

Ventilator setting in ICUs: comparing a Dutch with a European cohort

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ABSTRACT

Background: From data collected during the third International Study on Mechanical Ventilation (ISMV), we compared data from a Dutch cohort with a European cohort. We hypothesised that tidal volumes were smaller and applied positive end-expiratory pressure (PEEP) was higher in the Netherlands, compared with the European cohort. We also compared use of non-invasive ventilation (NIV) and outcomes in both cohorts.

Methods: A post-hoc analysis of a prospective observational study of patients receiving mechanical ventilation.

Results: Tidal volumes were smaller (7.6 vs. 8.1 ml/kg predicted bodyweight) in the Dutch cohort and applied PEEP was higher (8 vs. 6 cm H₂O). Fewer patients admitted in the Netherlands received NIV as first mode of mechanical ventilation (7.1 vs. 16.7%). Fewer patients in the Dutch cohort developed an ICU-acquired pneumonia (4.5 vs. 12.3%, $p < 0.01$) and sepsis (5.7 vs. 10.9%, $p = 0.03$), but more patients were diagnosed as having delirium (15.8 vs. 4.6%, $p < 0.01$). ICU and in-hospital mortality rates were 19% and 25%, respectively, in Dutch ICUs vs. 26% and 33% in Europe ($p = 0.06$ and 0.03).

Conclusion: Tidal volumes were smaller and applied PEEP was higher in the Dutch cohort compared with international data, but both Dutch and international patients received larger tidal volumes than recommended for prevention or treatment of acute respiratory distress syndrome. NIV as first mode of mechanical ventilation is less commonly used in the Netherlands. The incidence of ICU-acquired pneumonia is lower and of delirium higher in the Netherlands compared with international data.

KEYWORDS

Acute respiratory distress syndrome, mechanical ventilation, outcomes mechanical ventilation, tidal volumes

INTRODUCTION

Mechanical ventilation is a technique with an extensive history. Already in the 16th century, Vesalius described his techniques for keeping an animal alive during examination of its thoracic contents by putting a tube of reed into the trachea whereby air was brought into the lungs.¹ Early mechanical ventilation in humans was described in the 18th century by Hunter, who performed ventilation using bellows to artificially ventilate drowned patients through a tracheostomy.² In the same century, Kite described the technique of endotracheal intubation.³ After a period of negative pressure ventilation, induced by the invention of the iron lung in 1929, Ibsen finally introduced positive pressure ventilation outside the operating theatre in 1952. This development marked the birth of the modern intensive care unit (ICU).^{4,5}

A lot of research has been conducted since then to improve mechanical ventilation, which is common practice now in critically ill patients in ICUs all over the world. This research was important because, in spite of its advantages, it became obvious that mechanical ventilation had considerable disadvantages. An important example of these is a condition observed 50 years ago which is now known as acute respiratory distress syndrome (ARDS).^{6,7} Multiple studies concerning mechanisms of developing ARDS have been

conducted since then, questioning how to prevent patients receiving mechanical ventilation from developing ARDS. No clear recommendations concerning ideal tidal volumes in the prevention of developing ARDS are available, but large tidal volumes seem to be a risk factor whereas the use of lower tidal volumes seems to be beneficial.⁸⁻¹² More is known about how to treat patients with ARDS. Evidence for a strategy of mechanical ventilation with low tidal volumes was delivered in multiple studies, which showed a lower mortality when using a lung protective ventilation strategy.⁹⁻¹⁰ Another important variable in mechanical ventilation is the applied positive end-expiratory pressure (PEEP). A certain level of PEEP is needed to achieve the optimal lung volume at which the alveoli stay open. A low tidal volume prevents damage by limiting the energy transfer into the lungs by forced inspiration.¹¹

In 1998, 2004 and 2010, three large prospective cohort studies were conducted in mechanically ventilated patients in ICUs worldwide, including the Netherlands.^{12,13} The main objectives of these studies were to describe the utilisation of mechanical ventilation and the outcome of mechanically ventilated patients.

Literature about recommended ventilator settings is well known among clinicians in Dutch ICUs. An influential example is the paper written by Lachmann, which maintains that a certain level of PEEP is needed to prevent damage to the alveoli.¹¹ We therefore questioned whether the results from the participating units in the Netherlands differ from the results in other European ICUs or not and if our ventilator settings meet the evidence-based guidelines. Our main hypothesis was that tidal volumes are smaller and applied PEEP is higher in the overall cohort of patients receiving mechanical ventilation in the Netherlands compared with the European cohort. We especially expected to find lung protective mechanical ventilation strategies in the subgroup of patients with ARDS, since an earlier study showed a decline in tidal volumes in these patients and because this strategy was implemented in ICUs in the Netherlands.¹⁴ Furthermore we will describe the use of non-invasive mechanical ventilation (NIV) as first mode of mechanical ventilation, different modes of mechanical ventilation, sedation, and selective digestive decontamination (SDD) and outcomes, including events emerging during mechanical ventilation. We will compare these within the Dutch and European cohorts and discuss similarities and differences.

MATERIALS AND METHODS

Design

A post-hoc analysis of a prospective observational study of patients receiving invasive mechanical ventilation for at least 12 hours or NIV for at least one hour during a

one-month period starting in March 2010 was conducted in 494 ICUs in Europe, USA/Canada, Latin America, Africa, Asia and Oceania. To minimise practice changes in response to observation, only the investigator and research coordinators were aware of the exact aim and timing of the study. The protocol was approved by the research ethics board of each participating institution, which decided there was no need for informed consent.¹³ This article reviews only the results from the participating units from the Netherlands, compared with the results in the European cohort.

Protocol

During the study period, demographic data, daily ventilator variables, gas exchange, clinical management and complications of ventilation were recorded as well as ICU and hospital length of stay and mortality. A more extensive description of study design and protocol can be found in the original article.¹³

Statistical analysis

Data were checked for normal distribution by histogram and, when doubts arose about the normality of the distribution, by Q-Q plot. Data are expressed as median (interquartile range) and absolute and relative frequencies, as appropriate. To compare medians, the Mann-Whitney test was used. For comparing percentages, Fisher's exact test was used. Statistical analyses were performed using SPSS 16.0 and 20.0 (SPSS Inc., Chicago, IL.)

RESULTS

Characteristics of included patients

A total of 196 patients from seven ICUs were included in the Dutch cohort and 3081 patients from 185 ICUs

Table 1. Distribution of number of patients among Dutch ICUs

Hospital	Number of patients (% of total Dutch patients)
Medical Center Leeuwarden	30 (15.3)
Kennemer Gasthuis Haarlem	18 (9.2)
University Medical Centre Maastricht	52 (26.5)
Onze Lieve Vrouwe Gasthuis, Amsterdam	32 (16.3)
VU Medical Center, Amsterdam	30 (15.3)
Medical Center Haaglanden, The Hague and Leidschendam	24 (12.2)
Spaarne Hospital, Hoofddorp	10 (5.1)

in Denmark, France, Germany, Greece, Hungary, Italy, Poland, Portugal, Spain, Sweden and the UK. The distribution of number of patients among Dutch ICUs is shown in *table 1*. The characteristics of the included patients are shown in *table 2*. All characteristics of the Dutch cohort are similar to the European cohort, except for the body mass index, which was lower in the Netherlands, and the admission to the ICU of patients using NIV at home, which was more common in the European cohort.

Management during mechanical ventilation

An overview of the variables related to management of mechanical ventilation is shown in *table 3*.

In the European cohort, use of NIV previous to ICU admission was more common. This also applies to NIV as first mode of mechanical ventilation, which was used in 7.1% of Dutch patients vs. 16.7% in the European cohort ($p < 0.01$). On the first day of mechanical ventilation, 34 patients (17.3%) were hypercapnic ($\text{PaCO}_2 > 48$ mmHg) in

Table 2. Characteristics of included patients			
	The Netherlands	Europe	P-value
Participating units, n	7	185	
Patients included, n	196	3081	
Age, years	66.5 (56-75)	66 (53-76)	0.76
Female sex, n (%)	80 (40.8)	1098 (35.6)	0.15
Weight, kg	78.33 (66-89)	75 (65-85)	0.42
Body mass index, kg/m ²	25.4 (23-28.6)	26.2 (23.9-29.4)	< 0.01
Simplified acute physiology score II on admission, points	45 (34-60)	44 (33-56)	0.26
Noninvasive ventilation at home, n (%)	1 (0.5)	102 (3.3)	0.02
Main reason for mechanical ventilation, n (%)			
Chronic obstructive pulmonary disease	8 (4.1)	180 (5.8)	
Asthma	1 (0.5)	17 (0.6)	
Other chronic pulmonary disease	1 (0.5)	44 (1.4)	
Neurological disease	30 (15.3)	646 (21.0)	
Metabolic, n (% ¹)	4 (13.3)	103 (15.9)	
Overdose/intoxication, n (% ¹)	6 (20.0)	88 (13.6)	
Haemorrhagic stroke, n (% ²)	9 (30.0)	239 (37.0)	
Ischaemic stroke, n (% ²)	2 (6.7)	82 (12.7)	
Brain trauma, n (% ²)	5 (16.7)	102 (15.8)	
Other, n (% ²)	4 (13.3)	27 (4.2)	
Neuromuscular disease	1 (0.5)	26 (0.8)	
Postoperative	63 (32.1)	724 (23.5)	
Pneumonia	20 (10.2)	259 (8.4)	
Community acquired, n (% ³)	14 (70)	173 (67)	
Hospital acquired, n (% ³)	6 (30)	86 (33)	
Sepsis	19 (9.7)	254 (8.2)	
Acute respiratory distress syndrome	2 (1.0)	84 (2.7)	
Congestive heart failure	14 (7.1)	280 (9.1)	
Cardiac arrest	18 (9.2)	195 (6.3)	
Trauma	5 (2.6)	144 (4.7)	
Aspiration	1 (0.5)	83 (2.7)	
Other cause of acute respiratory failure	13 (6.6)	80 (2.6)	
Data are expressed, unless otherwise stated, as median (IQR). P-value < 0.05 is ¹for neurology; ²for pneumonia.			

Table 3. Variables related to management of mechanical ventilation

	The Netherlands	Europe	P-value
NIV before admission in the ICU, n (%)	2 (1.0)	190 (6.2)	< 0.01
NIV at admission in the ICU, n (%)	14 (7.1)	516 (16.7)	< 0.01
Mode of ventilation (% of time)			
A/C	4.1	31.6	
SIMV	0.1	2.7	
SIMV-PS	0.1	5.2	
PS	50.6	23.4	
PCV	13.0	7.4	
APRV/BIPAP	20.4	12.0	
PRVC	8.7	15.3	
CPAP	1.0	1.0	
ASV	1.7	0.8	
Other mode	0.3	0.5	
Ventilator settings over the course of invasive ventilation			
Lung protective ventilation ¹ , n (%)	79 (40)	1089 (35.3)	0.17
Tidal volume, ml/kg PBW	7.6 (6.6-8.6)	8.1 (7.3-9.2)	< 0.01
PEEP, cm H ₂ O	8.0 (6.0-9.5)	6.0 (5.0-8.0)	< 0.01
In patients with ARDS			
Tidal volume, ml/kg PBW	8.6 (7.4-9.7)	7.7 (6.6-8.8)	0.48
PEEP, cm H ₂ O	8.25 (8.0-8.5)	9.4 (7.0-12.1)	0.58
Total respiratory rate, breaths per minute	19 (16-22)	18 (15-20)	< 0.01
Sedation, n (%)	157 (80.1)	2306 (74.8)	0.11
As % of MV-duration	66.7 (21.3-100)	50.0 (0-100)	0.05
Analgesia, n (%)	137 (69.9)	2029 (65.9)	0.28
Neuromuscular blocking, n (%)	14 (7.1)	325 (10.5)	0.15
Liberation from mechanical ventilation met criteria ² , n (%)	187 (95.4)	2703 (87.7)	< 0.01
Scheduled extubation of patients met criteria, n (%)	105 (71.4)	1514 (86.1)	< 0.01
Unplanned extubation (% of patients 'at risk' ³)	42 (28.6)	245 (13.9)	< 0.01
NIV after extubation, n (% ⁴)	2 (1.4)	257 (14.6)	< 0.01
Reintubation (% of patients at risk ⁵)	14 (9.5)	251 (14.3)	0.14
After scheduled extubation	13 (12.4)	202 (13.3)	0.88
After unplanned extubation	1 (2.4)	49 (20.0)	< 0.01
Hours until reintubation	29.5 (10.3-52.5)	25 (6.0-68.0)	0.83
Tracheotomy, n (% of patients at risk ⁶)	15 (7.8)	440 (14.9)	< 0.01
Use of SDD, days per patient	2 (0-5)	0 (0-0)	< 0.01
During MV, days (% of total days with MV)	603 (65.5)	1900 (10.1)	
Days with MV and SDD	2 (0-3)	0 (0-0)	< 0.01
<p>Data are expressed, unless otherwise notated, as median (IQR). MV = mechanical ventilation, SDD = selective digestive decontamination; NIV = non-invasive positive-pressure ventilation; A/C = assist-control; SIMV = synchronised intermittent mandatory ventilation; PS = pressure support; PCV = pressure controlled ventilation; APRV/BIPAP = airway pressure release ventilation/biphasic positive airway pressure; PRVC = pressure regulated volume control; PEEP = positive end-expiratory pressure</p> <p>1: tidal volume below 6 ml/kg predicted body weight (PBW) or tidal volume below 8 ml/kg PBW and plateau or peak inspiratory pressure less than 30 cm H₂O 2: cohort excepting patients with successful NIV, 3: cohort excepting patients with a previous tracheotomy and patients with successful NIV, 5: scheduled and unplanned extubated patients, 4: scheduled and unplanned extubated patients, 6: cohort excepting patients with a previous tracheotomy and patients with successful NIV.</p>			

the Dutch cohort, whereas this percentage was 19.4% in Europe. In the European cohort, assist control was the most used mode of invasive ventilation, followed by pressure support (31.6 and 23.4%). In the Netherlands, pressure support was the most used mode (50.6%), followed by airway pressure release ventilation/biphasic positive airway pressure (20.4%) and pressure controlled ventilation (PCV, 13.0%). In the Netherlands, synchronised intermittent mandatory ventilation (SIMV) and SIMV-pressure support were rarely used (both 0.1% of time during mechanical ventilation), with higher percentages worldwide (2.7 and 5.2% respectively).

Tidal volumes per kilogram predicted bodyweight (PBW) were significantly lower in the Dutch cohort: 7.6 ml/kg vs. 8.1 ml/kg ($p < 0.01$) and applied PEEP was significantly higher (8.0 cm H₂O vs. 6.0 cm H₂O; $p < 0.01$). The proportion of patients receiving a pressure/volume limited ventilation strategy (tidal volume below 6 ml/kg actual body weight or tidal volume below 8 ml/kg actual body weight and peak or plateau inspiratory pressure less than 30 cm H₂O) was comparable in the two cohorts: 40% in the Netherlands vs. 35% in Europe.

In Dutch ICUs the median period on mechanical ventilation was three days, of which the median duration of sedation was two days. These periods were median four ($p < 0.01$) and two ($p = 0.3$) days, respectively, in other European ICUs. The corresponding duration of sedation expressed as a percentage of mechanical ventilation duration was 66.7% in the Netherlands and 50% in the European cohort ($p = 0.05$).

In the Dutch cohort, 95.4% met the criteria for liberation of mechanical ventilation. Of these 71.4% were indeed planned extubations, of which 87.6% successfully. In other European ICUs, a larger percentage (86.1%, $p < 0.01$) of patients who met the criteria were liberated from mechanical ventilation, but the same amount of extubations were successful. Unplanned extubation was more common in the Netherlands (28.6 vs. 13.9%) and was followed by reintubation in 2.4% of the cases in the Netherlands and in 20.0% of the cases in the European cohort. After extubation, 1.4% of the Dutch patients received NIV, versus 14.3% worldwide. When reintubation was necessary, duration until reintubation did not differ between the two cohorts.

Events emerging during mechanical ventilation and mortality

The most common adverse events during mechanical ventilation in the Netherlands were fever (21%) and delirium (16%). In the European cohort, fewer patients developed delirium (5%, $p < 0.001$), but more patients were recorded as having an ICU-acquired pneumonia (9.4%, $p = 0.007$). Expressed as days with ICU-acquired pneumonia per 1000 days of mechanical ventilation,

we found 28 days in the Dutch cohort and 99 days for European ICUs.

The median length of stay in the ICU in the Netherlands was four days (2-8), which was shorter than in the European cohort (six days, $p < 0.01$).

The predicted death rate was 38% for European ICU patients with a standardised mortality ratio (SMR) of 0.66 and 0.82 for ICU and in hospital mortality, respectively. Predicted death rate was 41% for Dutch ICU patients with SMRs of 0.46 and 0.58 for ICU and in hospital mortality. Actual ICU and hospital mortality after ICU admission was lower than predicted in both cohorts and higher in other European ICUs than in the Netherlands (19.4 and 25.0% compared with 25.5 and 32.7% European, $p = 0.06$ and 0.03 respectively). Mortality at day 28 after admission in the ICU was also lower in the Netherlands (18.4 vs. 24.5%, $p = 0.06$).

More detailed information concerning events emerging during mechanical ventilation and mortality can be found in *table 4*.

DISCUSSION

When comparing the study results to our hypothesis, we found that tidal volumes are indeed smaller and applied PEEP is higher in Dutch patients receiving mechanical ventilation. The difference in median tidal volumes is small though, despite its statistical significance. Concerning the median tidal volume in the Dutch cohort, another issue stands out. There is not much evidence for what the optimal tidal volumes in patients without ARDS would be, but a recent Dutch study found less patients with healthy lungs developing ARDS if they received small (6 ml/kg PBW) instead of larger (10 ml/kg PBW) tidal volumes.¹⁵ Considering this outcome, the lower median tidal volume of 7.6 ml/kg PBW in the Dutch cohort still implies a substantial number of patients receiving larger tidal volumes. However, more research has to be done on ARDS-preventing strategies in mechanical ventilation.

In the subgroup of patients with ARDS, both Dutch and European cohorts received larger tidal volumes and applied PEEP was higher when compared with these settings in the overall study population. In both the Dutch and the European cohort tidal volumes are larger than recommended.^{9,16} However, in both cohorts the subgroups of patients with ARDS were very small. Conclusions based on the aforementioned results may therefore be of limited value.

Of interest is the use of NIV in Dutch ICUs, the incidence of which is about 50% lower compared with the use of NIV in the European cohort. NIV is an especially beneficial mode of ventilation for patients with hypercapnic respiratory failure.¹⁷ While there may have been

Table 4. Events emerging over the course of mechanical ventilation and outcomes

	The Netherlands	Worldwide	P-value
Events emerging during mechanical ventilation			
ARDS, n (%)	16 (9.1)	178 (6.5)	0.21
ICU-acquired pneumonia, n (%)	8 (4.5)	329 (12.3)	< 0.01
Sepsis, n (%)	10 (5.7)	290 (10.9)	0.03
Barotrauma, n (%)	1 (0.6)	47 (1.8)	0.36
Renal failure, n (%)	17 (9.7)	224 (8.4)	0.58
Fever, n (%)	42 (23.9)	545 (20.4)	0.29
Delirium, n (%)	31 (15.8)	142 (4.6)	< 0.01
Outcomes			
Duration of ventilatory support, days	3 (2-6)	3 (2-8)	0.04
Length of stay in the ICU, days	4 (2-8)	6 (3-14)	< 0.01
Length of stay in the hospital, days	16 (7-32)	18 (9-34)	0.01
Mortality, n (%)			
In the ICU	38 (19.4)	786 (25.5)	0.06
At day 28 after admission in the ICU	36 (18.4)	756 (24.5)	0.06
In the hospital	48 (25.0)	979 (32.7)	0.03
Data are expressed, unless otherwise notated, as median (IQR). ARDS = acute respiratory distress syndrome; ICU = intensive care unit.			

unaccounted differences between the patients concerned, the percentages of hypercapnia on ICU admission were comparable. While we do not know the considerations of the treating physicians concerning the choice between invasive or non-invasive ventilation, the number of hypercapnic patients would lead us to expect more use of NIV in Dutch ICUs. Not choosing NIV might be related to the presence of contraindications as unconsciousness, airway obstruction, exhaustion, apnoea or excess amounts of sputum. If no contraindications are present, NIV should be considered the first mode of ventilation, because previous studies have shown that NIV can reduce the need for endotracheal intubation, with the associated risk of complications, length of stay in the ICU and hospital and mortality.¹⁸ Also of importance could be the weight Dutch clinicians put on the advantages of invasive mechanical ventilation, including lower work of breathing or more beneficial effects on circulation with higher possible levels of applied PEEP.

Another finding is the difference between the Dutch and European cohorts in the ventilator modes used. In the Netherlands, the most commonly used mode was pressure support, whereas in ICUs in Europe volume-controlled ventilator (VCV) modes are more commonly used. The collected data do not show an explanation for this difference. An obvious explanation would have been the use of sedation, but instead of less sedation we found sedation being more common in patients

receiving mechanical ventilation in the Netherlands. In the literature, little can be found about the benefit or disadvantages of different ventilation modes in critically ill patients. More is known about ventilation modes in patients with ARDS, but still obvious preference exists concerning the mode of ventilation. Patients with ARDS may benefit from PCV when compared with VCV, but this could also have been attributed to severity of illness.¹⁹ The substantial number of patients receiving larger tidal volumes than recommended, as mentioned above, could perhaps be explained by the mode of mechanical ventilation used. As pressure support was more often used in the Netherlands, and with pressure support tidal volumes may vary, it may be more difficult to achieve consistent tidal volumes of 6 ml/kg.

The higher prevalence of delirium in the Netherlands could have contributed to the amount of unplanned extubations, the incidence of which is high compared with both the European cohort and findings in previous literature.²⁰ On the other hand, less of the unplanned extubated patients were reintubated in the Dutch cohort compared with ICUs in Europe. We probably cannot draw any conclusions about this specific event, because of the small size of the Dutch cohort.

When looking at events emerging during mechanical ventilation, some prominent differences become clear. In both cohorts the percentage of patients with renal failure, defined as the need for renal replacement therapy,

was higher than the percentage present in the literature, suggesting a higher severity of illness. However, SAPS II scores at ICU admission were not higher in the Dutch cohort. A large prospective study found 4.2% of the ICU population in need of renal replacement therapy.²¹ Delirium is a common finding in ICU patients, especially when they receive mechanical ventilation. When compared with findings in literature, the percentage of patients with an ICU-acquired delirium in the Dutch cohort is low and in the European cohort even lower.²² It is questionable, however, if all patients with delirium were detected. In a recent study, concerning the Confusion Assessment Method adopted for the ICU (CAM-ICU), this method was found to have a sensitivity of only 47%.²³ The CAM-ICU is a widespread method for defining delirium, also in the Netherlands, and was used in the ICUs in the Dutch cohort. It is therefore likely that in our population not all patients with delirium were detected. We do not know the method for detection of delirium in the other ICUs in Europe. Sedation could have been of influence, because more sedation lowers delirium scores. In this study, we did not find this coincidence; sedation was even slightly more common in the Netherlands. The higher incidence of ICU-acquired pneumonia in the European cohort comes with an obvious less common use of SDD in European countries other than the Netherlands. This matches the findings in a large Cochrane review that showed an overall significant decrease in incidence of respiratory tract infections when SDD was used in patients receiving mechanical ventilation.²³ The difference in degree of SDD administration could also explain at least part of the lower mortality rates in Dutch ICUs, because the aforementioned review also showed a lower mortality rate within cohorts receiving topical and systemic SDD. The difference in mortality is probably not due to a difference in illness, according to the predicted death rates. What exactly caused the different mortality rates cannot be elucidated by this study and it is not possible to determine the share of settings in mechanical ventilation in these differences.

Limitations of the study

In spite of some conspicuous findings, the results of the Dutch cohort discussed in this article might not be completely accurate for common practice in Dutch ICUs. Collection of data was indeed conducted in all ventilated patients during one month, which provides an overview of common practice in ICUs in the Netherlands. However, data were collected in only seven ICUs, which is quite a small number of participating ICUs compared with the total amount of ICUs (about 100) in the Netherlands. Another limitation of the presented data is the moment of collection. This article is based on data collected in 2010, so it is very well possible that ventilator settings in ICUs have changed since then.

CONCLUSION

In this post-hoc analysis of a large international prospective observational trial, we found tidal volumes to be smaller and applied PEEP to be higher in a Dutch cohort compared with data from a European cohort, but both Dutch and international patients received larger tidal volumes than recommended for prevention or treatment of ARDS. NIV as first mode of mechanical ventilation is less commonly used in the Netherlands. The incidence of ICU-acquired pneumonia was lower and the incidence of delirium was higher in the Netherlands compared with international data.

DISCLOSURES

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