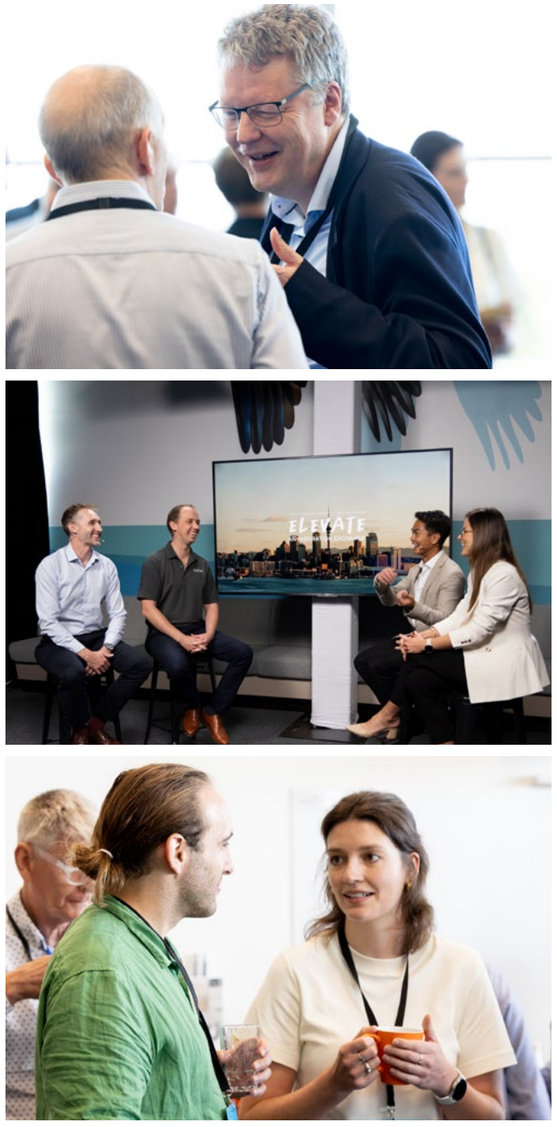
HIGHLIGHTS & KEY TAKEAWAYS
FROM

ELEVATE

NRSnet INAUGURAL MEETING | AUCKLAND 2023

NRSnet
Noninvasive Respiratory Support Network

CONTENTS



INTRODUCTION

In this summary of the first Noninvasive Respiratory Support Network meeting, held in Auckland, New Zealand, in late February to early March 2023, we present the meeting presentations and key takeaways.

This report includes a summary of the two educational days on-site at Fisher & Paykel Healthcare, exploring current and future research for Noninvasive Respiratory Support (NRS).

It covers current evidence and guidelines, clinical practice, the latest innovation from Fisher & Paykel, future research direction, knowledge translation methods, and exploratory workshops facilitated by international experts in the field of NRS.

Current NRS

Current body of evidence, current clinical practice and NRS physiology & technology

Prof. Laurent Brochard

NRS: Overview, current evidence, and practice
– Prof. Laurent Brochard

Prof. Laurent Brochard opened the meeting with a keynote on NRS therapies. He summarized the physiology of different types of respiratory failure and explained why some therapies would be more appropriate than others based on indications of certainties and levels of harm.

Munshi, Mancebo, Brochard NEJM 2022 [1]

He presented an overview of the physiology of noninvasive ventilation (NIV) and COPD (Chronic Obstructive Pulmonary Disease) patients with hypercapnic respiratory failure. He claimed that NIV was successful in treating COPD patients, given its mechanisms to increase tidal volume. However, despite the strong evidence for NIV therapy in decreasing intubation rates for patients with COPD, there was still many patient readmissions. Murphy et al, 2007 [2] had shown the potential benefit of domiciliary NIV in reducing readmission rates and mortality for acute COPD patients.

Prof. Brochard then went on to explain that there was very little data for obese patients; however, current evidence showed that NIV worked extremely well. The therapy also treated Cardiogenic pulmonary edema [3] and post-operative respiratory failure to deliver continuous positive pressure [4]. For hypoxemic respiratory failure, there was evidence that NIV might be beneficial if it succeeded; however, if NIV failed, it was likely to cause harm [5].

Insights from the LUNG SAFE study [6] showed a very high rate of failure for NIV use. Prof. Brochard overall warned the audience that there were risks with NIV for this type of population and therefore could not give a strong recommendation for its use.

New therapies such as Nasal High Flow (NHF) were introduced by Prof. Brochard as a potential alternative to reduce intubation for Hypoxemic respiratory failure given its advantages in reducing work of breathing, increasing deadspace washout [7], increasing expiratory resistance [8], and consequently decreased respiratory rate. He emphasized that the relationship between expiratory resistance, respiratory rate, and deadspace for NHF use was prominent to understand. Studying the relationship could provide the indication and type of flow used, which could contrast with hypoxemic respiratory failure.

Over the pandemic, sufficient evidence had been produced to prove that NHF use could also be beneficial for Covid-19 [9, 10,11]. Alternatively, the use of helmet NIV in a few studies provided a significantly lower intubation rate for Covid-19 patients in comparison to NHF [12], proving that there was much more to understand about the therapy and its potential applications.

The last point added by Prof. Brochard was how there needed to be a better focus on monitoring patients on NRS therapies by measuring work of breathing. Clinicians might have found it useful by monitoring tidal change in esophageal pressure to predict the timing of intubation for NIV patients with AHRF [13]. However, this might not have been the most practical approach for monitoring larger populations, so he declared a call to action on understanding more practical and better techniques for monitoring patients in the future.

Current body of Evidence
– Prof. Begum Ergan & Dr. Simon Oczkowski

As a starting point for the Current Body of Evidence, Prof. Begum Ergan and Dr. Simon Oczkowski referenced a summary of guidelines, their level of evidence, recommendations, and justifications:

- The ERS/ATS NIV guidelines for ARF [14]
- ESICM clinical practice guidelines on NHF for adults [15]
- ERS clinical practice guideline on NHF for adults [16].

Prof. Ergan then covered the ERS recommendations for both Peri-intubation preoxygenation and AHRF (including Covid-19), whereas Dr. Oczkowski reviewed the current evidence for post-operative patients, non-surgical patients after extubation, and acute hypercapnic respiratory failure. They reflected on the judgments of the panel, what they recommended, and further commentary on why they decided to base their recommendations.

The panel discussed the use of Non-Invasive Ventilation (NIV) and other Non-Invasive Respiratory Support (NRS) therapies in treating patients with respiratory conditions. The themes include medical treatment, patient care, and decision-making in a clinical setting.

Prof. Begum Ergan & Dr. Simon Oczkowski during the panel discussion

Current Clinical Practice
– Prof. Jean Damien Ricard

Prof. Ricard bridged the next session from current clinical evidence to how clinicians applied NRS therapies in the present day.

He aimed to create an interactive session involving vignettes, pro-con debates, and narratives that would engage the clinical audience to discuss and share ideas.

Primary Respiratory Support for Medical Patients
– Prof. Armand Mekontso Dessap

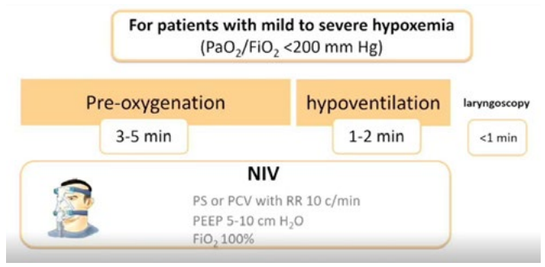
For the first part of the session, Prof. Armand Mekontso Dessap took to the stage and delivered two interactive vignettes on primary respiratory support for medical patients.

As an example, his first case study involved an 80-year-old woman with a renal graft and completely autonomous, who presented at the ED for dyspnea and was later diagnosed in the ward with pneumocystis pneumonia on BAL.
She was eventually transferred to the ICU where Armand and his colleagues navigated ways to treat her respiratory distress by using NHF then intubation. Unfortunately, by day 7, she had passed away from continued deterioration, complications, and her existing infections. He then encouraged the audience to discuss whether he chose the right initial support for the patient. Agreeance and lively discussions were had.

Prof. Armand Mekontso Dessap

Pre-escalation Debate
– Prof. Jean Pierre Frat & Prof. Jean Damien Ricard

Continuing to the next application, Prof. Ricard introduced a pro-con debate where Prof. Jean Pierre Frat defended the use of NIV for pre-escalation support, and Prof. Jean Damien Ricard represented NHF as a therapy of first choice.
Prof. Frat argued that NIV could be considered as a first-choice therapy for intubation because it would have a high FiO_2 with a maximum of 100% and it favored alveolar recruitment, increasing PaO_2. He referenced previous literature showing that NIV was the most efficient therapy for oxygenation compared to NHF and COT [22] and it had similarities with gas exchange compared to Invasive ventilation [23].
He further explained the efficiency of NIV during intubation for ARF in comparison to bag mask ventilation (BMV) from a trial that showed higher SpO_2 minimum and less frequent hypoxemia episodes with NIV [24].
Although many had favored NHF for apnoeic oxygenation during intubation, it was stressed that there had been trials where NHF and BMV had no significant difference during the apnea stage [25].
Prof. Frat also drew from literature explaining an approach where preoxygenation was optimized by using positive pressure [26] and from his own study, FLORALI 2, that there were less frequent episodes of severe hypoxemia with NIV than NHF [27]. After he reflected on potential causes of NHF Failure, he concluded that NIV would be the first choice over NHF during pre-escalation.



To defend NHF as the first choice for pre-escalation support, Prof. Ricard joined the stage. He started his argument with a summary of the determinants of hazards during intubation. He also stated that the patient's status [28], desaturation during the procedure, and whether one device could be used for preoxygenation and apnoeic oxygenation all mattered more than the device chosen.

Prof. Ricard implied that there needed to be an emphasis on looking at the immediate implications and long-term outcomes of intubation. This point was supported by trials that presented no differences between the devices during preoxygenation in regards to immediate serious adverse events and long-term ICU outcomes [27, 29, 30, 31].
Overall, he questioned whether it would be worth swapping NHF with a new face mask for intubation for a few minutes if studies proved

Prof. Jean Damien Ricard & Prof. Jean Pierre Frat defending NHF or NIV as first choice for Pre-escalation

there were no immediate or long-term outcomes, especially when a clinician could use the ROX index to help prevent NHF failure [1].
From a practical standpoint, he concluded if a patient initially received NHF then they should continue NHF, whereas if a patient initially received NIV for preoxygenation then the goal would be to maintain NIV with consideration to adding NHF for most severe patients to enhance apnoeic oxygenation.

The themes discussed in the Q&A included the importance of clinician skills in using NIV, the higher acceptability and ease of use of NHF, and the need for personalized care in medical treatment.

De-escalation Debate
– Dr. Salvatore Maggiore & Dr. Gonzalo Hernandez

Prof. Maggiore was welcomed on stage to start off the next debate on post-extubation support to defend NHF as the first choice therapy.

Before initiating the presentation, he asked the audience on what would be important for clinicians when deciding on a technique for their patients. A word cloud was formed with the below responses, and this was summarized as **safety, effectiveness, efficiency, and cost-effectiveness**.

Prof. Maggiore proposed that NHF was safer than NIV given that there were only mild NHF complications and no severe complications reported [20, 32]. He further determined that NHF showed effectiveness during weaning and post-extubation of ARF as he drew on from the physiological benefits such as increased dead space, reduced respiratory rate, increased inspiratory effort, comfort, and PEEP. He noted a few studies and guidelines that compared NHF's effectiveness, benefits and non-inferiority to NIV [15, 21, 33, 34]. He then presented that the use of NHF during post-extubation was efficient and cost-effective given that NIV is claimed to be a difficult technique.

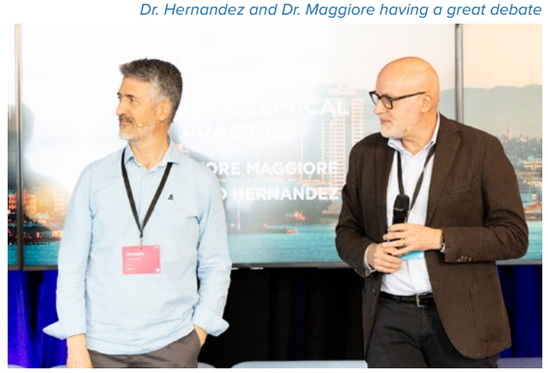
For Prof. Maggiore, NHF had ease of use, reduced workload, and a possible reduction of costs equivalent to hospital stay and ICU stay. Despite there being only one meta-analysis published on post-extubation and within it only two studies, both studies suggested that ICU and hospital stays decreased with the use of NHF compared to NIV [35].

Dr. Gonzalo Hernandez admitted that it was impossible to defend NIV as first-line therapy after extubation in all patients. Instead, he presented on NIV-based strategies and which patients should be receiving continued NIV as a de-escalation plan.

Hernandez explained the main objective was to understand how NIV could **improve performance, tolerance, and reduce adverse effects** for the patient. Firstly, he identified which patients were excluded from NIV-based strategies to then present the type of patients that would benefit from NIV post extubation [33, 36, 37, 38].
Studies showed that the more risk factors a patient would have, e.g., obesity or hypercapnia, the more likely they were to have a better response to NIV than NHF [36, 39].

Hernandez preferred the use of a 3-risk-factor approach to predict how to manage patients on NIV, and that would help improve the performance of NIV for patients combined with NHF [36].
Some study protocol designs were also noted to influence NIV-based strategies. Based on a few studies, Dr. Hernandez wanted

Dr. Hernandez and Dr. Maggiore having a great debate



to make a point that prolonging preventative therapy in a study was treating post-extubation failure. If a clinician were to escalate, it resulted in improving the treatment for more severe post-extubation failure [33, 37, 38].

In the case of improving a strategy and obtaining a significant reduction for reintubation, some studies mentioned a fixed period of time for prevention therapy with NIV use [34, 39, 40]. Different settings such as combined NHF, an optimized interface or humidified NIV could also improve patient outcomes and reduce reintubation [34, 36, 40].

To finish, Dr. Hernandez pointed out that the definition for reintubation needed to be adapted depending on what was selected and whether the study included a preventative, prolonged or escalation approach. Dr. Hernandez was hopeful that there would be more trials considering mortality as an outcome in the future.

The themes discussed in the Q&A included the importance of clinician skills in using NIV, the higher acceptability and ease of use of NHF, and the need for personalized care in medical treatment.

Weaning from NRS: NIV and NRS
– Prof. Lara Pisani

Prof. Lara Pisani presented on NRS weaning strategies for NIV and NHF. She stated that both NIV and NHF strategies for weaning were not very well defined and the techniques were unknown. Evidence and practice made it clear when NRS weaning started; however, not when they were stopped. Most weaning studies and guidelines concluded that there would be increased risks of complications, patient discomfort, and costs if weaning was delayed [41,42, 43].

Prof. Pisani explained that within a clinical practice setting, when to assess a patient's readiness for weaning depended on the level of experience of their clinician and whether they also used existing clinical criteria for weaning [44].
There were three different strategies presented for weaning ranging from:

- Abrupt NIV discontinuation
- A gradual decrease in ventilator support and duration of NIV
- A gradual decrease in the duration of NIV

Prof. Pisani reviewed several recent studies on COPD patients with AHRF against the 3 different protocols to determine which was better. No differences were found except for a shorter ICU stay between direct discontinuation and a Nocturnal NIV protocol [45, 46,47].
From most of the literature she reviewed amongst abrupt discontinuation, protocolized and non protocolized, there were overall no significant differences or relevance to NIV weaning strategies [48, 49 50, 51] apart from one study that indicated a reduction of NIV duration and ICU stay [52].

Prof. Pisani also noted NIV weaning strategies differed based on the underlying aetiology of ARF and the severity of the disease [53, 54]. Prof. Pisani then discussed how NHF was often paired in combination with NIV for weaning strategies. Although there were studies that showed no difference in total time comparing NHF and COT during breaks off NIV for ARF [55], one physiological study showed success in unchanged diaphragm displacement and improved patient comfort [56]. Other evidence showed that NHF was non-inferior to NIV during an initial ventilatory trial for COPD exacerbation [57].

Prof. Pisani added that technical advancements such as the new asymmetric cannula [58], improved the outcome of weaning with NHF by increasing deadspace clearance and positive airway pressure. She wanted the audience to reconsider the criteria for readiness to wean earlier [58], and ultimately that NHF was included in the criteria. Based on this, she proposed a new definition for weaning success in critically ill patients should include the absence of NIV (CPAP & Bi-level) and NHF 48 hours from extubation.

Lastly, Prof. Pisani understood that there were promising trials proposed and ongoing for NHF weaning in the future. She was hopeful that future results of the SLOWH trial would improve clinical practice on how patients were being weaned off NHF through either initial flow reduction, initial reduction of FiO_2 or a combined reduction [59].

The themes discussed with the audience included weaning COPD patients from NRS therapies, adherence to weaning programs, the potential benefits of NHF weaning, and the need for further studies to investigate the effectiveness of different therapies.

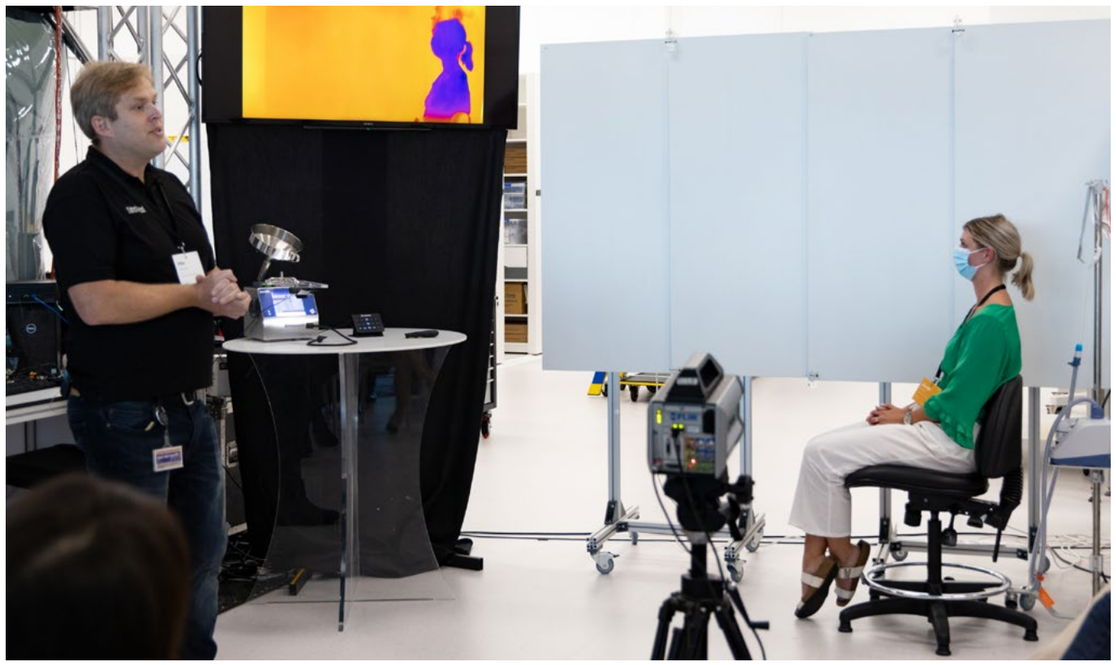
Prof. Pisani during her Weaning from NRS presentation

Current Clinical Practice Panel

The themes discussed in the panel included comparing NHF and NIV as palliative tools, conducting studies to assess their effectiveness, considering patient comfort and preferences, and personalization versus standardization in treatment.

Current body of evidence and clinical practice panel - (from left to right) Prof. Armand Mekontso Dessap, Prof. Begum Ergan, Prof. Jean Damien Ricard, Prof. Lara Pisani, Dr Simon Oczkowski, Dr Gonzalo Hernandez, Dr Salvatore Maggiore and Prof. Jean Pierre Frat

Dr. Stanislav Tatkov discussing ideas with Prof Kazuko Yamamoto



The Aerosols team presenting on their work

NRS physiology & technology
– Fisher & Paykel Healthcare

For the next segment of the day, Fisher & Paykel showcased their latest innovations in technology, research, and products, featuring the relationships between the engineers and motivated clinicians who worked together to solve clinical problems and improve patient outcomes.

The session introduced the journey of Dr. Matt Spence and his idea of humidifying air for mechanically ventilated patients with his partnership with Alf Melville, a designer from Fisher & Paykel.
It was this collaboration that started the progression and importance of Fisher & Paykel's principles around sustaining relationships to address unarticulated clinical needs.

Each presentation resonated with the company's origin story on humidification and acknowledged the importance of continued relationships and collaboration to drive the next innovation.

Two memorable presentations from this session included **Airborne transmission of disease – visualizing the invisible and Asymmetrical nasal high flow**.

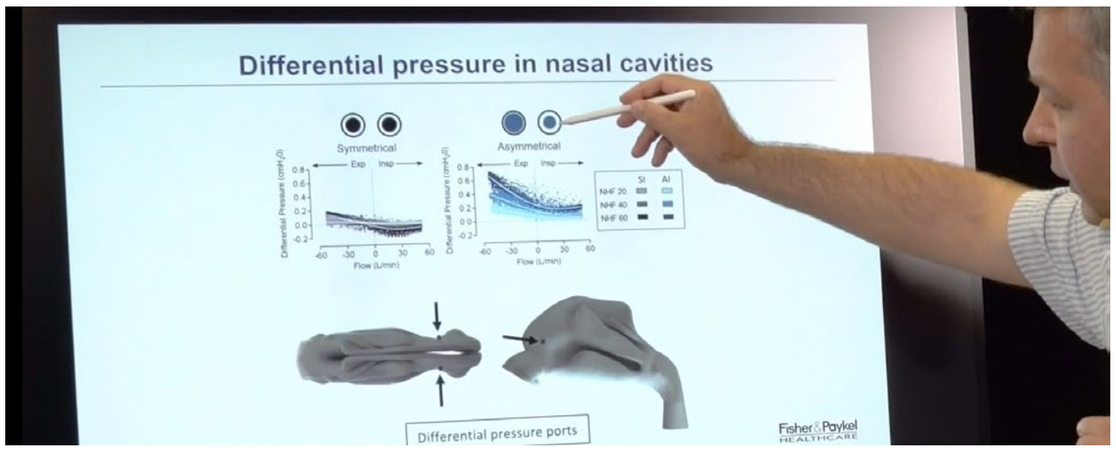
In the Airborne transmission of disease presentation by the Aerosols team and Dr. David Rapoport, the facilitators discussed their latest research on aerosol transmission.
They expanded on how their collaboration with Dr. Rapoport supported the depth of research in exploring the visualization of the plume created by patients, understanding how to measure respiratory bio-aerosols and the importance of protecting the healthcare workforce for future outbreaks.

Newspaper extract circa 1918, Influenza pandemic.

To find out more, the team created a website (https://www.fphcare.com/nz/hospital/adult-respiratory/optiflow/flow-matters/nhf-and-aerosols/) as a way to empower clinicians to make their own pragmatic decisions on how to avoid infectious plumes in the future.

Dr. Stanislav Tatkov and Kevin O'Donnell, both colleagues from Fisher & Paykel, introduced a new product called Duet, an asymmetric nasal cannula interface.
The duo provided an overview of their purpose in creating a new cannula for delivering nasal high flow and aimed to optimize the efficacy of the therapy.
Dr. Tatkov then guided the audience on his latest research on the physiology and mechanics of asymmetric prongs to improve deadspace clearance and positive airway pressure.
Since the presentation, these results have now been published in a journal article and video [58]. These can be accessed via the Journal of Applied Physiology and the American Physiological Society YouTube Channel.

Dr. Stanislav Tatkov presenting on the physiology and mechanisms of Duet.



Future of NRS

Future research, knowledge translation, exploratory workshops, and meta-panel

Keynote, day 2:

NHF in Acute Hypoxemic Respiratory Failure perspectives and considerations

– Prof. Massimo Antonelli

Prof. Massimo Antonelli began the second day by providing a brief overview of what had been done in NRS and possibilities for future research. He started the presentation by introducing how NHF had been utilized for mild ARDS (Acute Respiratory Distress Syndrome) patients and the benefits attributable to the therapy [60]. An issue highlighted was that spontaneous breathing increased the alveolar pendelluft, and it was still unknown whether NHF or COT could reduce the phenomena or whether positioning could impact patients. To support this, he highlighted a study that showed how helmet CPAP/NIV efficiently reduced the pendelluft compared to NHF. In the same study, the quasi-static compliance remained unchanged due to the differences in interfaces, highlighting the need for personalisation [61].

Prof. Antonelli then discussed the ESICM practice guideline, which outlined a strong recommendation for the use of NHF on hypoxemic respiratory failure patients [15]. However, in SOHO-COVID, HEVINOT and HELMET-COVID studies, NHF either did not show significant differences in mortality and median respiratory support when compared to other NRS therapies [62, 63, 64]. There were only differences in cumulative incidence of intubation amongst the therapies.

He then explored the immediate benefits of prone and awake positioning with NHF in AHRF patients. Aside from all the physiological benefits associated with prone positioning, he reported a meta-trial that improved ROX, respiratory rate, and SpO2/FiO2 for NHF patients in prone positioning compared to NHF patients. Longer-term outcomes were intubation, weaning from NHF but also not mortality [65].

In the last parts of his presentation, Massimo summarized the application of NHF in infant care, palliative care, and procedural trials such as endoscopy and bronchoscopy [66, 67, 68, 69]. All studies showed promising and beneficial results despite the endoscopy meta-analysis showing no difference in intubation but favoring the use of NHF regardless [68].

For a closing, Prof. Massimo Antonelli suggested that NHF could be used for mild to moderate ARDs and that the pandemic showed its use outside of the ICU. He also proposed that there needed to be more studies on combined NHF and NIV and that there were potential gaps of knowledge in physiology, the pediatric area, and palliative care for NHF.

Prof. Massimo Antonelli presenting online to a live audience

Future Research Direction: Medicine, Maths and Mechanics

– Prof. Nicholas Hart

Prof. Nick Hart took to the stage and outlined the next set of presentations on Future Research Direction – Medicine, Maths and Mechanics. He acknowledged naming the session Medicine, Maths and Mechanics as a testament to how clinical experts should work alongside the advancement of technology and hopefully match the momentum of the previous NRS technology and physiology session with clinical application and practice.

Prof. Nicholas Hart

Elective Care

– Prof. Anil Patel

Prof. Anil Patel shared the progression of ventilators he used from his early days to what could be in the future of elective care. In the next evolution of ventilators, industry have started creating machines that incorporated a NHF device. Prof. Patel believed this was where technology was advancing. Prof. Patel shared that an anesthetist's main objective was to provide balanced anesthesia. Following this, he engaged the audience to consider a new additional goal for elective care, **balanced ventilation**.

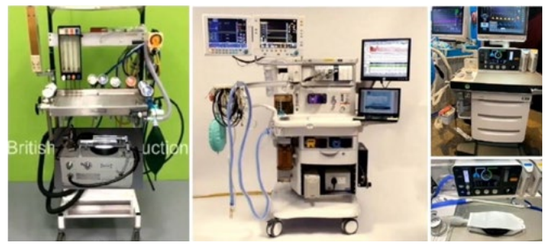
From the last 60 years since the application of positive pressure ventilation, Prof. Patel had analyzed that most research focused on the inspiratory phase of the cycle. The expiratory phase had essentially been forgotten as a passive phase. He stressed to the audience the need to further explore the expiratory phase.

In response to his call to action, he provided a range of solutions to the audience. He briefly introduced flow-controlled ventilation (FCV), a new technology mode in ventilators to control flow during active expiration. Another solution proposed was Negative Pressure Ventilation (NPV), which was used in the past but Prof. Patel established a charity-led team, Exovent that focused on creating a negative pressure support device for patients [70]. Currently, a prototype had been developed and tested on patients reproducing physiology and similar outcomes compared to the Iron lung.

Rather than in-series ventilation techniques where patients would be on one ventilatory therapy after another, Prof. Patel argued that clinicians should consider in-parallel ventilatory support techniques, which can be beneficial for patients with difficult airways to intubate. NHF, high-frequency jet ventilation, and low-frequency jet ventilation could all be used in tandem to maintain saturations [71]. Additionally, an in-parallel ventilatory technique with NHF, flow-controlled ventilation, and a tri-tube could also be successful in treating patients with obstructive tumors that limited intubation. Prof. Patel also promoted the potential use of both NHF and NPV where patients could receive benefits from each ventilatory support simultaneously.

Prof. Anil Patel, centre, chats with colleagues

The progression of ventilators Anil Patel used from his early days



To conclude, Prof. Patel highlighted that all pairings matched NHF synergistically. The challenge going forward would be to explore which patients and settings would benefit from all the solutions provided and understand whether AI would advance enough to predict personalised patient care.

Early intervention in trials of acutely ill patients
– Dr. Jonathan Casey

Dr. Casey outlined the main points he wanted to discuss with the audience. He focused on the importance of enrolling critically ill patients early (before ICU admission), addressing how enrolling these patients early could be feasible and proposals for future NHF trials.

First, he proposed that early intervention or prevention may be more effective than late-stage interventions. He reiterated that many treatments in critical illness were time sensitive however argued to the audience that time to intervene with supportive care therapies has been missed and should be considered.

Although outside of the NRS scope, Dr. Casey used his Isotonic fluids trial as an example to support his position on pre-ICU patient enrolment. Dr. Casey and the Vanderbilt team ran the SMART trial to evaluate whether the composition of saline or balanced crystalloid fluid impacted patient outcomes. During the trial, each patient in ICU was assigned a fluid which alternated every month. Towards the last 15 months of the trial, the research team expanded to ED and the OR to include pre-ICU patients. As a result of the trial, balanced crystalloids significantly reduced the incidence of persistent renal dysfunction and 30-day in-hospital mortality [72].

After the trial, secondary analyses reported that there were more positive impacts for patients who started the trial in ED over the ICU [73]. A similar secondary analysis from the BaSICs trial published nearly identical results establishing the benefit to including pre-ICU patients in trials [74].

Dr. Jonathan Casey discusses proposals for future NHF trials

Dr. Jonathan Casey with Justin Callahan from Fisher & Paykel Healthcare

The next point Dr. Casey wanted the audience to reflect on was if it were feasible to enroll patients early in ED. He acknowledged that there was difficulty enrolling patients admitted to the ED due to a range of barriers from brief windows of time between presentation and initiation of interventions to other reasons where some patients could not consent with their surrogates being absent. There were also significant trial design-related issues such as the heterogeneity of a study population and the requirement for a large cohort.

Dr. Casey introduced his Pragmatic Critical Care Research group which aimed to address these issues. The network was made of ED and ICUs at 20 centres across the US where they collaborated to produce trials together across the care continuum. To address the barriers to enrolling early in ED, the team utilised their knowledge and experience in the practice setting to adapt to make early enrolment feasible such as leveraging the electronic health record.

Concerning NHF, Dr. Casey reviewed all major multicentre trials and found that most started their studies within the ICU with less than 300 patients being enrolled in an ED setting. He proposed future trials should start their interventions early in the phase of illness, continue the intervention through ICU admission, enroll a large sample size to evaluate the effectiveness and enroll a broad generalizable population with eligibility criteria that could be applied to care after the trials.

Acute Care
– Prof. Paolo Navalesi

Prof. Paolo Navalesi believed the future direction of building NRS research for acute care should focus more on mechanisms and personalisation. He suggested evidence, where the effects of humidification levels influenced the production of cytokines over time [75] or studies that improved physiological benefits by advancing technology like Duet, should be progressed on [58]. He referred back to the trial comparing helmet NIV, helmet CPAP, and NHF with their respective physiological effects. Despite the study results, Paolo emphasized through the study's Pendelluft, dynamic lung strain, and Pressure time product graphs that there was a broad variability of the behaviour from some patients against the varied NRS therapy [61].

Next, Prof. Navalesi compared the CT scans, pictured below, from published case studies [76] and patient files. He claimed that for the first patient, NHF would not be applied as pressure would not be continuous during a patient's inspiration phase. Prof. Navalesi stressed that continuous pressure is required on these types of patients, otherwise during inspiration the positive effect is lost.

In comparison, the second patient had worse gas exchange and Prof. Navalesi recommended that applying continuous pressure for the patient would not generate any benefit. He believed that the ventilation-perfusion mismatch was the main contributor to the patient's respiratory failure and that they would benefit the most from NHF compared to other NRS therapies.

Over the pandemic, Prof. Navalesi originally used a flowchart he designed with Prof. Alexander De Moule [77] which illustrated an escalation of various NRS therapies. However, he wondered whether the application of combined CPAP and NHF through a helmet could have been a better approach for the same patients. By doing so, he reasoned that the inspiratory CO2 decreased, and the amount of extra pressure generated from NHF inside the helmet lowered

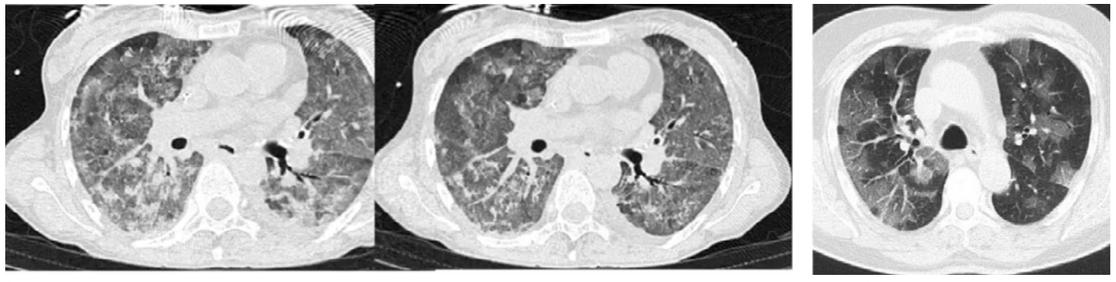
Prof. Paolo Navalesi

compared to standard NHF [78]. Instead of expiratory positive pressure benefits, Paolo believed that when CPAP and NHF were mixed, all the benefits attributed to full CPAP therapy.

Further to his presentation, Paolo presented a study that investigated redefining the Berlin definition of ARDs to include NHF [79]. He reported that the authors had difficulty broadening the ARDS definition as the level of severity would need to change for NIV. Paolo proposed that this type of research should also be progressed in the future.

Another proposition for future research was the potential of AI and big data [80]. Paolo reported that he is currently handling hospital data to generate a range of risks that would influence decision-making and other hospital applications. He argued that the use of algorithms may be a new approach to determining the phenotypes of patients who are likely to respond better to one form of treatment over the other [81].

Case studies of two patients discussed in Prof. Paolo Navalesi's presentation.



Patient 1 BEFORE AFTER Patient 2

Post-acute care
– Dr. Gerard Criner

Dr. Gerard Criner concentrated on patients with COPD at home for his presentation. Across the population of COPD at-home patients, Dr. Criner identified that patients would likely be older, fragile, severely symptomatic, predisposed to exacerbations of diseases, suffer from dyspnoea, cough, and sputum production with about 30% of the population suffered from anxiety or depression. Out of all the symptoms, a study reported dyspnoea as the most prominent symptom for COPD patients to occur during the day. Patients with more severe airflow obstruction would experience these symptoms 90% of the time [82].

Dr. Criner further argued that patients also experienced a multitude of comorbidities. Previous literature indiscated 91% of COPD patients had one comorbidity while 80% of patients had three or more comorbid conditions [83]. Overall, Dr. Criner stressed that these patients were a high-needs group based on their regular symptoms, comorbid conditions and overall disease, disrupting their daily living.

When hospitalised, the same patients had a further burden of disease and decreased quality of life. Dr. Criner argued that exposure to respiratory viruses and changes to the environment could lead to increased inflammation and mucus, generating air trapping for patients [84]. He proposed whether GOLD 3 or 4 patients with optimum treatment could also benefit from warm and humidified air to provide anti-inflammatory effects, slow down the respiratory rate, and decrease air trapping [85].

To understand what type of therapy should be designed for patients, Dr. Criner reviewed a meta-analysis that indicated how flow rates varied when a patient rested compared to when they exercised [86]. General exercise for a COPD patient at home would include walking to their kitchen, bathroom, and living quarters. Given the multitude of devices, Dr. Criner thought it would be impractical for them to switch over to another device and discontinue therapy when they walked around their home, so he suggested patients needed a machine with auto server sensor capabilities to detect a patients changing demand. He idealised an integrated machine that could facilitate sleep, provide medicines, and improve portability all at the same time while delivering NRS therapy.

Dr. Criner shared his thoughts about how the advancement of smart technology could potentially pair with early detection of ECOPD given that a study reported the relationship between early detection and shorter recovery period with improved clinical conditions for patients [87]. He reasoned that ‘exacerbation’ needed to be redefined with objective data to understand the signs of early detection. Given

Dr. Gerard Criner

that initiation points of exacerbation varied globally, and it depended on where patients lived based on the convenience of practice, Dr. Criner and colleagues created the Rome proposal.

The proposal classified measurable physiological changes of a patient that could be measured by tech against the type of severity of ECOPD to determine the onset of exacerbation [88]. He used the example of wearables to showcase the potential of tech collecting real-time objective data as a more seamless way of monitoring and diagnosing patients.

Overall, he concluded that new technology should be developed for the patient with it being smaller, easier to clean, use, and portable for rest and exercise. He also noted that it should be integrated with real-time wearable data, ease of use for delivery of other respiratory medicine, and more comfortable for patients.

Combined NRS therapies after extubation
– Prof. Arnaud Thille

As Prof. Arnaud Thille introduced his topic on combined NRS therapies after extubation, he presented the rates of reintubation and mortality for patients with ARDS then discussed the ERS NHF guidelines for post-extubation failure [89, 16]. Although there were no specific guidelines that recommended the use of combined therapies, the HIGH-WEAN study compared the use of combined NHF with alternating NIV to NHF alone on 650 high-risk extubation failure patients across. The trial resulted in a significant decrease in reintubation for those patients treated with NHF and NIV compared to those who had NHF alone. After 72 hours, the rate of reintubation for patients with combined therapy was lower than 10% after extubation [36].

To highlight his point on where the future should go for medicine, Prof. Thille proposed a potential RCT to guide the management of post-extubation failure. Previous trials comparing COT and NIV established the relationship between delayed effects of NIV and the risk of death [90]. The same evidence was incorporated in the 2017 ERS/ATS guidelines as a recommendation [14], however, Prof. Thille further shared that the recommendation did not outline the consequences of delayed reintubation with rescue NIV and that NHF had not been considered as an intervention in the setting.

Prof. Thille followed up with a HIGH-WEAN posthoc analysis to assess the management of either NHF with NIV or with NHF alone for patients with post-extubation respiratory failure. The results contrasted between a decreased risk of mortality and patients treated with NIV [91]. These results prompted Prof. Thille and his team to plan the Ventilo study, which aimed to compare alternating NHF with NIV and NHF alone for 670 patients with post-extubation respiratory failure (clinicaltrials.gov; NCT05686850).

Prof. Thille then considered whether the use of the ROX index could help guide decision making for reintubation in the future. He mentioned that he planned to use the ROX in his Ventilo study and HIGH-WEAN post hoc analysis. Initial results of the post hoc analysis reported how ROX was not predictive before extubation but very predictive an hour after extubation. These results will be confirmed and published soon however Prof. Thille proposed that in patients with AHRF, a ROX index threshold could be considered to help clinicians decide on reintubation [92].

For the future, Prof. Thille proposed a solution for engineers to integrate an automatic display of the ROX index on either monitoring screens or the NHF device. Each device could have a vital alarm to assist in reintubation decision-making for clinicians.

Prof. Arnaud Thille

Regarding the future of mechanics, Prof. Thille suggested that patient effort could guide the most adequate NRS therapy based on previous evidence where pressure could be counterbalanced by the patient and therapy [93].

In a further physiological study, the investigators reported that there was an inverse relationship between patient effort under NHF and patient effort under helmet NIV [94]. Prof. Thille advocated that these studies help match adequate NRS therapy and may be the extent of personalisation for patients. He concluded by showcasing a new physiological study his team is undergoing to assess tidal volumes and patient effort after extubation. He hoped to build a continuous partnerships with engineers to advance continuous monitoring of patient effort through simplified measures.

Future Research Direction:
Medicine, Maths and Mechanics Panel

The themes discussed in the panel included using big data and AI tools to strengthen recommendations and achieve personalized medicine, clarifying conditional recommendations, resetting the bar in certain areas, considering patient care and comfort, adjusting for heterogeneity in treatment effects, and the importance of global availability.

Knowledge Translation Methods
– Dr. Roman Jaeschke

After the break, Dr. Roman Jaeschke facilitated the next session on Knowledge Translation Methods and announced his McMaster colleagues Dr. Simon Oczkowski and Prof. Gordon Guyatt who were presenting on basics of meta-analysis, living, prospective and network meta-analysis and Trustworthy Clinical Practice guidelines.

Dr. Roman Jaeschke

Meta-analysis and its variations
– Dr. Simon Oczkowski

Dr. Simon Oczkowski re-joined the stage and provided a brief overview of the differences between narrative reviews, scoping reviews and systematic reviews. He emphasized that systematic reviews were normally completed to address a specific, focused clinical question (PICO) with minimized bias and aim to identify gaps for future research and methodological limitations of the existing literature.

He noted that there were critical appraisal tools like AMSTAR to judge whether a systematic review was trustworthy by checking on the writing of the protocol, the process of searching for literature, assessing the eligibility, data extraction and synthesis [95]. Dr. Oczkowski listed the advanced methods of systematic reviews and mentioned he was going to review three of them; Individual patient data, Prospective and Living.

Dr. Simon Oczkowski

Individual patient data meta-analysis (IPDMA) provided an approach where research could be analysed using individual participant data. The process is similar to a standard meta-analysis but could enable researchers to use the original primary data set allowing for larger sample sizes and analysis non comparable to the published work. This method explored capabilities in analysis such as time to event, new subgroup analyses and power to analyse data. Although there were clear benefits, Dr. Oczkowski reported that IPDMA was time consuming, costly, could lead to authorship issues and there was an inability to include studies without individual participant level data.

To address these challenges, Simon suggested the use of the Prospective meta-analysis method. In contrast to systematic reviews and meta-analyses being retrospective, prospective methods aim to identify studies and cohorts in the meta-analysis before results are known. The method could improve credibility by including hypotheses specified apriori, coordinating prospective inclusion criteria across multiple studies and pre-specifying sub group analyses.

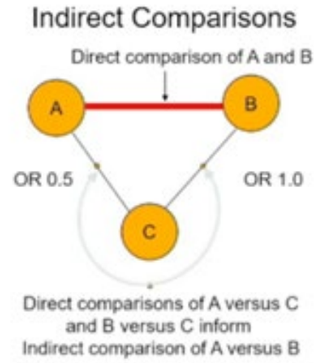
Lastly, Simon made a point that prospective methods could enable further IPDMA. He highlighted a study to the audience that used a prospective meta-analysis approach with its direct outputs of the harmonization of 3 large trials and prospective IPDMA [96].
Compared to the other approaches, living systematic reviews provided continual, active monitoring of the systematic search results. According to Dr. Oczkowski, the approach shortens the time between knowledge generation and translation as every prescribed time period, the researcher is actively monitoring the emerging literature and have it incorporated in their systematic review.

To conclude, Dr. Oczkowski suggested there could be potential to integrate technological innovations such as online platforms with linked data or AI algorithms. Dr. Oczkowski mentioned the Covid NMA, which is an established living Covid systematic review that helped generate large bodies of evidence and trustworthy clinical practice recommendations during Covid such as the WHO clinical practice guidelines during Covid.

Network Meta-analyses and Trustworthy CPGs
– Prof. Gordon Guyatt

Prof. Gordon Guyatt gave an overview on Network meta-analyses (NMA) and trustworthy guidelines for his presentation. He explained that it would be impractical to test and compare many of the existing disease states and their alternative treatments each so NMA provided a way to compare multiple treatments simultaneously through combining their direct and indirect comparisons.

To begin and involve the audience, he introduced an example below to establish the differences between direct comparisons and indirect comparisons. He expanded from the diagram that there would be an established direct comparison between treatments A and B however, a researcher might be able to make indirect inferences based on the A and B comparison to inform interactions with C.

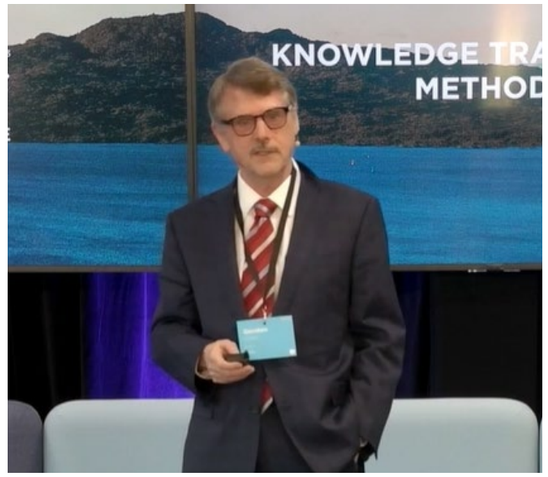


Indirect Comparisons between treatments A, B and C.

Prof. Guyatt forewarned the audience to be more skeptical with using indirect comparisons as proven evidence given that the three treatments may potentially vary in patients, application, the outcome measurements or a risk of bias [97].
To explain the variations of indirect comparisons, he showed a smoking cessation example involving first order, secondary order, and multiple order loop analyses. Indirect estimates can be pooled together for analysis to generate very strong inferences on a comparison between two treatments, especially if there was more evidence than the direct estimate. Gordon summarised his explanation by showing a NMA on fluid resuscitation which pooled indirect estimate results and direct estimates to provide a certainty of evidence [98].

Prof. Guyatt then covered six main standards to generate trustworthy guidelines, which included having an appropriate panel, having a

Prof. Gordon Guyatt



systematic review of best evidence, being explicit with values and preferences, rating the strength of recommendations, having up-to-date evidence, and presenting them optimally for their catered audience. He listed a mix of expertise normally represented in what made a good panel and all experts had the responsibility to advise the guidelines, however he noted that there could be possible conflicts of interests that needed to be openly declared and managed.

According to Prof. Guyatt, every single guideline required a systematic review as a foundation. In terms of systematic reviews approaches, GRADE is a gold standard approach widely endorsed globally. He suggested that all studies in a systematic review should be critiqued against a quality assessment criteria ranking confidence estimates. RCTs could potentially be rated lower if they had all the following biases, imprecisions, and inconsistencies whereas some observational studies could yield higher certainties of evidence. Prof. Guyatt recalled that resuscitating a patient on cardiac arrest was a good example of an intervention with high certainty of evidence based on observation and not on RCTs.

Prof. Guyatt noted that values and preferences came up as an issue on creating trustworthy guidelines as it involved trade-offs such as benefits and harms or burdens and costs. Predominantly in clinical guidelines, patient preferences were overlooked with regard to clinical decision due to burdens and harms. Prof. Guyatt advised that it is important to balance the trade-offs and be well-aware of making judgments based on implicit and unconscious bias. Next, Prof. Guyatt wanted the audience to understand how to rate the strength of recommendations. He believed that equity, costs, feasibility and acceptability should be considered when creating recommendations.

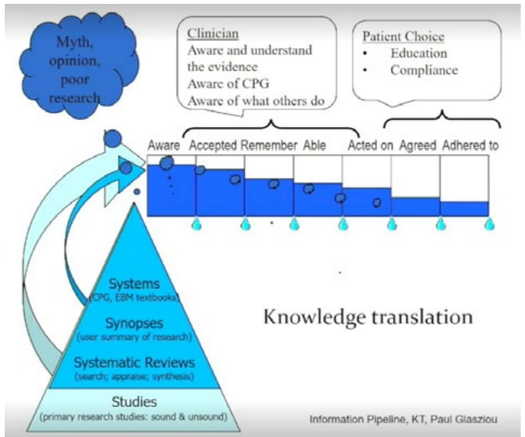
Knowledge Translation Panel

– Dr. Roman Jaeschke, Prof. Gordon Guyatt & Dr. Simon Oczkowski

Before Dr. Roman Jaeschke facilitated the Panel, he summarised where systematic reviews and clinical practice guidelines were positioned on the hierarchy of evidence then emphasized that the most difficult aspect that the audience must be aware of in knowledge translation was the journey of translating evidence for the clinician and patient. He used the leaky pipeline diagram to depict the stages at which knowledge shifts for the clinician to be aware, accept, remember, and practice recommendations while the patient must learn, accept and adhere to the recommended treatment. At any of these stages, Dr. Jaeschke stressed that even the strongest CPG recommendations could drop off.

The themes discussed in the panel included handling reviews such as Cochrane, navigating conflict of interests and industry influence on research outcomes, maintaining editorial independence, building trust in research results, and communicating research results to the public.

Leaky pipeline imagery and the stages of knowledge translation



Diversity Equity and Inclusion Workshop

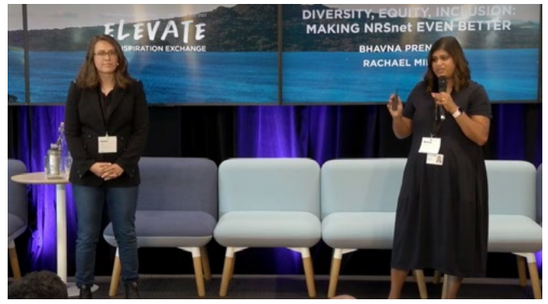
– Bhavna Prentice and Rachel Miller

Bhavna Prentice and Rachel Miller from Fisher & Paykel introduced the workshop. They expressed that as an organisation, Fisher & Paykel are on a Diversity, Equity and Inclusion (DEI) journey with the aim to embed the lens into everything that they do since DEI leads to better patient outcomes. For the purpose of the workshop, they wanted to integrate the network's perspective on DEI to build on future events. Before separating the audience into their groups, Rachel defined DEI and prompted the audience to reflect on the following questions:

- *List different groups and dimensions of diversity that you can think of that are underrepresented in events such as this one?*
- *How can we include these diverse groups in the future of NRSnet?*

After the groups came back from their discussions, two people from each group were invited to report back to the audience on their main points. In summary, the workshop groups listed that events such as NRSnet specifically underrepresented women, junior doctors, and health care professionals from Low to Middle Income countries. They suggested that it could be a goal for the next event to have an attendance portion dedicated to varying levels of gender, clinical experience and geo-economic position.

One group added that the best approach could come from leveraging on the network's connections to invite the most appropriate people from underrepresented groups and explore their barriers to attendance, if any. Ideas on virtual participation paired with a live meeting were proposed to address issues of distance, resource, language barriers and timing.



Rachel Miller, left, and Bhavna Prentice

Participants noted that for a long-term DEI goal, Fisher & Paykel could start a coalition of clinicians, policy makers and other industries to invest resources in LMIC spaces, solidify mentorships for the next generation of doctors and bring about systematic change for gender representation.

The groups also thought that involving patients, caregivers, nurses, respiratory therapists, economists, policy makers, implementation and tech specialists could provide more insight to understanding care outcomes, patient preferences and advancements for NRS. These divisions of professionals might further work with clinicians and engineers to understand how to use AI to streamline data or break down return of investment that these devices could contribute to the health system.

From Left, Prof Ioannis Pantazopoulos, Rachel Miller, Prof John Fraser, Prof Armand Mekontso Dessap, Dr Ivan Pavlov, Dr Jonathan Casey, Dr Gerard Criner, Dr Julie Cook and Bhavna Prentice

Exploratory Workshops

The audience was split into 4 workshop groups paired with two nominated facilitators to explore the adoption of clinical practice guidelines, monitoring and metrics of NRS for patients, the future of NRS therapies and treatment approaches for NRS.
Below is a summary of their report back:

Bridging the gap from Clinical Practice Guidelines publication to adoption
– A/Prof. Natasha Smallwood & Prof. Joan Ramon Masclans

Prof. Joan Ramon Masclans and A/Prof. Natasha Smallwood led their workshop group to investigate why there was poor uptake of CPGs, how it contributed to variations of care and the possible solutions.

The group agreed that the purpose of some guidelines were unclear and weren't always applicable to the complex patients, clinicians often encountered. For the future, they suggested that guidelines should only answer the questions that were prominent and current in clinical settings and distinguish what worked better in specific settings such as ICU or respiratory wards.

It was noted that some doctors preferred to deliver personalised care over following guidelines and if the recommendations were weak, clinicians would be more reluctant to adhere. The facilitators recognised that more evidence would be needed to strengthen the recommendations, so they mentioned the use of adaptive trial designs or a monitoring system to evaluate CPG success. It was also clear to the group that a lot more education and training across the hospital would be needed to accept and adopt guidelines.

Despite international guidelines being verified globally, the source of guidelines from international sources weren't always applicable in local settings and local standards produced by the national health system were mostly upheld over international guidelines. Therefore, the facilitators emphasized that clear institutionalised leadership and engagement across hospitals and governments were needed to enact clinical practice guidelines.

Prof. Joan Ramon Masclans and Associate Prof. Natasha Smallwood

Dr. Domenico Grieco

Dr. Salvatore Maggiore

Understanding what to measure for NRS Patients
– Prof. Salvatore Maggiore & Dr. Domenico Grieco

Prof. Maggiore and Dr. Grieco presented on what their group thought would be the most important parameters and tools for measuring NRS, the future state of monitoring, barriers to overcome and solutions to achieve the future state.

The workshop group identified tools essential in research and clinical practice for monitoring patients. For NHF, the ROX index, SpO2 and Respiratory rate were vital parameters for monitoring patients. Although the ROX was reliable for hypoxemic de novo ARF patients in clinical practice, there was currently no evidence to support its efficiencies in predicting intubation. The use of both SpO2 and respiratory rate in research was evident however it was unclear in clinical practice. For NIV, SpO2, respiratory rate, HACOR score, and Tidal volume were main parameters for measuring patients.

Based on evidence, the HACOR score showed good reliability in predicting intubation and tidal volume helped measure leaks during face mask NIV in clinical practice. The facilitators highlighted PaCO2 and dyspnoea as other possible measures with evidence in research but not in practice. The group also had a discussion on measuring patient preference in terms of tolerance, comfort and attitudes, however Dr. Grieco highlighted there was no standard approach to measure patient preferences.

Regarding the future state of monitoring patients and improving patient preferences, Prof. Maggiore highlighted the importance of how clinicians communicated to their patients as this had a possible impact on patient attitudes. The group indicated the importance of improving inspiratory effort measures in the future as it could help in clinical decision making through diaphragmatic thickening fraction or electric impedance tomography.

In the future, the group were hopeful that a new or existing tool would be able to decide on intubation. Prof. Maggiore referred that the ROX index can predict when to intubate but there is no evidence to suggest that the ROX index is used to intubate.

Lastly, the group imagined that international platform trial data and AI could be extrapolated into algorithms to help clinicians make a diagnosis, identify the severity of the patient, choose the most appropriate treatment strategy and monitor patients overtime.
The group identified that complexities, costs, and knowledge barriers of monitoring were often seen as barriers to progress however to improve the future state of NRS monitoring patients, the group believed that collaboration between clinicians and industry was key.

Prof. Lara Pisani and Prof. Stefano Nava

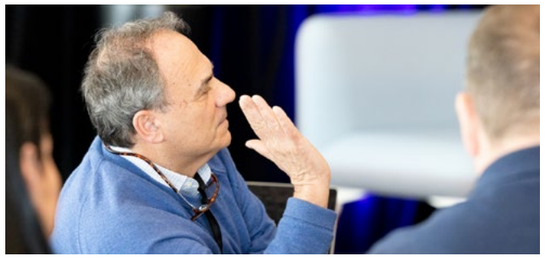
The Future of NRS
– Prof. Stefano Nava & Prof. Lara Pisani

Prof. Nava and Prof. Pisani worked with their group to understand the current utilisation of NRS therapies in acute settings, a reimagining of the perfect NRS therapy and barriers to device uptake. Overall, the group agreed that the current utilisation of NRS therapies were underutilised globally specifically in LMIC and rural regions due to resource limitations. Some countries such as the USA or Greece had fair utilisation of NHF however other therapies such as NIV had low uptake from a lack of education and rapid turnover of educated staff. The group considered reimbursement processes, high oxygen consumption and an absence of utilisation strategies across hospitals were significant for NHF underutilisation.

In terms of re-imagining the perfect NRS device for the future, the group hoped that there could be one device that integrated all 3 functionalities of NHF, NIV and CPAP. The one NRS device could do everything but could also have advanced monitoring metrics to automatically visualise the patient's upper airway anatomy, inspiratory effort, and gas exchange, which would then match the best interface and setting for the patient. Someone from the group wondered if an interface could be designed to generate combined NHF and NIV in the nares.

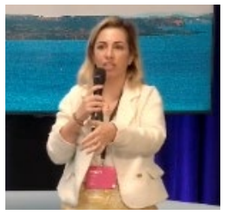
The facilitators acknowledged that their dream device could be engineered in the future however there were possibilities that some clinicians would be hesitant to use the NRS therapies altogether. The group recognised the opportunity to identify and build champion clinicians and patients to promote the usage and education of NRS rather than providing more research to convince clinicians to use the device. Those from the group believed that clinicians role modelling and providing results showing the technique is working will help the adoption of NRS therapies in the future. Prof. Stefano Nava ended the session with his opinion on the importance of needing a balanced team of champion clinicians and late adopters. He indicated that a mix of views would provide diverse perspectives needed to progress the next technology.

Prof. Stefano Nava



Dr. Ivan Pavlov

Treatment approach: Comprehensive vs Targeted
– Dr. Ivan Pavlov & Prof. Begum Ergan



Prof. Begum Ergan

Dr. Ivan Pavlov and Prof. Begum Ergan led their group to discuss whether treatment approaches should be comprehensive or targeted across a population and if targeted, who should be receiving the NRS therapy. Similar to the other workshops, the facilitators guided their group with a framework to go over the current state, the future of where they could go with NRS and the potential barriers withholding them from action. It was shared that NHF usage varied amongst the group based on cultures, hospital set up and resource availability across OR, ED and ward floors. Ivan was surprised there were even significant differences in NHF weaning strategies and when patients were transferred to and from the ICU. The group overall recognised that some hospitals were extremely liberal in the use of NHF across all clinical settings and most diseases, whereas other hospitals were a lot less liberal.

For the future, the group reached an agreement that they would see benefit in using NHF more frequently in more patients and more units. They rationalised that NHF was a safe procedure for all but there were possible risks associated to escalation delays, especially for junior staff who were inexperienced in monitoring their patients. The group reflected that they would need to classify signs of risks and although complicated, they reasoned that they would need to begin with a centralised definition for respiratory distress and work of breathing to ensure the safety of patients. In reference to Dr. Jaeschke's leaky pipe presentation, the group noted the process of dissemination was key in enabling adoption for a more comprehensive approach globally.

Potential barriers to a comprehensive NRS approach were mainly discussed as the availability of resources and how to match the supply of machines with staffing and unit capacity. For the efficacy of a comprehensive approach, there were consistent questions amongst the group in answering how to stop NRS therapy, how to wean NHF, when to wean and should they wean before the ICU. Workshop group 4 thought these questions could be good research topics in the future. They also wondered if NHF were deployed in all floors, whether the therapy could hide the severity of a patient's disease, potentially putting the patient at risk if their symptoms worsened. To address this, the group suggested that clinicians would need to identify those patients who would most likely benefit and observe beyond their saturation levels. This would be another area of clinical research where evidence should progress in the future.

Panel Discussion: Meeting Summary & Future Directions
– Dr. Nick Hill & Prof. Oriol Roca

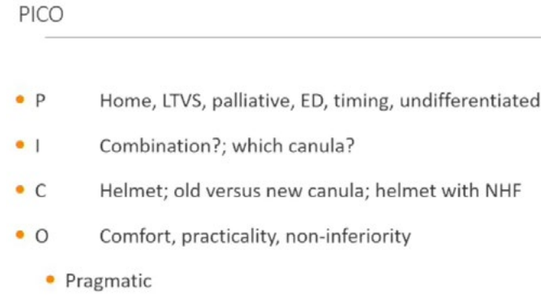
Dr. Nick Hill and Prof. Oriol Roca walked onto the stage and gave thanks to everyone who hosted, presented and partcipated. Dr. Hill reflected that he saw a need for such a meeting and thought that clinical and industry partnerships were important to create synergy in producing better products and addressing clinical gaps to improve patient care and outcomes. Dr. Hill and Prof. Roca shared a brief overview of the content from both days while also providing their opinions. They then reintroduced all session facilitators on stage across the past two days to answer how Covid shaped their experiences, learnings from the pandemic and whether there were any future research the session facilitators were interested in.

The themes discussed in the panel included changes in intubation criteria and NHF usage during the pandemic, education for nurses and medical students, adapting to new intubation criteria, and potential research questions for the future of NRS.

Dr. Nick Hill & Prof. Oriol Roca

Closing Remarks – Dr. Roman Jaeschke

Dr. Jaeschke closed the meeting by running through his main learnings from the last few days. Main themes he learnt were that Fisher & Paykel aimed to provide innovation and new solutions to clinical problems, the involvement of AI and new technology such as the asymmetric cannula, the return of negative pressure ventilation and the possible PICO questions drawn from everyone's presentations (as shown below).



For the future, he hoped that the efforts, cooperation, and communication he witnessed at the meeting could continue in the form of a community of practice. He proposed to the audience whether the NRS network would become an established forum for exchanging ideas, coordination of research, a system for future pandemics and a mechanism for liaising with non-clinicians.

Dr. Roman Jaeschke

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