WHO classification	Well-differentiated neuroendocrine tumor ^{1,2}	Well-differentiated neuroendocrine carcinoma ^{1,2}	Poorly differentiated neuroendocrine carcinoma ²
Biological behavior	Benign or uncertain malignancy	Low malignancy	High malignancy
Metastases	-	+	+
Ki-67 index (%)	<2	>2	>10
Infiltration, angioinvasion	-	+	+
Tumor size	≤2 cm >2 cm ^a	>2 cm >3 cm ^a	Any size



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Andamento epidemiologico negli anni

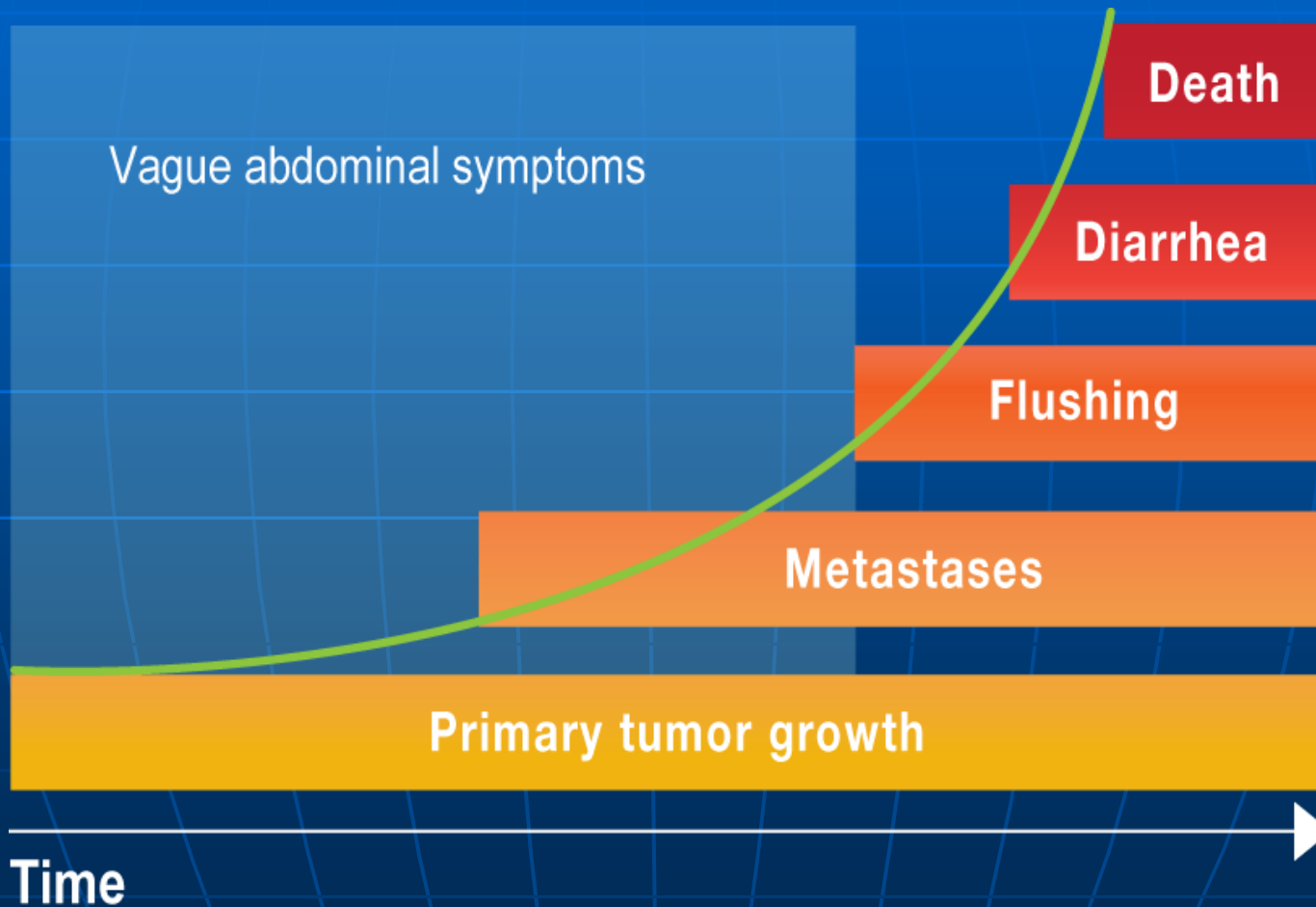
Storia clinica dei NETs

Indagine epidemiologica Cardarelli





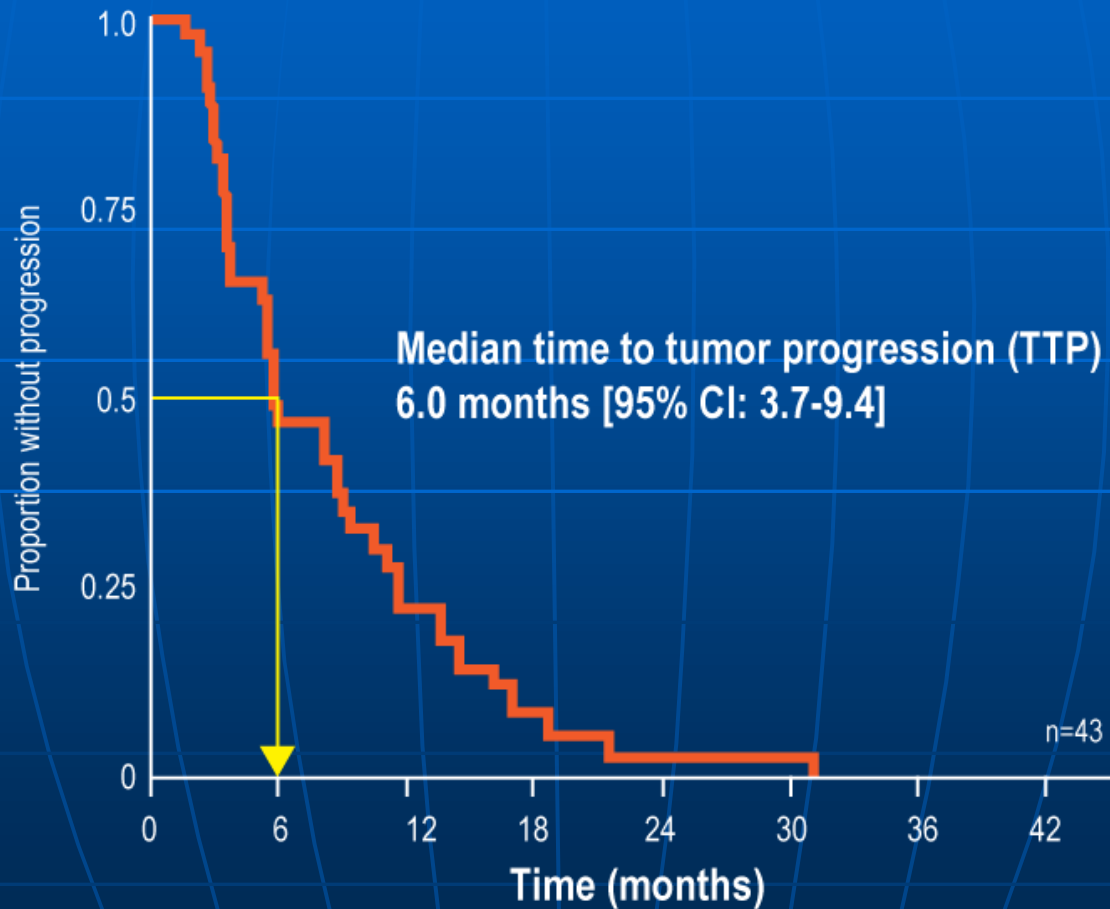
Natural History of a NET





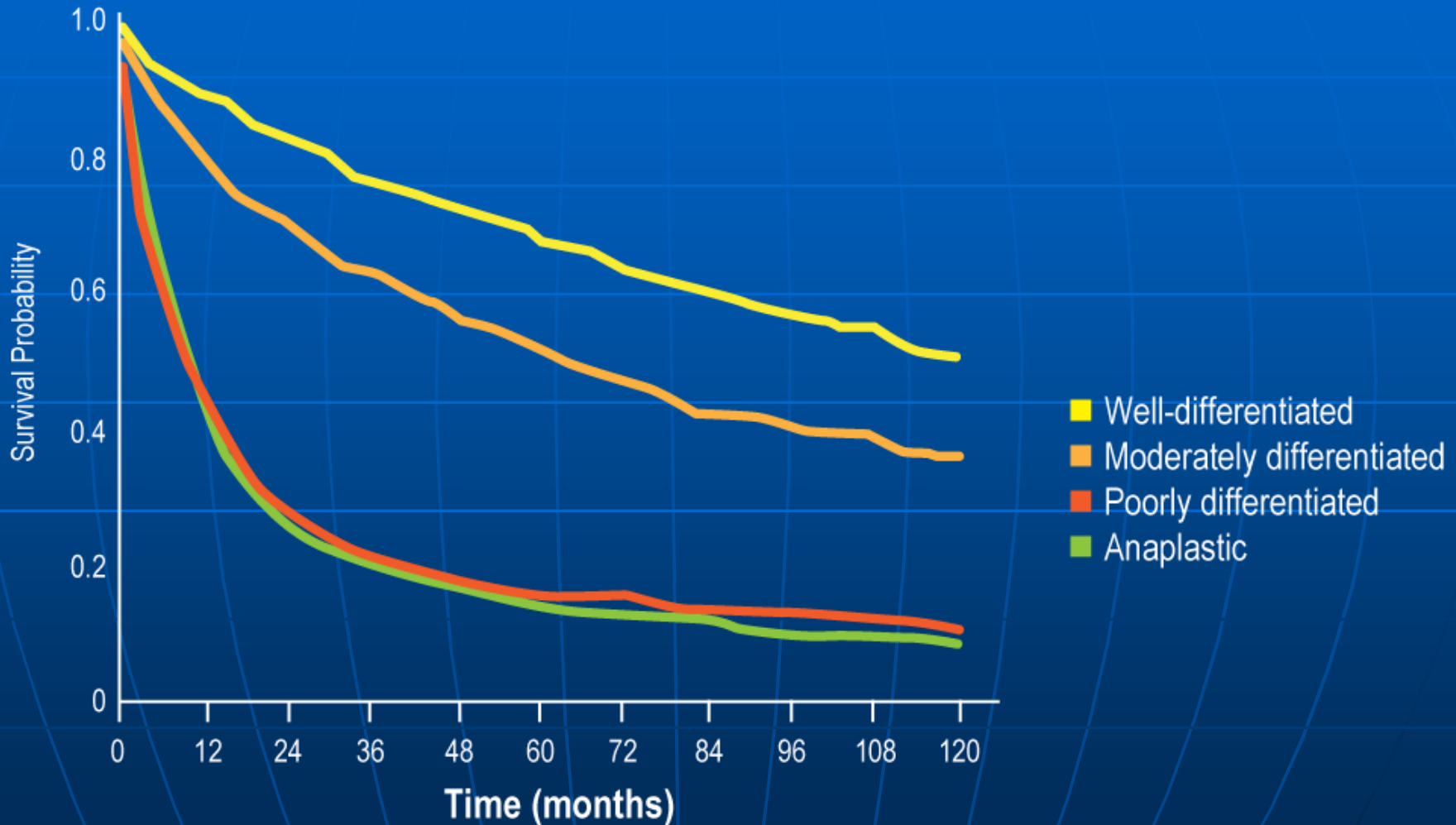
NET is a progressive disease

Outcomes in treatment-naive patients with locally inoperable or metastatic GEP-NETs randomized to placebo





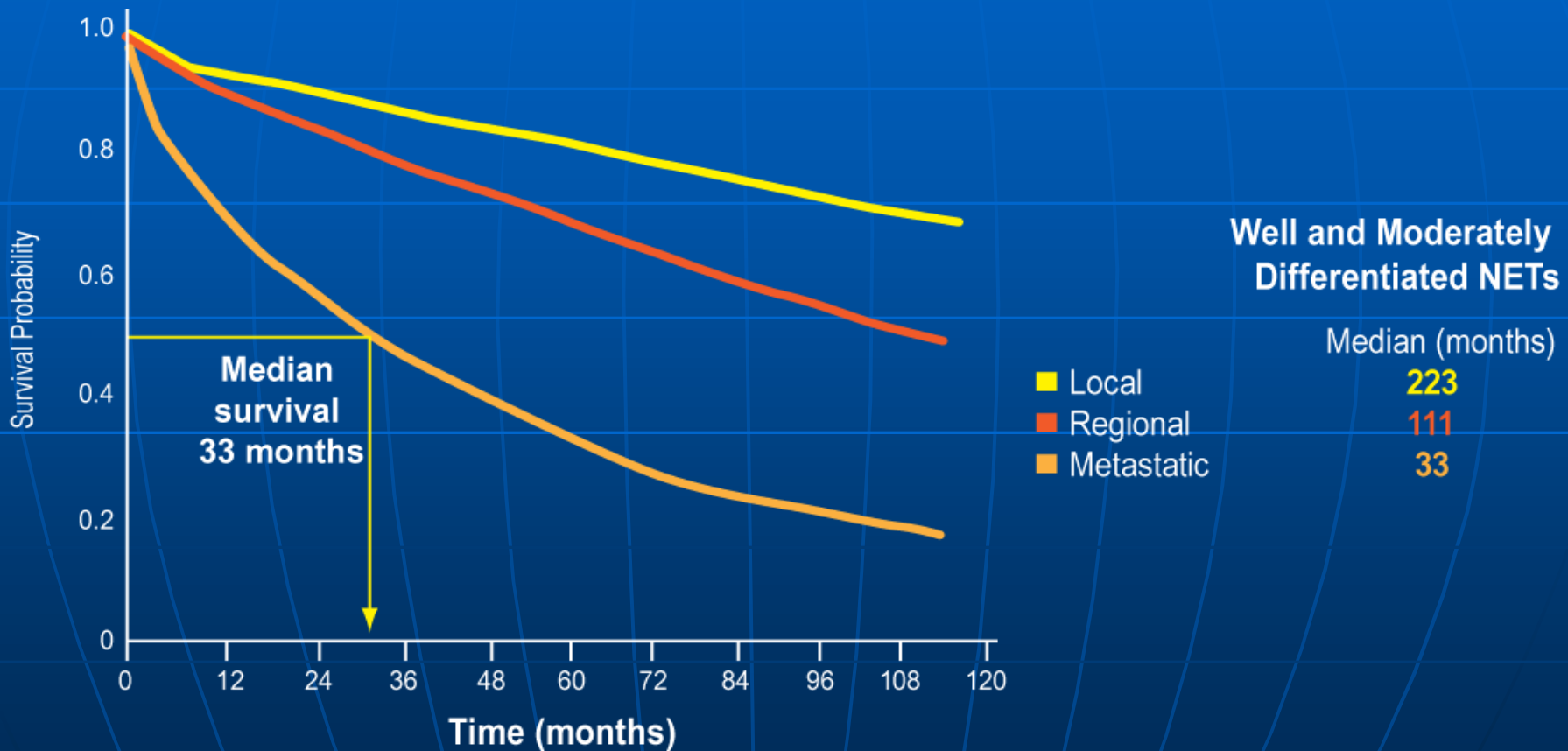
Survival is associated with tumor Grade





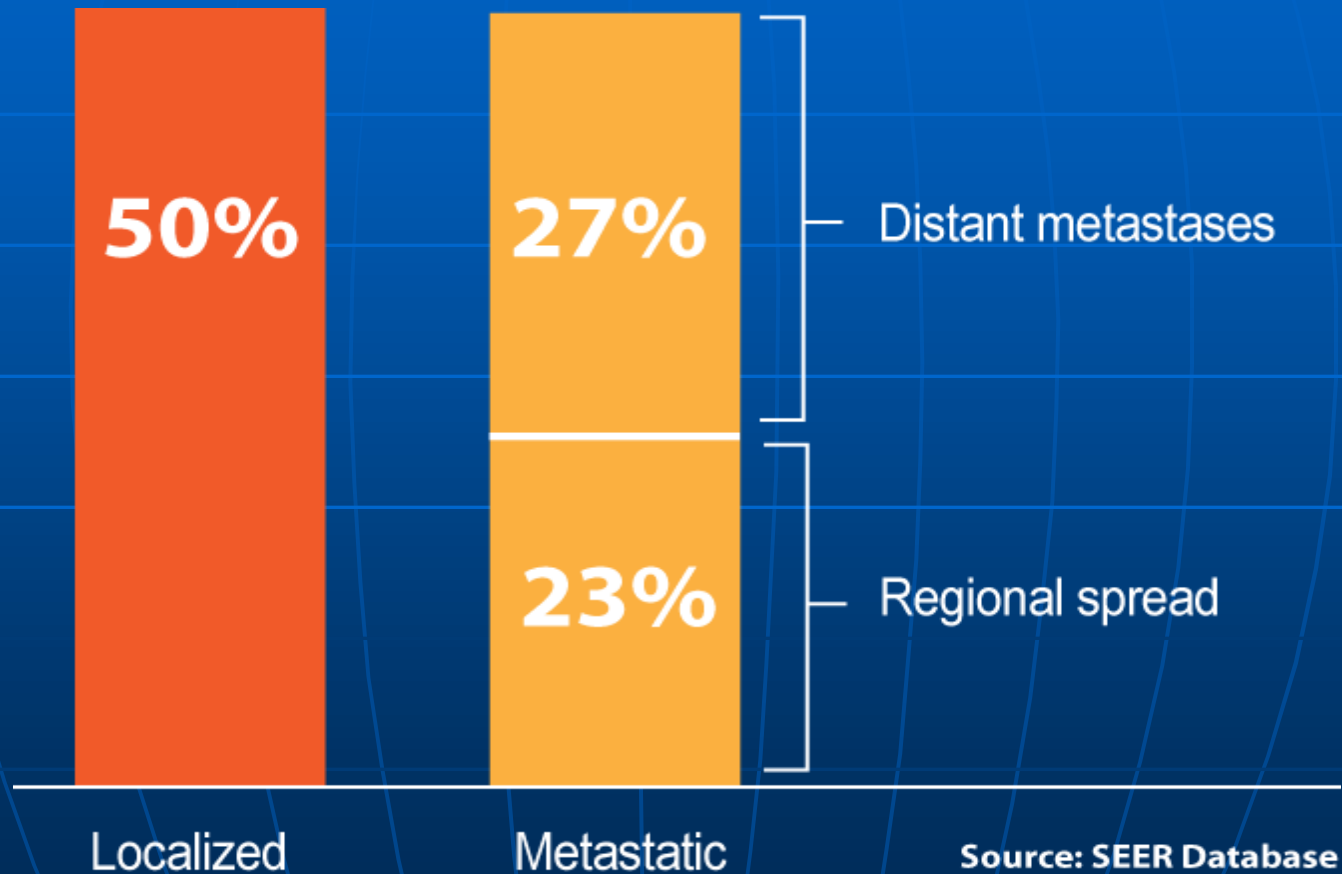
Survival Is Associated With Extension of Disease

33-Month Median Survival for Patients With Metastatic NETs





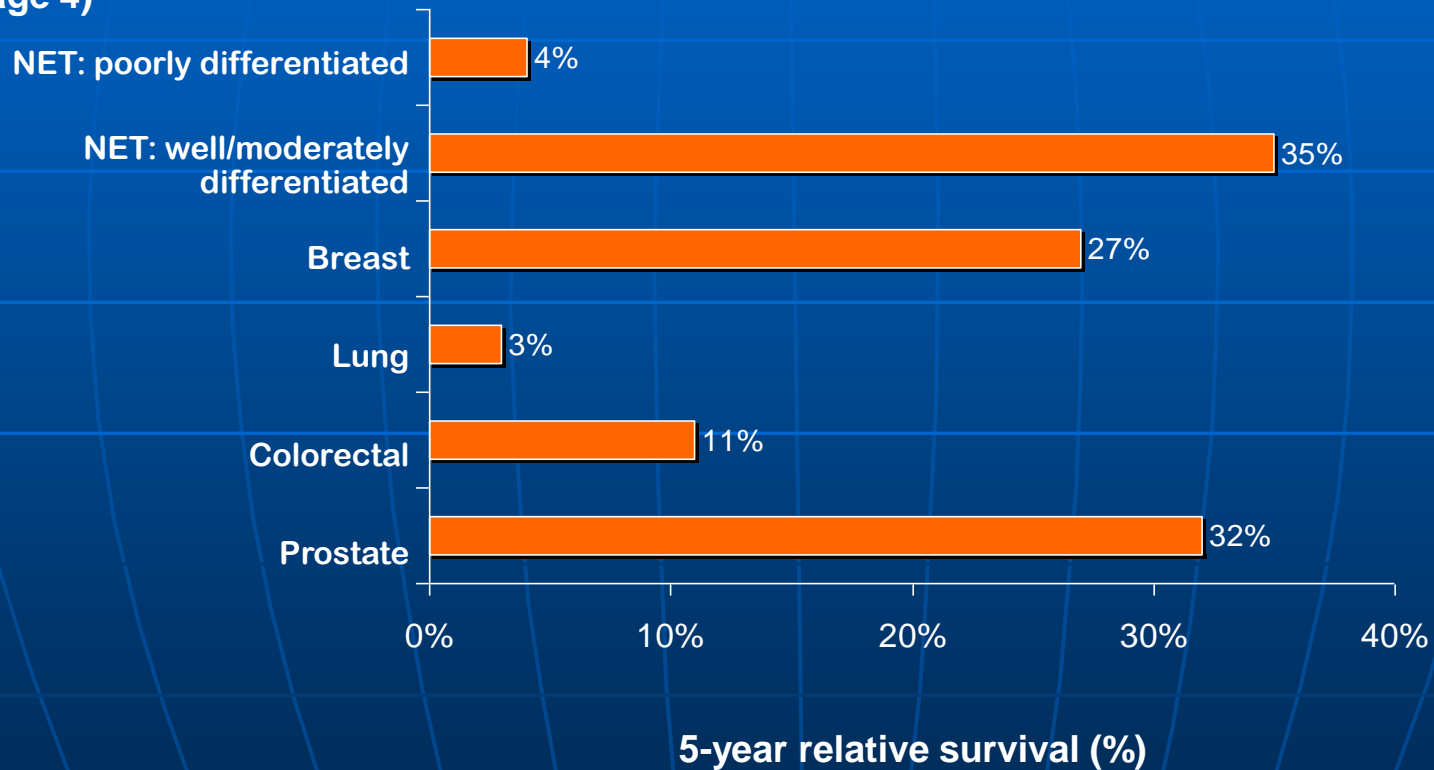
NETs are often Advanced at the time of diagnosis





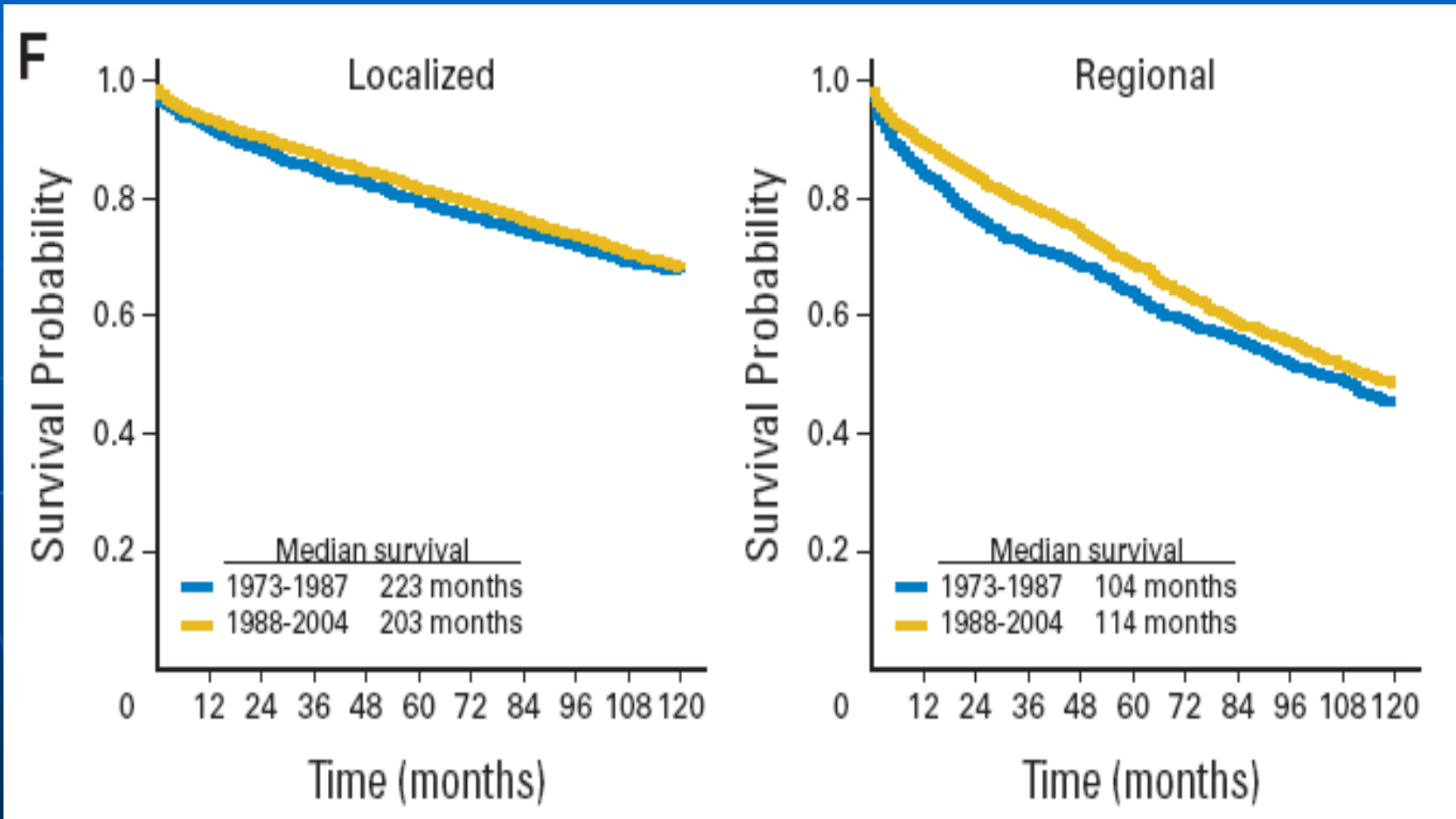
Survival in metastatic NETs is similar to other late-stage cancers

Metastatic tumor
(stage 4)





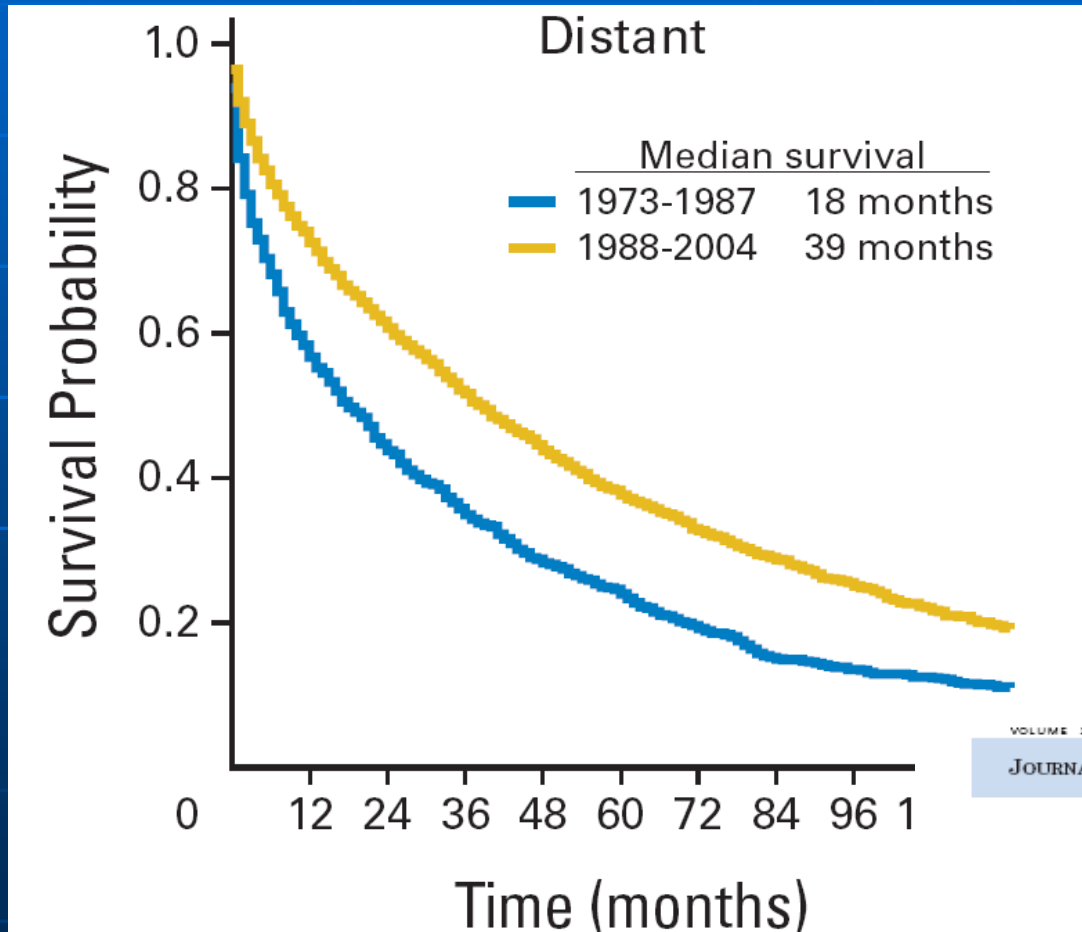
Tumori Neuroendocrini: come è cambiata la sopravvivenza negli anni



Yao JC et al. J Clin Oncol. 2008;26:3063-3072.



***Sopravvivenza dei pazienti con NETs metastatici:
significativamente superiore nel periodo 1988–2004 (post-octreotide)
rispetto al periodo 1973–1987 (pre-octreotide)***



*From an analysis of 35,825
cases of GEP-NETs
identified in the SEER registries*

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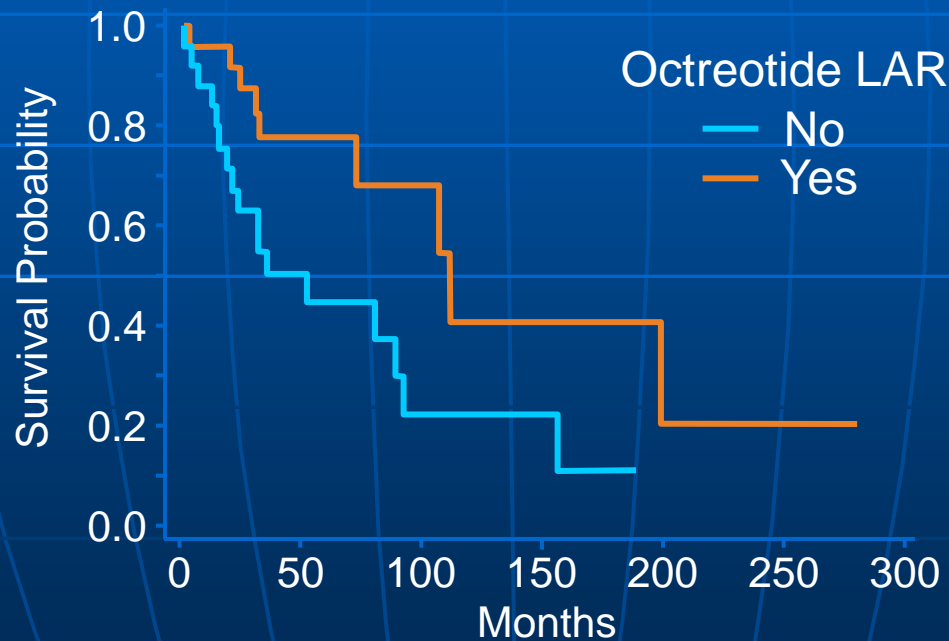
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**Retrospective database analysis
compared patients with advanced NET
receiving octreotide LAR (n=24) with those who did not (n=25)**

Median overall survival (OS) was significantly longer with octreotide LAR treatment (112 months vs 53 months; HR, 2.46; $P=.021$)

10-yr survival was 40% with octreotide LAR vs 22% without



Townsend A et al. *J Clin Gastroenterol.* 2010;44:195-199.



PROMID study

Placebo-Controlled, Double-Blind, Prospective, Randomized Study on the Effect of Octreotide LAR in the Control of tumour Growth in Patients with Metastatic Neuroendocrine MIDgut tumours: A Report from the PROMID Study Group

To evaluate the antiproliferative effect of octreotide LAR
Phase III, randomized, double-blind, placebo-controlled
18 centers in Germany (2001–2008)



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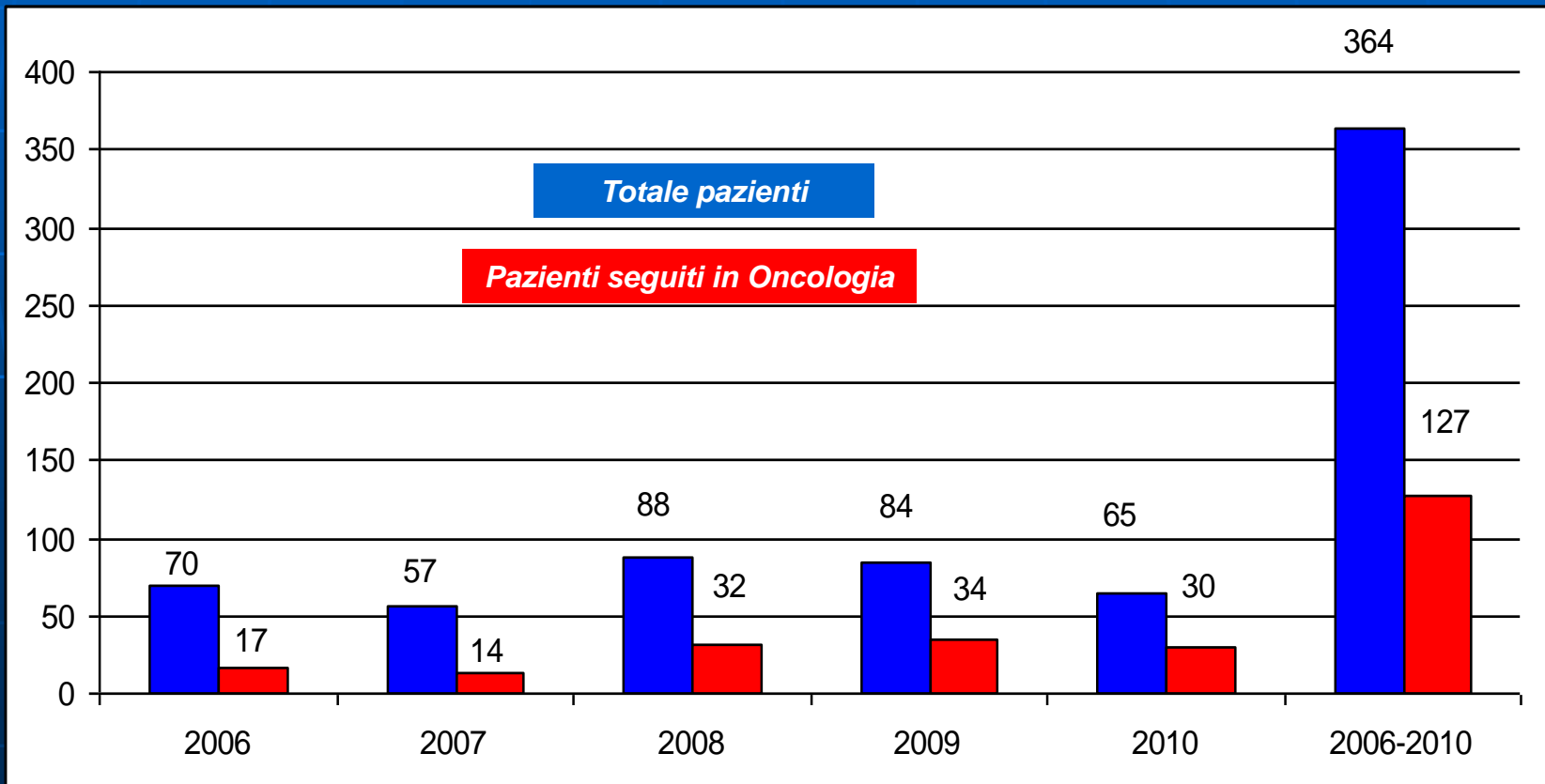


Obiettivi del progetto

- *analizzare l'incidenza dei NETs diagnosticati dall'Ospedale Cardarelli e di verificarne le correlazioni con fattori alimentari, ambientali e farmacologici*
- *verificare l'appropriatezza delle procedure di diagnosi, trattamento e monitoraggio dei pazienti affetti da NET*
- *valutare l'efficacia dei trattamenti disponibili – chirurgia, chemioterapia, terapia biologica, terapia radiometabolica – in coerenza con le linee guida internazionali, sulla sopravvivenza e sulla qualità della vita dei pazienti*



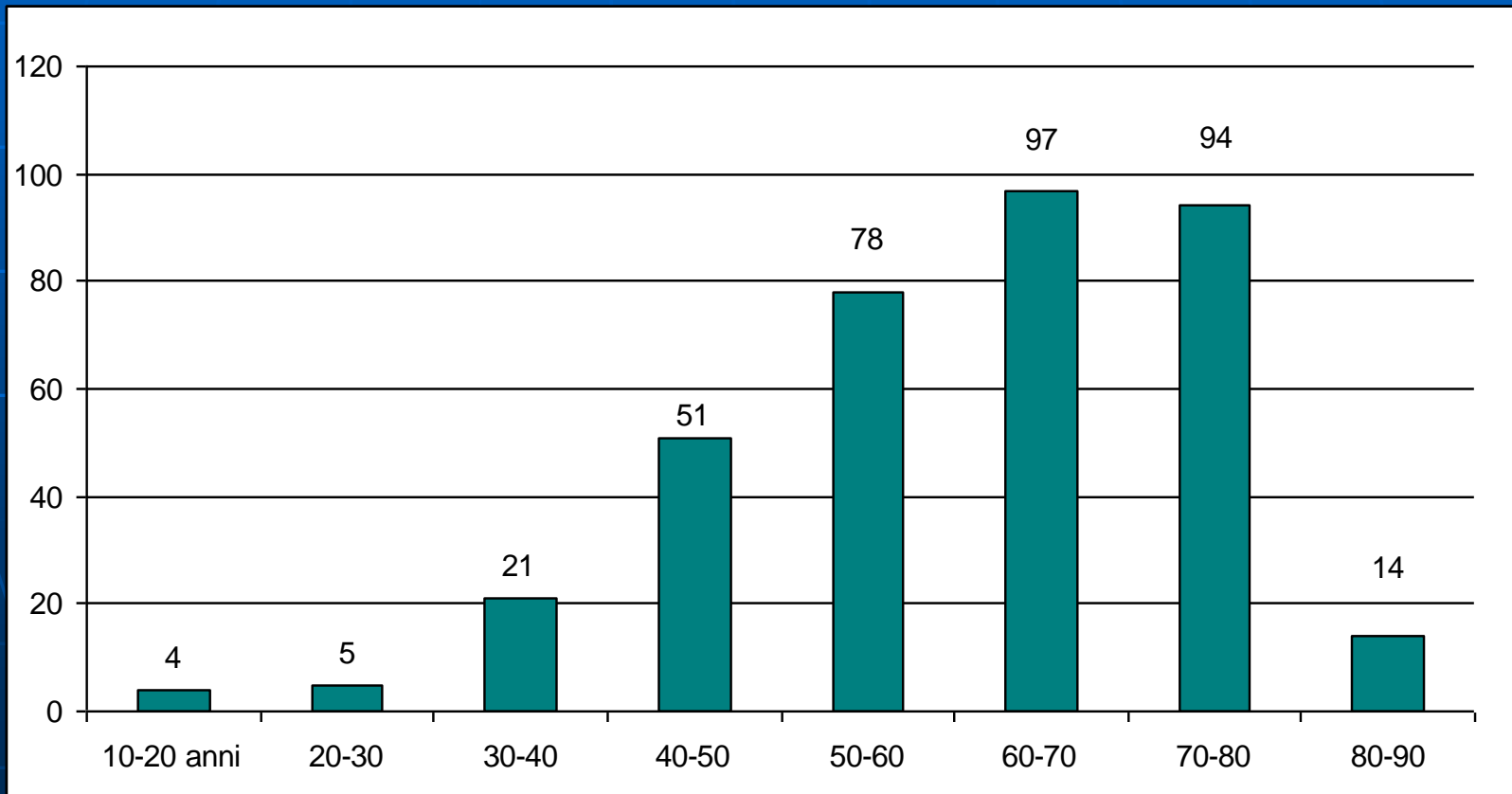
***Nuove diagnosi di Tumori Neuroendocrini effettuate
nell'Ospedale Cardarelli di Napoli nel periodo
01 gennaio 2006 – 15 ottobre 2010***





Nuove diagnosi NET nel periodo gennaio 2006–ottobre 2010

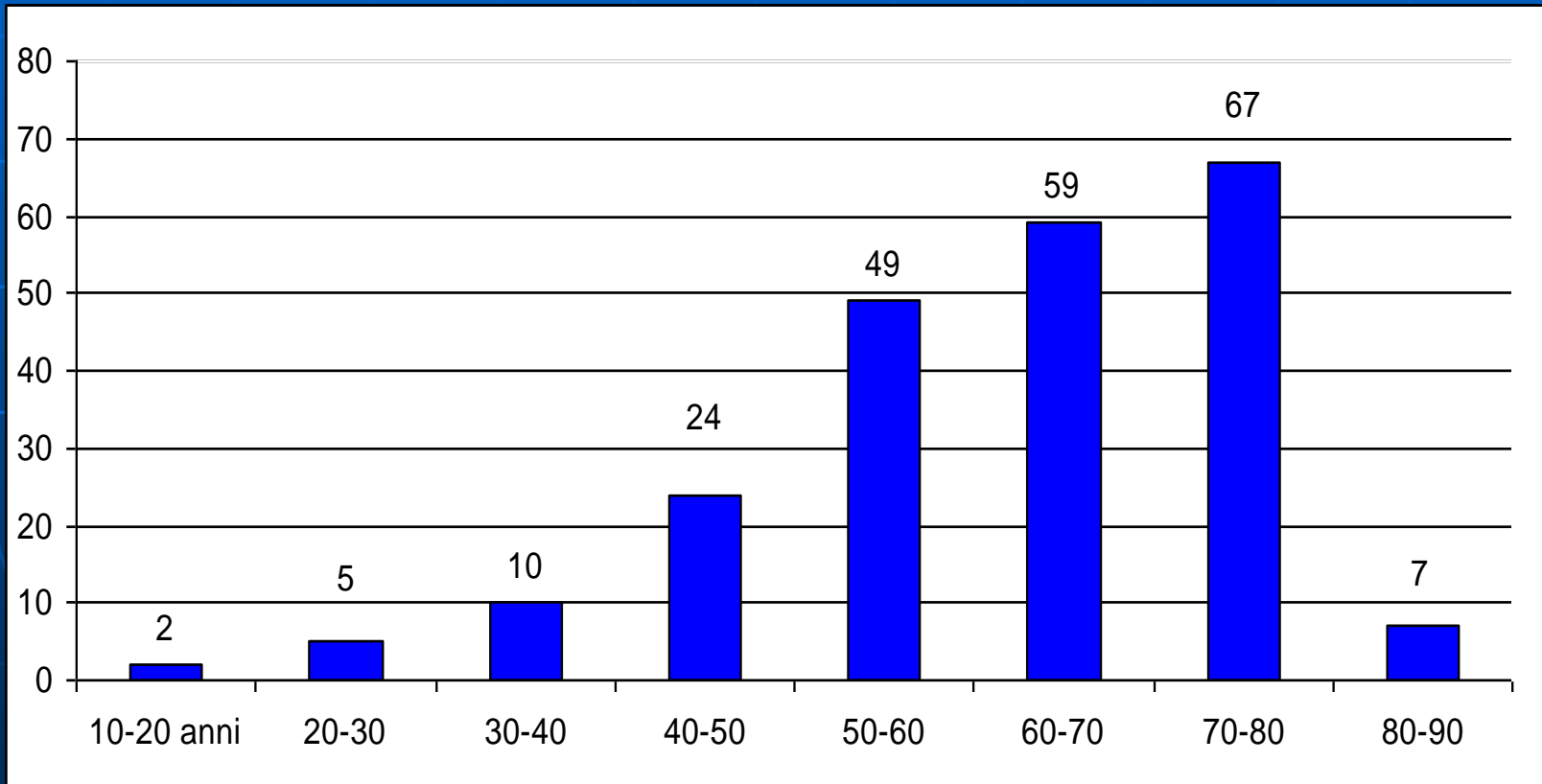
Età di insorgenza





Nuove diagnosi NET nel periodo gennaio 2006–ottobre 2010

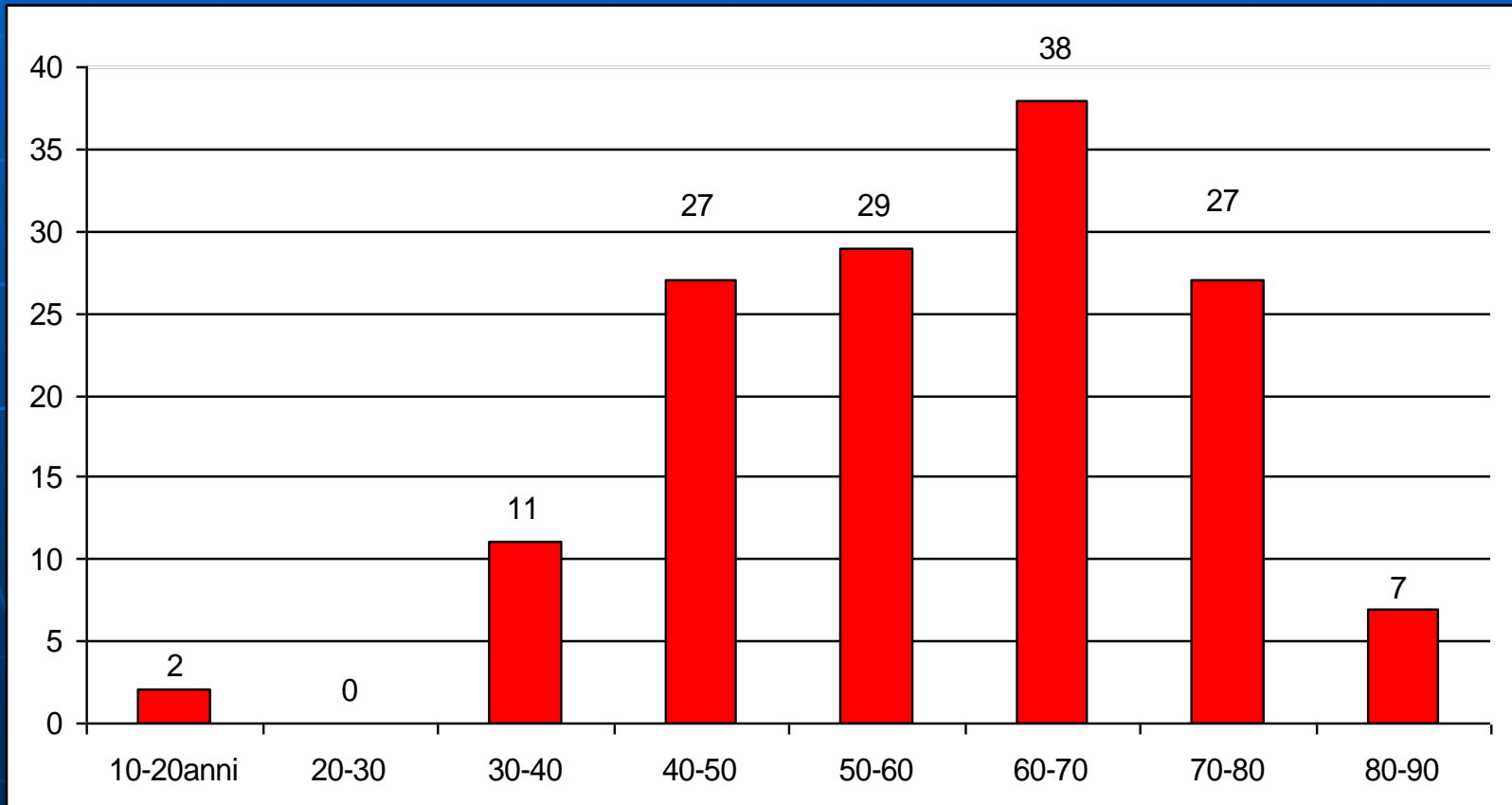
Età di insorgenza negli uomini





Nuove diagnosi NET nel periodo gennaio 2006–ottobre 2010

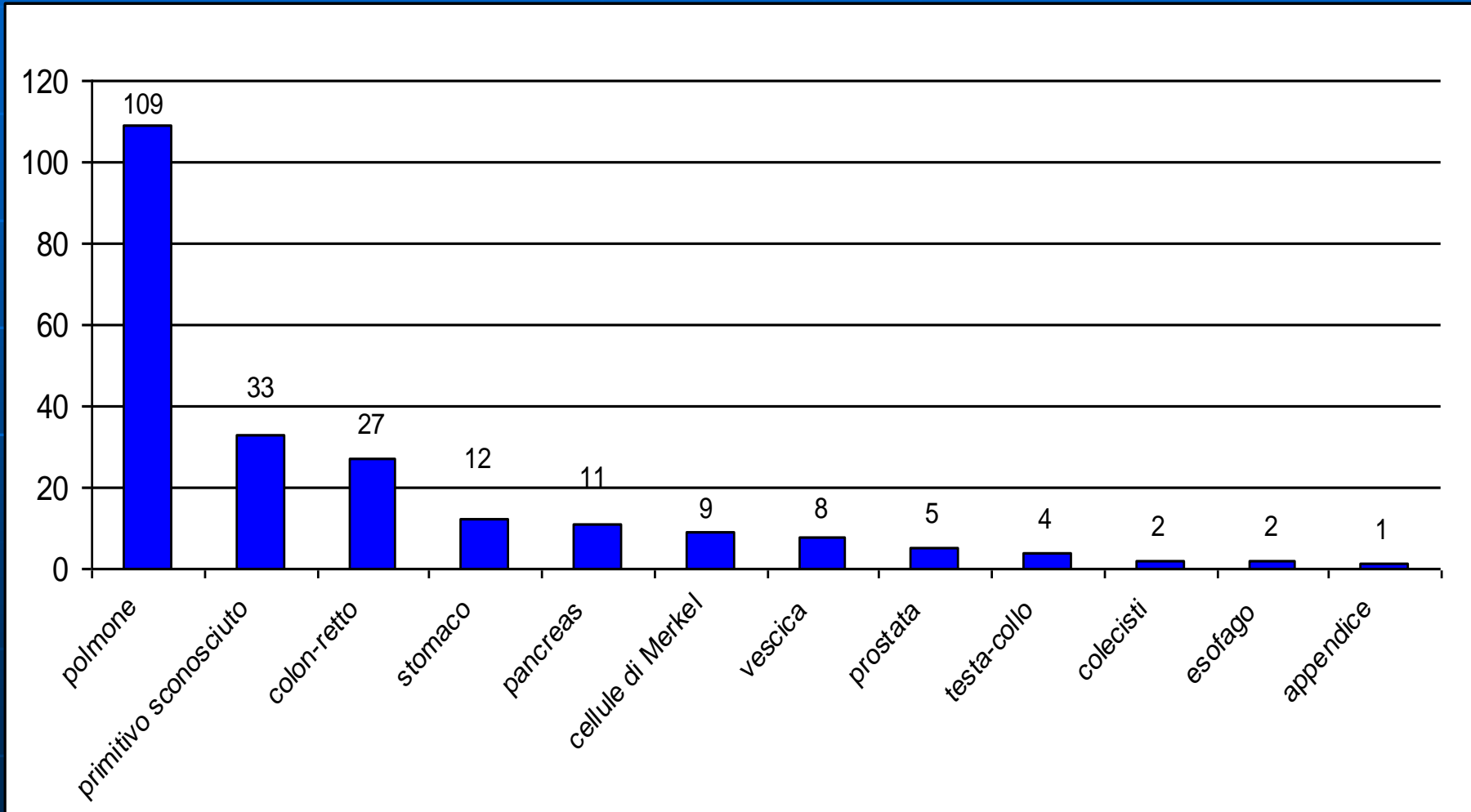
Età di insorgenza nelle donne





Nuove diagnosi NET nel periodo gennaio 2006–ottobre 2010

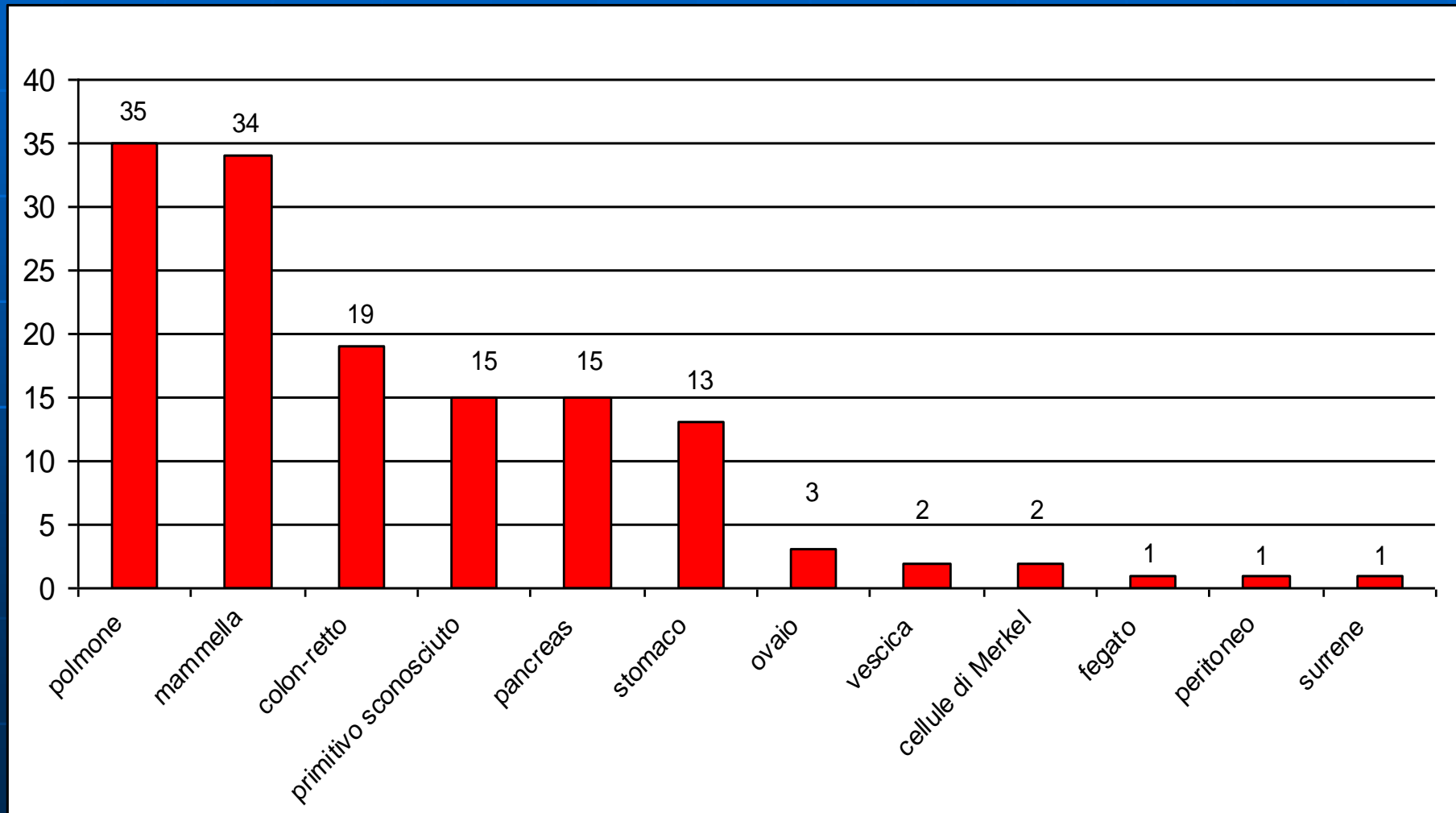
Sede primitiva negli uomini





Nuove diagnosi NET nel periodo gennaio 2006–ottobre 2010

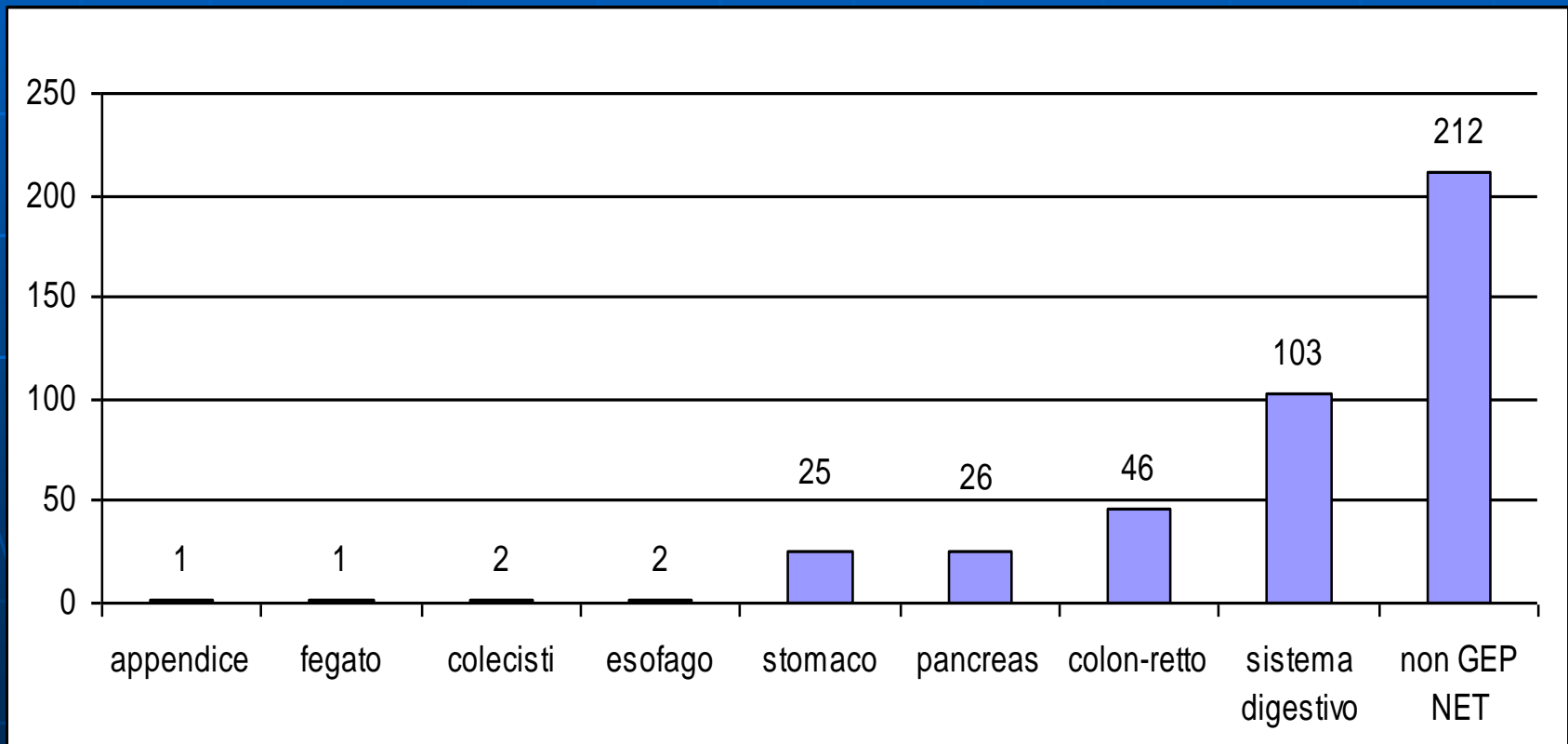
Sede primitiva nelle donne





Nuove diagnosi nel periodo gennaio 2006–ottobre 2010

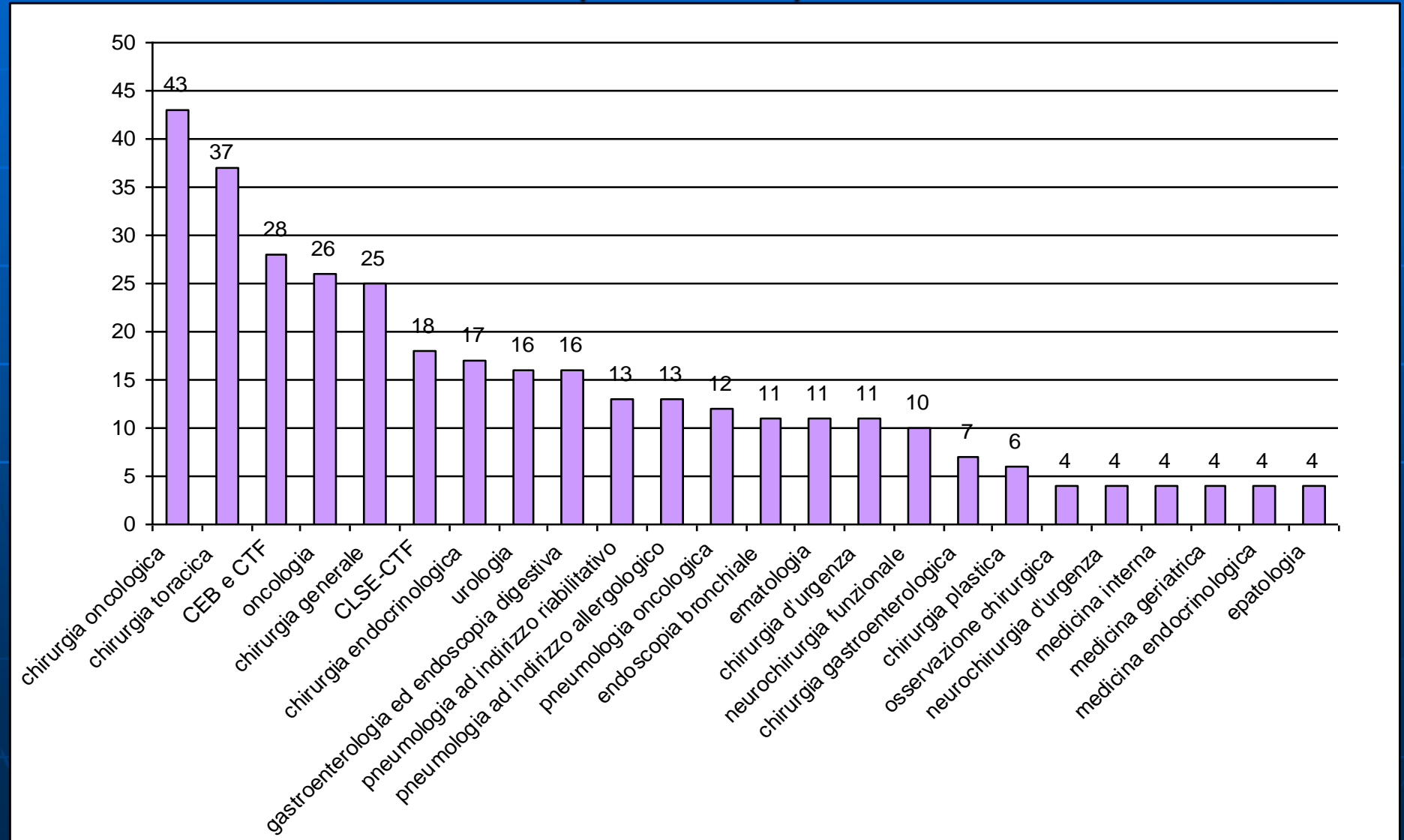
Suddivisione GEP-NET e non GEP-NET





Nuove diagnosi nel periodo gennaio 2006–ottobre 2010

Unità Operativa di provenienza





....la necessarietà dell'approccio multidisciplinare

Oscar Nappi, Anatomia Patologica, Presidente

Antonio Balzano, Gastroenterologia

Giacomo Carteni, Oncologia

Maurizio De Palma, Endocrinochirurgia

Guido De Sena, Chirurgia Oncologica

Eugenio Gragnano, Endocrinochirurgia

Secondo Lastoria, Medicina Nucleare INT Pascale

Carlo Molino, Chirurgia Videolaparoscopica

Guglielmo Monaco, Chirurgia Toracica

Pier Giorgio Rabitti, Medicina Interna-Pancreatologia

Luigia Romano, Radiologia

Francesco Scavuzzo, Endocrinologia

Rosalba Suozzo, Medicina Interna

Generoso Uomo, Medicina Interna- Pancreatologia

Raffaele Volpe, Endocrinologia

Ferdinando Riccardi, Oncologia, Segretario Scientifico

Mimma Rizzo, Oncologia

