

A Regional Audit of Tumour Markers

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North Middlesex University Hospital NHS Trust

On behalf of the Thames Biochemistry Audit Group

2nd June 2011

Response to the questionnaire

- There were a total of 25 replies to the questionnaire
- 8 responses were from Teaching Hospitals
- 17 responses were from Non-Teaching Hospitals

Question 1-Tumour markers offered-1

- **AFP**
- All 25 respondents perform the assay in house
- The turnaround time quoted ranged from 1 day to 1 week with the majority quoting 1 day.
- Most laboratories reported in kU/l with <6 kU/l being the most quoted reference range. A few reported in U/ml quoting between <6 and <12 U/ml. One laboratory reported <8 ng/ml, one <14 ug/l and one <20 ug/l
- One laboratory reported age related ranges in kU/l.
- **CA125**
- All 25 respondents perform the assay in house
- The turnaround time quoted ranged from 1 day to 1 week with the majority quoting 1 day
- Reference ranges quoted ranged from <23 kU/l to <36 kU/l with the majority quoting <35 kU/l

Question 1-Tumour markers offered-2

- **CA15-3**
- 17 of the respondents perform the assay in house. Reference ranges quoted range from <25 kU/l to <32 kU/l with the majority quoting <25 kU/L.
- Turnaround times ranged from 1 day to 3 days with the majority quoting 1 day.
- 8 respondents send the marker to another laboratory with the turnaround time ranging from 1 to 4 weeks, the majority quoting 1 week
- **CA19-9**
- 23 of the respondents perform the assay in house. Reference ranges quoted ranged from <27 kU/L to <37 kU/l, the majority quoting <31 kU/l. Turnaround time ranged from 1 day to 3 days with the majority quoting 1 day.
- 2 of the respondents send the marker to another laboratory with a turnaround time of 5-10 days

Question 1-Tumour markers offered-3

- **PSA**
- All 25 laboratories perform the assay in house
- Turnaround times quoted ranged from 1 day to 3 days with the majority quoting 1 day.
- 11 laboratories quoted age related ranges which varied from laboratory to laboratory
- Those not quoting age-related ranges quoted 0-4 ng/ml or ug/l.
- **CALCITONIN**
- 2 laboratories perform the assay in house. One of the laboratories quoted a turnaround time of 2 weeks.
- 23 laboratories send the marker to a reference laboratory with a turnaround time of 3 days to 4 weeks with the majority quoting 2 weeks
- The most quoted reference ranges were <4.8 ng/l for females, <11.8 ng/l for males

Question 1-Tumour markers offered-4

- **CEA**
- 24 laboratories perform the assay in house. Reference ranges quoted ranged from <3.4 ug/l to <5 ug/l with the majority quoting <4 ug/l
- Turnaround times quoted ranged from 1 day to 7 days with the majority quoting 1 day.
- One laboratory sends the marker to another laboratory
- **HCG**
- 21 laboratories perform the assay in house. Reference ranges quoted ranged from <2 IU/l to <10 IU/l, the majority quoting <4 IU/l
- 4 laboratories send the marker to another laboratory with a turnaround time of 1 to 2 weeks

Question 1-Tumour markers offered-5

- **HER2/NEU**
- 20 laboratories mentioned that they did not offer this assay
- 5 laboratories send the marker to another laboratory with a turnaround time of 2 weeks
- One laboratory quoted the result as either positive or negative
- **NSE-NEURONE SPECIFIC ENOLASE**
- 8 laboratories mentioned that they did not offer this assay
- 14 laboratories send the marker to another laboratory with a turnaround time ranging from 1 week to 4 weeks
- 3 laboratories perform the assay in house with a turnaround time ranging from 1 day to 4 weeks- two quoting 4 weeks
- Reference ranges quoted were <13 ug/l or <15 ug/l

Question 1-Tumour markers offered-6

- **THYROGLOBULIN**
- 20 laboratories send the marker to another laboratory with a turnaround time ranging from 2-3 weeks with the majority quoting 2 weeks
- 5 laboratories perform the assay in house with a turnaround time ranging from 1 day to 1 week with the majority quoting 1 week.
- Reference ranges quoted were <0.7 ug/l, <1 ug/l,<3 ug/l,<5 ug/l,<40 ug/l and 5-30 ng/ml-most quoted <5 ug/l-the Birmingham range
- **S100**
- 11 laboratories mentioned that they do not offer this assay.
- 12 laboratories send the marker to another laboratory with a turnaround time ranging from 1 week to 3 weeks,the majority quoting 2 weeks.
- 2 laboratories perform the assay in house,quoting 1 day
- Reference ranges quoted were normally <0.15 ug/l

Question 1-Tumour markers offered-7

- **INHIBIN A**

- This together with Inhibin B was not offered by 3 laboratories.
- 17 laboratories offered this together with Inhibin B. None offered Inhibin A alone.
- The most quoted reference range was <3.6 pg/ml for post menopausal women and 5-160 pg/ml for pre menopausal women

- **INHIBIN B**

- 5 laboratories offered Inhibin B alone, 17 offered this together with Inhibin A
- One laboratory measured Inhibin B in house
- The most quoted reference range was 25-325 pg/ml for males, <273 pg/ml for day 3 of the female menstrual cycle, <5 pg/ml for post menopausal women and <341 pg/ml for other females

Question 1-Tumour markers offered-8

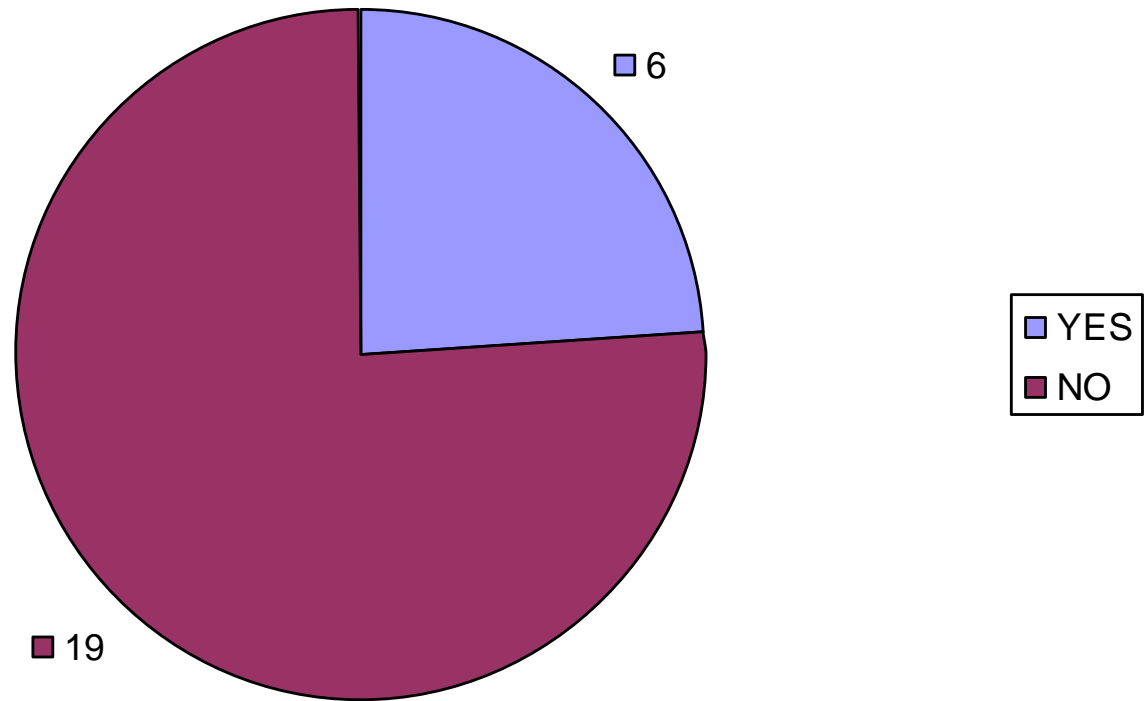
- **CHROMOGRANIN**
- 23 Laboratories send the marker to another laboratory with a turnaround time ranging from 2 to 3 weeks, the majority quoting 2 weeks
- 1 laboratory performs the assay in house
- 1 laboratory does not offer the assay
- Reference ranges quoted were <60 pmol/l for A and <150 pmol/l for B

- **CYFRA 21-1**
- 21 laboratories mentioned that they do not offer this assay
- 3 laboratories send the marker to another laboratory with a turnaround time of 1 to 2 weeks
- 1 laboratory performs the assay in house
- Reference ranges quoted were <3.3 ug/l

Question 1-Other markers offered

- **Placental Alkaline Phosphatase**-turnaround times quoted of 5-12 days and 1 month
- **Protein electrophoresis** with a turnaround time of 3 days
- **Urine catecholamines** with a turnaround time of 10-12 days
- **Squamous Carcinoma Cell Antigen(SCC)** with a turnaround time of 2 weeks
- **Gut hormones** with a turnaround time of 4 weeks
- **DHEAS** with a turnaround time of 1 week
- **Urine 5HIAA** with a turnaround time of 2 days-in house assay
- **Lactate Dehydrogenase** with a turnaround time of 2 hours and 3 days -in house assay
- **Prolactin** with a turnaround time of 2 hours-in house assay

Question 2-Does your laboratory have a guideline for the use of tumour markers?



Question 2a-Which clinicians were involved in the preparation of the guideline?

- Oncologists only
- Gastroenterologists and Urologists(GI markers and PSA)
- Oncologists,Consultant Haematologists,Chemical Pathologist and Consultant Clinical Scientist
- Oncologists and the Biochemistry laboratory
- Oncologists(CA125) Oncologists,Gastronterolgists and Consultant Clinical Scientist(CA199)
- Oncologists and Consultant Clinical Scientist

Question 2 b-What institutions were considered in devising the guidelines?

- ESTMO
- ISSTD
- WCN
- UK Nordic Myeloma Guidelines
- NACB-National Association for Clinical Biochemistry
- BMJ Article of 2009 by Sturgeon C et al
- EGTM
- Thames Audit Guidelines

Question 2c-For each tumour marker,list the relevant cancer as given in the guideline

- **AFP** Liver, testicular, Germ cell tumour, hepatocellular carcinoma-5,
 - **CA125** Ovary-5
 - **CA15-3** Breast-4
 - **CA199** Pancreatic, mucinoid ovarian, biliary, pancreatic-5
 - **PSA** Prostate-4
 - **Calcitonin** Medullary Carcinoma of the thyroid-4
 - **CEA** Colorectal-5
 - **Chromogranin** Carcinoid, neuroendocrine-1
 - **HCG** Seminoma, testicular, choriocarcinoma, trophoblastic disease-5
 - **Her 2/neu** Breast-3
 - **NSE** Squamous cell carcinoma-2
 - **Thyroglobulin**-Follicular cell carcinoma-4
 - **S100** Melanoma-1
 - **Inhibin B** Granuloma cell tumour of the ovary-1
- Not all respondents mentioned all markers in the guidelines and not all tumours were listed for each tumour marker

Question 2d-Are the guidelines readily available for junior doctors etc and 2e-Do representatives meet regularly with the oncologists etc to review these?

- **2d** Only four of those who have guidelines mentioned that these are readily available for junior doctors and other health professionals on the Trust intranet or other site
- **2e** There was no mention of regular meetings with the oncologists and other relevant clinicians to review the guidelines but two respondents mentioned that these were sent by email on an annual or bi-annual basis

Guideline information-1

- Letter issued by laboratory for GI tumour markers CEA and CA19-9-**West Hertfordshire**
- Guidance on requesting tumour markers in Pathology Users Handbook-general guidance,information on PSA,CEA,CA125,CA15-3,CA19-9 and AFP-**Eastbourne**
- Tumour marker guidelines-
specificity,screening,results,diagnosis,monitoring,protocols,assays,r
eference ranges,use of markers AFP,CA125,CA15-
3,Calcitonin,CEA,HCG,Her 2/neu,NSE,thyroglobulin,table of tumour
markers and their associated malignancies,references-**Southend**

Guideline information-2

- Investigation protocol for tumour marker testing-introduction,frequency of testing of tumour marker levels in chemotherapy,radiotherapy,those patients in remission,a section on tumour marker'screens' for patients with metastases but unknown primary tumour,patients with symptoms but no known malignant disease and a table listing the tumour type and whether a marker can be used for screening/early detection,diagnosis/case finding,staging/prognosis,detecting recurrence and monitoring therapy-**Royal Surrey County**
- Guidelines for the appropriate requesting of tumour markers-introduction,general information on specificity,screening,results,diagnosis,monitoring,interpretation,reference ranges,use of specific markers AFP,CA125,CA15-3,CA19-9,Calcitonin,CEA,HCG,Her 2/neu,NSE,thyroglobulin,PSA,references,table for each marker in terms of screening,diagnosis etc and factors that can influence interpretation of tumour markers-**North Middlesex**

16th December 2009

Dear Colleagues

Re: GI Tumour Markers

We are writing to you regarding the use of GI tumour markers (CEA, CA 19-9) in the diagnosis of gastrointestinal disease. These tumour markers have a low sensitivity and specificity when used in the diagnosis of gastrointestinal cancers – their role is in the monitoring and reassessment of known malignant disease, such as colorectal cancer or in the context of specialist investigation of upper GI cancer.

The use of these tests by non-specialists can lead to potentially misleading results and it has therefore been agreed that these tests are only available on the advice of specialists (Oncologists, GI surgeons and Gastroenterologists). This means that non-GI specialists will no longer have direct access to these tests.

If there is a concern that a patient may have a gastrointestinal malignancy then appropriate referral to a GI specialist should be made. Requests from other teams will no longer be processed through the Lab.

Yours sincerely

Medical Director/Director of Patient Safety
Consultant Gastroenterologist
Consultant Chemical Pathologist

14th October 2010

Dear Colleague

There has recently been a review of the number of requests for GI tumour markers (CEA and CA 19-9) in secondary and primary care. This has shown that the number of requests has gradually but significantly increased over time. The use of these tests has been reviewed by our local GP specialists. West Hertfordshire Hospitals Trust (WHHT) have implemented changes so that these tests can only be requested within the acute trust by specialists in GI cancer. These changes have resulted in a greater than 50% reduction in the number of GI tumour marker requests.

Whilst the number of requests from primary care is relatively small it is growing significantly. The local specialists have advised that GI tumour markers have a relatively low specificity and sensitivity for GI cancer and have no place in the diagnosis of cancer outside specialist centres. The low sensitivity (approximately 50% of colorectal cancers are negative for CEA and 97% of early cancers are negative for CEA) means that a negative result can give false reassurance. The 2 week cancer wait system is designed to provide a fast appropriate referral service for patients who may have bowel cancer and CEA estimation is not part of this algorithm.

In addition, the national Bowel Cancer Screening Programme is a well established evidence based system for screening for bowel cancer that does not include tumour markers.

CEA is useful in follow up after treatment for bowel cancer and is used as part of the algorithm for post colorectal cancer surveillance, organised through or on behalf of the GI oncologists and colorectal surgeons.

CA 19-9 has no place in the initial investigation of pancreato-biliary cancer and this tumour marker is only used in specialist circumstances when it may add to the interpretation of imaging studies.

Clearly there is a cost attached to these tests, but it is the additional costs that can accrue following these tests, eg referrals to GI outpatients/requests for colonoscopy in those found to have abnormal results which may be a false positive. Just as worrying is the possibility that in patients who have a false negative result, there may be reassurance that there is no significant pathology.

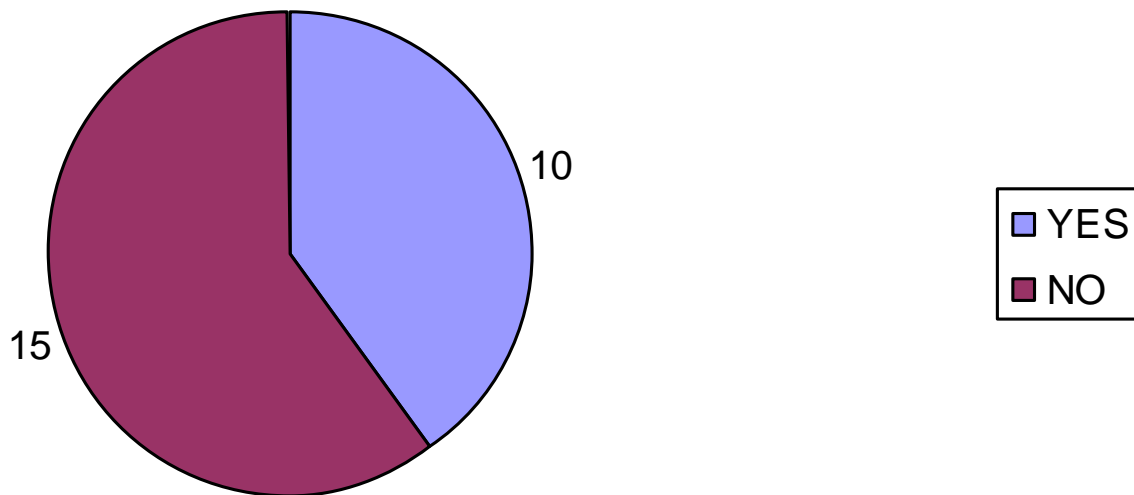
In summary, it is advised that requests for GI tumour markers should only be made when they are used as part of the management algorithm as advised above.

We would ask you to consider this information if you are requesting GI tumour markers in the future. We plan to review the level of demand over the next year.

Yours sincerely

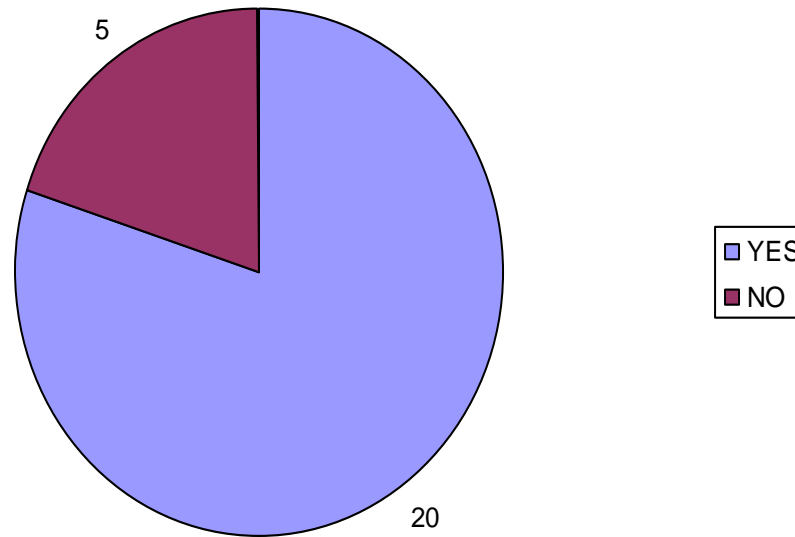
CEC Chair
PBC Leads/PBC Clinical Leads
Consultant in Public Health
Consultant Gastroenterologist

Question 3-Does the local laboratory carry out a local audit to review the tumour marker service?



The audits were carried out ranging from every 5 years,3 per year, 2 per year with most carrying this out or planning to do so on an annual basis

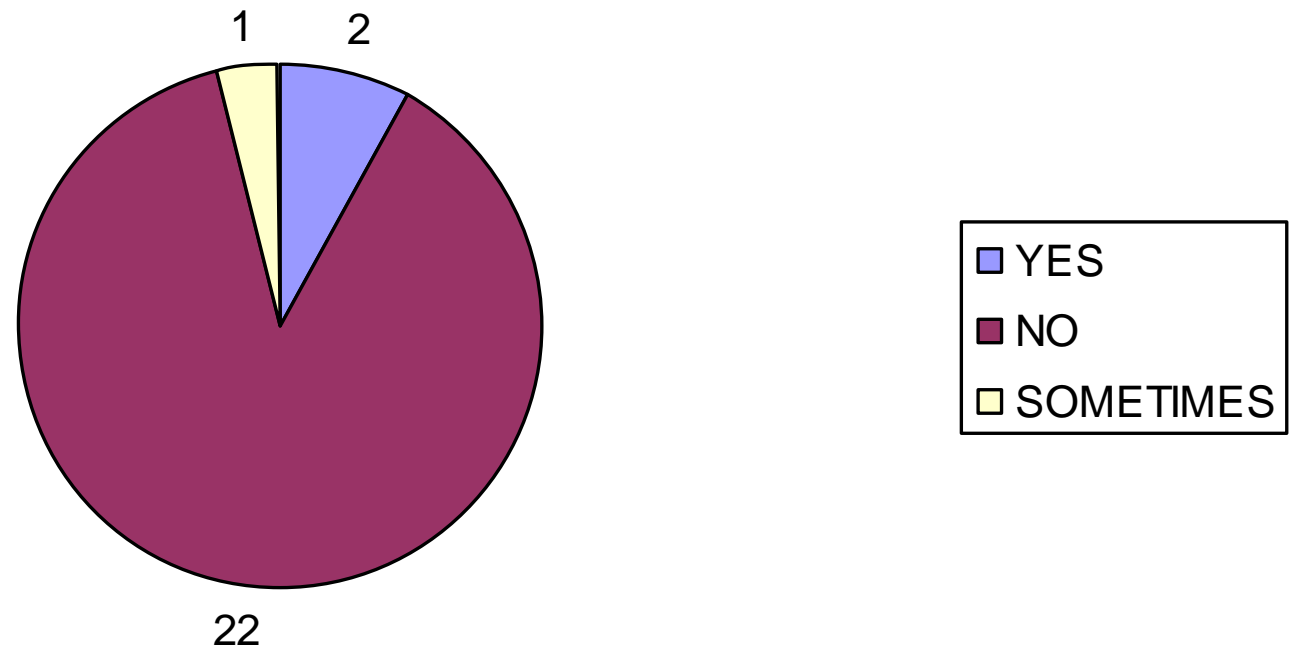
Question 4-Does the laboratory routinely vet requests for tumour markers?



Question 4-Tests vetted,who vets the requests and common reasons for rejection

- **4a.** Tests vetted were the referred tests,add on requests for tumour markers,all except PSA,CA19-9 and CA15-3,CA15-3 and thyroglobulin,CA19-9
- **4b** Consultant Clinical Scientist,Consultant Chemical Pathologist,Principal Biochemist,Senior Biochemist,Duty Biochemist,Trainee Clinical Scientist with supervision.
- **4c** Recently requested and unlikely to change in such a short space of time,frequency of requesting,requests from Accident and Emergency,screening requests,inadequate clinical information,wrong marker on the request form,screening for malignancy to determine the primary site of the metastases,CA19-9 used to diagnose cancer,patient not known to have relevant cancer,multiple tumours for diagnosis,wrong sample type,thyroglobulin in the case of hyper- or hypo-thyroidism,wrong sex of the patient,'fishing' exercise

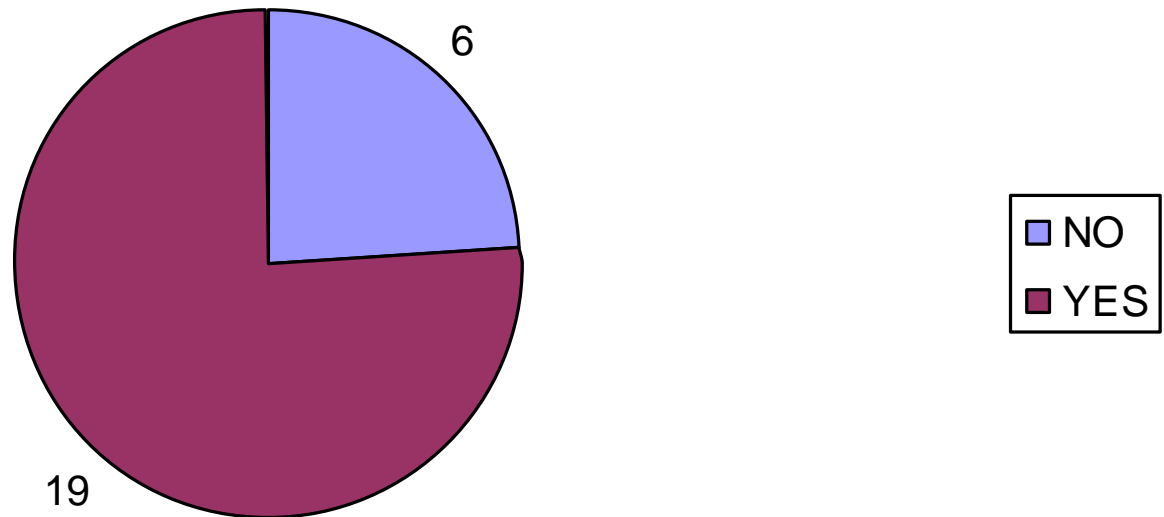
Question 5-Are tumour markers restricted to particular grades of clinical staff?



The laboratory mentioning sometimes stated requests for thyroglobulin only for oncology and metabolic consultants.

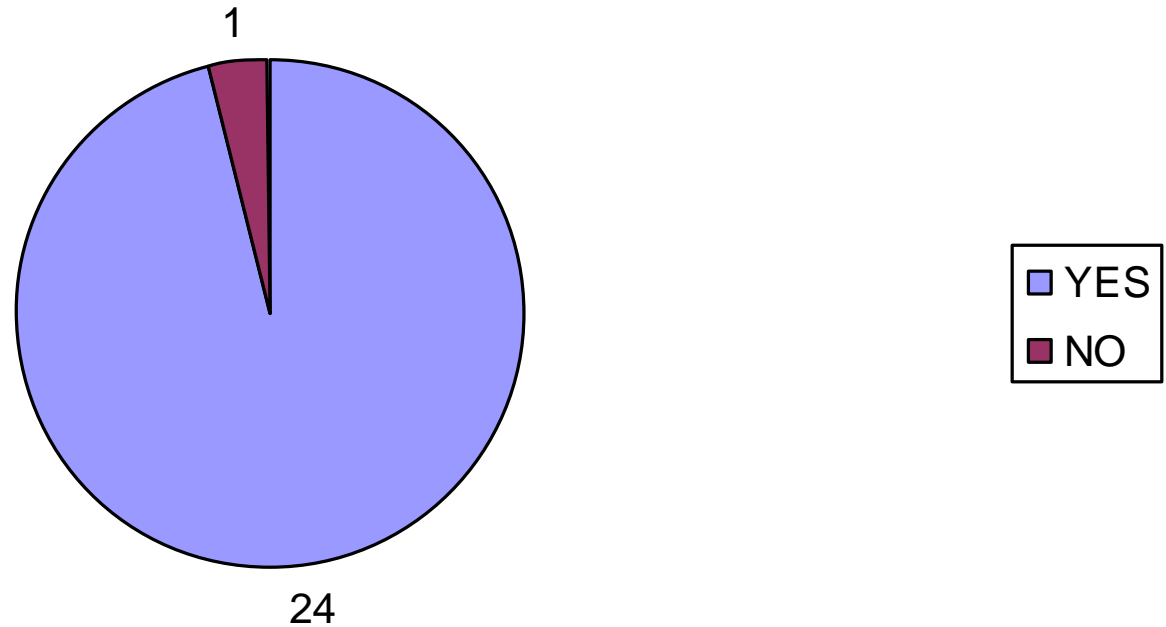
Those mentioning no mentioned non clinical staff and nurses

Question 5b-Are requests generally accepted from Accident and Emergency?



One laboratory responding yes said some were vetted and one responding yes that they were not accepted as general screening tests.

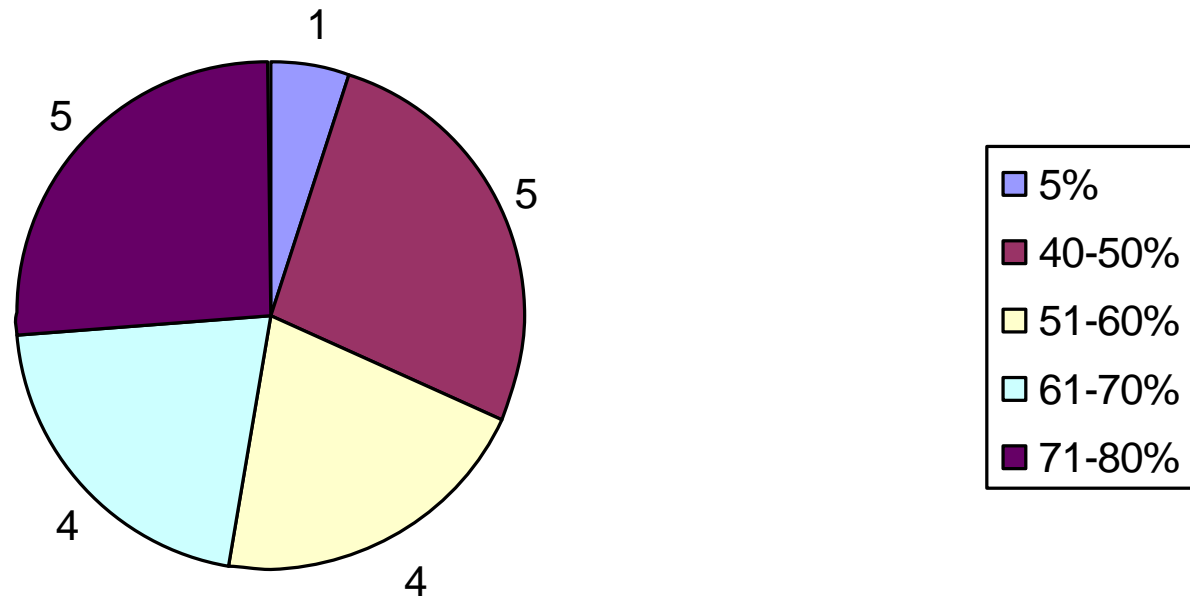
Question 6-Does the laboratory generally accept requests from GPs for tumour markers with the exception of PSA?



Question 6-If yes,under what circumstances are they accepted?

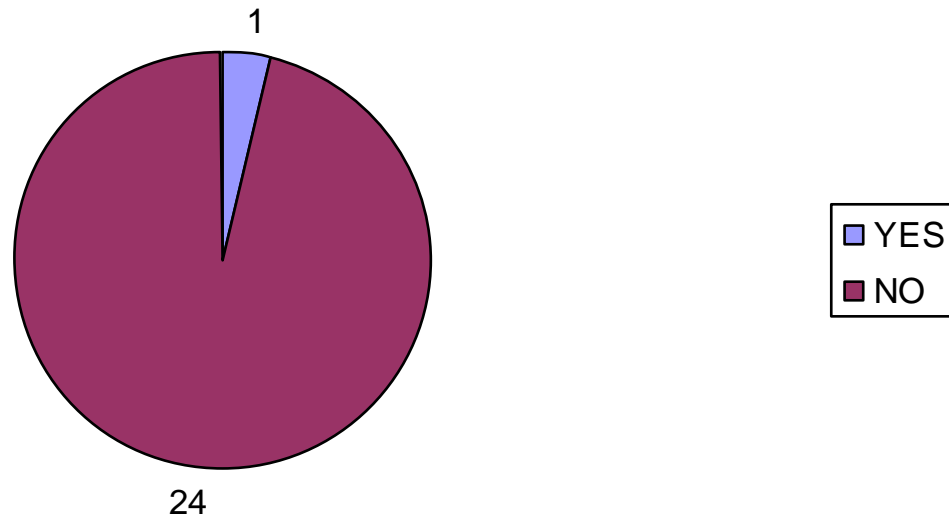
- 11 mentioned that they do not generally vet requests from GPs
- 4 mentioned that they tended to vet the referred tests
- 1 mentioned that they did not vet requests for CA125,CEA, CA15-3
- Ca 125 accepted due to the April 2011 NICE guidance on ovarian cancer
- CA19-9 and CEA accepted if already a known cancer and the tumour marker is being monitored in primary care
- Accepted if known malignancy or previous malignancy where the marker is appropriate
- Monitoring of known cancers
- Accepted if not used for screening
- Accepted if relevant clinical details
- One laboratory asked the GP to contact the laboratory to discuss
- Requested to do them by tertiary centre or secondary care for follow up

Question 6-Approximate % of requests for PSA from GPs?



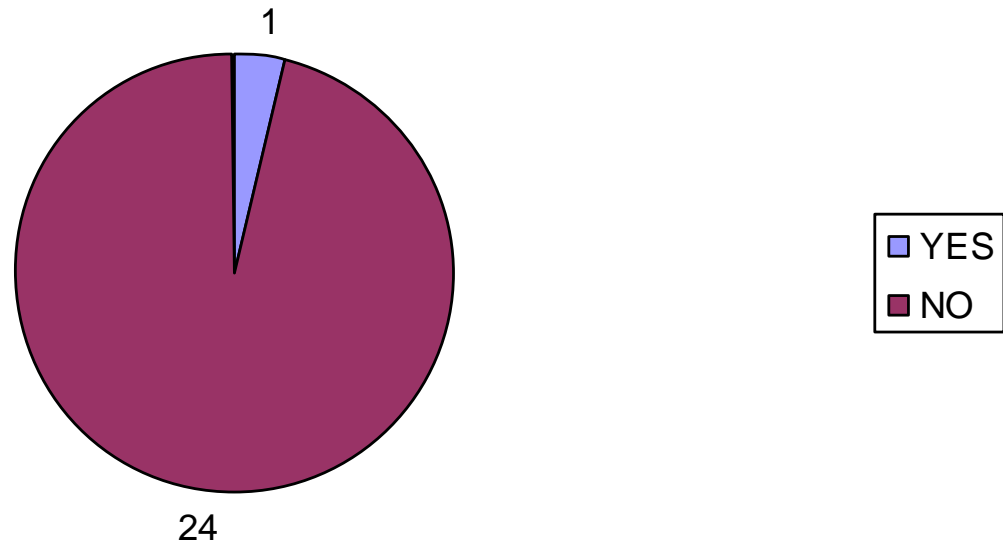
The laboratory quoting 5% was a London Teaching Hospital-UCLH

Question 7a-Does the EOS prevent ordering of tumour markers by source?

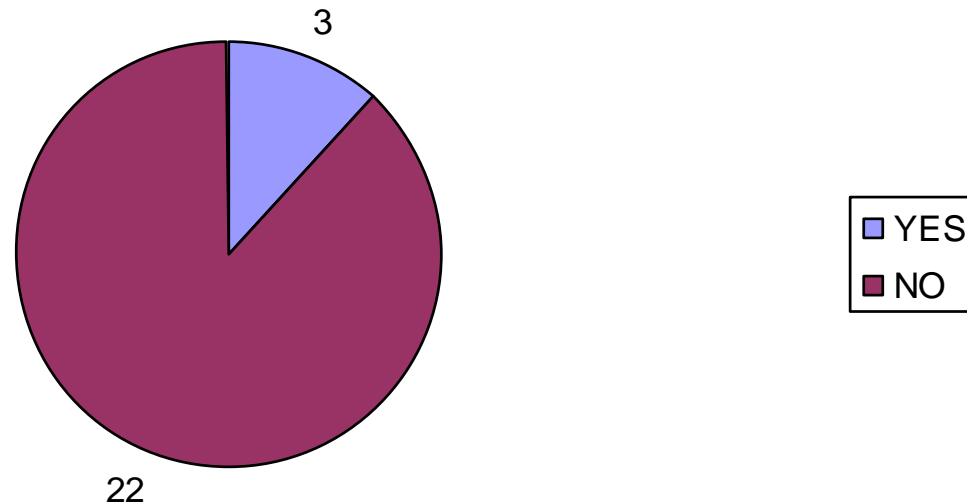


EOS Electronic ordering system

Question 7b-Does your EOS prevent ordering of tumour markers by clinician?

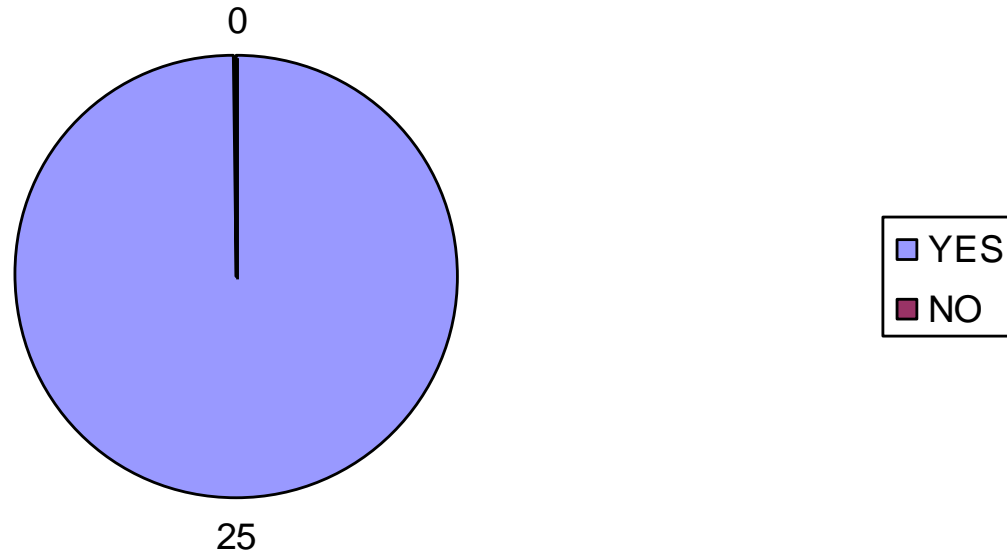


Question 7c-Does your EOS prevent ordering of tumour markers by interval at which the previous one was made?

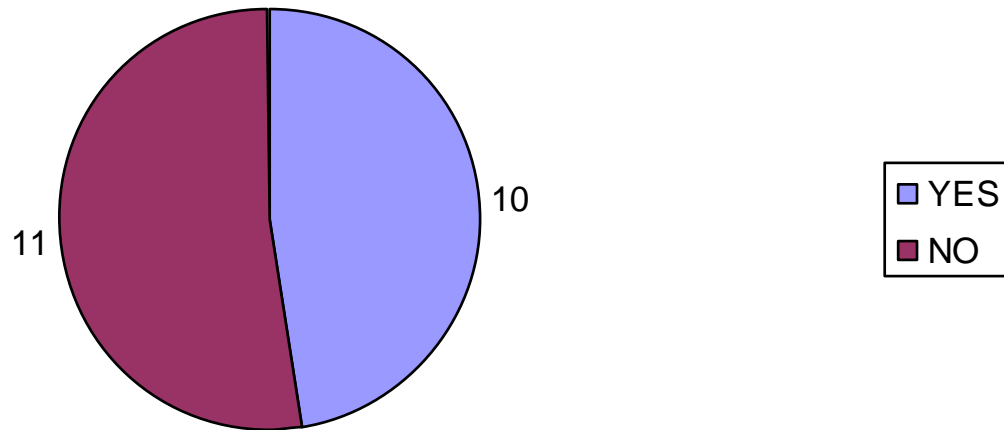


23 of 25 mentioned that it did not prevent a large number of tumour markers being requested

Question 8a-Are tumour markers offered Monday to Friday core hours?

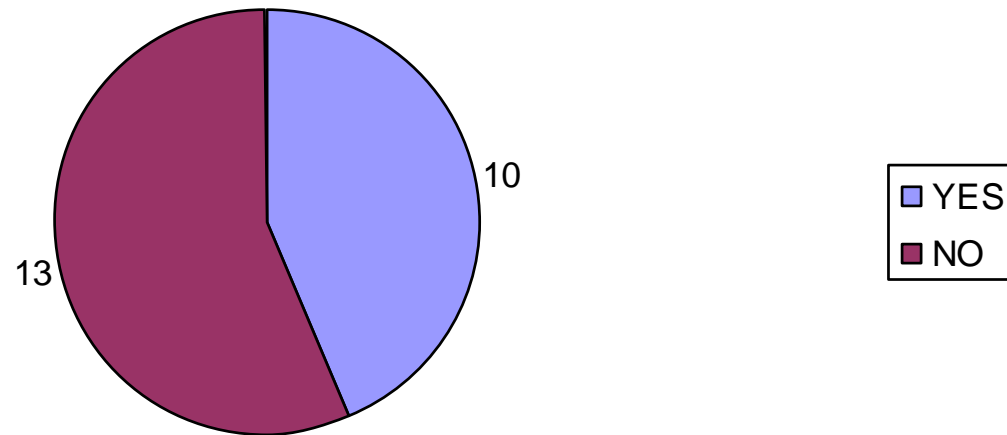


Question 8b-Weekends?



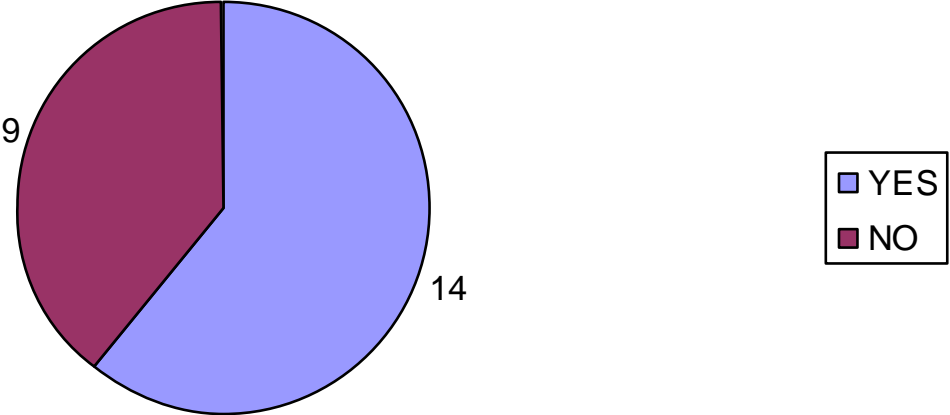
One laboratory mentioning yes did so after discussion with the Consultant on call and one would only do so for HCG

Question 8c-24/7



One mentioning yes stated for HCG only

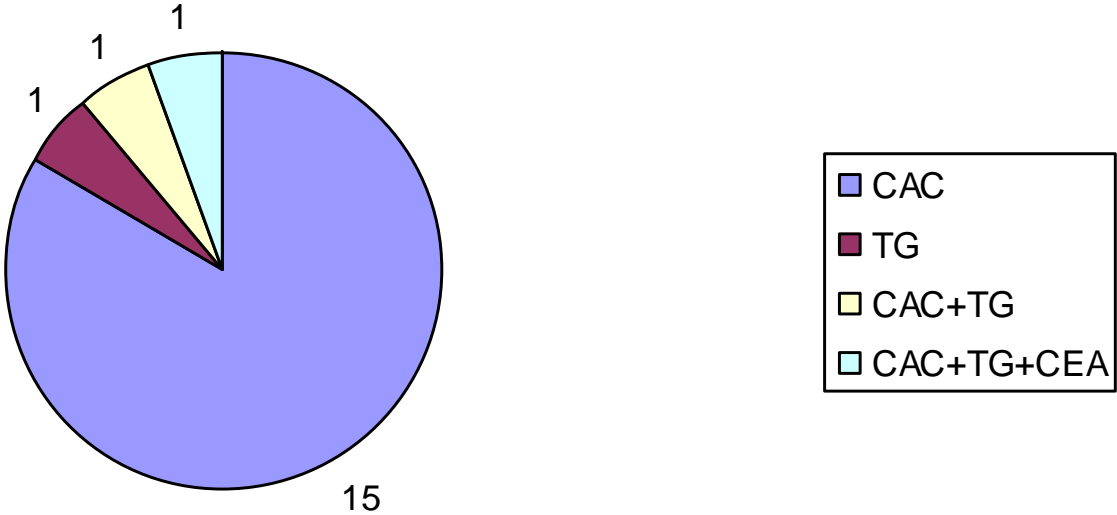
Question 8d-Urgently



Question 8d-If requested urgently, under what circumstances are they accepted?

- CA125 pre-operatively where the doctor failed to send a sample at the correct time
- Urgent request for HCG accepted for the Trophoblastic Disease Team Unit
- After discussion with the Consultant on call
- Patient has a mass and undergoing surgery and marker had not been requested
- Cancer waiting time samples
- Run for the Regional Cancer Centre who require urgent pre and post chemotherapy tumour marker levels
- Prolactin and HCG for immediate patient management

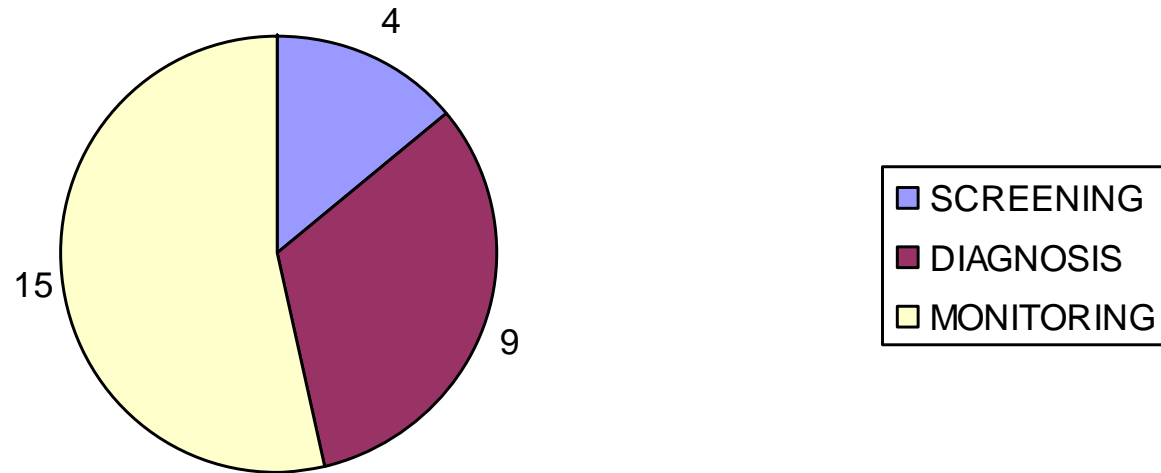
Question 9a-Tumour markers offered for medullary carcinoma of the thyroid



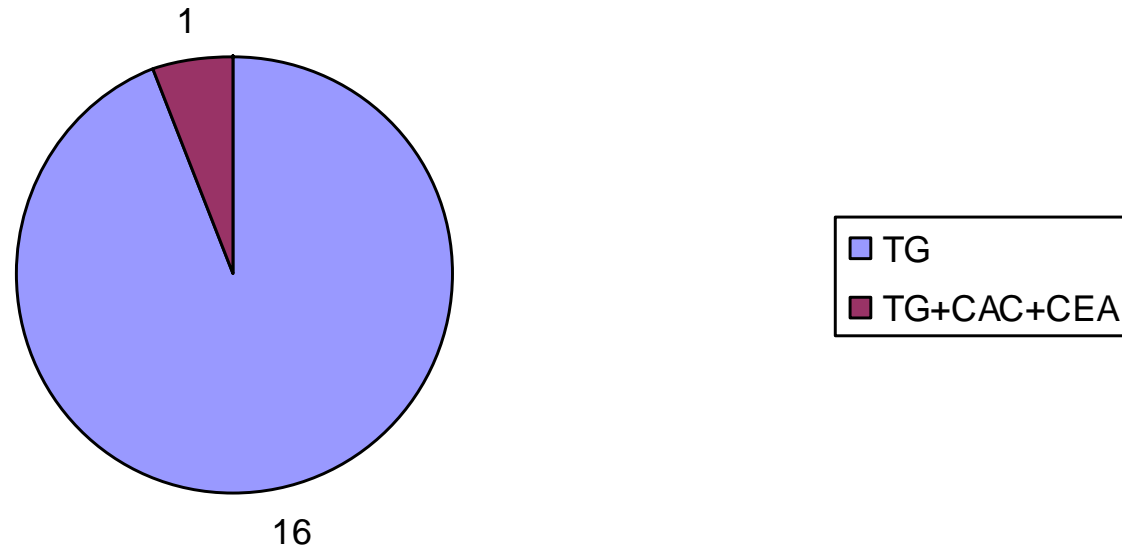
CAC Calcitonin

TG Thyroglobulin

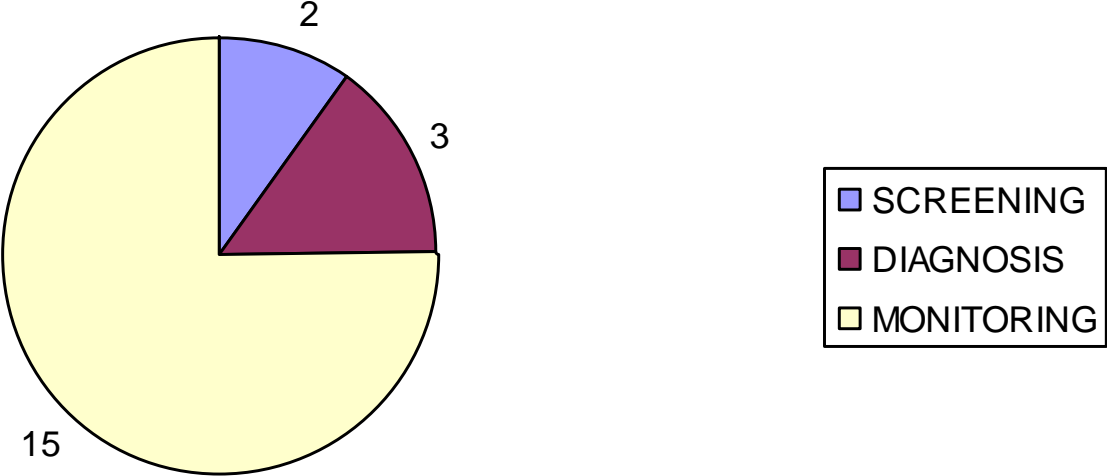
Markers for medullary carcinoma of thyroid



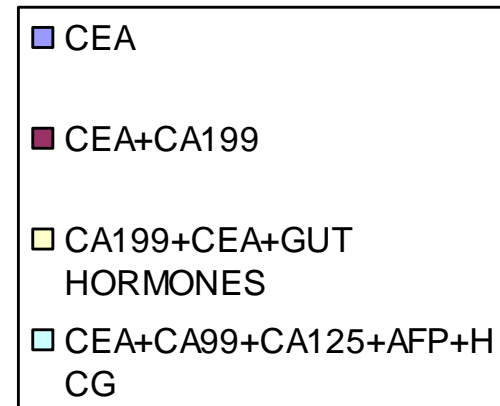
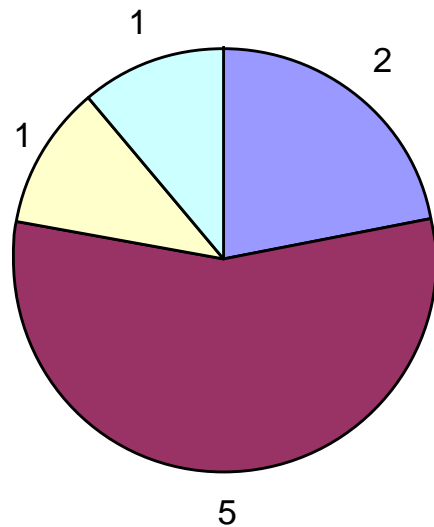
Question 9b-Tumour markers offered for papillary carcinoma of the thyroid



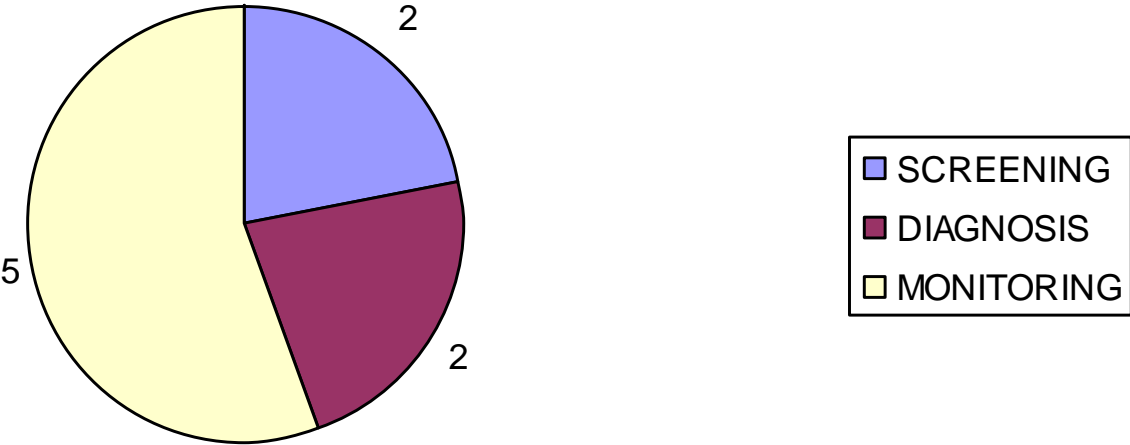
Markers for papillary carcinoma of the thyroid



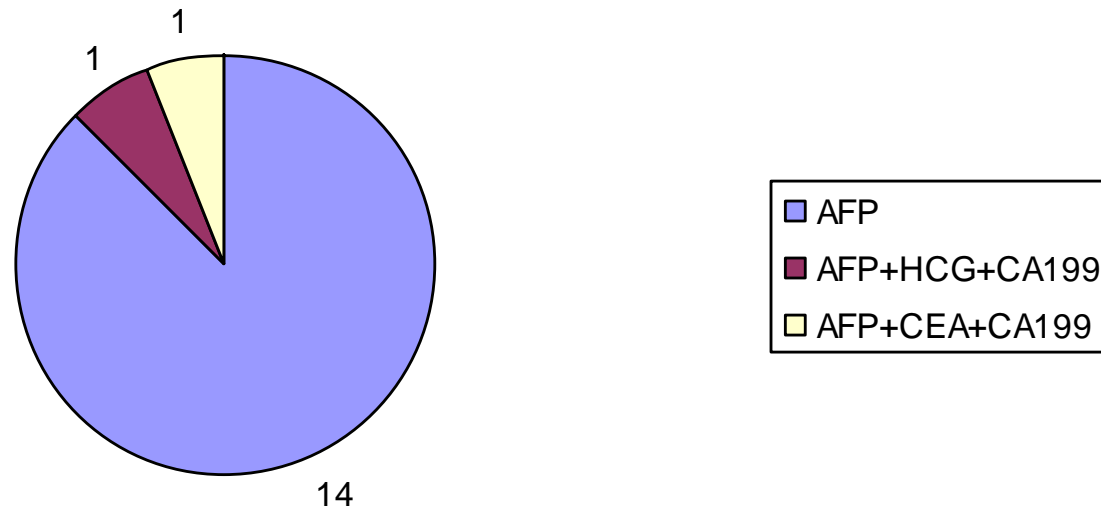
Question 9c-Tumour markers offered for carcinoma of the stomach



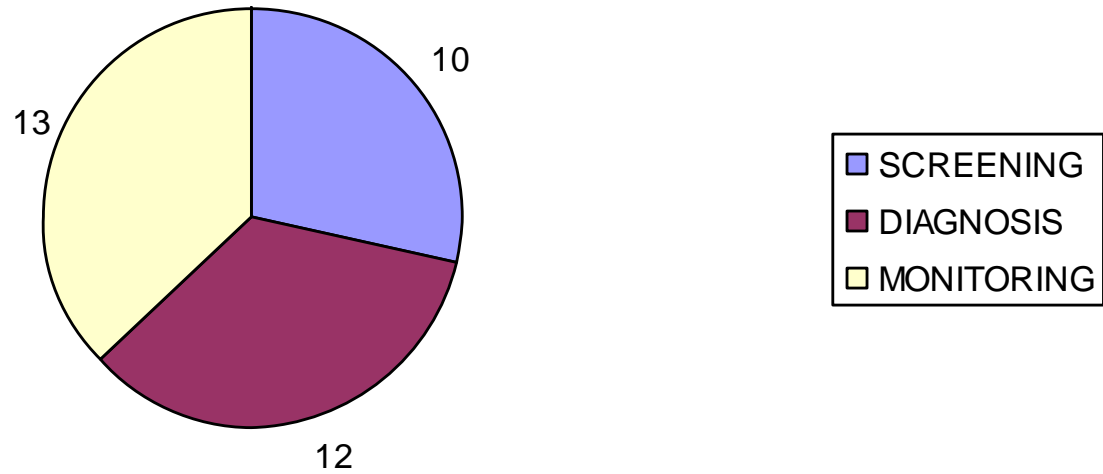
Markers for carcinoma of the stomach



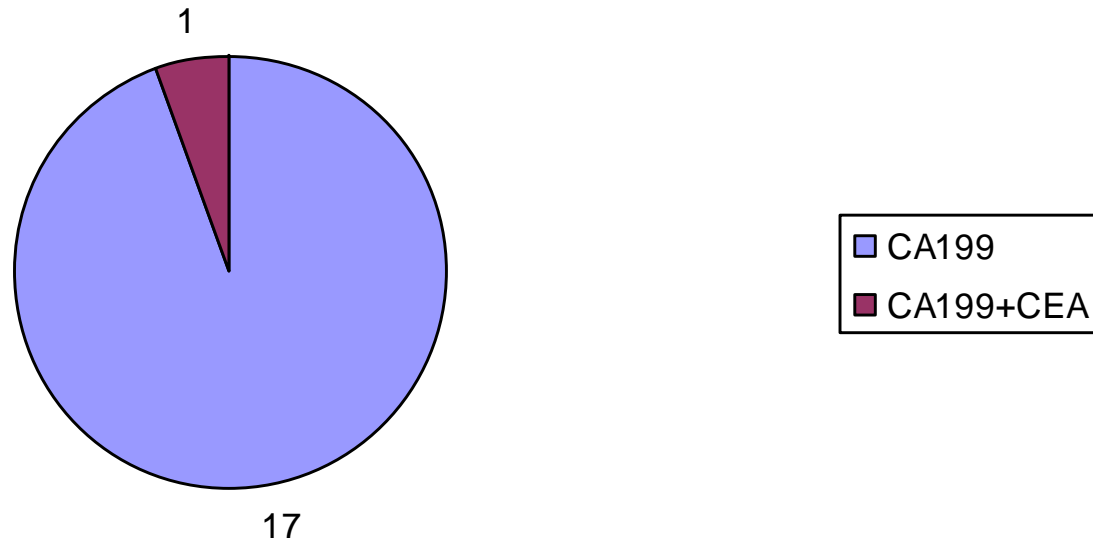
Question 9d-Tumour markers offered for carcinoma of the liver



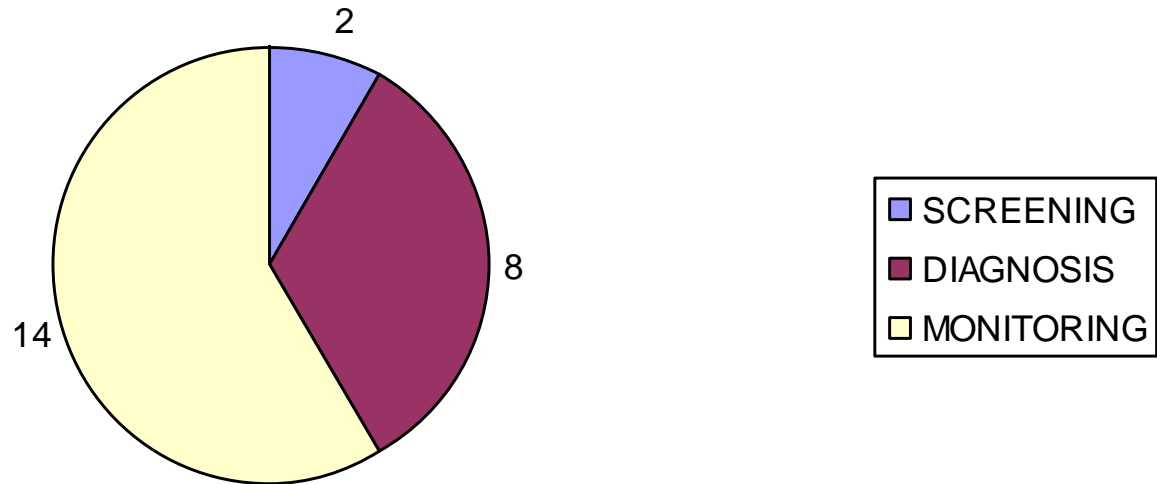
Markers for carcinoma of the liver



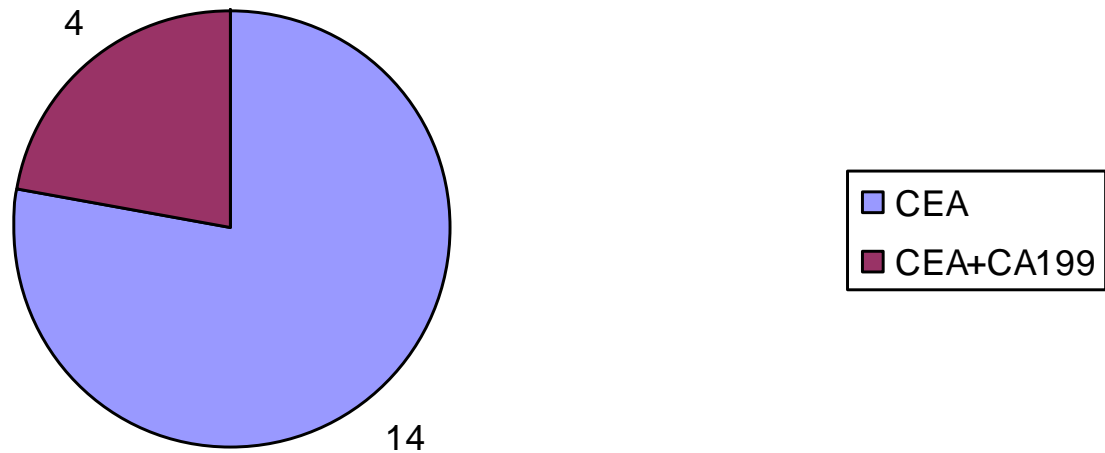
Question 9e-Tumour markers offered for carcinoma of the pancreas



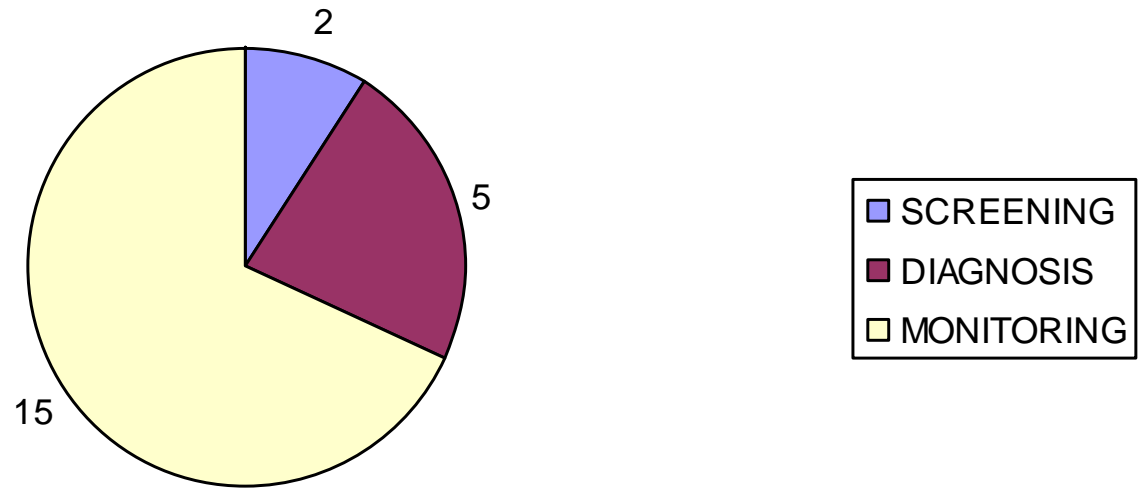
Markers for carcinoma of the pancreas



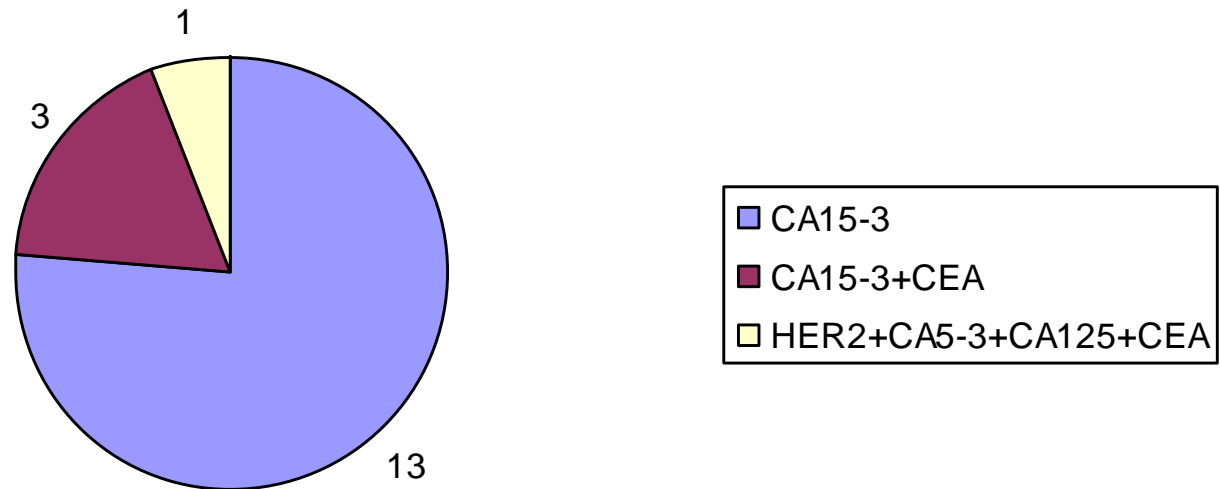
Question 9f-Tumour markers offered for carcinoma of the colon



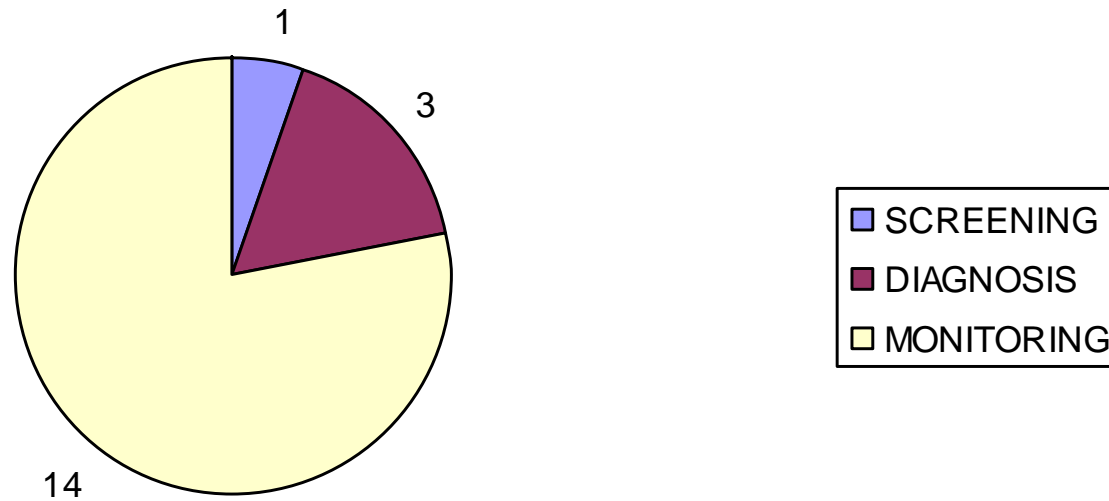
Markers for carcinoma of the colon



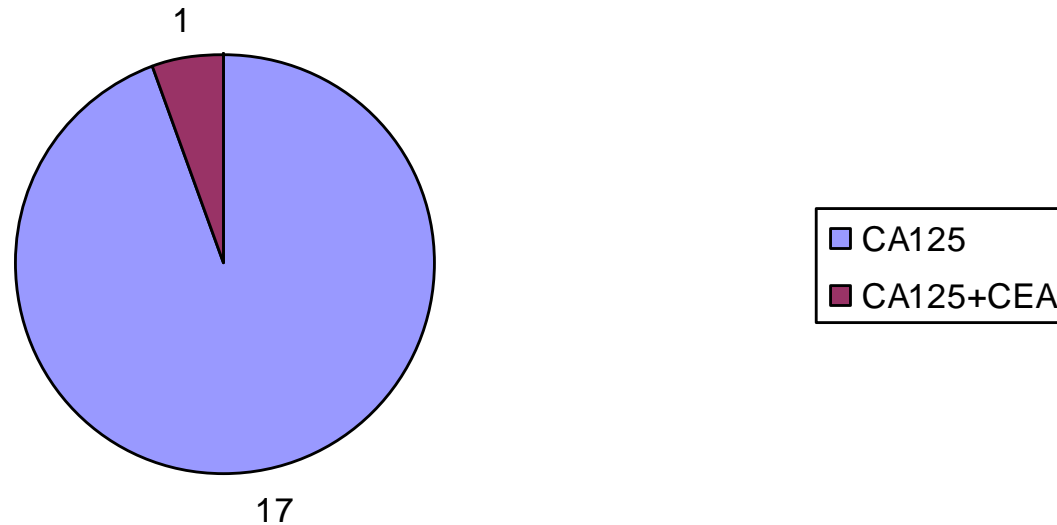
Question 9g-Tumour markers offered for carcinoma of the breast



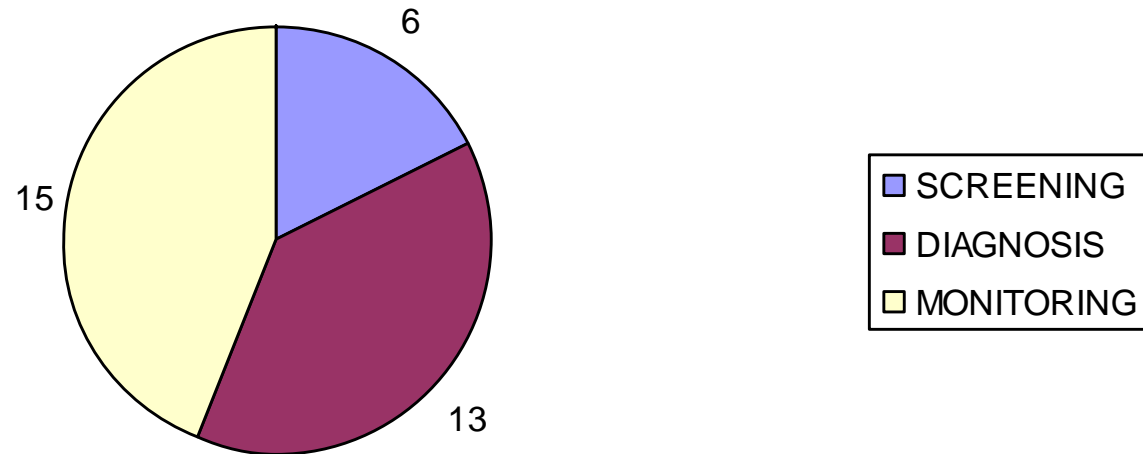
Markers for carcinoma of the breast



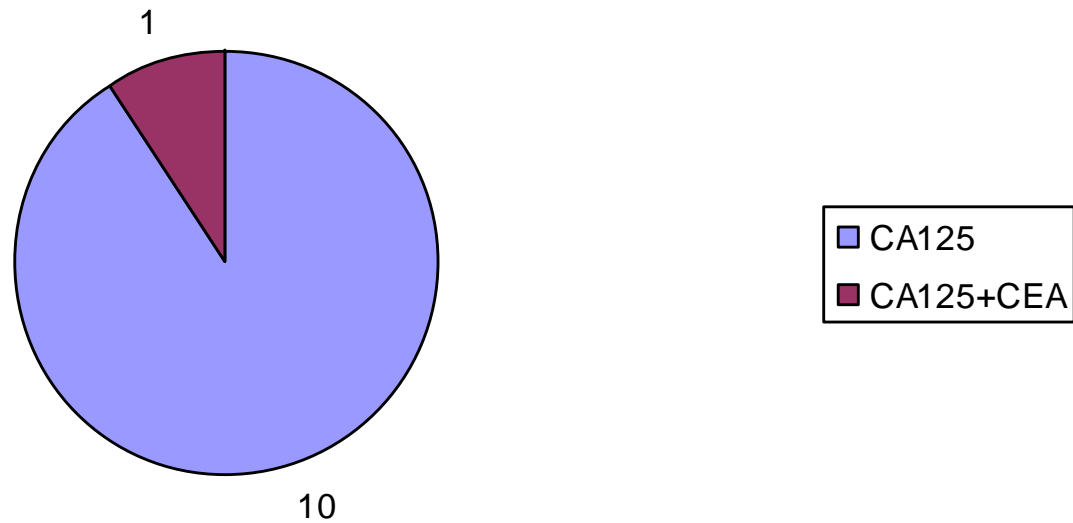
Question 9h-Tumour markers offered for carcinoma of the ovary



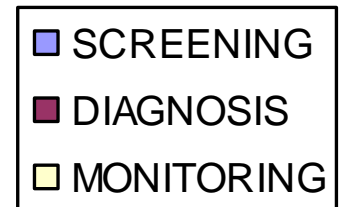
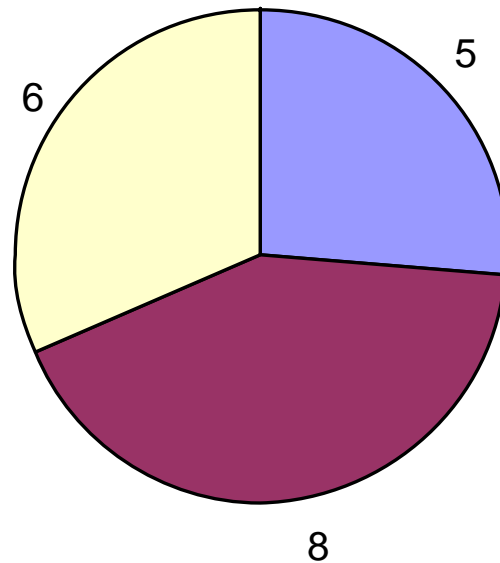
Markers for carcinoma of the ovary



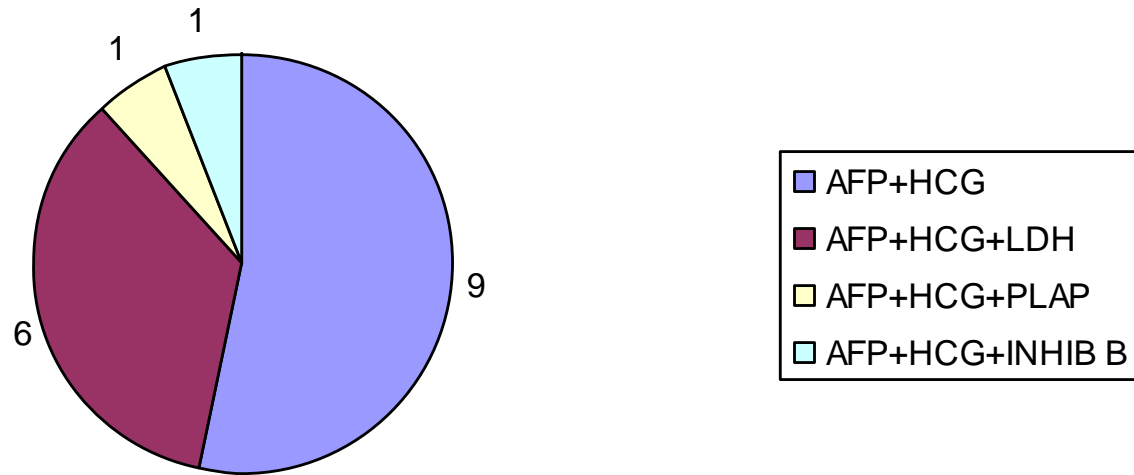
Question 9i-Tumour markers offered for ovarian cysts



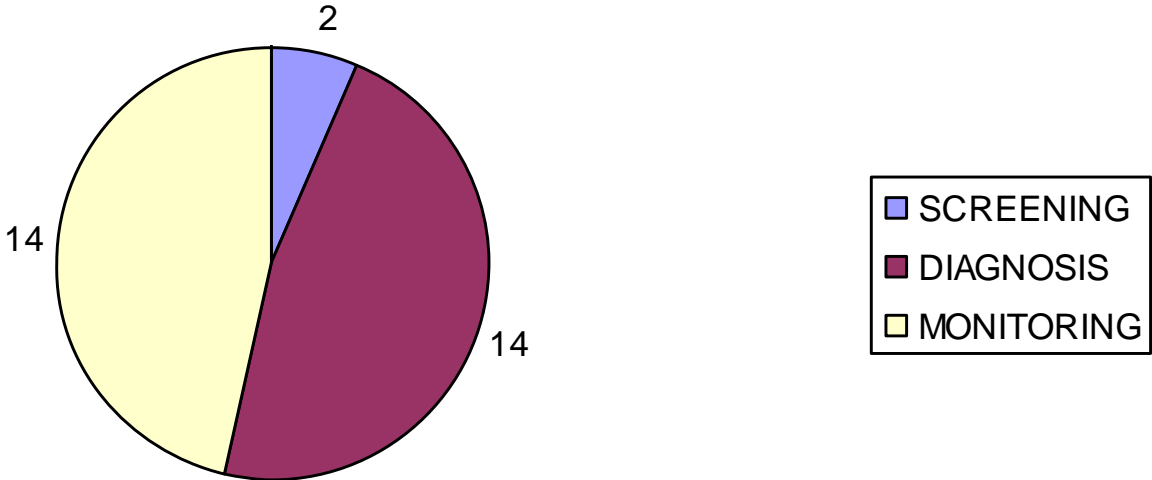
Markers for ovarian cysts



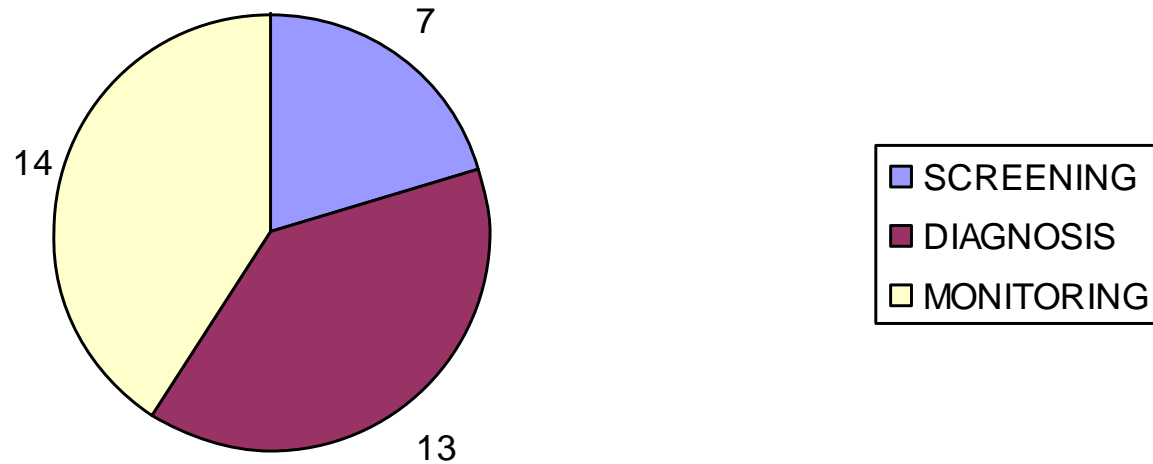
Question 9j-Tumour markers offered for carcinoma of the testes



Markers for carcinoma of the testes

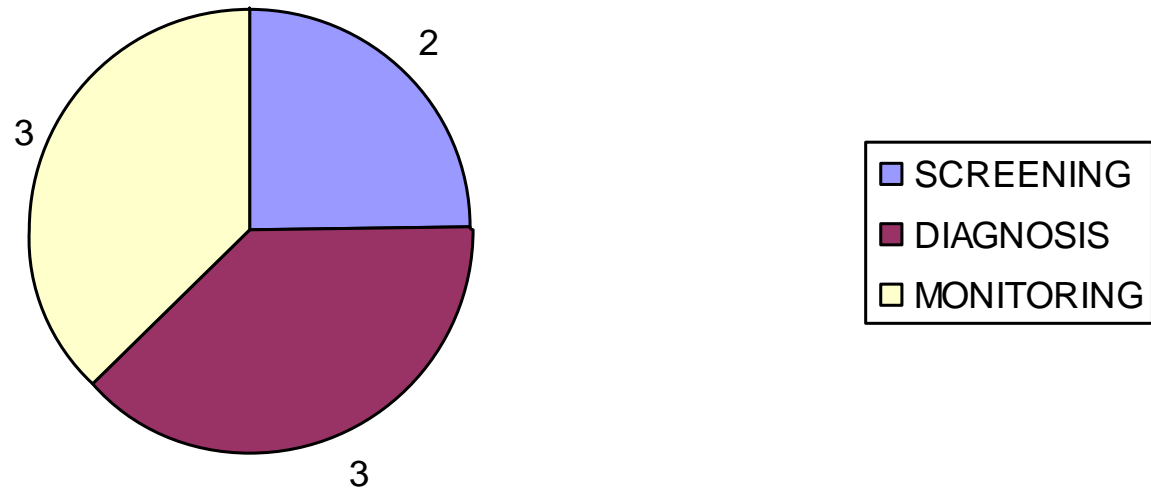


Question 9 k-Tumour markers offered for carcinoma of the prostate



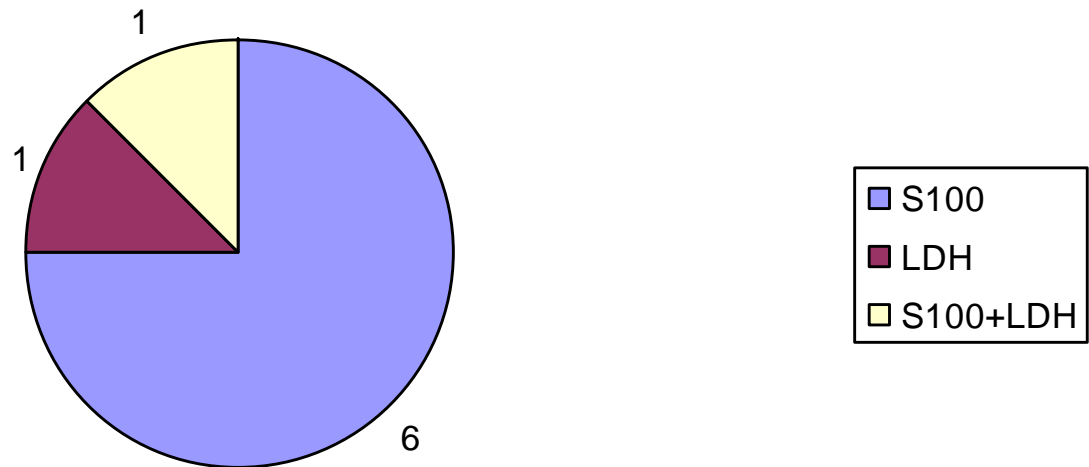
PSA mentioned as the only marker for carcinoma of the prostate

Question 9I-Tumour markers offered for ascites?cause

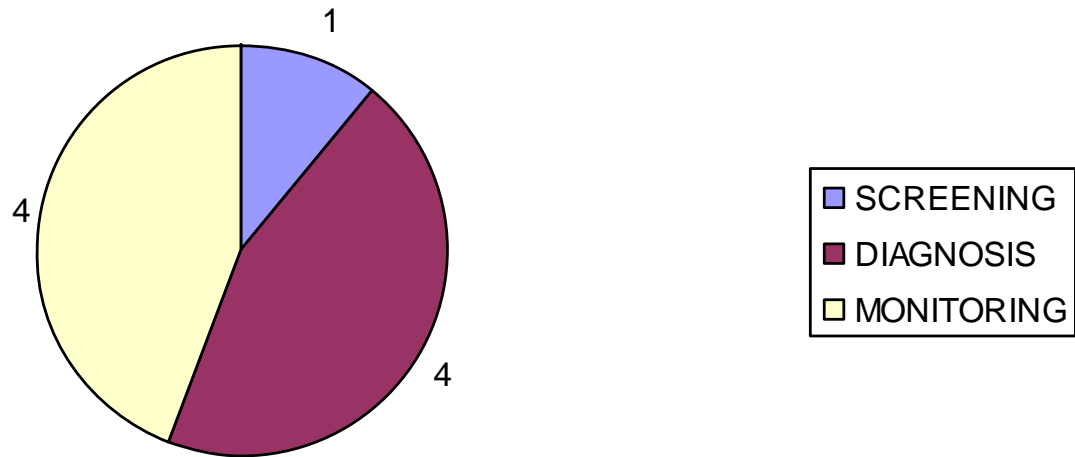


CA125 mentioned as the only tumour marker

Question 9m-Tumour markers offered for melanoma



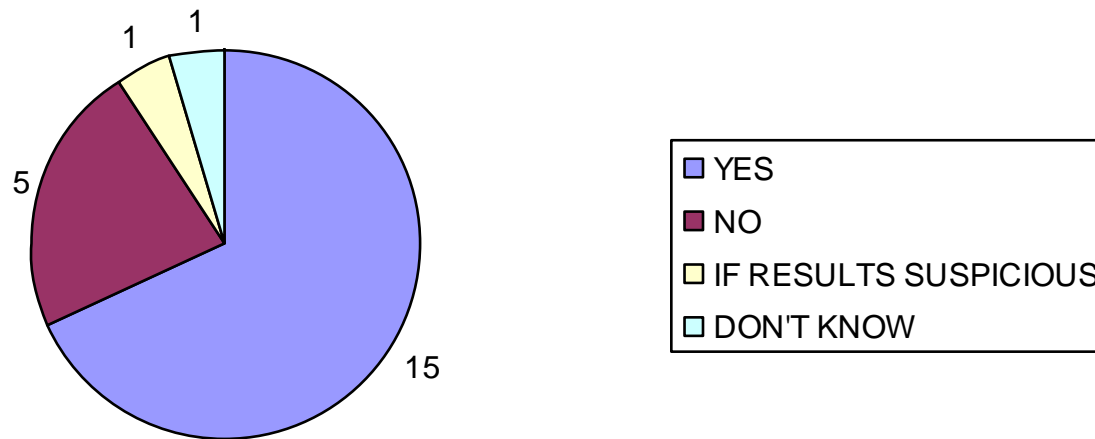
Markers for melanoma



Question 9n-Other markers

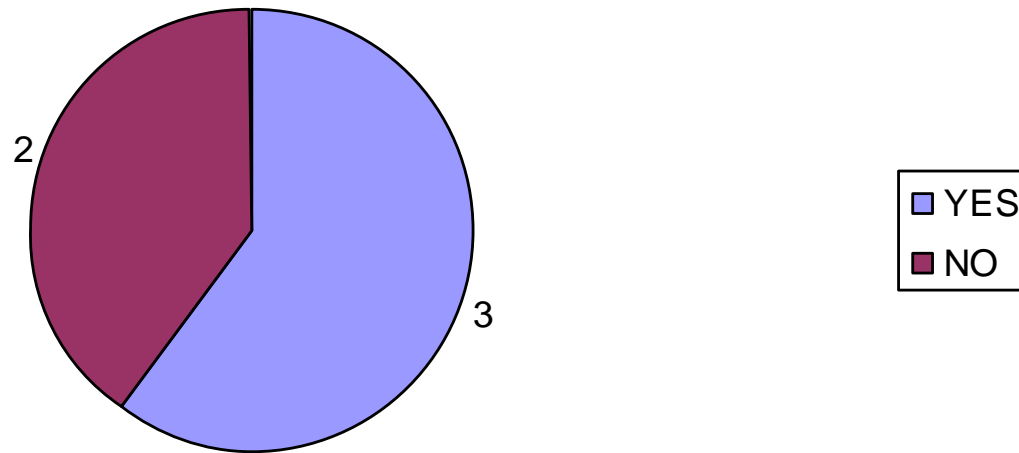
- **Liver 2° ? Cause** AFP +HCG,AFP+CEA+CA19-9,CEA+CA19-9
AFP+CEA+CA125+CA19-9
- **Bone 2° ?Cause** PSA,Alkaline Phos Isoenzymes,PSA+AFP
- **Lung 2° ?Cause** CA19-9+CEA+CA125,NSE
- **Brain 2° ?Cause** AFP+HCG,Chromogranin +NSE,CA125+CEA
- **Disseminated metastases?Cause** AFP+HCG,PSA+CA15-3
CEA+CA125+CA19-9

Question 10-When measuring thyroglobulin, does the referral laboratory that you use routinely measure TG antibodies?

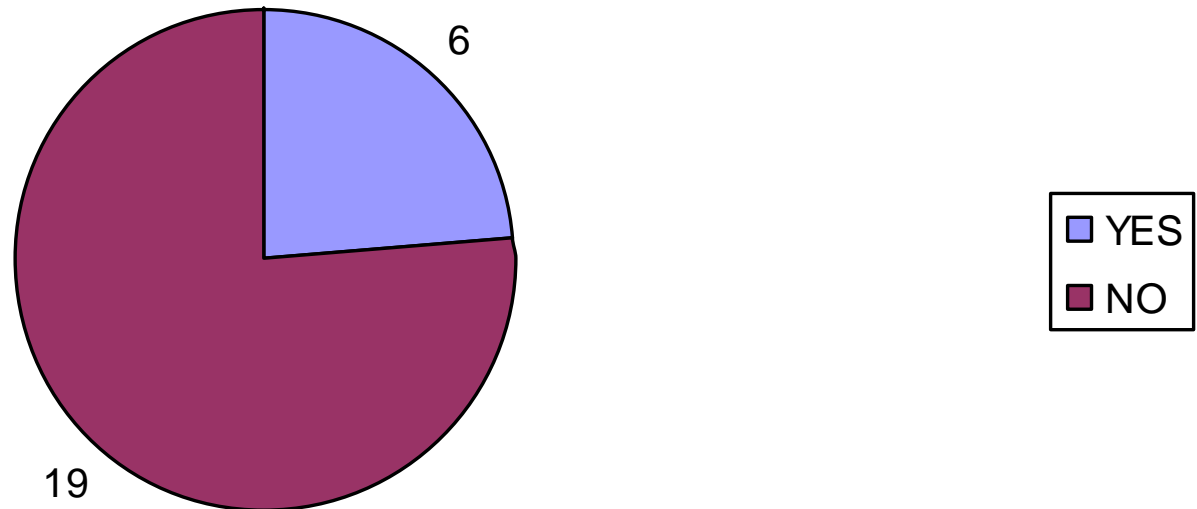


3 laboratories measure both thyroglobulin and thyroglobulin antibodies in house

Question 10b-If no, do you send the sample elsewhere for thyroglobulin antibodies?



Question 11-Does your laboratory ever measure tumour markers on fluids?



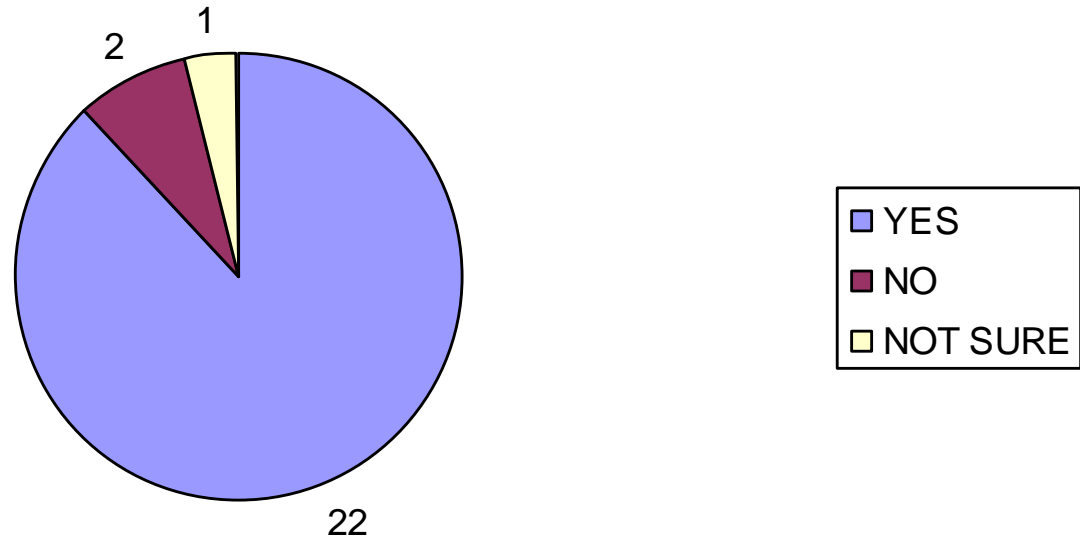
Question 11-What laboratories measure

- CSF HCG 4
- CSF AFP 5
- CYST FLUID CEA 4
- CYST FLUID CA19-9 3
- PLEURAL FLUID CEA 4
- PLEURAL FLUID CYFRA 21-1 1
- PLEURAL FLUID CA125 2
- FLUID HCG 1
- CSF CEA 1

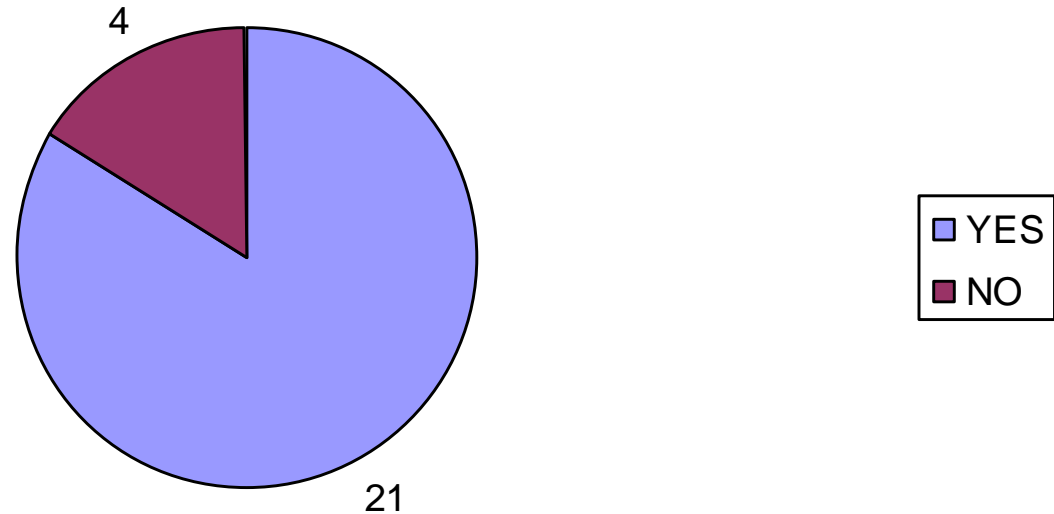
Question 11-Clinical situations when measured

- **CSF HCG** Diagnosing intracranial germ cell tumour, 2° intracranial metastases in trophoblastic disease, suspicion of CNS tumour
- **CSF AFP** Diagnosing intracranial germ cell tumour, craniopharyngioma, suspicion of CNS tumour
- **CYST FLUID CEA** GI tumour, pancreatic tumour, differentiation of premalignant or malignant pancreatic cysts from benign cysts
- **CYST FLUID CA19-9** Pancreatic tumour, differentiation of premalignant or malignant pancreatic cysts from benign cysts
- **PLEURAL FLUID CEA** To aid the differential diagnosis of malignant and non malignant tumours, ?malignant pleural effusion
- All but one laboratory mentioned that the method had not been validated for this matrix and that the results could not be interpreted

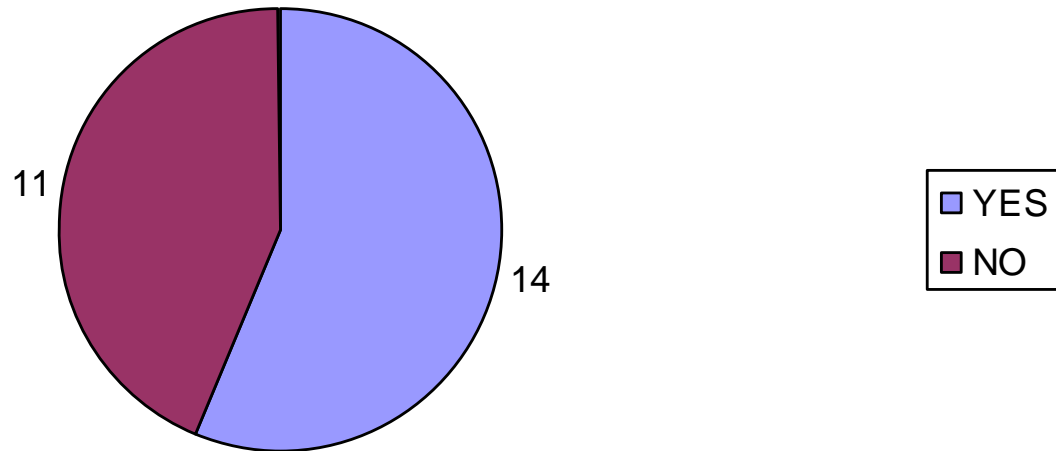
Question 12a-Does your laboratory measure CA125 for screening patients with a family history of ovarian cancer in a hospital setting?



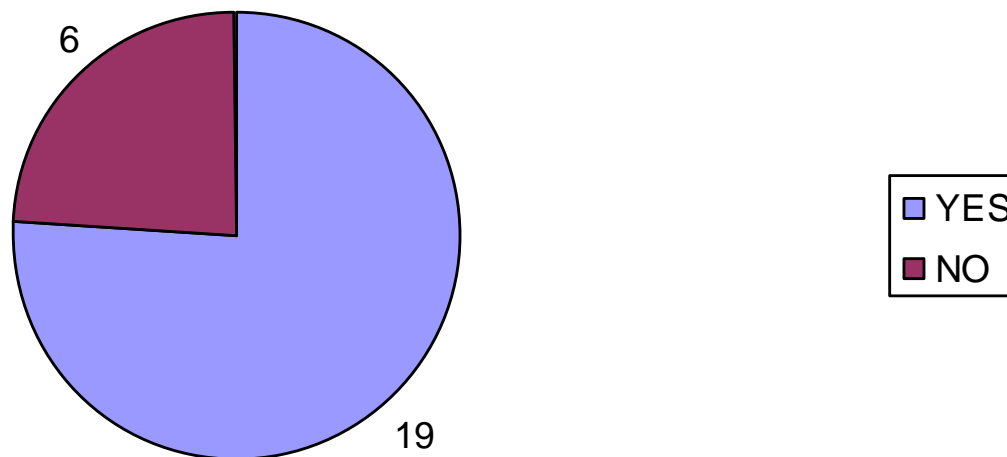
Question 12b-Does your laboratory measure CA125 for screening patients with a family history of ovarian cancer for GP patients?



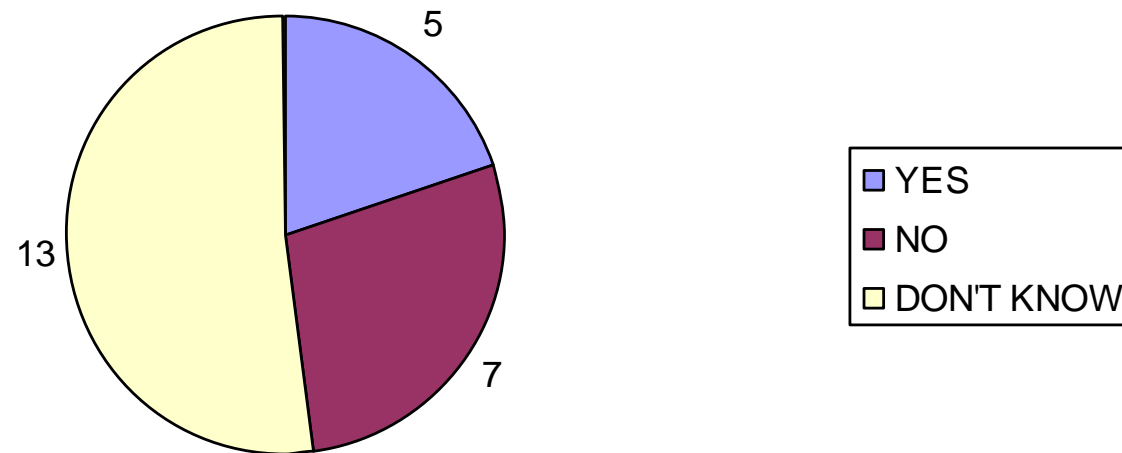
Question 13-Does your laboratory measure CA125 for screening asymptomatic patients for ovarian cancer?



Question 14-Does your laboratory intend to recommend the measurement of CA125 in primary care in women with symptoms suggestive of ovarian cancer as outlined in the April 2011 NICE guidelines?

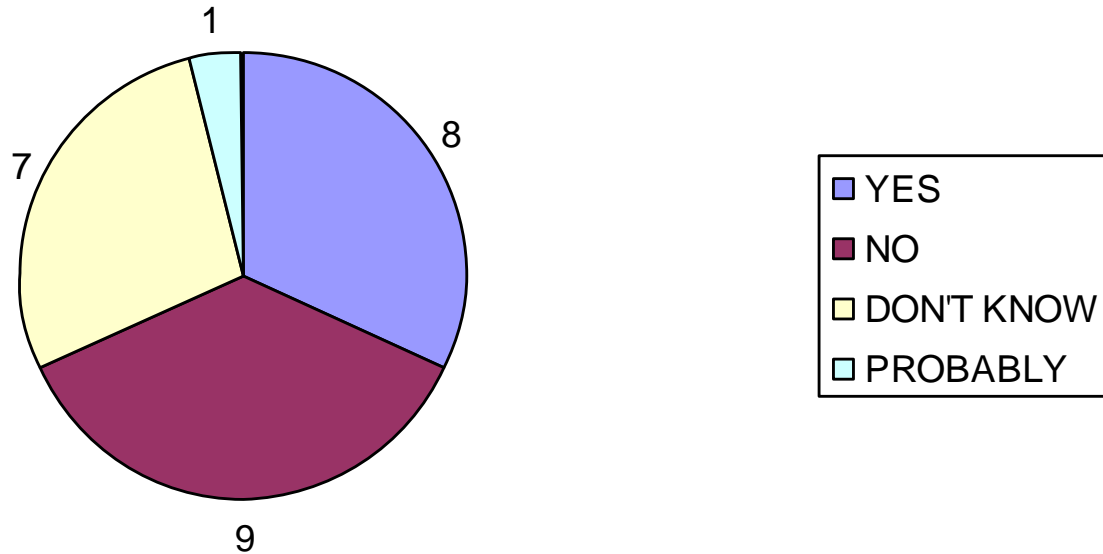


Question 15-Does your hospital calculate an RMI using the CA125 result after performing an ultrasound?

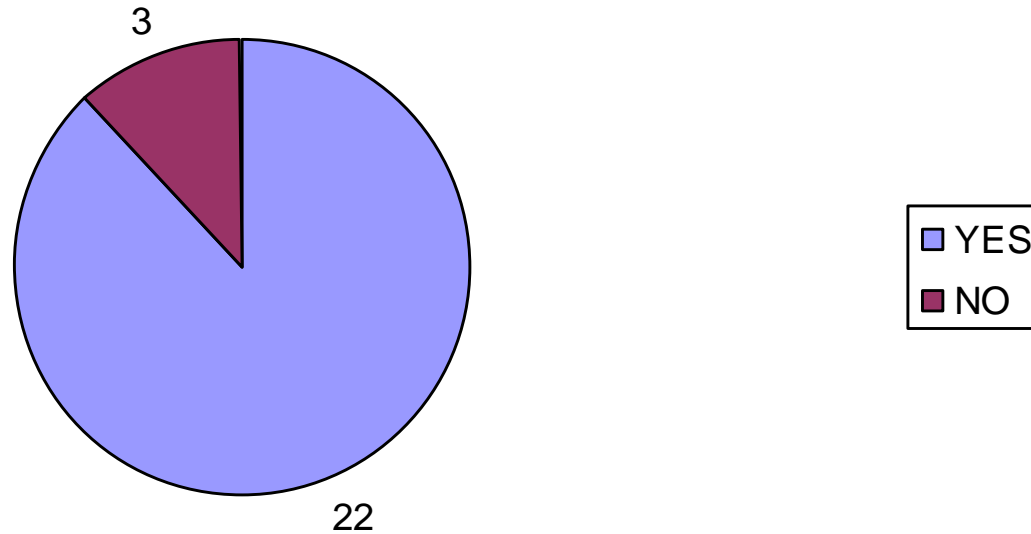


RMI Risk of Malignancy Index

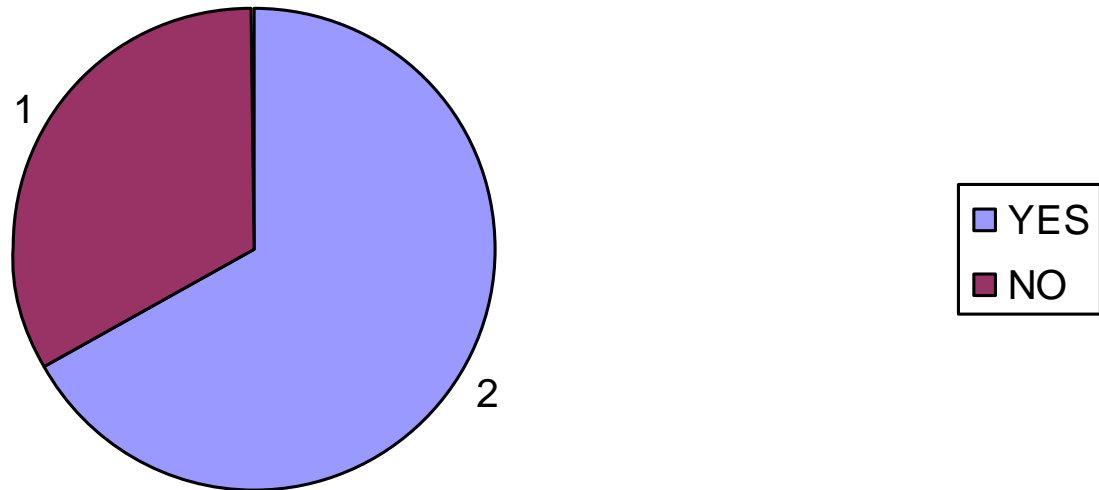
Question 16-Does your laboratory measure CA125 in the management of endometriosis?



Question 17a-Does your laboratory send HCG samples for monitoring hydatidiform mole to Imperial?

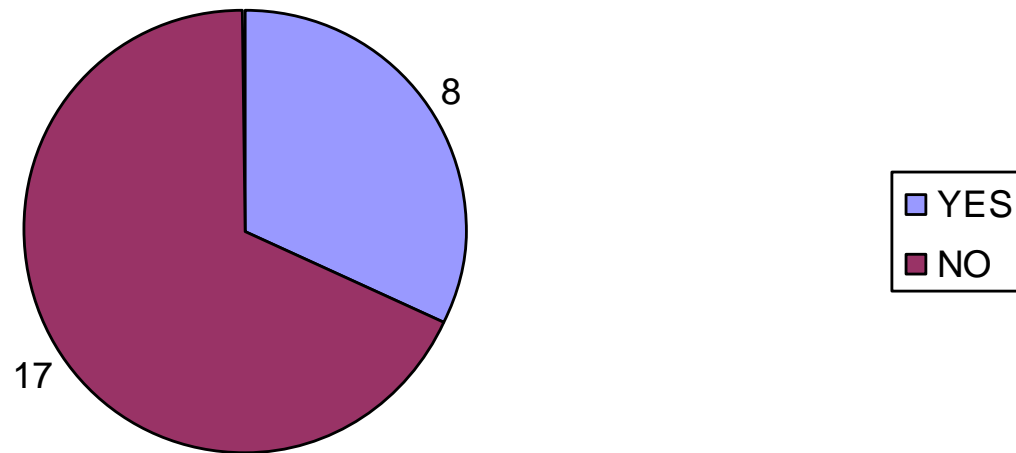


Question 17b-If no,do you monitor locally?



The laboratory responding no mentioned that these were sent directly without the involvement of the laboratory

Question 18-Does your laboratory offer free PSA?

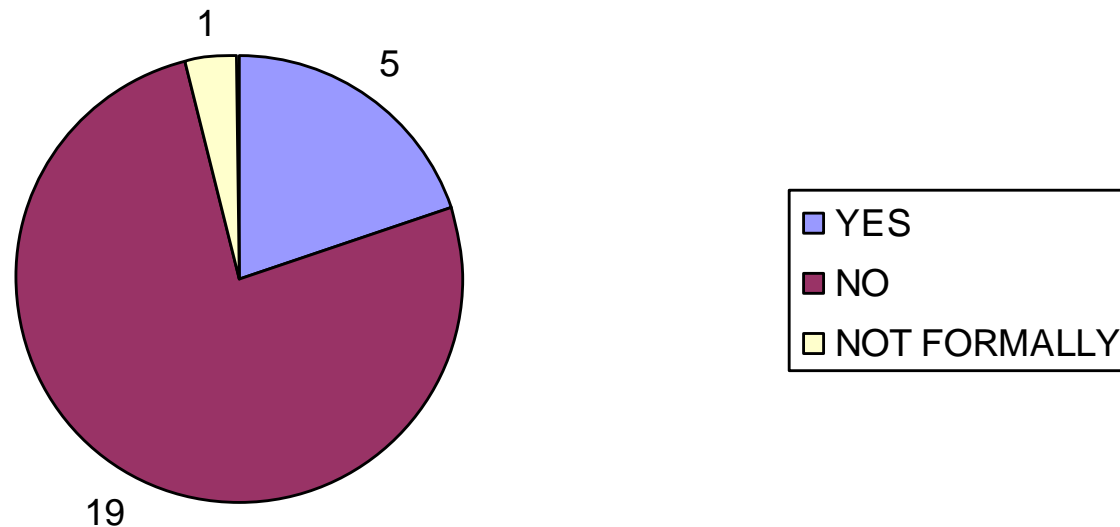


Two laboratories responding yes mentioned that this was sent away

Question 18 b-When free PSA is measured

- When requested by the Consultant Urologist-most given reason
- Differentiation of prostate cancer from BPH when the total PSA is between 2 and 10 ug/l
- When requested and when the total PSA is >4 ug/l
- When the total PSA is between 3 and 11 ug/l

Question 19-Does the laboratory issue recommendations when blood should be collected for PSA following procedures such as DRE etc?

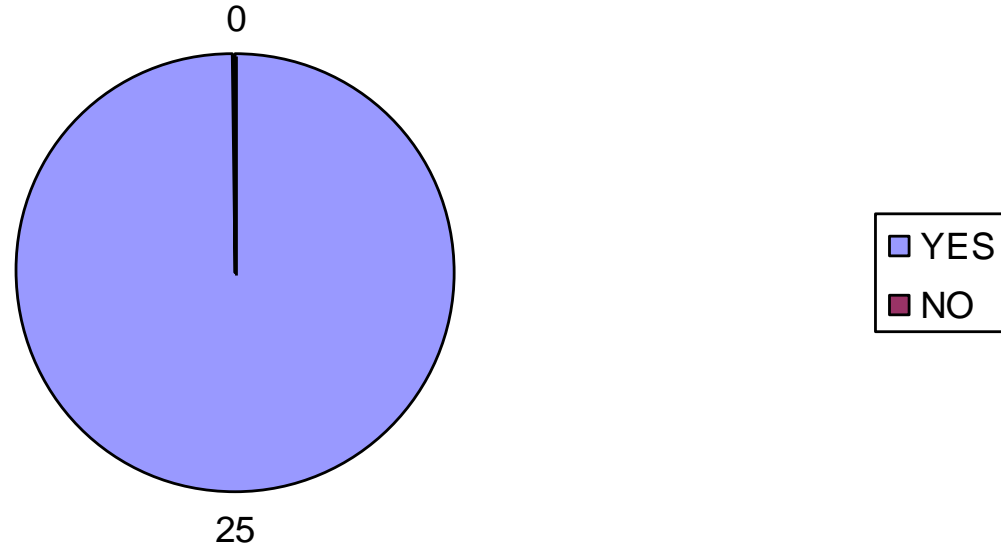


One laboratory responding no said they did not issue any official recommendations but if asked would advise at least 2 weeks

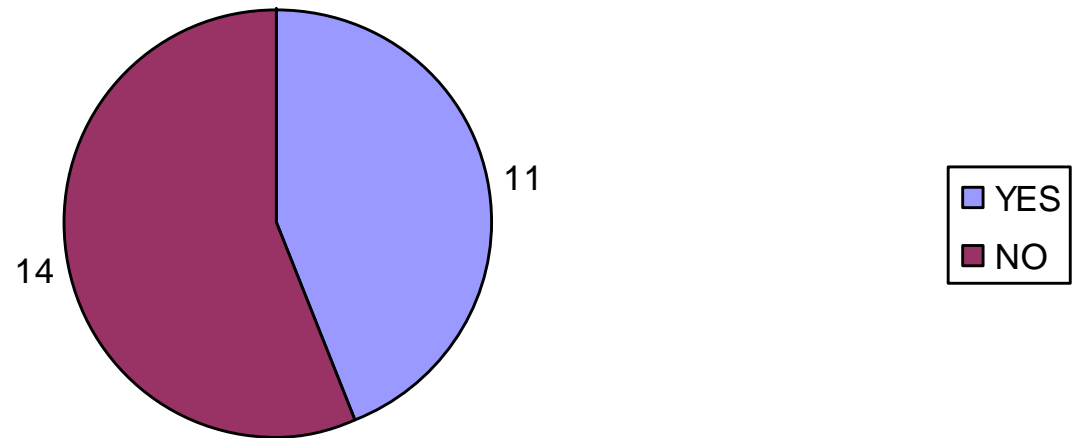
Question 19 b-Recommendations given

- Recommend collecting before the procedure.If prior collection not possible, recommend at least 3 days post DRE/ cystoscopy or 2 weeks post biopsy or surgery
- TUPR needle biopsy 6 weeks.DRE do prior procedure,intercourse 24 hours
- Bladder flow obstruction-after 1 week
- Blood should be collected prior to a DRE,If such an examination has taken place,then blood collection should be delayed for one week.Blood collection should be delayed for 48 hours after ejaculation,for at least six weeks if the subject has had a needle biopsy of the prostate gland or a transurethral resection of the prostate gland and should take place either before or delayed for one week after ultrasound or a rigid cystoscopy procedure and should take place prior to any period of sustained bicycle riding.

Question 20a -Does the laboratory report reference ranges for each tumour marker on the report?



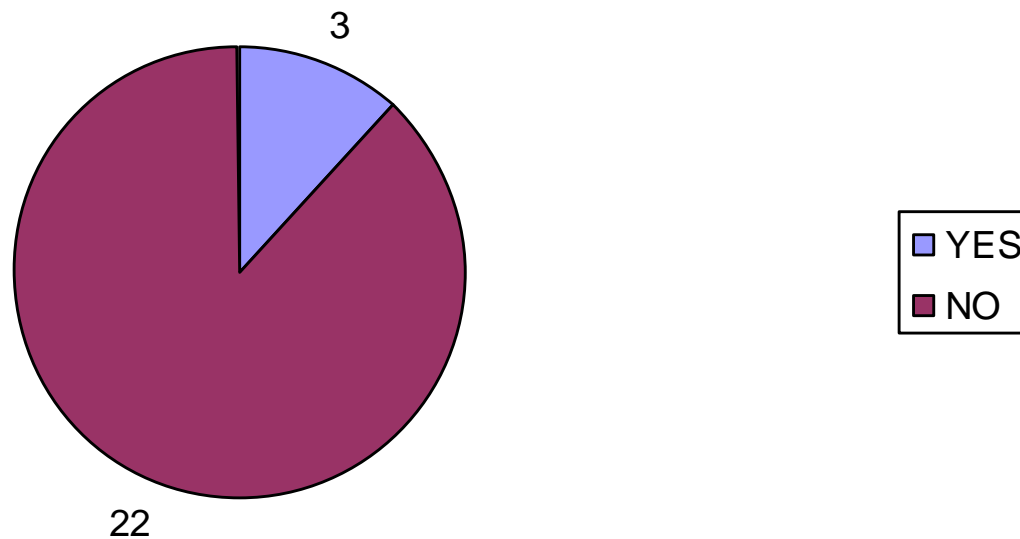
Question 20b-If yes,does your laboratory quote age-related ranges for PSA?



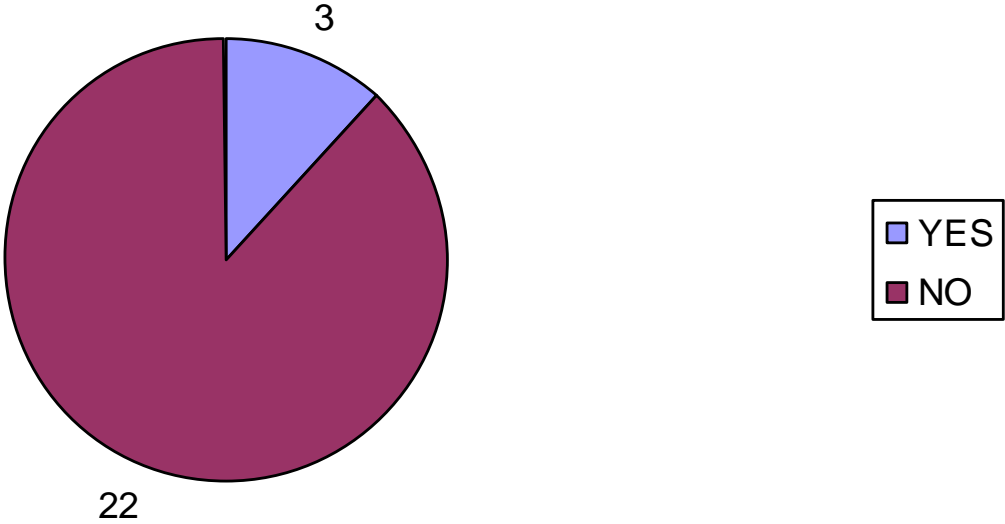
Question 20c-Age related ranges quoted for PSA

- <39 y <1.4,40-49y <2.0,50-59y <3.9,60-69 y <5.4 >70 y <6.2
- <50 y <2.5, 50-60 y <3.5,60-70 y <4.5,>70 y <5.5
- <40 y <1.4 40-50 y <2.0 50-60 y <3.1 >60 <4.1
- <49 y <2.5,50-59 y <3.5,60-69 y <4.5,70-79 y <6.5 ≠
- <49 y <2.5 49-59 y <3.5,59-69 y <4.5 >69 y <5.5
- <50 y <2.1 50-59 y <3.1 60-69 y <4.1 >70 y <4.9
- <49 y <2.5,50-59 y <3.5, 60-69 y <4.5 >70 y <5.5
- <44 y <2.4 45-49 y <2.8 50-54 y <3.3 55-59 y <3.8 60-64 y <4.5 65-69 y <5.3 >70 y <6.2
- <40 y <1.1 40-49 y <1.5 50-59 y <2.5 60-69 y <4.0 >70 y <4.9
- <49 y <2.5 <59 y <3.5 <69 y <4.5 <79y <6.5 y >79 y <7.5
- <60 y <3.0 <70 y <4.0 >70 y <5.0
- ≠ This laboratory quoted a different range for Afro Caribbean-<2.0,<4.0,<4.5 and <5.5 respectively

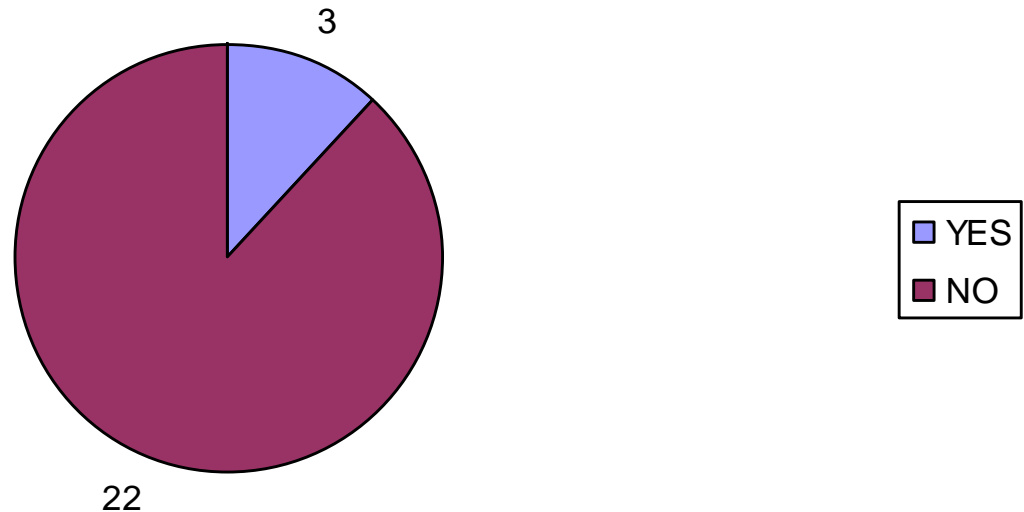
Question 20d-Does your laboratory comment on the report that reference ranges are not well defined and should be used for guidance purposes only?



Question 21-Does your laboratory state the method used on the report?

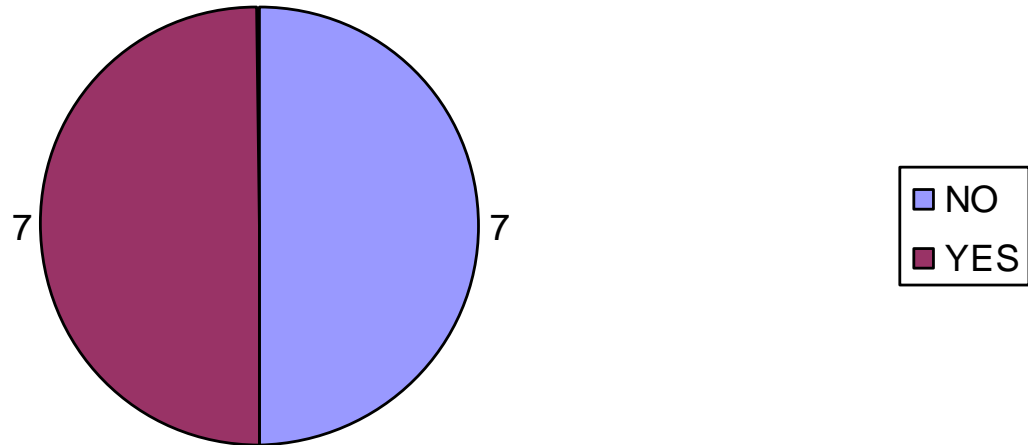


Question 22-Does your laboratory produce a cumulative report for tumour markers?

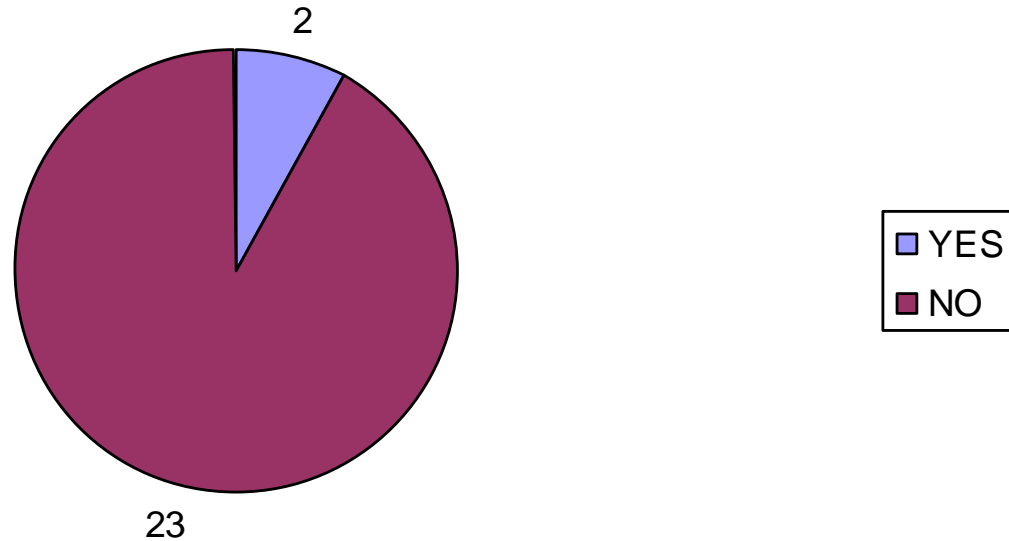


One laboratory reporting no mentioned that the electronic patient record has the ability to plot results over time

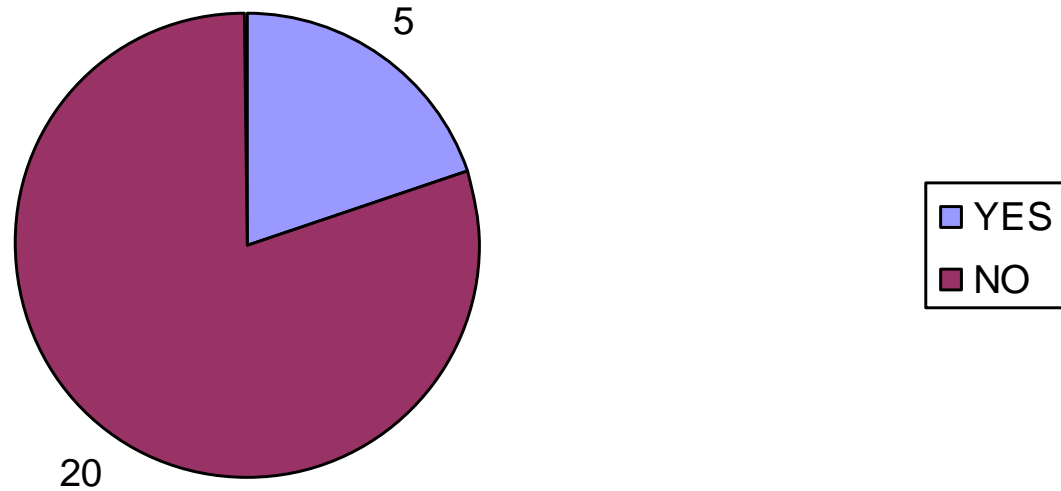
Question 22b-Are cumulative graphs from referral centres passed on to the requesting clinicians?



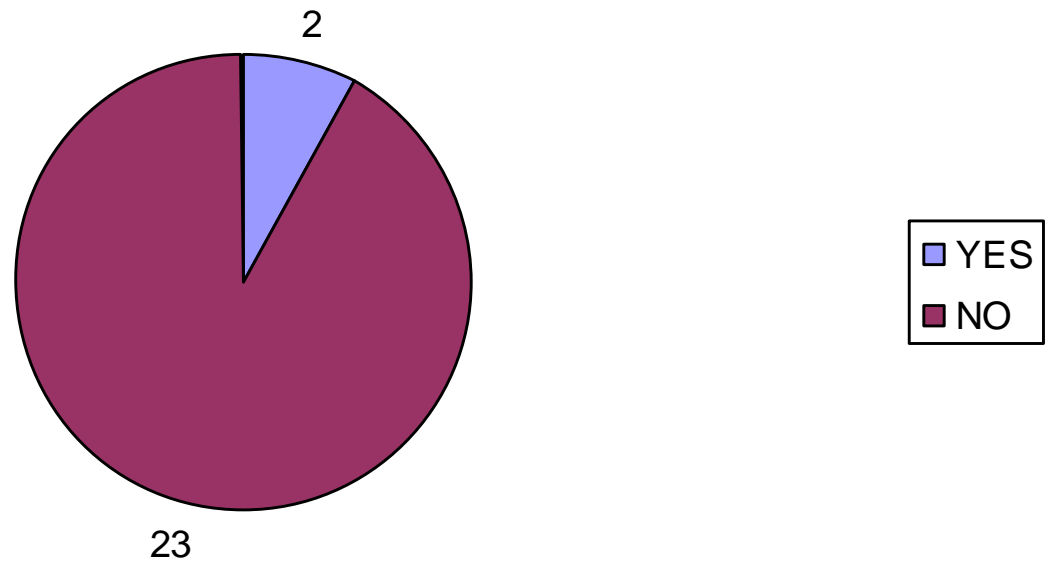
Question 23a-Does your laboratory comment on reports for oncology patients?



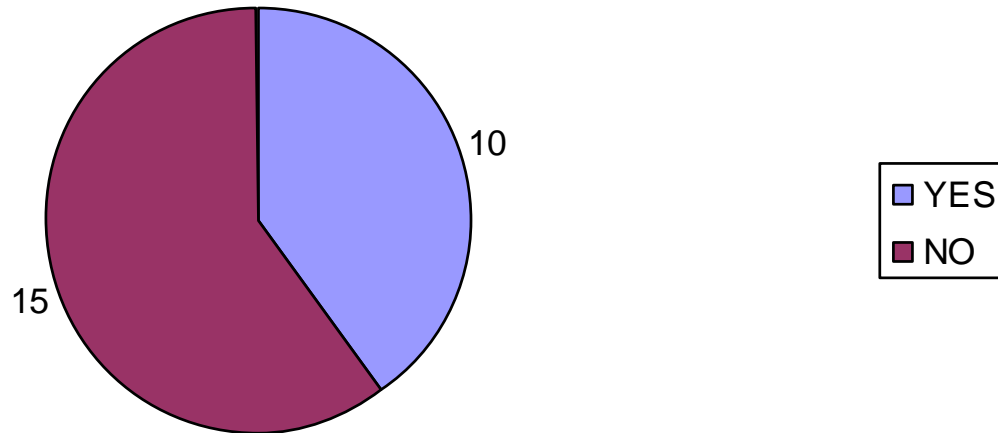
Question 23b-For medical/surgical patients?



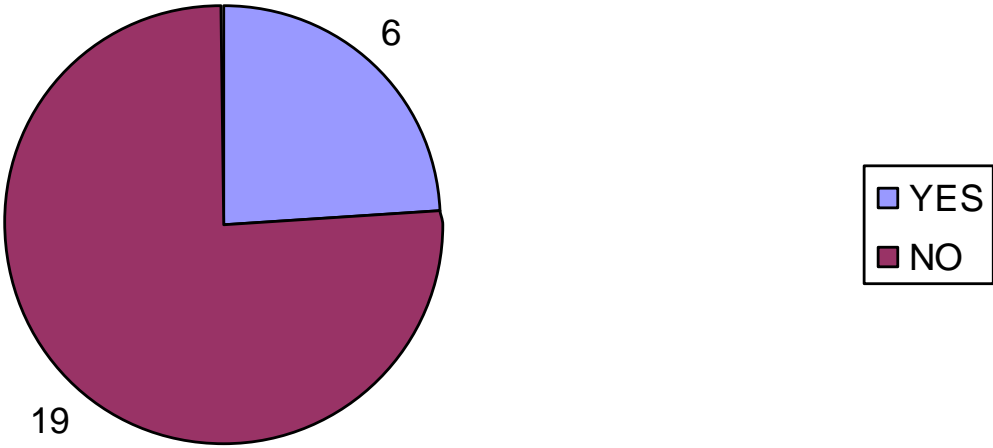
Question 23c-For gynaecology patients?



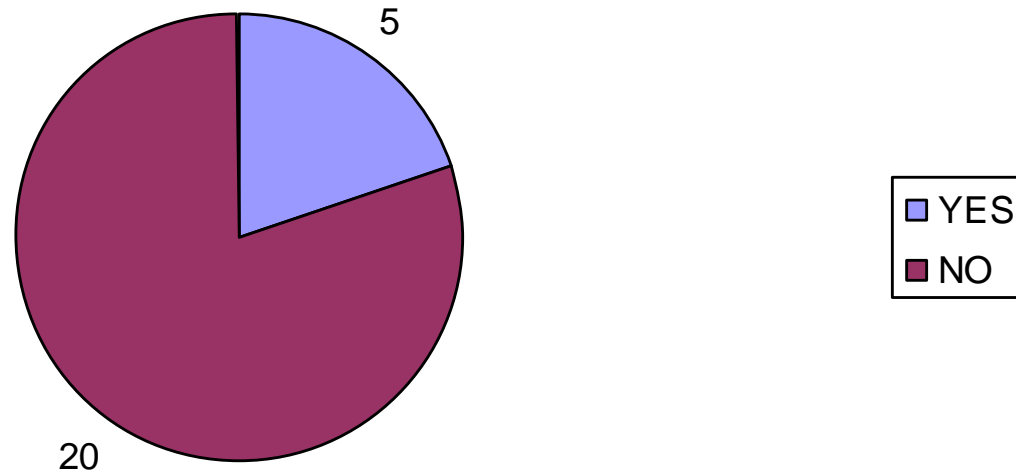
Question 23d-For GP patients?



Question 23e-For care of the elderly patients?



Question 23f-For gastroenterology patients?



Question 23-Type of comments made-1

- CA125-may be raised in pregnancy(<100 kU/l)menstruation(<100 kU/l),endometriosis,benign ovarian cysts,benign ascites,cirrhosis,renal failure,acute pancreatitis,peritonitis,pelvic inflammatory diseases,intra-abdomoinal cancers,advanced lung disease and breast cancer
- PSA-a range of 0.5-4.0 ug/l is considered to be normal although does not absolutely exclude a localised prostatic cancer.PSA is also raised in other conditions eg BPH,prostatitis,prostatic infarction,urinary tract infection,urethral catherisation,retention of urine,transurethral resection of the prostate(TURP) and prostate biopsy.A rise of >20%/year requires referral for further investigation
- PSA-A male with a PSA between 4 and 10 ng/ml has a 25% risk of prostate cancer with the risk increasing with an increasing PSA.Indications for a biopsy are a PSA>4 ng/ml and/or an abnormal feeling prostate gland.Higher PSA values are acceptable in elderly males.

Question 23-Type of comments made-2

- Use of tumour markers to screen for undiagnosed cancer is NOT recommended
- PSA-For moderately elevated results-Moderately elevated PSA,consistent with BPH or malignant neoplasm but exclude other causes eg: acute retention,infection
- PSA-Raised PSA?BPH,prostatitis or prostate cancer
- PSA-Due to poor specificity of total PSA,the<4 ug/l cut off is a guide to interpretation only.%free PSA measurement is recommended to help distinguish prostate cancer from BPH,particularly when the total PSA is in the range 2-10 ug/l.A % free PSA less or equal to 10% in a healthy male with a total PSA 4-10 ug/l increases the probability of biopsy positive prostate cancer approximately 3 fold

Question 23-Type of comments made-3

- General tumour markers-A rise/fall between the previous and current sample very rapid, half life/doubling time= x days. Please check primary sample tubes as sample sent is unlikely to belong to patient(Imperial)
- A rise/fall between previous sample and current sample has half life/doubling time= x days, reflecting....satisfactory response to treatment/therapy resistant disease(Imperial)
- A result significantly elevated. Please send a repeat sample to confirm(Imperial)
- Trophoblastic Disease and GCT tumour patient comments(Imperial)- If hydatidiform mole confirmed, please register.
- Please register for follow up. Forms already sent
- This result is consistent with a new pregnancy but does not exclude trophoblastic disease. Advised to see GP to be referred for an early scan to confirm/exclude pregnancy. Please keep us informed.

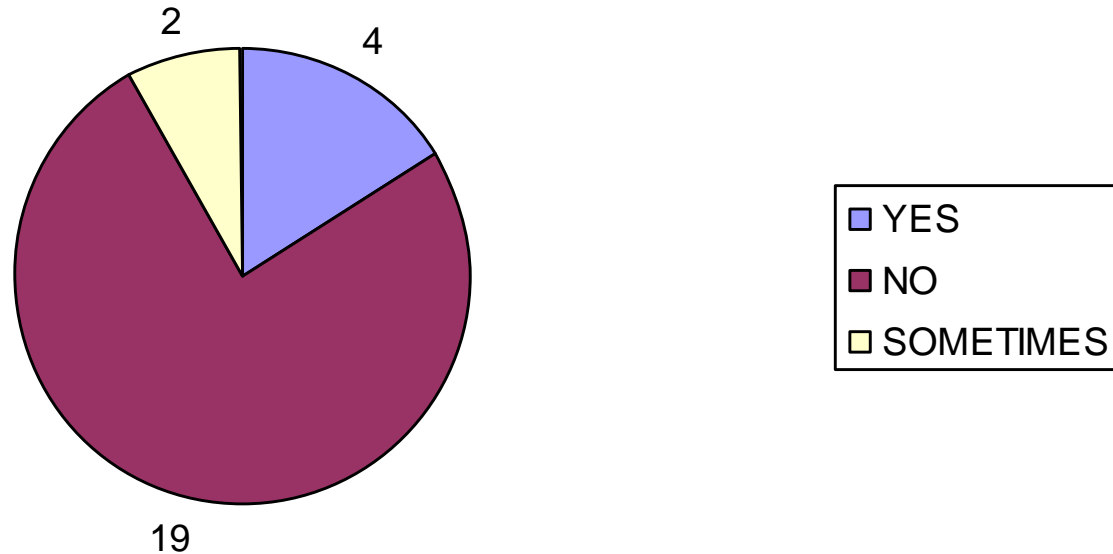
Question 23-Type of comments made-4

- Trophoblastic Disease and GCT tumour patient comments(Imperial)- In the absence of confirmation of pregnancy we are assuming all is well unless we hear to the contrary. Follow up has been discontinued until the pregnancy ends. We have asked her to contact us then.
- GCT follow up period has now been completed. No further requests will be issued from Charing Cross.
- Tumour marker levels rising. Close watch
- CA125-<35 IU/l does not rule out malignancy. Where diagnosis is uncertain, patient should be carefully monitored. Repeat the CA125 where symptoms persist or increase in frequency. Urgently refer if pelvic mass and/or ascites. See NICE guidelines-website given. CA125>35IU/L-ultrasound of the abdomen and pelvis recommended if not already performed. See NICE guidelines. Please note that CA125 may also be raised in benign conditions including PCOS and in non-ovarian pathologies

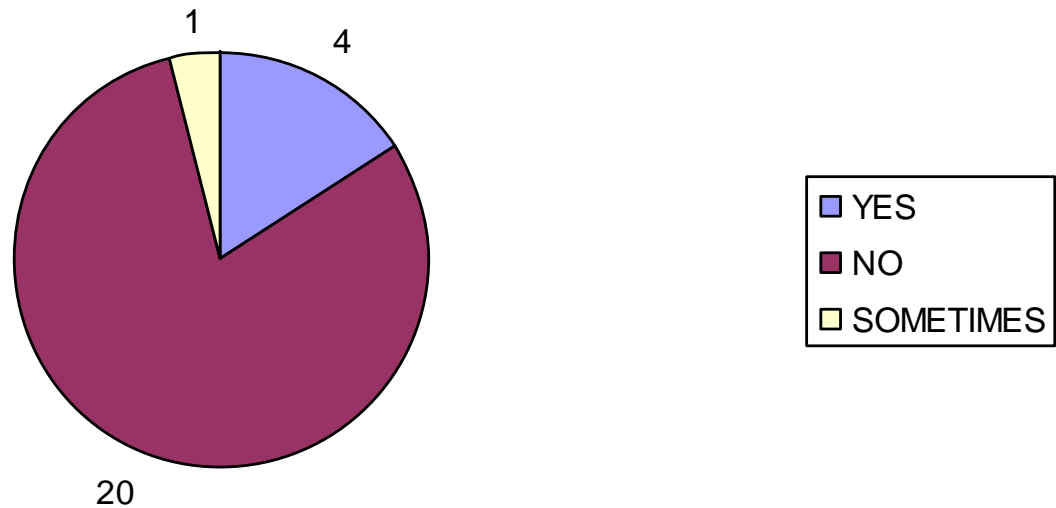
Question 23-Type of comments made-5

- PSA-Raised or rising PSA in an undiagnosed patient may be suggestive of malignancy(particularly if >10) but please note that PSA may also be markedly increased in UTI,BPH and post DRE.Please interpret in light of clinical history and refer for further investigation if indicated by NICE guidelines
- CA125-www.nice.org.uk/CG122 If symptoms suggest ovarian cancer and CA125 is 35 kIU/l or more,refer for ultrasound(NICE 2011) .Disease not excluded if <35 kIU/l.Assess clinically
- CA125-CA125 is not a sensitive test for ovarian cancer and may be normal in 50% of patients with stage 1 disease.A “normal” result does not exclude ovarian malignancy and any suspicion of ovarian malignancy should be followed up by ultrasound and pelvic examination
- CA125-CA125 has neither the sensitivity or specificity to be used alone for diagnosis of ovarian malignancy

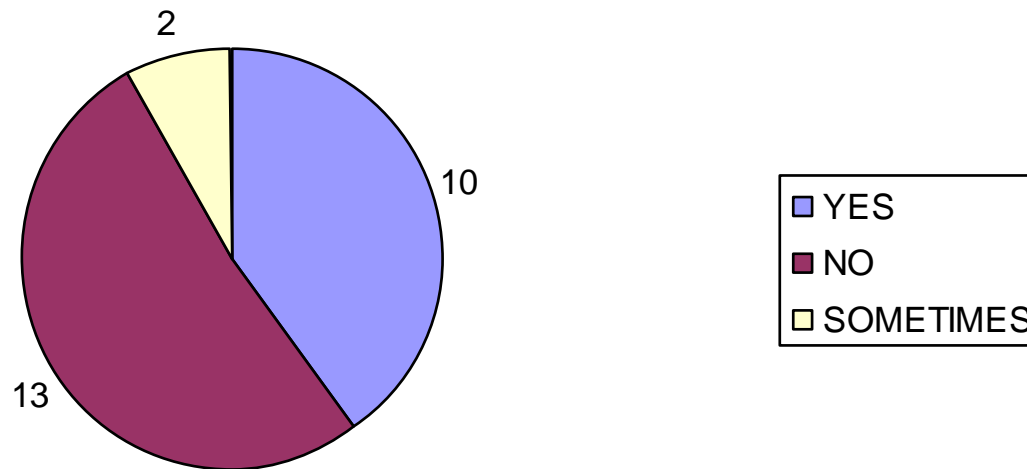
Question 24-Does your laboratory comment on the report regarding specificity of tumour markers?



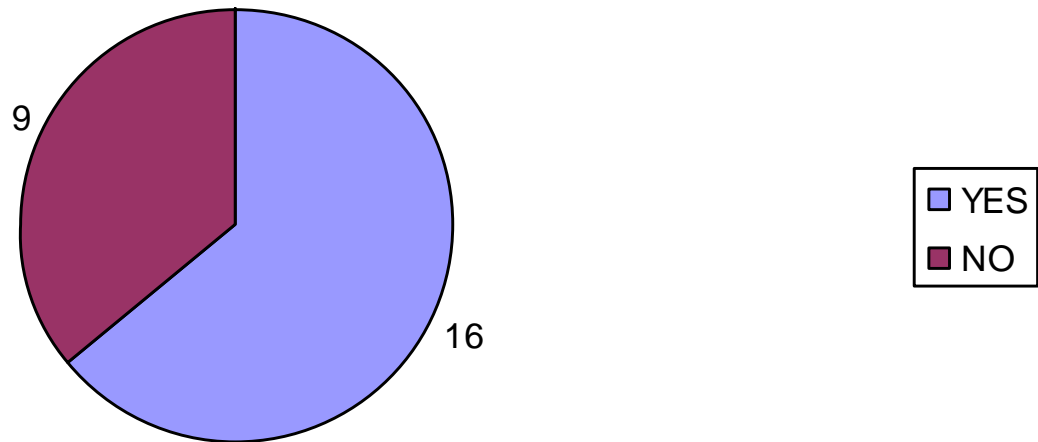
Question 25-Does your laboratory comment on the report that tumour markers are not recommended in those with vague symptoms?



Question 26-Does your laboratory comment on the report that tumour markers can be elevated in non-malignant conditions?



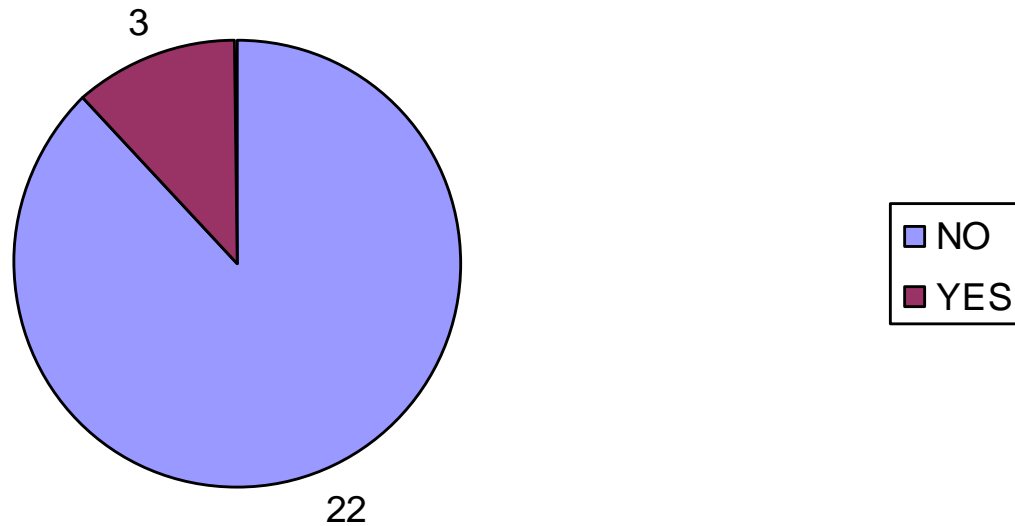
Question 27-Does the laboratory ever telephone tumour marker results?



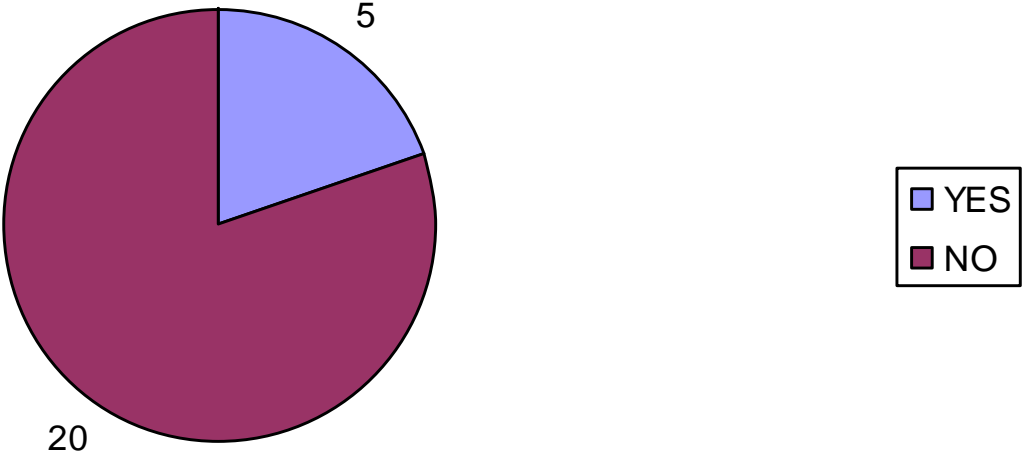
When tumour marker results are telephoned

- PSA>40 on the first occasion
- Very high results in patients not previously known to have cancer, mainly to GPs
- Pronounced increase
- If unexpected change after ensuring analytically correct
- Very high AFP in new patient eg: jaundice? cause
- Where indication of new diagnosis or relapse is indicated by result
- HCG results for recently admitted GTN patient
- At the clinical authorisers' discretion - depending on clinical details on the form and location of patient
- Unexpected raised PSA (very high) or raised AFP to ensure has reached the clinician
- Grossly elevated PSA or AFP
- First result when raised or if tumour marker has rapidly increased since last measurement
- Unexpected elevated results
- Very high result, especially when it may not be expected. Large increase in result for outpatients who are being monitored
- For fast track patients on chemotherapy
- At the discretion of the Duty Biochemist - high unexpected result from primary care or a large increase in someone being routinely monitored
- Very high result and a significant change in result

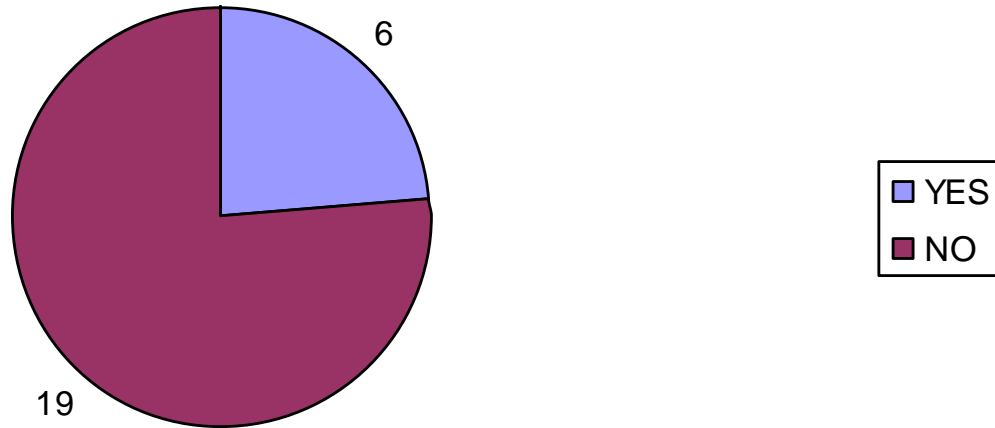
Question 28a-Has anyone from Biochemistry given a talk on the appropriate use of tumour markers to Oncology?



Question 28b-To non- oncology clinical staff?



Question 28c-To GPs?



Summary of the audit findings-1

- Most laboratories quote the kit insert as the source of their reference range
- Few laboratories have guidelines for tumour markers
- Few laboratories have carried out an audit of their tumour marker service
- Most laboratories perform some form of vetting of their tumour marker requests
- Most of the tumour markers are used for monitoring and additionally for diagnosis in carcinoma of the liver and carcinoma of the ovary
- Few laboratories measure tumour markers in fluids and where offered state that these matrices are not validated on their analysers
- Few laboratories offer free PSA with less than half quoting age-related ranges for total PSA

Summary of the audit findings-2

- All laboratories quote reference ranges for the tumour markers on their laboratory reports but few state that these reference ranges are not well defined and should be used as guidance only, the method used in their laboratory, the specificity of the tumour marker or that tumour markers are not recommended in those with vague symptoms.
- The tumour markers where most comments are made on the laboratory reports are PSA and CA125.
- Few laboratories mentioned that they have given talks to their oncologists, non-oncology clinical staff or GPs where the appropriateness of requesting tumour markers could be emphasised
- Most laboratories are aware of the NICE guidelines for ovarian cancer published in April 2011 and anticipate an increase in requests for CA125.



*National Institute for
Health and Clinical Excellence*

Quick reference guide

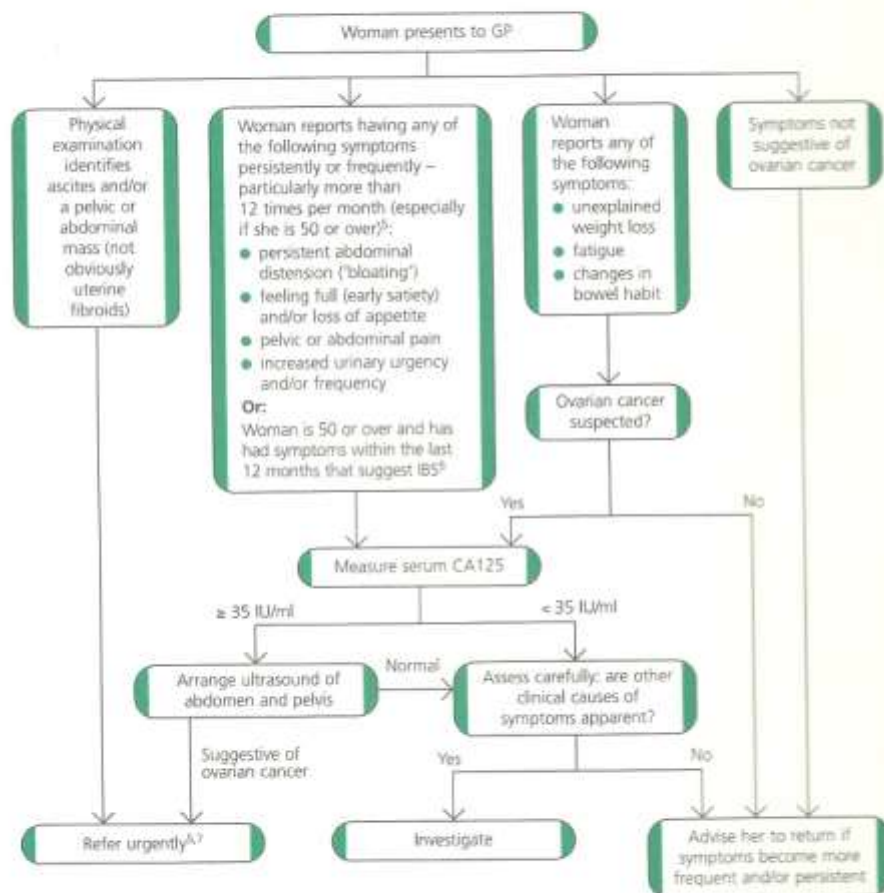
Issue date: April 2011

Ovarian cancer

The recognition and initial management of ovarian cancer



Detection in primary care



⁵ See also 'Referral guidelines for suspected cancer' (NICE clinical guideline 27; available at www.nice.org.uk/guidance/CG27) for recommendations about the support and information needs of people with suspected cancer.

⁶ See 'Irritable bowel syndrome in adults' (NICE clinical guideline 61; available at www.nice.org.uk/guidance/CG61). Irritable bowel syndrome (IBS) rarely presents for the first time in women of this age.

⁷ An urgent referral means that the woman is referred to a gynaecological cancer service within the national target in England and Wales for referral for suspected cancer, which is currently 2 weeks.

Aknowledgements-1

- University College Hospital
- Kings College Hospital
- Whittington Hospital
- Royal Surrey County Hospital
- Princess Alexandra Hospital
- Queen Elizabeth 2 Hospital
- Chertsey Hospital
- Queen's Hospital
- Charing Cross Hospital
- Newham Hospital
- St Mary's Hospital
- Southend Hospital
- St Thomas's Hospital

Acknowledgments-2

- Barts and the Royal London Hospital
- North Middlesex University Hospital
- Barnet and Chase Farm Hospitals
- St George's Hospital
- Wexham Park Hospital
- Bedford General Hospital
- Eastbourne Hospital
- Luton and Dunstable Hospital
- Royal Free Hospital
- Croydon Health University Hospital
- Hillingdon Hospital
- West Hertfordshire Hospital Trust

One laboratory's comment

- Our laboratory generally offers tumour markers to anyone who requests them. This is a matter of disagreement between the biochemists. The Consultant Biochemist feels it is up to the clinicians to decide what tests they require but the Senior Biochemist feels we should be more involved in giving advice and vetting tests. Obviously for tumour marker requests coming from the Regional Cancer Centre, even the Senior Biochemist trusts the clinician's judgement!