Reviewer’s report

**Title:** Patient advocate involvement in the design and conduct of breast cancer clinical trials requiring the collection of multiple biopsies

**Version:** 0  **Date:** 21 Jul 2017

**Reviewer:** Hazel Thornton

**Reviewer's report:**

I found this to be an interesting paper, clearly written, well structured and detailed.

The background, history and rationale for the increasing need to obtain multiple biopsies from breast cancer patients is well described and justified in this generally well written paper - as might be expected from this experienced authorship. However, as the title so clearly emphasises, this commentary is about the active involvement of patients in the work described. I therefore felt it was a pity that a better history of relevant involvement, especially with respect to the effect that such involvement has both on the attitude of Ethics Committees and prospective participants, was not so thoroughly indicated. Active involvement of patients and citizens - especially in breast cancer trials - is not new: this particularly difficult requirement of explaining the rationale for a difficult `ask` of prospective participants might have benefited from also providing more of a history so that any reader might appreciate the solid foundation there is for this type of collaboration leading to a better chance of successful recruitment and more acceptable trial propositions. [1] [2] At the same time, it is important that successful recruitment itself is not seen as the aim, since this could constitute manipulation for an objective other than the ultimate benefit of breast cancer patients. This criticism was highlighted and considered within the working group for an early research project in 1995/96: 'Using a Consumers' Advisory Group to increase accrual into trials' project (NCP/D18) see website report and (late) publication. [3]
The design and implementation of a randomised controlled trial for thrombolysis for acute ischaemic stroke around the year 2000 benefitted considerably on the input of patients, in various ways, as reported by Liedeke Koops and Richard Lindley in the BMJ in 2002. [4] Of especial interest was the acceptance by the Ethics Committee in passing this trial having appreciated the wide input of patients and carers into its design, especially in connection with the difficult decision-making for prospective participants in challenging circumstances.

Patient and citizen involvement in trial design and execution is continually evolving as medical developments occur. I believe it to be important to show that each new building block is placed on what has gone before so that readers can appreciate this history and evolution - that it is not a new phenomena but is growing, changing and responsive to demands and needs. [5]

Minor comments:

Line 20: "may not want to offer". Suggest perhaps `be diffident about offering`; `be wary of offering`; `fight shy of`; or `be reluctant to`.

Line 31: Grammar - `they are`, not `it is` (plural - `trials`).

Line 54: See comment above about motive. Maybe a small paragraph somewhere in the main paper about the ethics?

Line 58: Suggest insert `active` - i.e. encourage further active patient and participant.
Page 3. Line 8. `promote the acceptability`. I think it is important to mention somewhere in this abstract that acceptance is contingent on the fact that the rationale of the need for extra biopsies will be explained.

Page 4 line 34. `is delivered to individual patients in the future` is ambiguous. Would benefit from re-wording.

Page 5 line 30. `to assist communication with the Research Ethics Committee.` Reference to the thrombolysis/stroke trial [4] could be of benefit here.

Lines 35-37. `should be provided with detailed information` - important to re-iterate the importance too of emphasising the importance of explaining the rationale/reason for these increased biopsies - as in lines 24-27 of page 6.

Page 7 - issues around slow recruitment.

It might be useful to refer to the ProtecT trial. [6] Qualitative research was embedded into the ProtecT trial which proved valuable in addressing the issues about clinicians` reluctance to broach the topic confidently to potential participants. It found that they were inclined to leave the least popular option until last (active monitoring in this case) because they thought it would be unacceptable. The language they used was also found to be unsatisfactory; for example, men though that `watchful waiting` conveyed the idea that they would just watch while things deteriorate, and the term `active monitoring` was recommended. Use of `10 year survival` was problematic too. Altering the order of presentation of options and training in use of suitable language saw a rise in accrual rates.
Could training of clinicians be suggested perhaps?

Line 20: comma required after `biopsies`.

End of line 25: `whose consent to clinical trials` - `whose consent to participating in clinical trials`.

Perhaps mention the benefit of mutual education that this type of working provides - improving communication both ways?

REFERENCES;


"The House of Commons Health Select Committee in their Report on Breast Cancer Services (HMSO July 1995) endorses the activity of the CAG-CT by stating: "We believe that patient involvement at all stages of a trial, including initial design, is essential, and that initiatives such as the Consumers` Advisory Group for Clinical Trials are to be welcomed". (p.lvi.para 205). They state that patients should be seen as "full and active participants".

[3] Jo Marsden, Jane Bradburn Patient and clinician collaboration in the design of a national randomised breast cancer trial. Health Expectations 2004; 7 (1) 6-17. This describes the CAG-CT research project "Using a consumers` advisory group to increase accrual into trials", funded
by the NHS R&D (Cancer) Programme (NCP/D18) in 1995/6, based on a feasibility study which led to the multicentre U.K. Randomised Trial of Hormone Replacement Therapy (HRT) in Women with a History of Early Stage Breast Cancer. ISRCTN 29941643 (See INVOLVE website database.)


http://211.103.242.133:8080/ziyuan/CDDPdf/evd/200801/British%20Medical%20Journal/%E9%9A%8F%E6%9C%BA%E5%AF%B9%E7%85%A7%E8%AF%95%E9%AA%8C/bmj200232508415.pdf

"Consumer involvement can be a very important part of the development of new randomised controlled trials"

"The ideas of Hazel Thornton, Michael Baum, and Iain Chalmers prompted this research."


prostate cancer want wider access to prostate specific antigen testing: qualitative study. Alison Chapple, Sue Ziebland, Sasha Shepperd, Rachel Miller, Andrew Herxheimer, and Ann McPherson BMJ 2002 325: 737

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21st July 2017

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