Decomposing the Bundle: A Chronological Appraisal of Intraoperative Lung-Protective Ventilation and the Case for Driving Pressure

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Abstract

Background: Intraoperative lung-protective ventilation entered practice as a bundle of low tidal volume, positive end-expiratory pressure and recruitment manoeuvres, tested and adopted together. Trials isolating the individual components have been largely null, while driving pressure has emerged as a candidate mediating variable. The field illustrates a general problem — how to interpret a bundle whose parts have not been separately established — with direct consequences for setting the ventilator.

Methods: We conducted a structured narrative review, organised chronologically, of randomised trials and meta-analyses of intraoperative ventilation in adult surgical patients. For each landmark study we recorded what was believed before it, what it tested, and what it left standing, then appraised the mediation hypothesis.

Results: An initial trial of the full bundle reduced postoperative pulmonary complications. Trials isolating higher positive end-expiratory pressure with recruitment against lower pressure, at matched tidal volume, found no benefit in open abdominal surgery or in obesity, and signalled haemodynamic compromise and over-distension. A trial of low against conventional tidal volume alone also found no difference. An individual-patient-data meta-analysis found that driving pressure — tidal volume normalised to respiratory system compliance rather than predicted body weight — tracked complications better than either component. Later syntheses associate low tidal volume with driving-pressure-guided positive end-expiratory pressure with fewer complications.

Conclusion: The evidence is best read as identifying a mediator rather than as refuting the bundle. Tidal volume and positive end-expiratory pressure appear to matter to the extent that they alter driving pressure, which is measurable at the bedside and responds to the individual patient's mechanics. We propose setting tidal volume conservatively, treating driving pressure as the titration target, and diagnosing the reason a driving pressure is high before raising positive end-expiratory pressure.

Keywords: Mechanical Ventilation, Driving Pressure, Positive End-Expiratory Pressure, Postoperative Pulmonary Complications, Perioperative Medicine, Tidal Volume.

1. INTRODUCTION

Much of what anaesthetists do intraoperatively arrived as a package. Lung-protective ventilation is the clearest example: low tidal volume, positive end-expiratory pressure (PEEP) and periodic recruitment manoeuvres were adopted together, on the strength of trials that randomised them together, and have been taught together ever since.

Bundles are efficient to test and awkward to interpret. A trial that randomises three interventions simultaneously and finds benefit establishes that the package works. It cannot say whether all three components contributed, whether one carried the effect while the others were inert, or whether one was harmful and was more than offset by the others. That ambiguity is tolerable while the package is delivered intact. It becomes consequential the moment a clinician has to decide how much PEEP to apply to a particular patient, because the trial that justified the practice never asked that question.

The decade since intraoperative lung-protective ventilation was established has been, in effect, a sustained attempt to answer it. Trials have isolated the components, largely with null results; a mediation analysis has proposed a variable that unifies them; and individualised titration to that variable is now being tested. This review follows that sequence chronologically, because the order in which the evidence arrived is itself the argument. Figure 1 provides the spine.

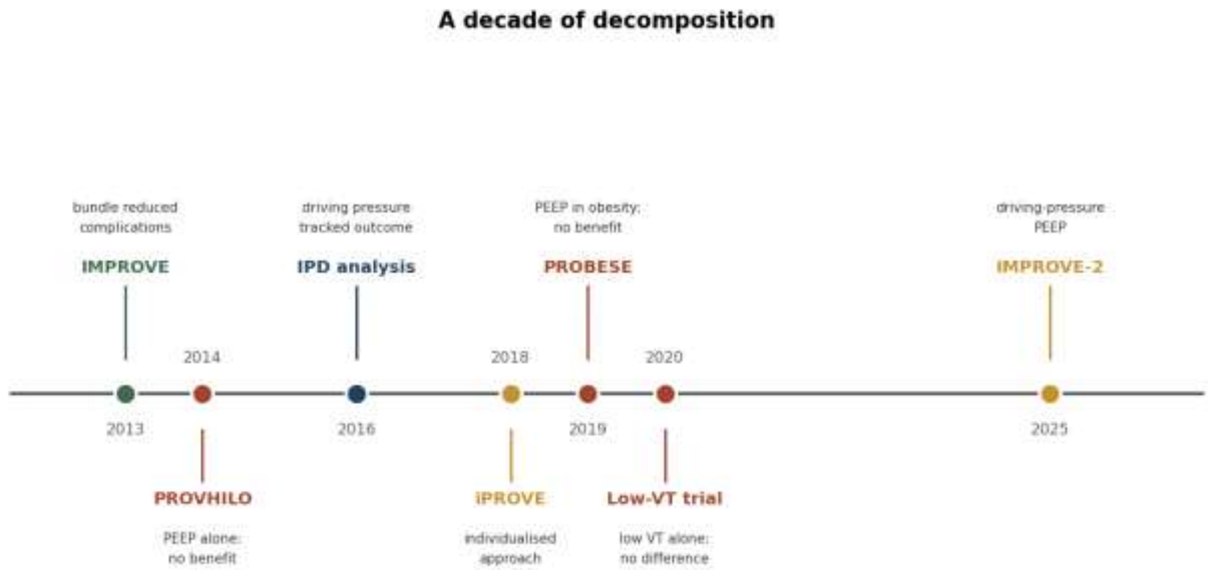

Figure 1. The chronology of intraoperative ventilation evidence. Studies above the line reported findings that advanced the protective or mediating hypothesis; those below isolated a component and found no benefit.

Objectives

We set out to trace how the evidence on intraoperative ventilation developed; to record for each landmark study what it tested and what it did not; to appraise the hypothesis that driving pressure mediates the effect of the individual components; to state the current evidence status of each component against each outcome; and to derive a practical approach to setting the ventilator that is consistent with the evidence as it stands.

2. METHODS

This is a structured narrative review rather than a systematic review. No protocol was registered and no formal screening was conducted; the studies discussed were selected as the landmarks that determined the direction of the field, and the review is therefore illustrative of that development rather than exhaustive of the literature. We searched for randomised trials, individual-patient-data meta-analyses and network meta-analyses of intraoperative ventilation strategies in adult surgical patients, with postoperative pulmonary complications as the outcome of principal interest.

No primary data were collected and no individual patient records were accessed, so institutional review board approval, informed consent and trial registration are not applicable. The evidence-status matrix in Section 3 and the ventilator-setting approach in Section 4 are the authors' synthesis, offered as proposals consistent with current evidence rather than as validated protocols or guidelines.

ACT I 2013 The Bundle Works

The foundational trial randomised patients undergoing major abdominal surgery to a protective strategy — low tidal volume with PEEP and periodic recruitment manoeuvres — or to conventional ventilation, and found fewer postoperative pulmonary and extrapulmonary complications in the protective arm [1]. Earlier meta-analytic work pointed the same way: low tidal volume was associated with less postoperative lung infection, and the combination of low tidal volume with PEEP and intermittent recruitment with reductions in infection, atelectasis, acute lung injury and length of stay [2].

The physiological rationale was well established from critical care. Ventilation with large tidal volumes produces cyclic over-distension and repetitive opening and closing of alveolar units, generating regional strain, inflammatory mediator release and, in susceptible lungs, injury that propagates systemically. Applying to healthy lungs during anaesthesia what had been proven in the injured lung was a reasonable extrapolation, and it appeared to be vindicated.

What the trial could not resolve is shown in Figure 2. Three interventions were randomised as one, and the design offered no way to apportion the benefit among them.

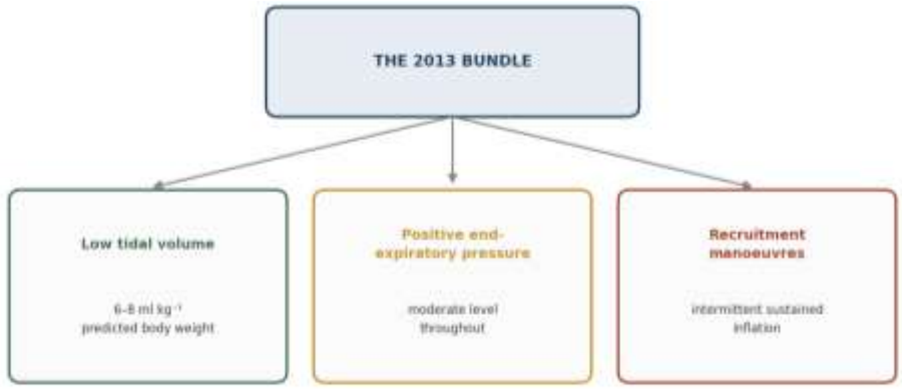

Figure 2. The components of the protective bundle as randomised. The trial established that the package worked; it could not establish which element was responsible.

ACT II 2014–2019 The PEEP Component Does Not

The natural next question was whether more PEEP was better. A multicentre trial in open abdominal surgery compared high PEEP of 12 cm H_2O with recruitment manoeuvres against low PEEP of 2 cm H_2O or less, with tidal volume held at 8 ml kg^{-1} predicted body weight in both arms — an unusually clean isolation of the PEEP component [3]. It found no reduction in postoperative pulmonary complications, and the higher-PEEP arm showed more haemodynamic compromise.

The result might have been dismissed as specific to that population. It was not. A subsequent trial applied the same contrast to patients with obesity, in whom the physiological case for higher PEEP is strongest because of reduced functional residual capacity and greater atelectasis, and again found no reduction in postoperative pulmonary complications [4]. An individualised open-lung approach was also evaluated [5]. A patient-level meta-analysis of three of these trials concluded that the accumulated evidence had consistently failed to demonstrate outcome improvement from higher PEEP, while demonstrating potential for over-distension-related injury and haemodynamic derangement [6].

Three isolations, two populations, no benefit (Figure 3, Table 1). This is a robust negative finding and it has a direct clinical implication: routinely escalating PEEP as a protective measure is not supported.

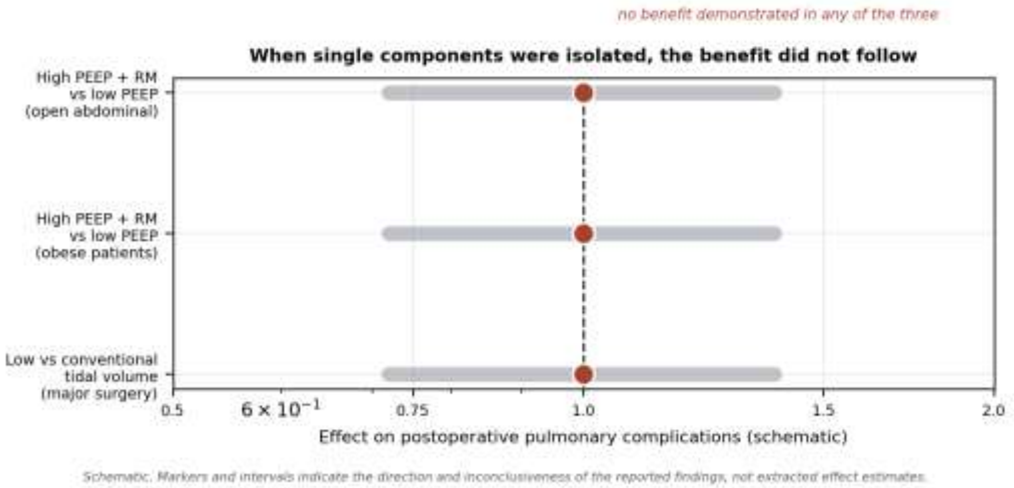

Figure 3. Schematic representation of the trials that isolated single components of the bundle. Markers and intervals indicate direction and inconclusiveness rather than extracted effect estimates.

Table 1. The landmark studies in sequence.

Year	Study	What it tested	What it found
2013	Bundle trial in abdominal surgery	Low tidal volume with PEEP and recruitment versus conventional ventilation	Fewer postoperative pulmonary and extrapulmonary complications
2014	High versus low PEEP, open abdominal surgery	PEEP 12 cm H_2O with recruitment versus ≤2 cm H_2O, tidal volume matched at 8 ml kg^{-1}	No reduction in complications; more haemodynamic compromise
2016	Individual-patient-data meta-analysis	Which ventilatory variable tracks complications	Driving pressure, not tidal volume or PEEP
2018	Individualised open-lung approach	Individualised versus standard protective ventilation in abdominal surgery	Contributed to the individualisation literature
2019	High versus low PEEP in obesity	PEEP with recruitment versus low PEEP in patients with obesity	No reduction in complications
2020	Low versus conventional tidal volume	Tidal volume isolated, in major surgery	No difference in postoperative pulmonary complications
2025	Driving-pressure-guided PEEP	Personalised driving-pressure-guided PEEP, pragmatic design	Reporting; see Act V

Sources: references [1,3–5,7,10,11]. Descriptions are summarised; readers should consult the primary reports for full design detail.

ACT III 2016 A Mediator Is Proposed

If neither PEEP nor, as it would later appear, tidal volume carries the effect in isolation, the possibility arises that both operate through a third variable. An individual-patient-data meta-analysis advanced exactly this proposal. Reasoning that respiratory system compliance is strongly related to end-expiratory lung volume, particularly in normal lungs, the investigators postulated that driving pressure — tidal volume normalised by respiratory system compliance — would predict postoperative pulmonary complications better than tidal volume normalised by predicted body weight, and found that it did [7].

The proposal is conceptually clean and physiologically attractive (Figure 4, Figure 5). Predicted body weight is a proxy for the size of a healthy lung. It is a poor proxy for the size of the lung actually available to receive a breath in an anaesthetised patient in the Trendelenburg position with a pneumoperitoneum and a retractor in the upper abdomen. Driving pressure uses the patient's own compliance as the denominator, and therefore expresses the breath relative to the lung that is genuinely participating.

Under this reading the earlier findings cohere rather than conflict. Lowering tidal volume reduces driving pressure and helps. Raising PEEP may reduce driving pressure by recruiting collapsed lung, in which case it helps, or may increase it by over-distending already-open lung, in which case it harms — and applied blindly to an unselected population, the two effects cancel, producing precisely the null results of Act II.

Two cautions are owed. The 2016 finding is an association within randomised datasets, not a randomised test of driving pressure as a target, and mediation inferred from observational structure within trials is weaker evidence than a trial of the mediator. And driving pressure measured at the airway reflects the whole respiratory system, so a high value may arise from chest-wall or abdominal loading rather than from the lung, in which case raising PEEP will not correct it. Table 2 sets out the arguments.

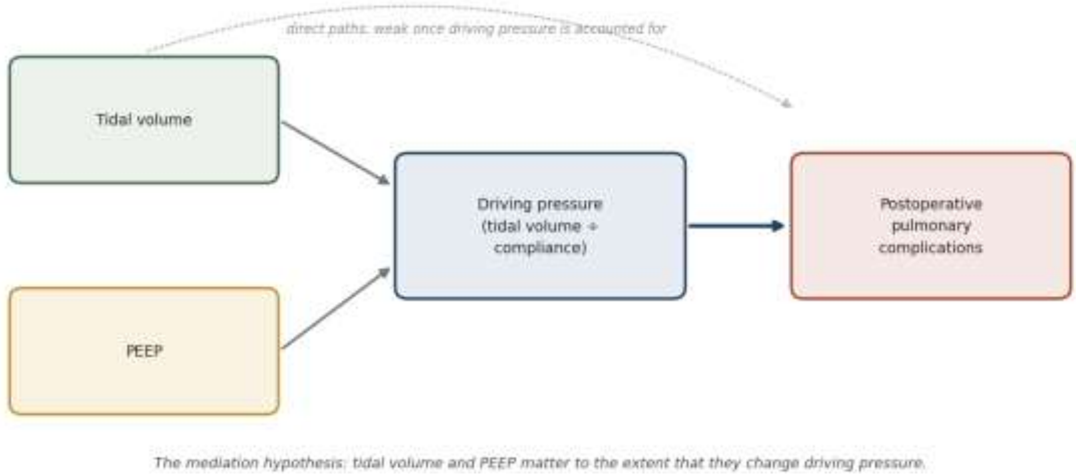

Figure 4. The mediation hypothesis. Tidal volume and PEEP are proposed to influence postoperative pulmonary complications principally through their effect on driving pressure.

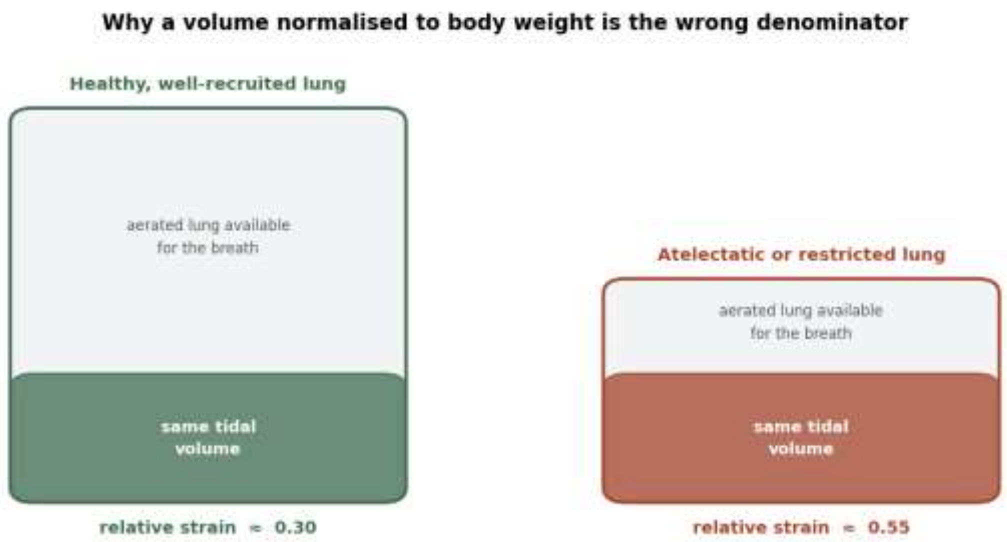

Figure 5. Why predicted body weight is an imperfect denominator. The same tidal volume imposes greater relative strain when less aerated lung is available to receive it.

Table 2. The driving-pressure mediation hypothesis appraised.

Claim	Supporting argument	Countervailing consideration
Driving pressure predicts complications better than tidal volume	Individual-patient-data meta-analysis found the association held for driving pressure but not for tidal volume normalised to predicted body weight	An association within trial datasets, not a randomised test of the variable as a target
PEEP helps only when it lowers driving pressure	Reconciles the null PEEP trials: recruitment and over-distension effects cancel across an unselected population	Not directly demonstrated; requires a trial randomising titration to driving pressure
Driving pressure reflects lung strain	Normalises the breath to the compliance actually available rather than to a population-average lung size	Airway driving pressure reflects the whole respiratory system, including chest wall and abdomen

Titrating to driving pressure will improve outcomes	Later syntheses report the combination of low tidal volume and driving-pressure-guided PEEP associated with fewer complications	Pragmatic randomised evidence is only now emerging

ACT IV 2020 Tidal Volume Alone Falters

If the mediation account is correct, then isolating tidal volume should also produce an equivocal result, because a change in tidal volume alters driving pressure only to the extent that compliance stays fixed, and because the contrast tested may be small relative to the range over which strain matters. A large randomised trial comparing low with conventional tidal volume in patients undergoing major surgery found no difference in postoperative pulmonary complications [10].

This is an awkward finding for the conventional teaching and it should not be smoothed over. Low tidal volume is the component of the bundle that clinicians regard as settled, and a well-conducted trial isolating it found nothing. Two readings are available. Under the mediation account, the trial tested a contrast in the numerator while leaving the denominator unmeasured, and would be expected to be equivocal. Under a sceptical account, the original bundle effect may have been smaller or more context-specific than believed, and the subsequent null results are simply what a smaller true effect looks like when components are separated.

The two readings are not currently distinguishable on the evidence, and honest practice should acknowledge that. What is not in dispute is that tidal volumes of 10 ml kg^{-1} or more, delivered without PEEP, have no constituency, and that the contemporary syntheses continue to support 6–8 ml kg^{-1} as the operating range [8,9].

ACT V 2019–2025 Individualisation

If the target is the mediator rather than either component, then the setting should be individualised to the patient's mechanics rather than fixed by protocol. A randomised trial in thoracic surgery examined ventilation guided by driving pressure [11]. Subsequent systematic reviews and meta-analyses have reported that low tidal volume combined with driving-pressure-guided PEEP is associated with a reduction in postoperative pulmonary complications, and have suggested an operating specification of 6–8 ml kg^{-1} tidal volume with PEEP set to reach the lowest driving pressure [8,9]. Network meta-analytic work reported that tidal volume of 8 ml kg^{-1} or less with PEEP of at least 5 cm H_2O was associated with reduced complications [12].

A multicentre pragmatic randomised trial of personalised driving-pressure-guided PEEP in patients at risk of postoperative respiratory failure has now reported [13]. Readers should consult that report directly; a review of this kind can note its arrival and its design but should not pre-empt the appraisal of a trial whose results will require the same careful separation of what was tested from what was assumed that this review has applied to its predecessors.

It is worth naming what would count as a satisfying end to this sequence. A trial randomising titration to driving pressure against a fixed protective protocol, with tidal volume matched, powered for postoperative pulmonary complications, and reporting the achieved driving pressure in both arms, would test the mediator as a target. Anything less continues to confound the variable with the means of reaching it — the same difficulty that has run through the whole decade.

3. WHERE THE EVIDENCE NOW STANDS

Figure 6 and Table 3 set out the position component by component and outcome by outcome. Three patterns are worth stating explicitly.

Evidence is strongest where it matters least. Every component has well-established effects on respiratory mechanics, and mechanics are not an outcome a patient experiences. Evidence weakens as the outcome becomes more clinically consequential, and no component of intraoperative ventilation has demonstrated a mortality effect in this setting.

The bundle retains better evidence than its parts. This is an uncomfortable but defensible position: the package has randomised support that no single component has independently reproduced. It is also exactly what one expects if a mediator is doing the work and the package changes it more reliably than any component alone.

Driving-pressure-guided titration has supportive but not definitive evidence. It is the most promising current direction and should be described as such rather than as established practice.

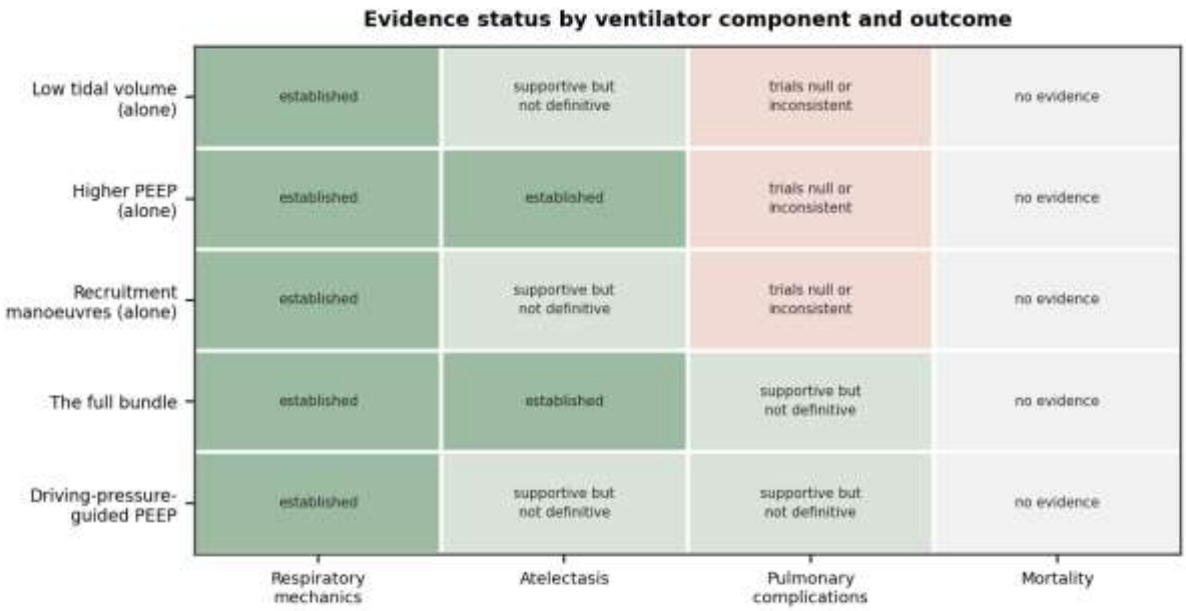

Figure 6. Evidence status by ventilator component and outcome. Certainty is highest for physiological endpoints and weakest for patient-centred ones.

Table 3. Component-by-component evidence summary.

Component	What the evidence supports	What it does not support	Practice implication
Low tidal volume	6–8 ml kg^{-1} predicted body weight as the operating range, endorsed by contemporary syntheses	That isolating it reliably reduces complications	Continue; set from measured height
Moderate PEEP	A modest level as a component of a protective package	Higher PEEP as a routine protective default	Use a modest starting value
Higher PEEP with recruitment	Nothing as a routine strategy; may reduce driving pressure in selected patients	Routine application in unselected patients or in obesity	Do not apply routinely
Recruitment manoeuvres	Transient improvement in mechanics	Independent outcome benefit	Reserve for defined indications
Driving-pressure-guided PEEP	Association with fewer complications in recent syntheses; pragmatic trials emerging	Established outcome benefit	Reasonable titration target; describe as promising

4. SETTING THE VENTILATOR

Figure 7 and Table 4 set out an approach consistent with the foregoing. Four points deserve emphasis.

Predicted body weight requires measured height. Tidal volume set from actual weight systematically over-ventilates patients with obesity, which is the population in whom the margin for error is smallest. This is a basic error that remains common, and correcting it is likely to matter more than any refinement discussed in this review.

Driving pressure is measurable without additional equipment. Plateau pressure minus PEEP, obtained with an inspiratory pause once conditions are steady, requires nothing that a modern anaesthetic ventilator does not already provide. That it is not routinely recorded is a matter of habit rather than capability.

A high driving pressure is a question, not an instruction. It may indicate derecruited lung, in which case a trial of higher PEEP is rational and should be retained only if driving pressure falls. It may equally indicate chest-wall or abdominal loading from positioning, pneumoperitoneum or retraction, in which case higher PEEP will add over-distension without addressing the cause. Distinguishing the two is the clinical skill this literature ultimately asks for.

The denominator moves during the operation. Compliance changes with position, insufflation, retraction, fluid administration and surgical duration. A driving pressure measured at induction describes a patient who no longer exists an hour later, and the measurement should be repeated after every substantial change.

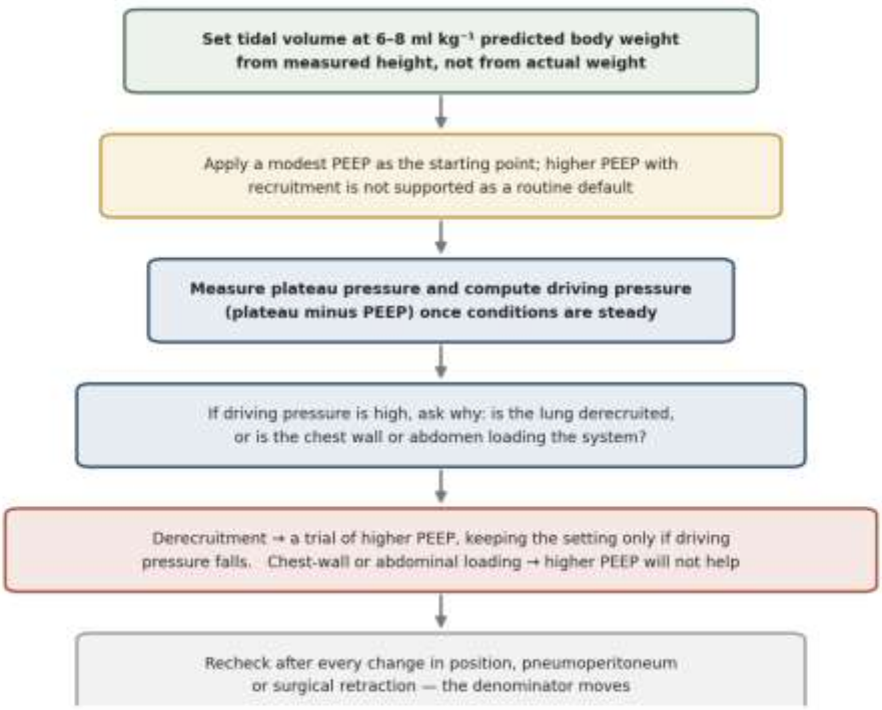

Figure 7. A proposed approach to intraoperative ventilator setting. This is the authors' synthesis and is not a validated protocol.

Table 4. Proposed settings with the evidential basis for each.

Setting	Proposal	Basis	Strength
Tidal volume	6–8 ml kg^{-1} predicted body weight, from measured height	Contemporary syntheses and network meta-analysis	Moderate
Starting PEEP	A modest level; do not escalate as a routine protective measure	Null results of the isolated PEEP trials	Moderate to strong

Measurement	Plateau pressure with inspiratory pause; compute driving pressure	Required to apply the mediation account	Practice standard
PEEP titration	Raise only if driving pressure falls; abandon the increase if it does not	Mediation hypothesis plus emerging titration evidence	Weak to moderate
Recruitment manoeuvres	Not routine; consider for defined derecruitment with haemodynamic tolerance	Absence of independent outcome benefit	Moderate
Reassessment	Repeat after position change, insufflation, retraction or major fluid shift	Compliance is not stable through an operation	Practice standard

Table 5. What this decade teaches about bundles in general.

Lesson	What happened here	Transferability
A bundle trial cannot apportion its own effect	Three components randomised together in the foundational trial	Applies to every care bundle in perioperative and critical care
Component trials are the necessary sequel, and are often null	Isolated PEEP and tidal volume trials found no benefit	Expect attenuation when components are separated
A null component trial does not refute the bundle	The package retains randomised support the components lack	Guards against over-reading isolation trials
A mediator can reconcile discordant findings	Driving pressure explains why PEEP helps some patients and harms others	Look for the normalising variable when components conflict
Mediators must themselves be randomised	Driving-pressure titration is only now being tested pragmatically	Mediation analysis generates hypotheses, not practice

Table 6. Research priorities.

Question	Design that would answer it	Priority
Does titrating to driving pressure improve outcomes?	Randomised comparison of driving-pressure-guided titration against a fixed protective protocol, tidal volume matched, powered for pulmonary complications	High
Is airway or transpulmonary driving pressure the better target?	Trial incorporating oesophageal manometry in patients with high abdominal or chest-wall load	High
Which patients benefit from recruitment?	Enrichment design selecting patients with demonstrated derecruitment	Moderate
Does the timing of measurement matter?	Comparison of single versus repeated intraoperative titration	Moderate
Is the tidal volume range still correct?	Dose-ranging trial within the 4–10 ml kg^{-1} interval, with driving pressure reported	Moderate

5. LIMITATIONS

This is a structured narrative review and not a systematic review; no protocol was registered, no screening process was documented, and the studies discussed were selected as landmarks rather than identified by a reproducible search. A systematic appraisal might include trials we have not discussed and weight the evidence differently.

The chronological structure imposes a narrative on a literature that did not develop as tidily as the account suggests. Trials overlapped, several populations were studied in parallel, and the mediation hypothesis was proposed before some of the component trials reported. Readers should treat the sequence as an organising device rather than as a claim about how the field reasoned at the time.

The evidence-status matrix in Figure 6 and the appraisals in Tables 2 and 3 are the authors' assessments against stated reasoning, not the output of a formal grading exercise. The matrix records the strongest available design for each cell and not the volume of evidence within it.

Figures 3 and 5 are schematic. Figure 3 conveys the direction and inconclusiveness of the isolation trials and does not display extracted effect estimates; Figure 5 illustrates the concept of strain relative to available lung and is not to scale. Neither should be used to derive quantitative conclusions.

Finally, the approach in Section 4 has not been prospectively evaluated. It is consistent with both the positive bundle evidence and the null component evidence, which not every current departmental protocol is, but consistency with existing evidence is a weaker claim than demonstrated benefit, and it should not be represented to trainees as established practice.

6. CONCLUSION

Intraoperative lung-protective ventilation was established as a bundle and has spent a decade being taken apart. Isolating higher PEEP with recruitment produced no benefit in two populations; isolating tidal volume produced no difference in a third trial; and driving pressure, which normalises the breath to the lung actually available to receive it, has emerged as the variable that tracks outcome across these datasets. The most coherent reading is that the components matter through the mediator rather than in themselves. That reading explains why the package worked, why the parts did not, and why higher PEEP helps some patients and harms others. It has not been confirmed by a trial randomising the mediator as a target, and it should be held as the best current account rather than as settled fact.

For the anaesthetist the practical consequence is modest and immediate. Set tidal volume conservatively from measured height, start with a modest PEEP, measure the driving pressure that results, ask why it is high before raising PEEP to correct it, and measure it again when the operation has changed the patient. None of that requires equipment that is not already in the room.

Declarations

Ethical approval: Not applicable.

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Conflicts of interes: The authors declare that there are no conflicts of interest regarding the publication of this paper.

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

Author contributions:

Name of Author	C	M	So	Va	Fo	I	R	D	O	E	Vi	Su	P	Fu
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C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
Va : **Va**lidation
Fo : **Fo**rmal analysis
I : **I**nvestigation
R : **R**esources
D : **D**ata Curation
O : Writing - **O**riginal Draft
E : Writing - Review & **E**diting
Vi : **Vi**sualization
Su : **Su**pervision
P : **P**roject administration
Fu : **Fu**nding acquisition

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