Author/s:
Edbrooke, L;Denehy, L;Patrick, C;Tuffaha, H

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Cost-effectiveness analysis of home-based rehabilitation compared to usual care for people with inoperable lung cancer

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Edbrooke Lara (Orcid ID: 0000-0002-4149-5578)

Title: Cost-effectiveness analysis of home-based rehabilitation compared to usual care for people with inoperable lung cancer.

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Authors: Lara Edbrooke[a,b,*], Linda Denehy[b,c] , Cameron Patrick[d] and Haitham Tuffaha[e].

Affiliations:

[a]Department of Physiotherapy, The University of Melbourne, Melbourne, Victoria, Australia

[b]Allied Health Department, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia

[c]Melbourne School of Health Sciences, The University of Melbourne, Melbourne, Victoria, Australia

[d]Statistical Consulting Centre, The University of Melbourne, Melbourne, Victoria, Australia

[e]Centre for the Business and Economics of Health, University of Queensland, Brisbane, Queensland, Australia

***Corresponding author:**

Lara Edbrooke

Address: Level 7, Alan Gilbert Building, 161 Barry St, Carlton, Victoria, Australia, 3010.

Email: larae@unimelb.edu.au

Phone: +61 3 400 830 945

Twitter handle: @LaraEdbrooke

ORCID: 0000-0002-4149-5578

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest statement

The authors report no conflicts of interest.

Author contributions

We confirm that all authors have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, and (2) drafting the article or revising it critically for important intellectual content. All authors have approved the final version which has been submitted.

Title: Cost-effectiveness analysis of home-based rehabilitation compared to usual care for people with inoperable lung cancer.

Abstract

Objective: Few economic evaluations of lung cancer rehabilitation exist. The aim of this study was to assess the cost-effectiveness of providing home-based rehabilitation for inoperable lung cancer.

Methods: A cost-utility analysis alongside a randomized controlled trial of rehabilitation compared with usual care. The primary outcome was quality-adjusted life years (QALYs) gained. The incremental cost-effectiveness ratio (ICER (95% CI)) and the net monetary benefit are reported. Value of Information (VOI) analysis assessed the need/value of more research.
Results: Seventy participants (34 intervention, 36 usual care), average (SD) age 63.0 (12.0) years, 32 (45.7%) stage IV. The average intervention cost was AU$3421 (AU$5352 usual care) and effect (QALY) was 0.30 (0.31 usual care). The ICER was AU$228,197 (-1,173,194 to 1,101,450) per QALY gained. The net monetary benefit was AU$1,508, favouring the intervention. The probability that the intervention was more cost-effective than usual care, at a willingness to pay threshold of AU$50,000, was 75%. VOI analysis showed that additional research to resolve decision uncertainty is potentially worthwhile.
Conclusion: A high degree of uncertainty exists regarding the cost-effectiveness of lung cancer rehabilitation. Further RCTs, powered for economic evaluations and utilising rehabilitation sensitive outcomes, are required to support translation of evidence into clinical practice.

Keywords: lung cancer, cost-effectiveness, rehabilitation, exercise, symptom management.

1. Introduction

Over two million people are diagnosed annually worldwide with lung cancer (Bray et al., 2018). Three-quarters of diagnoses occur once the disease has already spread beyond the primary site (National Comprehensive Cancer Network, 2018). Progress in the areas of lung cancer detection and medical treatment have contributed to gradual improvements in survival. Across all stages of lung cancer the five-year relative survival in Australia is now estimated at 19% (Australian Institute of Health and Welfare, 2019). Lung cancer is associated with a complex cluster and trajectory of symptoms (Cooley, 2000; Cooley, Short, & Moriarty, 2002; Sung et al., 2017), poor health-related quality of life (HRQoL) (Larsson, Ljung, & Johansson, 2012; Lee et al., 2011) and functional decline (Granger et al., 2014). These factors contribute to a high level of burden on patients (Fitzmaurice et al., 2017), their care givers (Borges et al., 2017; Seo & Park, 2019) and the healthcare system. In Australia, the second most common diagnosis associated with cancer-related palliative care hospital admissions is lung cancer (Australian Institute of Health and Welfare, 2019). Of all cancers lung cancer is ranked third, behind breast and colorectal cancer, in terms of direct costs to the healthcare system, costing a total of AU$0.6 billion annually (Goldsbury et al., 2018). Average case costs, associated with Medicare Benefits Schedule and Pharmaceutical Benefits Scheme items and hospital-based care, are AU$51,944 (Goldsbury et al., 2020).

With improvements in survival, greater attention to survival quality is essential. Rehabilitation interventions, including exercise, delivered at all stages along the cancer treatment continuum, are effective in improving cancer-related fatigue (Mustian et al., 2017), HRQoL, physical function (Buffart et al., 2017; Mishra et al., 2012) and minimizing postoperative complications (Assouline et al., 2020). These findings are well established in breast, prostate and colorectal populations and supported by emerging higher-quality evidence in lung cancer (Cavalheri et al., 2019; Cavalheri & Granger, 2017; Peddle-McIntyre et al., 2019; Rosero et al., 2019; Singh, Spence, Steele, Hayes, & Toohey, 2020; Zhou, Woo, & Larson, 2020).

Observational studies also demonstrate improved survival in people with higher levels of physical activity, including those with lung cancer (Cormie, Zopf, Zhang, & Schmitz, 2017; Jones et al., 2010). Current guidelines for people with cancer recommend regular exercise and physical activity to improve outcomes for all cancer types (Campbell et al., 2019; Cormie et al., 2018; Hayes, Newton, Spence, & Galvão, 2019). Despite twenty-one high-quality published oncology guidelines recommending rehabilitation and exercise, a significant gap still exists between these recommendations and clinical practice (Stout, Santa Mina, Lyons, Robb, & Silver, 2020). Barriers to translating evidence into practice may be reduced by providing those making decisions regarding allocation of healthcare resources with further evidence regarding the cost-effectiveness of rehabilitation interventions.

The majority of health economic evaluations of cancer rehabilitation interventions involve exercise alone and were conducted in breast cancer, with mixed findings (Khan, Mazuquin, Canaway, Petrou, & Bruce, 2019). Trial-based economic evaluations of multidimensional rehabilitation interventions compared to usual care, conducted in breast, head and neck, colon and cervical cancers, report all included studies demonstrate cost effectiveness ratios supporting the use of rehabilitation in cancer (Mewes, Steuten, Ijzerman, & van Harten, 2012). Rehabilitation trials in lung cancer have not included economic evaluations, resulting in scant evidence regarding the cost effectiveness of these interventions. Ha and colleagues modelled the cost-effectiveness of the 'Lifestyle Intervention and Independence for Elders' exercise program in patients with stage I-IIIA lung cancer following curative treatment completion (Ha et al., 2020). The intervention was cost-effective from an organisational perspective, but not from a societal perspective when costs such as lost productivity and transportation were included. The aim of this study was to assess the cost-effectiveness of a home-based rehabilitation program, involving exercise, symptom management and behaviour change, during and following treatment for inoperable lung cancer, compared to usual care.

2. Methods

2.1. RCT details and results

The economic evaluation was based on patient level data from a previously reported assessor-blinded, multi-site randomized controlled trial (ANZCTRN 12614001268639) of home-based rehabilitation, compared to usual care, for people with non-small cell lung cancer (NSCLC) (Edbrooke et al., 2019; Edbrooke et al., 2017). Briefly, the trial was conducted at three tertiary care hospitals in Melbourne, Australia. Multi-site ethical approval was received 26.6.14 (HREC/14/PMCC/27) and all participants provided written and informed consent. Eligible patients were adults with inoperable disease who were scheduled to receive or within four weeks of commencing active medical treatment to the primary tumour; an Eastern Co-operative Oncology Group Performance Status of <u><</u>2 (Oken et al., 1982); a Clinical Frailty Scale score of <7 (Rockwood et al., 2005); and a clinician-rated life expectancy of >6 months. Patients were excluded if they were non-English speaking; had met guidelines for physical activity over the past month (performed <u>></u>150 minutes of moderate-intensity physical activity each week); had comorbidities or bony metastases that prevented safe participation in unsupervised land-based exercise; had a concurrent or one-year history of active treatment for another malignancy; had recurrent disease with treatment for the primary disease <6 months prior to trial screening; or had currently unstable cognitive or psychiatric disorders. The intervention comprised eight weeks of individualised aerobic and resistance exercise, prescribed at moderate-intensity, combined with symptom management and behaviour change support. The intervention was delivered weekly using a combination of home-visits and telephone calls. Initial exercise prescription, performed by an experienced physiotherapist, occurred in the participant's home. Symptom management telephone support was provided by an experienced oncology nurse, with the Edmonton Symptom Assessment Scale used to guide sessions (Philip, Smith, Craft, & Lickiss, 1998). Following the eight-week program the intervention moved into a maintenance phase involving physiotherapy support alone. Usual care did not involve routine referral to an exercise professional or symptom management support during the trial recruitment period.

Outcomes, from the 92 participants recruited to the trial, were assessed at recruitment (baseline), nine weeks and six months post recruitment. The primary outcome was the between-group change in functional exercise capacity, measured by the six-minute walk test (6MWT), from baseline to nine-week follow-up. Secondary outcomes included survival and additional patient-reported outcomes including HRQoL using the Functional Assessment of Cancer Therapy-Lung (FACT-L) and the Assessment of Quality of Life (version one).

Key trial findings included no significant between-group differences for the 6MWT at either follow-up time point (Edbrooke et al., 2019). There were no significant between-group differences for patient-reported outcomes at nine weeks. However, at six months HRQoL (FACT-L), symptom severity and subscales of the exercise motivation questionnaire demonstrated significant between-group differences favouring the intervention group. Qualitative analyses revealed the intervention was well received by participants (Edbrooke, Denehy, Granger, Kapp, & Aranda, 2020).

2.2. Economic Evaluation

Reporting conforms to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement (Husereau et al., 2013). A patient-level health economic evaluation, from the perspective of the Australian healthcare-payer, of the costs associated with providing the six-month rehabilitation intervention compared to usual care was undertaken. Methods for data imputation due to missing data followed the same principles utilised for imputing data in the randomized controlled trial analysis of patient-reported clinical outcomes. A modified intention-to-treat analysis was conducted to avoid imputing data for deceased participants (Biering, Hjollund, & Frydenberg, 2015). The R multiple imputation for chained equations

(MICE) package was used to create 50 imputed datasets. Further details of the multiple imputation statistical analysis plan are provided in Appendix 1.

2.3. Health Economic Outcome – Quality Adjusted Life Years (QALYs)

The Assessment of Quality of Life (AQoL) questionnaire, version 1, was used to calculate QALYs (Hawthorne, Richardson, & Osborne, 1999). QALYs are a common measure of disease burden which represent life lived both in terms of quantity and quality. Higher QALYs are representative of a better HRQoL. The AQoL consists of 15 items representing 5 domains: illness, independent living, social relationships, physical senses and psychological well-being. A utility index, based on values from the Australian general population, is also derived from the AQoL domains, excluding the illness domain. Utility scores range from -0.04 (worst possible HRQoL, where 0.00 represents a HRQoL state which corresponds to death) to 1.00 (best possible HRQoL). It is a valid and reliable measure of HRQoL in lung cancer and has been found to be predictive of six-month survival in the inoperable population (Manser et al., 2006). QALYs, using the area under the curve method, during the six-month trial were determined for each participant by calculating the average utility score between outcome assessments multiplied by the time spent in that health state.

2.4. Measuring trial costs and healthcare utilisation

Resources associated with delivering the intervention and usual care were recorded during the trial and were calculated per participant. Intervention costs included the total time of all home visits performed by the physiotherapist and the total time of all telephone calls made by the physiotherapist and the nurse during the six months of the trial. A small fee was also included for the costs associated with printing the exercise diaries and symptom self-management booklets that intervention participants were provided with during the initial intervention session. As intervention participants were loaned physical activity monitors (pedometers) and free-weights during the trial, or used their own resources, these costs were not included in the total cost of delivering the intervention. Usual care costs included the total time of all telephone calls made by trial staff who performed monthly attention phone calls during the six months of the trial.

At nine weeks, and four and six months post-recruitment participants completed a questionnaire regarding their healthcare utilisation. The questionnaire was designed by the trial investigators specifically for use in the trial, following consultation with a senior health economist. Participants were asked to recall details of their healthcare utilisation since their recruitment to the trial or previous assessment (depending on the time point). This included information regarding the number of visits they had made to their general practitioner, the number of hospital admissions and the average number of nights stay associated with these hospital admissions. Timepoints for assessment were chosen to reduce potential bias associated with participant recall of healthcare utilisation (Bhandari & Wagner, 2006). Blinded assessors completed all assessments. The nine-week and six-month assessments were completed in person as this coincided with trial appointments for other outcome measures and the four-month assessment was conducted by telephone.

Resources consumed were priced using industry salaries in Australia and other national sources and reports. All costs are reported in Australian dollars (AU$). As the evaluation involved a six-month time period discounting was not applied. All staff were renumerated according to the University of Melbourne casual pay scales (The University of Melbourne, 2015) as outlined in Table 1. Two assumptions were made when calculating healthcare utilisation costs. Firstly, where costs were associated with general practitioner visits MBS Item 36 was applied (Department of Health, 2017). This item, involving a consultation of at least 20 minutes duration, was deemed appropriate given the complex nature of the trial participants who had inoperable lung cancer and often multiple co-morbidities. Secondly, overnight hospital admissions were assigned a cost of AU$1000 per day. This was based on the national average cost for a public hospital separation being estimated as AU$5,323

(Independent Hospital Pricing Authority, 2018) and the average length of hospital stay being five nights (Independent Hospital Pricing Authority, 2018).

2.5. Cost-effectiveness analysis

Two summary measures, the incremental cost-effectiveness ratio (ICER) and the net monetary benefit were calculated to assess the cost-effectiveness of the intervention. The average costs and the average effects (QALYs) were compared between the intervention and usual care groups to calculate the ICER. The ICER is the ratio of the between-group difference in costs (the numerator) and difference in effects (the denominator). The threshold of willingness to pay was set a priori at AU$50,000 per QALY; this is an implied threshold that is commonly used within the Australian setting (Bertram et al., 2016). The net monetary benefit was calculated by multiplying the between-group difference in effect by the threshold per QALY gain and subtracting the between-group difference in cost. A positive net benefit indicates that the intervention is cost-effective.

2.6. Uncertainty analysis

To characterise the uncertainty around the ICER non-parametric bootstrapping, from random sampling of the 70 intervention and usual care participants, was performed to generate 1000 cost and outcome pairs. These were graphed on the cost-effectiveness plane. Acceptability curves were plotted to depict the likelihood of the intervention being cost-effective given the willingness to pay per QALY. Value of information (VOI) analysis was conducted using the sample from the bootstrapping. VOI analysis quantifies the uncertainty in the results of the economic evaluation and informs if a decision can be made (i.e., to implement or reject the intervention) based on the results, or if additional evidence is required to reduce decision uncertainty (e.g., a larger RCT). This approach considers the probability of the intervention being cost effective, the consequences of uncertainty (i.e., the cost of making a wrong decision), and the size of the population affected by the decision to implement the intervention. We estimated the Australian lung cancer population size to be 7875 people over 5 years, based on the 5-year prevalence of lung cancer being 18,751, and conservatively assuming 42% are diagnosed with advanced lung cancer (Australian Institute of Health and Welfare, 2019). Microsoft Excel (2016) was used for all analyses.

3. Results

Seventy of the 92 participants recruited to the trial had complete data sets or met the criteria for data imputation and were included in the cost-effectiveness analysis. Flow of participants through the trial and completion of the AQoL and health economic questionnaire is shown in Figure 1. The main reasons for missing data, which did not differ significantly between groups, were participant death or withdrawal from the trial. Baseline demographic and clinical characteristics of participants (34 intervention, 36 usual care) are reported in Table 2. Participants were an average (SD) age of 63.0 (12.0) years, 38 (54.3%) male, 32 (45.7%) had stage IV disease and were receiving palliative intent treatment: primarily chemotherapy +/- radiotherapy (15 (21.4%)) or targeted therapy (8 (11.4%)). There was an average (SD) of 4.3 (17.6) days between trial randomisation and commencement of active treatment for lung cancer. No significant between-group differences were found with respect to participant demographic and clinical characteristics at baseline.

Cost-effectiveness analysis findings are presented in Table 3. Over the six months of the trial the average costs in the intervention group were AU$3421, compared with AU$5352 in the usual care group. This difference was largely due to fewer hospital admission costs in the intervention group. The average effect (QALY) was 0.30 in the intervention group compared to 0.31 in the usual care group. The ICER was AU$228,197 per QALY gained. The net monetary benefit was AU$1,508, suggesting the intervention is cost-effective. The results are most sensitive to the assumptions regarding in-patient hospital stay. However, even with a 50% reduction in hospitalisation cost per night, the intervention remains cost effective with an incremental net monetary benefit of $323.11. Figure 2 demonstrates a high level of uncertainty around the ICER with the majority of bootstrapped ICERs falling within the south-west and south-east quadrants. This distribution indicated that the intervention was commonly either less costly and less effective (south-west quadrant) or less costly and more effective (south-east quadrant) than usual care. The probability that the intervention was more cost-effective than usual care at the threshold willingness to pay per QALY gained of AU$50,000 was 75% (Figure 3). Value of Information analysis estimates that the expected monetary benefit of additional research to resolve this decision uncertainty (i.e., 75% probability of being cost effective or 25% margin of error), would be $370 per patient. Scaling this up to the population size (i.e., 7,875 over 5 years), the expected value of future research would be $2.9 million. This figure likely exceeds the cost of a future study, indicating that additional research is potentially worthwhile.

4. Discussion

This evaluation utilised two summary measures, the ICER and the net monetary benefit, to assess the cost-effectiveness at a patient level of home-based rehabilitation compared to usual care for people with inoperable lung cancer during and following treatment. At over AU$220,000, the ICER was well above the threshold willingness to pay set, mainly due to the small between-group difference in QALYs gained. The intervention had a net monetary benefit of approximately AU$1500 per participant with a 75% probability of being cost effective compared to usual care. Cost savings were largely attributable to the reduced number of hospital admissions observed in the intervention group compared to the usual care group during the six months of the trial. Being solely home-based the intervention was relatively low cost to deliver compared to supervised exercise interventions in other cancer populations (Edmunds et al., 2020; Kampshoff et al., 2018; van Dongen et al., 2019). The cost-effectiveness findings are in agreeance with findings from the clinical trial in which between-group differences, favouring the intervention group, were statistically significant for symptom severity and health-related quality of life and clinically significant for functional exercise capacity at six-month follow-up. It is likely that improvements in these clinical outcomes may be associated with fewer hospital admissions.

Study findings should be interpreted with caution given the large degree of uncertainty which exists around the incremental cost-effectiveness ratios reported and the limited number of other lung cancer rehabilitation cost-effectiveness analyses, precluding an evidence synthesis. At a willingness to pay (WTP) threshold of US$100,000/QALY gained, the 'Lifestyle Intervention and Independence for Elders' exercise program in patients with stage I-IIIA lung cancer following curative treatment completion was cost-effective from an organisational perspective with an ICER of US$79,504/QALY and 71% likelihood of cost effectiveness. However, potential issues with the modelling used in this study exist. Estimates of the probability of increasing exercise and study attrition were based on findings in breast cancer survivors and effectiveness estimates were derived from a program for older adults without cancer (Ha et al., 2020).

Economic evaluation findings of exercise interventions in other cancer types, such as breast cancer, may not be generalisable to lung cancer as multiple factors may differentially impact on exercise participation. These factors include demographic characteristics (such as the number and type of co-morbidities (Fowler et al., 2020)), level of social support and ability to access services (Lung Foundation Australia, 2018), symptom profiles and levels of symptom interference (Cheville et al., 2011), types of surgical or medical treatments received and presence of sarcopenia or cancer cachexia (Fearon et al., 2011). A systematic review of studies during and following breast cancer treatment, reported high-quality of included studies with three of the seven included studies found to be cost-effective compared to usual care. Study interventions included aerobic exercise or physiotherapy interventions aiming to restore upper limb function post-operatively (Khan et al., 2019). Cost-effectiveness of exercise compared with usual care in prostate cancer survivors who had received androgen-deprivation therapy and radiotherapy treatments (Edmunds et al., 2020) and following autologous stem cell transplant (van Dongen et al., 2019) concluded the interventions were not cost-effective. When comparing cost-effectiveness according to intensity of exercise prescribed, 12 weeks of high-intensity interval training was cost-effective when compared to moderate-to-low intensity training in a sample of mixed cancer survivors following chemoradiotherapy. This finding was largely attributable to the reduced healthcare costs in the high-intensity interval training group (Kampshoff et al., 2018). Several published protocols of ongoing RCTs involving exercise include health economic evaluations and these will add to the existing evidence base and allow an evidence synthesis. These include home-based exercise for patients with metastatic cancer being managed with targeted therapy (Joly et al., 2020) and two trials of prehabilitation (prior to surgery); high-intensity interval training in lung and oesophageal cancer (Sheill et al., 2020) and a multimodal program (exercise, nutrition, smoking cessation and cognitive behavioural therapy) in lung cancer (Barberan-Garcia et al., 2020).

There are several limitations of this economic analysis. The AQoL, a generic HRQoL questionnaire, was used to derive utility scores. Between-group differences in AQoL utility scores were not statistically significant at any time point during the trial. These findings are contrasted by those of the disease-specific quality of life questionnaire used in the trial, the Functional Assessment of Cancer Therapy – Lung (FACT-L). Using the FACT-L, intervention participants reported clinically and statistically significant improvements in HRQoL compared to the usual care group at six-months. These findings highlight the need for careful selection of outcomes; the trial was not powered to detect changes in HRQoL and the AQoL may not be sensitive to detecting changes associated with a rehabilitation intervention in lung cancer. Using a disease specific HRQoL questionnaire, such as the recently published FACT-8D algorithm, may have resulted in a difference in QALYs in favour of the intervention which was not found using the generic questionnaire (King et al., 2021). In addition, there are several aspects of this analysis which do not conform with the ISPOR good research practices task force report on cost-effectiveness analysis alongside clinical trials (Ramsey et al., 2015). We did not measure healthcare utilisation at baseline, therefore there is a possibility that differences between groups existed prior to trial recruitment. The small sample size meant that the trial was underpowered for economic analyses and did not permit analysis of subgroups, such as palliative versus radical treatment intent. However, this issue was addressed using VOI analysis to know if the intervention should be implemented given the uncertainty in the results. A larger RCT is potentially worthwhile to resolve this uncertainty. The trial involved limited duration follow-up with no modelling of outcomes beyond the trial. Given one quarter of the sample lived rurally we relied on patient recall of healthcare resource usage between assessment timepoints as many patients were admitted to hospitals other than the three recruitment hospitals.

5. Conclusion

This study is one of the first to investigate the cost-effectiveness of lung cancer rehabilitation. Patient-level analysis indicated that home-based rehabilitation during and following inoperable lung cancer treatment had a 75% likelihood of being cost-effective compared to usual care. However, the high degree of uncertainty associated with the findings and lack of other evidence in the area mean that further research is required and potentially worthwhile (or cost-effective). Our findings warrant further trials, powered for economic outcomes and utilising outcomes sensitive to rehabilitation interventions, to support the introduction of home-based lung cancer rehabilitation into standard care pathways.

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Tables

Table 1. Trial and healthcare utilisation costs

Item	**Value (AU$)**
Delivery of the intervention - physiotherapy	Other Academic activity - $49.32/hour†
Delivery of the intervention - nursing	Research Assistant Grade 1 - $42.61/hour
Printing of intervention exercise diary and symptom self-management booklet	$5.00 per participant
Delivery of the usual care telephone calls	$42.61/hour
Healthcare utilisation	
General practitioner visits	MBS Item 36 '*GP Professional attendance by a general practitioner at consulting rooms (other than a service to which another item in the table applies), lasting at least 20 minutes*' - $75.00 per visit
Hospital admissions	$1000 per night

Footnote: †this classification was used as it approximated the renumeration these staff received when working clinically as physiotherapists within the Victorian public hospital system at the time of the trial.

Table 2. Participant characteristics at baseline

	Intervention group (n=34)	Usual care (n=36)	p-value
Age, years (median IQR)	65.0 (54.0,76.0)	63.0 (57.5, 70.5)	0.724
Sex (male), n (%)	16 (47.1)	22 (61.1)	0.347
BMI (kg/m^2)	26.4 (4.5)	26.5 (4.4)	0.963
Histological type			
Squamous	6 (79.4)	8 (22.2)	0.227
Adenocarcinoma	27 (81.8)	24 (66.7)	
Other - large cell, adenosquamous, NOS, unknown	1 (2.9)	4 (11.2)	
EGFR or ALK mutation, n (%) 'yes'	9 (37.5)	7 (29.2)	0.508
	n=24 tested	n= 24 tested	
Disease stage			
IA/IB	2 (5.8)	1 (2.8)	0.76
IIIA	9 (26.5)	13 (36.1)	
IIIB	4 (11.8)	3 (8.3)	

IV	15 (44.1)	17 (47.2)	
Recurrent	4 (11.8)	2 (5.6)	
Metastases to brain	3 (8.8)	4 (11.1)	
Metastases to bone	4 (11.8)	4 (11.1)	
Time since diagnosis (days)	37.5 (22.0,55.0)	43.0 (29.0,55.0)	0.389
ECOG-PS, patient rated			
0	11 (32.4)	10 (27.8)	0.408
1	22 (64.7)	22 (61.1)	
2	1 (2.9)	4 (11.1)	
Clinical Frailty Scale score			
1-3	8 (23.5)	8 (22.2)	0.586
4	14 (41.2)	18 (50)	
5-6	12 (35.3)	10 (27.8)	
Colinet Co-morbidity Score	8.0 (7.0, 9.0)	8.0 (7.0, 9.0)	0.318
COPD	15 (44.1)	13 (36.1)	0.494

Cachexic at baseline n (%) 'yes'	11 (32.4)	13 (36.1)	0.937
Time from randomisation to commencing treatment (days)	5.1 (18.6)	3.5 (16.9)	0.659
Treatment intent at randomisation			
Radical	18 (52.9)	20 (55.6)	1
Palliative	16 (47.1)	16 (44.4)	
Intended/current anticancer treatment at baseline			
Radical chemoradiation	14 (41.2)	15 (41.7)	
Palliative chemotherapy	6 (17.7)	6 (16.7)	
Palliative chemotherapy and radiotherapy	1 (2.9)	2 (5.6)	
Targeted therapy	3 (8.8)	5 (13.9)	
Systemic clinical trial treatment	2 (5.9)	3 (8.3)	
Radical radiotherapy	2 (5.9)	2 (5.6)	
Stereotactic radiotherapy	2 (5.9)	2 (5.6)	
Palliative radiotherapy	3 (8.8)	0	
Palliative radiotherapy and targeted therapy	1 (2.9)	0	

Induction chemotherapy and surgical resection	0	1 (2.8)	
Prior treatment to metastatic sites			
Resection of cerebral metastasis	1 (2.9)	1 (2.8)	
WBRT/SABR for cerebral metastasis	2 (5.9)	0	
Resection of cerebral metastasis and WBRT/SABR	0	3 (8.3)	
Surgical spinal fixation	0	1 (2.8)	
Smoking history			
Never smoker	7 (20.6)	6 (16.7)	0.875
Ex-smoker	19 (55.9)	20 (55.6)	
Current smoker	8 (23.5)	10 (27.8)	
Smoking history pack years	30.0 (20.0, 44.0) n=27	30.0 (18.5, 51.0) n=30	0.968
Social situation			
Home alone independent	7 (20.6)	3 (8.3)	0.281
Home with family/friends/support/retirement village	27 (79.4)	33 (91.7)	

Rural residential status, n(%) 'yes'	8 (23.5)	10 (27.8)	0.894
Highest education level			
No formal schooling/some or finished primary schooling	6 (17.6)	4 (11.1)	0.938
Some secondary or high school	9 (26.5)	13 (36.1)	
Completed secondary or high school	7 (20.6)	6 (16.7)	
Some/completed trade, community or TAFE college	4 (11.8)	4 (11.1)	
Some university/currently enrolled	3 (8.8)	1 (2.8)	
Completed Bachelor/Masters or PhD degree	5 (14.7)	8 (22.2)	
Employment status			
Working/studying (full or part-time)	4 (11.8)	3 (8.3)	0.123
Temporary/permanent sick leave	4 (11.8)	11 (30.6)	
Not employed/taking time off/home duties	6 (17.6)	4 (11.1)	
Retired	20 (58.8)	13 (36.1)	
Other	0	1 (2.8)	

Footnote: Data are n (%), median (IQR) or mean (SD). Variables with no 'n' reported are complete. Abbreviations: ALK, anaplastic lymphoma kinase; BMI, body mass index; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor;

NOS, not otherwise specified; RT, radiotherapy; SABR, stereotactic ablative radiotherapy; TAFE, Technical and Further Education; WBRT, whole-brain radiotherapy.

Table 3. Cost-effectiveness analysis results

Variable	**Usual care**	**Intervention**	**Difference (95% CI)**	**ICER (mean (95% CI))**	**Net monetary benefit (mean (95% CI))**
Cost (AU$)	$5352.04 (1194.77)	$3421.28 (793.10)	-$1930.76 (-4741.44 to 879.92)	$228,197.37/QALY (-1,173,194.29, 1,101,450.03)	$1,507.72 (-3,014.76, 5,920.63)
QALYs	0.31 (0.02)	0.30 (0.02)	-0.01 (-0.06 to 0.04)		

Footnote: Values are mean (SE) unless specified. Correlations between change in costs and change in effect = -0.26 (usual care group), -0.11 (intervention group) and -0.21 (difference). ICER and net benefit confidence limits from bootstrapping.

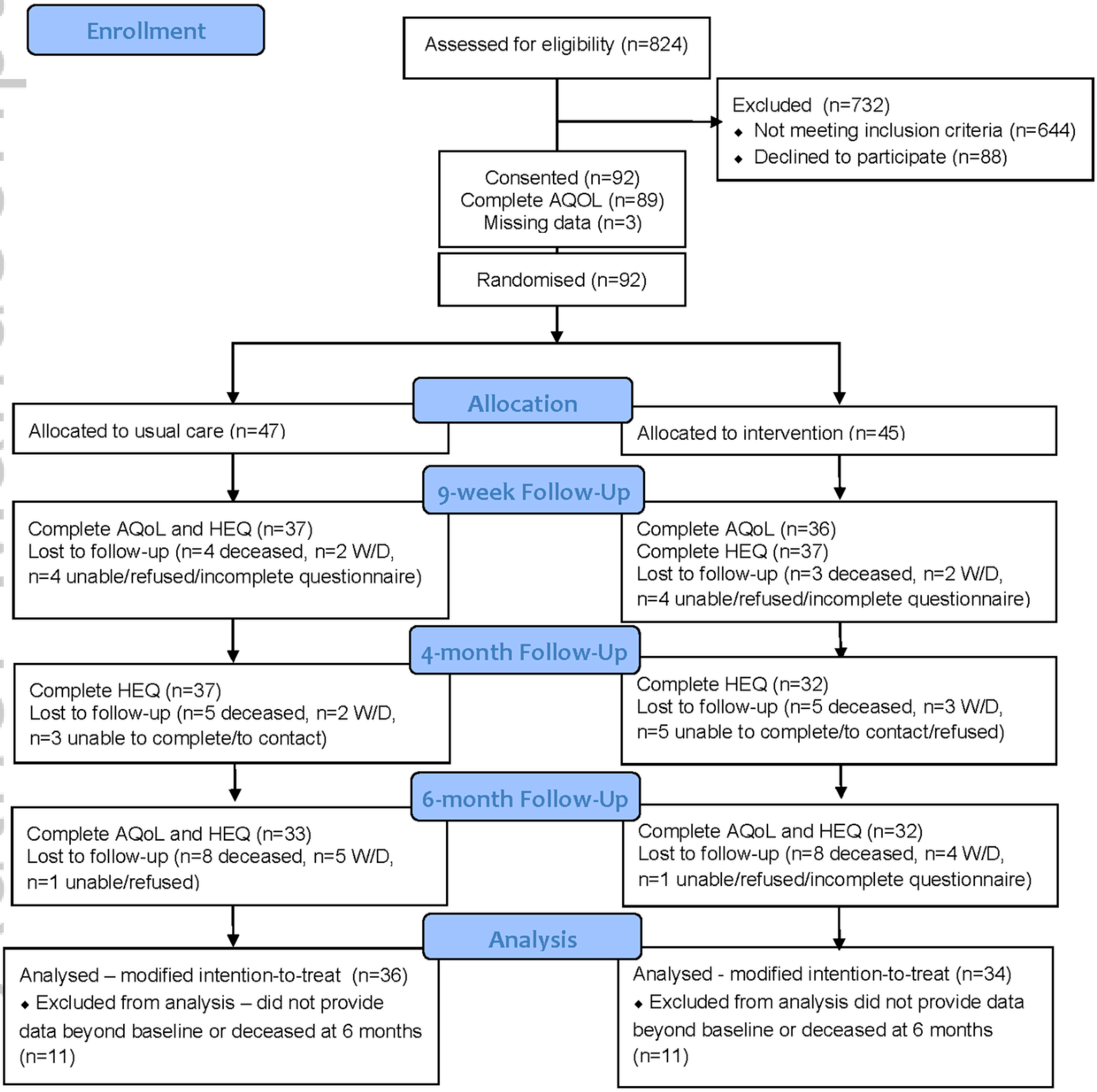
Figure legends

Figure 1. Flow of trial participants

Footnote: AQoL=Assessment of Quality of Life; HEQ=health economic questionnaire; W/D=withdrawn.

Figure 2. Cost-effectiveness plane

Figure 3. Cost effectiveness acceptability curve



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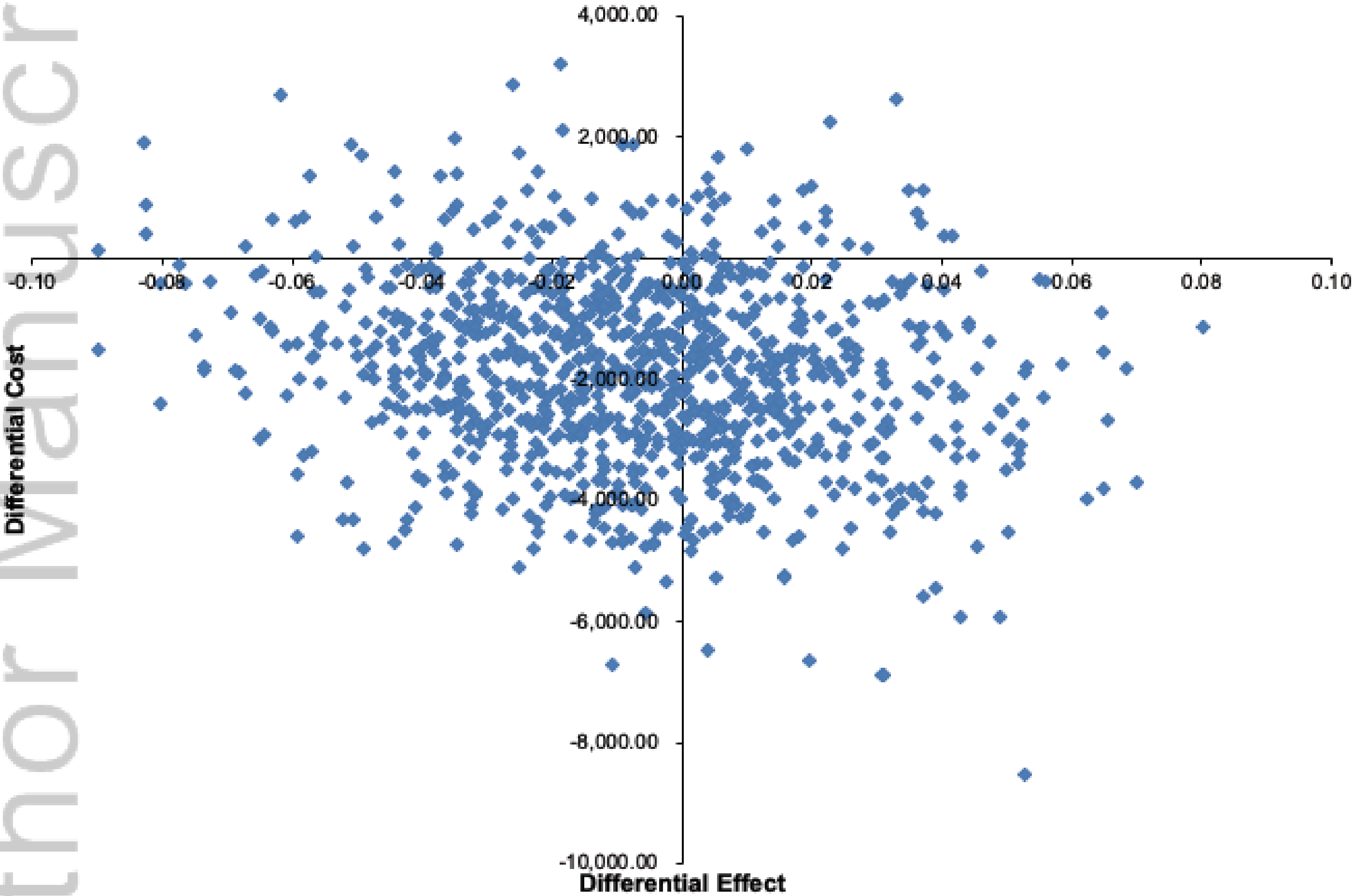

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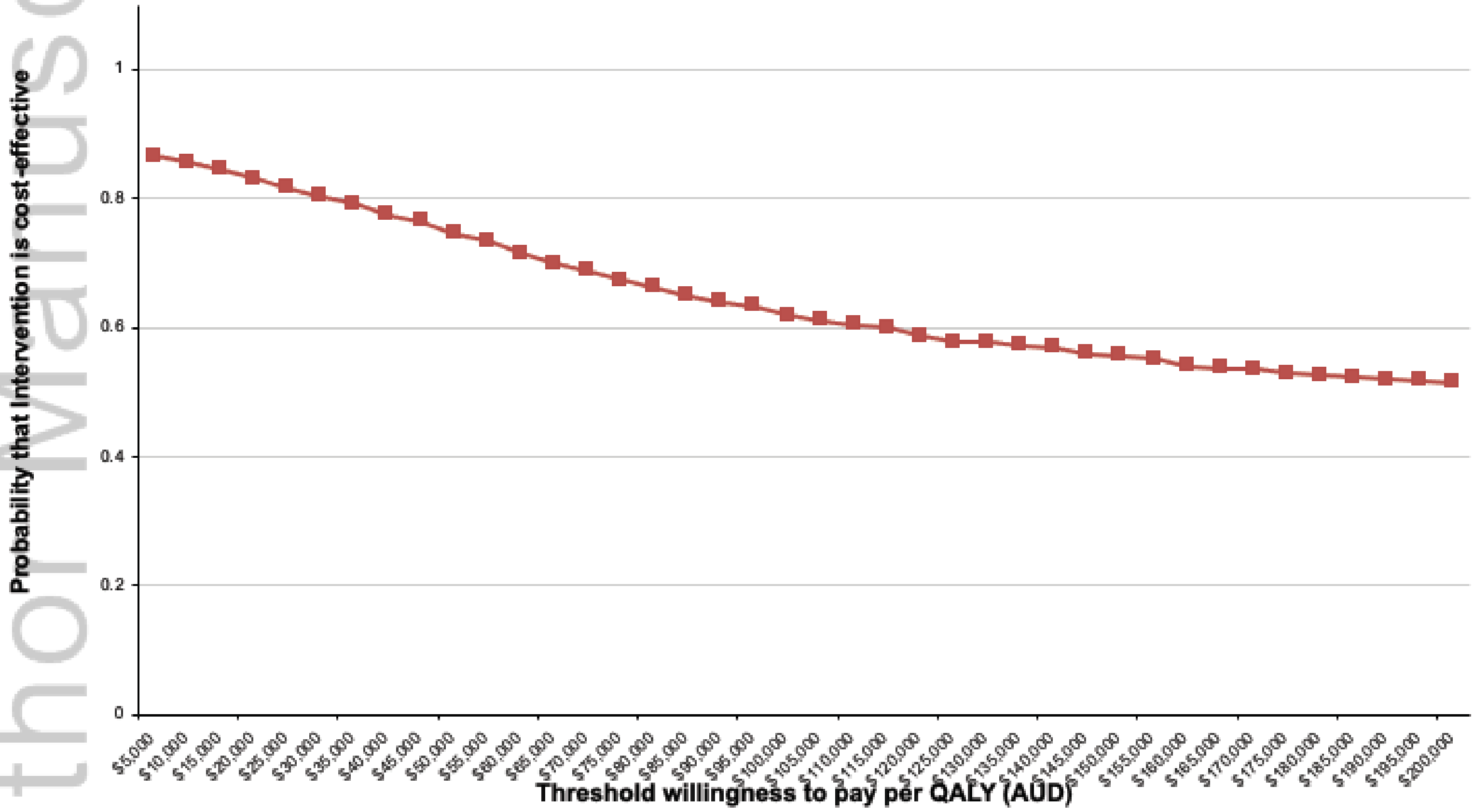

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