The Association for Clinical Biochemistry and Laboratory Medicine

Better Science, Better Testing, Better Care

A regional audit of pancreatic enzyme testing

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ACB Scotland National Autumn Meeting
Norton House Hotel, Edinburgh
10th November 2017

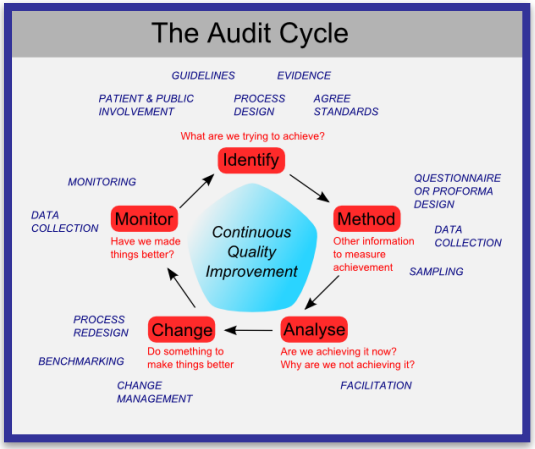
The Association for Clinical Biochemistry & Laboratory Medicine
Scotland Audit Group

The Association for Clinical Biochemistry & Laboratory Medicine

Scotland Audit Group

- Resurrected in 2015
- 12 local reps
- Meet quarterly
- Goal: 2-3 Regional audits/yr
- Links with NCBAG, SCBMDN
- Suggestions welcome!

Health Board	Local audit rep
NHS Greater Glasgow and Clyde	Jane McNeilly
NHS Ayrshire and Arran	Christopher Pitt, Suzanne MacKenzie
NHS Dumfries and Galloway	Julia Anderson
NHS Lanarkshire	Jacqueline McGuire
NHS Lothian	Jonathan Malo
NHS Borders	John O'Donnell
NHS Forth Valley	Mark Redpath
NHS Tayside	Rebecca McCann
NHS Fife	Heather Holmes
NHS Grampian	Fiona Brandie, Emma Dewar
NHS Highland	Heidi Mendoza
NHS Shetland	C/o Kevin Deans
NHS Orkney	C/o Kevin Deans
NHS Western Isles	C/o Ian Gilbert



Background

- Clinical features, together with elevation of pancreatic enzymes, are the key diagnostic indicators of acute pancreatitis (AP).
- Current British Society of Gastroenterology guidelines (2005) for the management of AP suggests a preference towards the measurement of lipase levels (Grade A, Level 1 evidence).
- Amylase is the most commonly measured enzyme in the UK due to the availability of cheap, easily automated methods.
- Main drawback of amylase is the lack of specificity for the pancreas.

Background

- Non-specificity of amylase can lead to diagnostic confusion.

Table 1. Some possible causes of hyperamylasaemia.	
Certain pancreatic disorders Acute pancreatitis Pancreatic pseudocyst Pancreatic carcinoma	Salivary gland disorders Mumps Salivary gland tumours, calculi or trauma Sjögren's syndrome After injection of contrast medium into salivary ducts for sialography Anorexia nervosa
Other abdominal conditions Acute cholecystitis or gallstones Intestinal obstruction or infarction Perforated peptic ulcer Abdominal trauma Toxic shock syndrome Ruptured ectopic pregnancy Ureteric calculi After ERCP	Miscellaneous causes Acute or chronic kidney disease Drugs, e.g. morphine, propofol, ephedrine, terbinafine, paracetamol overdose Acute myocardial infarction Diabetic ketoacidosis Glycogen storage disease type 1
Associated with malignant disease, including ectopic secretion	Macroamylasaemia

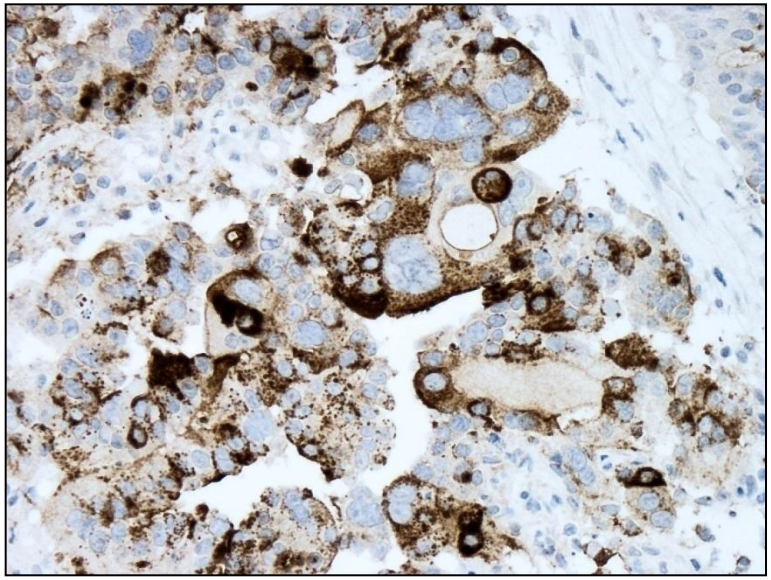
Crook M. *Ann Clin Biochem* 2013. 51(1) 5-7

Case

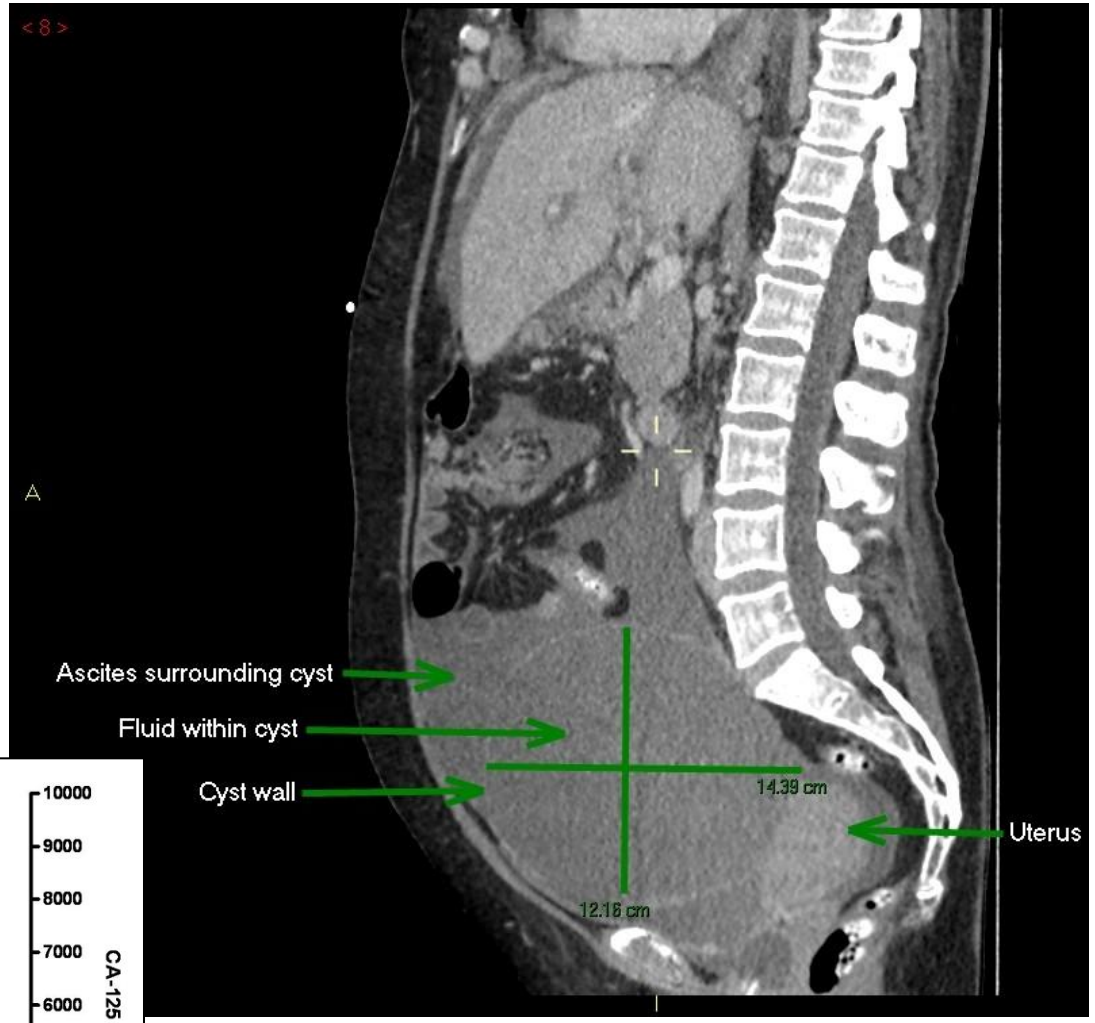
- Mrs VB, 56 years
- PC: Abdo distension, lower abdo discomfort
- HPC: Weight gain despite reduced appetite
- 3/12 history leg swelling due to persistent DVT (LMW heparin)
- No other medications
- No significant family history
- Ix: Amylase: 3163 U/L (RR <100)
- CT: “No peripancreatic stranding or pancreatic oedema to confirm pancreatitis”

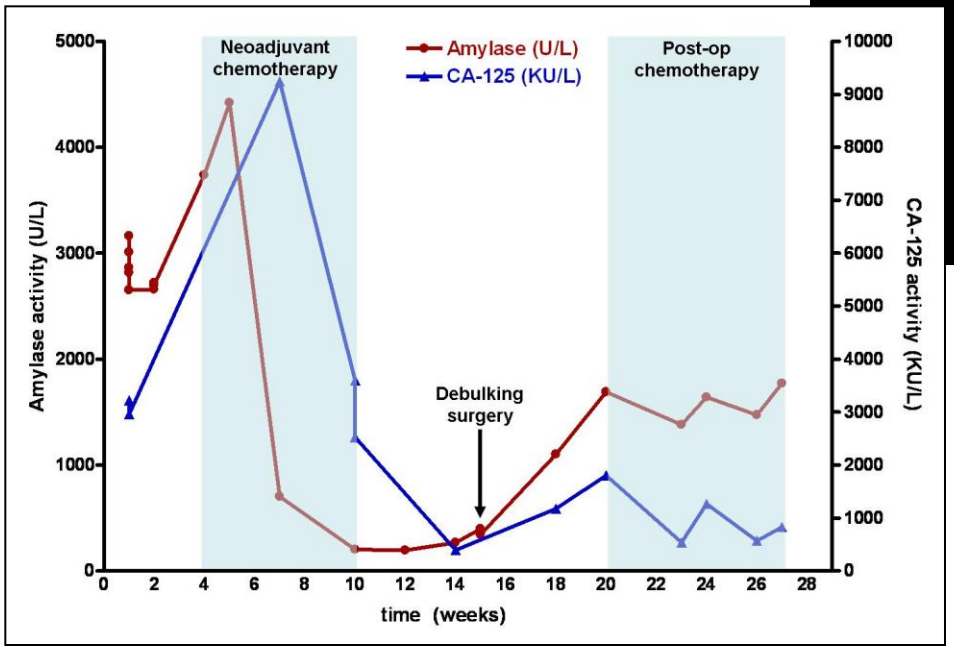
Case

- Further investigations:
- ?Macroamylase (Ig-bound)
  - Urine amylase: 28,436 U/L
  - Amylase:creatinine clearance ratio (ACCR): 4.5%
- Amylase isoenzymes (King's College Hospital)
  - Total amylase: 3076 IU/L (RR <100)
  - Pancreatic: 145 IU/L (RR <50)
  - Salivary: 2931 IU/L (RR <50)
- CA-125: 3216 KU/L (RR 0-35)



High grade serous carcinoma of probable ovarian origin (FIGO IIIB)





Logie JJ, et al. *BMJ Case Rep* 2015. doi:10.1136/bcr-2015-209780

Background

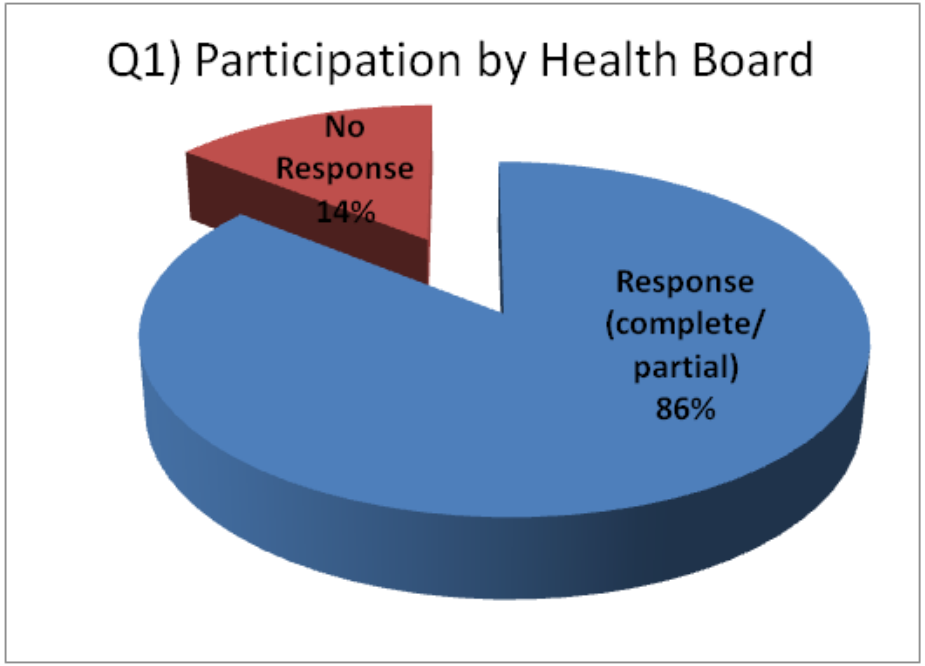
- Currently, there are no standards or guidance for pancreatic enzyme testing in Biochemistry laboratories across Scotland

Methods

- SurveyMonkey®
- 9 questions relating to:
  - Pre-analytical (order sets, clinical guidance)
  - Analytical (methods, workload ref ranges, TAT, costs, EQA) - local and send away
  - Post-analytical (interpretive comments, flags, cutoffs)
- Distributed 31st March 2016
- Closed 4th May 2016
- Link sent to Clinical Lead/HoD for the 14 Regional Health Boards plus local audit reps
- Data analysis in Microsoft® Excel®

Respondent information

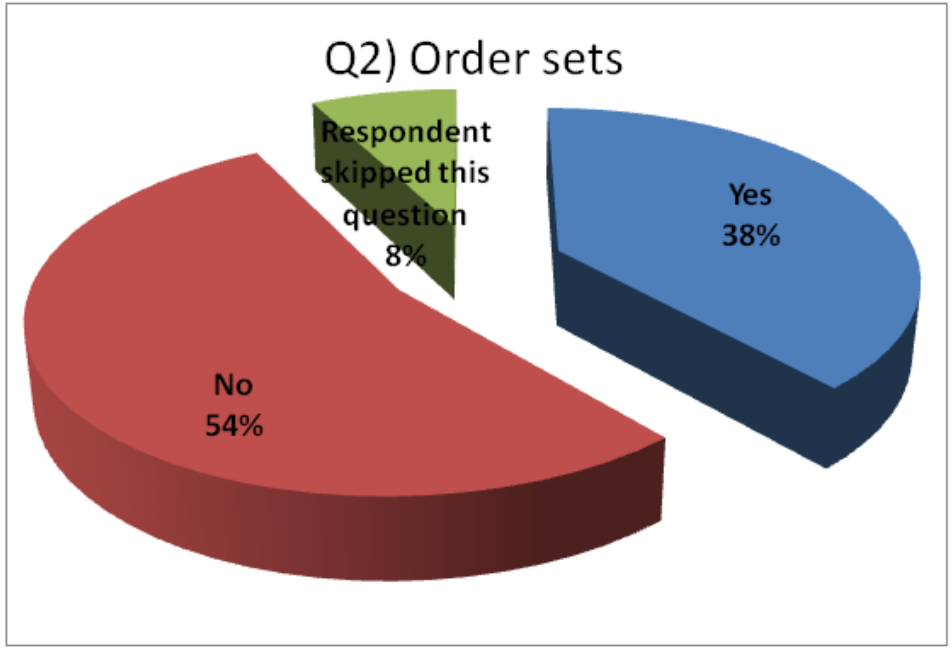
Q1: Please state the name of your hospital.



- 13 responses from 12/14 Health Boards ☺

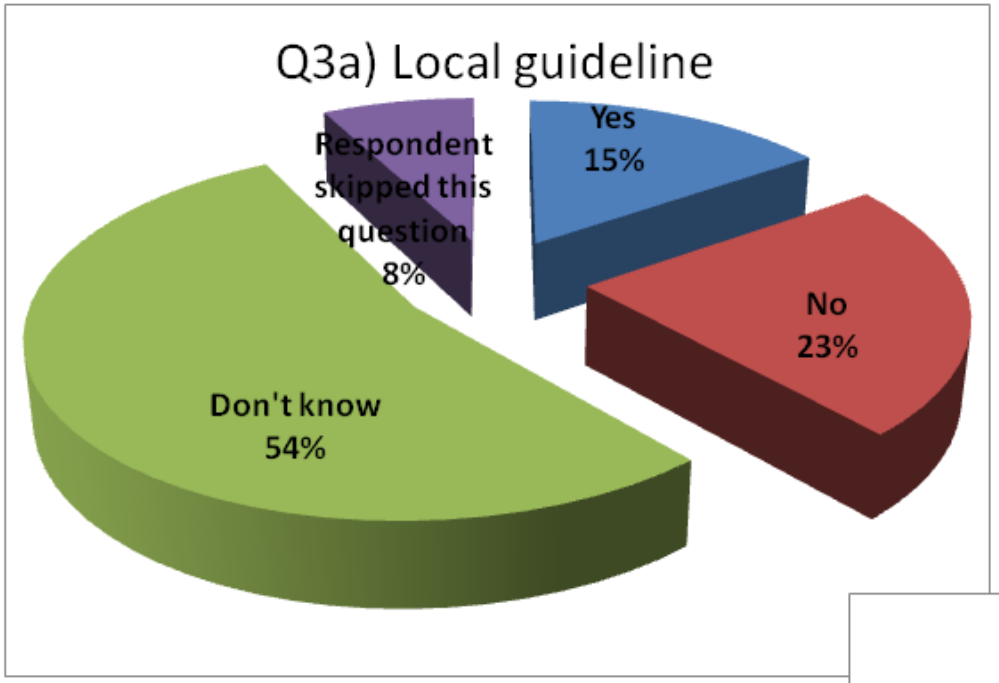
Pre-analytical

Q2: Does your laboratory include tests for acute pancreatitis in symptom/disease-specific order sets (e.g. abdominal pain or ?pancreatitis)?

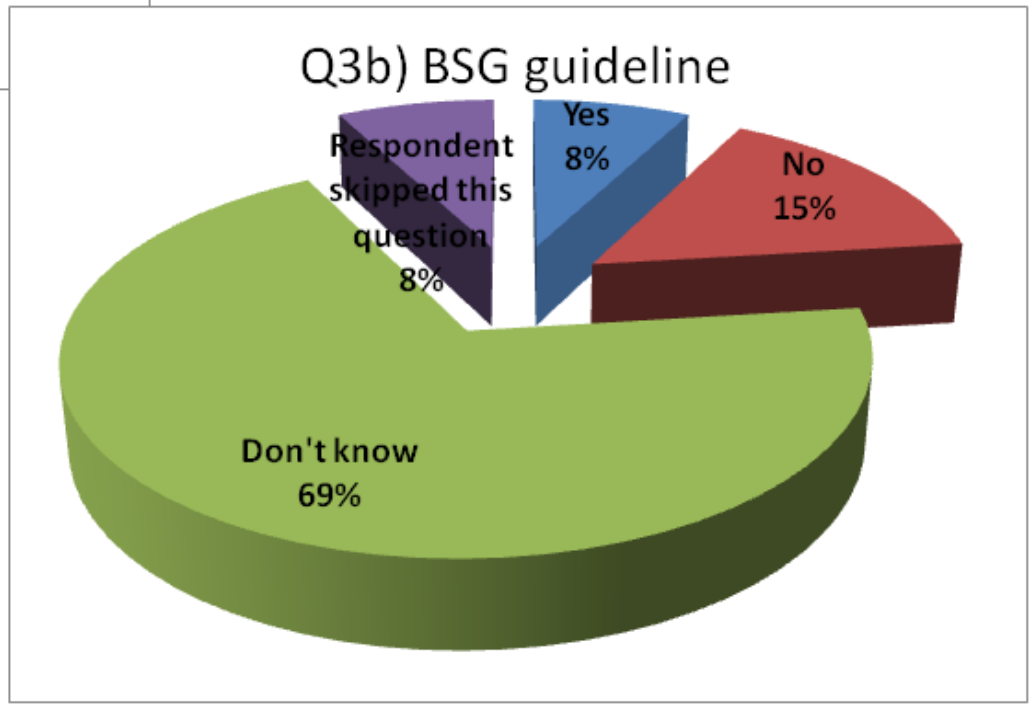


Q3: Are you aware of any criteria or guidelines used in your hospital for test requesting in cases of suspected acute pancreatitis?

a) Locally-developed guidelines



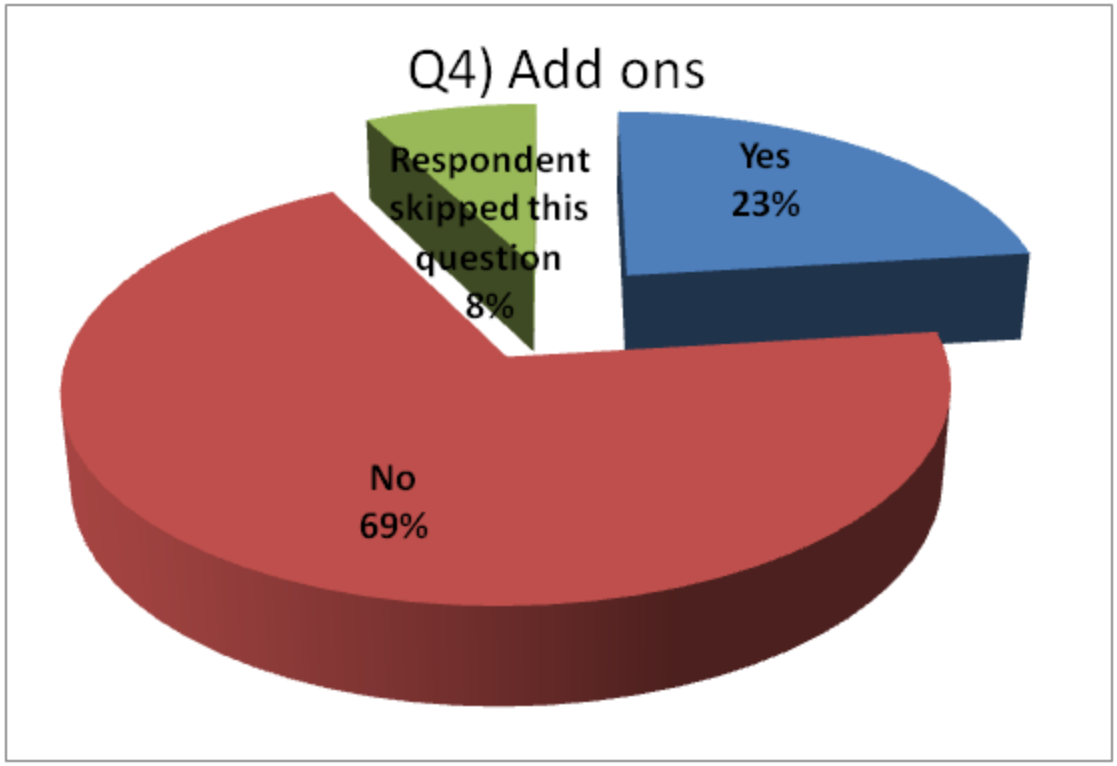
b) British Society of Gastroenterology guidelines, 2005



c) Other (please specify):

- One Health Board has a local guideline based on the British guidelines.

Q4: If your laboratory provides total amylase as a front-line test, do you add on lipase/amylase isoenzymes if total amylase is elevated (e.g. by LIMS reflex rules or DB intervention)?
Please provide relevant details

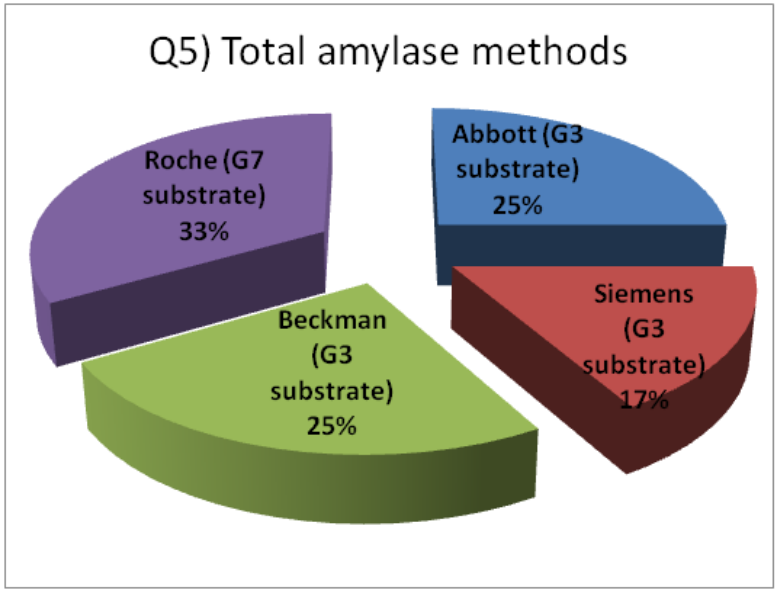


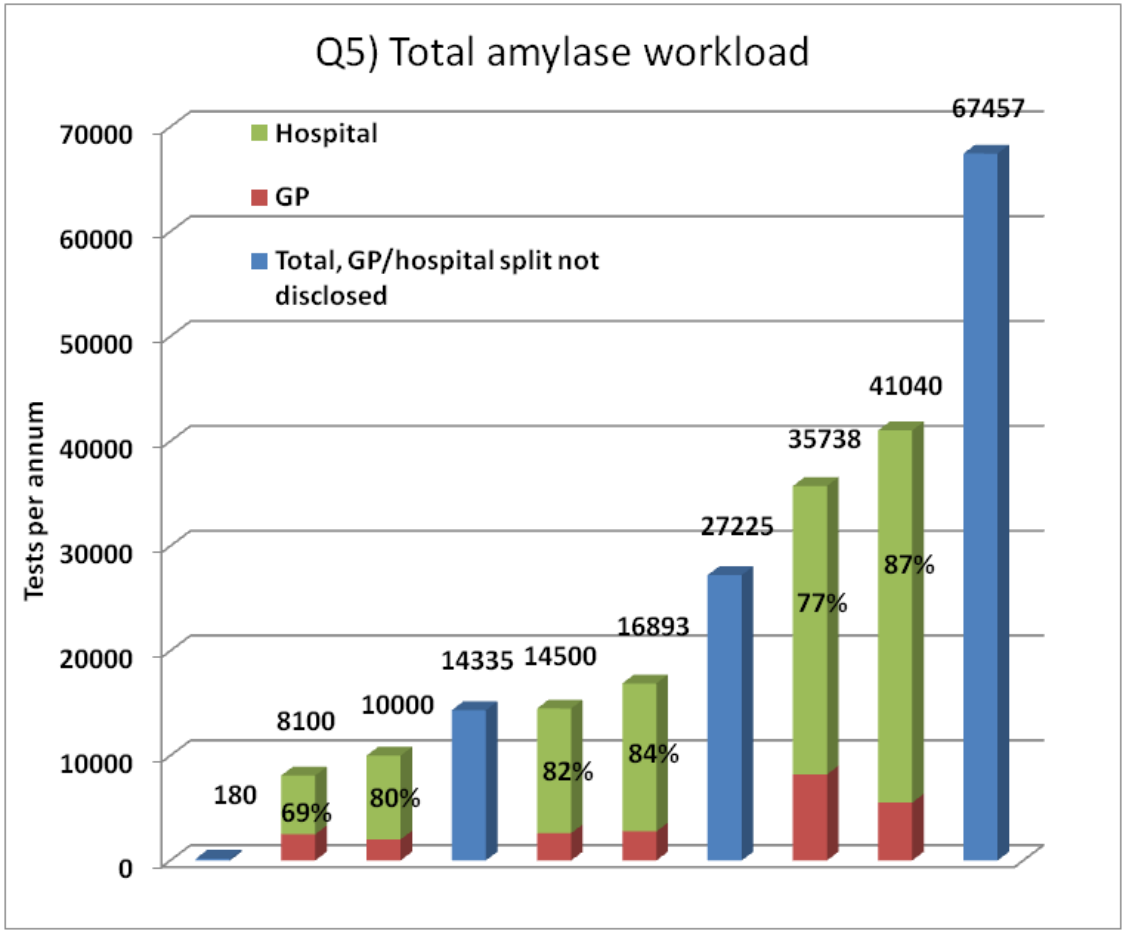
- Of those that add on other tests, this is done by the Duty Biochemist, and in some cases, the requesting clinician.

Analytical: Relating to tests provided locally (within your hospital)

Q5: Please provide the following details (for tests performed in house) :a) Method, b) Approximate workload (GP/hospital), Quoted TAT, d) Cost, e) Ref range/alert limits including source, f) EQA participation.

Total amylase (serum/plasma)





Analytical: Relating to tests provided locally (within your hospital)

Q5: Please provide the following details (for tests performed in house): a) Method, b) Approximate workload (GP/hospital), Quoted TAT, d) Cost, e) Ref range/alert limits including source, f) EQA participation.

Total amylase (serum/plasma)

Turnaround time

- <1 hour for emergency (A+E) requests, *n*=3
- <4 hours, *n*=2
- Same day, *n*=2
- <24 hours for non-emergency requests, *n*=3

Cost

- Respondents quoted a wide range of costs per test including: 15p, 19p, 89p, £2.00 and £4.80.

EQA participation

- UKNEQAS Clinical Chemistry scheme which includes amylase (*n*=9).

Reference ranges

- <100 U/L (*n*=7)
- <90 U/L (*n*=2)
- <85 U/L (*n*=1)
- One respondent quoted separate age-related ranges (<1 year 5-70 U/L, >1 year <100 U/L).
- The source of these was largely unknown however a few respondents disclosed these originated from a local study, or based on the West of Scotland Consensus Study (2007), or possibly from Tietz textbook.

Alert limits

- >2XURL (*n*=1)
- >3XURL (phone, *n*=1)
- >4XURL (phone *n*=1)
- >5XURL (*n*=4)
- Three respondents who declared alert limits stated these were based on RCPath guidance for telephoning abnormal results.

Pancreatic-specific amylase (serum/plasma)

- No laboratories perform this test in house.

Macro-amylase (serum/plasma)

- No laboratories perform this test in house.

Analytical: Relating to tests provided locally (within your hospital)

Q5: Please provide the following details (for tests performed in house): a) Method, b) Approximate workload (GP/hospital), Quoted TAT, d) Cost, e) Ref range/alert limits including source, f) EQA participation.

Lipase (serum/plasma)

Method	*Workload*	*Turnaround time*	*Cost*	*Ref range/ alert limit*	*EQA*
Quinine Dye	71/month, all inpatients	2 days	Not disclosed	8-78 U/L manufacturer range	Not disclosed

Urine tests (e.g. amylase, lipase)

Method

- The same method is used for urine amylase as serum amylase, in all laboratories that responded (*n*=8).

Turnaround time

- <1 hour for urgent requests (*n*=1)
- <3 hours (*n*=1)
- <4 hours (*n*=1)
- Same day (*n*=1)
- <24 hours (*n*=3)
- <72 hours (*n*=1)

Cost

- Respondents quoted a wide range of costs per test including: 15p, 19p, 89p and £2.00.

Workload

- The average workload is 91 (SD 64) tests per annum (*n*=8).
- Only a very small proportion (mean 6%) of these requests originate from primary care (*n*=2).

Reference ranges

- <100 U/L (*n*=1)
- 20-460 U/L (*n*=1)
- 120-648 U/24 hrs (*n*=1)
- <17 U/hr (*n*=1)
- <460 U/L (*n*=1)
- <600 U/L (*n*=2)
- <85 U/L (*n*=1).
- The source of these was largely unknown however one respondent disclosed this was based on local consensus.

EQA participation

- UKNEQAS scheme (*n*=3), RIQAS scheme (*n*=1), No EQA scheme (*n*=2).

Analytical: Relating to tests provided locally (within your hospital)

Q5: Please provide the following details (for tests performed in house): a) Method, b) Approximate workload (GP/hospital), Quoted TAT, d) Cost, e) Ref range/alert limits including source, f) EQA participation.

Fluid tests (amylase)

Method

- The same method is used for fluid amylase as serum amylase, in all laboratories that responded (*n*=7).

Turnaround time

- <1 hour for urgent requests (*n*=1)
- <3 hours (*n*=1)
- Same day (*n*=1)
- <24 hours (*n*=1)

Cost

- Respondents quoted a wide range of costs per test including: 19p, 89p and £2.00.

Workload

- The average workload is 278 (SD 206) tests per annum (*n*=8).
- Only a small fraction (~6%) of these requests originate from primary care (*n*=2).

Reference ranges

- No reference ranges or alert limits were disclosed.

EQA participation

- UKNEQAS scheme (*n*=1)
- No EQA scheme (*n*=4)

Other (e.g. amylase isoenzyme fractionation, macro-lipase)

- No laboratories provided details of any other relevant tests available in house.

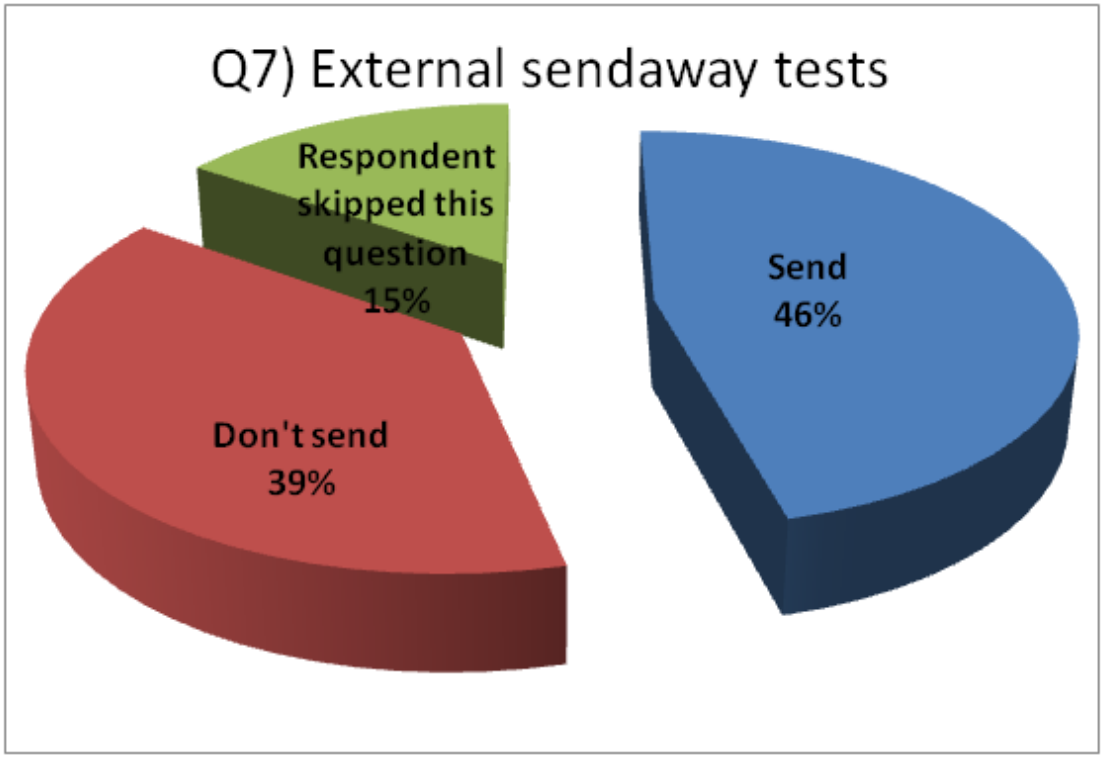
Analytical: Relating to send-away tests (within your Health Board)

Q6: Please provide details of tests sent to other laboratories within your health board (test, laboratory, method, approximate numbers, TAT).

- One hospital processed lipase which is available to other local hospitals within the same Health Board.

Analytical: Relating to send-away tests (outwith your Health Board)

Q7: Please provide details of tests sent to external laboratories (test, laboratory, method (if known), approximate numbers, TAT, cost).



Analytical: Relating to send-away tests (outwith your Health Board)

Q7: Please provide details of tests sent to external laboratories (test, laboratory, method (if known), approximate numbers, TAT, cost).

Lipase

- Three Health Boards send lipase requests to Huddersfield Royal Infirmary (1 on behalf of another 2 Health Boards):
  - Method: Siemens Advia 2400 (colorimetric, produces methylresorufin)
  - Reference range: 6-51 U/L
  - Workload: 24/ year, 20/ year, <20/ year, <5/ month, <2/ month
  - Cost: £25-£31 per test
  - Turnaround time: 28 days
- One Health Board sends approximately 7 request for lipase to an external laboratory (£25 per test) but did not disclose where.

Amylase Isoenzymes

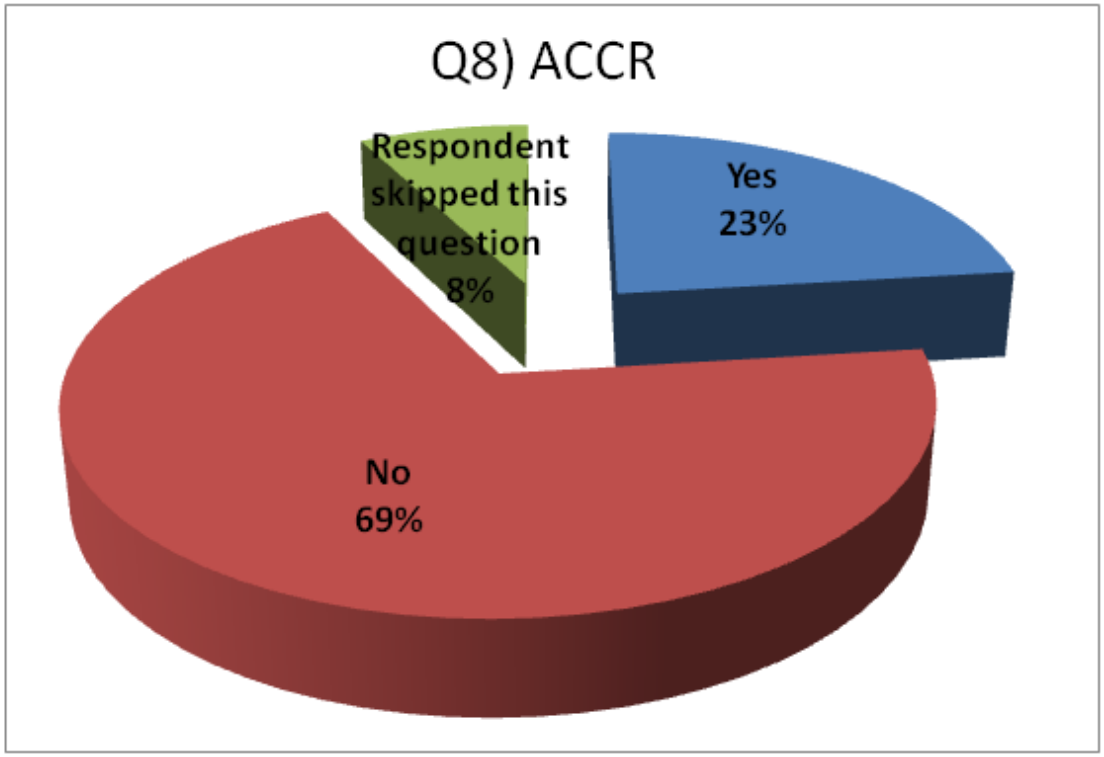
- One Health Board sends amylase isoenzymes requests to King's College London (ViaPath):
  - Method: Immunosubtraction & colorimetric assay
  - Reference range: Total amylase <100 U/L, pancreatic amylase <50 U/L and salivary amylase <50 U/L, pancreatic:total amylase ration (0.0-0.75)
  - Workload: <1 per year
  - Cost: £23 per test
  - Turnaround time: 28 days

Macro-amylase

- One Health Board sends macro-amylase requests to Southend University Hospital:
  - Method: Gel filtration chromatography
  - Reference range: 6-51 U/L
  - Workload: <1 per year
  - Cost: £20 per test.
  - Turnaround time: 28 days.
  - ***Note: Test no longer available***

Post-analytical: ACCR

Q8: Does your laboratory report amylase:creatinine clearance ratio (ACCR)?

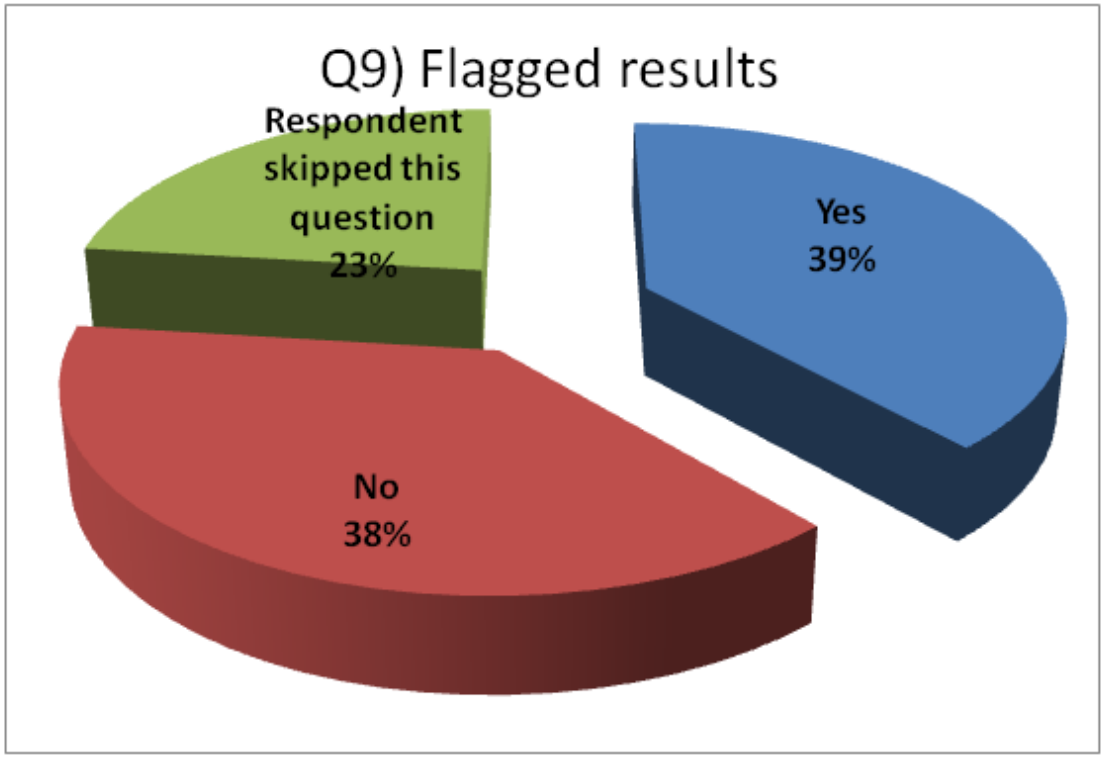


Of those that report ACCR:

- No locally agreed reference range (*n*=1)
- RR: 1-5% (*n*=1)
- RR: 1-6% (*n*=1)
- RR: 2-5% (*n*=1)
- < lower limit could be consistent with macro-amylase
- > upper limit could be consistent with pancreatitis or renal failure

Post-analytical: Interpretation of Results

Q9: Does your laboratory provide any interpretive comments or flags on reports (If so, please provide details). Alternatively, do you know which cut-off is used in local clinical protocols for diagnosis of acute pancreatitis?

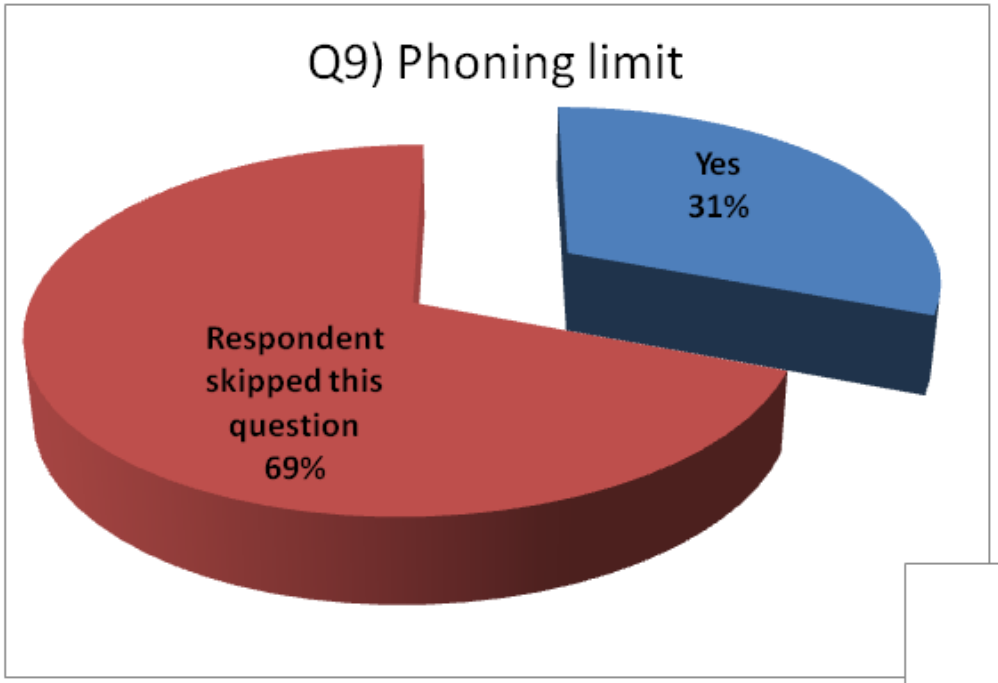


Of those that flag results:

- >URL (*n*=2)
- >5XURL (*n*=1)
- >delta change (*n*=1)
- Did not disclose details (*n*=1)

Post-analytical: Interpretation of Results

Q9: Does your laboratory provide any interpretive comments or flags on reports (If so, please provide details). Alternatively, do you know which cut-off is used in local clinical protocols for diagnosis of acute pancreatitis?

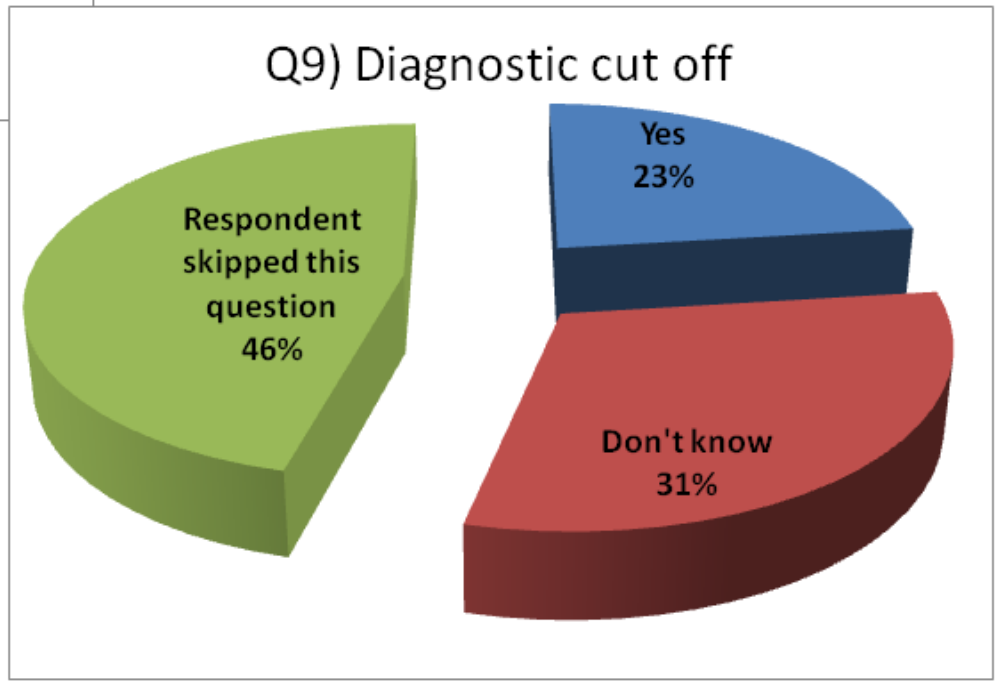


Phoning limits:

- >2X URL (*n*=1)
- >3X URL (*n*=1)
- >4X URL (*n*=1)
- >5 XURL (*n*=1)

Diagnostic cut off:

- >3X URL (*n*=3)
- Based on local protocols



Key findings	Recommendations
1) Only a small proportion of laboratories in Scotland include tests for acute pancreatitis in disease-specific order sets.	• Engage with gastroenterologists and Labs IT teams to develop solutions.
2) Very few laboratories are aware of guidelines for test requesting in cases of suspected acute pancreatitis.	• It is possible that guidelines have been developed without input from laboratories therefore there is an opportunity for laboratories to engage more with local clinicians around guideline development.
3) Most laboratories in Scotland are measuring amylase in cases of suspected pancreatitis despite National and International guidelines stating a preference for lipase.	• Engage with gastroenterologists on what is required.
4) Very few laboratories offer reflex or reflective testing using more specific pancreatic markers (*e.g.* lipase, amylase isoenzymes) when total amylase is elevated.	• Develop protocols for adding of more specific markers where total amylase is the first line test, in consultation with gastroenterologists.
5) There is marked variation in methods used and workload figures for total amylase.	• Probably reflects local circumstances.
6) There is generally close consensus for reference ranges for total amylase.	• Small differences probably attributed to the different platforms (and substrates) in use.
7) There was very little consensus in alert / phoning limits used for total amylase reporting.	• Recommend update of RCPath guidance.

Key findings	Recommendations
8) Most laboratories participate in EQA schemes for total amylase.	• Encourage participation.
9) Most laboratories offer urine and fluid amylase testing. There was wide variation in workload, turnaround time, cost and reference ranges. Only a few laboratories participate in an EQA scheme.	• Encourage EQA participation.
10) No Scottish laboratories offer pancreatic-specific amylase however one laboratory offers lipase testing which is available to other hospitals within their Health Board. Several laboratories are currently sending lipase requests to Huddersfield Royal Infirmary.	• There doesn't appear to be a strong case for a Regional amylase isoenzymes service. • Could lipase requests be sent to the laboratory in Scotland currently offering this?
11) No Scottish (or UK) laboratories offer macro-amylase testing by GFC.	• Consider a Regional macro-amylase service.
12) Only a small proportion of laboratories report ACCR, however of those that do, there is generally good agreement regarding cut-off.	• Consider harmonising ACCR reference range.
13) There was little consensus on phoning limits used. However of those that quoted a diagnostic cut-off, there was strong consensus for >3X URL.	• Consider harmonising phoning limits.

Acknowledgements

- ACB Scotland Clinical Audit Group
- Respondents

The Association for Clinical Biochemistry & Laboratory Medicine
Scotland Audit Group

Thank you!

Questions?