



Introduction

Although a variety of pancreatic function tests are nowadays available to diagnose pancreatic exocrine insufficiency (PEI), this is a condition poorly known in Spain and its diagnosis often differs among medical centers across the Country.

Objective

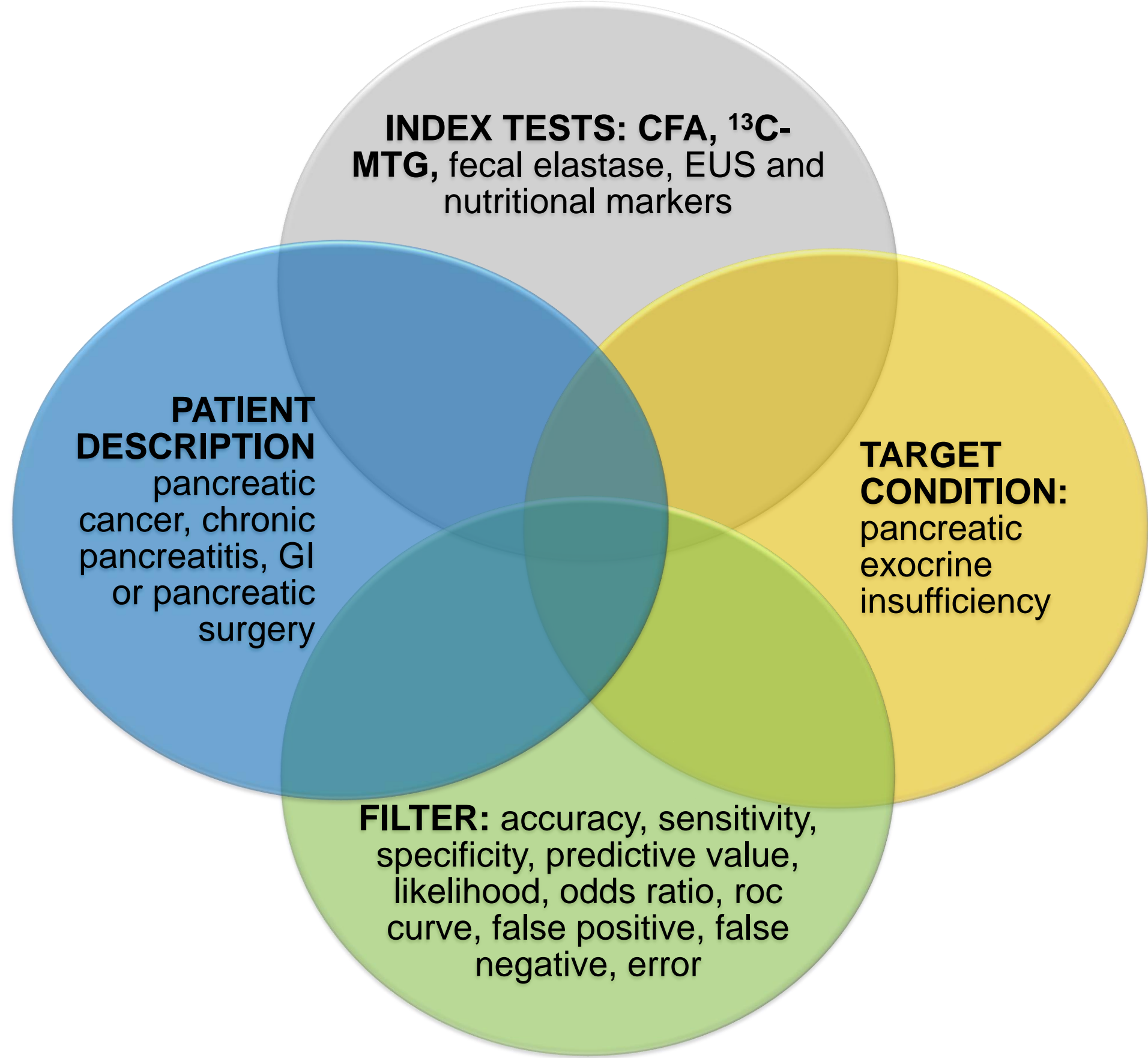
To systematically appraise the literature on the accuracy of four widely used tests to diagnose Pancreatic Exocrine Insufficiency (PEI) secondary to chronic pancreatitis (CP), gastrointestinal/pancreatic surgery or pancreatic cancer in Spain, namely: coefficient of fat absorption (CFA); mixed 13C-triglyceride breath test (13C-MTG); fecal elastase-I (FE-I); and serum nutritional markers (SNM).

Methods

Systematic review of the literature

A systematic review of the literature (until March, 2013) was performed in MedLine/PubMed, Cochrane Library, CRD, MEDION, ARIF, MEDES, IBECS, ISI WOK, SCOPUS. The search strategy was build according to Cochrane and NHS Centre for Reviews and Dissemination recommendations for reviewing diagnostic test accuracy studies and represented in Figure 1. Publications (original studies or reviews in English, Spanish, Italian, French or German) were included if they reported the accuracy of an index test for the diagnosis of PEI secondary to one of the selected patients' conditions in adults. Expert validation of the search strategy was sought through a consensus meeting.

Figure 1. Literature review search strategy



Expert consultation

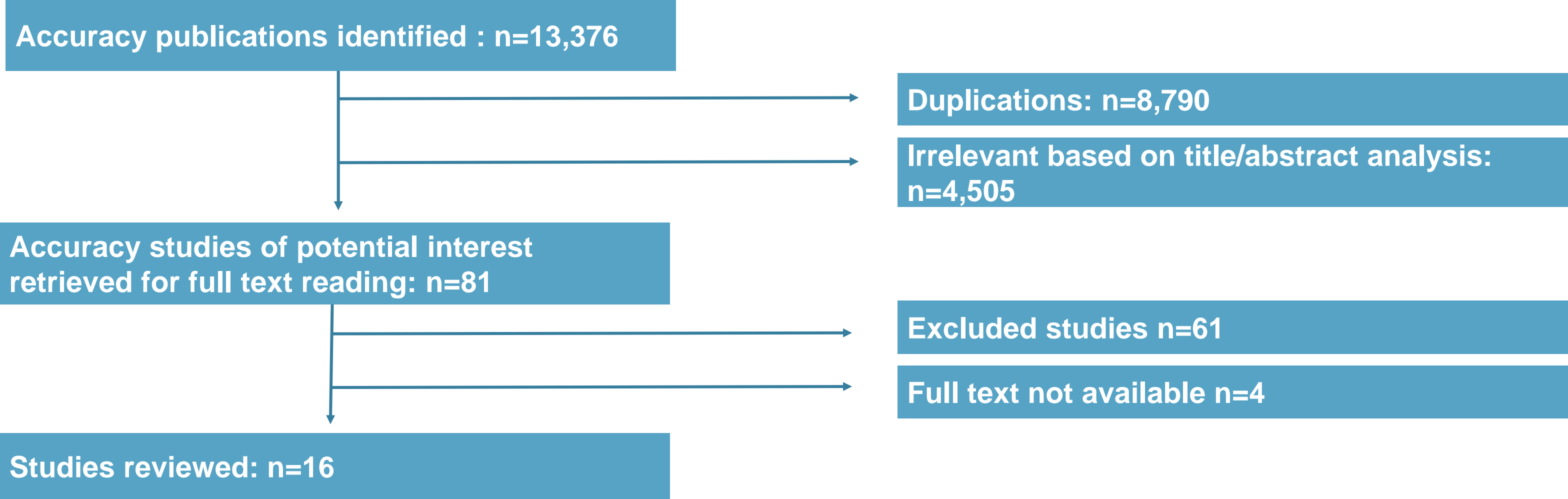
Experts were presented the results of the literature review and asked to give their opinion on the applicability of the accuracy values extracted from the literature to the usual clinical practice and to suggest new sources of information when needed. Two rounds of expert consultation were run, (one face-to-face and one by e-mail).

Results

Literature review

The literature search, including expert feedback on the search strategy, gave a total of 13,376 publications on the diagnostic accuracy of PEI tests were initially identified. Of these, 16 were selected. Three additional publications were identified by handsearch (references from other publications) and reviewed (Figure 2).

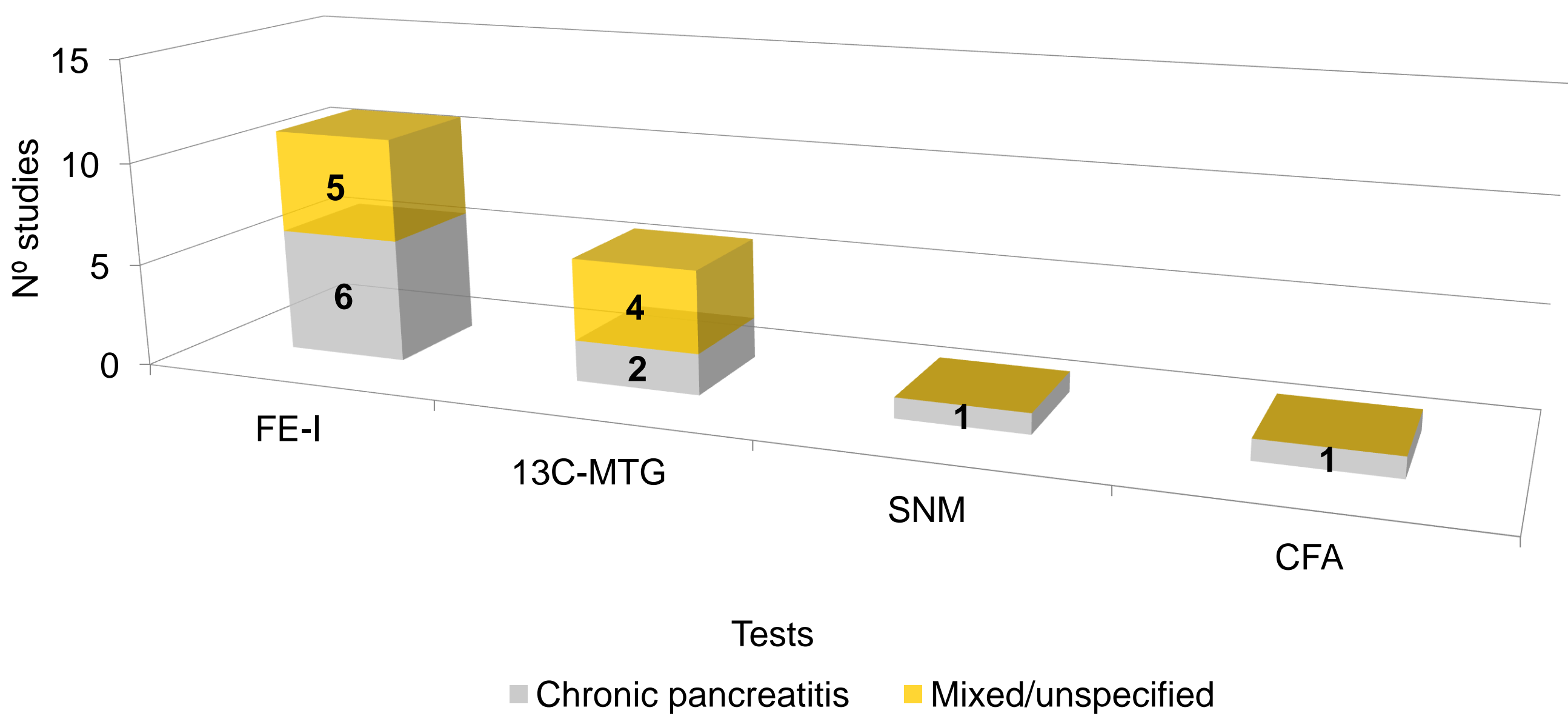
Figure 2. Selection process for test accuracy publications of the systematic review



After presenting the results to 4 experts, the papers related to Endoscopic Ultrasound (EUS), initially included as a diagnostic technique were excluded. The accuracy review finally included 14 papers from the systematic search and 3 from hand-search that:

- Contained information distributed per population and test as reported in Figure 3. The most studied population and test are CP and FE-I, respectively.
- Used different reference standards as represented in Figure 4. Most of the publications used a type of secretin/erulein test as reference standard for measuring test accuracy.
- Reported sensitivity and specificity values (assessed vs. different reference standards) that spanned wide ranges, when many publications were available per test and population, as represented in Table 1. FE-I is the test spanning the widest ranges of specificity and sensitivity values, in both populations of interest.

Figure 3. Distribution of the selected publications according to primary condition and test*



Results (continued)

Figure 4. Distribution of tests used as reference standard in the selected publications

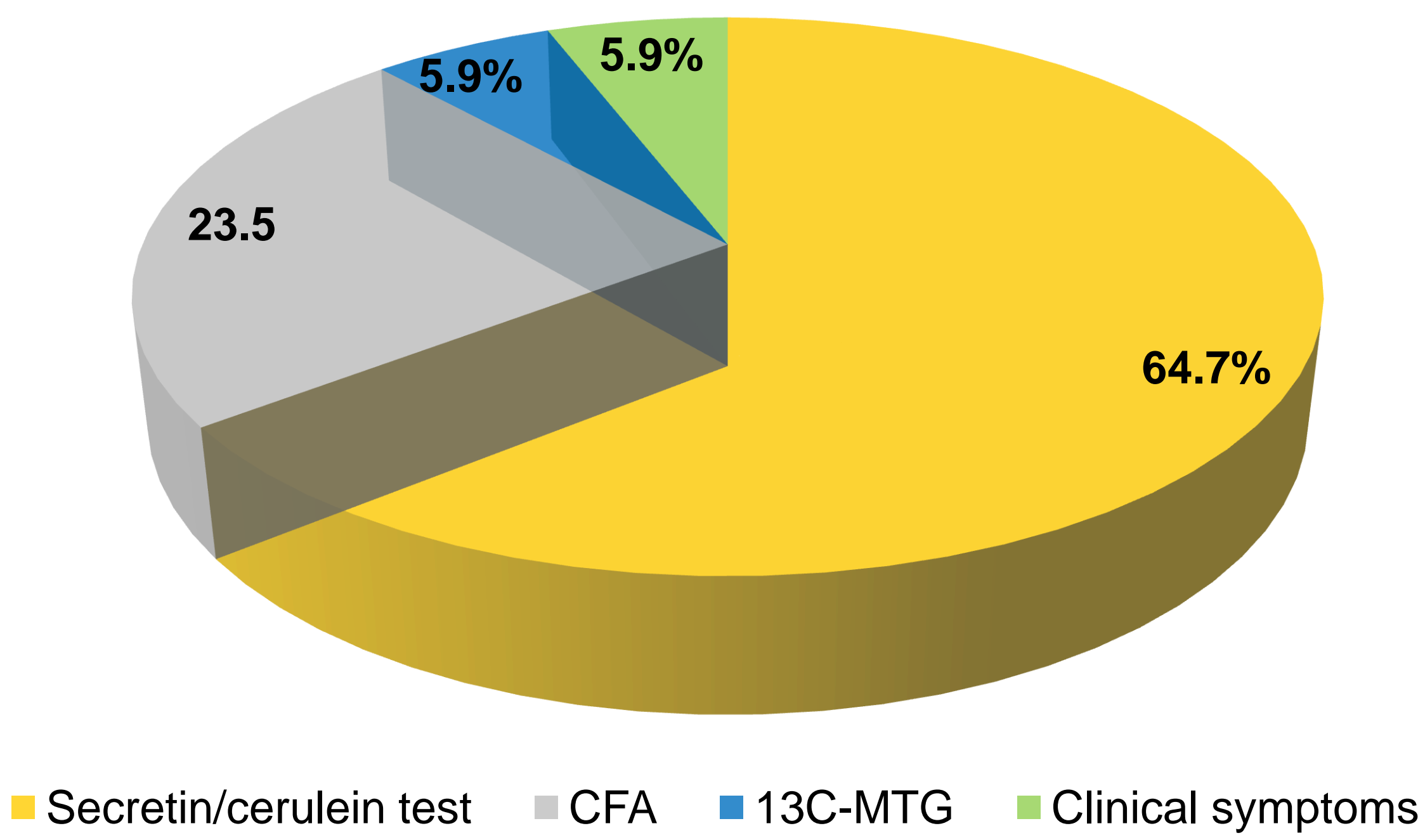


Table 1. Published ranges of accuracy of the tests in CP and cancer/surgery patients (assessed vs. different reference standards and with different cutoffs)

Index test	Chronic pancreatitis			Cancer/Surgery		
	Sensitivity range*	Specificity range*	Nº studies**	Sensitivity range*	Specificity range*	Nº studies**
FE-I	48-93%	57-100%	6	53-93%	35-94%	5
13C-MTG	81%	85%	2	69-100%	76-93%	4
CFA	56%	40%	1	NA	NA	0
SNM	100%	55%	1	NA	NA	0

*Cutoffs ranges are: FE-I <175-218µg/g; 13C-MTG <22-67% 13C recovery at 6-8h; CFA not specified; SNM at least one positive test significantly associated to PEI.
**One the papers include accuracy values for 2 different tests.

Expert consultation

When presented the accuracy data extracted from the literature, the experts advised:

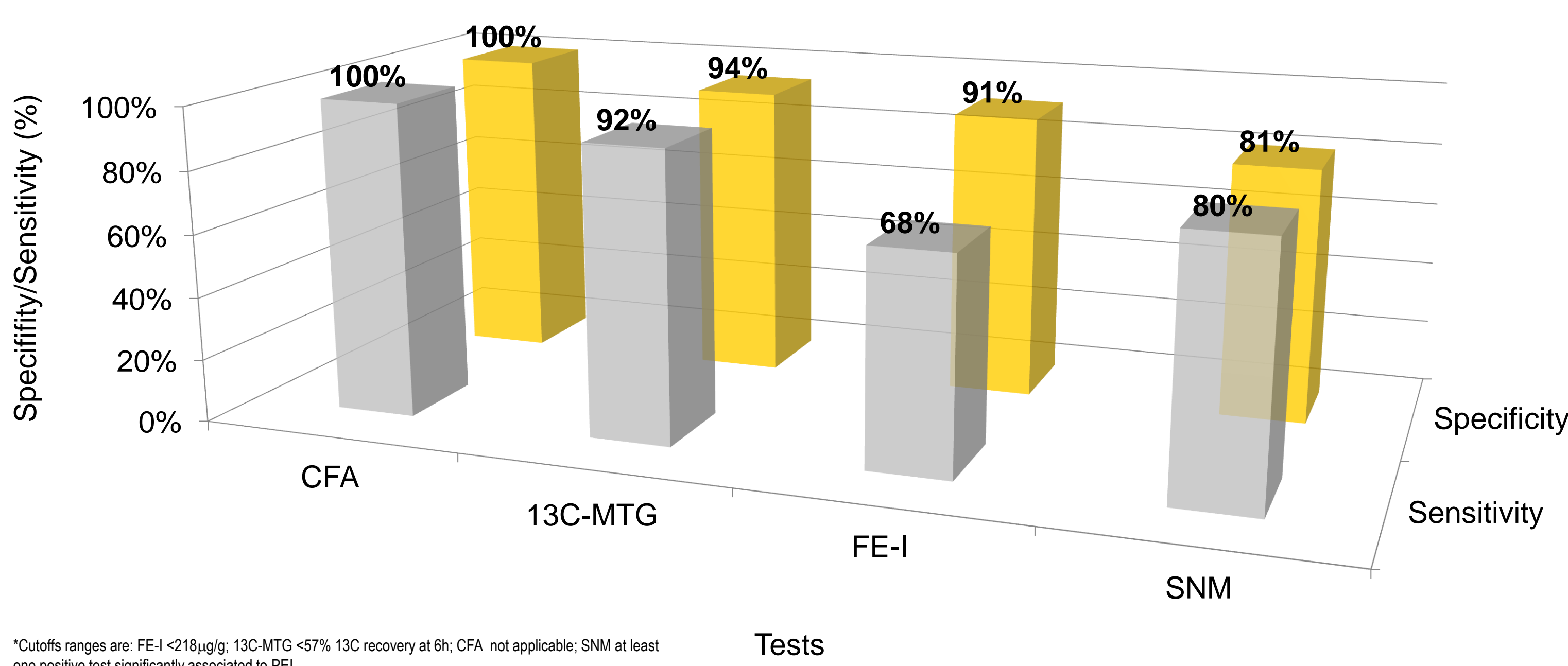
- Not to consider publications using the secretin/erulein test as the reference standard for accuracy of PEI diagnosis, because this test only measures pancreatic enzyme secretion, not exocrine insufficiency *per se*;
- To prioritize studies using the gold standard CFA (assumed accuracy 100%) or 13C-MTG test as reference standard for accuracy.

On the basis of these considerations:

- 4 publications using CFA as the reference standard were selected: FE-I sensitivity and specificity in 58 CP (cutoff <218µg/g:[1]) and 40 cancer/surgery patients (cutoff 200µg/g; [2]) were 68% and 98%, and 91% and 35%, respectively; 13C-MTG was ≥90% sensitive and specific in all populations [3,4].
- Sensitivity and specificity for SNM vs. MTG were 80% and 81%, respectively [5] and considered by experts as similarly accurate in the cancer/surgery population.

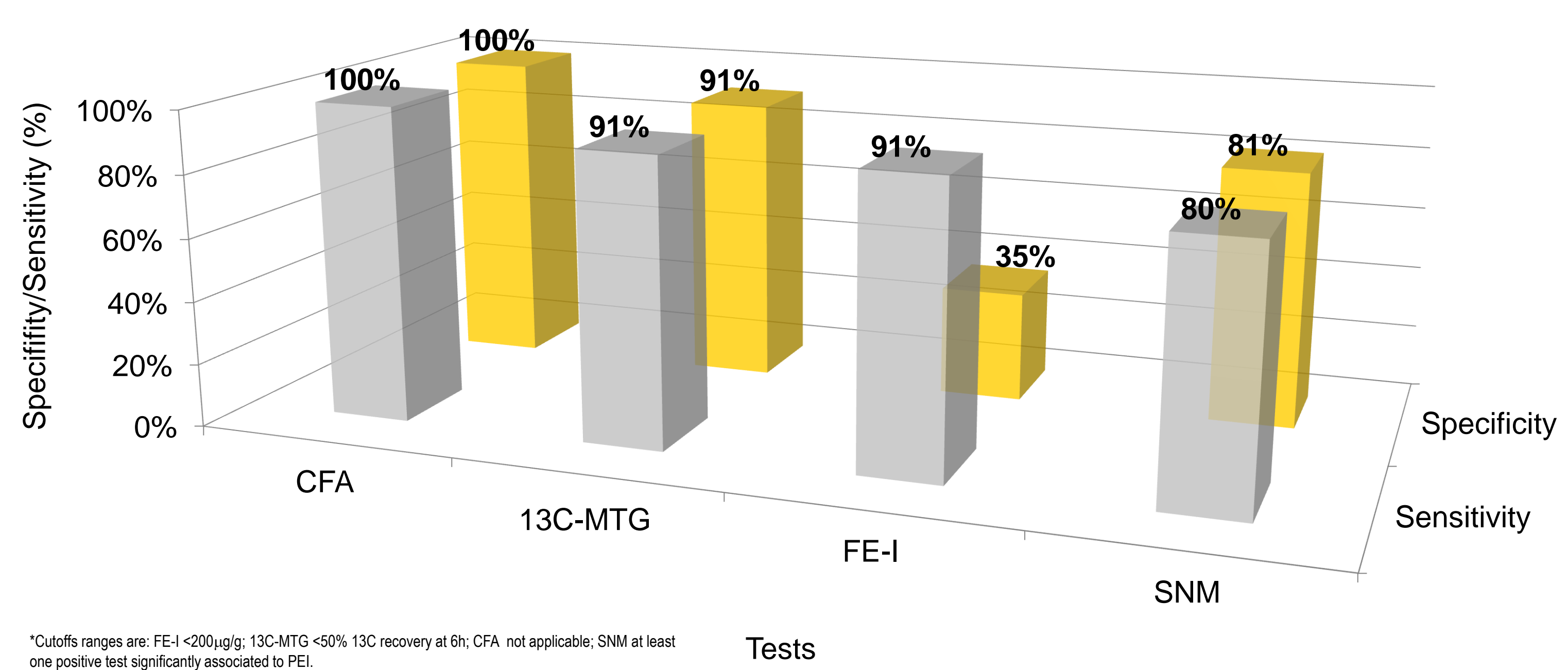
The extracted specificity and sensitivity values of the four tests in CP patients and cancer/surgery patients are reported in Figure 5 and Figure 6, respectively.

Figure 5. Diagnostic accuracy of the selected tests in patients with CP



*Cutoffs ranges are: FE-I <218µg/g; 13C-MTG <57% 13C recovery at 6h; CFA not applicable; SNM at least one positive test significantly associated to PEI.

Figure 6. Diagnostic accuracy of the selected tests cancer/surgery patients



*Cutoffs ranges are: FE-I <200µg/g; 13C-MTG <50% 13C recovery at 6h; CFA not applicable; SNM at least one positive test significantly associated to PEI.

Conclusions

This is the first systematic review to confirm the accuracy of four diagnostic tests for PEI in CP and cancer/surgery patients with the final selection of results being based on expert consensus to ensure that the data are representative of Spanish clinical practice. Cut-offs of these tests are crucial in determining their accuracy, for example at a cut of 100µg/g the sensitivity and specificity of FE-1 is 91.8% and 94.8%, respectively [6].These data, together with resource use and cost information from clinical practice will feed an economic tool to assess the cost of PEI diagnosis in Spain.

References

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