Survival benefits from follow-up of patients with lung cancer: a systematic review and meta-analysis

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CRD summary
The review concluded that some benefit was found from intensive follow-up strategies but due to potential for bias in the included studies the results should be interpreted with caution. Given the limited evidence base and limitations in the analytical methods the authors’ caution is warranted.

Authors' objectives
To determine the efficacy of after treatment follow-up strategies on survival and quality of life in patients with lung cancer.

Searching
MEDLINE, EMBASE, PsycINFO, CINAHL, British Nursing Index, The Cochrane Library, Current Controlled Trials, NIHR and NRR were searched up to August 2008. Search terms were reported. Reference lists were checked. It appeared that articles not in English were excluded once studies had been retrieved for full-text review.

Study selection
Randomised controlled trials, quasi-experimental and observational studies with a primary focus on follow-up interventions in adult patients (older than 18 years) following treatment for primary lung cancer and that reported at least one primary outcome (overall survival and asymptomatic survival) were eligible for inclusion. Secondary outcomes included quality of life and time to detection of recurrence. Follow-up was defined as care after treatment that was planned and multifaceted (programmes that included multiple types of assessment, not just individual types of imaging or tests, and ideally included symptom management, education, health promotion and psychosocial support).

Studies examined survival after follow-up regimes of varying intensity and time to symptomatic or asymptomatic recurrence. All cancer histological types – small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) – all treatment options – surgery, radiotherapy and/or chemotherapy – and all stages of lung cancer were included. Studies included patients with disease stages deemed appropriate for curative intent treatment (I to III). The median age range was 58 to 68 years.

The authors did not state how many reviewers were involved in the selection of studies.

Assessment of study quality
Methodological quality was assessed independently by two reviewers and discrepancies were resolved by discussion. Generalisability, reliability, validity, definition validity, theoretical basis and clinical versus statistical significance were considered.

Data extraction
Two reviewers independently extracted data to enable calculation of hazard ratios (HRs) and 95% confidence intervals (CIs). Methods used to estimate hazard ratios were reported in the paper.

Methods of synthesis
Pooled estimates were calculated using a fixed-effect model; Peto odds ratio (OR) was used for hazard ratio. Statistical heterogeneity was investigated using $X^2$ and $I^2$. Subgroup analyses were performed based on treatment intent (curative intent treatment included surgery alone or multimodal treatment and palliative treatment included chemotherapy and radiotherapy).

Results of the review
Nine studies (eight observational and one RCT) were included in the review (1,669 participants, range 75 to 358). The RCT failed to report how the randomisation sequence was generated and whether treatment allocation was concealed.
Seven of the observational studies were retrospective database cohort designs. The one prospective cohort study was considered to be relatively robust.

No significant difference was found between intensive follow-up and less intensive follow-up on overall survival for NSCLC (HR 0.83, 95% CI 0.66 to 1.05; four studies) and SCLC and advanced NSCLC (HR 0.86, 95% CI 0.65 to 1.13; two studies) subgroups. There was evidence of substantial heterogeneity for SCLC and advanced NSCLC subgroup analysis ($I^2=65\%$).

Asymptomatic recurrence was associated with a significantly longer survival time than symptomatic recurrence in patients with NSCLC after curative intent (OR 0.61, 95% CI 0.50 to 0.74; four studies); this outcome was not a predefined outcome of interest.

Quality of life outcomes were reported only in the RCT. A significant difference was found in favour of nurse-led (intensive) follow-up compared with standard care on measures of quality of life (dyspnoea less severe at three months, $p=0.03$; improved emotional functioning, $p=0.03$; less peripheral neuropathy at 12 months, $p=0.05$). No significant difference was found between intensive and less intensive follow-up for time to detection of recurrence (three studies) after curative treatment.

**Authors’ conclusions**

Some benefit was found from intensive follow-up strategies but due to potential for bias in the included studies the results should be interpreted with caution.

**CRD commentary**

The review question and inclusion criteria were somewhat broad and this was reflected in the heterogeneity found in the study designs, interventions and populations included in the review. The comprehensive literature search was initially unrestricted by language but it appeared that inclusion in the review was limited to studies in English; this raised the possibilities of language bias and omission of relevant data. Methods were used to minimise error and bias during data extraction and quality assessment; whether similar procedures were used during study selection was unclear. The methodological quality of the studies was assessed and some aspects were reported; the overall quality of the included studies was low.

The Peto method can be used to combine time-to-event data but may give biased answers where there is a lack of balance in treatment allocation within the individual studies. The authors acknowledged as a potential source of heterogeneity that the date from which survival analyses were calculated differed across studies due to variability in follow-up regimes. The authors also noted that in some studies the intensive programme resembled routine practice when compared with international guidelines.

The authors’ conclusion that these results should be interpreted with caution seems reasonable.

**Implications of the review for practice and research**

**Practice:** The authors stated that guidelines should be used to ensure regular contact with patients and carers is maintained and further treatment and symptom management initiated where required.

**Research:** The authors stated that well-designed randomised controlled trials with clearly defined patient groups and appropriate end-points were needed to confirm findings. Future research should consider patient and carer-centered outcomes to investigate the impact of follow-up regimes on living with lung cancer and psychological well-being. Additional research was suggested to further understanding of patients’ views of more intensive or invasive follow-up programmes or those using scanning techniques such as fluorodeoxyglucose-position emission tomography. Alternative approaches to follow-up should be developed for different disease subgroups and patient choice and these programmes should be evaluated through well-designed RCTs.

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