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Research

Preoperative physiotherapy is cost-effective for preventing pulmonary complications after major abdominal surgery: a health economic analysis of a multicentre randomised trial

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KEY WORDS

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Hospital costs
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Elective surgical procedures
Breathing exercises
Quality-adjusted life years

ABSTRACT

Question: Is preoperative physiotherapy cost-effective in reducing postoperative pulmonary complications (PPC) and improving quality-adjusted life years (QALYs) after major abdominal surgery? **Design**: Cost-effectiveness analysis from the hospitals' perspective within a multicentre randomised controlled trial with concealed allocation, blinded assessors and intention-to-treat analysis. **Participants**: Four hundred and forty-one adults awaiting elective upper abdominal surgery attending pre-anaesthetic clinics at three public hospitals in Australia and New Zealand. **Interventions**: The experimental group received an information booklet and a 30-minute face-to-face session, involving respiratory education and breathing exercise training, with a physiotherapist. The control group received the information booklet only. **Outcome measures**: The probability of cost-effectiveness and incremental net benefits was estimated using bootstrapped incremental PPC and QALY cost-effectiveness ratios plotted on cost-effectiveness planes and associated probability curves through a range of willingness-to-pay amounts. Cost-effectiveness modelling utilised 21-day postoperative hospital cost audit data and QALYs estimated from Short Form-Six Domain health utilities and mortality to 12 months. **Results**: Preoperative physiotherapy had 95% probability of being cost-effective with an incremental net benefit to participating hospitals of A$4,958 (95% CI 10 to 9,197) for each PPC prevented, given that the hospitals were willing to pay $45,000 to provide the service. Cost-utility for QALY gains was less certain. Sensitivity analyses strengthened cost-effectiveness findings. Improved cost-effectiveness and QALY gains were detected when experienced physiotherapists delivered the intervention. **Conclusions**: Preoperative physiotherapy aimed at preventing PPCs was highly likely to be cost-effective from the hospitals' perspective. For each PPC prevented, preoperative physiotherapy is likely to cost the hospitals less than the costs estimated to treat a PPC after surgery. Potential QALY gains require confirmation. **Trial registration**: ACTRN12613000664741. **[Boden I, Robertson IK, Neil A, Reeve J, Palmer AJ, Skinner EH, Browning L, Anderson L, Hill C, Story D, Denehy L (2020) Preoperative physiotherapy is cost-effective for preventing pulmonary complications after major abdominal surgery: a health economic analysis of a multicentre randomised trial. *Journal of Physiotherapy* ■:■–■]**

Introduction

With 300 to 500 operations per 100,000 people annually, abdominal surgery is the most common major surgery type performed in developed countries, with volumes increasing at 2 to 5% per year.[1–3] Patients having surgery account for a quarter of hospital bed days, yet accrue half of all hospital costs.[4] Existing large volumes, high costs and the increasing need for surgery suggest that methods to minimise hospital costs, whilst maintaining or enhancing service quality, are important to ensure long-term sustainability of hospital funding. Reducing postoperative complications could be one such method. Complications after abdominal surgery are the principal driver for increased costs, with higher expenditure on pharmaceuticals, diagnostic testing and lengths of stay in the intensive care unit and surgical ward.[5]

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Among the most common complications after major abdominal surgery are postoperative pulmonary complications (PPCs),[5,6] which range from mild atelectasis to severe hospital-acquired pneumonia and respiratory failure.[6] PPCs independently increase costs following major colorectal,[7] upper gastrointestinal[8] and renal surgery.[9] Even mild PPCs are associated with increased hospital utilisation.[6,10] PPCs are strongly associated with worse mortality[6–11] and health-related quality of life (HRQoL).[12] A recent multicentre randomised controlled trial,[11] the Lung Infection Prevention Post Surgery Major Abdominal with Pre-Operative Physiotherapy (LIPPSMAck-POP) trial, replicated previous findings,[13] confirming that a single preoperative physiotherapy education and training session halves PPC incidence with a number needed to treat of seven. Patients place high priority on preventing pneumonia after surgery, value preoperative physiotherapy and prefer individual face-to-face sessions.[14] Yet despite strong effectiveness,[11,13] patient preference[14] and international consensus that preventing PPC should be a key feature of perioperative care,[6] preoperative physiotherapy is seldom provided.[15,16] Uncertainty surrounding the economic cost/benefit of preoperative physiotherapy may be preventing the implementation of this highly efficacious patient-centred intervention.

Therefore, the research question for this planned within-trial health economic analysis was:

> Is preoperative physiotherapy cost-effective in reducing postoperative pulmonary complications and improving quality-adjusted life years (QALYs) after major abdominal surgery?

Methods

Design

This planned health economic evaluation was conducted within a multicentre, parallel-group, pragmatic, randomised controlled trial involving three diverse (rural, regional and metropolitan) government-funded hospitals in Australia and New Zealand[11] and reported in accordance with Consolidated Health Economic Evaluation Reporting Standards[17] (see Appendix 1 on the eAddenda). Detailed descriptions of the study design and methods are available[11,18] and briefly outlined here. Participants were randomly assigned via sealed opaque envelopes. Independent audit confirmed appropriate randomisation.[11] Participants, outcome assessors, postoperative physiotherapists, doctors, nurses, hospital administrators and statisticians were unaware of group assignment.

Participants

Inclusion criteria were: English speaking, age $\geq$ 18 years, and attending a pre-anaesthetic assessment clinic within 6 weeks of elective major abdominal surgery. Immobile patients and those having organ transplantation or hernia repair were excluded.

Interventions

At the pre-anaesthetic clinic all participants were seen by a physiotherapist for a 30-minute standardised social, functional and respiratory assessment. They were provided with a booklet containing information about postoperative pneumonia risk and prevention with early ambulation and breathing exercises. Control group participants received no further information or training from the physiotherapist.

Experimental group participants received an additional 30-minute one-on-one physiotherapy education and training session about the effect of anaesthesia and surgery on mucociliary clearance and lung volumes, and the consequences of bacterial stagnation in the lungs. They were educated that self-directed postoperative deep breathing and coughing exercises are vital to reduce the risk of pneumonia after surgery and directed to commence these immediately upon regaining consciousness and to perform 30 repetitions hourly until fully ambulant.

Preoperative interventions were delivered by physiotherapists with experience ranging from new graduates to > 10 years practice in acute care and surgery ward settings. Postoperative early ambulation was standardised and no additional prophylactic respiratory physiotherapy was provided.

Outcome measures

The cost-effectiveness of preoperative physiotherapy to prevent PPC and improve QALYs after major abdominal surgery was assessed using an incremental cost/utility analysis conducted from the hospital perspective as payer of the service. Incremental cost-effectiveness ratios were determined by dividing the difference between the experimental and control groups in net mean hospital costs per participant by the differences in PPC rates 14 days after surgery and QALYs 12 months from surgery.

Cost-effectiveness model inputs: 21-day hospital costs

Hospital costs for each treatment arm comprised the costs of providing the preoperative physiotherapy protocol and the costs of hospital resource use in the first 21 days after surgery.

Preoperative physiotherapy costs were estimated using salary rates in 2018 Australian dollars individualised to the experience level of each treating physiotherapist and costed to the maximum level within a band (see Appendix 2 on the eAddenda). Overheads of 25% were added (eg, superannuation, professional development, training, administration and backfill). New Zealand dollars were converted to Australian dollars using December 2018 exchange rates. Costings were based on control group participants receiving a 30-minute physiotherapy session and experimental group participants receiving 60 minutes. Booklet costs and clinic room hire were added (see Appendix 2 on the eAddenda). Administration costs to process referrals or coordinate bookings were not incorporated, as all participants attended an established clinic with an existing infrastructure.

Postoperative downstream hospital costs were estimated using a detailed patient-level costings model. Units of hospital activity were counted prospectively and daily by blinded trial assessors using the written and electronic medical records until 21 days after surgery or hospital discharge, whichever occurred first. Audited hospital activity included: bed days and location (ICU, surgical ward or residential rehabilitation); mechanical and non-invasive ventilation hours; antibiotic prescriptions; modes and days of oxygen therapy; number and type of imaging and pathology tests; and medical consultations outside standard rounds. These items of hospital activity were chosen as their consumption is associated with PPC.[5–11] Duration of hospital stay was cross-validated using hospital databases. Tariffs for items of hospital activity were derived from Australian healthcare authorities (see Appendix 2 on the eAddenda) and converted to 2018 Australian dollars using consumer price indices 2013 to 2018, as listed by the Australian Bureau of Statistics. Discounting of costs was not necessary as follow-up was within 12 months.[17]

Cost-effectiveness model inputs: quality-adjusted life years

QALYs were estimated using health utilities converted from HRQoL measures assessed with the Short-Form 36-item questionnaire (SF-36), a valid and responsive patient-reported outcome after abdominal surgery.[19] HRQoL data acquisition started from the 79th participant following receipt of funding for research assistant activities. Baseline responses were measured at the preoperative clinic within 6 weeks of surgery then repeated by phone with a masked assessor at 6 to 8 weeks after surgery. Postoperatively, if patients were unable to be contacted, a standardised letter, SF-36 questionnaire and self-addressed return-paid envelope were posted. Forms not returned within 2 weeks were considered lost to follow-up. Acquired SF-36 scores were converted to SF-six domains (SF-6D) health utilities using commercial software[a], providing values from 0 (death) to 1 (full health).[20] The SF-6D is valid and reliable for estimating health utilities after abdominal surgery.[21]

The typical trajectory of HRQoL after major elective colorectal and upper gastrointestinal surgery is of an immediate postoperative deterioration with a return to baseline HRQoL at 2 to 6 months and remaining stable within presurgery HRQoL levels to at least 1 year after surgery.[21–25] Therefore, baseline preoperative HRQoL scores were used to estimate each participant's 12-month health utility values as an alternative to reassessing HRQoL at 12 months directly from participants.[26] QALYs were calculated by multiplying the reported health utility state by the number of weeks spent in this health state. For participants who died, QALY estimates were censored to this date.[26] Calculations using the linear change area-under-the curve method[26] were applied to two time periods: baseline to 6 weeks (direct value) and 6 weeks to 1 year (estimated value). These values were summed to obtain 12-month QALYs. The maximum QALY for this study was 1, representing full health over the entire year. See Appendix 3 on the eAddenda for detailed descriptions of QALY calculations.

Cost-effectiveness

A cost-effectiveness analysis considers the additional cost of a new intervention relative to the improvement in outcomes gained compared with providing usual care or an alternative intervention. This is calculated by dividing the between-group net cost difference by the differences in treatment effects (eg, between-group difference in costs/difference in absolute risk reduction in PPC).[27,28] This is termed an incremental cost-effectiveness ratio.

To manage fundamental heterogeneity in hospital costs, health utilities and reduced statistical power regarding secondary outcomes, bootstrapping statistical techniques are considered essential in estimating cost-effectiveness within randomised controlled trials.[27,28] Bootstrapping is where the original trial's economic and clinical outcomes are run through a mathematical model using the variance in the original data to simulate hypothetical results if the same trial was conducted many hundreds or thousands of times over. These simulated cost-effectiveness ratios better represent the wide range of possible cost-effectiveness outcomes that could be expected in the population and not just from that sampled in the trial. These simulated cost-effectiveness ratios are then graphed on a cost-effectiveness plane (Figure 1A). The cost-effectiveness plane has four quadrants. The quadrant in which the cost-effectiveness ratios predominantly fall contributes to the decision by the purchaser of the intervention about whether or not the intervention is cost-effective and provides value for money. Interventions where all simulated cost-effectiveness ratios fall into the south-east quadrant (ie, net cost savings and improved outcomes compared with usual care or control) are always considered cost-effective.[28] Yet, because hospital cost accounting is highly variable, this lack of precision leads to estimated cost-effectiveness ratios often being scattered across a number of quadrants. This reflects the statistical possibility that in some circumstances the intervention is more effective than standard care but comes at a greater net cost (north-east quadrant).

Additional costs required by a hospital to fund a new treatment can be considered worthwhile if the improvement in clinical outcome is valued enough to pay more for it.[27] This is known as the willingness-to-pay amount.[29] Willingness to pay is an arbitrary figure regarded by the payer (eg, self-funded patient, hospital or government) as the amount of money considered worthwhile to pay for each unit of improvement in a desired outcome. For example, 1,000 surveyed Australians were willing to pay $82,000 (95% CI 77,000 to 88,000; 2007 data adjusted to 2018 Australian dollars) from their own funds for a hypothetical treatment if it improved their QALY.[30] From an Australian government perspective, although there is no explicit willingness-to-pay threshold currently stated, all new medications approved for public funding have cost less than $75,000 per QALY gain (2003 data adjusted to 2018 Australian dollars).[31]

Whereas the literature discussing willingness-to-pay thresholds for QALY improvements is extensive, no opinion has been published regarding what is considered a reasonable amount by a hospital to spend on PPC prevention. For the specific purposes of estimating the cost-effectiveness of preoperative physiotherapy in this trial, it was hypothesised that a hospital would be willing to pay to prevent PPC as long as it costs less than the treatment costs of a PPC. The additional cost burden independently attributed to PPCs in a 2008 study involving 46,000 major colorectal surgery patients across 600 US hospitals was $45,000 per PPC (2008 US dollars adjusted to 2018 Australian dollars).[7] This is currently the most methodologically robust assessment of additional hospital costs directly attributable to PPCs.

Due to the statistical chance of a new intervention costing more than usual care and the lack of certainty surrounding a hospital's willingness to pay to prevent PPCs or improve QALYs, cost-effectiveness is best determined using a cost-effectiveness acceptability curve.[28] This method provides the probability of an intervention being cost-effective over a range of willingness-to-pay amounts. The threshold on how much money is worthwhile spending on improving a clinical outcome will vary from hospital to hospital depending on the value placed on improving the target outcome and the extensive heterogeneity in the processes for funding

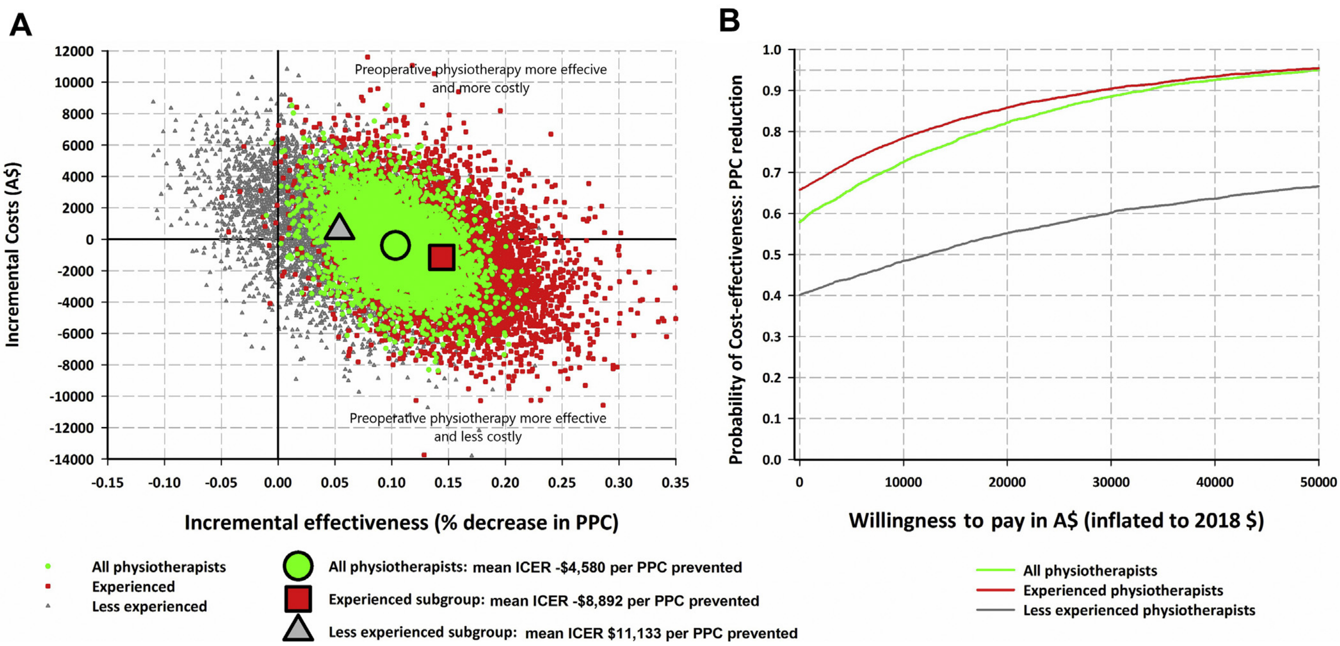

Figure 1. A and B. Cost-effectiveness plot and cost-effectiveness acceptability curve of preoperative physiotherapy versus information booklet to reduce postoperative pulmonary complications.

new services. A cost-effectiveness acceptability curve provides information to the decision-maker to guide this choice.

Due to the uncertainty surrounding an agreed willingness-to-pay amount for PPC prevention, the return on investment for a hospital paying for a preoperative physiotherapy service was calculated as an alternative measure of cost-effectiveness (net difference in cost between groups / cost of intervention). In circumstances where the mean incremental cost-effectiveness ratio indicated improved outcomes with cost savings, the incremental net benefit[32] to the hospital was also calculated (incremental net benefit = (willingness to pay × difference in treatment effects) – difference in costs between groups). A higher value equals greater cost-effectiveness.

Data analysis

This study was primarily powered to detect a treatment effect on PPC.[11,18] Bootstrapping methods were employed to manage the inherently limited power to detect significant differences in secondary outcomes, including costs and QALYs. To manage missing HRQoL data, characteristics of participants with complete data were compared with those with missing data. Fully conditional specification and predictive mean matching were used to make multiple imputations with chain equations, assuming that data were missed at random,[33] and adjusted for baseline utility to account for regression to the mean.[34]

Costs of hospital activity for individual items and the aggregate total were compared between-groups using adjusted mixed-effects linear regression analyses with logarithmic transformation of skewed data. Within-group and between-group differences for HRQoL, health utility and QALYs were analysed using adjusted repeated-measures mixed-effects linear regression. All outcomes were assessed by intention to treat. Bootstrapping of 5,000 paired incremental cost-effectiveness ratio estimates were performed and graphed on a cost-effectiveness plane and mean differences and confidence intervals were calculated.

Exploratory sub-group analyses were conducted by considering effects and costs separately in participants seen by experienced physiotherapists (≥ 10 years) or less-experienced physiotherapists. This was to analyse if the possible benefit of improved PPCs and mortality reduction detected when preoperative education was delivered by an experienced physiotherapist[11] is outweighed by the increased costs of employing a more experienced clinician.

Two sensitivity analyses were conducted. Cost-effectiveness analyses involve a number of assumptions and value judgements in constructing models for determining hospital costs and QALYs. Sensitivity analyses consider the stability of health economic findings by assessing the variation in results when areas of uncertainty are changed. This provides confidence in the primary findings or suggests areas requiring further research.[17,27] First, government hospital episode-of-care costs were used to compare groups. These costs were independently generated by hospital administrators and incorporated all direct (eg, theatre time, personnel, equipment and medications) and ancillary costs (eg, cleaning, catering and building overheads) for the whole hospital episode of care from admission to hospital discharge. This is the primary process of hospital cost accounting in Australia.[35] Second, only health utilities where a full set of preoperative and postoperative HRQoL data were collected directly from a patient were considered to calculate QALYs.

All outcomes, including costs and HRQoL, were adjusted for imbalances in age, respiratory comorbidity and surgical category detected at baseline.[11] Analyses were conducted using commercial software[b] by the trial's statistician. Methodology, data, results and interpretation were validated by two independent health economists.

Results

Characteristics of participants

Detailed participant characteristics have been published already.[11] Median age was 65 years (IQR 52 to 75) and most were male (61%). Their surgical procedures were oncological (69%), major colorectal (49%), urological (26%), or upper gastrointestinal/hepatobiliary procedures (24%). Operations were generally > 2 hours (64%) via upper midline (49%) or subcostal (18%) incisions.

Flow of participants

From June 2013 to August 2015, 504 patients were eligible for inclusion, with 441 (88%) randomly assigned: 219 to the control group and 222 to the experimental group.[11] Nine (2%) participants were withdrawn. Data for PPC, mortality and hospital costs were available for all 432 participants. Baseline characteristics of the cohort and treatment effects for PPC and mortality have been published already.[11] The flow diagram of HRQoL data acquisition is shown in Appendix 4 on the eAddenda. Preoperative HRQoL was obtained in 315 participants (73%). Missing preoperative HRQoL was proportionally higher in the experienced physiotherapist sub-group (Table 1 on the eAddenda) as HRQoL acquisition did not start until the 79th participant, when only experienced physiotherapists were actively recruiting. There was a 69% (217/315) follow-up rate 6 weeks after surgery. Follow-up was similar between groups (114/160 (71%) experimental; 103/155 (66%) control) and between sub-groups. Participants who acquired a postoperative complication or had an extended hospital stay were more likely to have missing 6-week postoperative HRQoL data (Table 1 on the eAddenda).

Cost-effectiveness model inputs: 21-day hospital costs

Across the whole cohort the primary cost contributors for the first 21 postoperative hospital days were surgical ward (64%), ICU bed days (19%) and diagnostic testing and imaging (7%), as shown in Table 2. The cost of the intervention inclusive of salary, overheads, room hire and consumables was an additional $52 (95% CI 51 to 53) per participant compared with control group participants, or $27 (95% CI 26 to 28) when using available clinic rooms. Following surgery, experimental group participants consistently tended to consume fewer postoperative hospital resources across all assessed items compared with control participants (Table 2). Individual items with a 95% confidence interval estimate closest to the statistically significant cost saving were: usage of oxygen therapy, sputum cultures, blood cultures and antibiotics prescribed for respiratory complications. The between-group difference in adjusted total 21-day hospital costs was $458 saved (95% CI −4,490 to 4,697) favouring the experimental group. This mean estimate of net savings provided a return on investment of approximately 800% ($8 saved by the hospital for every $1 spent on physiotherapy to provide education and breathing exercise training to patients before surgery), although the precision of this single-trial estimate was low, as shown by the wide confidence intervals.

Cost-effectiveness model inputs: quality-adjusted life years

Adjusted within-group and between-group HRQoL are reported in Table 3 on the eAddenda. Six weeks following surgery, physical domains had declined up to 30% in both groups, whilst emotional and mental health domains were unaffected. No between-group differences were detected in HRQoL at 6 weeks or QALYs at 12 months (MD 0.020, 95% CI −0.008 to 0.045).

Cost-effectiveness for PPC reduction

As previously reported,[11] preoperative physiotherapy halved PPC incidence (27% versus 13%, adjusted hazard ratio 0.48, 95% CI 0.30 to 0.75). A large proportion of incremental cost effectiveness ratios fall in the south-east quadrant of the cost-effectiveness graph (Figure 1A), giving a 60% probability that the preoperative intervention was either cost-neutral or cost-saving to the hospitals (Figure 1B). At a willingness-to-pay threshold of $45,000 (the estimated additional cost to the hospital to treat patients with PPC),[7] preoperative physiotherapy had a 95% probability of being cost-effective to prevent PPC, giving an incremental net benefit to the hospitals of $4,958 saved

Table 2
21-day hospital costs and effects of preoperative physiotherapy versus standard care.

Parameter	Costs/unit of use	Whole cohort (n = 432)		Experimental (n = 218)		Control (n = 214)		Difference between groups Experimental minus control	
		Mean (SD) units	Mean (SD) costs	Mean (SD) units	Mean (SD) costs	Mean (SD) units	Mean (SD) costs	Mean (95% CI)	*p* value
Costs									
Preoperative physiotherapy									
physiotherapist salary	$45 to 55/hr	0.75 (0.25)	$41 (17)	1 (0)	$52 (10)	0.5 (0)	$25 (1)	$27 (26 to 28)	<0.0001
room hire	$50/hr	0.75 (0.25)	$38 (13)	1 (0)	$50 (0)	0.5 (0)	$25 (0)	$25 (25 to 25)	<0.0001
booklet	$5/booklet	1 (0)	$5 (0)	1 (0)	$5 (0)	1 (0)	$5 (0)	$0 (0 to 0)	1.0
Hospital ward use									
ICU/HDU stay	$3,000/d	1.4 (2.8)	$4,188 (8,438)	1.3 (2.9)	$3,867 (8,633)	1.5 (2.7)	$4,514 (8,242)	−$647 (−2,244 to 950)	0.43
surgical ward stay	$1,500/d	9.5 (8.5)	$14,153 (12,710)	9.2 (8.5)	$13,728 (12,774)	9.7 (8.4)	$14,586 (12,554)	−$858 (−3,254 to 1,538)	0.55
sub-acute stay	$800/d	1.0 (5.4)	$779 (4,292)	0.82 (4.5)	$659 (3,630)	1.1 (6.1)	$902 (4,879)	−$243 (−1,055 to 569)	0.55
Ventilation support									
mechanical ventilation	$1,500/d	0.25 (1.4)	$377 (2,057)	0.22 (1.2)	$330 (1,727)	0.28 (1.6)	$425 (2,349)	−$95 (−484 to 294)	0.63
non-invasive ventilation	$500/d	0.04 (0.3)	$21 (143)	0.04 (0.3)	$18 (135)	0.05 (0.3)	$23 (151)	−$5 (−32 to 22)	0.72
high-flow oxygen	$100/d	0.18 (0.9)	$36 (130)	0.16 (0.9)	$33 (124)	0.20 (1.0)	$40 (136)	−$7 (−32 to 18)	0.54
standard oxygen	$20/d	3.0 (2.8)	$60 (57)	2.8 (2.7)	$56 (53)	3.2 (3.0)	$65 (60)	−$9 (−20 to 2)	0.11
Imaging and pathology									
sputum cultures	$50/test	0.3 (0.8)	$14 (40)	0.22 (0.6)	$11 (32)	0.33 (0.9)	$17 (47)	−$6 (−14 to 2)	0.13
blood cultures	$50/test	0.3 (1.1)	$17 (55)	0.25 (0.9)	$12 (46)	0.42 (1.3)	$21 (63)	−$9 (−19 to 1)	0.11
all other pathology	$30/test	40.4 (55.5)	$1,213 (1,666)	38.0 (58.3)	$1,139 (1,749)	43.0 (52.6)	$1,289 (1,578)	−$150 (−465 to 165)	0.35
chest X-rays	$70/test	2.0 (3.2)	$142 (231)	1.8 (2.8)	$129 (214)	2.2 (3.5)	$155 (247)	−$26 (−70 to 18)	0.24
chest CTs	$450/test	0.1 (0.4)	$42 (162)	0.07 (0.3)	$31 (122)	0.12 (0.4)	$53 (195)	−$22 (−53 to 9)	0.17
all other imaging	$100/test	1.1 (2.8)	$110 (278)	1.0 (3.2)	$104 (326)	1.2 (2.2)	$116 (219)	−$12 (−65 to 41)	0.63
Antibiotics									
respiratory indication	$100/d	1.2 (3.0)	$121 (297)	0.94 (2.8)	$94 (286)	1.5 (3.1)	$149 (309)	−$55 (−111 to 1)	0.05
all other indications	$100/d	2.9 (4.4)	$169 (311)	1.8 (3.4)	$181 (335)	1.6 (2.8)	$156 (285)	$25 (−40 to 84)	0.42
Medical visits									
out of round visits	$300/visit	1.9 (2.8)	$573 (854)	1.8 (2.7)	$544 (817)	2.0 (3.0)	$603 (891)	−$59 (−221 to 103)	0.43
MET calls	$1,000/call	0.12 (0.5)	$116 (493)	0.11 (0.5)	$106 (473)	0.13 (0.5)	$127 (513)	−$21 (−114 to 72)	0.55
Total 21-day costs, unadjusted			$22,201 (24,142)		$21,143 (24,290)		$23,282 (23,998)	−$2,139 (−6,706 to 2,428)	0.19
Targeted costs model, adjusted[a]					$21,867 (24,455)		$22,325 (21,724)	−$458 (−4,697 to 4,490)	0.42
Sensitivity analysis: whole episode-of-care costs[a]			$31,829 (26,845)		$30,900 (25,165)		$32,767 (28,469)	−$1,867 (−6,946 to 3,212)	0.47
Effects									
pulmonary complications[a]					27 (12%)		58 (27%)	−10% (−14 to −5)	0.001
12-month mortality[a]					16 (7%)		23 (11%)	−1.6% (−4.5 to 3.7)	0.46
QALY, imputed data set, unadjusted					0.671 (0.19)		0.642 (0.19)	0.029 (0.002 to 0.055)	0.015
QALY, imputed data set, adjusted[ab]					0.667 (0.19)		0.647 (0.19)	0.020 (−0.008 to 0.045)	0.08
Sensitivity analysis: QALY complete cases only[ab]					0.656 (0.22)		0.659 (0.20)	−0.003 (−0.05 to 0.04)	0.89

All costs are in 2018 Australian dollars. Raw unadjusted cost data are mean (SD) and mean difference (95% confidence interval) with *p*-values estimated using mixed effects linear regression.
ICU = intensive care unit, HDU = high dependency unit, CT = computerised tomography, MET = medical emergency team, QALY = quality-adjusted life years.
[a] Adjusted for age, respiratory comorbidity, surgical category using multiple regression and Poisson regression.
[b] Adjusted for baseline utility.

(95% CI 10 to 9,197), as shown in Figure 1B. At a lower willingness-to-pay threshold of $18,000 there was an 80% probability of cost-effectiveness. See Appendix 5 in eAddenda for graphed incremental net benefits for willingness-to-pay amounts from $0 to $60,000.

Cost-utility for QALY improvement

Bootstrapped estimates indicated that preoperative physiotherapy was likely to improve QALYs 12 months after surgery; however, due to the spread of incremental cost-effectiveness ratios across both the south-east and north-east quadrants (Figure 2A), there is uncertainty if this comes at an additional cost or is cost saving to the hospital. Given a willingness-to-pay threshold of $50,000 per one QALY gain, preoperative physiotherapy had 73% probability of being considered value for money (Figure 2B), with an incremental net benefit favouring the experimental group of $1,458 (95% CI −3,490 to 5,697).

Sub-group analyses

Within the experienced physiotherapist sub-group (see Table 4 on the eAddenda), the mean adjusted hospital cost savings favouring the experimental intervention were stronger ($1,156 saving per participant, 95% CI −5,300 to 6,937) with an 80% probability of cost-effectiveness at a willingness-to-pay threshold of $10,000 (Figure 2B). Large and significant 12-month QALY gains were also detected in the experimental group treated by more experienced physiotherapists (adjusted MD 0.051, 95% CI 0.015 to 0.088, $p = 0.01$), with a 90% probability of improving QALYs within a willingness-to-pay threshold of $50,000 (Figures 2A and 2B).

Sensitivity analyses

Government episode-of-care costings were $31,829 per participant (SD 26,845), with the adjusted between-group cost differences more strongly favouring the experimental group than the targeted costing model (Table 2). Preoperative physiotherapy had a 95% probability of being cost-effective in preventing PPC at a willingness-to-pay threshold of $45,000, giving an incremental net benefit to hospitals of $6,367 (95% CI 1,288 to 11,446). When QALYs were calculated using health utilities from complete cases only, cost-utility was reduced, giving an incremental net benefit of $308 (95% CI −4,640 to 4,547) per QALY gained.

Discussion

A PPC is a high-cost event with severe negative consequences to patients and hospitals.[4–10] A PPC is > 15 times more common than a cardiac complication, has similar effects on in-hospital mortality, and is responsible for more than doubling the baseline cost of abdominal surgery, costing a hospital approximately $45,000 to treat.[7] Large randomised controlled trials have found that a single preoperative physiotherapy education and training session reduces PPC incidence by 25 to 75%.[11,13] By reducing PPC risk after major abdominal surgery, respiratory physiotherapy has been associated with reduced hospital length of stay,[36] antibiotic usage[36] and reintubation rates.[37] However, the LIPPSMAck-POP trial is the first with a detailed audit of hospital resource use and a thorough health economic analysis. When accounting for the cost of introducing the service, there was a 60% likelihood that preoperative physiotherapy resulted in overall cost savings to participating hospitals through reductions in downstream hospital resource use. In circumstances where a net cost may be incurred to provide preoperative physiotherapy to prevent PPCs, it is reasonable to consider that hospitals would be willing to pay for this as long as it costs less than treating a PPC. This trial found that if a hospital is willing to pay $18,000 to prevent one PPC (ie, less than half the cost of a PPC), preoperative physiotherapy is 80% likely to be cost-effective.

A consistent signal of reduced costs of downstream hospital resource use was found in the experimental group participants, with an estimated return on investment of $8 saved postoperatively for every $1 spent on preoperative physiotherapy. Given the inevitable wide confidence intervals in a cost-benefit analysis based on a single trial, the level of precision around this estimate is low. A recent prehabilitation trial that halved postoperative complication rates following high-risk major abdominal surgery[38] reported wide variance in costing data and a non-significant difference in postoperative hospital costs favouring the experimental group ($536 net saving, 95% CI −1,626 to 3,113; costs converted to Australian dollars at 2018 exchange rates).[39] Randomised controlled trials rarely have large enough sample sizes to overcome the wide variance in patient-level resource use and costs and are generally unable to detect primary significance in cost measures. A cost-benefit analysis (simple comparison in net costs between a new intervention and usual care or control) not only requires exceptionally large clinical trials to definitely prove a fiscal benefit from a new intervention, but also does not

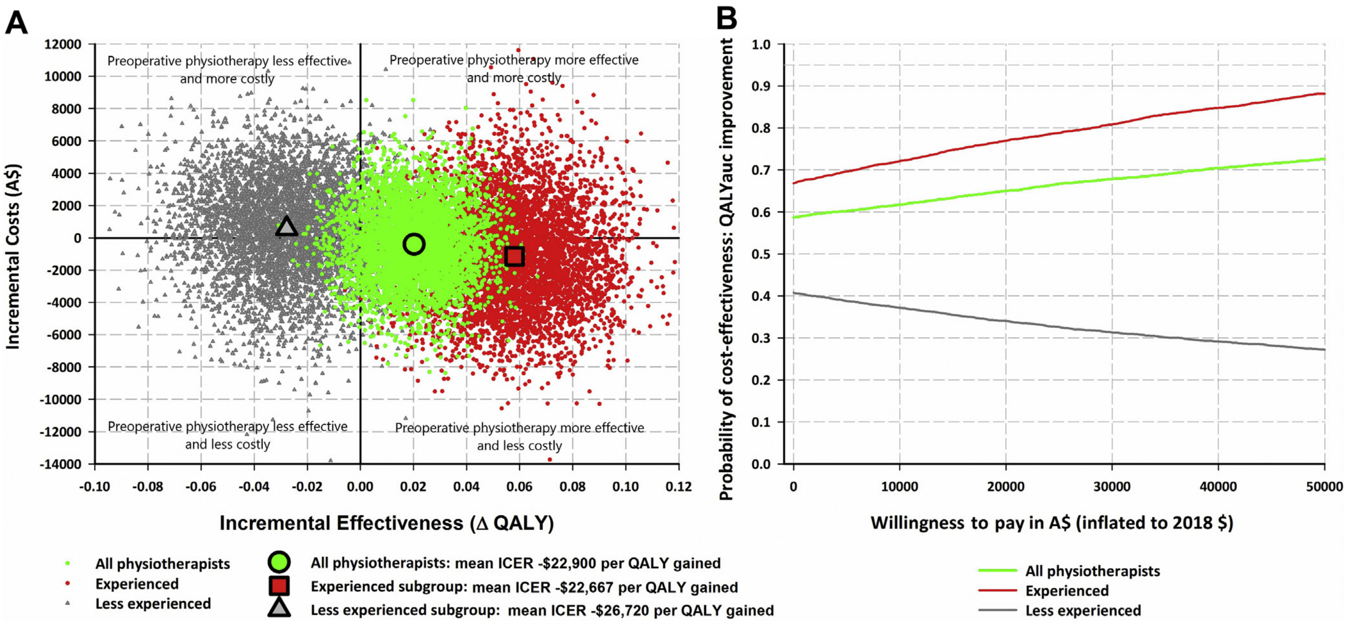

Figure 2. A and B. Cost-utility plot and cost-effectiveness acceptability curve of preoperative physiotherapy versus information booklet to improve quality-adjusted life years.

incorporate societal or consumer beliefs on the value of incurring additional costs for improved benefits.[27]

A cost-effectiveness analysis considers the relative relationship between treatment costs and how effective the treatment is in improving the desired outcome. This value is then placed in the context of how much a consumer would be prepared to pay in order to gain an improvement in the desired outcome. For this trial, most cost-effectiveness ratios fell in the south-east quadrant of the cost-effectiveness plane, indicating an overall mean cost saving to hospitals and reduced risk of PPCs for patients when compared with usual care. The probability that preoperative physiotherapy is cost-neutral or entirely cost-saving to the hospitals was 60% (Figure 1B). However, due to the very wide standard deviations in hospital costings, the statistical chance of preoperative physiotherapy costing the hospital more than is saved in downstream ward costs cannot be discounted. If the benefit gained in reducing PPC incidence and improving QALYs after major surgery are important to a hospital, they may be willing to pay to instigate a preoperative physiotherapy service to achieve this. Within this trial there was a 5% chance that the preoperative physiotherapy service cost the hospitals more to prevent one PPC than the estimated $45,000 it costs to treat a PPC. The probability of preoperative physiotherapy being cost-effective to prevent PPCs at a reasonable cost was therefore 95%. The consistent signal of individual hospital activity savings favouring the experimental group and independent hospital episode-of-care costings demonstrating a stronger reduction in costs strengthens the likelihood that preoperative physiotherapy truly reduces downstream hospital costs and constitutes a dominant strategy in preventing PPCs.

Improved value for money appears to be gained by hospitals if experienced physiotherapists provide the intervention, with greater PPC reductions,[11] reduced postoperative mortality,[11] large significant QALY gains and a stronger signal towards reducing downstream hospital costs. Even when accounting for the additional costs of employing a more experienced physiotherapist, there was an 80% probability of cost-effectiveness at a willingness-to-pay threshold of less than a quarter of the estimated cost of treating a PPC,[7] with a possible return on investment in the order of 1,800% (ie, $18 saved for every $1 spent on an experienced physiotherapist). Further research is required to confirm these experience-related effects, to determine what qualities and attributes regarding treatment from an experienced practitioner may make it more effective and whether these factors are trainable in others.

Although the probability of cost-effectiveness for preoperative physiotherapy to prevent PPCs is strong, there is less certainty surrounding its ability to improve HRQoL and QALYs at a reasonable cost. Sensitivity analysis of complete QALY data indicated fragility around the result. There are some limitations to the trial that could explain this. HRQoL data acquisition started after a fifth of all patients had been recruited. This incomplete baseline data set and a 31% missing 6-week follow-up rate led to imputed measures comprising 50% of all health utility results. As a consequence, the trial's HRQoL estimates have inherent uncertainty and may not truly represent the whole population. Countering this concern, the large declines detected in HRQoL physical domains but not mental health domains within 2 months of surgery were congruent with other studies.[12,39]

Patients who develop postoperative complications tend to have poorer HRQoL compared with patients without complications.[12] An intervention that halves PPCs after major abdominal surgery could improve HRQoL trajectory at 6 weeks. This was not detected in this trial, perhaps due to inherently reduced power for this secondary outcome and/or a response bias. Participants who suffered a postoperative complication were more likely to be missed to follow-up, minimising power to detect a treatment response of preventing PPCs on short-term HRQoL. Whilst the imputed data set demonstrated an improved signal towards improvements, these findings are uncertain and need to be confirmed in a trial with adequate follow-up and power.

The time point of data collection could also have impacted the sensitivity of detecting an effect on HRQoL. After major abdominal surgery, HRQoL tends to normalise around 2 months.[21–25] Assessment of HRQoL at an earlier time point (eg, 4 weeks) may have more sensitivity at detecting possible differences associated with prevention of postoperative complications. Improvements in 4-week postoperative SF-36 physical domains have been reported following an intensive preoperative exercise and behavioural therapy intervention that halved postoperative complications.[39] A multimodal intervention targeting physical fitness might impact postoperative HRQoL physical domains more than a unimodal intervention targeting a single postoperative complication, as studied in this trial.

This study was conducted in Australia and New Zealand. The best estimate of costs to hospitals attributable to a PPC after abdominal surgery is currently derived from a large US-based study.[7] To the authors' knowledge this is the most methodologically robust data in this field; however, US costs might not be directly comparable with hospitals operating within a universal public healthcare system. Cost-effectiveness interpretations could be improved if comparative PPC costs from similar healthcare funding structures in the LIPPSMAck-POP trial were available. Additionally, this health economic analysis does not include the costs of the additional physiotherapy required if participants contracted a PPC, hospital costs beyond 21 days, or medical and societal costs following hospital discharge, including primary healthcare use, hospital readmissions and productivity. It is possible that the experimental intervention could have better cost-effectiveness if these outcomes were included. Providing some support for this assumption is the observation that whole episode-of-care cost data demonstrated a between-group cost difference four times the magnitude of the restricted cost accounting modelling.

The decision on whether or not something is cost-effective comes down to the purchaser or consumer (ie, the hospital) deciding if the benefit (ie, a reduction in PPC or an improvement in QALY) is worth paying a certain amount to achieve. The determination of the cost-effectiveness of preoperative physiotherapy will be a valuation made by each hospital based on local ideals to prevent PPCs and improve patient QALYs after surgery whilst considering the strength of evidence, generalisability to a local context and the reported probabilities of cost-effectiveness. The LIPPSMAck-POP trial found a 60% probability that preoperative physiotherapy was cost-neutral or entirely cost-saving in preventing PPCs. At this estimate, millions of dollars of healthcare funding could be saved if preoperative physiotherapy is instigated as standard care to the 50 million patients who undergo major abdominal surgery every year in Europe, Australia and the USA alone.[1–3] Alternatively, there is a 40% probability that reducing the PPC rate and improving QALYs after surgery with preoperative physiotherapy would require additional funding over and above standard care. In this case, there is a 95% probability that preoperative physiotherapy is cost-effective if a hospital is willing to pay anywhere up to $45,000 for the service to prevent one PPC with an incremental net benefit of $4,958 (95% CI 10 to 9,197) in the hospital's favour for each PPC prevented.

This is the first multicentre randomised controlled trial investigating PPC prophylaxis with a comprehensive analysis of postoperative hospital use and a robust integrated health economic analysis. Preoperative physiotherapy is a highly efficacious treatment that halves the incidence of a serious postoperative complication,[11,13] is valued by patients,[14] is non-harmful,[11] and is highly likely to be cost-effective from a hospital's perspective in preventing PPCs after major abdominal surgery.

What was already known on this topic: Before major abdominal surgery, a single physiotherapy session involving education and training markedly reduces the incidence of postoperative pulmonary complications. Uncertainty about the cost-effectiveness of preoperative physiotherapy may be making some hospitals reluctant to institute this intervention.

What this study adds: Preoperative physiotherapy aimed at preventing postoperative pulmonary complications is highly likely to be cost-effective from the hospitals' perspective. Improved cost-effectiveness and quality-adjusted life-year gains were detected when experienced physiotherapists delivered the intervention.

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Footnotes: [a] SF-6D software, University of Sheffield, Sheffield, UK. [b] Stata Version 14.1, StataCorp, College Station, USA.

eAddenda: Tables 1, 3 and 4 and Appendices 1, 2, 3, 4 and 5 can be found online at https://doi.org/10.1016/j.jphys.2020.06.005.

Ethics approval: The Tasmanian Human Research Ethics Committee, Australia (H0011911) and Health and Disability Ethics Committee, New Zealand (14/NTA/233) approved this study. All participants were provided with written and verbal information about the study. Those willing to be involved provided signed consent prior to randomisation into the trial.

Competing interests: The funders had no role in study design, data collection, data analysis, data interpretation or writing of the report. The corresponding author had full access to all data in the study and had final responsibility of the decision to submit for publication.

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