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SAPERE AUDE

Te Whare Wānanga o Otago

**A BRIEF HISTORY
OF ASYNCHRONY**

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Editor-in-Chief, Journal of Mechanical Ventilation

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Declaration

Shareholder in **TIRO MEDICAL LIMITED (5024040)** <https://app.companiesoffice.govt.nz/co/5024040>
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absolutelymaybe.plos.org/2018/09/24/scientific-advocacy-and-biases-of-the-ideological-and-industry-kinds/

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Asynchrony is bad!

Why is minimising asynchrony is important?

Asynchrony is associated with:

Prolonged ventilator support, sleep disorders, poor lung aeration, longer stay in the intensive care unit and mortality

Or more simply put: =>**BADNESS**

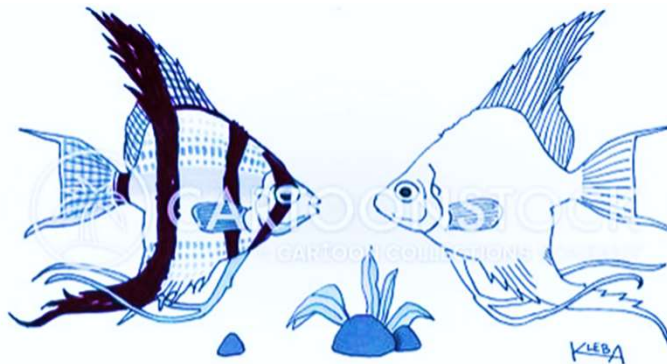


de Wit M, et al , *Crit Care Med* 2009 Thille AW et al, *Int Care Med* 2006 Colombo D, et al *Crit Care Med* 2011
 Blanch L, et al *Int Care Med* 2015 Bosma K, *Crit Care Med* 2007 Kacmarek RM, *Minerva Anes* 2016;

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Recognising Asynchrony

To manage asynchrony you first have to recognise it!...



"I hardly recognised you without makeup"

...To improve asynchrony you have to measure it!

<https://www.cartoonstock.com/directory/r/recognise.asp?expanded=CX906583>

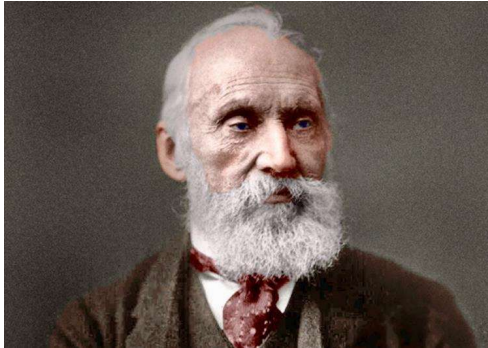
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The importance of measurement

"If you cannot measure it, you cannot improve it."

"When you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot measure it, when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind."

-Lord Kelvin



Lord Kelvin, a Scottish mathematician, who formulated the first and second laws of thermodynamics. *Science*, 09/08/2020, <https://www.facebook.com/scientetune/photos/a.104936004563873/152838873106919/?type=3&theater> accessed 25/08/2023

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A Brief history of Asynchrony- Definitions

RESPIRATORY CARE

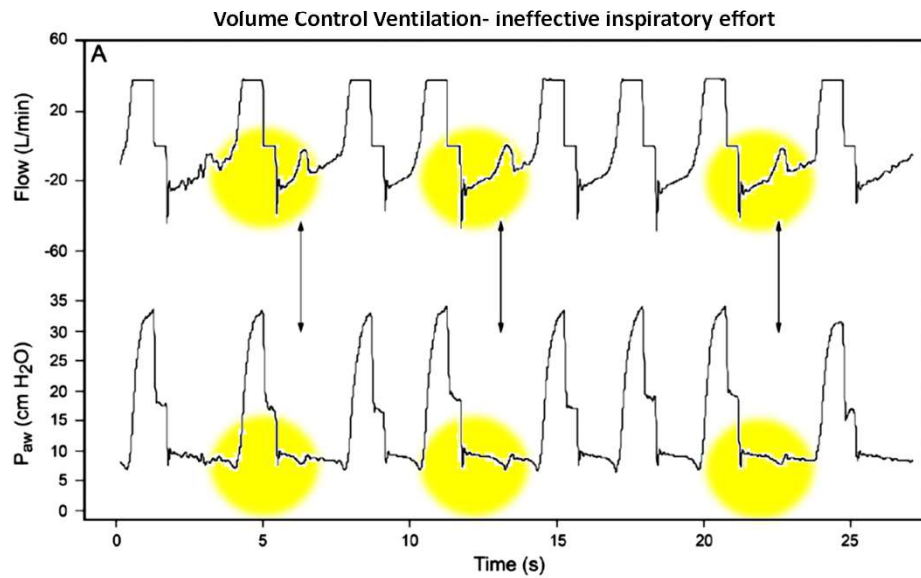
Types of asynchronies

Inspiratory Period	During the Transition From Inspiration to Expiration	Expiratory Period
<ul style="list-style-type: none"> · Trigger delay · Inspiratory flow mismatching · Short cycling · Prolonged cycling · Reverse triggering 	<ul style="list-style-type: none"> · Double triggering due to short cycling or reverse triggering · Expiratory muscle contraction due to prolonged cycling 	<ul style="list-style-type: none"> · Ineffective inspiratory effort · Auto-triggering · Expiratory muscle contraction

Subirà C, de Haro C, Magrans R, Fernández R, Blanch L. Minimizing asynchronies in mechanical ventilation: current and future trends. *Respiratory care*. 2018 Apr 1;63(4):464-78.

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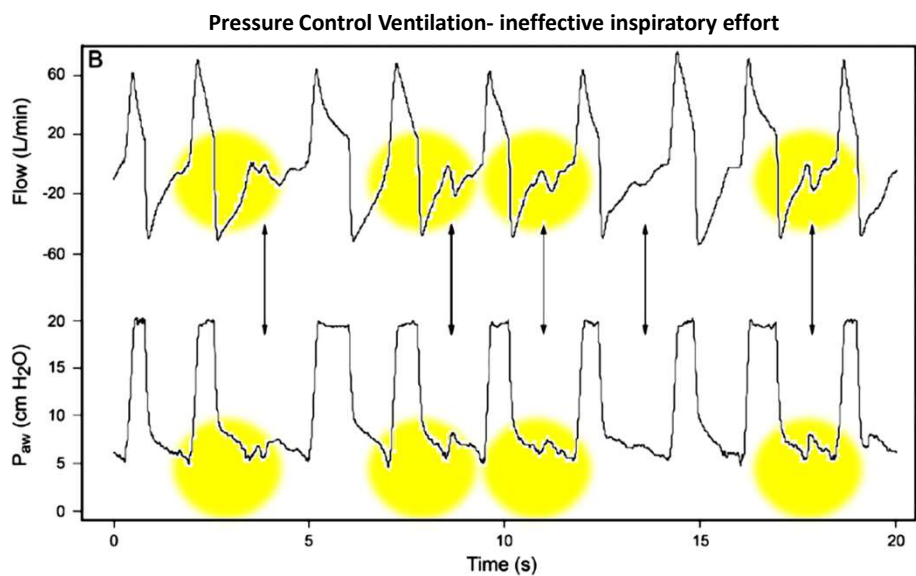
A Brief history of Asynchrony- Definitions



Subirà C, de Haro C, Magrans R, Fernández R, Blanch L. Minimizing asynchronies in mechanical ventilation: current and future trends. *Respiratory care.* 2018 Apr 1;63(4):464-78.

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A Brief history of Asynchrony- Definitions

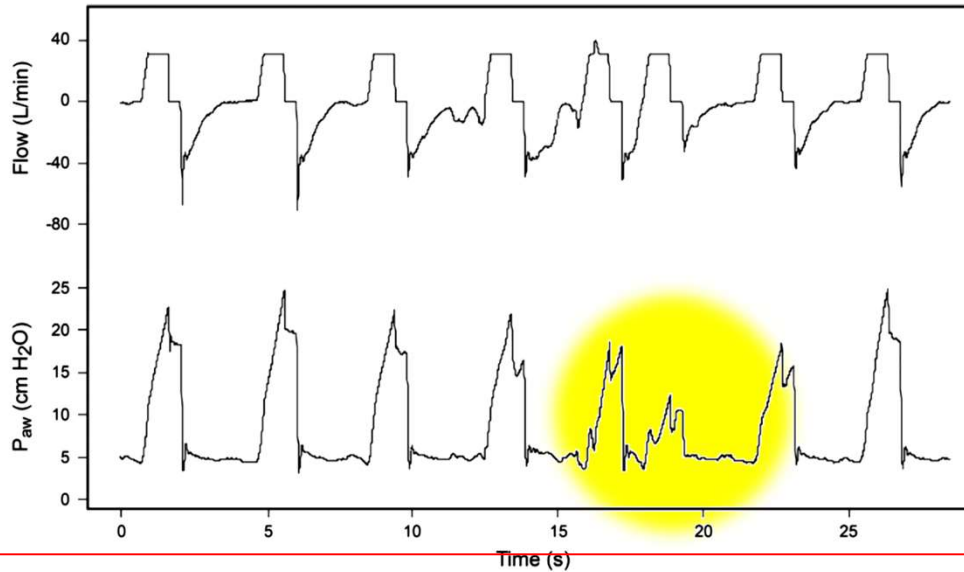


Subirà C, de Haro C, Magrans R, Fernández R, Blanch L. Minimizing asynchronies in mechanical ventilation: current and future trends. *Respiratory care.* 2018 Apr 1;63(4):464-78.

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A Brief history of Asynchrony- Definitions

Volume Controlled Ventilation, (constant flow) inspiratory flow mismatching

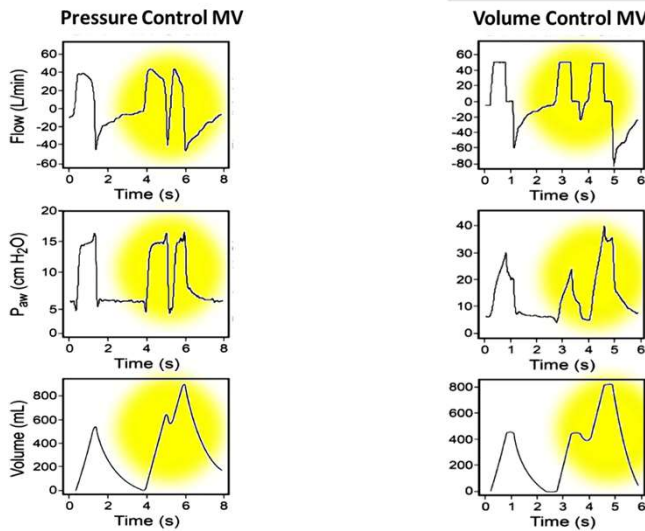


Subirà C, de Haro C, Magrans R, Fernández R, Blanch L. Minimizing asynchronies in mechanical ventilation: current and future trends. *Respiratory care.* 2018 Apr 1;63(4):464-78.

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A Brief history of Asynchrony- Definitions

Double triggering in pressure and volume controlled modes

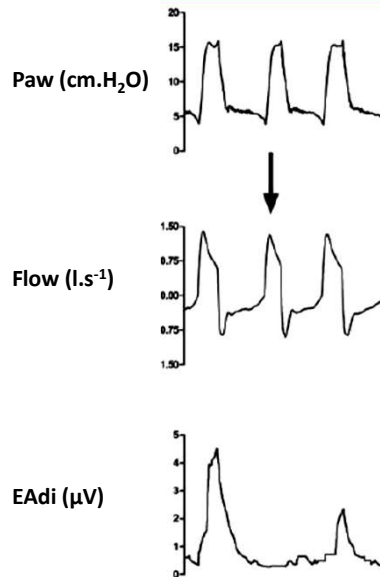


Subirà C, de Haro C, Magrans R, Fernández R, Blanch L. Minimizing asynchronies in mechanical ventilation: current and future trends. *Respiratory care.* 2018 Apr 1;63(4):464-78.

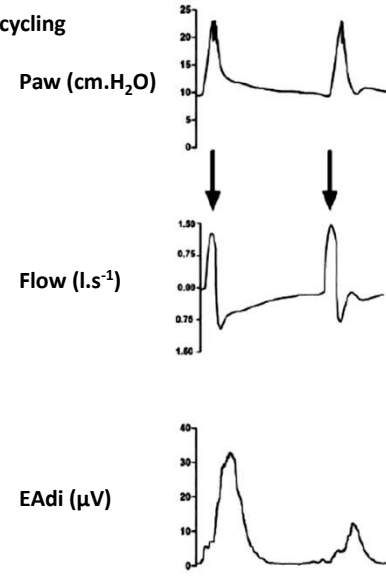
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A Brief history of Asynchrony- Definitions

Auto triggering



Premature cycling

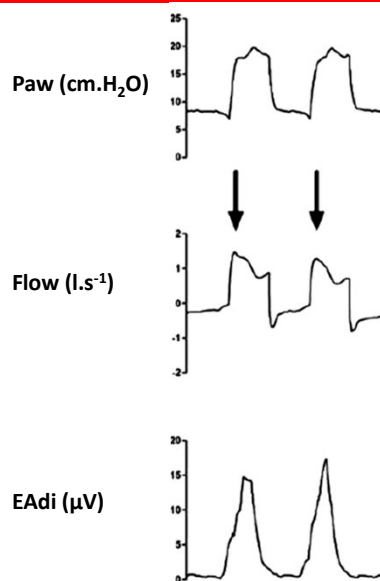


Garofalo E, Bruni A, Pelaia C, Liparota L, Lombardo N, Longhini F, Navalesi P. Recognizing, quantifying and managing patient-ventilator asynchrony in invasive and noninvasive ventilation. *Expert Review of Respiratory Medicine*. 2018 Jul 3;12(7):557-67.

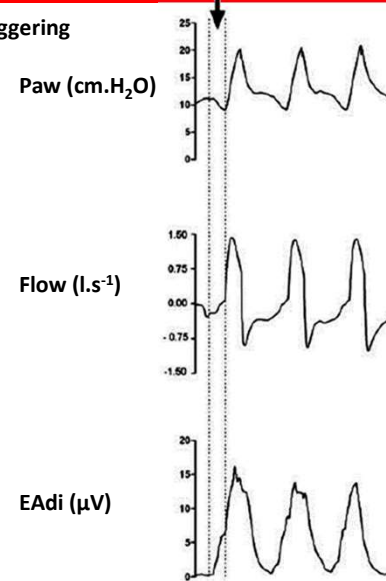
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A Brief history of Asynchrony- Definitions

Delayed cycling



Delayed triggering

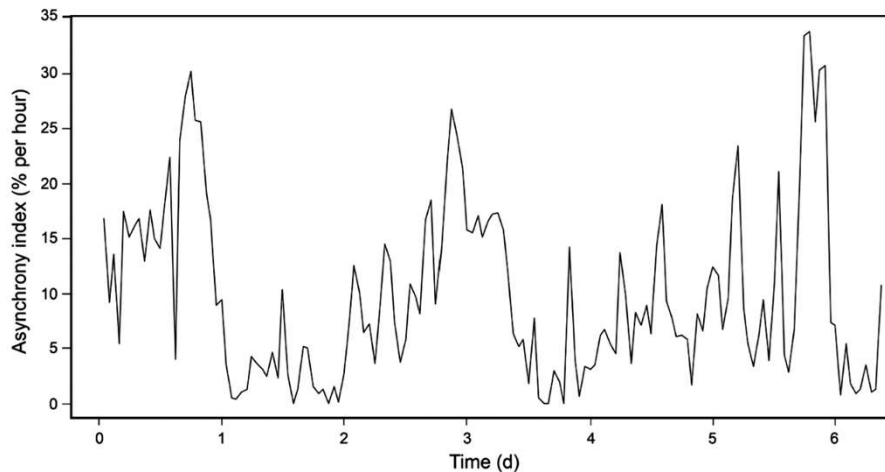


Garofalo E, Bruni A, Pelaia C, Liparota L, Lombardo N, Longhini F, Navalesi P. Recognizing, quantifying and managing patient-ventilator asynchrony in invasive and noninvasive ventilation. *Expert Review of Respiratory Medicine*. 2018 Jul 3;12(7):557-67.

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Defining Asynchrony Index

$$AI \% = \frac{\text{Asynchronous Breaths}}{\sum \text{Ventilator cycles} + \text{non-triggered breaths}}$$



Subirà C, de Haro C, Magrans R, Fernández R, Blanch L. Minimizing asynchronies in mechanical ventilation: current and future trends. *Respiratory care. 2018 Apr 1;63(4):464-78.*

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A Brief history of Asynchrony- Strategies

Strategies for Managing Asynchronies

Asynchrony	Action
Inspiratory flow mismatching	Increase gas flow; decrease respiratory drive and assess adequacy of analgesia and sedation; check for dyspnea.
Short or prolonged cycling	Increase or decrease inspiratory period; check cycling off in pressure support; use proportional modes.
Double triggering	Increase ventilator inspiratory time; try pressure support, titrating flow termination criteria to improve synchrony, or proportional modes; consider paralyzing agents if tidal volume is too elevated (> 8 mL/kg) in ARDS or in patients with risk factors for developing lung injury.
Double triggering due to reverse triggering	Decrease sedation; check breathing frequency; consider paralyzing agents if tidal volume is too elevated (> 8 mL/kg) in ARDS or in patients with risk factors for developing lung injury.
Expiratory muscle contraction due to prolonged cycling	Reduce inspiratory period by checking cycling off and tidal volume; check for comfort.
Ineffective inspiratory efforts	Check trigger sensitivity and excessive air trapping; check for excessive assistance (excessive set frequency and or inspiratory time during controlled modes or excessive pressure support ventilation level); counterbalance auto-PEEP by using external PEEP; check for dyspnea; consider proportional modes.
Auto-triggering	Check trigger sensitivity; check for leaks and water in the ventilator circuit.
Expiratory muscle contraction during expiration	Check for excessive assistance; check for air trapping and auto-PEEP.

Subirà C, de Haro C, Magrans R, Fernández R, Blanch L. Minimizing asynchronies in mechanical ventilation: current and future trends. *Respiratory care. 2018 Apr 1;63(4):464-78.*

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A brief review of asynchrony

Intensive Care Med (2008) 34:1477–1486
DOI 10.1007/s00134-008-1121-9

ORIGINAL

Arnaud W. Thille
Belen Cabello
Fabrice Galia
Aissam Lyazidi
Laurent Brochard

Reduction of patient-ventilator asynchrony by reducing tidal volume during pressure-support ventilation

12 patients with more than 10% of ineffective breaths on pressure-support ventilation were randomly assigned to pressure support reduction, insufflation time reduction, and change in end-expiratory pressure.

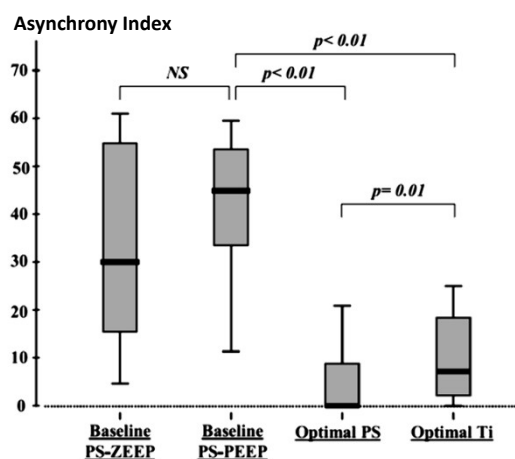
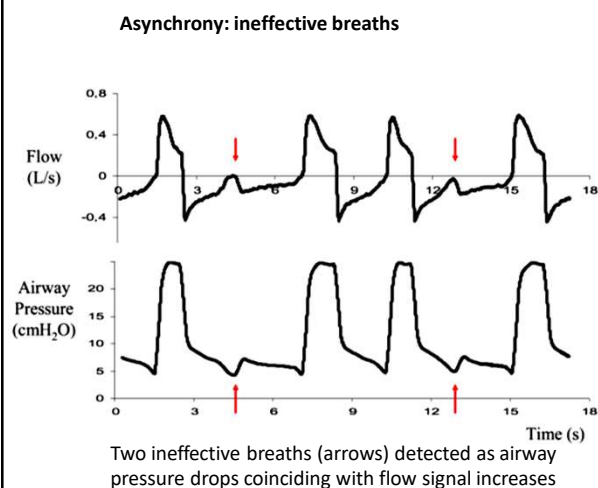
Results:

- **Reducing pressure support** from 20cm H₂O to 13 reduced tidal volume from 10.2 to 5.9 ml/kg, and **reduced ineffective triggering, from 45% of respiratory efforts [IQR 36–52] to 0% [0–7], (p < 0.01)** completely abolishing ineffective triggering in two-thirds of patients.
- **Reducing the insufflation time decreased the asynchrony index from 45% [IQR 36–52] to 7% [3–15], (p < 0.01)** and also reduced PEEPi

Thille AW, Cabello B, Galia F, et. al. Reduction of patient-ventilator asynchrony by reducing tidal volume during pressure-support ventilation. *Intensive Care Medicine*. 2008 Aug;34:1477-86.

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A Brief history of Asynchrony- Clinical Studies



Thille AW, Cabello B, Galia F, et. al. Reduction of patient-ventilator asynchrony by reducing tidal volume during pressure-support ventilation. *Intensive Care Medicine*. 2008 Aug;34:1477-86.

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A Brief history of Asynchrony- Clinical Studies

Intensive Care Med (2015) 41:633–641
DOI 10.1007/s00134-015-3692-6

ORIGINAL

Lluís Blanch
Ana Villagra
Bernat Sales
Jaume Montanya

Asynchronies during mechanical ventilation are associated with mortality

Prospective, observational study of 50 ICU patients
Using *Better Care*TM

Software distinguishes modes and detects ineffective inspiratory efforts during expiration (IEE), double-triggering, aborted inspirations, and short and prolonged cycling to compute the asynchrony index (AI) for each hour.

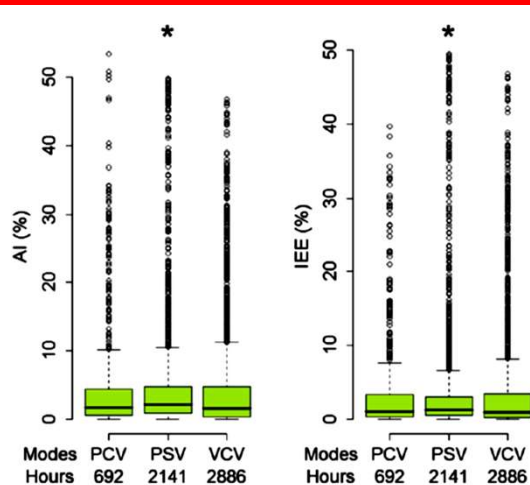
Results:

- 7,027 h of MV comprising 8,731,981 breaths
- AI was 3.41 % [IQR 1.95–5.77]; the most common asynchrony overall and in each mode was IEE [2.38 % (IQR 1.36–3.61)].
- Patients with AI >10 vs ≤10 %, had similar reintubation and tracheostomy rates, but higher ICU and hospital mortality and a trend toward longer duration of MV.

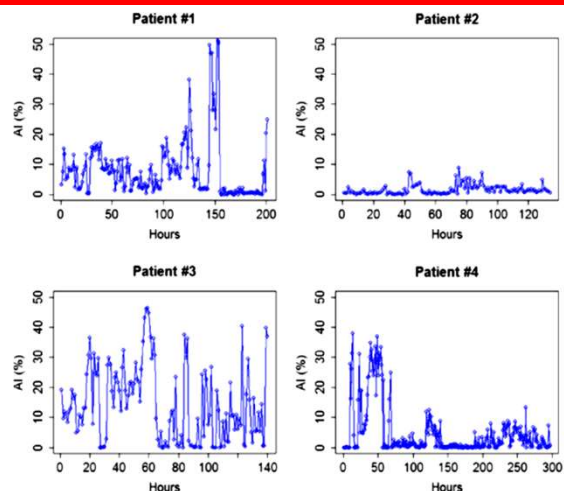
Blanch L, Villagra A, Sales B, Montanya J, Lucangelo U, Luján M, García-Esquirol O, Chacón E, Estruga A, Oliva JC, Hernández-Abadía A
Asynchronies during mechanical ventilation are associated with mortality. *Intensive care medicine*. 2015 Apr;41:633-41

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A Brief history of Asynchrony- Clinical Studies



Box, whiskers, and outliers (circles) showing the asynchrony index (AI) and proportion of inefficient expiratory efforts (IEE) during different modes of mechanical ventilation. * $p < 0.001$

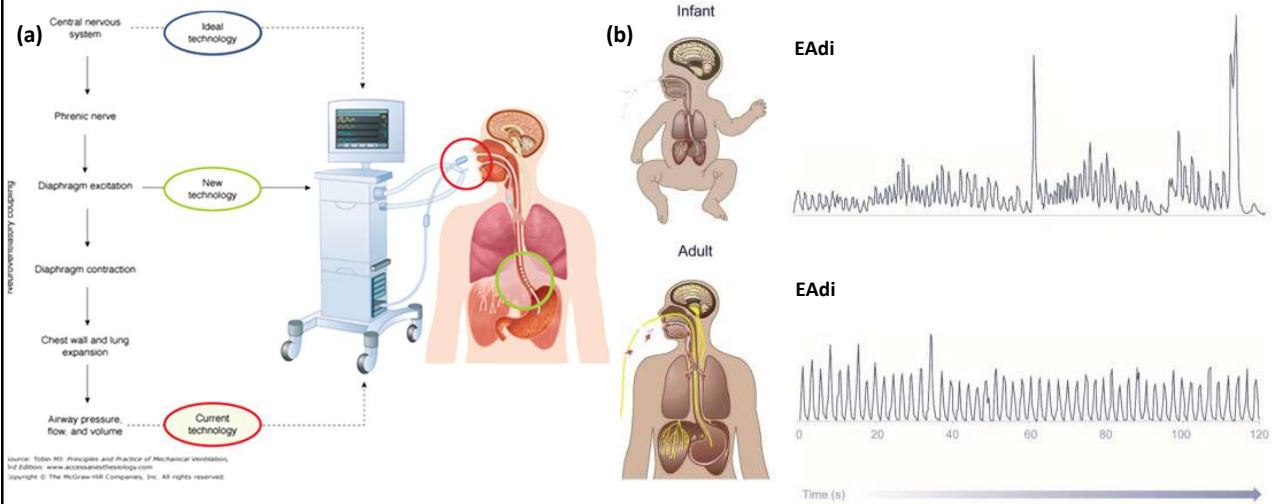


Asynchrony index (AI), (%)/hour, in 4 patients.
There are periods of almost no asynchronies alternating with high levels of asynchronies

Blanch L, Villagra A, Sales B, Montanya J, Lucangelo U, Luján M, García-Esquirol O, Chacón E, Estruga A, Oliva JC, Hernández-Abadía A
Asynchronies during mechanical ventilation are associated with mortality. *Intensive care medicine*. 2015 Apr;41:633-41

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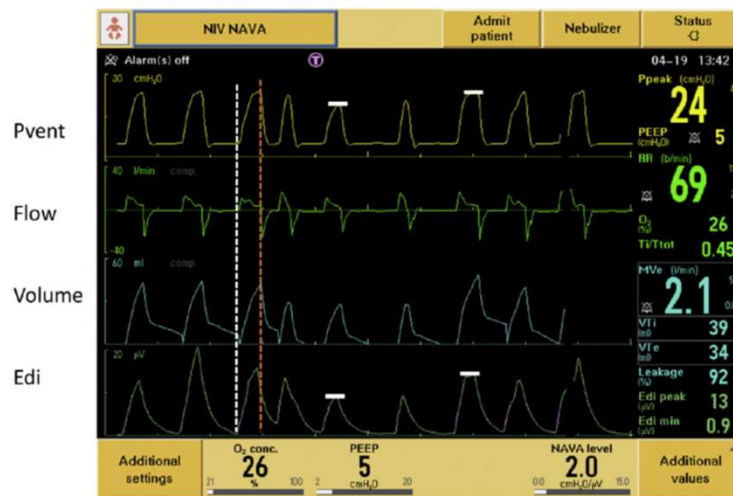
A Brief history of Asynchrony- Clinical Studies in NAVA



(a) Tobin MJ. *Principles and practice of mechanical ventilation, 3rd Edition McGraw-Hill Companies Inc.*
 (b) Stein H, Beck J, Dunn M. Non-invasive ventilation with neurally adjusted ventilatory assist in newborns. *Seminars in Fetal and Neonatal Medicine 2016 Jun 1 (Vol. 21, No. 3, pp. 154-161). WB Saunders.*

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A Brief history of Asynchrony- Clinical Studies in NAVA



Ventilator and diaphragm electrical activity waveforms during non-invasive neurally adjusted ventilatory assist (NIV-NAVA) in a premature neonate.

Stein H, Beck J, Dunn M. Non-invasive ventilation with neurally adjusted ventilatory assist in newborns. *Seminars in Fetal and Neonatal Medicine 2016 Jun 1 (Vol. 21, No. 3, pp. 154-161). WB Saunders.*

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A Brief history of Asynchrony- Clinical Studies

RESEARCH

Open Access



Critical Care

Impact of prolonged assisted ventilation on diaphragmatic efficiency: NAVA versus PSV

Patients on CMV for ≥ 72 hours or more were randomized to be ventilated for 48 hours with PSV ($n = 12$) or NAVA ($n = 13$). Neuro-ventilatory efficiency (NVE) (tidal volume/diaphragmatic electrical activity) and neuro-mechanical efficiency NME (pressure generated against the occluded airways/diaphragmatic electrical activity) were measured during 3 SBTs (0, 24 and 48 hours). Breathing pattern, diaphragmatic electrical activity and pressure time product of the diaphragm were assessed every 4 hours

Results:

NAVA

- **NVE increased** from 27 ± 19 ml/ μ V at baseline to 62 ± 30 ml/ μ V at 48 hours ($p < 0.0001$)
- **NME increased** from 1 ± 0.6 to 2.6 ± 1.1 cmH₂O/ μ V at 48 hours ($p = 0.033$)
- **AI = 5.39 [3.78– 8.36]**

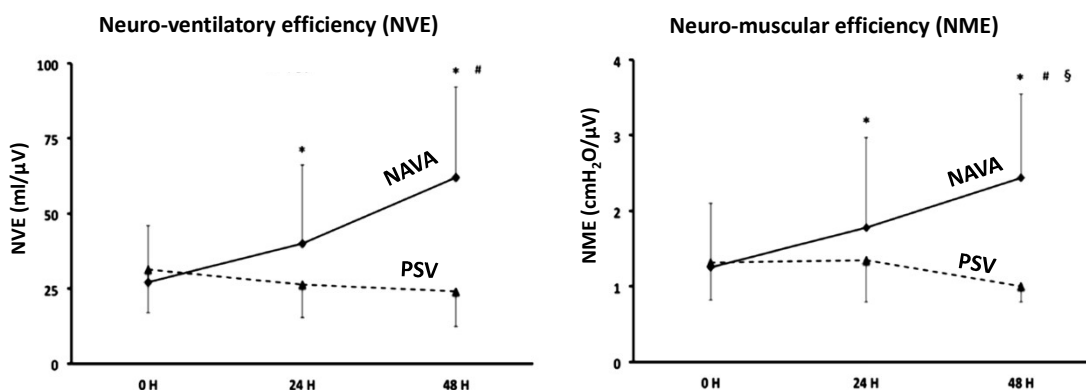
PSV

- **No change in NVE and NME**
- **AI = 9.48 [6.38– 21.73]**

Di Mussi R, Spadaro S, Mirabella L, et.al. Impact of prolonged assisted ventilation on diaphragmatic efficiency: NAVA versus PSV. *Critical Care*. 2015 Dec;20:1-2.

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A Brief history of Asynchrony- Clinical Studies



NVE and NME during SBTs in patients randomized to NAVA or PSV

The NVE and NME trends significantly different ($p < 0.0001$ for NVE and $p = 0.033$ for NME).

Key messages:

- After prolonged controlled mechanical ventilation 48 h of **NAVA improves diaphragm efficiency; prolonged PSV does not**
- Patient ventilator interactions were different between NAVA and PSV, which likely explains the differential impact on diaphragmatic efficiency.

Di Mussi R, Spadaro S, Mirabella L, et.al. Impact of prolonged assisted ventilation on diaphragmatic efficiency: NAVA versus PSV. *Critical Care*. 2015 Dec;20:1-2.

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A Brief history of Asynchrony- Clinical Studies

RESEARCH

Open Access



Neurally adjusted ventilatory assist and proportional assist ventilation both improve patient-ventilator interaction

PSV, NAVA, and PAV were set to obtain a tidal volume (V_T) of 6 to 8 ml/kg (PSV100, NAVA100, and PAV100) in 16 intubated patients. Assistance was decreased by 50% (PSV50, NAVA50, and PAV50) and then increased by 50% (PSV150, NAVA150, and PAV150) with all modes.

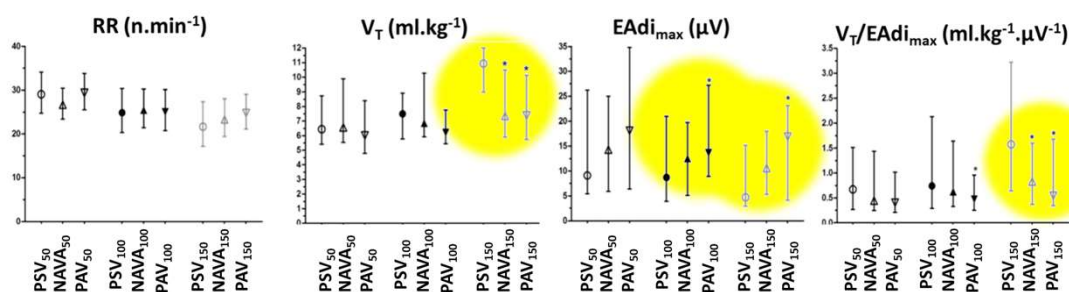
Results:

- **When PAV and NAVA were increased by 50% V_T remained acceptable** (medians 7.4 and 7.4 ml/kg) **but with PSV it increased** (10.9 ml/kg) ($P < 0.05$).
- **EAdi was higher with PAV** than with PSV at level100 and level150.
- **The coefficient of variation of V_T was higher with NAVA100 (19%) and PAV100 (21%)** vs. PSV100 (13%), ($P < 0.05$).
- **Ineffective triggering was lower with PAV and NAVA** ($P < 0.05$), but double triggering was higher with NAVA than with PAV and PSV ($P < 0.05$).

Schmidt M, Kindler F, Cecchini J, et. al. Neurally adjusted ventilatory assist and proportional assist ventilation both improve patient-ventilator interaction. *Critical Care*. 2015 Dec;19(1):1-1.

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A Brief history of Asynchrony- Clinical Studies



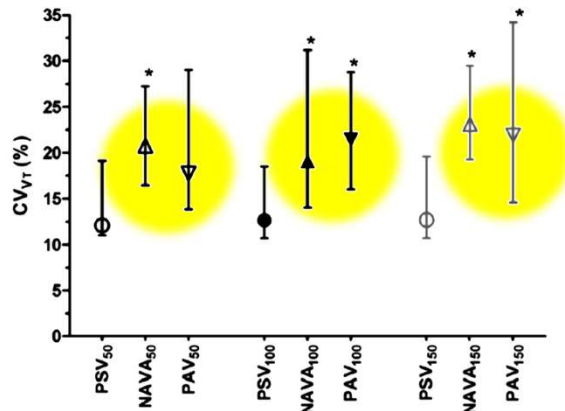
Support level 50% 100% 150% 50% 100% 150% 50% 100% 150% 50% 100% 150%

Impact of ventilator mode and level of assistance on the major descriptors of breathing pattern and diaphragmatic electrical activity (EAdi). **PSV results in a high V_T relative to the EAdi indicating over inflation and decoupling of diaphragm-ventilator interaction** $P < 0.05$ with PSV. Data are expressed as median and interquartile range.

Schmidt M, Kindler F, Cecchini J, et. al. Neurally adjusted ventilatory assist and proportional assist ventilation both improve patient-ventilator interaction. *Critical Care*. 2015 Dec;19(1):1-1.

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A Brief history of Asynchrony- Clinical Studies



Impact of ventilator mode and level of assistance on the coefficient of variation of tidal volume (CVVT).

- **PAV and NAVA both restore “natural” variability** of breathing.
- **The increase in breath-to-breath variability** observed during NAVA and PAV is due to “unmasking” of the underlying variability in central respiratory neural output and **is a direct result of improvement of neuromechanical coupling.**

Schmidt M, Kindler F, Cecchini J, et. al. Neurally adjusted ventilatory assist and proportional assist ventilation both improve patient-ventilator interaction. *Critical Care*. 2015 Dec;19(1):1-1.

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A Brief history of Asynchrony- Clinical Studies

ORIGINAL



Neurally adjusted ventilatory assist as an alternative to pressure support ventilation in adults: a French multicentre randomized trial

A multicentre RCT of 128 intubated adults with acute respiratory failure in 11 intensive care units were assigned to NAVA or PSV. The primary outcome was probability of remaining in a partial ventilatory mode (either NAVA or PSV) throughout the first 48 h without any return to assist-control ventilation.

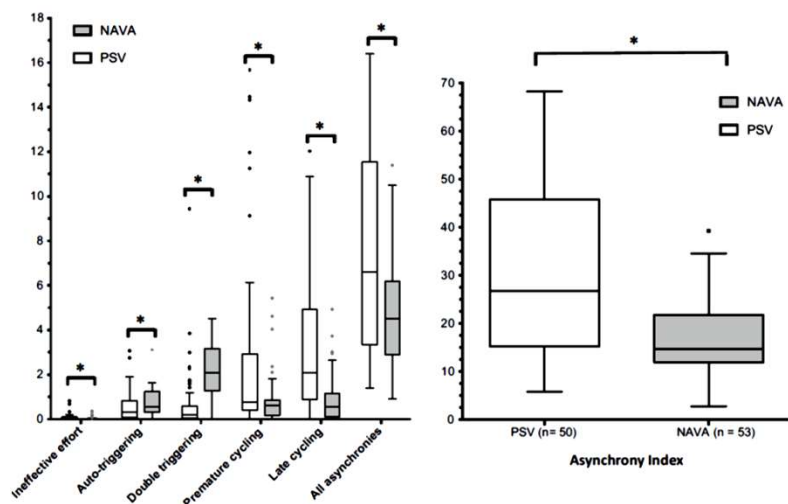
Results:

- Proportion of patients remaining in partial ventilatory mode in first 48 h was 67.2% (NAVA) vs. 63.3% (PSV) (P = 0.66)
- **Asynchrony index was 14.7 vs. 26.7 %** (P < 0.001)
- **More ventilator-free days (VFDs) at day 7 (1.0 day [1.0–4.0] vs. 0.0 days [0.0–1.0])** (P < 0.01)
- VFDs at day 28 were 21 days [4–25] vs. 17 days [0–23] (P = 0.12)
- 28 d mortality rate was 15.0 vs. 22.7 % (P = 0.21)
- **Post-extubation noninvasive mechanical ventilation was 43.5 vs. 66.6 %** (P < 0.01).

Demoule A, Clavel M, Rolland-Debord C, et.al. Neurally adjusted ventilatory assist as an alternative to pressure support ventilation in adults: a French multicentre randomized trial. *Intensive Care Medicine*. 2016 Nov;42:1723-32.

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A Brief history of Asynchrony- Clinical Studies



Rates and prevalence of main patient-ventilator asynchronies. Median and IQR for the main ventilator asynchronies (left) and the asynchrony index (right). $p < 0.05$

Demoule A, Clavel M, Rolland-Debord C, et.al. Neurally adjusted ventilatory assist as an alternative to pressure support ventilation in adults: a French multicentre randomized trial. *Intensive Care Medicine*. 2016 Nov;42:1723-32.

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A Brief history of Asynchrony- Clinical Studies

RESPIRATORY CARE

Neurally-Adjusted Ventilatory Assist Versus Noninvasive Pressure Support Ventilation in COPD Exacerbation: The NAVA-NICE Trial

40 subjects with COPD and acute hypercapnic respiratory failure randomized to either NIV-NAVA (n=20) or NIV-PSV (n=20)

Results:

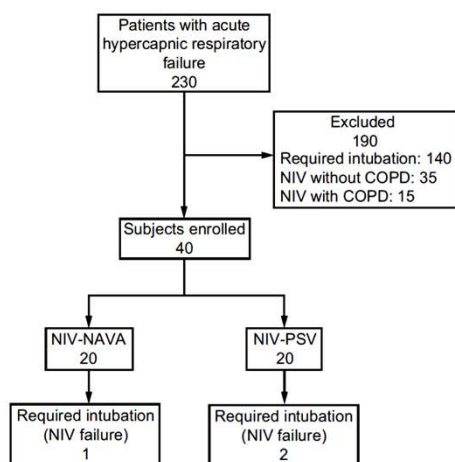
NIV-NAVA significantly reduced the total number of asynchrony events compared to NIV-PSV. median, [IQR]) 22 [15-32.5] vs. 65 (50.75-104.25), $P = .002$.

Severe asynchrony (AI > 10%) was lower in NIV-NAVA than in NIV-PSV. 2 vs. 14 events, $P < .001$.

Tajamul S, Hadda V, Madan K, et. al. Neurally-adjusted ventilatory assist versus noninvasive pressure support ventilation in COPD exacerbation: the NAVA-NICE Trial. *Respiratory care*. 2020 Jan 1;65(1):53-61.

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A Brief history of Asynchrony- Clinical Studies



Flow chart. NIV = noninvasive ventilation; NAVA = neurally adjusted ventilatory assist; PSV = pressure support ventilation.

Comparison of Asynchrony Index and Types of Asynchrony

	NIV-NAVA	NIV-PSV	P
Asynchrony index			
30 min after initiation	6.02 ± 2.36	14.33 ± 8.63	< .001
Day 1	4.42 ± 2.03	12.06 ± 7.98	.002
Day 2	3.05 ± 2.29	8.43 ± 6.61	.001
Day 3	1.88 ± 2.09	5.07 ± 3.38	.001
Day 4	0.74 ± 0.89	3.88 ± 3.96	.007
Types of asynchrony			
Ineffective efforts	1 (0–3)	10 (8.5–18)	< .001
Auto triggering	0 (0–0)	5.5 (2.5–9.5)	< .001
Double triggering	11.5 (10–14)	19.5 (14–29)	.004
Premature cycling	0 (0–4.25)	15 (9–22.5)	< .001
Delayed cycling	8 (3.5–9.25)	13 (8–17.25)	.01
Total asynchrony	22.5 (15–32.5)	65 (50.75–104.25)	.002

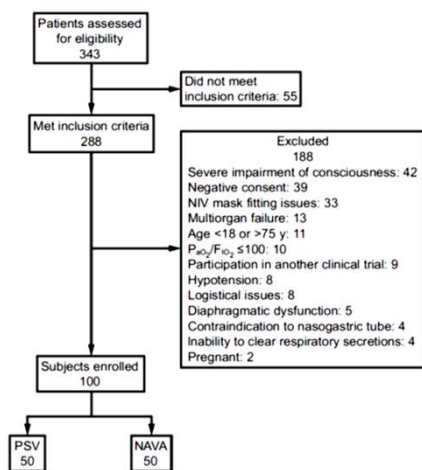
Data are presented as mean SD or median (IQR). NIV-NAVA: n = 20; NIV-PSV: n = 20 .

Tajamul S, Hadda V, Madan K, et. al. Neurally-adjusted ventilatory assist versus noninvasive pressure support ventilation in COPD exacerbation: the NAVA-NICE Trial. *Respiratory care*. 2020 Jan 1;65(1):53-61.

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A Brief history of Asynchrony- Clinical Studies

Comparing Noninvasive Ventilation Delivered Using Neurally-Adjusted Ventilatory Assist or Pressure Support in Acute Respiratory Failure



RCT of NAVA compared with PSV in NIV in 100 consecutive subjects with de novo acute respiratory failure. Primary outcomes were NIV failure and 28-d mortality.

Results:

- **No diff. in NIV failure** (30% vs 32%, P = .83) or 28-d mort. (18% vs 34%, P = .07)
- **Lower asynchrony index with NAVA** (6.7 vs 44.8, P < .001)
- **Lower NIV-related complications with NAVA** (32% vs 58%, P = .01)

Specifically, NAVA resulted in:

- **Better muscle unloading**; lower peak EAdi values compared to the PSV arm
- **Less abdominal distension** (6% vs. 20%) and skin ulcers (14% vs 36%)
- **In a post hoc analysis of exacerbation of COPD there was 20% reduction in 90-d mortality** (attributable to lower in-hospital mortality, which might have contributed to better 90-d mortality)

Prasad KT, Gandra RR, Dhooria S, et al., Agarwal R, Sehgal IS. Comparing noninvasive ventilation delivered using neurally-adjusted ventilatory assist or pressure support in acute respiratory failure. *Respiratory Care*. 2021 Feb 1;66(2):213-20.

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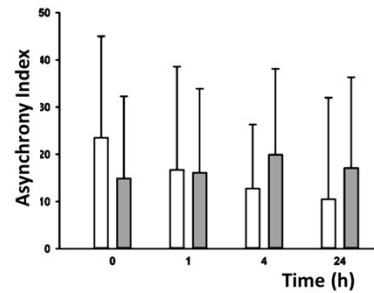
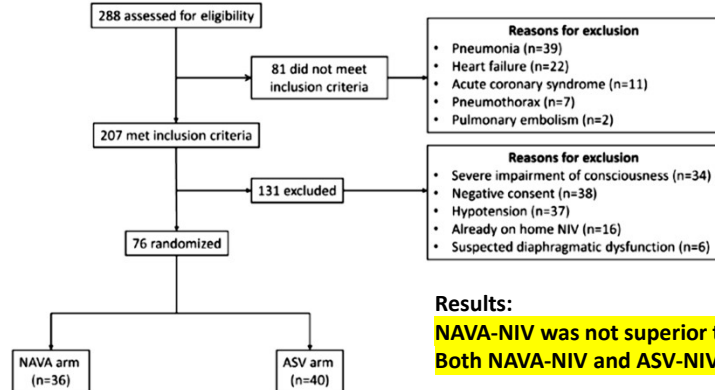
A Brief history of Asynchrony- Clinical Studies



ELSEVIER

A randomized controlled trial comparing non-invasive ventilation delivered using neurally adjusted ventilator assist (NAVA) or adaptive support ventilation (ASV) in patients with acute exacerbation of chronic obstructive pulmonary disease

RCT of 76 patients comparing NAVA-NIV with ASV-NIV in consecutive subjects with acute exacerbation of COPD.



Results:

NAVA-NIV was not superior to ASV-NIV in reducing NIV failure rates in AECOPD. Both NAVA-NIV and ASV-NIV had similar asynchrony index and 90-day mortality.

Chhabria BA, Prasad KT, Dhooria S, et.al. A randomized controlled trial comparing non-invasive ventilation delivered using neurally adjusted ventilator assist (NAVA) or adaptive support ventilation (ASV) in patients with acute exacerbation of chronic obstructive pulmonary disease.

Journal of Critical Care. 2023 Jun 1;75:154250.

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A Brief history of Asynchrony- Paediatric Clinical Studies



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A Brief history of Asynchrony- Paediatric Clinical Studies

RESEARCH

Open Access



Neurally adjusted ventilatory assist (NAVA) allows patient-ventilator synchrony during pediatric noninvasive ventilation: a crossover physiological study

13 NIV patients in PICU successively ventilated in conventional NIV (30 minutes), in NIV-NAVA (60 minutes), and then again in NIV (30 minutes). Electrical activity of the diaphragm (EAdi) and airway pressure simultaneously recorded to assess patient-ventilator synchrony.

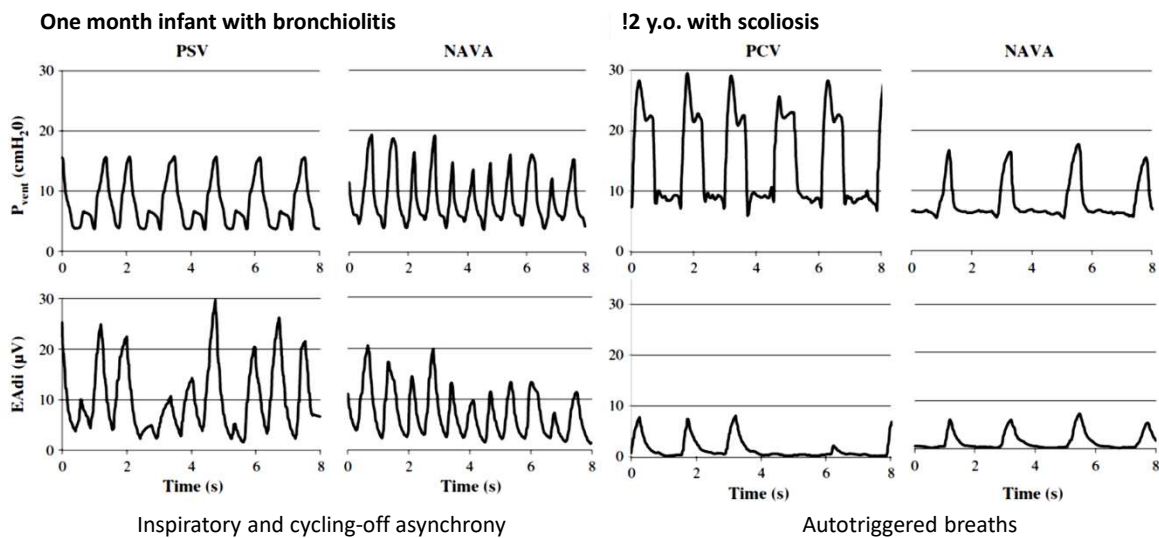
Results:

- **Inspiratory trigger dys-synchrony and cycling-off dys-synchrony shorter in NIV-NAVA** compared with both conventional NIV periods (both $P < 0.05$).
- **Wasted efforts were decreased in NIV-NAVA, 0% [0 to 0] versus 12% [4 to 20] and 6% [2 to 22], $P < 0.01$.**
- **Total time spent in asynchrony reduced from 27% [19 to 56] and 32% [21 to 38] to 8% [6 to 10] in NIV-NAVA ($P = 0.05$)**

Ducharme-Crevier L, Beck J, Essouri S, Jouvét P, Emeriaud G. Neurally adjusted ventilatory assist (NAVA) allows patient-ventilator synchrony during pediatric noninvasive ventilation: a crossover physiological study. *Critical Care*. 2015 Dec;19(1):1-0.

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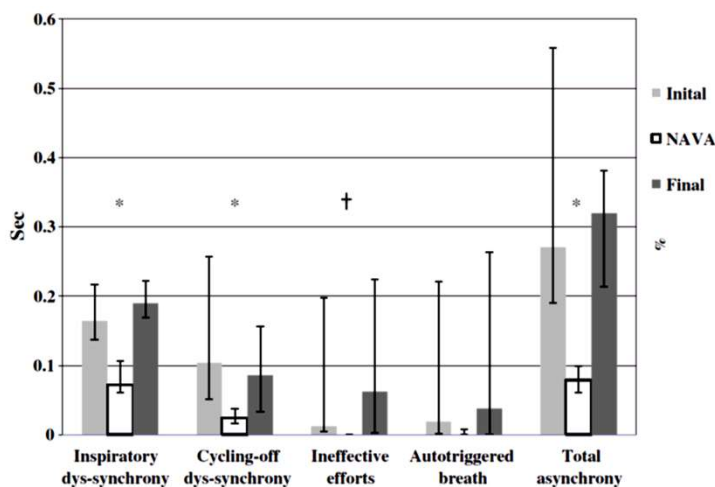
A Brief history of Asynchrony- Paediatric Clinical Studies



Ducharme-Crevier L, Beck J, Essouri S, Jouvét P, Emeriaud G. Neurally adjusted ventilatory assist (NAVA) allows patient-ventilator synchrony during pediatric noninvasive ventilation: a crossover physiological study. *Critical Care*. 2015 Dec;19(1):1-0.

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A Brief history of Asynchrony- Paediatric Clinical Studies



Inspiratory dys-synchrony (ms), cycling-off dys-synchrony (ms), ineffective efforts (%) and autotriggered breaths (%) in initial conventional NIV, NIV-NAVA, and final conventional NIV. *P ≤ 0.05 and † P < 0.01

Ducharme-Crevier L, Beck J, Essouri S, Jouvét P, Emeriaud G. Neurally adjusted ventilatory assist (NAVA) allows patient-ventilator synchrony during pediatric noninvasive ventilation: a crossover physiological study. *Critical Care*. 2015 Dec;19(1):1-0.

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A Brief history of Asynchrony- Paediatric Clinical Studies

RESEARCH

Open Access

Annals of Intensive Care



Patient-ventilator asynchrony during conventional mechanical ventilation in children

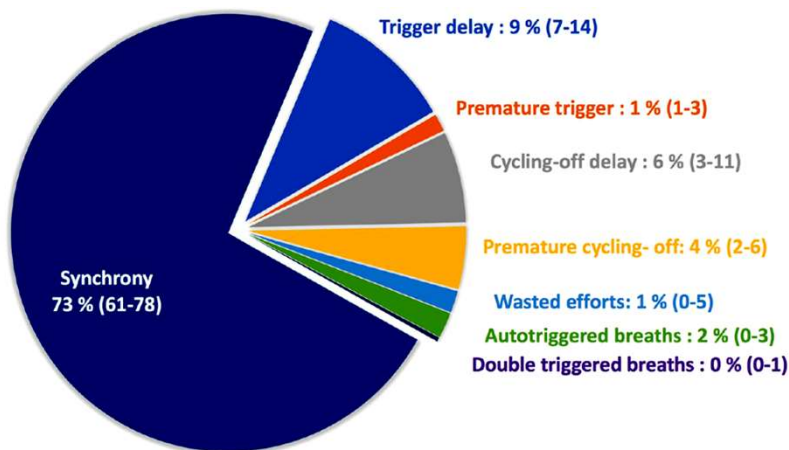


Prospective observational study using NAVA used to detect asynchrony in a PICU
Ventilator mode and setting according to local practice. No written protocol regarding ventilation or sedation management

Mortamet G, Larouche A, Ducharme-Crevier L, Fléchelles O, Constantin G, Essouri S, Pellerin-Leblanc AA, Beck J, Sinderby C, Jouvét P, Emeriaud G. Patient-ventilator asynchrony during conventional mechanical ventilation in children. *Annals of Intensive Care*. 2017 Dec;7(1):1-1.

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A Brief history of Asynchrony- Paediatric Clinical Studies



Results:

- 52 Children, median age = 6 mo.
- 27% [IQR 22–39] of time in conflict with ventilator. 20% due to cycling-off errors and trigger delays
- NeuroSync index of 45%, (confirming the high prevalence of asynchrony)

Mortamet G, Larouche A, Ducharme-Crevier L, Fléhelles O, Constantin G, Essouri S, Pellerin-Leblanc AA, Beck J, Sinderby C, Jouvett P, Emeriaud G. Patient-ventilator asynchrony during conventional mechanical ventilation in children. *Annals of Intensive Care.* 2017 Dec;7(1):1-1.

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A Brief history of Asynchrony- Meta-Analysis

LETTER



Asynchrony index in pressure support ventilation (PSV) versus neurally adjusted ventilator assist (NAVA) during non-invasive ventilation (NIV) for respiratory failure: systematic review and meta-analysis

9, mostly feasibility, studies (6 adult, 3 paediatric), 5 RCTs; 4 Observational studies 96 patients.

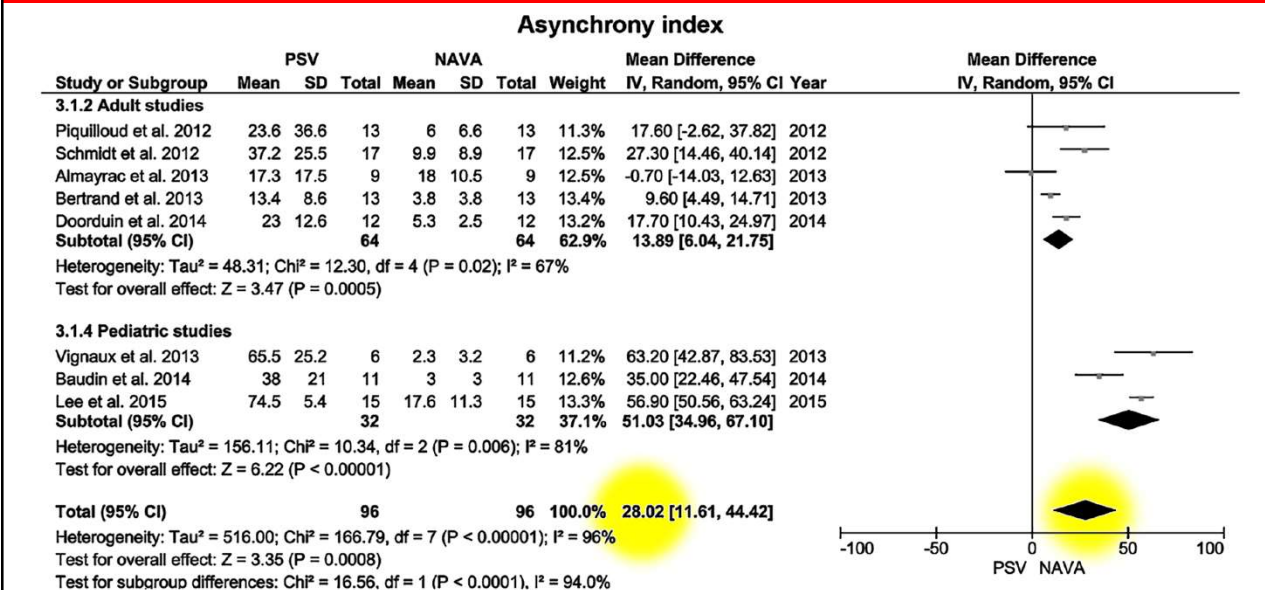
Severe asynchrony (asynchrony index >10%)

Study or Subgroup	PSV		NAVA		Weight	Risk Ratio		M-H, Random, 95% CI
	Events	Total	Events	Total		M-H, Random, 95% CI	Year	
Cammarota et al. 2011	8	10	0	10	7.2%	17.00	[1.11, 259.87]	2011
Schmidt et al. 2012	17	17	8	17	45.5%	2.06	[1.26, 3.38]	2012
Piquilloud et al. 2012	9	13	3	13	27.7%	3.00	[1.04, 8.63]	2012
Bertrand et al. 2013	6	13	1	13	12.3%	6.00	[0.83, 43.13]	2013
Vignaux et al. 2013	5	6	0	6	7.3%	11.00	[0.74, 163.49]	2013
Total (95% CI)		59		59	100.0%	3.43	[1.57, 7.51]	
Total events	45		12					
Heterogeneity: Tau ² = 0.29; Chi ² = 6.56, df = 4 (P = 0.16); I ² = 39%								
Test for overall effect: Z = 3.08 (P = 0.002)								

Sehgal IS, Dhooria S, Aggarwal AN, et.al. Asynchrony index in pressure support ventilation (PSV) versus neurally adjusted ventilator assist (NAVA) during non-invasive ventilation (NIV) for respiratory failure: systematic review and meta-analysis. *Intensive care medicine.* 2016 Nov;42:1813-5.

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A Brief history of Asynchrony- Meta-Analysis



Sehgal IS, Dhooria S, Aggarwal AN, et al. Asynchrony index in pressure support ventilation (PSV) versus neurally adjusted ventilator assist (NAVA) during non-invasive ventilation (NIV) for respiratory failure: systematic review and meta-analysis. *Intensive care medicine*. 2016 Nov;42:1813-5.

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A Brief history of Asynchrony- Meta-Analysis

RESEARCH

Open Access



Annals of Intensive Care

Proportional modes versus pressure support ventilation: a systematic review and meta-analysis

Parallel-group and crossover randomized studies were included, which examined the efficacy of proportional modes in comparison with PSV in mechanically ventilated adults.

Primary outcomes were (1) asynchrony index (AI), (2) weaning failure, and (3) duration of mechanical ventilation.

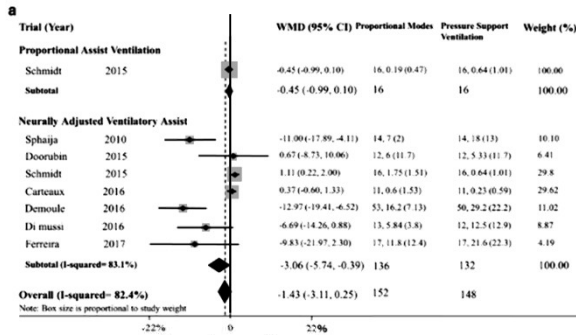
- **The use of proportional modes was associated with a reduction in patients with severe AI > 10%** (RR 0.15; 95% CI 0.04–0.58; p = 0.006; PAV—two studies, and NAVA—five studies), compared with PSV.
- Compared with PSV, use of **proportional modes were associated with a reduction in weaning failure** (RR 0.44; 95% CI 0.26–0.75; p = 0.003; PAV—three studies) and **duration of mechanical ventilation** (WMD – 1.78 days; 95% CI – 3.24 to – 0.32; p = 0.017; PAV—three studies, and NAVA—two studies).
- Reduced duration of mechanical ventilation was found with PAV but not with NAVA. (no studies available)

Kataoka J, Kuriyama A, Norisue Y, Fujitani S. Proportional modes versus pressure support ventilation: a systematic review and meta-analysis. *Annals of Intensive Care*. 2018 Dec;8(1):1-2.

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A Brief history of Asynchrony- Meta-Analysis

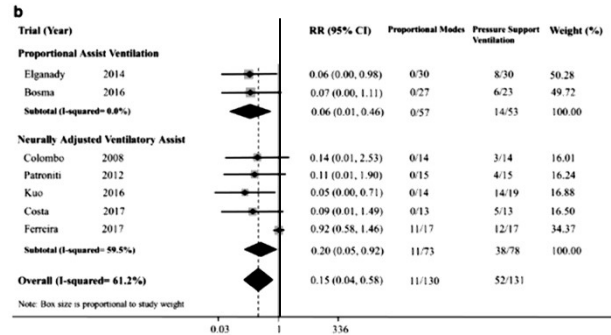
Risk of asynchrony (AI as continuous outcome)



Favours Proportional modes Favours PSV



Relative risk of severe asynchrony (AI >10%)



Favours Proportional modes Favours PSV



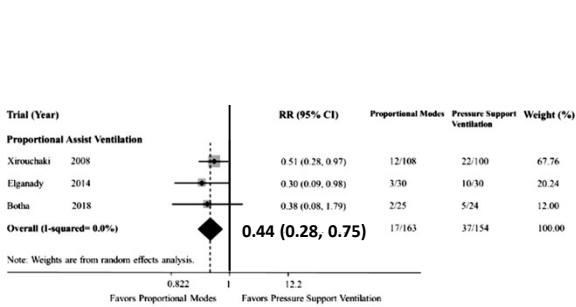
a AI as a continuous outcome, **b** AI as dichotomous if patients with AI > 10%. RR = risk ratio, WMD =weighted mean difference

Kataoka J, Kuriyama A, Norisue Y, Fujitani S. Proportional modes versus pressure support ventilation: a systematic review and meta-analysis. *Annals of Intensive Care. 2018 Dec;8(1):1-2.*

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A Brief history of Asynchrony- Meta-Analysis

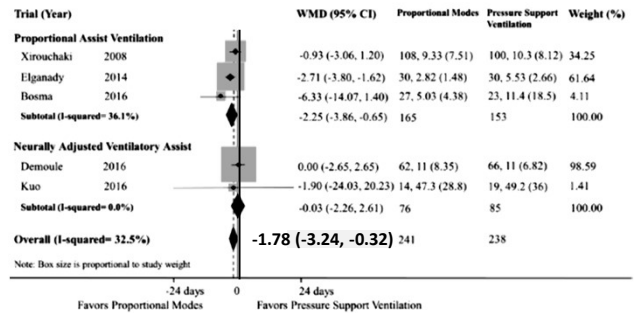
Relative risk of weaning failure (only PAV studies)



Favours Proportional Modes Favours Pressure Support Ventilation



Relative risk of duration of mechanical ventilation



Favours Proportional Modes Favours Pressure Support Ventilation



Kataoka J, Kuriyama A, Norisue Y, Fujitani S. Proportional modes versus pressure support ventilation: a systematic review and meta-analysis. *Annals of Intensive Care. 2018 Dec;8(1):1-2.*

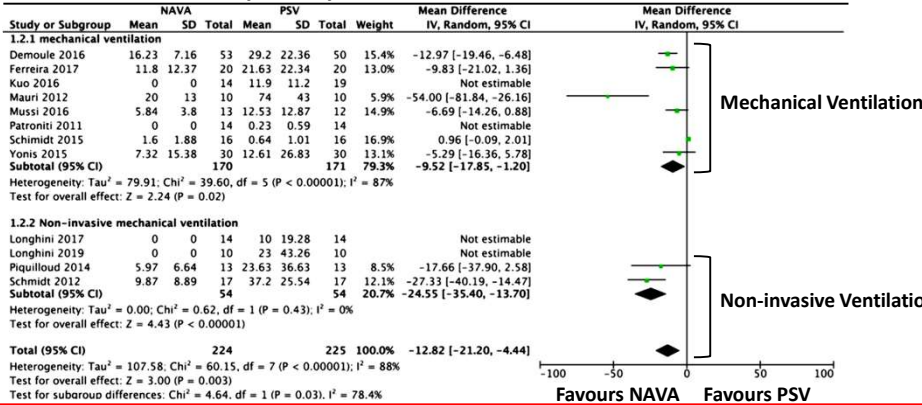
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A Brief history of Asynchrony- Meta-Analysis

Original Article

Neurally adjusted ventilatory assist versus pressure support ventilation in patient-ventilator interaction and clinical outcomes: a meta-analysis of clinical trials

Asynchrony Index NAVA vs PSV

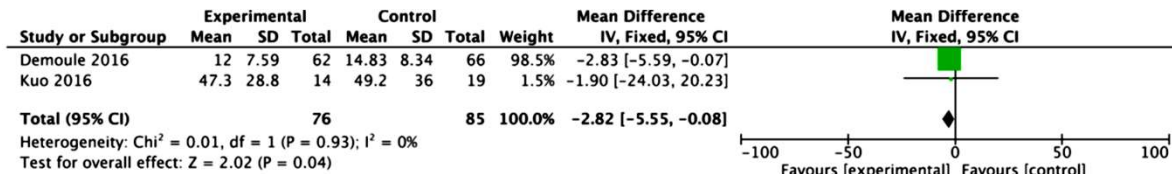


Chen C, Wen T, Liao W. Neurally adjusted ventilatory assist versus pressure support ventilation in patient-ventilator interaction and clinical outcomes: a meta-analysis of clinical trials. *Annals of Translational Medicine*. 2019 Aug;7(16).

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A Brief history of Asynchrony- Meta-Analysis

Duration of ventilation



Chen C, Wen T, Liao W. Neurally adjusted ventilatory assist versus pressure support ventilation in patient-ventilator interaction and clinical outcomes: a meta-analysis of clinical trials. *Annals of Translational Medicine*. 2019 Aug;7(16).

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A Brief history of Asynchrony- Clinical Studies

RESPIRATORY CARE

Neurally adjusted ventilatory assist (NAVA) versus pressure support ventilation (PSV) during non-invasive ventilation (NIV): systematic review and meta-analysis

The PubMed, Cochrane Library, Web of Science, OpenGrey, and Embase databases were searched for appropriate clinical trials comparing NIV-NAVA with NIV-PSV for adult subjects. Comparisons of asynchrony index (AI), types of asynchrony, and clinical outcomes were pooled.

Results: (15 studies; 615 subjects).

By comparison of NAVA to Pressure Support Ventilation (PSV):

- **AI lower** ([MD] -14.70 [95% CI -23.20 to -6.19]), $P < .001$).
- **AI lower in COPD exacerbation** (MD -14.56 [95% CI -21.04 to -8.09], $P < .001$) and non-COPD (MD -3.02 [95% CI -4.44 to -1.61], $P < .001$).
- **Severe asynchrony lower** (OR 0.06 [95% CI 0.03-0.11], $P < .001$).
- **Inspiratory trigger delay lower** (MD -129.60 [95% CI -148.43 to -110.78], $P < .001$).
- **Longer ICU length of stay** (MD 1.22 [95% CI 0.44-2.00], $P = .002$).
- **Higher discomfort** (MD 0.62 [95% CI 0.02-1.21], $P = .040$).



Teng W, Sang L, Cao L. Neurally adjusted ventilatory assist (NAVA) versus pressure support ventilation (PSV) during non-invasive ventilation (NIV): systematic review and meta-analysis. *Respiratory Care*. 2022 Feb 17.

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What do we need to think about?

Some questions to ponder....

- Why is asynchrony software not available for use on all patients undergoing ventilation? Is this another case of the proverbial, "If you don't take a temperature, you can't find a fever?"
[Roy Basch's rules from House of God]
- Is this why is asynchrony is so poorly appreciated at the bedside?
- Why, in spite of two decades of application of PROPORTIONAL breathing assistance modes (NAVA and PAV), have these modes not become more readily available and adopted? Should they be available on all ventilators?



https://www.modernanalyst.com/Resources/BusinessAnalystHumor/tabid/218/ID/6133/Hospital_Medical_Software_Design.aspx
(accessed 4 Sept 2023)

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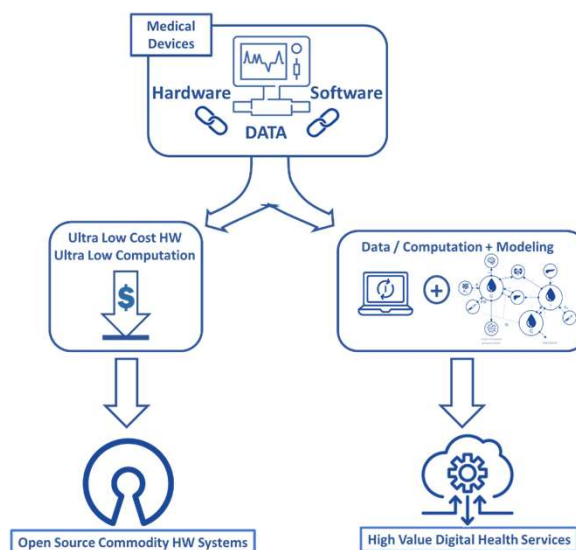
What do we need to think about?

- Vaccine development during Covid-19 pandemic took about 18 months. However, new developments in mechanical ventilation may take more than the clinical career of many clinicians! (>30 years)
- This lack of progress is not just limited to proportional ventilation modes, but all innovations in mechanical ventilation.
- Failure to translate ventilation research into clinical practice at the bedside fails to correct the harm and excess mortality from poor practices in mechanical ventilation



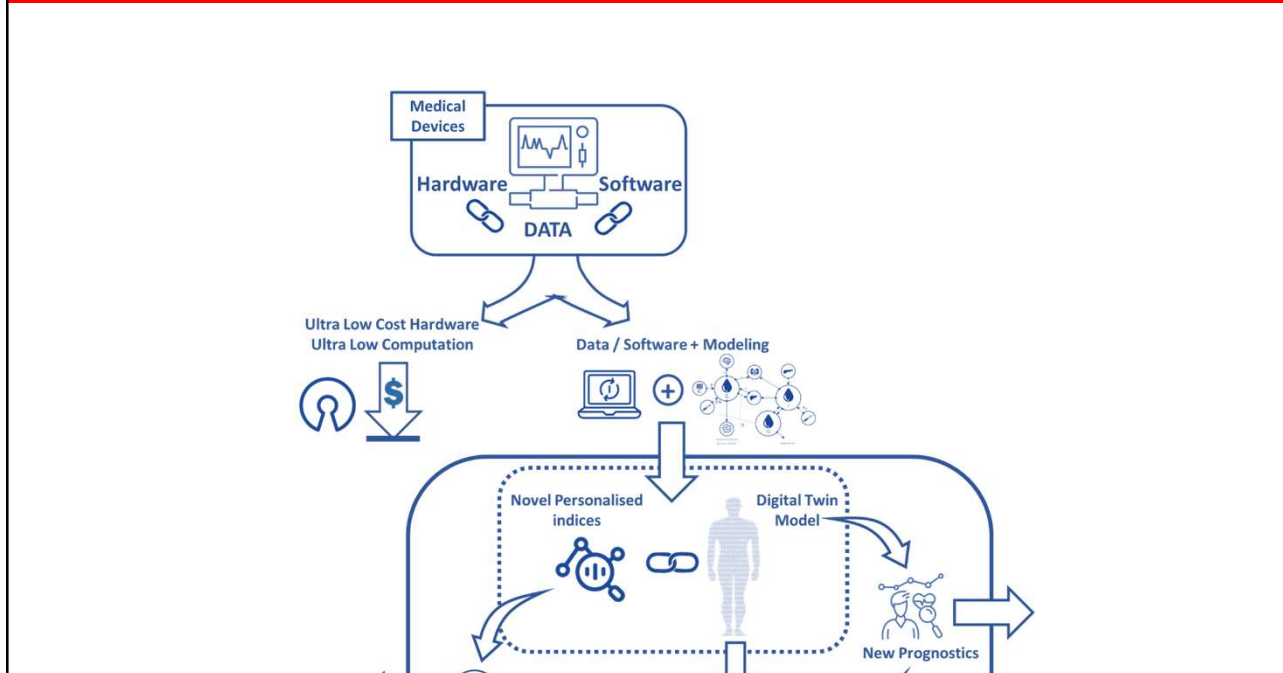
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The business model is not fit for purpose. How can we fix this??

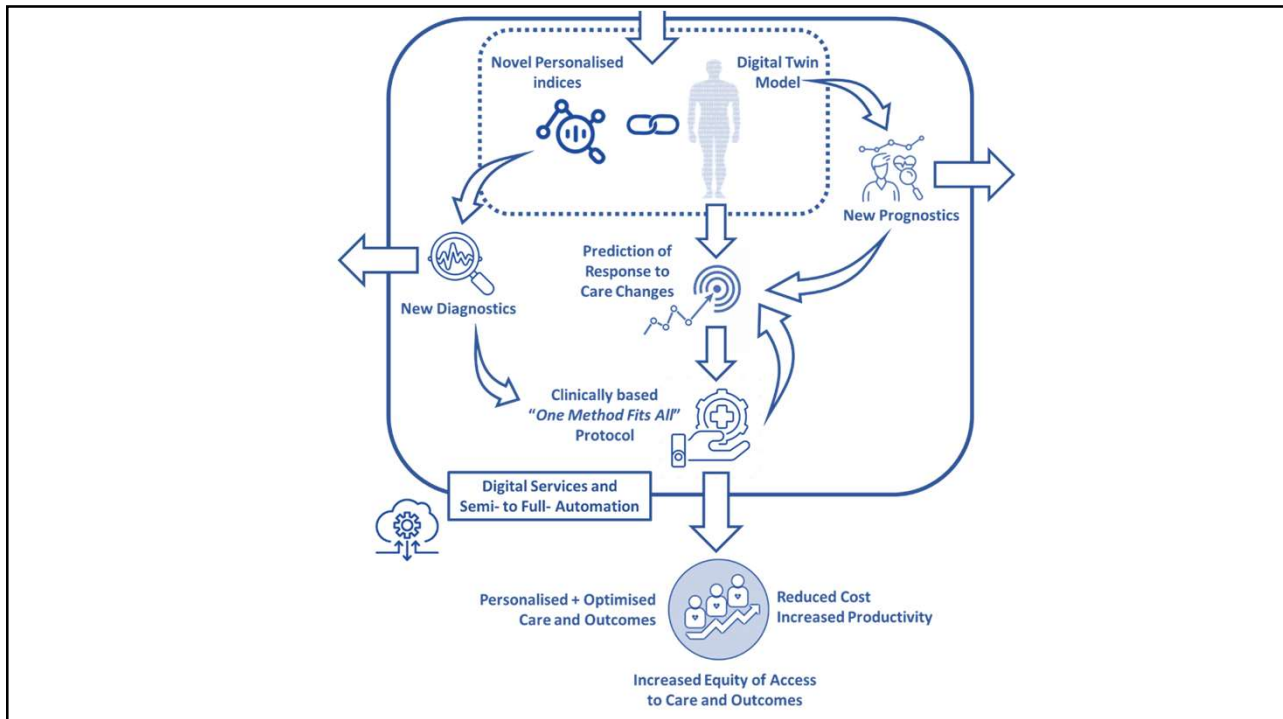


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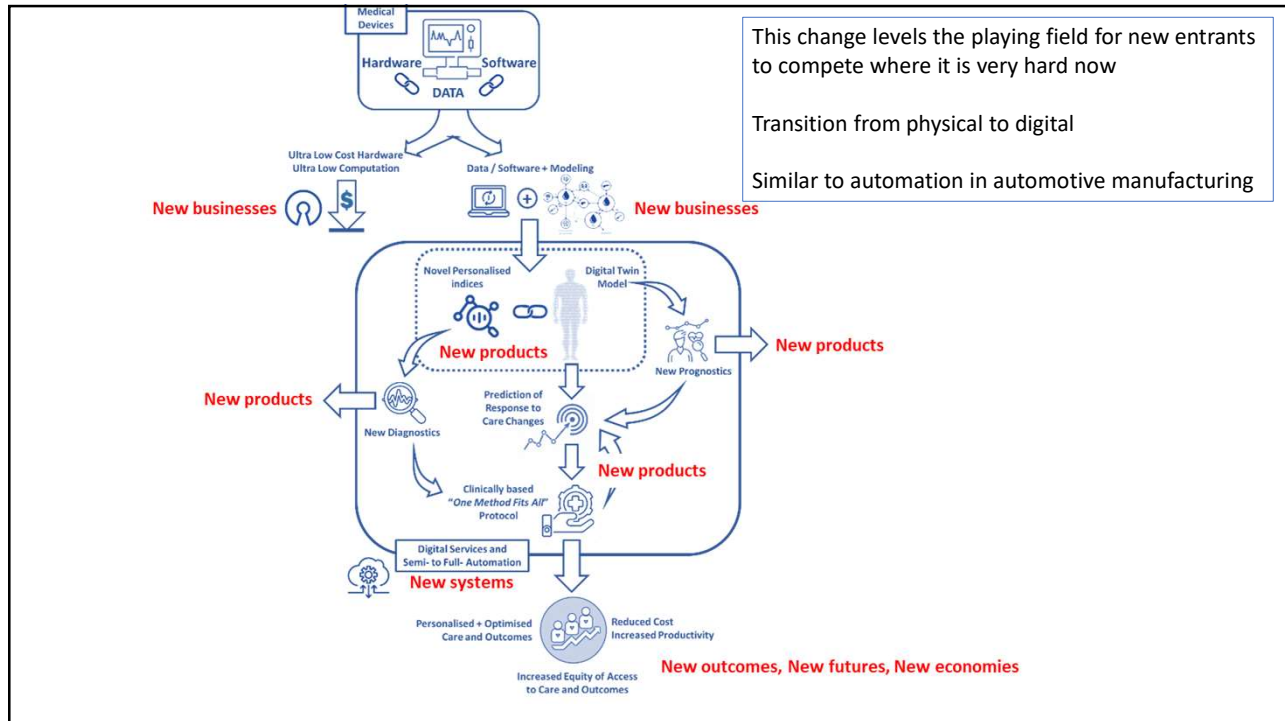
The business model is not fit for purpose. How can we fix this??



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It's time to revolutionise care and transform devices and systems!

Yesterday Today Future

Thank You

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