PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

This paper was submitted to the BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open where it was re-reviewed and accepted.

ARTICLE DETAILS

TITLE (PROVISIONAL)	A randomized controlled trial of hospital-based case management to improve colorectal cancer patients' health-related quality of life and evaluations of care
AUTHORS	Wulff, Christian ; Vedsted, Peter; Søndergaard, Jens

VERSION 1 - REVIEW

REVIEWER	Blazeby, Jane University of Bristol, School of Social and Community Medicine
REVIEW RETURNED	07-May-2012

GENERAL COMMENTS	This is a 1:1 parallel randomised trial comparing standard care with a case management systems for patients with colorectal cancer. It is a single country and centre study. The intervention comprises dedicated nurse led care, and access during diagnosis, staging and treatment, the standard arm (in the same centre) is simple access to a member of the surgical team. the primary end point is the global QOL score in the QLQ-C30. There are a lack of RCTs examining processes of care and therefore this is a novel piece of work There are a number of methodological weaknesses in the study which lead to bias and weaken the results of the study. It is unclear why the global score of the C30 was selected for the primary outcome, what was the rationale for using this measure and what are the hypothesised reasons for global health to be different because of better access/information to care. The global health scale comprises two items, one assessing physical function and the other overall QOL - this may not be sensitive enough to the intervention. The intervention is complex with interacting and interdependant components (the expertise of the nurse, the hospital, the patient and services), some pilot work was undertaken but there is a lack of modelling and theory to underpin this service and the selection of outcomes to evaluate the impact of the intervention The ad hoc items selected and developed to evaluate the procedure are not yet validated and therefore information they yield is of uncertain value. It is also a pity that responses were dichotomised as data will have been lost. It is likely that they may have been contamination between the caregivers in the hospital betwen each arm and a cluster design may have been a better option In other countries, case management is often performed by a clinical nurse specialist who is also allocated to the patient and the whole care

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	pathway in the UK is managed through a multi-disciplinary team - this study therefore may not be generalisable outside of the country in which is was performed In summary this interesting, but the findings may not be generalisable to other healthcare systems and there are weaknesses in the design and choice of outcome measures

REVIEWER	Frizelle, Frank Christchurch hospital, Surgery
REVIEW RETURNED	07-May-2012

GENERAL COMMENTS	This manuscript deals with an aspect of cancer care , were their increasing demands to provide. There has been no data to support this demands or to negate this, as such this is a manuscript which at last provides that and as a result I expect will be well cited. The results to me are surprising. No doubt someone will repeat the study. I would have been interested in the outcome measures such as length to time treatment took and missed appointments . It is a well written manuscript, the stats look correct. It is readable . I would support publication, however I am not certain that it "fits" in the BMJ though if published in BMJ this allows excellent access to it.

- The manuscript received a third review at the BMJ but the reviewer did not give permission for their comments to be published.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 2

Comments:
This is a 1:1 parallel randomised trial comparing standard care with a case management system for patients with colorectal cancer. It is a single country and centre study. The intervention comprises dedicated nurse led care, and access during diagnosis, staging and treatment, the standard arm (in the same centre) is simple access to a member of the surgical team. The primary end point is the global QOL score in the QLQ-C30. There is a lack of RCTs examining processes of care and therefore this is a novel piece of work

There are a number of methodological weaknesses in the study which lead to bias and weaken the results of the study.

It is unclear why the global score of the C30 was selected for the primary outcome, what was the rationale for using this measure and what are the hypothesised reasons for global health to be different because of better access/information to care. The global health scale comprises two items, one assessing physical function and the other overall QOL - this may not be sensitive enough to the intervention.

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Response: The purpose of the trial was to assess whether increased focus on well-coordinated care (as to patients' treatment, information and health care relations) would improve 'the patient experience' (patient evaluations) and as a consequence patients' well-being. EORTC QLQ-C30 was chosen as the instrument to measure well-being as the instrument incorporates overall well-being (the global quality of life subscale) and five functioning scales. The global quality of life subscale was chosen as the primary HRQoL variable and the functioning scales as secondary outcomes. The EORTC QLQ-C30 was chosen among various HRQoL instruments because it is validated, translated into Danish, and is the most used cancer-generic HRQoL instrument in Europe and also in the colorectal cancer setting.
Before conducting the study we had no reasons to believe that the subscales of the EORTC QLQ-C30 should not be responsive in our CRC setting. Meanwhile the RCT, a paper by Uwer et al (PMID: 21859485) have questioned responsiveness of the global quality of life subscale in a group of colorectal cancer patients. Retrospectively, we acknowledge that the study could have been improved by running a 'responsiveness' study in the setting and context where the RCT was conducted.

The intervention is complex with interacting and interdependent components (the expertise of the nurse, the hospital, the patient and services), some pilot work was undertaken but there is a lack of modelling and theory to underpin this service and the selection of outcomes to evaluate the impact of the intervention.
Response: We tested a pragmatically developed complex intervention based on the concept of case management. The hypotheses that CM improves patient evaluations and patients' well-being are some of the commonly used reasons for implementing case management although the correlations have not been scientifically established.

The ad hoc items selected and developed to evaluate the procedure are not yet validated and therefore information they yield is of uncertain value.
Response: "We argue that it is acceptable to analyse non-validated items in a trial as long as items are presented by their exact wording and analysed item-by-item." This statement has been added to the weaknesses section.
It is also a pity that responses were dichotomised as data will have been lost.
Response: It is uncommon to analyse single item responses after linear transformation because of the ordinal nature of the response categories.

It is likely that they may have been contamination between the caregivers in the hospital between each arm and a cluster design may have been a better option
Response: That it correct and has already been discussed in the section discussing weaknesses. A cluster randomized design might have been superior but would also have been much more expensive and was hindered by our budget. In the weaknesses section we have argued that we find 'significant' contamination unlikely.

In other countries, case management is often performed by a clinical nurse specialist who is also allocated to the patient and the whole care pathway in the UK is managed through a multi-disciplinary team - this study therefore may not be generalisable outside of the country in which is was performed
Response: Various models of case management are implemented in different countries and setting. None of these models can be seen as 'the CM model', because both definitions and description of case management are numerous and broad. Moreover, very few research studies have so far tried to establish effectiveness of different CM models. This is just one study elucidating effectiveness of one model of CM. Naturally, present study needs to be followed by further health services research focusing on other methods of improving continuity of care for cancer patients. We did our best to

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describe the content of the tested model and hope that the submitted paper regarding methods and feasibility of the trial will soon be published so particularly interested readers can obtain extra information about the complex intervention.

The case managers were member of the MDT – this fact has now been underlined.

In summary this interesting, but the findings may not be generalisable to other healthcare systems and there are weaknesses in the design and choice of outcome measures

Please enter your name: Jane M Blazeby

Job Title: Professor of Surgery

Institution: University of Bristol

[...]

Reviewer: 3

Comments:
This manuscript deals with an aspect of cancer care, were their increasing demands to provide. There has been no data to support this demands or to negate this, as such this is a manuscript which at last provides that and as a result I expect will be well cited.
The results to me are surprising. No doubt someone will repeat the study.
I would have been interested in the outcome measures such as length to time treatment took and missed appointments.
Response: We plan to analyse such data in another study as we find such process outcomes important.

It is a well written manuscript, the stats look correct.
It is readable.
I would support publication, however I am not certain that it "fits" in the BMJ though if published in BMJ this allows excellent access to it.

Please enter your name: Frank Frizelle

Job Title: Professor of Surgery

Institution: University of Otago; Christchurch

[...]

VERSION 2 – REVIEW

REVIEWER	Fowzia Ibrahim Statistician King's Musculoskeletal Clinical Trials Unit Department of Academic Rheumatology Weston Education Centre

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	King's College London Denmark Hill London SE5 9RJ
REVIEW RETURNED	24-Aug-2012

THE STUDY	Although the authors acknowledge the missing data is mainly due to death, one way to assess the estimates wouldn't be biased by missing data which are more marked with the CM group than controls is to carry out sensitivity analysis, I wonder why the authors didn't try to carry out this analysis? Furthermore, CM patients who withdrew between 30-52 weeks, couldn't you impute their data at week 52 by using the availability of previous data points? I would suggest that the authors should at least attempt to carry out sensitivity analysis. I think the authors should also adjust for multiple comparisons

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