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Nama V, Nordin A, Bryant A

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[Intervention Review]

Patient-reported outcome measures for follow-up after gynaecological cancer treatment

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ABSTRACT

Background

Cancer is a leading cause of death worldwide. Gynaecologic cancer treatment is known to have the potential for a major impact on quality of life (QoL). Patient-reported outcome measures (PROMs) is an umbrella term that covers a range of potential types of measurement but is used specifically to refer to self reports by the patient of their health and well-being. Use of QoL and cancer-specific questionnaires as alternatives to follow-up may have immense psychological benefit to the patient and cost benefit to the healthcare system.

Objectives

To evaluate the effectiveness of PROMs as an alternative to routine follow-up of women after treatment for gynaecological cancers to identify recurrences, affect overall survival and assess psychological benefit.

Search methods

We searched the Cochrane Gynaecological Cancer Group Trials Register, MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) up to November 2012. We also searched registers of clinical trials, abstracts of scientific meetings and reference lists of review articles.

Selection criteria

We searched for randomised controlled trials (RCTs) and non-RCTs with concurrent comparison groups (of adequate quality that used statistical adjustment for baseline case mix using multivariable analyses) that compared PROMs or QoL questionnaires versus traditional follow-up with multiple visits to the hospital in women after treatment for gynaecological cancers. Studies that involved women completing PROMs at intervals and submitting results for assessment by their cancer care team or structured interviews of women during their follow-up were included in the analysis.

Data collection and analysis

Two review authors independently assessed whether potentially relevant studies met the inclusion criteria. We found no studies and therefore analysed no data.

Main results

The search strategy identified 2524 unique references, of which all were excluded.

Authors' conclusions

We found no evidence to make an informed decision about PROMs for follow-up after gynaecological cancer. Ideally, RCTs which are multicentre or multinational or both, or well-designed non-randomised studies are needed that use multivariable analysis to adjust for baseline imbalances, to compare follow-up strategies and improve current knowledge.

PLAIN LANGUAGE SUMMARY

Benefits of patient-reported measures of health and well-being versus traditional follow-up after treatment of gynaecological cancer

Background

Cancer is a leading cause of death worldwide. The traditional method of follow-up involves multiple visits to the hospital to check, for example, whether the cancer has come back (recurrence). This may cause anxiety among the patients and its cost effectiveness is questionable. Clinician and patient groups have asked for a consideration of alternative model approaches; since most recurrences are symptomatic, follow-up of patients after treatment for gynaecological cancer may be accomplished by patient-related outcome measures (PROMs) rather than routine follow-up visits. PROMs is an umbrella term that covers a range of potential types of measurements, but is used specifically to refer to self reports by the patient of their health and well-being. Use of PROMs as alternatives to follow-up may have immense psychological benefits for the patient and cost benefit to the healthcare system. There is currently no evidence to determine whether PROMs are better or worse in helping women to live longer and better after gynaecological cancer rather than follow-up visits. It is also unclear whether PROMs are beneficial in terms of patient satisfaction or quality of life.

Study Characteristics

We performed an extensive literature search to identify randomised controlled studies that compared PROMs to routine follow up.

Key findings

No studies suitable for inclusion in our review were found. This highlights the need for good-quality studies comparing PROMs to standard follow-up. Evidence from adequately-powered studies at low risk of bias are needed.

BACKGROUND

Description of the condition

Cancer is a leading cause of death worldwide (American Cancer Society 2010). Globally, a woman's risk of developing cancer of the ovaries, uterus or cervix by the age of 65 is 2.2%; cancers of the vulva and vagina are less common. Gynaecological cancers account for 25% of all new cancers diagnosed amongst women aged up to 65 years in developing countries, compared to 16% in the developed world (GLOBOCAN 2008). Gynaecologic cancer treatment is known to have the potential for a major impact on quality of life (QoL). Beyond treatment and disease management, long-term issues of living with a diagnosis of cancer and effects of treatments are emerging as major issues in cancer care.

Follow-up of women treated for gynaecological cancers is aimed at early identification of recurrences in order to improve survival. It also helps in identifying physical, psychological, functional and sexual morbidity as a consequence of diagnosis and treatment. Current protocols in place for follow-up of women, after treatment of gynaecological cancers to detect recurrences, are not evidence-based. The traditional method of follow-up (Kew 2006) involves multiple visits to hospital that generate anxiety among the women (Kew 2009) and its cost effectiveness is questionable. There is no evidence that the traditional method of follow-up identifies recurrences earlier or improves overall survival. Patient groups have called for a consideration of alternative models (Lydon 2009) and since most recurrences are symptomatic, follow-up of women with gynaecological cancer may be accomplished by patient-reported outcome measures (PROMs).

Description of the intervention

The purpose of PROMs is to get patients' own assessment of their health and health-related quality of life – PROMs questionnaires do not ask about patients' satisfaction with or experience of healthcare services, or seek their opinions about how successful their treatment was. The questions can be asked by paper and pencil questionnaires, interviews, or, increasingly commonly, by electronic means (e.g. via a computer, or a handheld electronic device). For example, enquiring about trouble taking a long walk could be used as a score to help assess physical functioning. A question about feeling nauseated could contribute to a score to assess symptoms. A questionnaire that measures a single aspect of health is described as uni-dimensional. A questionnaire that measures multiple dimensions of health is termed multi-dimensional (e.g. questionnaires that include global QoL, functional scales and symptoms scales). Questionnaires may be generic (designed to be used in any disease population and cover a broad aspect of the construct measured) or condition-targeted (developed specifically to measure those aspects of outcome that are of importance for people with a particular medical condition). The answers patients give to the PROM questions provide detailed information on a variety of aspects of their health and quality of life. However, in order to provide an overall assessment of a patient's health, and to make comparisons (for example, before versus after treatment, or between subgroups of patients), it is necessary to sum up the answers the patient has provided to each question. PROMs instruments achieve this in a number of different ways.

Why it is important to do this review

Use of PROMs as alternatives to follow-up may have psychological benefit to the patient and cost benefit to the healthcare system. Follow-up using PROMs may have the potential to affect identification of recurrence and overall survival.

OBJECTIVES

To evaluate the effectiveness of PROMs as an alternative to routine follow up of patients after treatment for gynaecological cancers to identify recurrences, affect overall survival and assess psychological benefit.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs)

We did not expect to identify any relevant RCTs, so non-randomised studies (NRS) with concurrent comparison groups were eligible: Quasi-RCTs, prospective and retrospective cohort studies, and case series of 30 or more participants. We excluded case-control studies, uncontrolled observational studies and case series of fewer than 30 participants.

In order to minimise selection bias for NRS, we included only studies that used statistical adjustment for baseline case mix using multivariable analyses (e.g. disease severity, age, comorbidity, and type of cancer, grade of cancer, treatment modalities).

Types of participants

We included women (18 years and older) diagnosed with a gynaecological malignancy and who had received treatment with surgery, radiotherapy or chemotherapy, either as the only treatment or in combination.

Types of interventions

Intervention: PROMs used as intervention in follow-up of women after treatment for gynaecological cancers, e.g. PROMs at intervals and submitting results for assessment by their cancer care team, or specific interviews with non-clinical staff to fill PROMs, or PROMs used as alternatives to follow-up to triage women who need to visit a gynae-oncologist.

Control: Traditional follow-up with multiple visits to the hospital. Traditionally, women with gynaecological cancers are followed up by routine clinic visits. The frequency and duration of follow-up is variable between centres.

Types of outcome measures

Primary outcomes

Overall Survival (OS): survival until death from all causes. We planned to assess survival from the time when women completed treatment.

Secondary outcomes

- Recurrence/progression-free survival (PFS).
- Participant satisfaction, measured using a validated scale.

- Quality of life (QoL), as measured by a validated scale in the intervention group at the end of the trial.
- Cost effectiveness.

Search methods for identification of studies

Electronic searches

We sought papers in all languages and carried out translations when necessary.

Electronic searches

See: Cochrane Gynaecological Cancer Group methods used in reviews.
We searched the following electronic databases:

- The Cochrane Gynaecological Cancer Review Group's Trial Register;
- Cochrane Central Register of Controlled Trials (CENTRAL), Issue 11, 2012;
- MEDLINE to November 2012;
- EMBASE to November 2012.

The MEDLINE (1985 to November 2012), to identify RCTs comparing the use of PROMs in follow-up of women treated for gynaecological cancers are presented in Appendix 1, Appendix 2 and Appendix 3 respectively.

We identified all relevant articles found on PubMed, and using the 'related articles' feature, we conducted a further search for newly-published articles.

Searching other resources

Unpublished and Grey literature

We searched Metaregister, Physicians Data Query, www.controlled-trials.com/rct, www.clinicaltrials.gov and www.cancer.gov/clinicaltrials for ongoing trials.

We searched for conference proceedings and abstracts through ZETOC (zetoc.mimas.ac.uk) and WorldCat Dissertations.

Handsearching

We handsearched reports of conferences in the following sources:

- Gynecologic Oncology (Annual Meeting of the American Society of Gynecologic Oncologist);
- International Journal of Gynecological Cancer (Annual Meeting of the International Gynecologic Cancer Society);
- British Journal of Cancer;
- British Cancer Research Meeting;
- Annual Meeting of European Society of Medical Oncology (ESMO);
- Annual Meeting of the American Society of Clinical Oncology (ASCO);
- Oxford University PROM Group Database.

Data collection and analysis

Selection of studies

We downloaded all titles and abstracts retrieved by electronic searching to a reference management database (Endnote), and removed duplicates. Two review authors (VN, AN) independently examined the remaining references. We excluded those studies that clearly did not meet the inclusion criteria and obtained copies of the full text of potentially relevant references. Two review authors (VN, AN) independently assessed the eligibility of the retrieved papers, and excluded all of them at this stage, as they clearly did not meet the inclusion criteria. Reasons for exclusion are documented in the table Characteristics of excluded studies. We did not identify any ongoing RCTs which met our inclusion criteria from our searches of the grey literature. In future updates of this review, we will employ the methods detailed in the Differences between protocol and review section below.

RESULTS

Description of studies

Results of the search

The search strategies identified 2524 unique references. Two review authors independently read the abstracts of these and excluded articles which obviously did not meet the inclusion criteria. We retrieved 11 full-text articles. The full-text screening of these 11 studies excluded all of them for the reasons described in the table of Characteristics of excluded studies. Searches of the Cochrane Database of Systematic Reviews (DARE), the System for Information on Grey Literature in Europe (SIGLE) and Oxford Patient Reported Outcomes Measurement Group website (Oxford PROM group) using the keyword 'Patient related outcome measures and gynaecological cancers' yielded no relevant references.

Included studies

No studies met our inclusion criteria.

Excluded studies

We obtained the full text for 11 references, but excluded all of them from the review for the following reasons:

- Two references (Chase 2010) were reviews of PROMs. We checked the references in these reviews, but none of them met our inclusion criteria.
- Vistad 2011 was a review of follow-up routines in gynaecological cancer.
- Ashing Giwa 2010, Gupta 2008 and Greimel 2002 were studies that looked at predictors of survival.
- Klee 1997, Lerman 2012 and Seow 2011 were studies looking into quality of life in women after treatment for gynaecological cancers.
- Greimel 2011 assessed quality of life in long-term ovarian cancer survivors.
- Greimel 2003 looked into the validity and reliability of questionnaires.
- Jordan 2012 was a questionnaire survey looking at the use of patient reported symptom assessment in gynaecological oncology practice.

For further details of all the excluded studies see the table Characteristics of excluded studies.

Risk of bias in included studies

We found no studies and therefore could not apply the 'Risk of bias' tool.

Effects of interventions

No data were available.

DISCUSSION

Summary of main results

We did not identify any studies that evaluated the role of patient-reported outcome measures (PROMs) as an alternative to routine follow-up in women treated for gynaecological cancer. Therefore the question of using PROMs as alternatives to routine follow-up remains unanswered. We specified overall survival (OS) as the primary outcome of interest, as it is a major objective of routine follow-up. Although we specified OS as our primary outcome and identification of recurrence as a secondary outcome, these have to be analysed in the context of cancer site, stage and other morbidities. Studies are needed to randomise early-stage cancers to no follow-up and follow-up with PROMs. Initial trials could explore the possibility of using routine follow-up in combination with PROMs to evaluate the sensitivity of the PROMs in identifying recurrences or other morbidity from treatment. For patients with poor prognosis and performance status, quality of life (QoL) should perhaps be the main focus. For healthier patients with early-stage cancers, achieving longer-term survival may be paramount.

Overall completeness and applicability of evidence

When we initiated this review, PROMs were inconsistently used in the follow-up of women after treatment. With increasing emphasis on cancer survivorship and quality of life (QoL), PROMs are increasingly implemented as part of the routine follow-up and are firmly established as an integral part of clinical trials. We are not aware of examples where they are routinely being used as alternatives for follow-up for gynaecological oncology patients.

Quality of the evidence

No studies met the inclusion criteria for this review, so there is no evidence to assess.

Potential biases in the review process

We performed a comprehensive search, including a thorough search of the grey literature, and all references were checked by two reviewers independently. We were not restrictive in our inclusion criteria with regards to types of studies, as we did not expect to find any randomised controlled trials. We were mindful that many potentially eligible non-randomised designs would have been prone to selection bias, hence we planned to only include studies that used appropriate statistical adjustment for important baseline imbalances to get studies of adequate quality. Therefore, we attempted to ensure that we did not overlook any relevant evidence by searching a wide range of sources and ensuring the review was not based on poor quality evidence by excluding case reports and poor quality retrospective studies.

The greatest threat to the validity of the review is likely to be publication bias, i.e. studies that did not find the treatment to have been effective may not have been published. We were unable to assess this possibility as we did not find any studies that met the inclusion criteria.

Agreements and disagreements with other studies or reviews

None of the excluded studies had the same objective as our review. There were two studies (Ashing Giwa 2010; Greimel 2011) which showed that survival was related to QoL and better QoL scores correlated with survival. However it cannot be extrapolated that patients with poorer quality of life are at risk of recurrences or needing intervention. The bias lies in the fact that women with early-stage cancers have an improved quality of life, as they are less likely to need radical treatment and are also likely to survive longer.

None of these studies used PROMs as a tool to identify recurrences. Traditionally, all women treated for gynaecological cancers have been followed up in clinics, and there is a reluctance to move away from traditional follow-up.

AUTHORS' CONCLUSIONS

Implications for practice

We are unable to make any evidence-based recommendations, as we found no studies assessing patient-reported outcome measures (PROMs) as an intervention and comparing it to routine follow-up.

Implications for research

High-quality, comparative studies are required, preferably using a randomised controlled trial (RCT) format. Firstly, studies should adequately ascertain the best form of clinical follow-up for women treated for gynaecological cancer, and secondly, should compare the benefits and risks of routine follow-up with a model restricted to routine assessment of symptoms and well-being by PROMs. Women identified as at risk of recurrence or treatment-related morbidity would be identified by the PROMs for clinical assessment and interventions.

Ideally, a large RCT is needed to compare the risks and benefits of following women after treatment for gynaecological cancer either with routine follow-up or with PROMs. Trials involving follow-up are difficult due to their length, time and cost in different healthcare systems. It also needs active participation from women being followed up after their treatment. The trials should also consider exploring other follow-up routines like patient-initiated follow-up or telephone follow-up. Although gynaecological cancer accounts for only 2% of all malignancies (GLOBOCAN 2008), there is a lack of evidence to support routine follow-up of these women as it is currently practiced, i.e. multiple visits to the hospital with no consensus on use of PROMs during these follow-up visits.

ACKNOWLEDGEMENTS

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The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR, NHS or the Department of Health

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Ashing Giwa 2010 *{published data only}*

Ashing-Giwa KT, Lim JW, Tang J. Surviving cervical cancer: does health-related quality of life influence survival? *Gynecologic Oncology* 2010;**118**(1):35-42. [PMID: 20382414]

Chase 2010 *{published data only}*

Chase DM, Watanabe T, Monk B J. Assessement and significance of quality of life in women with gynecologic cancer. *Future Oncology* 2010;**6**(8):1279-887.

Greimel 2002 *{published data only}*

Greimel E, Thiel L, Peintinger F, Cegnar I, Pongratz E. Prospective assessment of quality of life of female cancer patients. *Gynecologic Oncology* 2002;**85**(1):140-147.

Greimel 2003 *{published data only}*

Greimel E, Bottomley A, Cull A, Waldenstron A C, Arraras J, Chauvenet L, et al. An international field study of the reliability and validity of a disease-specific questionnaire module (the QLQ-OV28) in assessing the quality of life of patients with ovarian cancer. *European Journal of Cancer* 2003;**39**(10):1402-8.

Greimel 2011 *{published data only}*

Greimel E, Daghofer F, Petru E. Prospective assessment of quality of life in long-term ovarian cancer survivors. *International Journal of Cancer* 2011;**128**(12):3005-11.

Gupta 2008 *{published data only}*

Gupta D, Grutsch JF, Lis CG. Patient satisfaction with quality of life as a prognostic indicator in ovarian cancer patients treated in an integrative treatment setting. *Journal of the Society of Integrative Oncology* 2008;**6**(3):98-104.

Jordan 2012 *{published data only}*

Jordan S, Osann K, Wenzel L, Arroyo A, Tewari K, Chase D. Can patient-reported symptom assessment be useful in a gynecologic oncology office practice? A prospective study using the Edmonton Symptom Assessment Scale (ESAS) in a diverse population. In: Gynecologic Oncology; Conference: 2012 Annual Meeting of the Western Association of Gynecologic Oncologists, WAGO 2012 Huntington Beach, CA United States. 2012.

Klee 1997 *{published data only}*

Klee M, Groenvold M, Machin D. Quality of life of Danish women: population-based norms of the EORTC QLQ-C30. Quality of Life Research 1997;**6**(1):27-34.

Lerman 2012 *{published data only}*

Lerman R, Jarski R, Rea H, Gellish R, Vicini F. Improving symptoms and quality of life of female cancer survivors: A randomized controlled study. *Annals of Surgical Oncology.* 2012;**19**(2):373-8.

Seow 2011 *{published data only}*

Seow H, Barbera L, Sutradhar R, Howell D, Dudgeon D, Atzema C, et al. Trajectory of performance status and symptom scores for patients with cancer during the last six months of life. *Journal of Clinical Oncology* 2011;**29**(9):1151-8.

Vistad 2011 *{published data only}*

Vistad I, Moy BW, Salvesen HB, Liavaag AH. Follow-up routines in gynecological cancer - time for a change? *Acta Obstetricia et Gynecologica Scandinavica* 2011.;**90**(7):707-18.

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American Cancer Society. Cancer Projected To Become Leading Cause Of Death Worldwide In 2010. ScienceDaily; www.sciencedaily.com /releases/2008/12/081209111516.htm (accessed 30 June 2013).

Deeks 2001

Deeks JJ, Altman DG, Bradburn MJ. Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Davey Smith G, Altman DG, editors(s). Systematic Reviews in Health Care: Meta-Analysis in Context. 2nd edition. London: BMJ Publication Group, 2001.

Dersimonian 1986

DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled Clinical Trials* 1986;**7**(3):177-88.

GLOBOCAN 2008

Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. GLOBOCAN 2008: Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer. globocan.iarc.fr 2010;**2.0**.

Higgins 2003

Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**(7414):557-60.

Higgins 2011

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Kew 2006

Kew FM, Cruickshank DJ. Routine follow-up after treatment for a gynecological cancer: a survey of practice. *International Journal of Gynecological Cancer* 2006;**15**(1):380-4.

Kew 2009

Kew FM, Galaal K, Maderville H. Patients' views of follow-up after treatment for gynaecological cancer. *Journal of Obstetrics and Gynaecology* 2009;**29**(2):135-42.

Lydon 2009

Lydon A, Beavery K, Newbery C, Wray J. Routine follow-up after treatment for ovarian cancer in the United Kingdom (UK): patient and health professional views. *European Journal of Oncology Nursing* 2009;**13**(5):336-43.

Parmar 1998

Parmar MK, Torri V, Stewart L. Extracting summary statistics to perform meta-analyses of the published literature for survival endpoints. *Statistics in Medicine* 1998;**17**(24):2815-34.

RevMan 2012 [Computer program]

The Nordic Cochrane Centre, The Cochrane Collaboration Review Manager (RevMan). Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012.

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Nama 2013

Nama V, Nordin A, Bryant A. Patient-Reported outcome measures for follow-up after gynaecological cancer treatment. *Cochrane Database of Systematic Reviews* 2013, Issue 1. Art. No: CD010299. [DOI: 10.1002/14651858.CD010299]

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ashing Giwa 2010	Compared health-related quality of life outcomes to survival in all participants treated for cervical cancer.
Chase 2010	Study on assessment techniques and significance of quality of life in women with gynaecologic cancer.
Greimel 2002	Identifies the predictors of quality of life.
Greimel 2003	Evaluates different questionnaires.
Greimel 2011	A study on quality of life in ovarian cancer survivors.
Gupta 2008	Study to identify the quality of life markers that predict survival.
Jordan 2012	Study to evaluate the parameters in QoL to target treatment in during follow up visits.
Klee 1997	Creation of population-based norms.
Lerman 2012	Randomised controlled trial comparing the benefit of mindfulness-based stress reduction in improving quality of life.
Seow 2011	Symptoms scores in palliative care setting.
Vistad 2011	Evaluates different follow-up schedules and techniques used in Norway.

APPENDICES

Appendix 1. MEDLINE search strategy

Medline Ovid

1. exp Genital Neoplasms, Female/
2. exp Ovarian Neoplasms/
3. ((gynecologic* or gynaecologic* or uter* or cervi* or ovar* or endometri* or vagina* or vulva* or fallopian*) adj5 (cancer* or tumor* or tumour* or neoplas* or malignan* or carcinoma* or adenocarcinoma*)).mp.
4. 1 or 2 or 3
5. "Outcome Assessment (Health Care)"/
6. "Quality of Life"/
7. (quality of life or QOL).mp.

8. 6 or 7
9. exp Questionnaires/
10. (questionnaire* or interview* or self-report* or measure* or instrument* or scale* or tool* or construct*).mp.
11. 9 or 10
12. 8 and 11
13. (patient* adj5 (report* or relate*) adj5 (outcome* or measure*)).mp.
14. 5 or 12 or 13
15. 4 and 14
16. randomized controlled trial.pt.
17. controlled clinical trial.pt.
18. randomized.ab.
19. placebo.ab.
20. clinical trials as topic.sh.
21. randomly.ab.
22. trial.ti.
23. exp Cohort Studies/
24. (cohort* or retrospective* or prospective*).mp.
25. Comparative Study/
26. (comparative or comparison).mp.
27. (case* and series).mp.
28. 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27
29. 15 and 28

key: mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier, sh=subject heading, pt=publication type, ab=abstract, ti=title

Appendix 2. EMBASE search strategy

Embase Ovid

1 exp female genital tract tumor/
2 ((gynecologic* or gynaecologic* or uter* or cervi* or ovar* or endometri* or vagina* or vulva* or fallopian*) adj5 (cancer* or tumor* or tumour* or neoplas* or malignan* or carcinoma* or adenocarcinoma*)).mp.
3 1 or 2
4 outcome assessment/
5 exp "quality of life"/
6 (quality of life or QOL).mp.
7 5 or 6
8 exp questionnaire/
9 (questionnaire* or interview* or self-report* or measure* or instrument* or scale* or tool* or construct*).mp.
10 8 or 9
11 7 and 10
12 (patient* adj5 (report* or relate*) adj5 (outcome* or measure*)).mp.
13 4 or 11 or 12
14 3 and 13
15 exp "controlled clinical trial (topic)"/
16 crossover procedure/
17 double-blind procedure/
18 randomized controlled trial/
19 single-blind procedure/
20 random*.mp.
21 factorial*.mp.
22 (crossover* or cross over* or cross-over*).mp.
23 placebo*.mp.
24 (double* adj blind*).mp.
25 (singl* adj blind*).mp.
26 assign*.mp.
27 allocat*.mp.
28 volunteer*.mp.

29 cohort analysis/
30 (cohort* or retrospective* or prospective*).ti,ab.
31 comparative study/
32 (comparative or comparison).ti,ab.
33 case study/
34 (case* adj5 series).ti,ab.
35 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34
36 14 and 35
37 (exp animal/ or nonhuman/ or exp animal experiment/) not human/
38 36 not 37

key: [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]

Appendix 3. CENTRAL search strategy

#1 MeSH descriptor: [Genital Neoplasms, Female] explode all trees
#2 MeSH descriptor: [Ovarian Neoplasms] explode all trees
#3 ((gynecologic* or gynaecologic* or uter* or cervi* or ovar* or endometri* or vagina* or vulva* or fallopian*) near/5 (cancer* or tumor* or tumour* or neoplas* or malignan* or carcinoma* or adenocarcinoma*))
#4 #1 or #2 or #3
#5 MeSH descriptor: [Outcome Assessment (Health Care)] this term only
#6 MeSH descriptor: [Quality of Life] this term only
#7 (quality of life or QOL)
#8 #6 or #7
#9 MeSH descriptor: [Questionnaires] explode all trees
#10 (questionnaire* or interview* or self-report* or measure* or instrument* or scale* or tool* or construct*)
#11 #9 or #10
#12 #8 and #11
#13 (patient* near/5 (report* or relate*) near/5 (outcome* or measure*))
#14 #5 or #12 or #13
#15 #4 and #14

WHAT'S NEW

Date	Event	Description
5 January 2022	Amended	No longer for update as any future update will require the development of a new protocol reflecting current Cochrane methodological criteria.

HISTORY

Protocol first published: Issue 1, 2013
Review first published: Issue 11, 2013

CONTRIBUTIONS OF AUTHORS

VN and AN searched for relevant studies and individually examined each potentially relevant full-text reference. AB drafted methodological and statistical sections of the review as well as various sections of the discussion. VN drafted clinical sections of the review and AN added expertise.

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources

- No sources of support provided

External sources

- Department of Health, UK

  NHS Cochrane Collaboration programme Grant Scheme CPG-10/4001/12

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We changed the title from patient related outcome measures to patient-reported outcome measures. Some use these terms are interchangable, but the most appropriate terms used in the majority of the literature is patient-reported outcome measures and hence the change in the title. We did not find any studies that met our inclusion criteria. In future updates of the review, we will employ the following methods:

Searching other resources

Unpublished and Grey literature

We will approach major co-operative trials groups active in this area.

Selection of studies

We will obtain copies of the full text of relevant references. Two review authors (VN, AN) will independently assess the eligibility of retrieved papers, resolving disagreements by discussion. We will document reasons for exclusion.

Data extraction and management

For included studies, we will abstract data as recommended in chapter 7 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will include data on the following:

- author, year of publication and journal citation (including language);
- country;
- setting;
- inclusion and exclusion criteria;
- study design, methodology;
- study population;
- total number enrolled.

Participant characteristics

- age;
- co-morbidities;
- primary or recurrent disease;
- primary treatment;
- subgroups of gynaecological cancers;
- adjuvant treatment received;
- intervention details: PROM or traditional follow-up.

Type of measures used (generic or disease-specific or combination)

- interview or self assessment;
- risk of bias in study (see Assessment of risk of bias in included studies);
- duration of follow-up;
- outcomes:overall survival (OS), recurrence/progression-free survival (PFS), quality of life (QoL):
  - for each outcome: Outcome definition (with diagnostic criteria if relevant);
  - unit of measurement (if relevant);
  - for scales: upper and lower limits, and whether high or low score is good;
  - results: Number of participants allocated to each intervention group;
  - for each outcome of interest: sample size; missing participants.

Data on outcomes will be extracted as below.

- For time-to-event (OS and recurrence/PFS) data, we will extract the log of the hazard ratio [log(HR)] and its standard error (SE) from study reports; if these are not reported, we will attempt to estimate them from other reported statistics using the methods of Parmar

1998. The HR compares the risk of death/recurrence among women followed up by PROM with the risk of death among women with conventional follow-up methods; hence a HR less than one indicated better survival in PROM.

- For dichotomous outcomes (number of participants who died or had disease recurrence if it was not reported as time-to-event data), we will extract the number of participants in each treatment arm who experienced the outcome of interest and the number of participants assessed at end point, in order to estimate a risk ratio (RR).
- For continuous outcomes (e.g. QoL), we will extract the final value and standard deviation (SD) of the outcome of interest and the number of participants assessed at end point in each treatment arm at the end of follow-up, in order to estimate the mean difference (if trials measured outcomes on the same scale) or standardised mean differences (if trials measured outcomes on different scales) between treatment arms, and its standard error.

We will extract both unadjusted and adjusted statistics, if reported.

Where possible, all data extracted will be those relevant to an intention-to-treat (ITT) analysis, in which all participants randomised are analysed in the groups to which they were assigned.

We will note the time points at which outcomes were collected and reported.

Two review authors (VN, AN) will abstract data independently onto a data abstraction form specially designed for the review, resolving any differences by discussion.

Assessment of risk of bias in included studies

We will assess the risk of bias in included randomised controlled trials (RCTs) in accordance with guidelines in the *Cochrane Handbook of Systematic Reviews of Interventions* using the Cochrane Collaboration's tool and the criteria specified in chapter 8 (Higgins 2011). This will include assessment of:

- sequence generation;
- allocation concealment;
- blinding (of participants, healthcare providers and outcome assessors);
- incomplete outcome data:
  - we will record the proportion of participants whose outcomes were not reported at the end of the study. We will note if loss to follow-up was not reported. Satisfactory level of loss to follow-up for each outcome is coded as:
    - yes, if fewer than 20% of participants were lost to follow-up and reasons for loss to follow-up were similar in both treatment arms;
    - no, if more than 20% of participants were lost to follow-up or reasons for loss to follow-up differed between treatment arms;
    - unclear if loss to follow-up was not reported.
- selective reporting of outcomes;
- other possible sources of bias.

If we do not identify any included RCTs and include relevant observational studies that meet the inclusion criteria, we will assess risk of bias in accordance with the following additional criteria:

Cohort selection.

1. Were relevant details of criteria for assignment of participants to interventions provided?
   - Low risk of bias (e.g. yes).
   - High risk of bias (e.g. no).
   - Unclear risk of bias.
2. Was the group of women who received the experimental intervention (PROM intervention) representative?
   - Low risk of bias (e.g. yes, as they were representative of women with gynaecological cancer).
   - High risk of bias (e.g. no, as group of participants was selected).
   - Unclear risk of bias (e.g. selection of group was not described).
3. Was the group of women who received the comparison intervention (standard follow-up) representative?
   - Low risk of bias (e.g. yes, as drawn from the same population as the experimental cohort).
   - High risk of bias (e.g. no, as drawn from a different source).
   - Unclear risk of bias (e.g. selection of group was not described).

We will assess cohort comparability on the basis of study design or analysis of cohort differences:

Were there differences between the two groups or were differences controlled for, in particular with reference to age, FIGO (International Federation of Gynecology and Obstetrics) stage, histological cell type, and grade of tumour, treatment modalities?

- Low risk of bias, if at least two of these characteristics were reported, and any reported differences were controlled for;
- High risk of bias, if the two groups differed, and differences were not controlled for;
- Unclear risk of bias, if fewer than two of these characteristics were reported, even if there were no other differences between the groups, and other characteristics were controlled for.

Two review authors (VN, AN) will apply the 'Risk of bias' tool independently and will resolve differences by discussion or by appeal to a third review author (AB). We will present results in both a risk of bias graph and a risk of bias summary.

Measures of treatment effect

We will use the following measures of the effect of treatment:

- for time-to-event data, we will use the HR;
- for dichotomous outcomes, we will use the risk ratio;
- for continuous outcomes, we will use the mean difference between treatment arms.

Dealing with missing data

We will not impute missing outcome data for any of the outcomes. If data are missing or only imputed data are reported we will contact trial authors to request data on the outcomes only among participants who were assessed.

Assessment of heterogeneity

We will assess heterogeneity between studies by visual inspection of forest plots, by estimation of the percentage heterogeneity between trials which cannot be ascribed to sampling variation (Higgins 2003), by a formal statistical test of the significance of the heterogeneity (Deeks 2001) and, if possible, by subgroup analyses (Subgroup analysis and investigation of heterogeneity). If there is evidence of substantial heterogeneity, we will investigate and report the possible reasons for this.

Assessment of reporting biases

We will generate funnel plots corresponding to meta-analysis of the primary outcome if more than 10 studies were selected to assess the potential for small study effects. When there is evidence of small-study effects, we will consider publication bias as only one of a number of possible explanations.

Data synthesis

If sufficient, clinically similar studies are available, we will pool the results in meta-analyses and report the 95% confidence interval (CI) of the pooled estimate.

- For time-to-event data, we will pool HRs using the generic inverse variance facility of Review Manager 5 (RevMan 2012).
- For any dichotomous outcomes, we will calculate the risk ratio for each study and will then pool these.
- For continuous outcomes, we will pool the mean differences between the treatment arms at the end of follow-up if all trials measured the outcome on the same scale, otherwise we will pool standardised mean differences.

We will use random-effects models with inverse variance weighting for all meta-analyses (Dersimonian 1986).

Subgroup analysis and investigation of heterogeneity

Where possible, we will perform subgroup analyses, grouping the studies by:

- tumour site;
- treatment modalities.

Sensitivity analysis

We will carry out a sensitivity analysis excluding studies at high risk of bias.

INDEX TERMS

Medical Subject Headings (MeSH)

Follow-Up Studies; Genital Neoplasms, Female [*therapy]; *Outcome Assessment, Health Care; *Self Report

MeSH check words

Female; Humans