White Paper

Service provider
Machine learning

Opening the "Black Box"

Ebenbuild research program aims to provide clinicians with personalized digital twins of the human lung for the first time. The Ebenbuild prototype solution has the potential to transform mechanical ventilation therapy and may improve survival and recovery rates for patients with acute respiratory distress syndrome (ARDS).

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Simulation snapshot of a digital lung twin. The coloring indicates different levels of air velocity and tissue strain.

Executive Summary

The Covid-19 pandemic has brought to the world's attention the valuable work carried out by intensive care unit (ICU) clinicians across the globe. Without mechanical ventilation therapy, many more patients with acute respiratory distress syndrome (ARDS), from Covid-19 complications and other causes, would have sadly passed away.

Given the equipment clinicians have available to inform ventilation therapy, their success in treating patients is even more impressive. Currently, doctors and nurses have little way of understanding the impact of mechanical ventilation on the different parts of a patient's lung. They rely on simple written formulas, experience, and, in many cases, trial and error to inform treatment.

However, ARDS care could be about to enter a new era thanks to a pioneering research program from Ebenbuild, which is fusing patient data with sophisticated machine learning algorithms and physics-based computer simulation. By opening the "black box" that is the human lung, physicians could personalize ventilation therapy to bring many more ARDS patients to a full recovery.

Business challenge: Improving survival and recovery of ARDS patients

Respiratory diseases are on the rise. Chronic obstructive pulmonary disease (COPD), which includes chronic bronchitis and emphysema, is the fourth leading cause of death in the US[1]. Cases of tuberculosis, bronchiectasis, and cystic fibrosis are also increasing. Together with the Covid-19 pandemic, this upsurge in lung diseases has created the perfect storm for critical care physicians treating respiratory illness.

In 2020, an estimated eight million people suffered from ARDS—a life threatening condition that causes fluid to leak into the lungs. Another 40 percent of cases passed unrecognized[2]. These instances of ARDS put a huge strain on ICUs, since all ARDS patients require mechanical ventilation. And sadly, despite the best efforts of critical care physicians, mortality rates for ARDS remain high. Over two million recorded ARDS patients die every year[3]. Of the survivors, another two million will suffer from chronic conditions, potentially for the rest of their lives[4]. And some will experience long-lasting physical and psychological side effects and will be unable to work again[5].

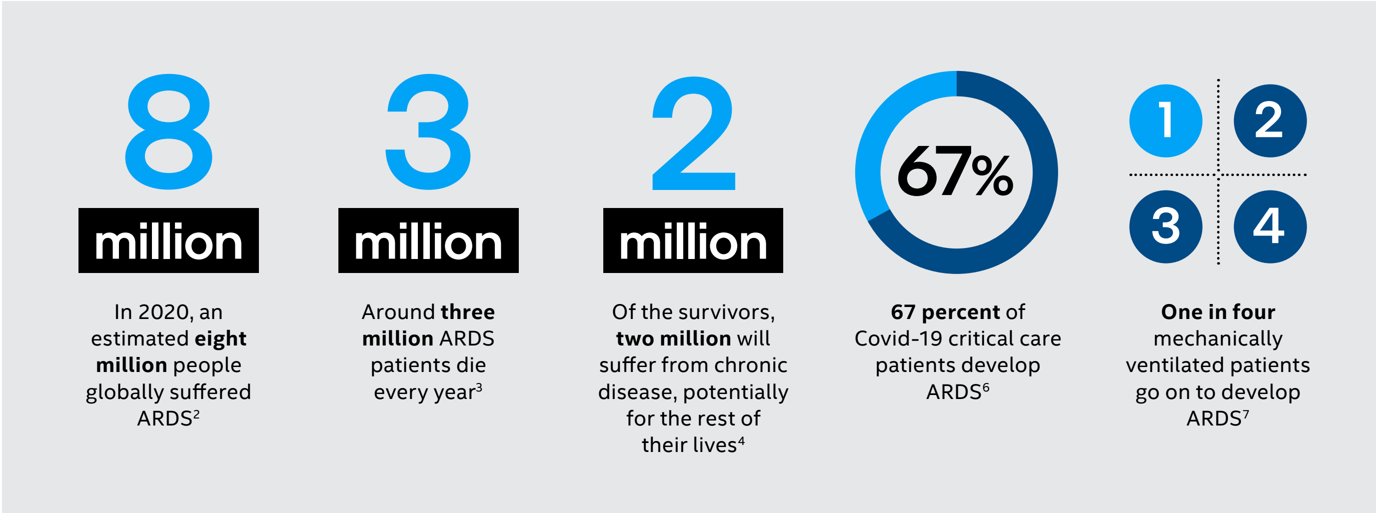

Figure 1. Acute respiratory distress syndrome (ARDS) is a life-threatening condition in which the lungs become severely inflamed and can't provide the body with enough oxygen.

While Covid-19 is the most pressing cause of ARDS currently—with up to 67 percent of Covid-19 critical care patients developing the condition[6]—there are many other reasons why patients develop ARDS. These include pneumonia, pulmonary hemorrhage, trauma, burns, shock, transfusion, sepsis, and aspiration. However, one of the most surprising causes for ARDS is the treatment itself—mechanical ventilation. Around one in four mechanically ventilated patients go on to develop ARDS[7] due to inadequate treatment. The cause, primarily, is not the physician, but the equipment.

Clinical care physicians do the absolute best job they can with the tools they have available. But, they often lack the equipment to provide insight into how the patient's lung responds to ventilation. Currently, they mostly refer to simple formulas to calculate how much air a patient needs to breathe and set up the ventilator accordingly. From there, physicians often rely on experience and trial and error to iteratively fine tune the ventilator settings to suit the patient's needs. Throughout, they have little visibility of the impact of their treatment on the inside of the lung. This lack of visibility of ventilator-induced lung overstretch can cause lung damage, inflammation, or even death.

Clinical care physicians have an urgent need for an imaging solution that provides a clear picture of the inside of the lung so they can improve mechanical ventilation for each individual patient. By reducing ventilator-inflicted lung damage, clinicians could boost survival and recovery rates for ARDS patients.

Precision ventilation therapy

Healthcare technology provider Ebenbuild has launched a research program to increase the odds of survival and recovery of those needing artificial ventilation due to ARDS. Up until now, clinical care physicians have had little visibility of the inside of a patient's lung. To all intents and purposes, the lung has been a "black box". Following the research program, Ebenbuild hopes this will no longer be the case. Ebenbuild wants to provide physicians with precise information and data from inside the lung, so they can set the best possible protective ventilation protocol for each individual patient. Not only in specialist clinics, but anytime, in any hospital.

Here's how Ebenbuild anticipates a digital twin solution could work. The clinician records a query via a web application at the patient's bedside—see figure 2. This query automatically uploads the patient's electronic medical records, CT scan, and any other medical images to the cloud through a so-called virtual private network (VPN) channel. Here, the Ebenbuild solution would process this data with machine learning (ML) algorithms to create a personalized digital twin of the patient's lung. The technology behind this digital twin utilizes advanced numerical simulation algorithms. Mechanically, this twin behaves exactly like its real counterpart, providing physicians with a detailed picture of the state of the patient's lung function and mechanics. Currently it takes around 30 minutes for the work-in-progress solution to deliver this information. The long-term goal is for a solution to return these results in near real-time to the patient's bedside. Using the digital twin, physicians could quickly identify the regions of the lung that are diseased and quantify the extent of any lung damage caused by the current ventilation pattern. The physician could then use this information to optimize the ventilator settings according to each patient's needs.

Research program value: More effective, efficient treatment

For the first time, physicians could act and react quickly to personalize ventilation therapy, helping to minimize lung damage in ARDS patients. Fewer instances of lung damage, together with more effective ventilation, could enable doctors to bring patients to a full recovery more quickly. More effective treatment may boost survival rates and minimize the long-term physical and psychological side effects of ARDS for patients and society as a whole. For example, in Germany alone, an estimated 25,000 people are unable to return to work following mechanical ventilation for ARDS[5]. Helping these people back into employment could be hugely beneficial to the individual's wellbeing and may help to ease pressure on social services.

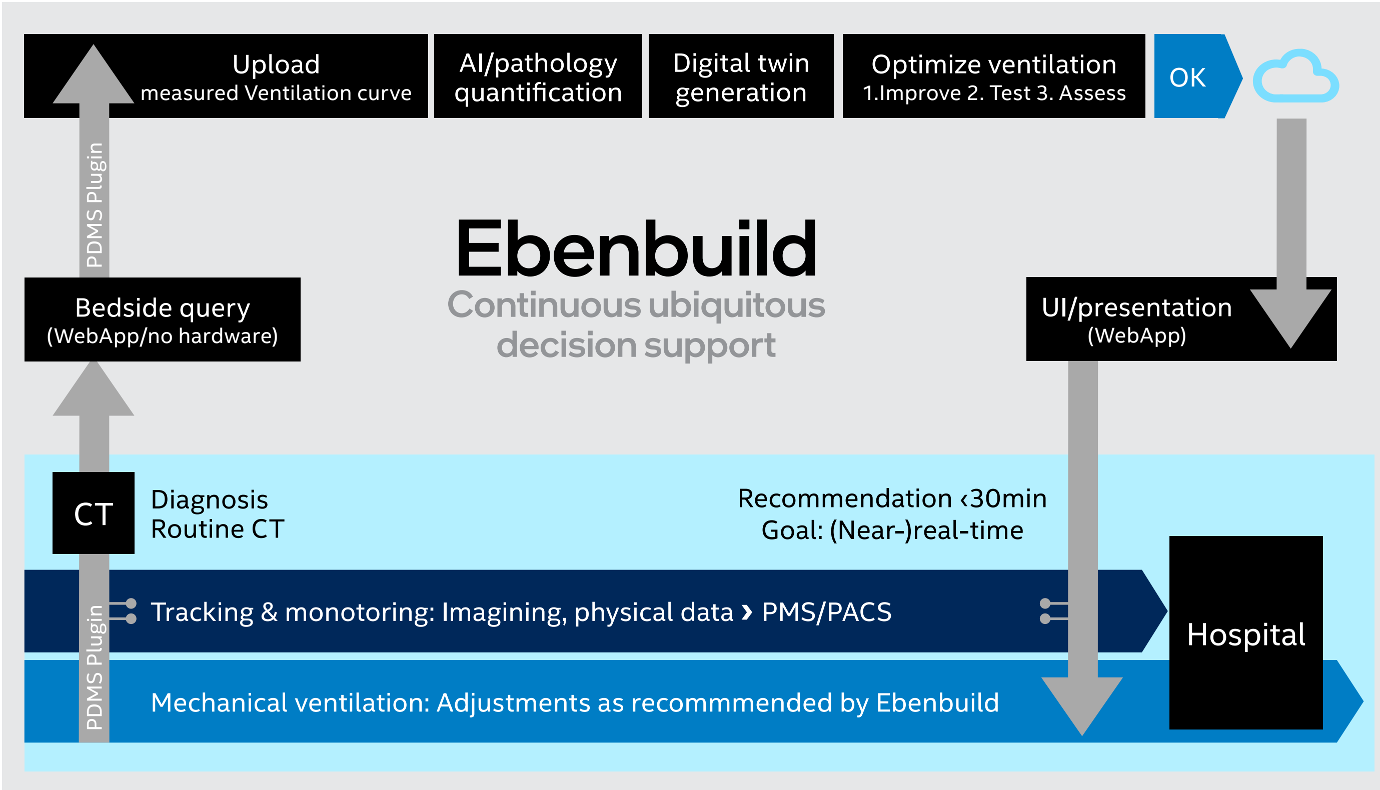

Figure 2. The prototype Ebenbuild solution aims to clinicians with tailored recommendations for mechanical ventilation to support treatment anytime, in any hospital.

Since they would have a picture of the patient's lung, clinical care physicians could carry out ventilation therapy with more confidence. They could work more effectively and more productively and accelerate clinical decision-making. Ebenbuild estimates that doctors could reduce the time taken to set up the ventilator and also minimize the number of ventilator readjustments.

For the healthcare providers, greater efficiency could mean reduced costs. The more effectively physicians can treat an ARDS patient, the faster they may be able to take back mechanical ventilation. Ebenbuild expects that doctors and nurses could reduce the average ventilation period per patient by two to four days, which could translate into acute care cost savings of up to EUR 6,000 per patient[8]. Since healthcare providers in regions like the United States (US) and the European Union (EU) are reimbursed a fixed sum to treat each ARDS patient[9], no matter how long treatment takes, they could use any money left over to treat other patients.

Research program architecture: Personalized digital twin

The Ebenbuild research program runs in the public cloud. Dynamically increasable computing power would enable Ebenbuild to efficiently scale any resulting solution in line with demand—a critical capability, especially during a global pandemic.

Using the Intel® Distribution for OpenVINO™ toolkit, Ebenbuild's developers optimized pre-trained artificial intelligence (AI) inference models to run on Intel® hardware, accelerating performance of the computer vision cluster.

For fast data processing and visualization in the simulation cluster, Ebenbuild used the Intel® Math Kernel Library (Intel® MKL) and Intel C++ Compiler to optimize its application to run on the Intel® Xeon® Platinum 8174 processor.

Confidential Computing, powered by Intel® Software Guard Extensions (Intel® SGX), enables Ebenbuild to process data from multiple sources and transfer it to the cloud without exposing it, even to the cloud administrators.

> "Confidential Computing, running on Intel® Software Guard Extensions, allows us to reassure healthcare providers that the privacy, confidentiality, and integrity of sensitive patient data is maintained."
>
> **Dr. Kei W. Müller,**
> CEO and Co-Founder,
> Ebenbuild

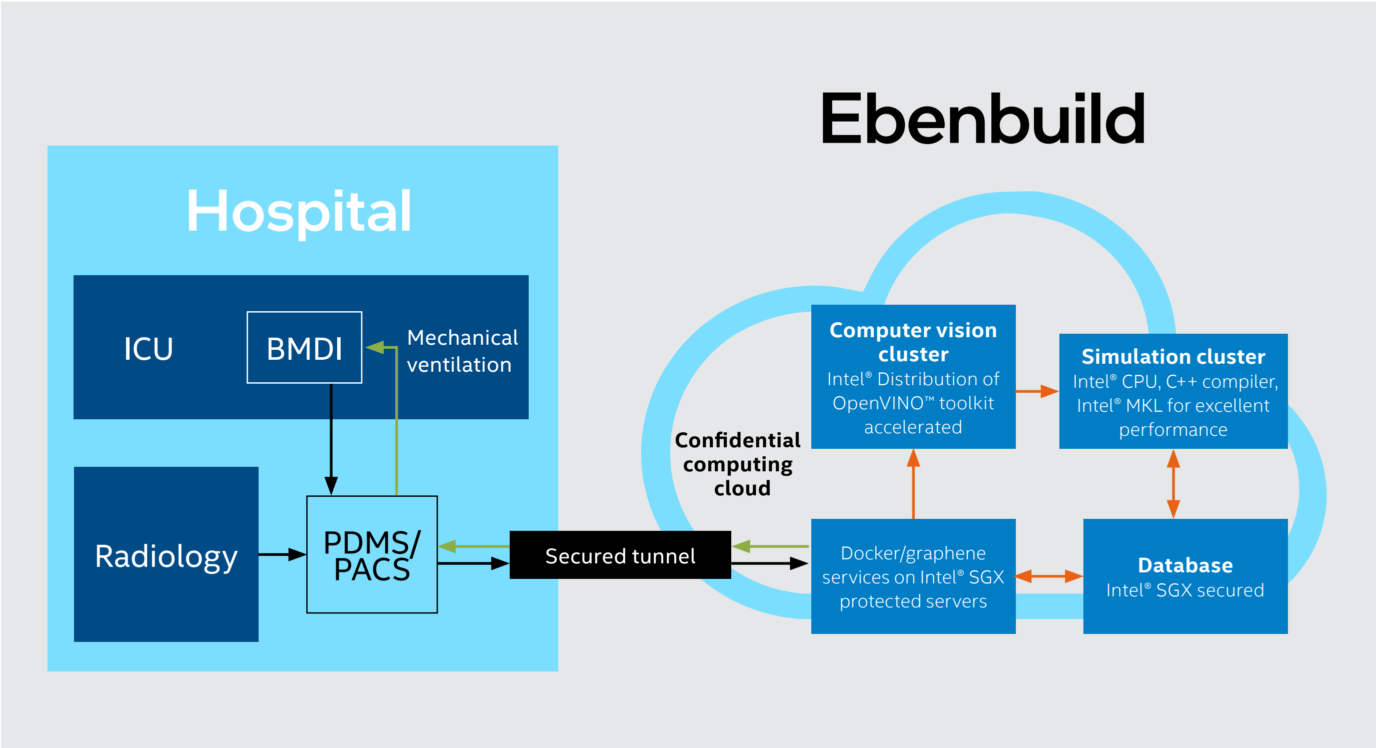

Figure 3. The prototype Ebenbuild software as-a-service (SaaS) solution runs on the public cloud for optimized performance and high scalability.

Finally, Ebenbuild was one of the beneficiaries of Intel's Covid-19 Response and Readiness Initiative. This financial support allowed Ebenbuild to fast track its machine learning research and roll out a test environment for the research program to quantify the potential damage of Covid-19 on the human lung.

Conclusion

Currently the success of mechanical ventilation therapy is dependent on the expertise and experience of the attending clinicians. By providing doctors and nurses with an assessment of a patient's lung condition, Ebenbuild aims to improve the quality and outcome of treatment for patients anytime, in any hospital. Healthcare providers could also benefit from improved efficiency and cost savings.

Ebenbuild will soon be entering clinical trials and is seeking approval from regulatory agencies. It intends to enter the market in mid-2023. Beyond this, the company plans to extend the use of its digital twin research program. Firstly, to cover different applications, such as optimizing pulmonary drug delivery from inhalers and nebulizers. And secondly, for the predictive modeling and visualization of further organs, such as the liver.

Learn More

- **Ebenbuild personalized digital twin**
- **Intel® Distribution of OpenVINO™ toolkit**
- **Intel® Software Guard Extensions (Intel® SGX)**
- **Intel® Xeon® Scalable processors**

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[1] Chronic Obstructive Pulmonary Disease: An Overview: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4106574/#:~:text=Chronic%20obstructive%20pulmonary%20disease%20(COPD,%2C%20cancer%2C%20and%20cerebrovascular%20disease.

[2] Definition and Epidemiology of Acute Respiratory Distress Syndrome: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5537110/

[3] Epidemiology, Patterns of Care, and Mortality for Patients with Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries: https://pubmed.ncbi.nlm.nih.gov/26903337/

[4] Extrapolated from the incidences and calculations given in: Epidemiology of Acute Lung Injury: https://pubmed.ncbi.nlm.nih.gov/12682453/ and Incidence and Outcomes of Acute Lung Injury: https://www.nejm.org/doi/full/10.1056/NEJMoa050333

[5] Long-term Outcome After the Acute Respiratory Distress Syndrome: Different From General Critical Illness? https://pubmed.ncbi.nlm.nih.gov/29189296/

[6] Risk Factors Analysis of COVID-19 Patients with ARDS and Prediction Based on Machine Learning: https://www.nature.com/articles/s41598-021-82492-x

[7] Acute respiratory distress syndrome in mechanically ventilated patients with community-acquired pneumonia: https://erj.ersjournals.com/content/51/3/1702215#:~:text=They%20reported%20that%20ARDS%20occurred,moderate%20and%20severe%20ARDS%2C%20respectively

[8] The average ICU ventilation time for ARDS is around 14-17 days: https://www.nejm.org/doi/full/10.1056/nejmoa050333. A reduction of two to four days (or 12 to 25 percent) has been report for decision support systems for ventilation cases: https://pubmed.ncbi.nlm.nih.gov/32878764/. The incremental cost of ventilation per day is dependent on location but ranges from EUR 1,000-2,000: https://journals.lww.com/ccmjournal/Abstract/2005/06000/Daily_cost_of_an_intensive_care_unit_day__The.13.aspx. Taking the median average cost of EUR1,500, a reduction in the average ICU ventilation period of two to four days equates to up EUR 6,000.

[9] In all major healthcare regions, e.g. the United States (US) or the European Union (EU), treatments are coded, e.g. by means of Operation and Procedure (OPS) codes or (International Classification of Diseases 10th Revision (ICD-10) codes, which are summarized into diagnose-related groups (DRGs). Which procedures (codes) are included in a DRG varies from region to region, but the principle is the same. Reimbursement amounts are calculated based on a list of included coded procedures/ treatments (updated annually) and are fixed to a certain amount. In cases where a patient can be categorized into one or the other DRG, the hospital receives a reimbursement amount.

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