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Evaluation of a Digital Health Model of Care for the Management of Adults With Symptomatic Malignant Pleural Effusion

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Keywords: digital health | malignant pleural effusion | nursing care | patient-reported outcomes | teleultrasound

ABSTRACT

Background: The management of malignant pleural effusion (MPE) is inconsistent across health services. Many centres do not routinely offer all treatment options for MPE, with indwelling pleural catheter (IPC) being a primary example. This may be due to lack of specialist expertise or nursing capability to support the community-based treatment. New approaches are required to improve access to MPE treatments. This proof-of-concept study examines the feasibility of a virtual model of care for MPE, known as the specialist ambulatory pleural service (SAPS) model of care. This model will be compared with current approaches at other health services in the state, in terms of healthcare utilisation and costs. It will also assess health-related quality of life in individuals with MPE and report patient, carer and nurse experiences with the SAPS model of care.

Methods: A prospective, multi-centre, mixed-methods study will be performed. Participants with symptomatic MPE requiring intervention will be consecutively enrolled. The primary outcome is pleural effusion-related hospitalisation from enrolment to death or end of study participation. Secondary outcomes include: Overall hospitalisation, unplanned pleural effusion-related outpatient and emergency department (ED) visits, pleural-related healthcare costs, adverse events, overall survival, percentage of screened patients recruited, percentage dropped out/lost to follow up, percentage of scheduled home visits carried out, percentage of teleultrasound assessments completed, technical issues, percentage of symptom logbooks completed, quality of life, longitudinal symptom monitoring, participant and nursing attitudes to the SAPS model of care, patient activation measure and a stakeholder interview of the SAPS model of care implementation.

Discussion: Digital health may improve access to MPE treatments by reducing barriers to specialist care and facilitating training and support for community staff. This trial assesses the SAPS model of care, providing data on barriers and facilitators to its implementation, its efficacy, costs and qualitative outcomes.
Trial Registration: Australia New Zealand Clinical Trial Registry: ACTRN12623000063617; https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=384448&isReview=true.

1 | Additional Trial Registration Information

Date of registration: 18/01/2023.

Funding of the trial: HCF Foundation; Victorian Nurse and Midwifery Trust.

Name and contact information for the trial sponsor: Dr Justine Ellis, Research Operations Manager, Northern Health Research Development and Governance Unit.

Role of sponsor: Responsible for initiating, managing, and/or financing the trial, and for carrying the medico-legal responsibility associated with its conduct.

2 | Introduction

2.1 | Background and Rationale

Malignant pleural effusion (MPE) has a reported incidence of 660 cases per million population [1, 2]. In Australia, it is estimated to affect 10,000 people each year and can complicate most types of cancer. MPE represents an incurable stage of disease and is often associated with breathlessness, functional limitation and impaired quality of life (QoL). It is a frequent cause of hospitalisation and unplanned healthcare utilisation [3]. The burden of MPE-related healthcare continues to rise due to overall improvements in cancer survival. Data from Western Australia previously identified a doubling of inpatient care costs for MPE over a 5-year period, with costs now exceeding AUD 10 million annually [4]. In the United States, MPE is estimated to account for over 125,000 hospital admissions each year, has an inpatient mortality rate of 11% and a total cost of USD 5 billion each year [5]. Survival from diagnosis of MPE ranges from 13 to 484 days, being influenced primarily by performance status and cancer type [6]. Even in previous randomised controlled trials of MPE interventions, over 30% of participants did not survive beyond 3 months [7, 8].

There are two main treatment approaches for MPE: use of indwelling pleural catheters (IPC) or chemical pleurodesis via an intercostal drain (ICD) [9–11]. Each have their respective advantages and drawbacks; however, they are considered comparable for symptom control and QoL outcomes [7, 12, 13]. Due to the high risk of recurrence and poor prognosis [14], a key aspect of MPE management is to use the fewest procedures to manage symptoms, optimise physical function and avoid hospitalisation. While still regularly performed in some centres, the role of pleurodesis via a thoracoscopic approach, for example, video-assisted thoracoscopic surgery (VATS) or local anaesthetic thoracoscopy (LAT) has diminished due to the more invasive nature of the procedure and data suggesting no better pleurodesis success rates compared to ICD pleurodesis [15]. A disadvantage of chemical pleurodesis, regardless of approach, is a failure rate of 20%–30% [13, 15, 16], often necessitating at least a second procedure being performed (usually with a hospital admission) in these individuals to manage recurrence of MPE.

Determining the choice of treatment involves an in-depth discussion of individual wishes and preferences. However, many health services within the Australian healthcare system do not offer IPC as a standard option or lack the infrastructure required to provide ongoing support of individuals with IPC. This may result in a higher number of procedures being performed, with greater hospitalisation. A recent survey of clinicians who regularly manage MPE confirmed a lack of clinical support in the community as a major barrier to recommending IPC as a treatment option [17].

Improving access to MPE treatments and IPCs in particular, therefore represents a key step to improving the quality of MPE care. In 2019, the Pleural Medicine Unit (PMU) was established at Northern Health. A major objective of the PMU was to support individual choice by improving local access to evidence-based therapies for MPE. In response to access issues related to the coronavirus-2019 (COVID-19) pandemic, a virtual model of care for individuals with MPE was successfully piloted in 2020 (one person with malignant ascites, managed with an indwelling peritoneal catheter was included) [18]. This model replaced outpatient hospital attendance for people with newly diagnosed MPE, with home visits performed by a trained nurse, who could facilitate a telehealth consultation (including bidirectional video and audio) with a respiratory physician. The nurse was able to perform an ultrasound assessment which was streamed to the physician (teleultrasound), who could in turn provide real-time feedback on image acquisition and make immediate management decisions. The nurse could also provide education for individuals regarding MPE, provide information on treatment options, support management of IPC where applicable and undertake procedures such as IPC drainage and dressing change, pleural fluid sampling from an IPC and phlebotomy. This model of care was designated the specialist ambulatory pleural service (SAPS).

Extending the reach of the SAPS model of care at Northern Health would allow greater access to MPE care, particularly in regional areas or areas where limited treatment options are available. It would aim to develop local expertise in managing MPE and allow individuals with MPE to spend less time receiving care within hospitals. This real-world study will provide a comparison of the SAPS model of care (Figure 1) with the existing approach

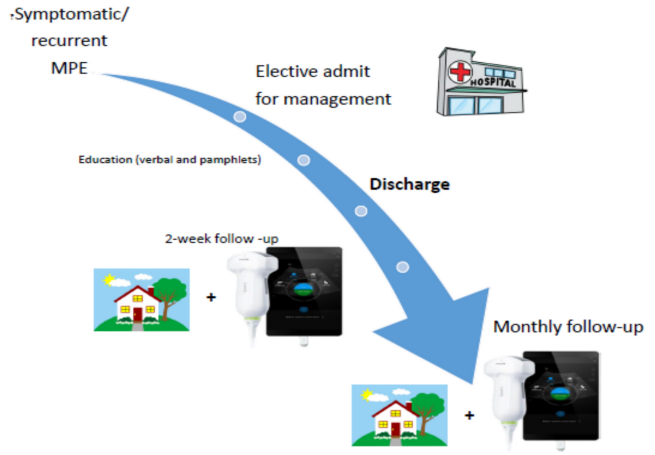

FIGURE 1 | The proposed SAPS model of care.

to MPE management currently in use at other large local health services, to ascertain the impact of this approach.

2.2 | Objective

The primary aim of this study is to determine the feasibility of integrating telehealth and teleultrasound into an ambulatory model of care (SAPS) for the management of MPE and compare outcomes to the existing model of care across three other health services.

This study consists of six objectives:

- *Objective 1*: To determine healthcare utilisation of individuals with MPE according to the model of care employed at their health service.
- *Objective 2*: To determine the feasibility of longitudinal symptom monitoring using patient-reported outcome measures (PROMs) in individuals with MPE.
- *Objective 3*: To determine healthcare costs between the SAPS model of care and the standard model of care.
- *Objective 4*: To ascertain consumer acceptability of the SAPS model of care.
- *Objective 5*: To ascertain nursing acceptability of the SAPS model of care.
- *Objective 6*: To receive feedback on the SAPS model of care by various stakeholders in patient care.

2.3 | Trial Design

Prospective, pragmatic, mixed-methods study comparing the SAPS model of care with the inpatient model of care for MPE (Figure 2).

There are six parts corresponding with the listed objectives:

- *Part 1*: Comparing healthcare utilisation of individuals with MPE according to the model of care employed at their health service.

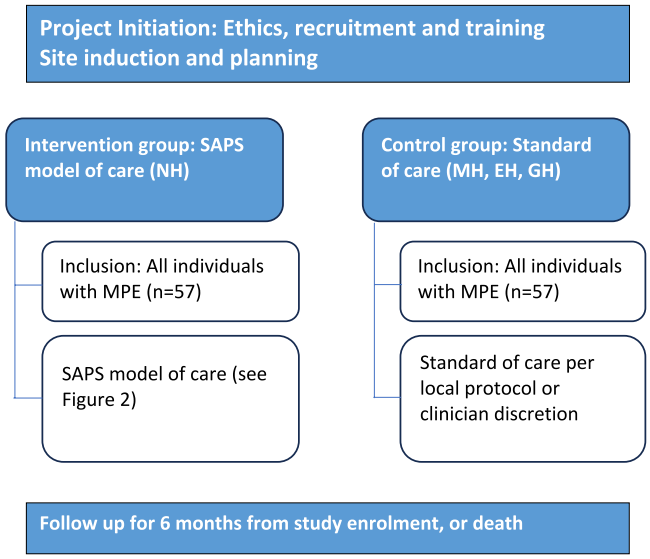

FIGURE 2 | Project overview.

- *Part 2*: Feasibility of longitudinal symptom monitoring using PROMs in individuals with MPE
- *Part 3*: Comparison of healthcare costs between the SAPS model of care and the standard model of care
- *Part 4*: Describe the consumer experience associated with the SAPS model of care
- *Part 5*: Describe the nursing experience associated with the SAPS model of care
- *Part 6*: Describe stakeholder experience in the implementation of the SAPS model of care

3 | Methods

3.1 | Participants, Interventions and Outcomes

3.1.1 | Study Setting

Intervention group

- Northern Health (NH), Epping, Victoria, Australia.

Comparison group

- Melbourne Health (MH), Parkville, Victoria, Australia.
- Grampians Health (GH), Ballarat, Victoria, Australia.
- Eastern Health (EH), Box Hill, Victoria, Australia.

3.1.2 | Eligibility Criteria

- Age of 18 years or older
  - Inpatients or outpatients at Northern, Melbourne, Grampians and Eastern Health
- Diagnosis of MPE
  - Defined as a pleural effusion in which malignant cells are identified in pleural fluid or on pleural biopsy.

- An MPE may also be diagnosed based on the presence of a large exudative effusion without other causes in an individual with disseminated extra-thoracic malignancy [7, 8, 12, 19, 20]

- Participants can be enrolled prior to, or after a definitive pleural procedure for MPE management has been performed.

At the intervention site (NH), individuals are identified after referral to the PMU for management of MPE. Participants who are medically unwell (per treating clinician's discretion) or with known cognitive impairment will be excluded from the requirement to complete questionnaires/surveys and interviews. Health service data for Part 1 of this study will be collected from these participants with the consent of a substitute decision maker.

Those admitted to the comparison sites with an MPE during the study period will be identified through two sources. First, primary discharge diagnostic codes for acute care episodes (defined using the International Classification of Diseases (ICD) version 10) will be audited and episodes with the code C782: 'Secondary malignant neoplasm of pleura' will be extracted from the electronic health information of each health service. Second, the pathology database of each health service will also be audited to identify pleural pathology diagnosed either by cytology or histopathology. Results identified and extracted from these sources will be evaluated by the investigators and verified through the examination of relevant medical records to determine eligibility. All results identified for individuals that meet the inclusion criteria will be included. In cases where there is uncertainty with regards to the diagnosis of MPE, inclusion will be determined by consensus of at least two of the investigators including the coordinating principal investigator.

3.1.3 | Who Will Collect Informed Consent?

At the intervention site (NH), individuals will be approached by the site research staff (as per the Delegation Log) upon the diagnosis of MPE. Consecutively identified individuals with MPE will be offered trial entry and enrolled after providing informed consent. In circumstances where a participant does not have the capacity to consent, consent by a substitute decision-maker will be sought in accordance with the State of Victoria's Guardianship and Administration Board Act.

The study has been granted ethics approval by the Royal Melbourne Hospital Research, Governance and Ethics Unit (HREC/85858/MH-2022). A waiver of consent has been sought and approved, and will apply for the participants in the comparison groups (Melbourne Health, Grampians Health and Eastern Health) as the study is accessing routinely collected information from patient records and hospital administrative data.

3.1.4 | Interventions

Upon enrolment at the intervention site, individuals will have their MPE managed at the discretion of the treating team, which may include IPC, VATS, chemical pleurodesis (via chest tube or thoracoscopy), or a combination approach. After the procedure, follow up will be according to the SAPS model of care. Personalised education, information booklets and IPC consumables (where applicable) will be provided to the participants. Participants will be given a logbook to monitor breathlessness and pain up to 1 month from enrolment.

A portable tablet and access to a broadband connection (mobile 4G/5G) will be used by a pleural nurse to facilitate review in the community. Fortnightly video calls (using the secure video call platform; Phillips Reacts [21]) and home visits for the first month (post-definitive procedure), then monthly will be scheduled in addition to as-needed home visits. Home visits throughout the study period will be attended by the trained pleural nurse who will review progress, educate, perform teleultrasound with real-time (remote) physician supervision and ensure PROMs are obtained.

Philips Lumify handheld ultrasound devices will be used for the purpose of remote assessment, with Reacts videoconferencing software incorporated in the device. Participants will also be provided with a 24-h on-call number to report worsening of symptoms or to assist with troubleshooting of IPC-related issues (Figure 3).

3.1.5 | Participant Withdrawal Criteria

Participants can opt out of the trial at any stage without providing a reason. Participant data up to the point of withdrawal will be retained, as described in the Participant Information and Consent Form. Participants withdrawing from the study will return to receiving standard care.

Alternatively, participants can opt out of completing PROMs but remain in the study. Additionally, participants may opt out of home visits and instead attend follow-up appointments in the outpatient clinic while continuing to complete PROMs.

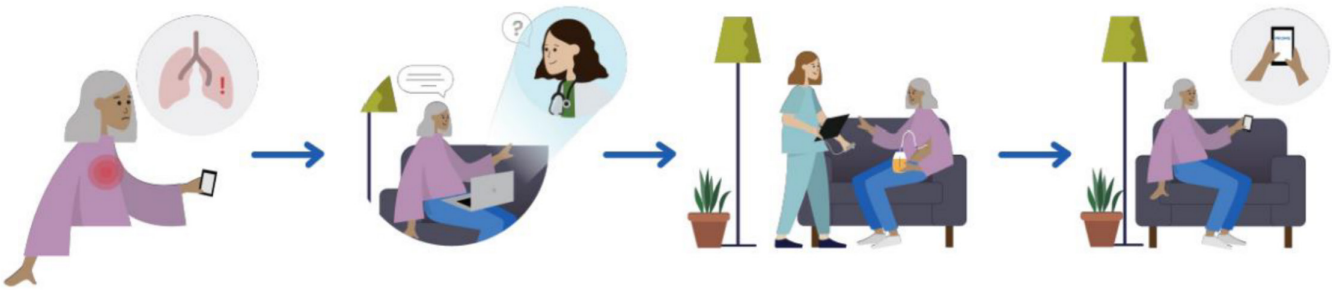

FIGURE 3 | Pathway for managing MPE-related concerns under the SAPS model of care.

3.1.6 | Primary Outcome

Pleural effusion-related hospitalisation, in days and percentage of survival time from enrolment to death or end of study participation.

3.1.7 | Secondary Outcomes (All Sites)

- Overall hospitalisation, in days and percentage of survival time from enrolment to death or end of study participation
- Unplanned pleural effusion-related outpatient and emergency department (ED) visits from enrolment to death or end of study participation
- Pleural-related healthcare costs
- Adverse events
- Overall survival

3.1.8 | Secondary Outcomes (Intervention Site Only)

- Percentage of screened patients recruited
- Percentage dropped out/lost to follow up
- Percentage of scheduled home visits carried out
- Percentage of teleultrasound assessments completed
- Technical issues encountered
- Percentage of symptom logbooks completed
- Health-related quality of life using EQ-5D-5L [22] and ICEpop CAPability Measure for Adults (ICECAP-A) [23]
- Symptom measurement (Visual analogue scale for breathlessness and pain)
- Health information technology usability evaluation scale (Health-ITUES) [24]
- Carers' experience survey
- Nurses' experience survey
- Patient activation measure (PAM) [25]
- Qualitative evaluation (semi-structured interviews of participants and study nurse)
- Evaluation of the SAPS model of care implementation (stakeholder interview)

3.1.9 | Participant Timeline

Participation flow is outlined in Table 1.

3.1.10 | Sample Size

This study will be powered to detect a cumulative length of hospital stay difference of 6 days or more between the groups (80% power; $\alpha = 0.05$) based on the AMPLE study [12], with the estimated mean in the control group considered to be 12 (SD,12) days based on a one-sided test. There is no established minimal

TABLE 1 | Schedule of participant treatment, follow up and data collection.

Timepoint	Day 0 (enrolment)	Discharge	Day 14	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6
Baseline information[a]	x								
MPE education	x	x							
VAS dyspnoea and pain (logbook)		x	x	x					
Determine drainage regimen		x							
Assess for pleurodesis[b]			x	x	x	x	x	x	x
EQ-VAS		x	x	x	x	x	x	x	x
EQ-5D-5L		x	x	x	x	x	x	x	x
ICECAP-A		x	x	x	x	x	x	x	x
PAM	x						x		
Healthcare utilisation questionnaire			x	x	x	x	x	x	x
Health-ITUES			x	x	x	x	x	x	x
Nurse survey			x	x	x	x	x	x	x
Carer survey			x	x		x	x	x	x
Economic evaluation[a]									x
Ultrasound	x		x	x	x	x	x	x	x

[a]Outlined in the following section.
[b]If pleurodesis is achieved: Schedule IPC removal. If not achieved and lung is expandable, consider chemical pleurodesis. If the lung is non-expandable consider changing the regimen to symptom-guided.

clinically important difference for this endpoint, but 50% reduction in the mean hospital stay was considered a clinically meaningful effect size for the purposes of the sample size calculation.

A total sample size of $N = 114$ will be required ($n = 57$ per group). The overall recruitment target of 114 allows for a lost-to-follow-up rate of approximately 10%.

TABLE 2 | Light's effusion grading.

0	No fluid
1	Blunting of the costophrenic angle
2	< 25% but more than blunting
3	25% but > 50% of hemithorax
4	50%–75% of hemithorax
5	> 75% of hemithorax

3.2 | Data Collection, Management and Analysis

3.2.1 | Data Collection Methods

Data for this study will be collected and entered in a secured database provided by REDCap (Research Electronic Data Capture). A system of data validation checks will be implemented and applied to the database. The accuracy of the data will be verified by comparing study data to source documents.

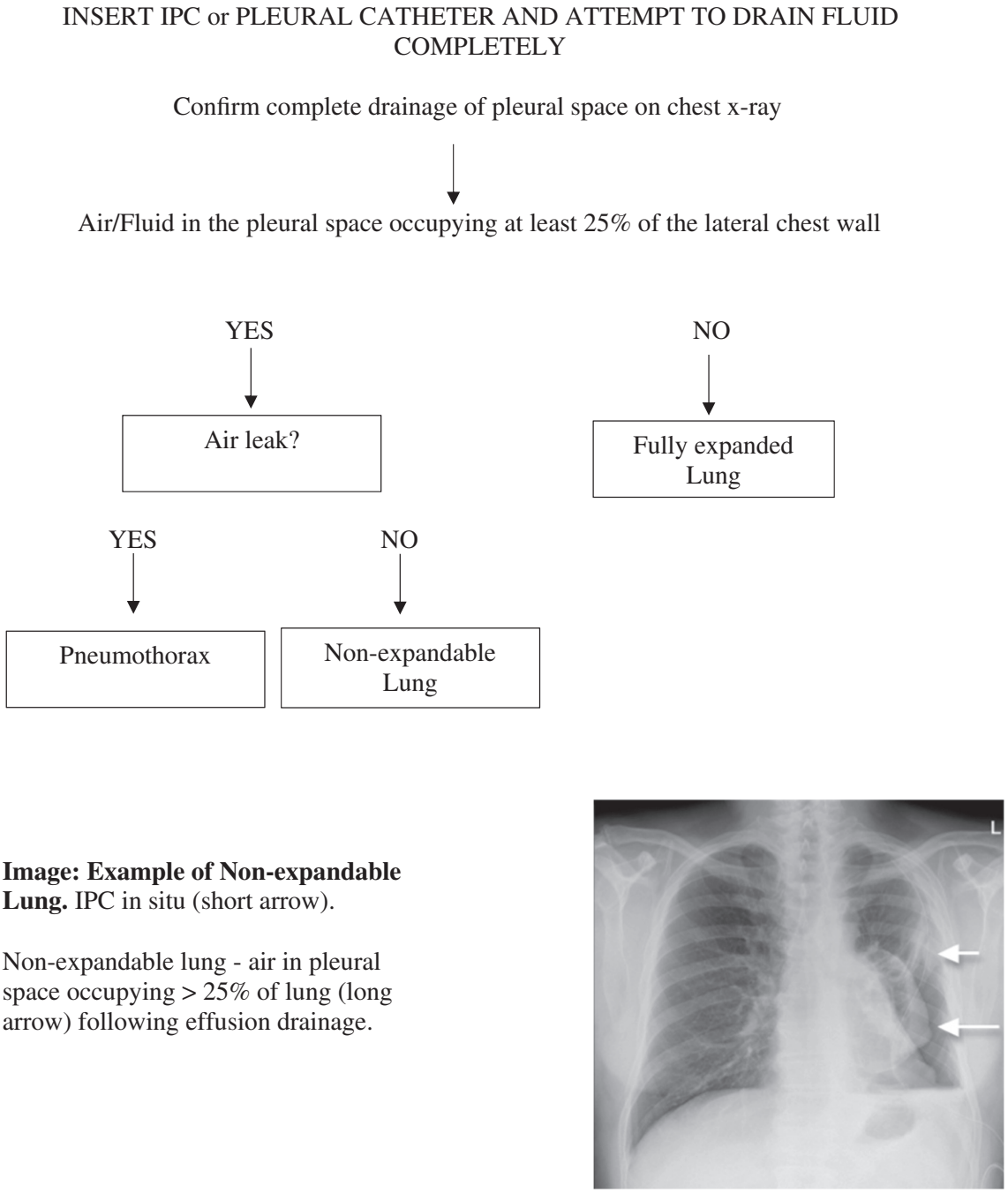

FIGURE 4 | Standard operating procedure (SOP) for diagnosing non-expandable lung.

Participant and nurse interviews will be performed by an experienced researcher not involved in the clinical care of trial participants. Guiding interview questions have been developed using the Health Information Technology Usability Evaluation Model (Health-ITUEM) [26]. Consecutive participants will be invited to participate in the interview, with the expectation that $n = 12–16$ one-hour interviews will be required for theme saturation. To ensure consistency of approach, one researcher will conduct all interviews related to the study.

The non-identifiable data described below will be collected for each eligible patient from NH, MH, EH and GH medical records:

3.3 | Baseline Assessment

Patient data
Patient characteristics: date of birth, gender, ethnicity, smoking status
Clinical information
- Diagnosis, initial assessment date, diagnosis date
- Comorbidities
- Previous chemotherapy
- Previous radiotherapy
- ECOG performance status
- Cancer type

Blood and/or pleural fluid tests
- Blood tests: Serum haemoglobin, white cell count, C-reactive protein (CRP)
- Pleural fluid: pH, lactate dehydrogenase (LDH), protein, glucose and fluid culture

Imaging
- Thoracic ultrasound
  - Presence of pleural effusion (ipsilateral and contralateral hemithorax)
  - Size of pleural effusion (depth and rib spaces)
  - Presence of septations within effusion
  - Assessment of lung sliding (6-point assessment)
  - Other ultrasound findings
- Chest x-ray
  - Effusion size grading [27] (Table 2)
  - Trapped lung (Figure 4)

Baseline intervention
Analgesia used (local and oral)
Thoracentesis
- Type of intercostal catheter
- Video-assisted thoracoscopic surgery (VATS)
- Date of surgery
- Duration from diagnosis to surgery
- Duration from referral to surgery

Intrapleural therapy (tPA/DNAse, sclerosant for chemical bedside pleurodesis)
If indwelling pleural catheter in situ
- Drainage regime
- Drainage volume
- Spontaneous pleurodesis (Figure 5)
- Complications

Percutaneous or surgical pleural or lung biopsy if required
Procedural complications
- Pneumothorax—seen on CXR post-procedure:
  - Conservatively managed
  - Requiring intercostal catheter
  - Prolonged air leak (defined as air leak lasting more than 72 h)
  - Pneumothorax ex vacuo (CXR showing pneumothorax despite no bubbling evident on UWSD)
- Haemothorax—detected on CXR post procedure
- Drain migration—evidenced by subcutaneous emphysema on any CXR
- Infection
- Site infection (ICC)
  - Pleural infection
  - Visceral perforation
- Symptomatic loculation post IPC insertion
- IPC blockage needing intervention

Baseline questionnaires (from participants at NH only)
28-day logbook for VAS breathlessness and pain
EQ-VAS
EQ-5D-5L
ICECAP-A
PAM

Follow-up
Logbook for VAS breathlessness and pain (up to 28 days)
EQ-VAS
EQ-5D-5L
ICECAP-A
PAM (collected once after 3 months)
Healthcare utilisation questionnaire
Health-ITUES
Nurse survey
Carer survey (as applicable)
Teleultrasound

Health service-specific data
Admission data
Time from admission to procedure (days)
Time from procedure to discharge (days)
Total hospital length of stay (days)
Time to diagnosis (days)
Final diagnosis
Survival as defined in days from enrolment
Re-interventions (ipsilateral pleural procedures)
Re-admissions
- All re-admissions (planned or unplanned) during the duration of follow-up with the pleural service will be recorded
- Presentations that were clearly unrelated to the pleural procedure will then be excluded. The focus will be in identifying pleural re-admissions involving the ipsilateral side in which the pleural intervention was originally performed. In cases where there is uncertainty with regards to the cause of re-presentation, the case will be reviewed by a senior respiratory physician.

Health economics data
- Pleural-related hospital length of stay
- Cost of ultrasound machine and skilled personnel
- Type of pleural catheter
- Treatment of complications, where applicable (hospitalisation, re-intervention, antibiotic therapy, diagnostic imaging, surgery)
- Surgery (figure based on procedure)
- For each home visit:
  - Distance travelled by study nurse
  - Time spent travelling
  - Fuel costs
  - Time with study participant
  - Consumables used
- Other out of hospital costs:
  - Patient-reported visits to their General Practitioner, imaging/pathology or other hospital, in relation to their pleural effusion
- All hospitals: Diagnosis-related Group (DRG) and Weighted Inlier Equivalent Separations (WIES) or National Weighted Activity Unit (NWAU)

Other qualitative data (intervention site only)
Semi-structured qualitative interview with study participants ($n = 12–16$)
Semi-structured qualitative interview with all study nurses

3.3.1 | Data Management

Procedures for the handling and analysis of data will be conducted according to the ICH GCP guidelines and the National Statement on Ethical Conduct in Human Research (2007)—*Updated 2018* and in accordance with local policies and procedures.

Data collected will be stored according to the Australian Code for the Responsible Conduct of Research for clinical trials and

local policy guidelines for research data archiving. Access to the final trial dataset will only be available to the research team at the lead site.

3.3.2 | Confidentiality

The database will be stored in a secure shared drive, which is safeguarded against unauthorised access. All future research projects requiring the use of the information in the database will require a separate ethics application and the published data will be non-identifiable.

To comply with local regulations regarding use and disclosure of protected health information (PHI), patient identifiers (e.g., name, date of birth, medical record number) will not be collected as part of this study. Investigators will access the medical record of their patient and enter required data into the database. The database will be maintained for an infinite amount of time. The protected health information will not be reused or disclosed to

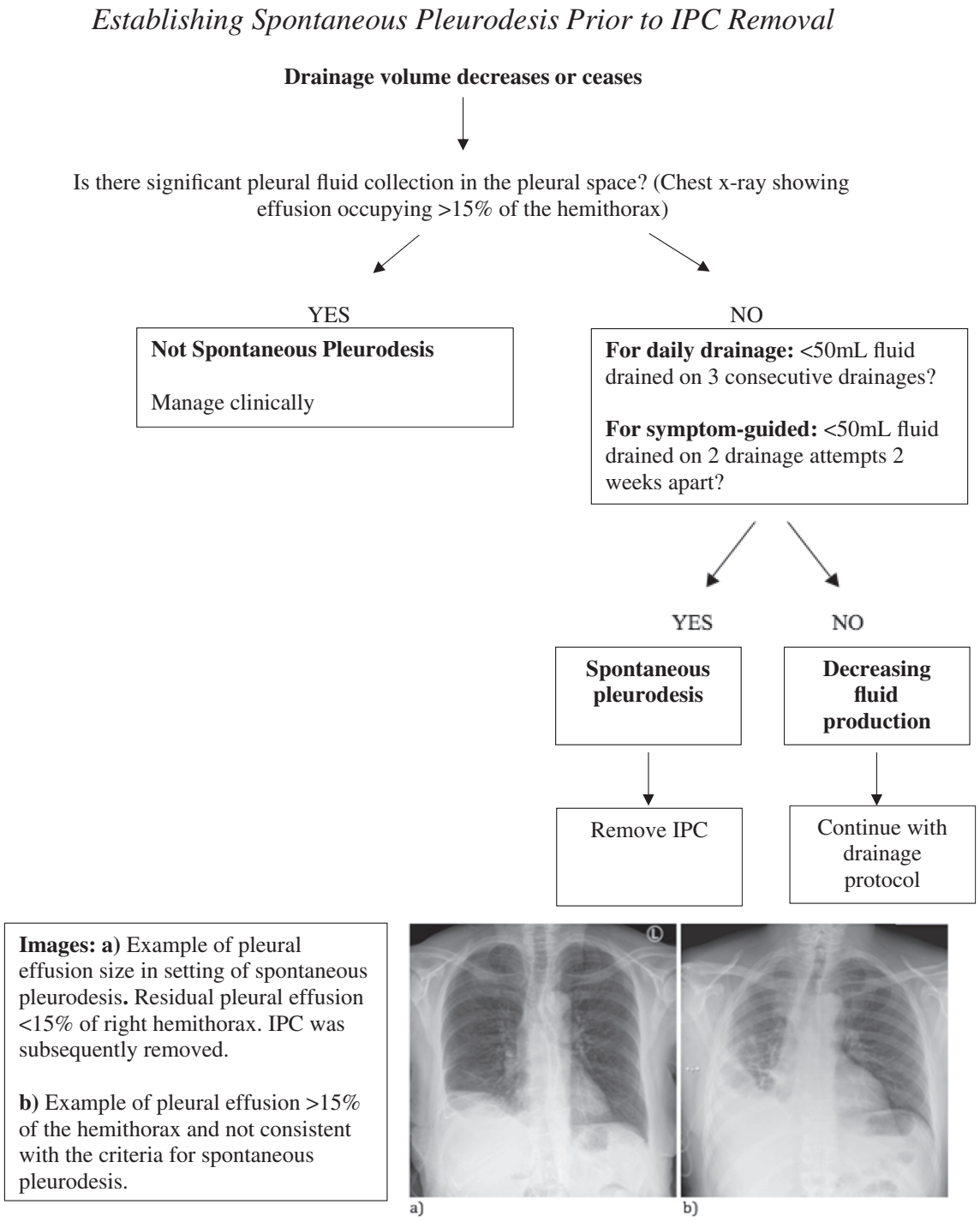

FIGURE 5 | Standard operating procedure (SOP) for establishing spontaneous pleurodesis in individuals with IPC.

any other person or entity, except as required by law, for authorised oversight of the research project.

Future research that is not defined in this protocol wishing to access the REDCap database will need institutional review board/ethics board approval before obtaining access to the REDCap database.

3.3.3 | Statistical Analysis

Data analysis will be on an intention-to-treat basis overseen by a biostatistician. For continuous outcomes, normality will be tested using a Shapiro–Wilk test and if normally distributed, differences between groups will be analysed using *t* tests; otherwise, a Mann–Whitney *U* test will be used. Subsequent regression analyses for the primary outcome may be undertaken to adjust for any noted characteristic or clinical differences between the intervention and control groups. For categorical variables and outcomes, differences between groups will be analysed using Chi Square tests or Fisher's exact tests.

3.3.4 | Health Economic Analysis

The health economic analysis will involve a comparison of health care costs between the intervention and control groups. Healthcare costs will be calculated from hospital records and patient self-report. As participants are not randomised between the two approaches, there may be unobserved differences in the baseline patient characteristics. To adjust for these differences in the cost comparison, we will conduct a difference-in-differences analysis and fit a regression model for cost with an indicator for the programmes and baseline characteristics as explanatory variables. Depending on the distribution of costs, we will select an appropriate model for the analysis [28] with the candidates being generalised linear models (GLM), mixture models, parametric models based on skewed distributions outside the GLM family of distributions, two-part models and Tobit models. For the intervention group where EQ-5D-5L health utility values are collected, we will also examine how the QoL of the participants changes over time and which factors contribute most to these changes using a fixed effects regression model.

3.3.5 | Implementation Evaluation of the SAPS Model of Care

An evaluation of the SAPS model of care will be performed to assess its reliability, efficiency and scalability. An expert panel report will be produced via analysis of nursing and participant surveys and interviews, using the WHO mobile health evidence reporting and assessment criteria [29].

3.4 | Monitoring

3.4.1 | Data Monitoring

After data have been entered into the study database, a system of data validation checks will be implemented and applied to the database. The study database will be updated in accordance with the resolved query reports. All changes to the study database will be documented.

3.4.2 | Harms

Given the nature of the study, inclusion in the interventional cohort is not expected to influence the clinical risk posed to participants. The information routinely collected as part of the individual's attendance and admission (as relevant) to the hospital is entered electronically.

3.4.3 | Auditing

Audits, if any, will be carried out by an independent compliance monitoring officer.

3.4.4 | Safety Reporting

All adverse events occurring during the study period will be documented and reported. A Data and Safety Monitoring Committee, comprising three independent members, will oversee the monitoring of all adverse events. For each adverse event, the investigator will provide the onset, end, intensity, treatment required, outcome, seriousness and action taken. Serious Adverse Events (SAEs) will be reported immediately to both the local ethics committee and the Data and Safety Monitoring Committee using the Serious Adverse Event Report Form, including a documented causal relationship assessment. An SAE is defined as any AE thatresults in death; is life-threatening; results in persistent or significant disability/incapacity; prolongs hospitalisation by ≥ 24 h; is deemed serious for any other reason such that it is thought to jeopardise the patient and may require medical or surgical intervention to prevent one of the other outcomes listed in the above SAE definitions.

3.4.5 | Trial Monitoring and Oversight

A Trial Steering Committee, comprising the investigators and trial coordinators, will be responsible for the supervision of the trial in its entirety. It will be responsible for ensuring the completion of the trial to clinical and ethical standards. The Data and Safety Monitoring Committee will oversee the monitoring of adverse events and the ethical conduct of the study.

4 | Discussion

It is anticipated that the SAPS model of care will reduce pleural-related hospitalisation and enhance the utilisation of an ambulatory care model that focuses on person-centredness, satisfaction and improving outcomes that are important to people with MPE. The model is intended to empower individuals with MPE by educating them on their management choices and facilitating those choices through digital modalities. It is expected that satisfaction will be high with an approach to care that maximises time away from hospital.

Additionally, it is hoped that the study will provide the impetus for upskilling of community nurses to improve management of pleural disease. This will support a case to develop infrastructure to provide better clinical support for people in the community with IPCs.

The strengths of the study include the multi-centre (metropolitan [NH, MH, EH] and regional [GH]) collaboration, enabling direct comparison of outcomes related to the SAPS model of care. Additionally, this is a real-world, pragmatic study, meaning that there are no exclusion criteria beyond that of MPE diagnosis. To our knowledge, this will be the first study in which the actual cost of MPE management is examined in a prospective fashion.

Limitations of the study include that only one centre is designated as the intervention site, with the results susceptible to potential health service-specific biases. The study does not account for potential pre-existing differences between sites which could influence outcomes independently of the intervention. Qualitative analyses are subject to bias given the lack of blinding of participants, study nurses and the lack of a control arm. There are possible losses to follow-up of trial participants relocating to a different state or country, as healthcare data outside Victoria cannot be accessed. Given the geographic location of the primary recruitment site, cellular network coverage may be inconsistent and affect the quality of teleultrasound consultations.

The outcomes from the study will guide future planning for a regional or state-wide pleural service to support people with pleural disease. The SAPS model of care may also be extended to the management of individuals with pneumothorax [30] or transudative pleural effusion [31] (such as heart-failure related pleural effusion) in the future as more evidence emerges for ambulatory management of these pleural diseases.

Author Contributions

Conceptualisation: Victor Duong, Kirstin Tirant, Pierce Marsden, Liam M. Hannan and Sanjeevan Muruganandan. Project administration: Victor Duong and Kirstin Tirant. Data collection/enrolment: Victor Duong, Kirstin Tirant, Urooj Raza Khan, Pierce Marsden, Daniel Steinfort, Nicholas Wilsmore, Wasek Faisal, Sanjeevan Muruganandan. Data curation: Victor Duong, Kirstin Tirant. Formal analysis: Victor Duong, Kirstin Tirant, Urooj Raza Khan, Mani Suleiman, An Duy Tran, Paul Amores. Resources: Sanjeevan Muruganandan. Supervision: Sanjeevan Muruganandan. Protocol preparation: Victor Duong, Liam M. Hannan and Sanjeevan Muruganandan. All authors reviewed and approved the final submission.

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We acknowledge the contribution of Natalie Tirant for the graphics used in the protocol. Aparna Prasad (research assistant) currently administrates the study and oversees quality control of the collected data. Victoria Justice and Maureen Goodwin (research nurses) conduct home visits and perform data collection. Open access publishing facilitated by The University of Melbourne, as part of the Wiley - The University of Melbourne agreement via the Council of Australian University Librarians.

Ethics Statement

The study has been granted approval by the Royal Melbourne Hospital Research, Governance and Ethics Unit (reference: HREC/85858/MH-2022). Study investigators will ensure that any amendments to the protocol are approved by the ethics committee and signed by both participants entering the trial and those currently in the trial, if affected by the amendment.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The research team at the lead site will have access to the final trial dataset. Supporting data including standard operating procedures, details of data management procedures, case report forms and datasets generated and/or analysed during the current study will be available to the scientific community with as few restrictions as possible, while retaining exclusive use until publication of major outcomes. Data requests from qualified researchers should be made to SM (sanjeevan.muruganandan@nh.org.au).

Trial Status at Submission

Recruitment state date: 1 September 2023.

Estimated completion of recruitment: 1 August 2025.

Protocol Amendments Since Registration

Protocol version 3.1/16.5.24.

Dissemination Policy

The study results will be disseminated through national and international conference presentations and publications in peer-reviewed journals.

References

1. B. Chernow and S. A. Sahn, "Carcinomatous Involvement of the Pleura: An Analysis of 96 Patients," *American Journal of Medicine* 63, no. 5 (1977): 695–702, https://doi.org/10.1016/0002-9343(77)90154-1.

2. M. Marel, M. Zrůstová, B. Stasný, and R. W. Light, "The Incidence of Pleural Effusion in a Well-Defined Region. Epidemiologic Study in Central Bohemia," *Chest* 104, no. 5 (1993): 1486–1489, https://doi.org/10.1378/chest.104.5.1486.

3. T. S. Yang, D. W. Hsia, and D. W. Chang, "Patient- and Hospital-Level Factors Associated With Readmission for Malignant Pleural Effusion," *Journal of Oncology Practice/ American Society of Clinical Oncology* 14, no. 9 (2018): e547–e556, https://doi.org/10.1200/jop.18.00201.

4. E. T. H. Fysh, G. W. Waterer, P. A. Kendall, et al., "Indwelling Pleural Catheters Reduce Inpatient Days Over Pleurodesis for Malignant Pleural Effusion," *Chest* 142, no. 2 (2012): 394–400, https://doi.org/10.1378/chest.11-2657.

5. N. Taghizadeh, M. Fortin, and A. Tremblay, "US Hospitalizations for Malignant Pleural Effusions: Data From the 2012 National Inpatient Sample," *Chest* 151, no. 4 (2017): 845–854, https://doi.org/10.1016/j.chest.2016.11.010.

6. A. O. Clive, B. C. Kahan, C. E. Hooper, et al., "Predicting Survival in Malignant Pleural Effusion: Development and Validation of the LENT Prognostic Score," *Thorax* 69, no. 12 (2014): 1098–1104, https://doi.org/10.1136/thoraxjnl-2014-205285.

7. H. E. Davies, E. K. Mishra, B. C. Kahan, et al., "Effect of an Indwelling Pleural Catheter vs Chest Tube and Talc Pleurodesis for Relieving Dyspnea in Patients With Malignant Pleural Effusion: The TIME2 Randomized Controlled Trial," *Journal of the American Medical Association* 307, no. 22 (2012): 2383–2389, https://doi.org/10.1001/jama.2012.5535.

8. S. Muruganandan, M. Azzopardi, D. B. Fitzgerald, et al., "Aggressive Versus Symptom-Guided Drainage of Malignant Pleural Effusion via Indwelling Pleural Catheters (AMPLE-2): An Open-Label Randomised Trial," *Lancet Respiratory Medicine* 6, no. 9 (2018): 671–680, https://doi.org/10.1016/s2213-2600(18)30288-1.

9. M. E. Roberts, N. M. Rahman, N. A. Maskell, et al., "British Thoracic Society Guideline for Pleural Disease," *Thorax* 78, no. Suppl 3 (2023): s1–s42, https://doi.org/10.1136/thorax-2022-219784.

10. A. C. Bibby, P. Dorn, I. Psallidas, et al., "ERS/EACTS Statement on the Management of Malignant Pleural Effusions," *European Respiratory Journal* 52, no. 1 (2018): 1800349, https://doi.org/10.1183/13993003.00349-2018.

11. D. J. Feller-Kopman, C. B. Reddy, M. M. DeCamp, et al., "Management of Malignant Pleural Effusions. An Official ATS/STS/STR Clinical Practice Guideline," *American Journal of Respiratory and Critical Care Medicine* 198, no. 7 (2018): 839–849, https://doi.org/10.1164/rccm.201807-1415ST.

12. R. Thomas, E. T. H. Fysh, N. A. Smith, et al., "Effect of an Indwelling Pleural Catheter vs Talc Pleurodesis on Hospitalization Days in Patients With Malignant Pleural Effusion: The AMPLE Randomized Clinical Trial," *Journal of the American Medical Association* 318 (2017): 1903–1912.

13. P. Sivakumar, D. B. Fitzgerald, H. Ip, et al., "The Impact of Outpatient Versus Inpatient Management on Health-Related Quality of Life Outcomes for Patients With Malignant Pleural Effusion: The OPTIMUM Randomised Clinical Trial," *European Respiratory Journal* 63, no. 2 (2024): 2201215, https://doi.org/10.1183/13993003.01215-2022.

14. R. C. Boshuizen, A. D. Vincent, and M. M. van den Heuvel, "Comparison of Modified Borg Scale and Visual Analog Scale Dyspnea Scores in Predicting Re-Intervention After Drainage of Malignant Pleural Effusion," *Supportive Care in Cancer* 21, no. 11 (2013): 3109–3116, https://doi.org/10.1007/s00520-013-1895-3.

15. R. Bhatnagar, H. E. G. Piotrowska, M. Laskawiec-Szkonter, et al., "Effect of Thoracoscopic Talc Poudrage vs Talc Slurry via Chest Tube on Pleurodesis Failure Rate Among Patients With Malignant Pleural Effusions: A Randomized Clinical Trial," *Journal of the American Medical Association* 323, no. 1 (2020): 60–69, https://doi.org/10.1001/jama.2019.19997.

16. N. M. Rahman, J. Pepperell, S. Rehal, et al., "Effect of Opioids vs NSAIDs and Larger vs Smaller Chest Tube Size on Pain Control and Pleurodesis Efficacy Among Patients With Malignant Pleural Effusion: The TIME1 Randomized Clinical Trial," *Journal of the American Medical Association* 314, no. 24 (2015): 2641–2653, https://doi.org/10.1001/jama.2015.16840.

17. C. Sidhu, G. Wright, C. J. Peddle-McIntyre, A. L. Tan, and Y. C. G. Lee, "Management of Malignant Pleural Effusion and Trapped Lung: A Survey of Respiratory Physicians and Thoracic Surgeons in Australasia," *Internal Medicine Journal* 54, no. 7 (2024): 1119–1125, https://doi.org/10.1111/imj.16366.

18. K. Tirant, L. Hannan, J. Roberts, and S. Muruganandan, "Digital Health to Extend Victoria's First Specialized Pleural Service," *Respirology* 27 (2022): 36.

19. R. Bhatnagar, E. K. Keenan, A. J. Morley, et al., "Outpatient Talc Administration by Indwelling Pleural Catheter for Malignant Effusion," *New England Journal of Medicine* 378, no. 14 (2018): 1313–1322, https://doi.org/10.1056/NEJMoa1716883.

20. M. M. Wahidi, S. Shofer, K. Mahmood, et al., "Randomized Trial of Pleural Fluid Drainage Frequency in Patients With Malignant Pleural Effusions the ASAP Trial," *American Journal of Respiratory and Critical Care Medicine* 195, no. 8 (2017): 1050–1057, https://doi.org/10.1164/rccm.201607-1404OC.

21. Koninklijke Philips N.V, "Improve Patient Evaluation and Treatment With Remote Virtual Guidance," accessed March 22, 2025, https://www.philips.com.au/healthcare/sites/lumify-handheld-ultrasound/products/reacts-tele-ultrasound.

22. M. Herdman, C. Gudex, A. Lloyd, et al., "Development and Preliminary Testing of the New Five-Level Version of EQ-5D (EQ-5D-5L)," *Quality of Life Research* 20, no. 10 (2011): 1727–1736, https://doi.org/10.1007/s11136-011-9903-x.

23. H. Al-Janabi, T. N. Flynn, and J. Coast, "Development of a Self-Report Measure of Capability Wellbeing for Adults: The ICECAP-A," *Quality of Life Research* 21, no. 1 (2012): 167–176, https://doi.org/10.1007/s11136-011-9927-2.

24. R. Schnall, H. Cho, and J. Liu, "Health Information Technology Usability Evaluation Scale (Health-ITUES) for Usability Assessment of Mobile Health Technology: Validation Study," *JMIR mHealth and uHealth* 6, no. 1 (2018): e4, https://doi.org/10.2196/mhealth.8851.

25. J. H. Hibbard, J. Stockard, E. R. Mahoney, and M. Tusler, "Development of the Patient Activation Measure (PAM): Conceptualizing and Measuring Activation in Patients and Consumers," *Health Services Research* 39 (2004): 1005–1026, https://doi.org/10.1111/j.1475-6773.2004.00269.x.

26. W. Brown, 3rd, P. Y. Yen, M. Rojas, and R. Schnall, "Assessment of the Health IT Usability Evaluation Model (Health-ITUEM) for Evaluating Mobile Health (mHealth) Technology," *Journal of Biomedical Informatics* 46, no. 6 (2013): 1080–1087, https://doi.org/10.1016/j.jbi.2013.08.001.

27. R. W. Light, J. T. Rogers, D. Cheng, and R. M. Rodriguez, "Large Pleural Effusions Occurring After Coronary Artery Bypass Grafting. Cardiovascular Surgery Associates, PC," *Annals of Internal Medicine* 130, no. 11 (1999): 891–896, https://doi.org/10.7326/0003-4819-130-11-199906010-00004.

28. B. Mihaylova, A. Briggs, A. O'Hagan, and S. G. Thompson, "Review of Statistical Methods for Analysing Healthcare Resources and Costs," *Health Economics* 20, no. 8 (2011): 897–916, https://doi.org/10.1002/hec.1653.

29. S. Agarwal, A. E. LeFevre, J. Lee, et al., "Guidelines for Reporting of Health Interventions Using Mobile Phones: Mobile Health (mHealth) Evidence Reporting and Assessment (mERA) Checklist," *British Medical Journal* 352 (2016): i1174, https://doi.org/10.1136/bmj.i1174.

30. R. J. Hallifax, E. McKeown, P. Sivakumar, et al., "Ambulatory Management of Primary Spontaneous Pneumothorax: An Open-Label, Randomised Controlled Trial," *Lancet* 396, no. 10243 (2020): 39–49, https://doi.org/10.1016/s0140-6736(20)31043-6.

31. S. P. Walker, O. Bintcliffe, E. Keenan, et al., "Randomised Trial of Indwelling Pleural Catheters for Refractory Transudative Pleural Effusions," *European Respiratory Journal* 59, no. 2 (2022): 2101362, https://doi.org/10.1183/13993003.01362-2021.