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Observation, aspiration, or tube-thoracostomy for primary spontaneous pneumothorax: A systematic review, meta-analysis and cost-utility analysis

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Observation, aspiration, or tube-thoracostomy for primary spontaneous pneumothorax: A systematic review, meta-analysis and cost-utility analysis

Short title: Pneumothorax management: a cost utility analysis

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Trial registration: This trial was not registered. No patient level data was used or accessed.

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MINI-ABSTRACT

Systematic review, meta-analysis and cost utility analysis of management strategies for primary spontaneous pneumothorax were conducted. With careful patient selection, observation may be the most effective and lowest cost management strategy.

ABSTRACT

Background: Primary spontaneous pneumothorax (PSP) has several commonly used management strategies: observation, aspiration, and chest tube (CT). Economic modelling of pooled data comparing techniques has not been performed.

Research question: Based on studies from the past 20 years, approach to management of PSP delivers the highest utility?

Study design and methods: A systematic review of PSP management strategies (observation, aspiration or CT) was conducted in Medline and EMBASE from January 1, 2000 to April 10, 2020. Text screening, bias assessment and data extraction was performed by two authors. Inclusion and exclusion criteria were defined a priori. The primary outcome was PSP resolution following the initial intervention. Secondary outcomes were PSP recurrence, length-of-stay, rate of surgical management, and complications. Meta-analysis compared treatment arms; dichotomous outcomes were reported as risk ratios (RR) and continuous outcomes as mean difference. A cost-utility analysis within the Canadian healthcare system context with deterministic and probabilistic sensitivity analyses were performed.

Results: 5179 articles were identified; after screening, 22 articles were included. Most trials had high risk of bias but randomized trials were lower risk. Compared to CT, observation (Mean difference (MD):5.17, confidence interval (CI):3.75-6.59, $p<0.01$ I^2=62%) and aspiration (MD:2.72 CI:2.39-3.04, $p<0.01$, I^2=0%) had shorter length-of-stay. Compared to observation, CT (RR:0.81, CI:0.71-0.91, $p<0.01$, I^2=62%) and aspiration (RR:0.73, CI:0.61-0.88, $p<0.01$, I^2-=67%) had higher resolution without additional intervention. Two-year recurrence rates did not differ between management strategies. Observation had the best utility (0.82) and lowest cost; observation was the optimal strategy in 98.2% of Monte-Carlo simulations.

Interpretation: Observation is the dominant choice compared to aspiration and CT for PSP. It should be considered as the first line therapy in appropriately selected patients.

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Primary spontaneous pneumothorax meta-analysis and cost utility analysis

Primary spontaneous pneumothorax (PSP) is the presence of air in the pleural space without an inciting event such as trauma and without underlying pulmonary pathology[1,2]. It leads to progressive pulmonary collapse and respiratory compromise. PSP is thought to be due to rupture of air-containing blisters (or bullae) formed under the visceral pleura of the lung[3–5]. It's incidence ranges between 6-24 per 100,000 in European populations (France, Sweden, United Kingdom)[2,5,6] and 39-66 per 100,000 in Korea[7], though it's incidence is lower in pediatric cohorts and is equally common in boys and girls age 9 or less[3]. Hospitalization rates are also lower than incidence rates but hospitalization rates in Minnesota, USA (13.7/100,000 for males and 3.2/100,000 for females) are similar to those in the United Kingdom (16.7/100,000 for males and 5.8/100,000 for females)[6]. PSP is roughly 3 times more common in males over the age of 10[8] and is most common in the second and third decade of life[5].

The most common clinical management strategies are close observation, needle aspiration and tube thoracostomy. The current British Thoracic Society consensuses guidelines recommend aspiration with a pleural drain under 14 French in size for symptomatic pneumothorax or those greater than 2 cm on chest radiographs, and observation for those that are asymptomatic and smaller than 2 cm[4]. The health state of a patient with PSP is reduced form their normal healthy state as they typically have several symptoms including shortness of breath, chest pain, cough and/or hypoxia. Additionally, they are restricted from traveling in the months after a PSP. Successful management of PSP will return them to a normal health state and permit travel again. The question is what is the most appropriate management strategy. Standard (aspiration) and traditional (chest tube) modes of treatment for PSP can be costly and can involve admission to the hospital which affects patients' wellbeing and financial position. Contrarily, observation could be associated with a higher chance of recurrence which would result in more days being symptomatic and lost healthy days resulting in a lower overall health state over the year. Recent studies have questioned if aspiration is necessary by examining the effectiveness of observation of larger pneumothoraxes versus aspiration[1,9]. Additionally, despite widely cited guidelines and the original very similar guidelines published in 2003[10], chest tube (CT) placement remains common in many clinical centres around the world.

Robust Canadian cost and epidemiologic data was not available however the Canadian population is very diverse with an ethnic mix similar to the United States with large East Asian minorities representing 9.4% of the Canadian population[11]. The annual health care cost for PSP in the United States (US) was over $130 million US dollars (USD) in 2000[12]. It has likely grown significantly since that time. Additionally, its cost is quite different based on whether outpatient or inpatient management is undertaken. A nationwide study in Korea between 2002 and 2013 found that the average cost of patients' management in an outpatient setting was 94.50 USD (2018 dollars) while those managed in an inpatient setting was 2,523 USD[7]. Overall, PSP represents a significant burden on healthcare systems around the world given its relatively high incidence and the cost associated with current guideline-based therapy.

Previous systematic reviews have examined differences between the various management techniques for PSP[13–15] but have not been updated since more recent high-quality studies have been published comparing aspiration with other interventions such as observation[1] or a Heimlich device[16]. Reviews that have been performed since these high quality studies were published have pooled all interventions together (aspiration, chest tube and surgery) as a single intervention[17] or included surgical intervention as a comparison arm[18]. In addition, none have compared observation with aspiration or CT, have not examined the difference in costs between the management strategies nor have they performed an economic analysis of different management strategies. Our study aims to use data compiled from our systematic review and meta-analysis using the latest high-quality studies comparing three PSP treatment strategies: (1) observation, (2) needle aspiration and (3) CT and Canadian medical cost data to create an economic model for all three treatment pathways to guide future treatments strategies for PSP.

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METHODS

Systematic review

A systematic search of Medline and EMBASE was designed and conducted by a trained research librarian (Author JP) asking: what is the cost utility of different management strategies (observation, aspiration, or tube thoracostomy) in patients presenting with PSP. The search strategy was divided into two key concepts: condition (primary spontaneous pneumothorax and related terms), and intervention (specifically observation, aspiration, or tube thoracostomy and synonymous terms) while limiting results to studies published between January 1, 2000 and April 10, 2020 (Appendix A). Observation was defined by monitoring a PSP without inserting any form of pleural drain or the performance of any other procedure to evacuate air. Aspiration was defined by either needle aspiration of air or the use of a small-bore pig-tail (under 14 French) catheter to briefly evacuate air followed by clamping or otherwise sealing so that no further air could escape. Chest tube was defined as either a large (14 French or larger) or small-bore chest tube that was inserted and placed to a suction device for ongoing evacuation of extra pleural air.

Systematic abstract and full-text screening, bias assessment and data extraction was performed by two authors. Inclusion and exclusion criteria were defined a priori. Studies were included if they had at minimum two comparative arms comparing PSP management with observation, aspiration, and/or tube thoracostomy. Studies must also have been either randomized control trials, prospective or sequentially collected retrospective cohorts, or case control studies with a defined outcome being assessed. There were no restrictions on age study subjects as the incidence is highest from age 15-34 but begins to increase significantly at age 10[2]. Excluding pediatric patients would exclude an important and significant subset of PSP patients. We also did not restrict studies to one particular geographic region. Only articles published in English, French or Spanish were included. Studies were excluded if pneumothoraxes studied were not PSP (e.g., secondary spontaneous pneumothorax), the study did not have comparative arms, or if they only compared surgical interventions. If a study reported outcomes on PSP and another type of pneumothorax, only data regarding PSP were extracted for analyses.

Primary outcome was resolution following the initial intervention. Secondary outcomes were PSP recurrence, length of hospital stay, and complications due to PSP treatment. We also collected participant demographics including age (mean), male gender (%), BMI (mean), and current smoker (%). Conflict between reviewers was resolved through consensus. Bias was assessed in each included study according to the Cochrane collaboration guidelines[19] using Covidence software[20]. A low risk of bias score was ascribed to studies if at least 5 of the 7 categories were graded as having a low risk of bias. Moderate risk of bias studies had 3 or 4 low risk assessments and high risk studies had fewer than 3 low risk scores[19].

Data extraction was carried out using Covidence software and meta-analysis was conducted using Review Manager[21] using a random effects model. Dichotomous outcomes are reported with risk rations and continuous outcomes with mean difference along with 95% confidence intervals (CI). Heterogeneity between studies was assessed using the chi-square test reported in RevMan (Cochran's Q test) and I^2 tests and pooled results with high heterogeneity (I^2 greater than 70%) is reported in summary only. Subgroup analysis for randomized controlled trials was conducted when more than one study was available.

Economic evaluation and sensitivity analysis

A decision tree was constructed prior to data extraction (Appendix B) and then a cost utility analysis was conducted using the pooled meta-analysis data and utilities from a prior publication[22]. The decision tree had three arms – chest tube, aspiration and observation. The aspiration and observation arms included if the initial treatment was successful or not. If not successful a chest drain was placed. If this was not successful then surgery was performed. If there was a recurrence in either the initially successful or successful after chest drain then the patients received a chest drain and surgery. For the chest tube arm, it was the same as the other two arms but did not include a node for success of treatment before a chest tube was placed. The cost utility analysis was conducted from the Canadian healthcare system perspective – a single-payer publicly funded healthcare system.

Costs of care for PSP was derived form multiple sources. The physician billing costs were identified in the Schedule of Benefits from the Ontario Ministry of Health[23]. Administrative data from our tertiary care children's hospital for PSP patients was used to asses cost of care during admission. Microcosted operating room expenses (including wages and supplies along with pre-operative and recovery room costs), microcosted emergency room visit costs, average cost per radiographic investigation and length of stay multiplied by average cost per day for surgical admissions were used to calculate total admission cost. Costs are reported in 2021 Canadian Dollars (CAD). Cost utility analysis was used to assess the three interventions using our pooled review data. Where there were more than 2 randomized controlled trials (RCT) with over 100 participants overall only RCT data was used in the model, for other data points the entire pooled data was used to derive node frequency estimates (Appendix C, e-Table 1). Utility was derived from a study by Morimoto *et al*[22] and estimated when not reported by Morimoto *et al*. Economic modelling was performed from the perspective of a single payer public health care system. Canadian inflation rates from the Bank of Canada inflation calculator[24] were used to adjust costs to 2021 CAD when costs were incurred before 2021. Mean exchange rate in 2021 was 1.2535 CAD = 1 USD[25]. The study horizon was 1 year; utility did not need adjustment for inflation in the model. The utility used in the model represents 2 months during which the patient experienced their firsts PSP then may have experienced a recurrence. The remaining 10 months were assumed to have a utility of 0.95 and were not included in the estimated utility for the model as it did not contribute to a change in utility. The cost of each arm of the model was calculated using TreeAge Pro 2021, R2.1 (TreeAge Software, Williamstown, MA).

Deterministic and probabilistic sensitivity analyses of the model were performed. One-way deterministic analysis was performed by changing single decision point frequency within a given range to assess each node's effect on the overall outcome of the model. Probabilistic modelling was performed by Monte Carlo simulation with 10,000 iterations. Ranges used in the Monte Carlo simulation were based on mean, maximum and minimum node frequencies reported in identified studies. The base case node frequency was based on the pooled data as described previously. The 95% confidence intervals (CI) were based on the 2.5th and 97.5th centiles of the Monte Carlo simulation and are displayed graphically. The Incremental Cost-Effectiveness Ratio (ICER) was determined with a willingness to pay (WTP) of $70,000 Canadian Dollars based on Cameron *et al*[26] assessment of WTP in 2009 in Canada of 50,000 CAD (range 20,000 CAD to 100,000 CAD) and inflation from 2009 to 2021 of 26.3%[24].

RESULTS

There were 5179 non duplicate articles identified. After abstract screening (5036 articles excluded) and full-text screening (121 articles excluded), 22 articles were included for data extraction[1,9,27–46] (Figure 1). Chest tube and aspiration were compared in 18 studies, chest tube and observation in 9 studies and aspiration and observation in 9 studies (Figure 1). All identified studies were conducted in publicly funded hospitals and all but one (Ramouz *et al*[45]) were conducted in high income countries. Demographic data (Appendix C, e-Table 2) found mean or median age was 16 or 17 years for pediatric studies and in the mid-twenties for most adult studies. Aspiration versus observation was not exclusively based on the BTS guidelines in any study. Prospective studies such as Brown *et al*[1] used predefined inclusion criteria and included pneumothoraxes that were moderate to large in size in all arms of their studies. In the retrospective studies, no study reported using the BTS guidelines to exclusively guide who should undergo aspiration and who should be observed – in the end it was up to the clinician to determine the management strategy for each patient. We did not detect a bias towards small pneumothoraxes in the less invasive management strategies for RCT trials but we were unable to fully assess this in the retrospective studies. The largest study to compare observation with another intervention was prospective and did not have any difference in in pneumothorax size[1] however smaller and retrospective studies either had a difference[33,46] or did not report pneumothorax size by study arm[27,32,36] or at all[29–31,39,40,43]. All studies were strongly skewed towards male sex and patients were almost exclusively 13 years of age or older – only two studies identified a very small number of children under 13 years of age[36,46].

Bias assessment identified high risk of bias for all studies for blinding of participants and personnel due to the nature of the interventions (Appendix C, e-Table 3). Overall, included studies that were randomized controlled trials had lower risk of bias based on our evaluation of study design, data collection and interpretation. Only three studies employed allocation concealment for the data analysis[28,34,38] and outcome assessor blinding[1,28,43]. Risk of bias for differences in pneumothorax size in each arm could not be excluded.

Traditional chest tube vs aspiration

Sixteen studies were identified. Seven were RCTs[28,34,37,38,41,44,45] and one was a prospective cohort with a very small aspiration arm[30]. The remaining eight studies were retrospective[29,32,35,40,43] of which three[31,36,42] had very small aspiration arms. Aspiration had a shorter length of stay vs CT (Figure 2) with a mean difference (MD) of 2.72 days (95% Confidence interval [CI] 2.39-3.04 days, $p<0.01$, $I^2=0\%$, 5 studies). There was no difference when excluding retrospective trials (MD 2.74, $p<0.01$, 4 studies). When comparing pneumothorax resolution following the primary intervention there is a clear trend towards favouring aspiration vs CT when all studies are included however there is very high heterogeneity ($I^2=88\%$) so pooling was not performed. When examining only randomized controlled trials heterogeneity was low (Figure 3). There was a trend towards favouring aspiration (Risk ratio [RR] 1.08, CI: 0.97-1.20, $p=0.17$, $I^2=19\%$) in the randomized controlled trials but it was not statistically significant. There was no difference between the two arms in terms of pneumothorax recurrence up to 2 years following the intervention (RR 1.09, CI:0.80-1.49, $p=0.5$, $I^2=0\%$). Only one RCT study reported if pneumothorax resolved if a CT was inserted after failed aspiration[44] (no difference) and one study reported the recurrence rate following failed primary management with insertion of a CT[45] (no difference). Three RCT studies reported complication rates for which there was a trend towards favouring aspiration (RR 2.83, CI: 0.94-8.53, $p=0.06$, $I^2=34\%$).

Traditional chest tube vs observation

Ten studies were identified. All but one were retrospective cohort studies[27,29,31–33,36,39,40,43] and one was a prospective cohort with a very small observation arm[30]. Only two studies reported length of stay comparing CT with observation of PSP, both of which were retrospective cohort studies with moderate risk of bias. Overall, both studies identified shorter length of stay in the observation arm (Mean difference 5.17 days, CI:3.75-6.59, $p<0.01$, $I^2=62\%$). Six retrospective studies and no prospective studies reported resolution of PSP following CT versus observation. Overall, CT was more likely to lead to resolution of the PSP (RR 0.81, CI:0.71-0.91, $p<0.01$, $I^2=62\%$, Figure 4). There was no difference in recurrence following successful initial treatment strategy up to two years follow-up (RR 1.20, CI: 0.85-1.68, p=0.3, I^2=0%). No studies reported recurrence following initial treatment success when comparing CT and observation and one study[33] reported lower complications with observation versus CT.

Aspiration versus observation

Nine studies were identified. Two were prospective trials – one RCT[1] and one cohort study[30] – while the remaining sever were retrospective[29,31,32,36,40,43,46]. Three of the identified studies had less than 10 patients in one of the arms[30,31,36]. Only one RCT study compared length of stay following aspiration versus observation; it found shorter length of stay with observation[1]. Five studies reported the success rate for observation vs aspiration of PSP; all studies found higher rates of resolution with aspiration but when pooled there was high heterogeneity (I^2=89%). After removing one outlier (Chan *et al.* 2009[32]) the heterogeneity fell to an acceptable level (Figure 5). The remaining 4 pooled studies found aspiration resulted in higher PSP resolution than observation (RR 0.73, CI: 0.61-0.88, p<0.01, I2-=67%). There was no difference in recurrence rates between each arm (RR 1.29, CI: 0.77-2.16, p=0.33, I2=16%, 5 studies) though Brown *et al*[1] did report lower recurrence rate with observation which differs from all other included studies. No studies reported success rate following CT placement for recurrence or rate of resolution following CT placement for failed aspiration or observation. One well designed prospective study[1] reported a lower complication rate in the observation arm when comparing aspiration and observation.

Cost utility modelling

The cost of each management arm based on the economic model were $14,658 CAD for CT placement, $13,126 CAD for aspiration and $6,408 CAD for observation. Estimated utility represents 2 months in a one-year period during which a PSP occurred and a recurrence may have occurred. The utility for each management arm was 0.77 for CT placement, 0.79 for aspiration and 0.82 for observation. The observation arm dominates the other two arms meaning it results in a more desirable (higher) utility with lower cost and results in a negative ICER. Deterministic sensitivity analysis identified model variables that did not have large effects on overall outcomes (Appendix C, e-Table 4) and were left constant in probabilistic modelling. Distributions, ranges and means used in probabilistic modelling are reported in Appendix C (e-Table 5) for the remaining variables. For an explanation of economic modelling terminology please refer to Appendix C of Eamer *et al*, 2020[47].

After Monte Carlo simulation with 10,000 iterations the optimal strategy was observation in 98.2% of simulations, aspiration in 1.8% of simulations and CT in <0.1% of simulations. When comparing Observation and aspiration (Figure 6) or CT (Figure 7), observation was the dominant choice. When aspiration and CT were compared (Appendix D, e-Figure 1), aspiration was favoured over CT. When all three study arms were pooled, aspiration and chest tube were both dominated by observation as the initial treatment modality of choice in appropriately selected patients (Appendix C, e-Table 6). The cost effectiveness acceptability curve demonstrates that changing the willingness-to-pay to between $0 CAD to $100,000 CAD did not change the outcome of the analysis – observation remained the dominant choice (Appendix D – e-Figure 2). Using the model to estimate the rate of surgical intervention in each arm, observation resulted in 19.1% surgical intervention rate, aspiration resulted in 31.5% surgical intervention rate and CT resulted in 36.2% surgical intervention rate. Due to selection bias in most included studies determining statistical significance is not possible.

DISCUSSION

There has been a significant volume of research over the past 20 years as to what intervention, if any, is the most appropriate for management of PSP. Current guidelines have shifted away from CT placement and yet CT placement remains quite common in many physicians' clinical practice. Additionally, current guidelines recommend aspiration of PSP however recent studies have suggested equivalent or improved outcomes with simple observation in appropriately selected patients. Recent publications by Brown *et al.* have supported the implementation of an observation protocol with good long-term outcomes and minimal morbidity[1]. Three previous systematic reviews have examined PSP studies. The first review identified was published in 2019 and found that aspiration was favoured over CT in randomized trials as there was shorter length of stay with no difference in immediate success rate, recurrence rate, rate of surgical intervention or complication rate[13]. A second review examining the same study methodology published one year later also compared aspiration with CT[14]. This review identified decreased complication rate, operation rate and length of stay in the aspiration arm when compared to CT but a higher initial success rate in the CT arm. The final review identified also examined only randomized trials and compared all treatment techniques for PSP[15]. They found no difference between aspiration and CT arms for recurrence but that aspiration reduced hospital length of stay. None of the identified studies compared aspiration or CT with observation and economic modelling has not been done on pooled data.

Interestingly Brown *et al* found decreased recurrence rate in those who underwent observation as opposed to aspiration[1]. While the study was well designed it had slow enrollment with only 30% of eligible patients getting enrolled. The other four studies that examined recurrence in this comparison found no difference[29–31,43] in recurrence rates and the biologic basis for lower recurrence rates with observation in the in the randomized trial is unclear. It is important to note that studies that used observation had strict criteria for who would qualify for observation that included such parameters as degree of shortness of breath, blood pressure, social reliability/ability to easily return to hospital for reassessment and the size of pneumothorax. Conversely, many of the retrospective reviews that were included did not report the size of pneumothorax in each arm of their study or did not report the size at all. This raises the concern that there is bias (smaller PSP were observed and larger had an intervention). It should be noted that size of pneumothorax hasn't been reliably shown to increase risk of recurrence[48]. Any future PSP management algorithm should account for patient biopsychosocial factors that could contribute to worse outcomes or incomplete follow-up.

Younger age of patients has been linked with higher recurrence rates in some studies[8] but not others[48]. Our demographic data was reported in such a manner that we were unable to examine this reliably. However, the large population-based study by Hallifax *et al*[8] did find that a younger age (defined as age 15-34) did have a higher recurrence rate. This age group would correspond to most of the patients included in the studies we identified based on reported mean or median age. This suggests that the recurrence rates that we have used should represent the higher end of recurrence for any age group.

The data from the identified studies over the past 20 years suggests that observation results in a shorter length of stay compared with either aspiration of CT drainage, however both aspiration and CT were more likely to result in resolution of PSP with the initial intervention. This means that there is a higher failure rate with observation, however, no studies identified any major morbidity in patients who failed with observation initially. Those that failed with observation initially faired well when a CT was placed and the rate of surgical intervention may be lower in the observation arm after accounting for surgery on recurrent PSP – though this may be influenced by selection bias within the included studies. There was also no difference between any of the three arms in recurrence rates up to two years out from initial PSP presentation. Additionally, though the data is limited by lower quality data and low rates of reporting, there is evidence within the identified studies that there is a lower complication rate in the observation arm when compared to both aspiration and CT interventions.

This begs the question; what management strategy derives the most utility for patients given the cost and morbidity of CT placement, hospital admission, surgical intervention and the risk of recurrence of PSP. Based on our review of the literature in the last 20 years and using the cost of inpatient care in the Canadian healthcare system, the most desirable long-term outcomes from the patient's perspective (i.e., highest utility) were achieved with initial observation of PSP. Additionally, the lowest cost was derived from treating PSP with observation first in the setting of a well controlled and defined treatment algorithm such as the one used by Brown *et al*[1]. There have been criticism of Brown *et al* for screening a large number of patients who ended up being excluded and the low symptom burden based on reported breathlessness and pain. This may suggest that some selection bias was present but doesn't mean that observation isn't an appropriate management strategy in carefully selected patients. It is important to recall that our analysis found that utility was higher in the observation group and that costs were lower. This means that no mater how much people are willing to pay for an improved outcome observation is the preferred initial management as it gives higher utility with lower expected cost.

It is uncommon for a medical intervention to improve patient outcomes when compared to traditional care while at the same time reducing the cost of that care. Given this, and the increasing evidence that observation is safe and effective in appropriately selected patients presenting with PSP, observation should be considered in all patients presenting with PSP who meet predefined criteria. Additionally, given that aspiration is favoured over CT placement, aspiration should be considered second line therapy in well selected PSP patients presenting with recurrence or who have failed a trial of observation. Hallifax *et al*[16] also found that ambulatory management of PSP with a Heimlich valve is safe and cost-effective[49] at the expense of higher adverse events. This supports, to a certain extent, the findings of our review – observation of PSP in an ambulatory setting is safe and improves cost-utility – with the caveat that the Hallifax study was comparing aspiration with ambulatory Heimlich valve use which is an intervention that we did not include in our analysis.

Limitations

This study is limited by several factors. First, not all nodes within the model had robust prospective pooled data to draw from. This increases the risk that errors introduced by subpar study designs into our model would affect our outcomes. We have controlled for this in several ways including not pooling data together for meta-analysis when the I^2 was too high, limiting the pooled data used in the economic model to prospective randomized trials when able, and using bootstrapped sensitivity

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analysis of the model. It is also encouraging that the trial not only fits what we expected to see before performing the analysis, but was also the dominant choice (lower cost and higher utility) for the observation arm. It is also important to note that our chest tube versus observation arm does not contain any prospective randomized trials. This limits our ability to corroborate retrospective findings with prospective findings. We are comforted that the findings in this arm fit with the overall trend that favors observation over aspiration and aspiration over chest tube insertion. Second, systematic reviews are always prone to reporting bias and we cannot discount the fact that negative studies that may have affected our conclusions and the model may not have been published. We were unable to find any negative studies published as abstracts suggesting our findings represent a real effect.

Third, cost data used for admission cost is based on average cost per bed per day on a pediatric surgical ward at a single institution. It is an accepted method of costing admission but not as accurate as microcosting and disease specific costing methods. The operating room costs were disease specific but the total number of cases was low so costs could be inaccurate. To limit this effect both admission cost per day and operating room expenses were assumed to have a 95% confidence interval of ±15% in deterministic modelling. Both admission cost and operating room cost had a small, but not negligible effect, when compared to other factors on the models' outcomes in deterministic sensitivity analysis. Additionally, costing for complications could not be conducted on a patient level. However, by using length of stay to calculate cost we have captured the additional admission days that a complication will result in. Due to data specific to complication related treatment costs, we cannot calculate additional costs such as antibiotic use, ICU admissions or re-operation. Overall, we did not find a difference in complication rates between the aspiration and chest tube arms. Complications were lower in the observation arms in the minority of studies that reported this outcome. This supports our conclusion that costs are lower in the observation arm.

Fourth, healthcare costs are highly variable from country to country. Our data uses worldwide patient outcome data (though it is skewed towards East Asian and European ethnic populations) but uses Canadian healthcare cost data. Comparison of healthcare costs from country to country has its challenges due to differences in health spending but the overall trend of lower costs due to shorter length of stay with observation, or even aspiration, should hold true in most healthcare systems. Additionally, we have used our local centre's cost (pediatric tertiary care centre) for calculating cost including admission costs, surgical costs and physician billing. There should be no difference in costs between adult care and pediatric care for PSP in our region. Generalizing cost to all patient ages is reasonable as our cost for physician billing are not dependent on patient age, surgical supplies are ordered by our regional health authority and nursing pay is based on a regional contract for all hospitals.

Finally, not all states of health were accounted for in the study we used to determine our utilities for the model and we did not have standard deviation for the utility assessment. We estimated the standard deviation using the range rule which is an acceptable method of estimation though not ideal. Additionally, several states of health were estimated based on extrapolation from the known utility values. This may have introduced errors, but in our opinion the estimated values should represent a reasonable estimate based on the known utility values. Additionally, one of the four estimated values (utility of healthy state) did not end up contributing meaningfully to model variation in deterministic modelling and therefore was excluded for probabilistic sensitivity analysis.

INTERPRETATION

There has been a shift away from CT management of PSP towards either aspiration or observation over the past 20 years though tubes continue to be commonplace in many centres. BTS guidelines currently recommend aspiration for larger pneumothoraxes but our review and model suggest that observation may be the best initial management strategy in appropriately selected patients'. Observation may provide better patient health utility at lower cost and, possibly, with lower complication rates than either CT placement or aspiration of PSP.

Take-home point

Study question: Based on studies from the past 20 years, what approach to management of primary spontaneous pneumothorax has the highest utility?

Results: After systematically searching 20 years of publications, we identified 22 articles. The data suggests that observation and aspiration had shorter lengths of stay compared to chest tube insertion, recurrence rate at 2 years was equal between the three groups and economic modeling suggesting observation had the highest utility and lowest cost compared to aspiration and chest tube insertion.

Interpretation: Observation is the dominant choice compared to aspiration and chest tube insertion for primary spontaneous pneumothorax. It should be considered as the first line therapy in appropriately selected patients.

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Primary spontaneous pneumothorax meta-analysis and cost utility analysis

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FIGURES

Figure 1: Prisma flow diagram of included and excluded articles

Figure 2: Chest tube vs aspiration pooled length of stay favours aspiration.

Figure 3: Chest tube vs aspiration resolution after initial intervention

Figure 4: Chest tube versus observation resolution after initial treatment modality

Figure 5: Aspiration versus observation of primary spontaneous pneumothorax resolution with primary intervention only.

Figure 6: Probabilistic sensitivity analysis by Monte Carlo simulation - Incremental cost effectiveness scatter plot for 10,000 simulations of Observation versus aspiration for primary spontaneous pneumothorax

Definitions: WTP – willingness to pay, ICE – incremental cost effectiveness, ellipse represents 95% confidence interval, green dotes below WTP threshold, red dots above.

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Figure 7: Probabilistic sensitivity analysis by Monte Carlo simulation - Incremental cost effectiveness scatter plot for 10,000 simulations of Observation versus chest tube for primary spontaneous pneumothorax

Definitions: WTP – willingness to pay, ICE – incremental cost effectiveness, ellipse represents 95% confidence interval, green dotes below WTP threshold, red dots above.

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ABREVIATIONS

CAD – Canadian dollars
CI – confidence interval
CT – Chest tube
ICER – Incremental cost effectiveness ratio
MD – Mean difference
PSP - Primary spontaneous pneumothorax
RCT – Randomized controlled trial
RR – Risk ratio
US – United States
USD – United States Dollars

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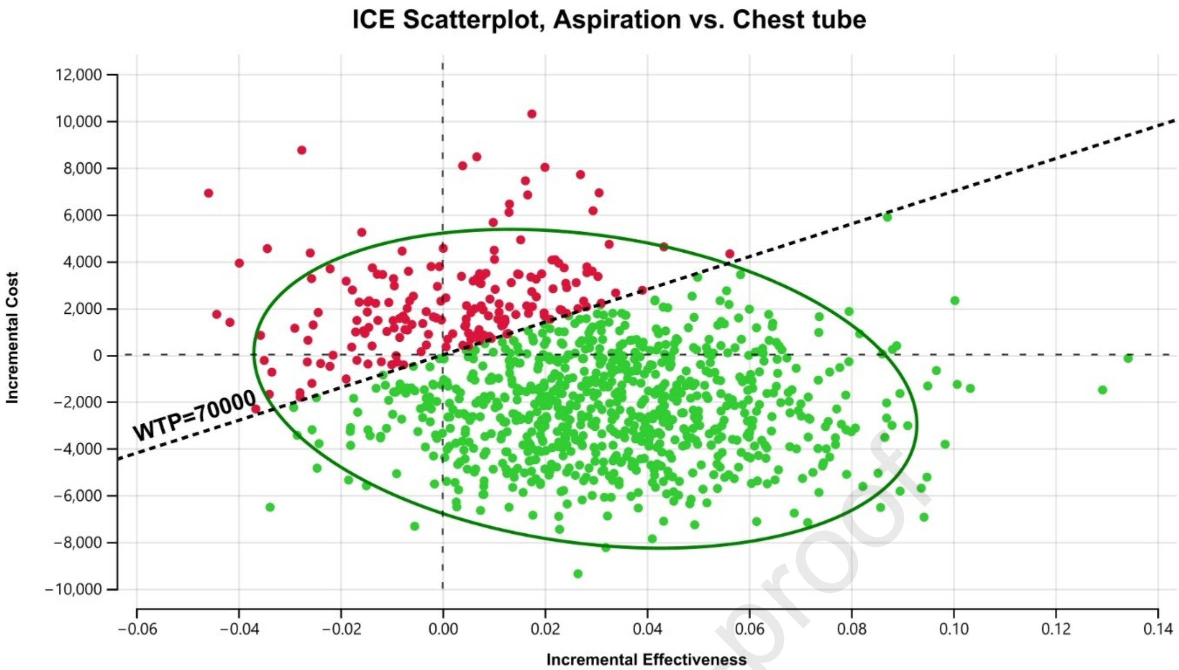

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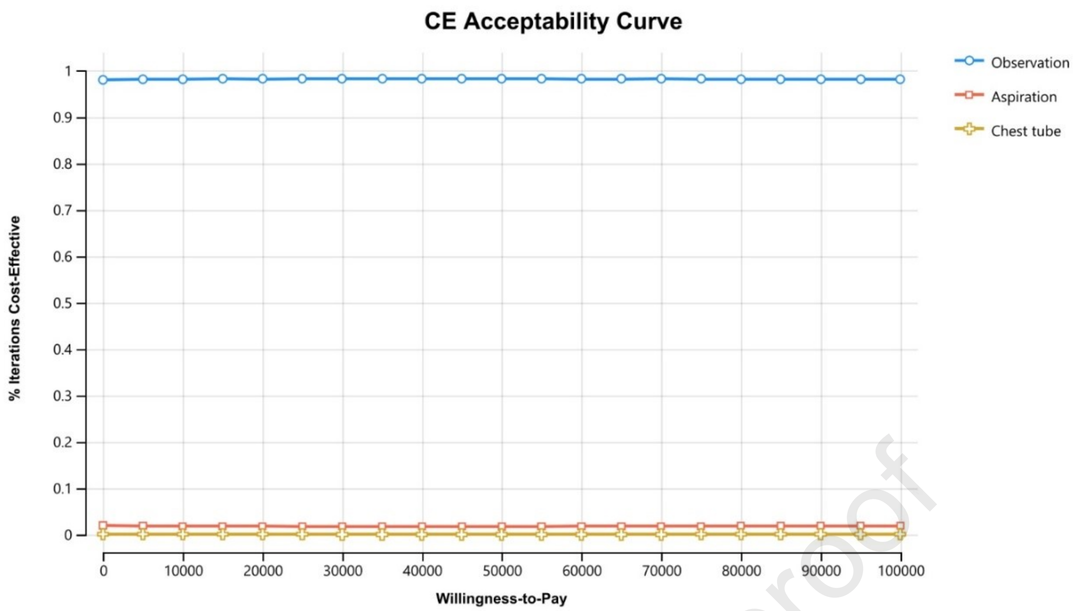

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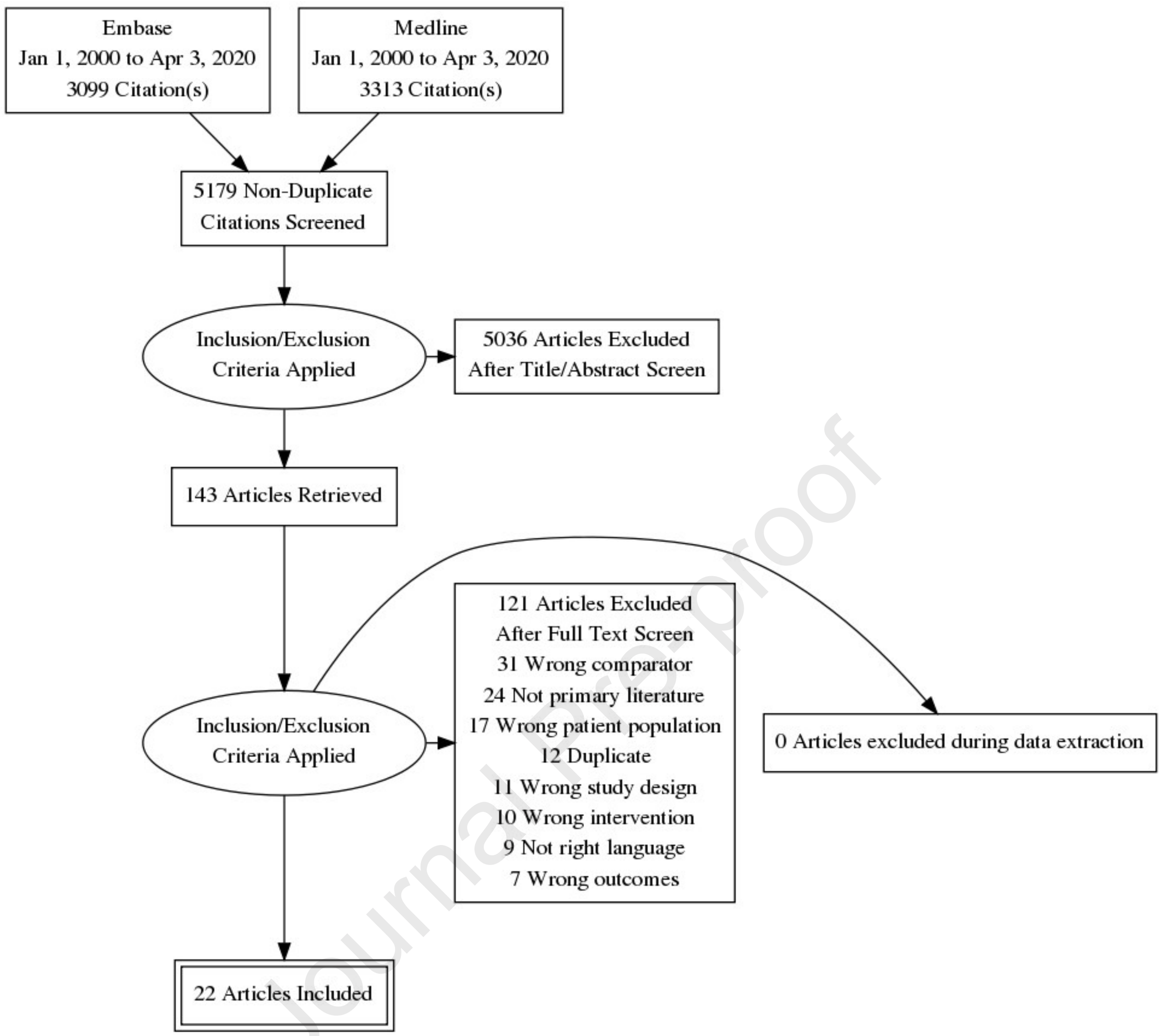

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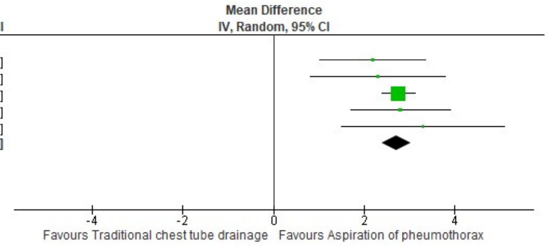
Study or Subgroup	Traditional chest tube drainage Mean	SD	Total	Aspiration of pheumothorax Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Baseline								
Ayed 2006	4.04	2.9	72	1.85	3.9	65	7.8%	2.19 [1.03, 3.35]
Lee 2010	6.9	3	24	4.6	1.9	18	4.7%	2.30 [0.81, 3.79]
Ramouz 2018	4.15	1.07	35	1.39	0.34	35	75.6%	2.76 [2.39, 3.13]
Noppen 2002	4.5	2.7	33	1.7	1.6	27	8.6%	2.80 [1.70, 3.90]
Kim 2019	5.4	3.6	19	2.1	1.8	21	3.3%	3.30 [1.51, 5.09]
Subtotal (95% CI)			**183**			**166**	**100.0%**	**2.72 [2.39, 3.04]**

Heterogeneity: Tau² = 0.00; Chi² = 1.57, df = 4 (P = 0.81); I² = 0%
Test for overall effect: Z = 16.45 (P < 0.00001)

Test for subgroup differences: Not applicable



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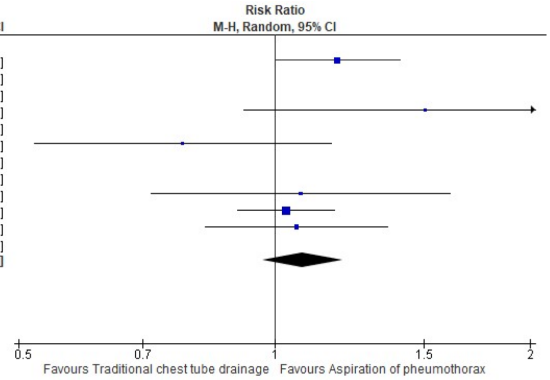
Study or Subgroup	Traditional chest tube drainage Events	Total	Aspiration of pneumothorax Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 Baseline						
Ayed 2006	63	72	48	65	27.9%	1.18 [1.00, 1.40]
Chan 2009	283	382	15	81	0.0%	4.00 [2.52, 6.34]
Ganaie 2019	21	34	4	35	0.0%	5.40 [2.07, 14.11]
Ho 2011	18	25	11	23	4.6%	1.51 [0.92, 2.46]
Kelly 2008	47	64	24	48	0.0%	1.47 [1.07, 2.02]
Kim 2019	12	19	17	21	6.7%	0.78 [0.52, 1.17]
Kuo 2013	15	23	6	8	0.0%	0.87 [0.53, 1.43]
Lee 2010	24	36	18	23	0.0%	0.85 [0.62, 1.17]
Noppen 2002	21	33	16	27	6.6%	1.07 [0.72, 1.61]
Ramouz 2018	33	35	32	35	38.6%	1.03 [0.91, 1.17]
Thelle 2017	29	37	31	42	15.7%	1.06 [0.83, 1.36]
Tomlow 2016	50	55	37	60	0.0%	1.47 [1.19, 1.83]
Subtotal (95% CI)		**221**		**213**	**100.0%**	**1.08 [0.97, 1.20]**
Total events	176		155			

Heterogeneity: Tau² = 0.00; Chi² = 6.16, df = 5 (P = 0.29); I² = 19%

Test for overall effect: Z = 1.37 (P = 0.17)



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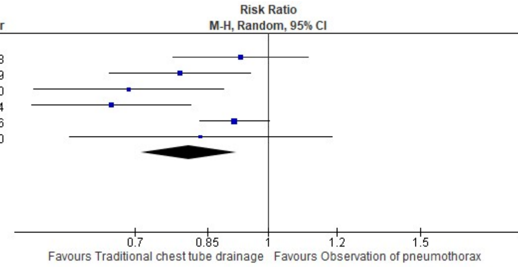
Study or Subgroup	Traditional chest tube drainage Events	Total	Observation of pneumothorax Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
2.2.1 Baseline							
Kelly 2008	47	64	72	91	18.3%	0.93 [0.77, 1.11]	2008
Chan 2009	283	382	7	7	17.8%	0.79 [0.65, 0.95]	2009
Lee 2010	24	36	12	12	13.5%	0.69 [0.53, 0.89]	2010
Chew 2014	36	58	50	53	16.1%	0.66 [0.53, 0.81]	2014
Tomlow 2016	50	55	37	37	25.2%	0.91 [0.83, 1.00]	2016
Gariepy 2020	15	23	25	32	9.1%	0.83 [0.59, 1.18]	2020
Subtotal (95% CI)		**618**		**232**	**100.0%**	**0.81 [0.71, 0.92]**	
Total events	455		203				

Heterogeneity: Tau² = 0.01; Chi² = 13.18, df = 5 (P = 0.02); I² = 62%
Test for overall effect: Z = 3.27 (P = 0.001)



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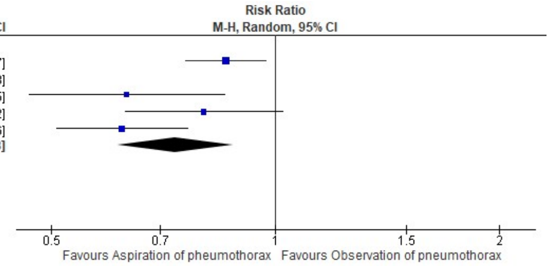
Study or Subgroup	Aspiration of pheumothorax Events	Aspiration of pheumothorax Total	Observation of pneumothorax Events	Observation of pneumothorax Total	Weight	Risk Ratio M-H, Random, 95% CI
3.2.1 Baseline						
Brown 2020	95	131	137	162	32.8%	0.86 [0.76, 0.97]
Chan 2009	15	81	7	7	0.0%	0.20 [0.12, 0.33]
Kelly 2008	24	48	72	91	18.5%	0.63 [0.47, 0.85]
Lee 2010	18	23	12	12	22.6%	0.80 [0.63, 1.02]
Tomlow 2016	37	60	37	37	26.1%	0.62 [0.51, 0.76]
Subtotal (95% CI)		**262**		**302**	**100.0%**	**0.73 [0.61, 0.88]**
Total events	174		258			

Heterogeneity: Tau² = 0.02; Chi² = 8.97, df = 3 (P = 0.03); I² = 67%

Test for overall effect: Z = 3.38 (P = 0.0007)



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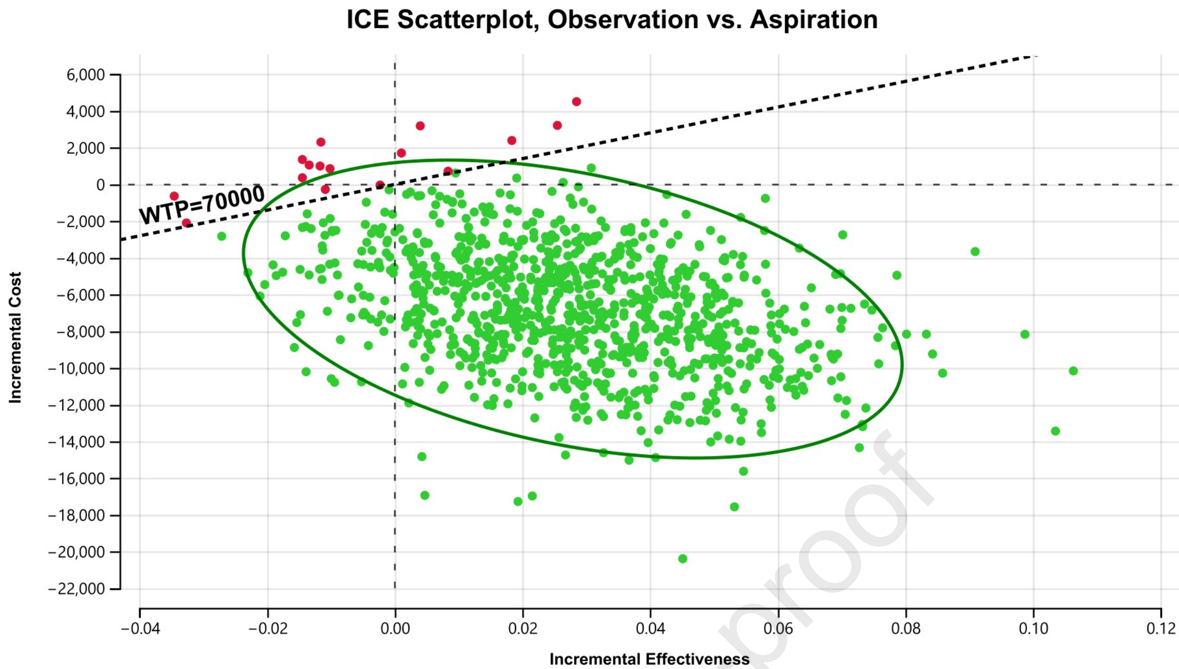

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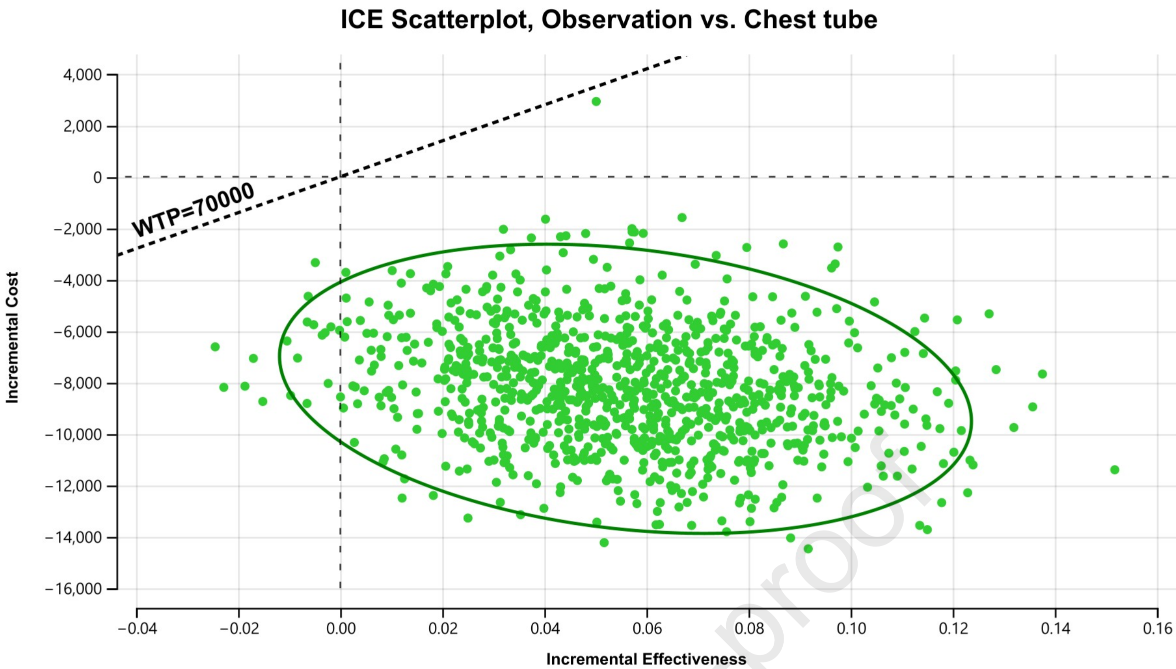

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APPENDIX A: DATABASE SEARCH ALGORITHMS

Embase

Date of Export: April 13, 2020

Database: Embase <1996 to 2020 April 10>
Search Strategy:
----
1 spontaneous pneumothorax/ (2968)
2 ((Unilateral or Spontaneous or primary or tension or pressure or chronic or nontraumatic or non-traumatic) adj2 Pneumothora*).ti,ab,kw. (5090)
3 PSP.ti,ab,kw. (8308)
4 (ruptured pleural adj2 (blebs or bullae)).ti,ab,kw. (2)
5 (spontaneous rupture adj4 (subpleural bleb or bulla)).ti,ab,kw. (2)
6 ((air or gas) adj4 (pleural cavity or air in the pleural space)).ti,ab,kw. (153)
7 (collaps* adj3 lung).ti,ab,kw. (1891)
8 or/1-7 (15301)
9 therapy/ (381872)
10 conservative treatment/ (76231)
11 ((Traditional or Observational) adj3 (Management or intervention)).ti,ab,kw. (4594)
12 ((standard or Usual) adj3 Care).ti,ab,kw. (103835)
13 Standard management.ti,ab,kw. (2275)
14 (interventional adj2 (treatment or management)).ti,ab,kw. (8122)
15 conservative.ti,ab,kw. (110614)
16 chest tube/ (7735)
17 ((chest or drainage or thorax or pleural) adj2 tube*).ti,ab,kw. (14547)
18 drainage tube/ (1687)
19 thorax tube/ (186)
20 pleural catheter/ (628)
21 tunneled pleural catheter/ (178)
22 catheter/ or suction catheter/ (54768)
23 drainage catheter/ or malecot catheter/ or pericardial drainage catheter/ or tenckhoff catheter/ (2164)
24 ((suction or catheter or catheters) adj2 drain*).ti,ab,kw. (5140)
25 (pigtail catheter* or drainage catheter* or pleural catheter* or suction catheter* or malecot catheter* or (pericardial adj2 catheter*) or tenckhoff catheter*).ti,ab,kw. (4462)
26 thorax drainage/ (8628)
27 ((Chest or intercostal or thorax or thoracic or tube) adj3 drain*).ti,ab,kw. (10985)
28 thoracostomy/ (957)
29 Thoracostom*.ti,ab,kw. (2679)
30 needle decompression.ti,ab,kw. (252)
31 thoracocentesis/ (8199)
32 "aspiration, puncture and suction"/ or aspiration/ or catheter aspiration/ or suction/ or suction drainage/ (39816)
33 (Aspiration* or pleurocentes?s or thoracentes?s or Thoracocentes?s).ti,ab,kw. (102272)
34 or/9-33 (825943)
35 8 and 34 (3233)
36 spontaneous pneumothorax/th (263)
37 35 or 36 (3299)
38 animals/ not humans/ (539809)
39 37 not 38 (3284)
40 limit 39 to yr="2000 -Current" (3099)

Medline

Date of Export: April 13, 2020

Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present (April 10, 2020)

Search Strategy:

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1 PNEUMOTHORAX/ (16719)
2 ((Unilateral or Spontaneous or primary or tension or pressure or chronic or nontraumatic or non-traumatic) adj2 Pneumothora*).ti,ab,kw,kf. (6276)
3 PSP.ti,ab,kw,kf. (5969)
4 (ruptured pleural adj2 (blebs or bullae)).ti,ab,kw,kf. (2)
5 (spontaneous rupture adj4 (subpleural bleb or bulla)).ti,ab,kw,kf. (2)
6 ((air or gas) adj4 (pleural cavity or air in the pleural space)).ti,ab,kw,kf. (127)
7 (collaps* adj3 lung).ti,ab,kw,kf. (1538)
8 or/1-7 (25182)
9 Therapeutics/ (8456)
10 Conservative Treatment/ (2780)
11 ((Traditional or Observational) adj3 (Management or intervention)).ti,ab,kw,kf. (3583)
12 ((standard or Usual) adj3 Care).ti,ab,kw,kf. (62292)
13 Standard management.ti,ab,kw,kf. (1474)
14 (interventional adj2 (treatment or management)).ti,ab,kw,kf. (3767)
15 conservative.ti,ab,kw,kf. (104806)
16 Chest Tubes/ (2883)
17 ((chest or drainage or thorax or pleural) adj2 tube*).ti,ab,kw,kf. (11176)
18 Catheters/ (4681)
19 (pigtail catheter* or drainage catheter* or pleural catheter* or suction catheter* or malecot catheter* or (pericardial adj2 catheter*) or tenckhoff catheter*).ti,ab,kw,kf. (3222)
20 ((Chest or intercostal or thorax or thoracic or tube) adj3 drain*).ti,ab,kw,kf. (8802)
21 Drainage/ (42060)
22 Thoracostomy/ (1434)
23 Thoracostom*.ti,ab,kw,kf. (2242)
24 needle decompression.ti,ab,kw,kf. (167)
25 Thoracentesis/ (291)
26 Suction/ (12366)
27 (Aspiration* or pleurocentes?s or thoracentes?s or Thoracocentes?s).ti,ab,kw,kf. (87148)
28 or/9-27 (333583)
29 8 and 28 (4673)
30 Pneumothorax/th (2741)
31 29 or 30 (5891)
32 animals/ not humans/ (4656322)
33 31 not 32 (5754)
34 limit 33 to yr="2000 -Current" (3313)

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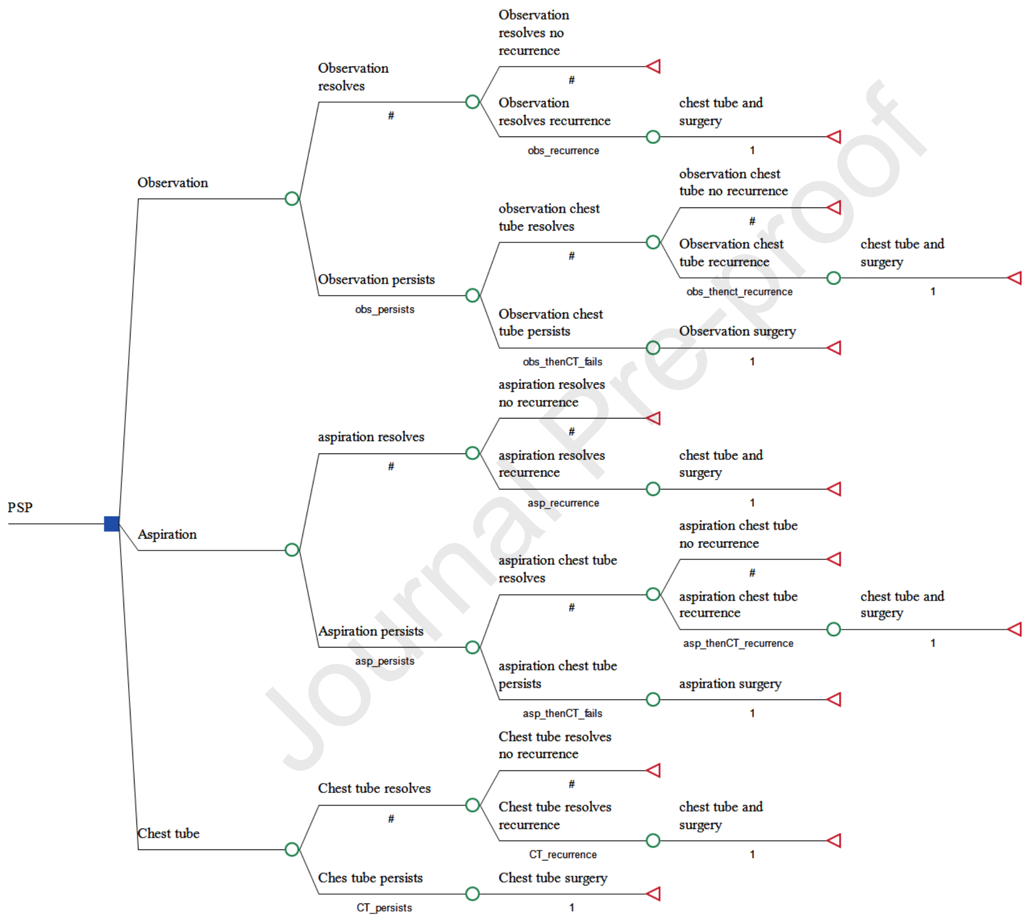
APPENDIX B: ECONOMIC EVALUATION DIAGRAM

Economic model decision tree for three different management strategies: Observation (no up-front drainage of pneumothorax), aspiration (small bore chest tube – under 14 French – drainage with temporary pleural drain or needle) and large bore chest tube (pleural drain 14 French or larger left in-situ for ongoing pleural drainage).



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Study	Title	Trial design	Number of patients enrolled			
			Total	Chest tube	Aspiration	Observation
Ayed 2006	Aspiration versus tube drainage in primary spontaneous pneumothorax: A randomised study	RCT	137	72	65	
Brown 2014	Spontaneous pneumothorax; a multicentre retrospective analysis of emergency treatment, complications and outcomes	Retrospective cohort	159			159
Brown 2020	Conservative versus interventional treatment for spontaneous pneumothorax	RCT	316		154	162
Chan 2009	Management of patients admitted with pneumothorax: A multi-centre study of the practice and outcomes in Hong Kong	Retrospective cohort	476	319	81	76
Chew 2014	Conservative versus invasive treatment of primary spontaneous pneumothorax: A retrospective cohort study	Retrospective cohort	111	58		53
Desmettre 2019	First line simple aspiration versus chest tube drainage in first episodes of primary spontaneous pneumothorax: A French Multicenter, prospective, randomized study (the expred study)	RCT	379	190	189	
Ganaie 2019	How should complete lung collapse secondary to primary spontaneous pneumothorax be managed?	Retrospective cohort	69	34	35	
Gariepy 2020	Management and recurrence of spontaneous pneumothorax in children	Retrospective cohort	59	23	4	32
Ho 2011	A randomized controlled trial comparing mini chest tube and needle aspiration in outpatient management of primary spontaneous pneumothorax	RCT	48	25	23	
Hui 2006	Adolescent primary spontaneous pneumothorax: A hospital's experience	Retrospective cohort	63	44		19
Kelly 2008	Outcomes of emergency department patients treated for primary spontaneous pneumothorax	Retrospective cohort	203	64	48	91
Kim 2019	A Prospective Randomized Trial Comparing Manual Needle Aspiration to Closed Thoracostomy as an Initial Treatment for the First Episode of Primary Spontaneous Pneumothorax.	RCT	40	19	21	

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Kuo 2013	Small-bore pigtail catheters for the treatment of primary spontaneous pneumothorax in young adolescents	Retrospective cohort	31	23	8	
Lee 2010	Management of primary spontaneous pneumothorax in Chinese children	Retrospective cohort	71	36	23	12
Noppen 2002	Manual aspiration versus chest tube drainage in first episodes of primary spontaneous pneumothorax: A multicenter, prospective, randomized pilot study	RCT	60	33	27	
Ramouz 2018	Randomized controlled trial on the comparison of chest tube drainage and needle aspiration in the treatment of primary spontaneous pneumothorax	RCT	70	35	35	
Robinson 2015	Management of paediatric spontaneous pneumothorax: A multicentre retrospective case series	Retrospective cohort	120*		23	65
Shih 2011	Clinical manifestations of primary spontaneous pneumothorax in pediatric patients: An analysis of 78 patients	Retrospective cohort	57*	39		10
Thelle 2017	Randomised comparison of needle aspiration and chest tube drainage in spontaneous pneumothorax	RCT	79	37	42	
Tomlow 2016	Treatment of a spontaneous primary pneumothorax (SPP) in a large teaching hospital	Retrospective cohort	152	55	60	37
Vernejoux 2001	Spontaneous pneumothorax: Pragmatic management and long-term outcome	Prospective cohort	65*	32	4	6
Yap 2017	Epidemiology and outcomes of paediatric primary spontaneous pneumothorax in Singapore	Retrospective cohort	100*	58	2	26

RCT: Randomized controlled trial, * not all patients included in the study met inclusion criteria for intervention type

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Study	Traditional chest tube						Aspiration						Observation						Overall*				
	Age**	Male	Large PSP	PSP size	BMI**	Smoker	Age**	Male	Large PSP	PSP size	BMI**	Smoker	Age**	Male	Large PSP	PSP size	BMI**	Smoker	Age**	Male	Large PSP	BMI**	Smoker
Ayed 2006	23.5	95.8%	NR	NR	19.8	76.4%	24.38	90.8%	NR	NR	19.1	81.5%											
Brown 2014																			26 (20-41)	81.0%	37.1%	NR	NR
Brown 2020							26.4	84.4%		67.5%	21.4	49.3%	26.1	87.7%		63.6%	21.3	42.5%					
Chan 2009																			NR	NR	73.7%	NR	NR
Chew 2014			72.4%												32.7%				37 (18-NR)	75.0%		NR	82.0%
Desmettre 2019																			27	NR	NR	NR	NR
Ganaie 2019	30.5	76.0%	NR	NR	NR	74.0%	30	69.0%	NR	NR	NR	82.0%											
Gariepy 2020																			16 (10-17)	85.0%	81.0%	NR	NR
Ho 2011	24.3	92.0%	96.0%		NR	36.0%	26	91.3%	95.6%		NR	30.4%											
Hui 2006																			16.5	87.3%	NR	"low"	19.1%
Kelly 2008	33	73.0%	NR	NR	NR	NR	26.5	69.0%	NR	NR	NR	NR	21	65.0%	NR	NR	NR	NR					
Kim 2019	24.8	88.2%		65.6%	20.7	15.8%	24	95.0%		56.0%	20.2	23.8%											
Kuo 2013	16	82.6%		59.1%	NR	NR	16	87.5%		44.8%	NR	NR											
Lee 2010	16	96.0%	NR	NR	17		16	78.0%	NR	NR	18												14.0%
Noppen 2002	28.9	84.8%		63.6%	21	81.8%	28.2	74.0%		62.1%	20.9	59.2%											
Ramouz 2018	49.8	83.0%		49.3%	22.3	36.0%	48.9	88.0%		53.8%	21.2	46.0%											
Robinson 2015			48.1%						55.6%						15.0%				15.3 (0.1-18)	68.0%		NR	NR
Shih 2011																			16.8	88.5%	59.0%	18.2	11.5%
Thelle 2017	40.9	84.1%		57.0%	22.1	44.3%	40.5	84.4%		47.5%	21.3	47.6%											
Tomlow 2016																			32.2 (NR-NR)	80.5%	NR	NR	NR
Vernejoux 2001																			30	75.4%	NR	NR	80.0%
Yap 2017																			17.1 (13-18)	93.2%	NR	"low"	11.1%

* Overall demographic data is only reported if cohort specific data was not reported, ** continuous variable presented as mean unless skewed data then presented as median with range in brackets, NR: Not reported, Large PSP: % enrolled with greater than 2 cm distance between pleura and chest wall at the hylum or greater than 50% pneumothorax, PSP size: mean PSP size (% hemithorax) in cohort, PSP: Primary spontaneous pneumothorax

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Study	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Other sources of bias	Trial design
Ayed 2006	Low	High	High	Unclear	Unclear	Low	Low	RCT
Brown 2014	High	High	High	High	Unclear	Low	Low	Retrospective cohort
Brown 2020	Low	High	High	Low	Low	Low	Low	RCT
Chan 2009	High	High	High	High	High	Low	Low	Retrospective cohort
Chew 2014	High	High	High	Unclear	Low	Low	Low	Retrospective cohort
Desmettre 2019	Unclear	Unclear	High	Unclear	Unclear	High	Low	RCT
Ganaie 2019	High	High	High	High	Low	Unclear	Low	Retrospective cohort
Gariepy 2020	High	High	High	High	Low	Low	Low	Retrospective cohort
Ho 2011	Low	Low	High	High	Low	Low	Low	RCT
Hui 2006	High	High	High	High	Low	High	Low	Retrospective cohort
Kelly 2008	High	High	High	Unclear	Unclear	Unclear	Low	Retrospective cohort
Kim 2019	Low	High	High	Unclear	Low	Unclear	Low	RCT
Kuo 2013	High	High	High	High	Low	Unclear	High	Retrospective cohort
Lee 2010	High	High	High	Low	Low	Low	Low	Retrospective cohort
Noppen 2002	Low	Low	High	High	Low	Low	Low	RCT
Ramouz 2018	Unclear	Unclear	High	Unclear	Low	Unclear	Low	RCT
Robinson 2015	High	High	High	High	Unclear	Unclear	Low	Retrospective cohort
Shih 2011	High	High	High	Unclear	Low	Unclear	Low	Retrospective cohort
Thelle 2017	Low	Low	High	Low	Low	Unclear	Low	RCT
Tomlow 2016	High	High	High	Unclear	Unclear	Unclear	Unclear	Retrospective cohort
Vernejoux 2001	High	High	High	High	Low	Unclear	Low	Prospective cohort
Yap 2017	High	High	High	High	Unclear	High	Unclear	Retrospective cohort

RCT: Randomized controlled trial

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Variable description	Value	Notes
Cost of chest tube	$ 200.00	Administrative data
Cost of chest tube insertion	$ 76.80	Ministry of health billing schedule
Cost of computed tomography	$ 139.85	Administrative data
Cost of chest X-ray	$ 62.60	Administrative data
Cost of emergency physician assessment	$ 106.80	Ministry of health billing schedule
Cost for care in emergency department	$ 86.45	Administrative data
Cost of surgeon consult	$ 98.55	Ministry of health billing schedule
Cost of pathologist assessment of surgical specimen	$ 103.20	Ministry of health billing schedule
Cost of pigtail for aspiration	$ 120.00	Administrative data
Surgeon billing for VATS bullectomy	$ 672.00	Ministry of health billing schedule
Probability of failed aspiration followed by successful chest tube then recurrent PSP	10.0%	Pooled review data
Probability of failed observation followed by successful chest tube then recurrent PSP	25.6%	Pooled review data
Utility derived during a healthy state - no PSP and not during month of admission	0.95	Expert opinion
Length of stay (days) following VATS bullectomy	5.5	Pooled review data

Definitions: PSP - Primary spontaneous pneumothorax, VATS - Video assisted thoracoscopic surgery, all costs reported in 2021 Canadian Dollars

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Category	Variable description	Base case	Range			St Dev	Distribution	Notes
Cost	Cost of admission per day	$ 2,295.65	$1,951.30	-	$2,640.00	$172.17	Normal	& and ^
	Operating and recovery room hospital costs for VATS bullectomy (physician billing excluded)	$ 3,997.67	$3,398.02	-	$4,597.32	$299.83	Normal	& and ^
Model node frequencies	Probability PSP persists following aspiration	25.5%	8.6%	-	40.7%	8.0%	Normal	*
	Probability of recurrent PSP following aspiration	20.7%	16.8%	-	29.2%	3.1%	Beta	*
	Probability failed aspiration followed by failed chest tube	59.0%	18.2%	-	75.8%	14.4%	Beta	
	Persistent PSP following primary chest tube placement	15.8%	5.7%	-	36.8%	7.8%	Beta	*
	Recurrent PSP following successful chest tube management	24.2%	15.8%	-	27.3%	2.9%	Beta	*
	Persistent PSP following initial observation	13.7%	0.0%	-	21.9%	5.5%	Beta	
	Recurrent PSP following successful observation management	15.1%	7.5%	-	38.5%	7.8%	Beta	
	Probability failed observation followed by failed chest tube	60.0%	45.0%	-	75.0%	7.5%	Normal	^ (1 study only)
Length of stay	Length of stay (days) - Observation arm	1.45	0.60	-	3.50	0.725	Gamma	
	Length of stay (days) - Aspiration arm	3.97	1.39	-	6.10	1.18	Gamma	*
	Length of stay (days) - Chest tube arm	4.32	4.04	-	5.4	0.340	Gamma	*
Utility	Utility during admission for PSP - managed with **observation**	0.5	0.43	-	0.57	0.035	Normal	#
	Utility during the month after discharge from hospital following **observation** of PSP	0.75	0.68	-	0.82	0.035	Normal	#
	Utility during admission for PSP - managed with **aspiration**	0.45	0.33	-	0.58	0.063	Normal	Morimoto et al.
	Utility during the month after discharge from hospital following **aspiration** of PSP	0.7	0.63	-	0.77	0.035	Normal	#
	Utility during admission for PSP - managed with **chest tube**	0.45	0.33	-	0.58	0.063	Normal	Morimoto et al.
	Utility during the month after discharge from hospital following **chest tube** drainage of PSP	0.63	0.51	-	0.76	0.063	Normal	Morimoto et al.
	Utility during admission for PSP - managed with VATS bullectomy	0.37	0.25	-	0.49	0.060	Normal	Morimoto et al.
	Utility during the month after discharge from hospital following VATS bullectomy for PSP	0.82	0.7	-	0.93	0.058	Normal	Morimoto et al.

Legend: VATS - video assisted thoracoscopic surgery, PSP - primary spontaneous pneumothorax, St Dev - standard deviation (estimated with range rule), RCT - Randomized controlled trial, & Hospital administrative data, ^ assumed standard deviation of 7.5% from mean, * RCT data, # expert opinion, all costs reported in 2021 Canadian Dollars

Strategy	Cost (CAD)	Incremental cost (CAD)	Effectiveness	Incremental effectiveness	ICER	Net monetary benefit (CAD)
Observation	6,408.32		0.82			34,714
Aspiration	13,125.62	6,717	0.79	-0.03	-243,101	26,615
Chest tube	14,658.29	8,249	0.77	-0.06	-149,655	23,708

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APPENDIX C: TABLES FOR META-ANALYSIS AND ECONOMIC MODELING

e-Table 1: Study characteristics, design and participants

e-Table 2: Study demographic outcomes

e-Table 3: Quality assessment of included trials according to Cochrane collaboration bias assessment guidelines based on high, low or unclear risk of bias

e-Table 4: Constant variables for economic model Monte Carlo simulation based on deterministic modelling

e-Table 5: Economic model base case values, range used in economic modelling, distribution type, study design and description

e-Table 6: Cost effectiveness rankings for Observation, aspiration and chest tube with net monetary benefit for each arm

Legend: CAD – Canadian dollars, ICER – Incremental Cost Effectiveness Ratio (Incremental cost/incremental effectiveness)

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APPENDIX D

e-Figure 1: Probabilistic sensitivity analysis by Monte Carlo simulation - Incremental cost effectiveness scatter plot for 10,000 simulations of aspiration versus chest tube for primary spontaneous pneumothorax.

Definitions: WTP – willingness to pay, ICE – incremental cost effectiveness, ellipse represents 95% confidence interval, green dotes below WTP threshold, red dots above.

e-Figure 2: Cost effectiveness acceptability curve for three primary spontaneous pneumothorax management strategies

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