

Improved outcomes by lung protective strategy in patients with acute respiratory distress syndrome

China Medical University Hospital, Taiwan

How-Yang Tseng, Attending Physician; Wei-Cheng Chen, Director of Respiratory Intensive Care Unit; and Chuen-Liang Chen, Information Vice Superintendent

Executive Summary

Acute Respiratory Distress Syndrome (ARDS) is a critical condition with a high mortality rate and is an important complication of COVID-19. The mortality rate among elderly and septic patients can reach as high as 80%. Patients' survival can be improved through adequate ARDS management, including early diagnosis, a lung-protective ventilation strategy (using a low tidal volume of approximately 6-8 ml/kg of predicted body weight [PBW] and maintaining a low plateau pressure of < 30 cm H₂O), and prone positioning for appropriate patients with severe disease. However, the recognition of ARDS and the implementation of effective therapies are limited among clinicians.

Due to these reasons, we launched an ARDS improvement project that led to an increase in the ARDS recognition rate from 52.2% to 74.4%. Compliance with the lung protective strategy also improved significantly, rising from 30.4% to 75.6%. Furthermore, the ICU mortality rate saw a notable decrease from 56.5% to 39.8%. **(Table 1)**

Define the Clinical Problem and Pre-Implementation Performance

According to clinical practice guidelines from the American Thoracic Society, European Society of Intensive Care Medicine, and Society of Critical Care Medicine in 2017, guidelines published in the British Medical Journal in 2019, and guidelines from the Japanese Society of Intensive Care Medicine, Japanese Respiratory Society, and Japanese Society of Respiratory Care Medicine in 2021, it is suggested that a lung protective strategy (with a tidal volume \leq 6-8 ml/kg of predicted body weight) be implemented for all patients with ARDS.

Although lung protective strategy is associated with improved survival in patients with acute respiratory distress syndrome (ARDS), the implementation of effective therapies remains low. The **LUNG SAFE trial** revealed that only **half** of the patients with mild ARDS and **three-quarters** of the patients with severe ARDS were properly recognized. Additionally, less than **66%** of patients with ARDS received a lung protective strategy, as indicated by a low tidal volume of 8 mL/kg or less of predicted body weight.

China Medical University Hospital (CMUH), a tertiary referral center in Taiwan, operates a medical ICU with 40 beds and admits an average of 1300 patients into the ICU each year. Among these admissions, approximately 200 cases are diagnosed with ARDS. Prior to the implementation of the project, only **52.2%** of the patients with ARDS were recognized, and merely **30.4%** received a lung-protective strategy. Consequently, both the ICU and hospital mortality rates were alarmingly high, at **56.5%** and **78.3%**, respectively. **(Table 1)**.

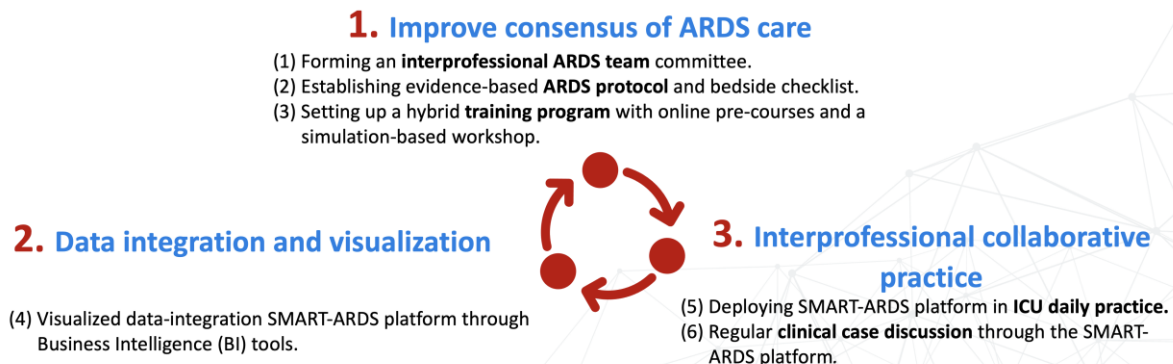
Table 1 Characteristics of patients with acute respiratory distress syndrome

	Pre-implementation (n=23)	Intervention-SOC group (n=62)	Intervention-BI assisted group (n=86)	Maintain phase (n=315)	p value
Male	13 (56.5%)	44 (71%)	53 (61.6%)	211 (67%)	0.480
Age, years	67.8 (14.8)	68.6 (15.4)	67.7 (14.9)	68.2 (14.0)	0.982
BW, kg	60.5 (15.6)	62.2 (13.5)	60.5 (12.2)	60.5 (13.4)	0.821
BMI, kg/m ²	22.7 (5.1)	23.4 (4.1)	22.7 (4.1)	23.0 (4.7)	0.801
Comorbidities					
Cancer	12 (52.2%)	22 (35.5%)	41 (47.7%)	111 (35.2%)	0.088
Modified Charlson score	5 (5-7)	5 (3-7)	5 (4-6.8)	7 (4-9)	<0.001
Severity of illness					
APACHE II score	28 (24-35)	29 (21.5-34.5)	28.5 (23-34.8)	30 (26-35)	0.370
Shock	15 (65.2%)	49 (79%)	62 (72.1%)	264 (83.8%)	0.024
ARDS severity at diagnosis					0.676
Mild	6 (26.1%)	10 (16.1%)	16 (18.6%)	60 (19%)	
Moderate	8 (34.8%)	31 (50%)	43 (50%)	168 (53.3%)	
Severe	9 (39.1%)	21 (33.9%)	27 (31.4%)	87 (27.6%)	
Recognition rate	12 (52.2%)	40 (64.5%)	64 (74.4%)		0.100
Vt-PBW≤8	7 (30.4%) ^a	38 (61.3%) ^{a,b}	68 (79.1%) ^b	238 (75.6%) ^b	<0.001
Vt-PBW≤6	4 (17.4%)	8 (12.9%)	17 (19.8%)	57 (18.1%)	0.737
NMB	9 (39.1%) ^a	43 (69.4%) ^{a,b}	60 (69.8%) ^b	181 (57.5%) ^{a,b}	0.013
Prone	4 (17.4%)	24 (38.7%)	38 (44.2%)	115 (36.5%)	0.123
ECMO	0	3 (4.8%)	3 (3.5%)	9 (2.9%)	0.689
Duration of IMV, day	11 (6-24)	14 (6-27.5)	10 (5-26)	16 (6-36)	0.133
ICU mortality	13 (56.5%) ^{a,b}	36 (58.1%) ^b	34 (39.5%) ^{a,b}	125 (39.8%) ^a	0.027
Hospital mortality	18 (78.3%)	42 (67.7%)	42 (48.8%)	169 (56.1%)	0.023
ICU LOS, day	13 (8-21)	14 (8.5-24)	10 (6-15.8)	14 (7-22)	0.048
Hospital LOS, day	19 (11-34)	23 (10-39.5)	29 (15-51.5)	32 (15-60)	0.023

BW = body weight, BMI = body mass index, APACHE = Acute Physiology and Chronic Health Evaluation

Design and Implementation Model Practices and Governance

In comparison to a similar group of ARDS patients in Taiwan (Chan et al., Journal of the Formosan Medical Association, 2019, 118, 378-385), our study revealed that the patients with ARDS were predominantly elderly, with a mean age of 68.1 (compared to 59.8 as recorded in the local data). Additionally, there was a higher rate of patients with a history of cancer (38.3% vs. 13.3% in the local data), a higher incidence of shock status (80.2% vs. 53.2% in the local data), and a higher APACHE II score (30 vs. 23.6 in the local data). Furthermore, 81% of the patients demonstrated moderate to severe ARDS, as indicated by the P/F ratio. These findings highlight the need for improved ARDS care. Therefore, since September 2020, the CMUH ICU has begun implementing a series of changes to better address the challenges of ARDS diagnosis and management. These changes include three key elements: **1.** Improving consensus on ARDS care among team members, **2.** Implementing data integration and visualization tools, and **3.** Encouraging interprofessional collaborative practice. The changes are being implemented step by step. It takes approximately one week to train the ICU team members to become familiar with the virtual tools. However, it is essential to repeat the above steps 1 to 3 in order to continuously improve consensus on ARDS care, promote the usage of the virtual tools, and ensure their adoption among a broader range of multidisciplinary ICU team members.



(1) **Forming an interprofessional ARDS team committee:** We formed an interprofessional ARDS team committee comprised of the ICU director, ICU case manager, intensivists, nurse practitioners, residents, nurses, respiratory therapists, pharmacists, nutritionists, and technicians of information technology (IT). The multidisciplinary team discussed important issues such as setting up an ARDS protocol, arranging a team education program, and building a *SMART-ARDS platform* for ARDS screening and monitoring of lung protective strategy.

(2) **Establishing evidence-based ARDS protocol (Fig 1) and bedside checklist:** The ARDS team committee developed the CMUH ARDS protocol based on a literature review of current guidelines. It was established through multiple rounds of discussion and is regularly reviewed and updated to reflect the latest evidence.

(3) **Setting up a hybrid training program with online pre-courses and a simulation-based workshop:** To provide a more effective learning program, we established a hybrid training program comprised of online pre-courses and annual simulation-based workshops. The educational department adjusted the program based on the analysis of pre-test and post-test results from the trainees.

(4) **Visualized data-integration SMART-ARDS platform by Business Intelligence (BI) (Fig 2):** BI was used to integrate scattered data related to ARDS such as PaO₂/FiO₂ ratios, tidal volume per predicted body weight, APACHE II score, usage of neuromuscular blockers, prone positioning, use of vasopressors, continuous venovenous hemofiltration (CVVH), and ECMO. All these data were presented visually on a dashboard to help physicians screen for ARDS patients and monitor the implementation of lung protective strategies. An IT group consisting of IT technicians and ICU clinicians was enlisted and received training in BI to design the platform.

(5) **Deploying SMART-ARDS platform in ICU daily practice:** After setting up the SMART-ARDS platform, clinicians discussed the clinical course for specific patients with team members. Directors could detect ARDS patients and monitor the implementation of lung protective strategy. The chief nurse could adjust the workforce based on the severity distribution shown on the dashboards.

(6) **Regular clinical case discussion through the SMART-ARDS platform:** To improve the recognition of ARDS, regular case discussions were held twice a week to screen new patients and enhance awareness of ARDS among the medical team. Previously, clinicians spent approximately one hour systematically reviewing arterial blood gas data and checking chest X-rays for all 40-bed ICU patients to identify those at high risk. However, with the implementation of the smart platform, this process only takes half an hour. Furthermore, after the introduction of AI-assisted chest x-ray detection, the entire systematic screening process was replaced by the SMART-ARDS platform.

In order to improve compliance with the standard of care for ARDS, interprofessional discussions took place during weekly ICU ward rounds to monitor patient progress and ensure adherence to the recommended protocols. To evaluate overall outcomes, such as the proportion of ARDS cases and mortality rates, the team utilizes a retrospective panel in the SMART-ARDS platform to review challenging cases and establish a consensus on best practices.

Figure 1. CMUH ARDS management protocol

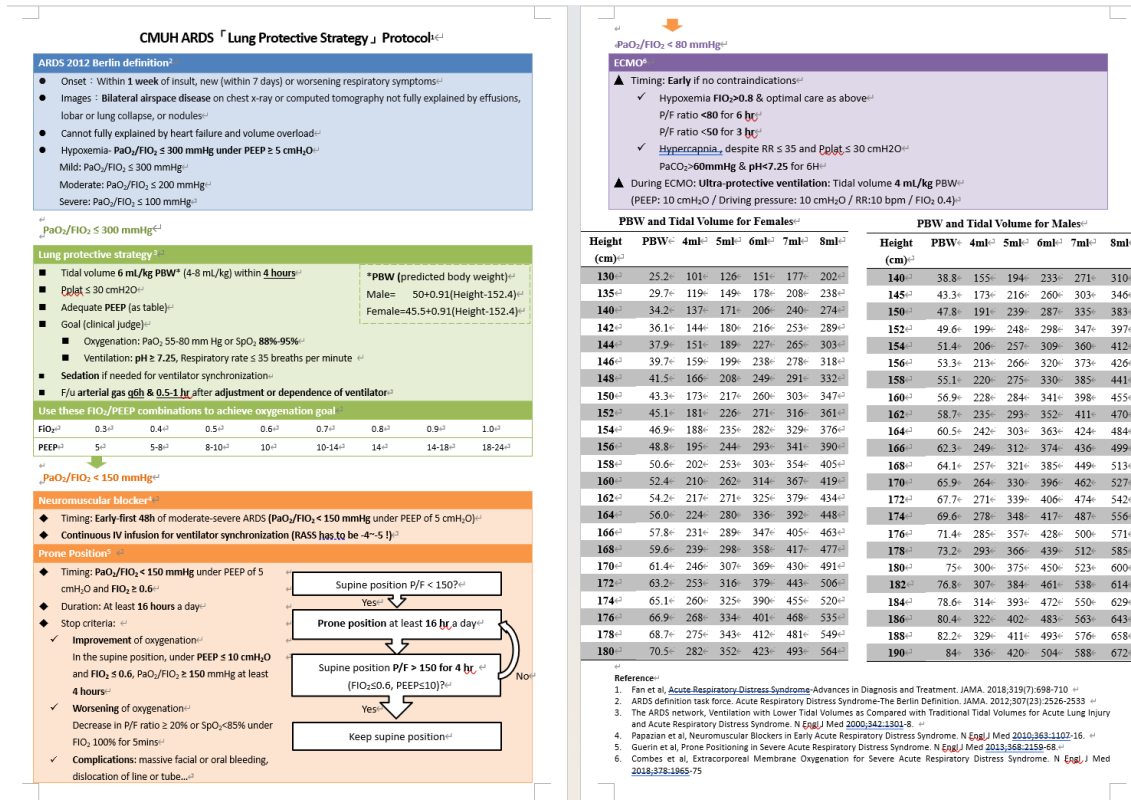


Figure 2. Visualized data-integration SMART-ARDS platform

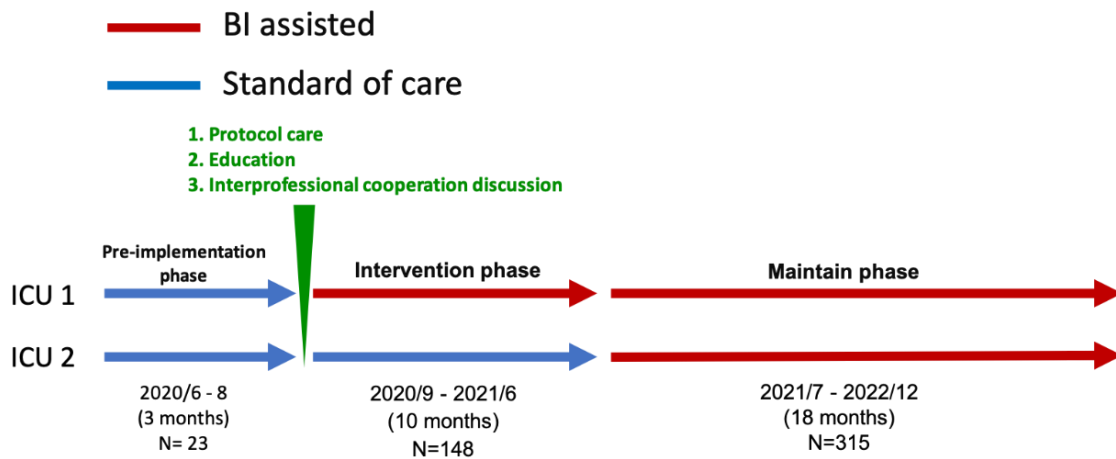


Clinical Transformation enabled through Information and Technology

Timeline of the ARDS Improving Project (Fig 3)

The CMUH hospital has two Medical Intensive Care Units (ICUs). Prior to implementation, we collected three months' worth of data from both ICUs to establish performance baseline. This information is presented in the "Pre-Implementation Performance" section. During the intervention phase, education for healthcare providers and protocolized care of ARDS was provided in both ICUs, and a *SMART-ARDS platform* was introduced and applied in one of the ICUs. The outcomes of intervention phase were published in "**Critical Care**" journal (Crit Care. 2022 Aug 22;26(1):253. doi: 10.1186/s13054-022-04091-0.). Due to its success, the system was implemented in both ICUs beginning in July 2021 and is still in use today. During the maintenance phase, our focus is on ensuring that the system is functioning correctly and efficiently, and addressing any issues that may arise.

Figure 3. Timeline of the ARDS Improving Project



Integrated data visualization for data-driven decision support in ICU (Fig 4)

A real-time interactive visualized dashboard- *SMART-ARDS platform* was established through Power Business Intelligence, Power BI (Microsoft Corporation, Redmond, Washington) for ARDS information integration, which enables clinicians to screen patients with ARDS, monitor the condition of lung protective strategy, and assist in interprofessional discussion and clinical decision.

Before implementing the platform, it is essential to ensure that all key items, such as the APACHE II score, P/F ratio, PBW, and others, are available in the hospital information system (HIS). The *SMART-ARDS platform* is connected directly to the hospital information system (HIS) for real-time and retrospective monitoring and automatically detects the International Statistical

Classification of Diseases (10th version; ICD-10) coding of ARDS. The real-time dashboard is updated every 5 minutes, and the retrospective dashboard allows clinicians to access information in any period.

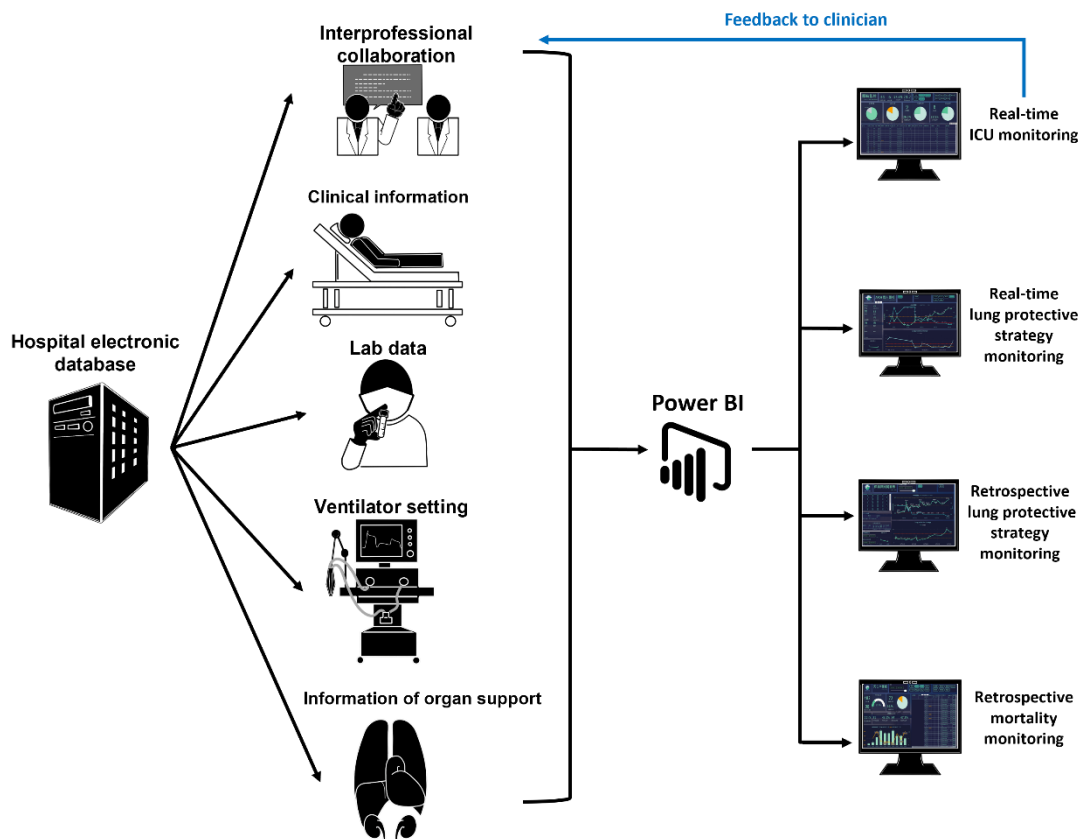
The real-time dashboard was used to:

1. provide a timely diagnosis of ARDS by rapidly screening the PaO₂/ FiO₂ ratio in every ICU patient.
2. monitor the in-time percentage of ARDS patients in the ICU.
3. provide a pie chart to demonstrate the current condition of organ support, including the use of mechanical ventilation, CVVH, inotropic agents, or ECMO in patients with ARDS.
4. further understand the utility of neuromuscular blockade and prone positioning in patients with moderate-to-severe ARDS.
5. determine the trend of disease severity and lung protective strategy by using the serial data from the PaO₂/FiO₂ ratio, FiO₂, and tidal volume/PBW (V_t/PBW) to create a line chart.

The retrospective dashboard could display the following information:

1. ARDS incidence
2. in-ICU and in-hospital mortality rates among patients with ARDS.
3. the trend of in-ICU mortality visualized into line and column charts.
4. a quick review of the implementation of lung protective strategy in every patient with ARDS during ICU admission presented as a line chart.

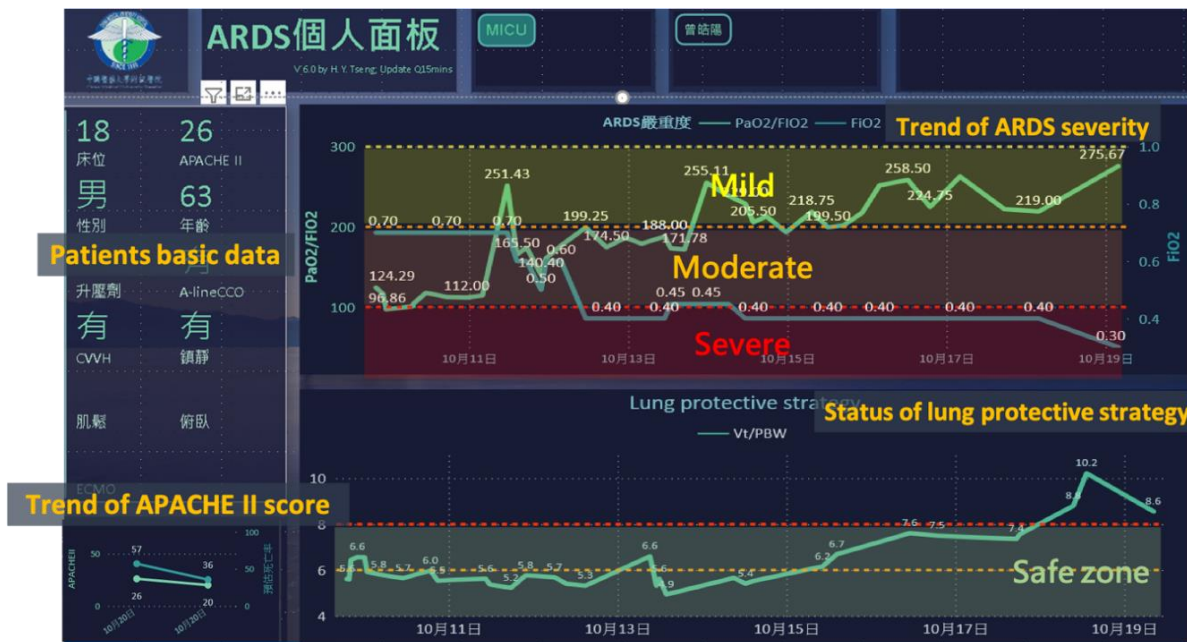
Figure 4. An interactive visualized platform was established through Power BI for data-driven decision support.



Implementation of SMART-ARDS platform into ICU clinical practice

The ICU at CMUH has implemented the SMART-ARDS platform into daily practice, including morning meetings, daily ward rounds, weekly ICU team rounds, interprofessional team discussions, teaching for junior staff, and even explanations of the state of illness to patients' families. Warning notifications for high-risk patients and for patients who have not received lung protective strategy will be automatically transmitted to clinicians (Fig 13). The use of this system makes it easier to understand the disease severity and the status of lung protection due to its easy-to-understand graphics, which are easier to read and more concise than a lot of scattered words and numbers. With the assistance of this system, clinicians and interprofessional team members can stay alert and easily monitor the dynamic severity trends of ARDS and compliance with low tidal volume ventilation strategies. This is especially important during the high prevalence season of ARDS or pandemics, such as COVID-19 when clinicians must manage many patients with ARDS at the same time (Fig 5)

Figure 5. The real-time dashboard to monitoring the trend of severity of ARDS and lung protection.

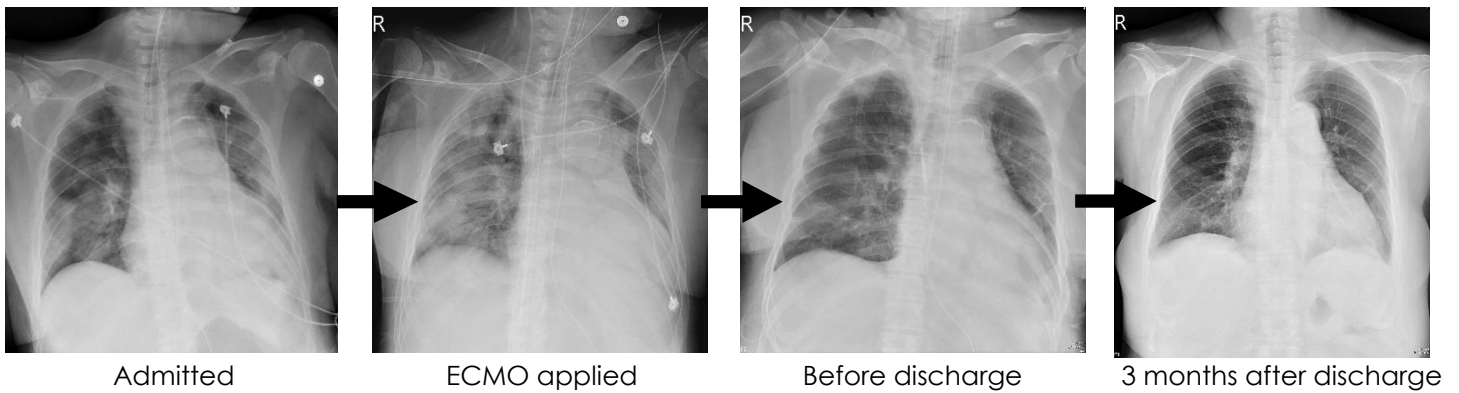


Successful clinical case

A patient with COVID-19 developed ARDS as a critical complication. The CMUH SMART-ARDS platform assisted the ARDS specialist team to successfully reverse the patient's critical condition.

Ms. Chang, a 46-year-old woman with a history of hypertension and nephropathy underwent a kidney transplantation surgery 10 years ago. She tested positive for COVID-19, had shortness of breath, and the concentration of her oxygen saturation was dropping dramatically. A chest X-ray showed bilateral diffuse pulmonary infiltrations (**Fig 6**). She was diagnosed with "acute respiratory distress syndrome (ARDS)". Ms. Chang immediately underwent endotracheal intubation and was transferred to the negative pressure isolation ICU at the China Medical University Hospital. Due to her rapidly deteriorating condition, extracorporeal membrane oxygenation (ECMO) emergent use was initiated, and an interprofessional ARDS expert team was gathered. The team utilized the visual SMART-ARDS platform in real-time to assist their clinical decisions and prescribed the proper antibiotics and antivirals. With 15 days of ECMO support, Ms. Chang's condition improved. After 35 days in the hospital, she became stable, recovered, and was successfully discharged.

Figure 6. The series of changes of chest x-ray



Improving Adherence to the Standard of Care

Improvement of the ARDS recognition:

Carefully monitoring potential ARDS cases can lead to a timely diagnosis which is an important first step in improving the outcome of patients with ARDS in the ICU. The recognition rate of ARDS is defined as the percentage of ICD-10 codes made on the hospital information system (HIS) by the attending primary care physician and the diagnosis made by three other intensivists retrospectively. The ARDS recognition rate was only 52.2% during the pre-implementation phase. In the standard-of-care (SOC) group of the intervention phase, the ARDS recognition increased to 64.5% through protocolized care, education, and interprofessional cooperation. With the assistance of the SMART-ARDS platform, the recognition rate significantly increased to 74.4% in the BI-assisted group (**Fig 7-1**). **Figure 7-2** displays the trend of the recognition rate using monthly data points. It reveals that the issue extends beyond just percentages, but also includes absolute numbers. With timely intervention, we can diagnose more patients with ARDS and potentially save lives. Following the intervention phase, the SMART-ARDS platform replaced all systemic screening for ARDS recognition.

Figure 7-1. Improved recognition rate of ARDS between different phases

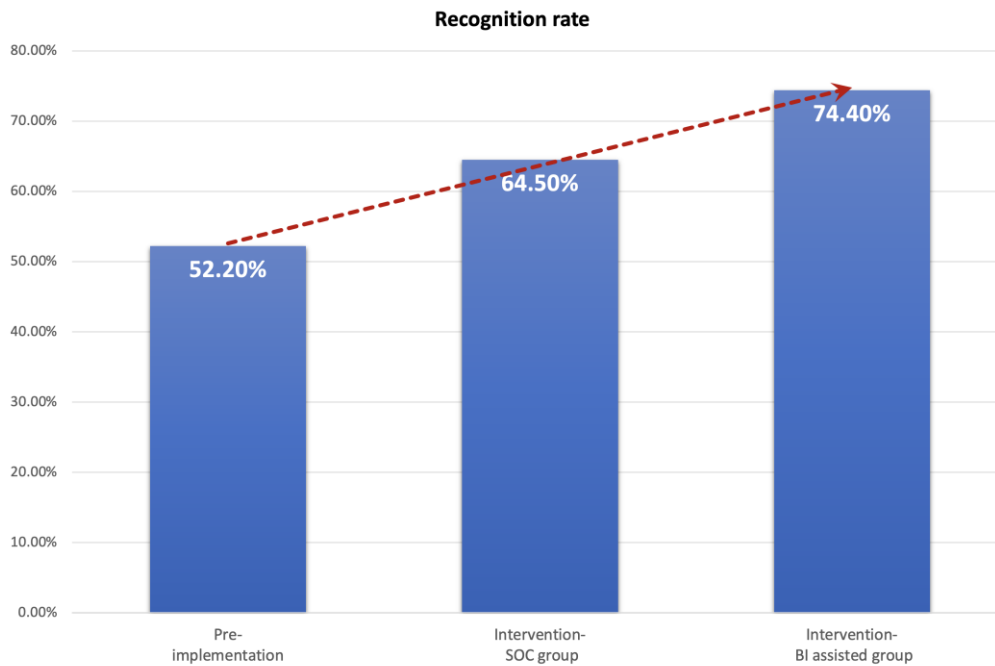
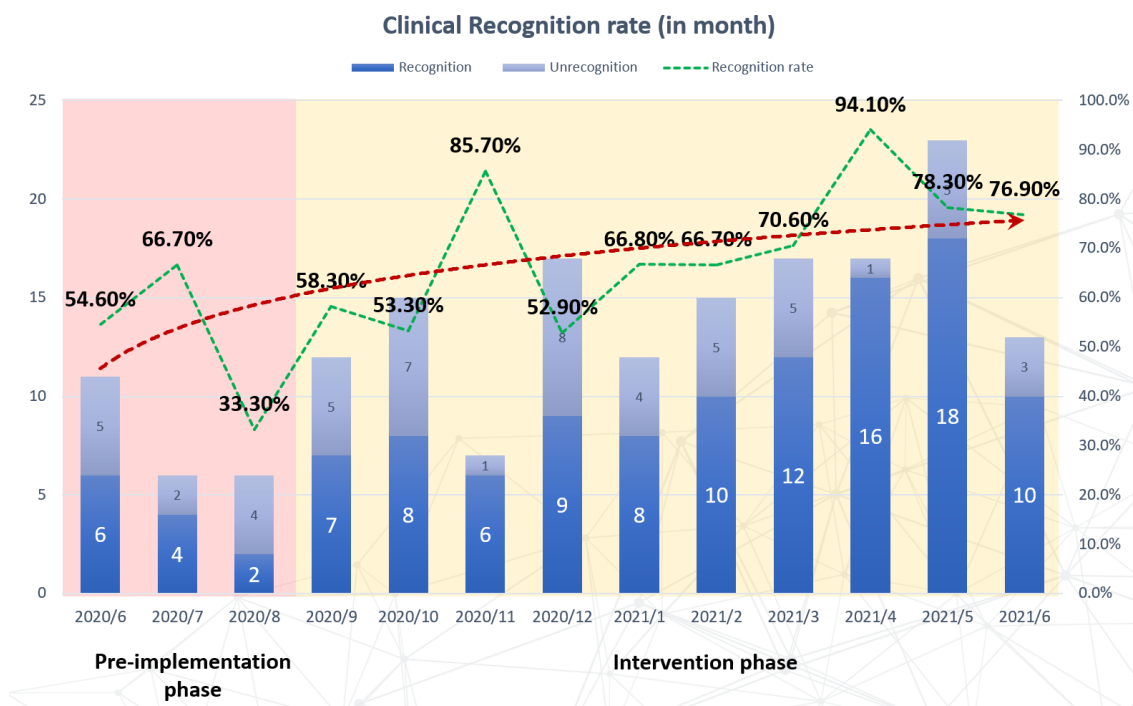


Figure 7-2. Improved recognition rate of ARDS in monthly data points



Improvement of compliance to low tidal volume ventilation within 24h from ARDS onset

Although the lung protective strategy and adjunctive interventions are associated with improved survival in patients with acute respiratory distress syndrome (ARDS), the implementation of effective therapies remains low. Therefore, the initiation of the lung protective strategy (defined as tidal volume/predicted body weight ≤ 8 mL/kg) timely and safely should be the first approach in ARDS management.

Thus, we defined the numerator as patients receiving low tidal volume ventilation within 24h from ARDS onset. And the denominator was all patients with ARDS. In a large global LUNG-SAFE study (JAMA, 2016), 66% of the patients across all the ICUs received the lung protective strategy. We have adapted this as our benchmark.

In the intervention phase, the implementation of lung protective strategy within 24h from ARDS onset was significantly increased in the BI-assisted group compared to the standard-of-care group. Furthermore, during the 18 months maintain phase, the implementation rate of lung protective strategy remained higher than the benchmark set by the LUNG-SAFE study, with 75.6% of patients receiving lung protective strategy within 24h from ARDS onset. The trend line also indicated that compliance with the lung protective strategy increases between different phases (**Fig 8**).

Figure 9-1 demonstrates the trend in compliance with the lung protective strategy over the past 31 months. The horizontal axis represents time (in quarters) and the vertical axis represents the percentage of patients who receive the lung protective strategy within 24h of an ARDS onset. In the pre-implementation phase, compliance with a lung protective strategy was initially poor but improved during an intervention phase, with some quarters falling below the benchmark. The performance then continued to improve during a maintenance phase, with the percentage of patients receiving lung protection within 24 hours from ARDS onset steadily surpassing the benchmark and even reaching over 80% in 2022 Q4. The trend of compliance to the lung protection strategy between two ICUs were shown in **Figure 10**.

There are certain clinical conditions that are not suitable or contraindicated for the implementation of the lung protective strategy, such as refractory shock status, refractory acidosis, brain injury with increased intracranial pressure, or toxicologic emergencies. We have also documented cases during the maintenance phase where the lung protective strategy was deemed unsuitable. **Figure 9-2** illustrates the compliance trend with the lung protective strategy during the maintenance phase using monthly data points. After excluding the clinically unsuitable cases, the compliance with the lung protective strategy is presented in **Figure 9-3**. With the assistance of the SMART-ARDS platform, we can initiate the lung protective strategy to the best of our ability as soon as possible. Weekly interprofessional case-based discussions will be arranged to address uncertain or protocol-unfollowed cases, aiming to hold individuals accountable for performance improvement (**Fig 13**).

Figure 8: Improved compliance of lung protective strategy between different phases

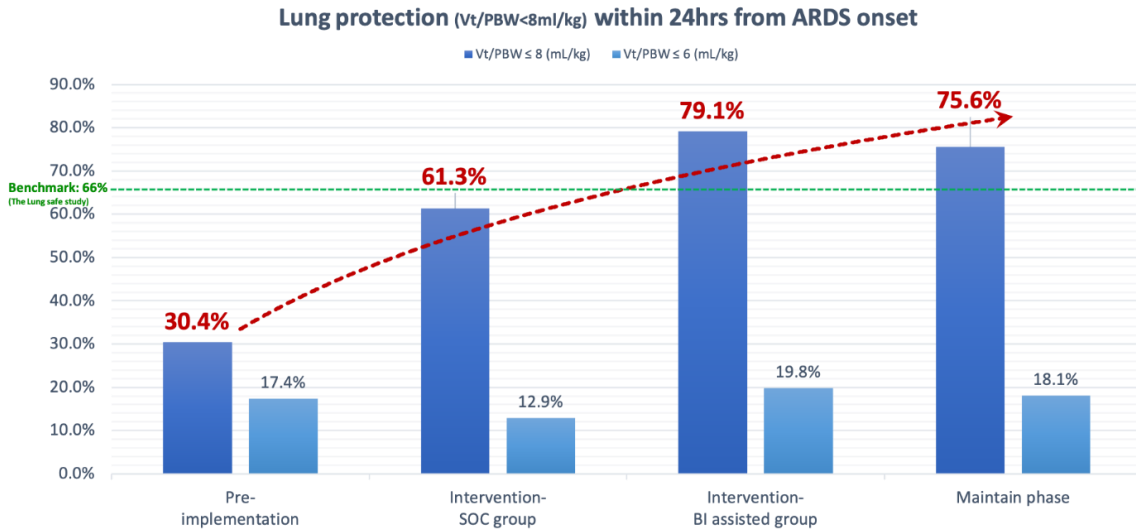


Figure 9-1. Trend of compliance to the lung protective strategy over time (in quarters)

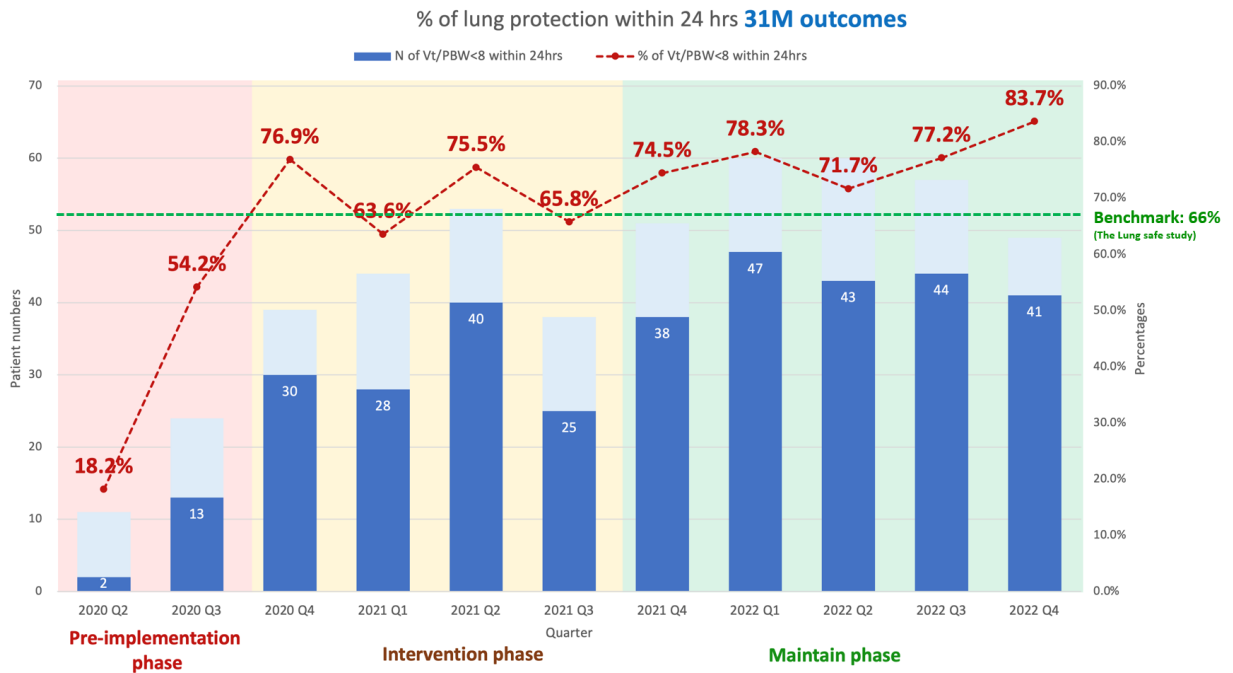


Figure 9-2. Trend of compliance to the lung protective strategy over time (in months) during the maintenance phase.

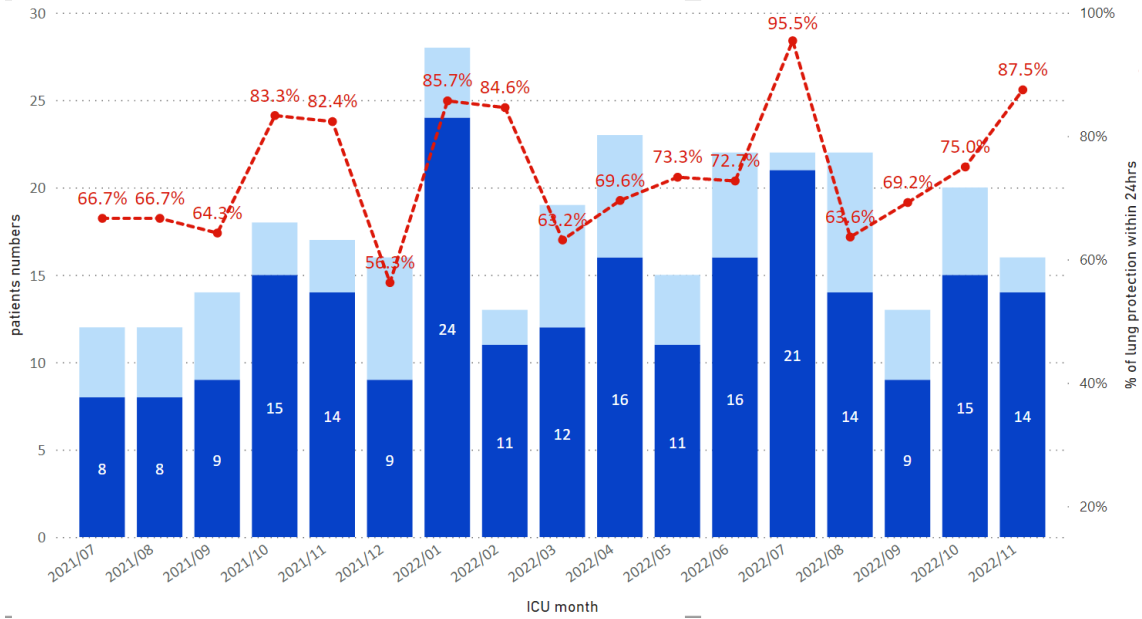


Figure 9-3. Trend of compliance to the lung protective strategy over time (in months) during the maintenance phase. (Exclude clinical unsuitable cases)

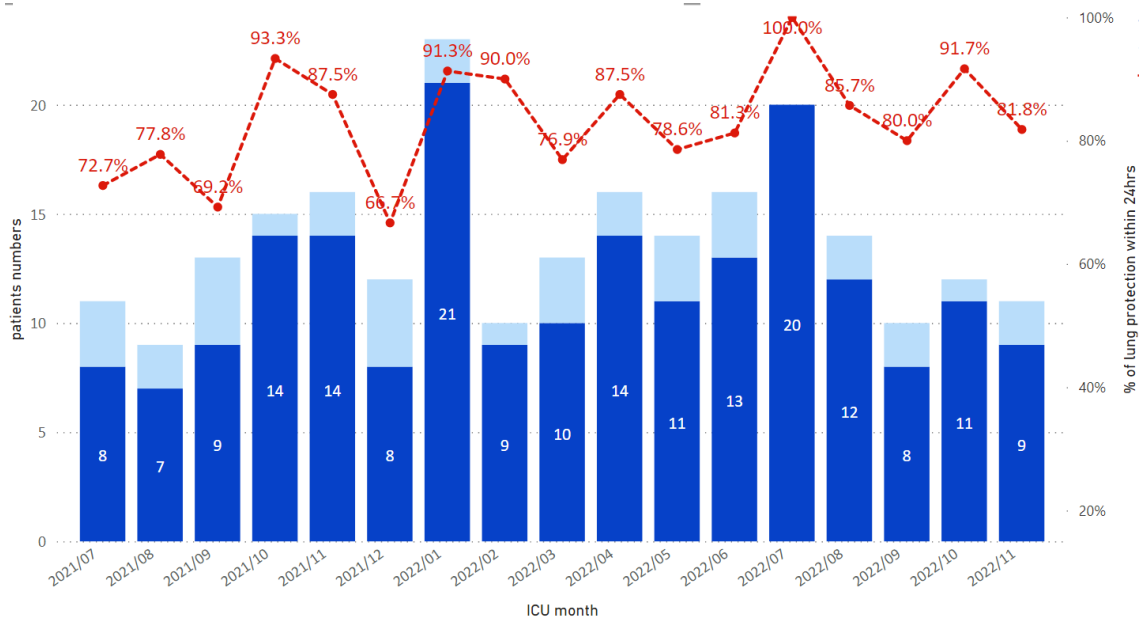
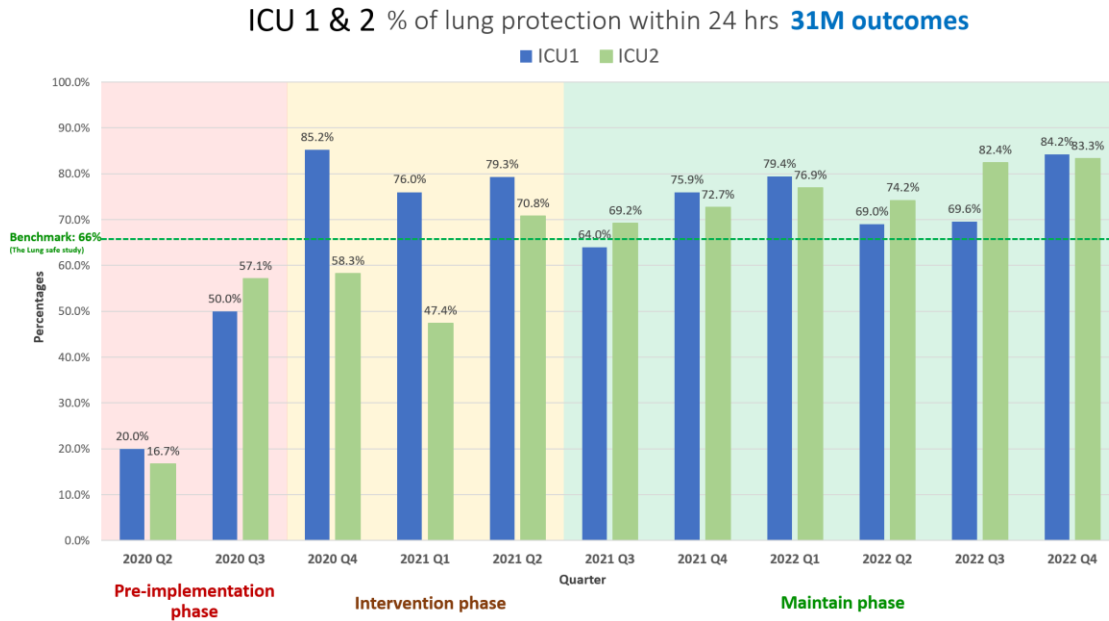


Figure 10. Trend of compliance to the lung protective strategy between two ICUs over time (in quarters)



Improving Patient Outcomes

Mechanical ventilation with low tidal volume in patients with ARDS can reduce mortality and increase the number of ventilator-free days. High tidal volume ventilation shortly after ARDS leads to high ICU mortality. Through the improvement of ARDS recognition and compliance with lung protective strategies, the outcomes for patients with ARDS also improved. In the intervention phase, the ICU mortality rate was 39.5% in the BI-assisted group, which was significantly lower than that of the SOC group (58.1%). During the 18-month maintenance phase, the ICU mortality remained steadily lower than it was before. The trend line revealed that ICU mortality decreased between the different phases (**Fig 11-1**).

As mentioned above, despite the fact that the patients with ARDS in the CMUH ICU were predominantly elderly, with a mean age of 68.1, and had a high rate of patients (38.3%) with a history of cancer, it was observed that 80.2% of cases experienced shock status, and their disease severity was high (APACHE II score: 30). Notably, 81% of these patients exhibited moderate to severe ARDS, as indicated by the P/F ratio. Implementing increased adherence to lung protective strategies resulted in improved survival for these individuals. (**Fig 11-2**).

Figure 11-1. Decrease of ICU mortality between different phases

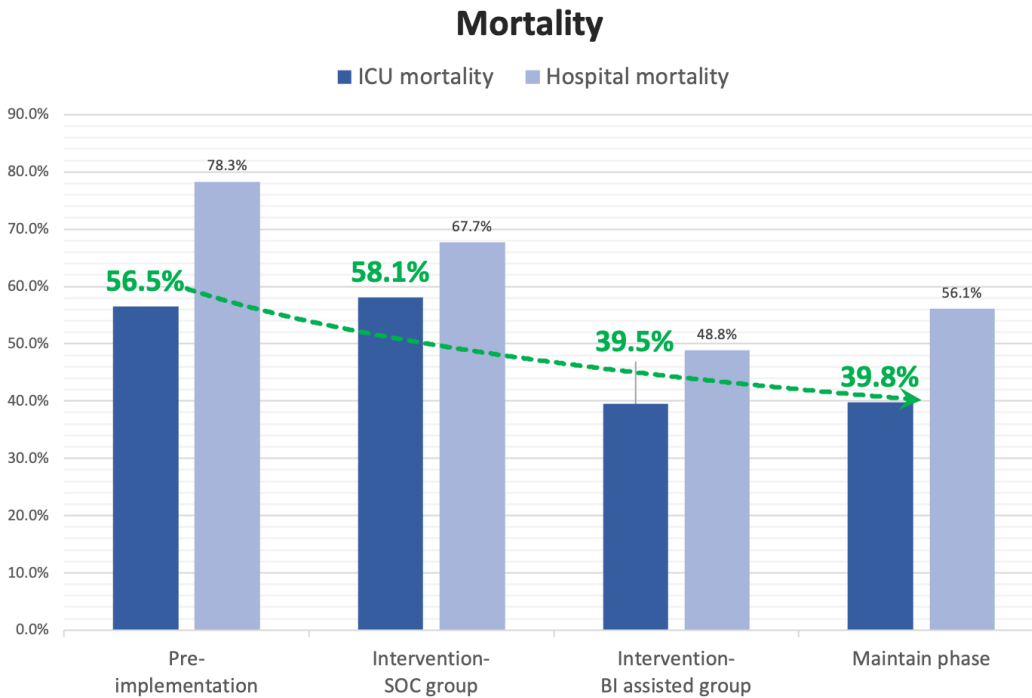


Figure 11-2 Comparison of ICU and hospital mortality rates among different cohorts.

	Bellani et al., JAMA, 2016. 315(8): p. 788-800.	Chan et al. Journal of the Formosan Medical Association (2019) 118, 378-385	Tseng et al. Critical Care (2022) 26:253	Kao KC, et al. Sci Rep. 2018 Sep 7;8(1):13459	Crit Care Med . 2016 Jul;44(7):1361-9.	
	2016 The Lung Safe study	2016 Local data in Taiwan	Our performance baseline	Our Cohort with ARDiTeX assistance	2015 Local data for elderly in Taiwan	2016 ARDS cohort of elderly in Spain
Age of Cohort	61	59.8	67.8	67.7	>65	>66
Disease severity of Cohort	SOFA: 10.1 (day 1) APACHE II: -	SOFA: - APACHE II: 23.6	APACHE II: 28	APACHE II: 28.5	APACHE II:24	APACHE II:22
Diagnostic rate	51.3%	-	52%	74.4%	-	-
Compliance of low tidal volume ventilation (<8 ml/kg PBW)	<66%	-	30%	79.1%	-	-
Mortality	ICU mortality: 35.3% Hospital mortality: 40% 28-days mortality: 34.8%	30-days mortality: 23.2%	ICU mortality: 56% Hospital mortality: 78%	ICU mortality: 39.5% Hospital mortality: 48.8%	Hospital mortality: 63.9%	Hospital mortality: 66%

Accountability and Driving Resilient Care Redesign

To actively detect gaps in current ARDS care, artificial intelligence (AI) was included in the BI tool to monitor performance and drive care redesign.

Empowering ARDS detection through AI-integrated BI tools

Utilizing machine learning on the data of ARDS patients may provide insights and new strategies for improving ARDS detection and lowering its mortality rate. CMUH ICU has implemented an "ARDS AI imaging detection system" into the BI-based *SMART-ARDS platform* **(Fig 12)**, which can automatically detect bilateral infiltrates on CXR with an AUC of 0.91. The *SMART-ARDS platform* detects highly suspicious ARDS patients and automatically transmits warning messages to clinicians. Real-time monitoring and warning allow the clinical team to quickly identify patients with ARDS and intervene with proper treatment to decrease the mortality rate **(Fig 13)**.

Driving compliance of lung protective strategy workflow

The compliance with lung protective strategies is automatically transmitted to the clinical team through real-time messages **(Fig 13)**. By receiving active warning messages from the system, the clinical team can easily stay alert about the current tidal volume and monitoring the rapidly changing condition of ARDS. Cases with uncertain diagnosis or non-compliance with lung protective strategy will be reviewed and promptly reminded by the case manager and ICU director at the same time.

Establishing a real-time data-driven culture for ARDS care decision-making

Real-time visualization and integration of information could improve ARDS management by enabling data-driven decision making and transparency, which can in turn facilitate holding individuals accountable for performance improvement. The *SMART-ARDS platform* can parse compliance and outcomes data at both the patient and clinician level and visualize it for every member of the ARDS team. Real-time monitoring can be used to track ARDS prevalence **(Fig 14)** and demonstrate the trend of ICU and hospital mortality **(Fig 15)** following implementation of the project. It is also reviewed and discussed during the weekly ICU ward rounds, which can improve communication and coordination among healthcare providers to ensure that patients receive the right care at the right time. This successful project has established a patient-centric, data-driven decision-making culture for the diagnosis and management of ARDS.

Figure 12. Integration of AI-assisted detection tools into BI system to provide new strategies to improve ARDS care. Which utilizing machine learning on auto-detection of bilateral infiltration on chest X-ray

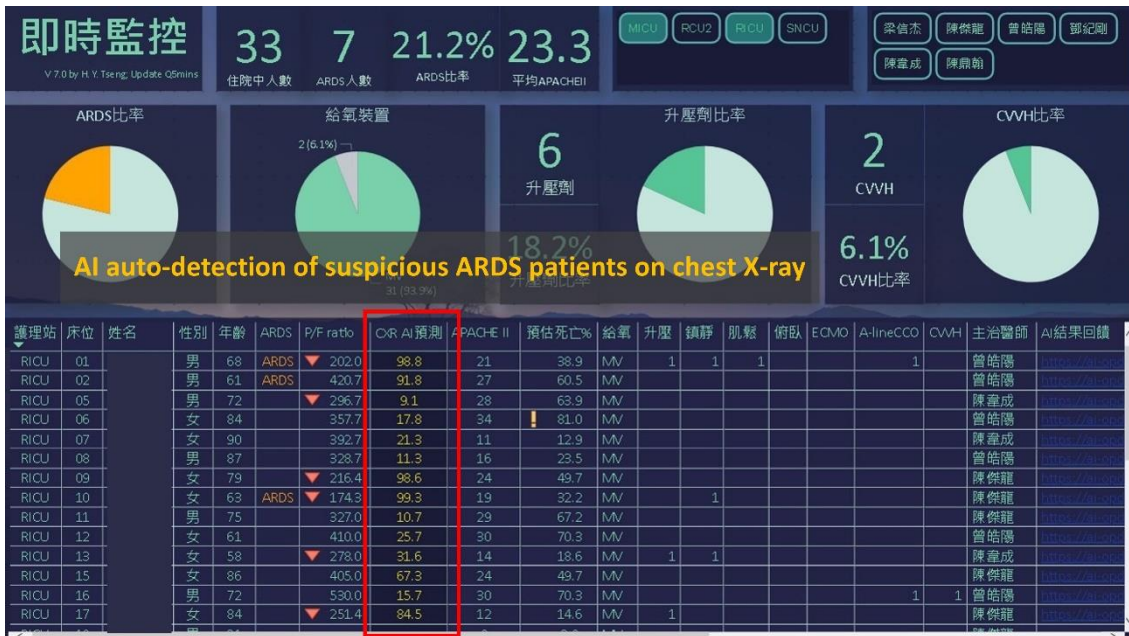


Figure 13 Building a data-driven decision-making culture in the care of ARDS

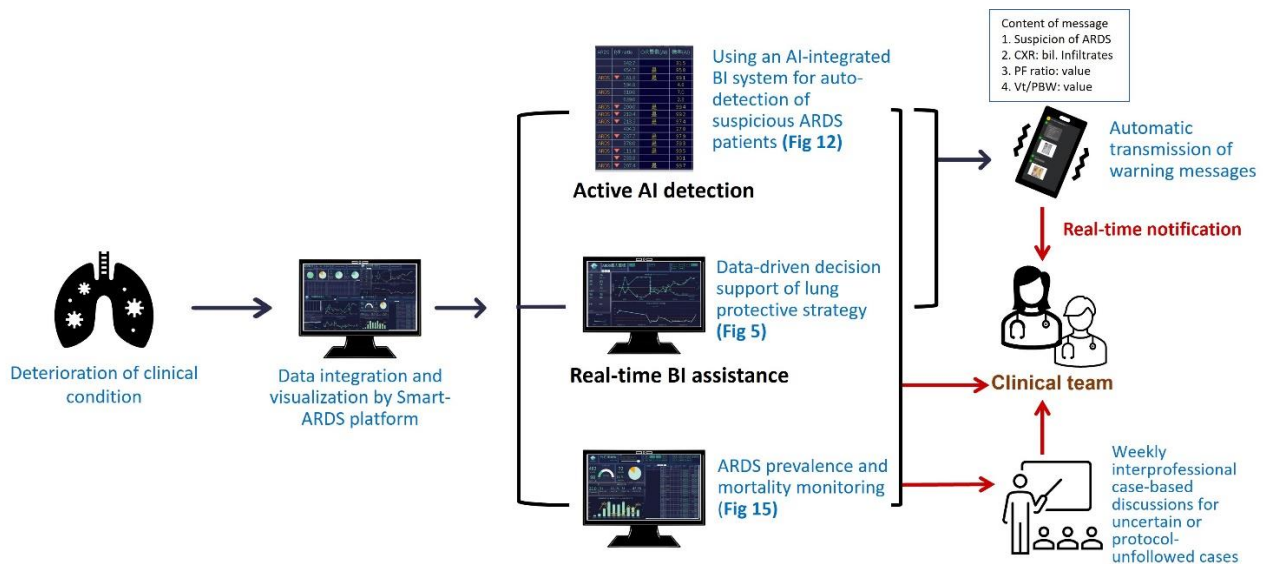


Figure 14. The real-time monitoring of ARDS prevalence

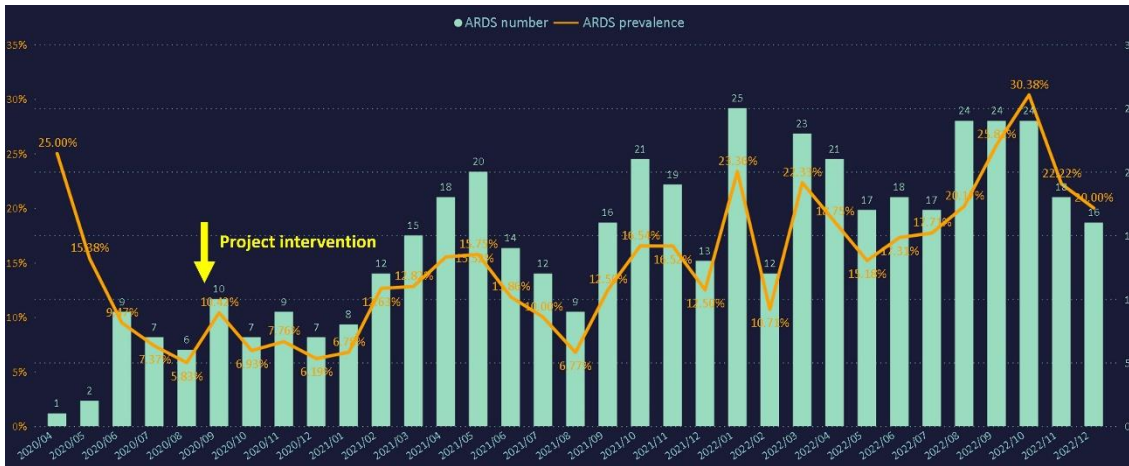


Figure 15. The real-time monitoring the trend of mortality in patients with ARDS

