Reviewer's report

Title: Views of general practitioners on the role of CA125 in primary care to diagnose ovarian cancer

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Reviewer: Marcia Hall

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My comments are below. I should disclose that I was a participant on the NICE group that recommended that GPs have access to CA125 as part of their tools to identify women with ovary cancer.

1. Is the question posed original, important and well defined?

The question is important although not exactly original. However given the very recent adoption of the NICE guidance in the UK, and so no previous work has been published on this in this country other than the papers quoted. The endpoints are certainly not clear and this is really a descriptive piece of work based on a very small response to a survey.

2 Are the data sound and well-controlled?

Not really applicable to this submission – yes as far as they are presented

3 Is the interpretation (discussion and conclusion) well balanced and supported by the data?

Although the limitation of poor response to the survey (8%) has been mentioned – it should be mentioned again within the body of the discussion and conclusion text. Eg within the first para as this states that GPs are well aware of the typical symptoms... well the 8% that answered are aware.

The data is clearly presented, such that it is, but great emphasis is placed on the referral into secondary care of women with raised CA125 but no US evidence of ovary cancer. Although seemingly contrary to the NICE guidance it would be more helpful to explore why this is so rather than state it factually – simply because women can have ovary cancer with normal imaging.

However, mention is made of the acceptance that women with ovary cancer can have a normal CA125, confirming the general opinion that both US and CA125 are both important parts of a difficult jigsaw. It would make more sense to point out that this survey of well informed and self-selected participants confirms this fact!

It would be interesting to mention in the discussion if NICE had NOT recommended that GPs have access to CA125 would there be any impact? – questions on this would have been helpful too – eg reassure patients whose
CA125 is normal and reassure GP too! Fewer GPs involved on NICE group agreed but in fact GP don’t see it very often....and the 6 secondary care doctors were – radiologist, 2 x gyn onc surgeon, 2 x med onc and 1 x cancer unit gynaecologist. The scope for development of these guidelines was very broad – ranging from the diagnostic issues discussed here but also including whether lymph node dissection should be done – what radiology was appropriate, was histology always required and what chemotherapy was needed – hence the inclusion of all the secondary care doctors.

It would be sensible to discuss the limitations that the NICE process has in forming guidelines – it HAS to be (apparently) didactic and direct (NO ambiguity allowed). Health economics are also an integral part of the NICE process. These are the two reasons why the algorithm states CA125 first (cheaper than US for everyone) and will not allow both investigations at once (although practically it is very likely that this is what will happen).

Finally although mention is made of the aim of these guidelines in expediting the diagnosis of such patients in order to improve treatment outcomes, the discussion also needs to reiterate the latest theory that many of these serous cancers probably arise from the fallopian tube and are thus ‘advanced’ (stage II/III) from the start whenever this happens to have been discovered. Expediting confirmation of this will therefore only reassure the patient that there is indeed ‘something wrong’ but is most unlikely to alter outcomes until our therapy has improved. Explaining these unpleasant facts is often the most important and helpful way for a GP to ease some of the anxiety induced by waiting for results.

4. Are the methods appropriate and well described and are sufficient details given to evaluate and / or replicate work?

Yes methods well described although of limited application given very poor response. Pity that the same survey couldn’t have been given to a captive audience say at GP seminars on cancer and perhaps on another unrelated topic (in order to reduce self-selection issue). I think the addition of such replica surveys, although of smaller numbers might strengthen your case. Somewhat surprised that GPs do not recognise endometriosis as likely precursor to malignancy.

5. What are the strengths and weaknesses of the methods?

There was a distinct lack of any questions about bowel habit. This is a major symptom of ovary cancer – many patients will be labelled as having irritable bowel syndrome because of their frequent complaints of alternating diarrhoea and constipation. Patients rarely offer up these symptoms, particularly if something else is troubling them but very often the co-existence of bowel problems significantly raises your concern about ovary cancer. This is a very common feature of patients with serous ca ovary and these patients often get referred to the gastroenterologists and then onto oncology. Also important to remind GPs that IBS is part of ‘normal’ spectrum – just that these people’s bowels reflect stress more readily than the average. Additional questions such as
what do GP’s think abdominal bloating is? can it be “normal” (YES)

See above answer. Case histories are so borderline there wasn’t really any correct answer for either scenario – so I am not sure exactly what they were designed to show except that any pathway could have been correct for these patients. Would be more helpful to have given ‘correct’ answers – so more likely to refer 2WW if post menop but probably no real necessity for urgent referral and review of bloating and repeat CA125 more sensible in younger age group. Again – no information on bowel habit which GP should have asked about if bloating main symptom.

6. Can the writing, organisation, tables and figures be improved?

What revisions are requested.

Cannot really draw conclusions from survey as it stands – not only very few GPs answering but also no bowel symptoms included in any of the survey. I cannot recommend this for publication but if the survey were repeated and perhaps validated as discussed above it might then be a more helpful addition to the literature

Are there any ethical or competing interests issues you would like to raise

No ethical / competing issues