A practical approach to diagnostic appraisals

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A diagnostic appraisal pathway

1. Technology
2. Role?
3. Submission/Topic Selection
4. Focus?
5. Scope
6. Application?
7. Protocol
8. Delivery?
9. Report & Guidance
What is the aim of a diagnostic appraisal?

Does the test have a potential role in the NHS?

• What does the test add to what is already being provided?

Accuracy versus clinical benefit

• Does the test result in benefits perceived by the patient?

Clinical benefit

• Improved health outcomes
• Changes to management
• Reassurance?
Topic selected – SonoVue ✅
Potential position in the care pathway

Replacement of an existing test

- Improved discriminatory value
- Better patient experience/fewer adverse effects
- Quicker
- Cheaper

Addition to an existing test

- Improved discriminatory value
- Improved coverage

Triage

- Sensitive test which could be used to rapidly rule-out further investigation with more invasive/expensive tests
Scoping and question setting

Contrast enhanced ultrasound of the liver using SonoVue® (sulphur hexafluoride microbubbles)

- Target group – adults who require liver imaging by ultrasound techniques

- Other indications – echocardiography, Doppler of the macrovasculature, Doppler of the microvasculature (including breast and liver lesions)

- Existing treatments and comparators: US, CT and MRI (all with and without contrast), biopsy and first generation microbubble contrast agents.
Final scope published ✔
Research question

To compare the clinical and cost-effectiveness of contrast enhanced ultrasound (CEUS) using the contrast agent SonoVue® with contrast-enhanced CT and contrast-enhanced MRI for the assessment of adults with focal liver lesions (FLL), in whom previous liver imaging has been inconclusive.

- Cirrhosis surveillance
- Detection of liver metastases from colorectal cancer
- Incidentally detected focal liver lesions
Final protocol published ✔
Direct vs. ‘linked-evidence’ approach

- Trial data to address the question: do patients who undergo the diagnostic test have better health outcomes than those who do not?

- Accuracy + prognostic link between the target condition and morbidity/mortality + effective intervention

- SonoVue® – three clinical applications = three cost-effectiveness models

- Comparators – other contrast-enhanced imaging modalities
Modelling approach

published model for cirrhosis surveillance

new cirrhosis model modified
compare confirmatory imaging methods and allow uncertainty

published model for liver metastases detection

new metastases model modified
compare imaging methods after inconclusive ultrasound

new incidental focal liver lesions model
Combination and modification
change to point of diagnosis (hepatocellular carcinoma)
change to handling of false positives and false negatives
Conclusion of the SonoVue® assessment

Systematic review

• SonoVue® could provide similar diagnostic performance to other imaging modalities (CECT and CEMRI) for the three main clinical applications considered

Cost-effectiveness analyses

• SonoVue® instead of CEMRI was cost-effective. SonoVue® instead of CECT was considered cost-effective in the surveillance of cirrhosis and characterisation of incidentally detected focal liver lesions, with similar costs and effects for the detection of CRC liver metastases
Report submitted ✓
“SonoVue® is recommended for use with ultrasound for examining abnormal-looking areas in the liver that are noticed, but cannot be properly identified, using normal ultrasound. These areas may have been noticed during routine scanning. If they were noticed when looking for cancer that has spread from another part of the body, SonoVue® is recommended if the person cannot have or does not want a CT (computed tomography) scan. If they were noticed in someone with cirrhosis who is having their liver checked, SonoVue® is recommended if the person cannot have or does not want an MRI (magnetic resonance imaging) scan.”
The future – companion diagnostics

• Trial data are generally available for test and treatment
• Different trials may use different tests, but trials do not usually compare tests
• No reference standard test – tests may select different populations

Possible approaches

• Compare accuracy of test(s) to predict response to treatment
• Compare treatment effects obtained when participants are selected using different tests

Problem

• Other variables may effect these measures
References


