



# Economic variations in patterns of care and outcomes of patients receiving invasive mechanical ventilation in China: a national cross-sectional survey

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**Background:** Ventilation practice may be affected by economic variations, which might result in different outcomes to mechanically ventilated patients. We aimed to investigate the important effect of economic variations in patients with mechanical ventilation (MV) in China.

**Methods:** We carried out a national prospective multicentre cross-sectional observational study over 1 month of all patients receiving invasive MV for more than 24 hours in 20 intensive care units (ICUs), including patient characteristics, practice of MV, weaning modalities and outcomes, including probability of weaning and survival. Based on the 2012 World Bank classification of counties, patients were divided into high-income and middle-income groups according to gross domestic product per capita in their province of origin.

**Results:** Of the 483 patients enrolled, 291 (60.2%) were from high-income provinces and 192 (39.8%) were from middle-income provinces. Tidal volume, peak pressure, plateau and driving pressure were significantly lower, and the proportion of patients receiving protective ventilation (71.1% vs. 59.9%,  $P=0.014$ ) was significantly higher in the high-income group than in the middle-income group. The probability of weaning within 28 days was significantly greater in the high-income group than in the middle-income group ( $P=0.046$ ). Patients in the high-income group had significantly higher median numbers of ventilator-free days within 14 and 28 days than those in the middle-income group ( $P<0.05$ ). Although the patients did not differ in terms of their demographics, survival within 28 days was significantly higher in the high-income group than in the middle-income group ( $P=0.025$ ). Driving pressure, positive end-expiratory pressure and spontaneous breathing trial were independently associated with hospital mortality.

**Conclusions:** Important economic differences exist in the management of MV and patient outcomes. Higher income is associated with a higher proportion of protective ventilation, lower driving pressure, shorter weaning and better survival in mechanically ventilated patients in China.

**Keywords:** Respiration, artificial; economics; China; ventilator weaning; in-hospital mortalities

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## Introduction

Mechanical ventilation (MV) is the cornerstone in the supportive management of patients with acute respiratory failure and has been reported to be used in about one-third of patients in intensive care units (1-3). MV did not become widely available in China until the 1980s. Meanwhile, with the rapid development of the country's economy, healthcare system and international communication, the use and patient outcomes of patients with MV have been deeply influenced. However, an imbalanced economic development between the southeast coast and other regions has led to the imbalanced development of healthcare. Important economic variations in patterns of care have been described for the use of interventions such as blood transfusion (4), amputation (5), aneurysm repair (6), carotid revascularization (7), and outcomes of acute respiratory distress syndrome (ARDS) patients (8).

Understanding the economic variations in the management of patients with MV could lead to effective interventions to improve care. However, little information is available about the economic variations in management and outcomes of patients with MV in different provinces of China. Considering that China's economy and medical development are extremely uneven, the hypothesis of the present study is that economic differences between different provinces in China will lead to differences in the management of MV and in patient outcomes. Therefore, we conducted a national observational study to investigate the effect of economic variations on management and outcomes in mechanically ventilated patients in China.

## Methods

### Study design

We report *post hoc* analysis data describing the economic variations of patients with invasive MV from a multicentre observational cohort study in China. The study was a 1-month (August 31, 2012, to September 30, 2012) prospective observational study to describe the implementation of MV and the outcomes of mechanically

ventilated patients in Chinese intensive care units (ICUs). The 1-month period was arbitrarily decided upon by the researchers to enroll more than 400 patients in the 20 participating ICUs. All 20 participating ICUs were closed ICUs in tertiary teaching hospitals in metropolitan cities, managed by full-time ICU doctors. Participating ICUs were selected according to convenience. The protocol was approved by the Institutional Ethics Committee of Zhongda Hospital (the core centre, Approval No. 2012ZD11KY09.0). Informed consent was waived due to the observational nature of the study. The trial was registered at [clinicaltrials.gov](http://clinicaltrials.gov) (NCT01666834).

### Study population

All patients who were admitted to participating ICUs during the study period were screened for eligibility. During the enrolment period, patients who received invasive MV for more than 24 hours were enrolled. We excluded those patients who were younger than 18 years old and who have been invasively ventilated prior to the study.

### Data collection and definitions

Our data surveillance panel was organized by clinical experts to monitor every patient who was admitted to the participating ICUs to ensure that all patients with MV for more than 24 hours were sequentially included in our study. After the researchers had completed the case report form (CRF), an independent monitoring team screened the data of every patient who was admitted to the participating ICU during the study period to avoid missing any patient with MV.

For every enrolled patient, patient characteristics, underlying diseases, severity of illness, causes of MV, weaning process, and patient outcome were recorded. Ventilation settings, breathing patterns, sedative and analgesic were recorded on the first day of MV. Acute Physiology and Chronic Health Evaluation (APACHE) II score was assessed based on the worst variables recorded during the first 24 hours of ICU admission (9). All data

were recorded at 9 a.m. each day, and the mean value of respiratory parameters in one minute was recorded. During assisted-controlled ventilation, plateau pressure and driving pressure analyses were confined to patients ( $n=448$ ) in whom no evidence of spontaneous ventilation was detected (set and measured respiratory rates were equal). Plateau pressure was measured as airway pressure when the inspiratory flow rate was zero. Driving pressure was defined as plateau pressure minus positive end-expiratory pressure (PEEP). Protective ventilation was defined as tidal volume  $\leq 8$  mL/kg of predicted body weight (PBW) and plateau pressure  $\leq 30$  cmH<sub>2</sub>O. Ventilator-free days within 14 and 28 days after enrolment were recorded. If patients died during the 14- or 28-day period after enrolment, the number of ventilator-free days within 14 and 28 days was zero. All-cause ICU mortality, hospital mortality, 28-day mortality, ICU length of stay and hospital length of stay were recorded.

We used the gross domestic product (GDP) per capita in the province where each ICU is located to define high-income and middle-income groups. According to the 2012 World Bank countries classification of high-income countries, patients in the province with a GDP per capita over 12,615 US dollars per year were placed into the high-income group, while those with a GDP per capita between 1,046 to 12,615 US dollars per year were placed into the middle-income group.

Weaning classification was defined as follows: no weaning: comprising patients who never experienced any separation attempt. Short weaning: the first attempt resulted in a termination of the weaning process within 1 day (successful separation or early death). Difficult weaning: the weaning was completed after more than 1 day but in less than one week after the first separation attempt (successful weaning or death). Prolonged weaning: weaning was still not terminated 7 days after the first separation attempt (by success or death) (10). Separation attempt from MV: a spontaneous breathing trial (SBT) with or without extubation, or an extubation directly performed without identified SBT (whatever the type: planned or unplanned extubation) (10). Successful weaning: extubation without death or reintubation within the next 7 days, whichever came first.

### Statistical analysis

Statistical analysis was performed using SPSS 17.0 and STATA 14.1. Data are presented as the median (interquartile range). Continuous variables were compared with the use of

one-way ANOVA or the Mann-Whitney test. Comparisons of proportions were made using Pearson's chi-squared or Fisher's exact tests. Nonparametric fitting was used to show the association between hospital mortality and tidal volume, peak pressure, plateau pressure and driving pressure graphically. Multivariate logistic regression analysis was used to detect the risk factors for hospital survival. Factors found to be significantly different between groups in univariate analysis were included in multivariate logistic regression analysis. Missing data were ignored during analysis. A significant difference was defined as  $P < 0.05$ .

## Results

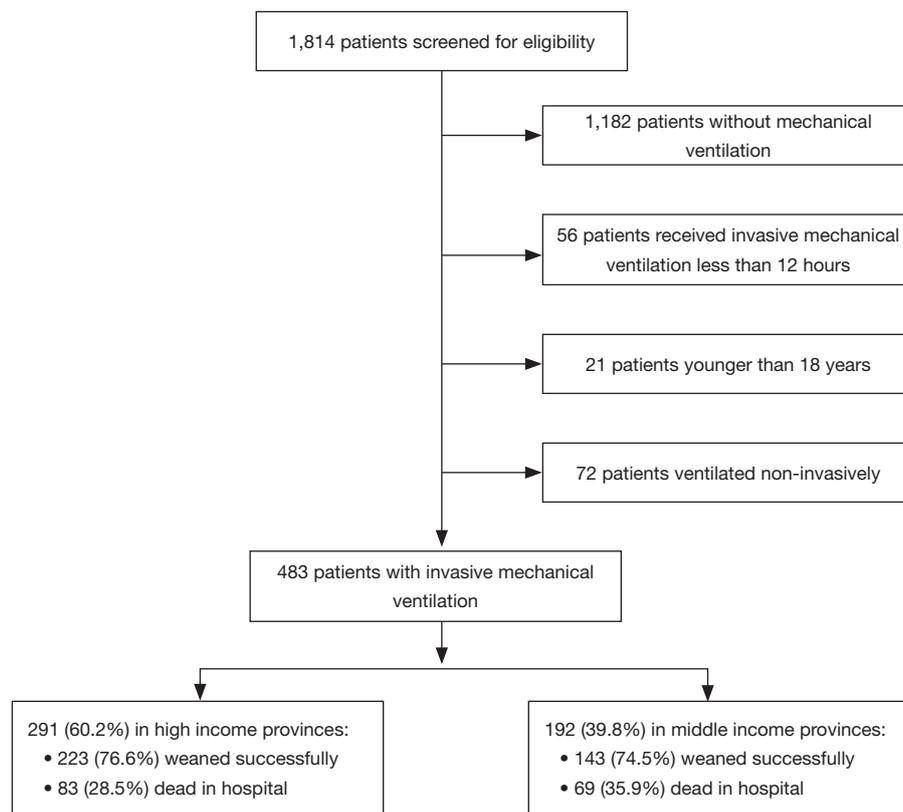
### Participating ICUs and patient characteristics

The doctor/bed ratio and nurse/bed ratio were comparable between ICUs from high-income and middle-income provinces (*Table S1*). Of these 483 participants, 291 (60.2%) were recruited from high-income provinces and 192 (39.8%) from middle-income provinces (*Figure 1*). Age, APACHE II score and comorbidities were not different between the high-income and middle-income groups (*Table S2*). As the causes of MV, ARDS was more common in the high-income group than in the middle-income group; however, coma was more common in the middle-income group than in the high-income group (*Table 1*).

### MV

Synchronized intermittent mandatory ventilation + pressure support ventilation (SIMV + PSV) was the most popular mode used on the first day (385/483, 79.7%). Tidal volume, peak pressure, plateau and driving pressure were significantly lower in the high-income group than in the middle-income group (*Table 2*). The proportion of patients receiving protective ventilation (defined as a tidal volume  $\leq 8$  mL/kg of predicted bodyweight and plateau pressure of  $\leq 30$  cmH<sub>2</sub>O) was higher in the high-income group (71.1%) than in the middle-income group (59.9%) ( $P=0.014$ ) (*Table 2*). After adjusting ARDS and coma at baseline, patients in the high-economic district were more likely to receive lung-protective ventilation [odds ratio (OR) 2.28; 95% CI: 1.51–3.41,  $P < 0.001$ ].

More patients received lower driving pressure ( $< 15$  cmH<sub>2</sub>O) and tidal volume ( $< 6$  mL/kg of PBW) in the high-income group than in the middle-income group (*Figure 2A,B*). As shown in *Figure 2C*, more patients in the



**Figure 1** Flow chart of patient screening and enrolment.

high-income group distributed more in the low plateau pressure ( $P < 0.05$ ). In all mechanically ventilated patients, with the increase of peak pressure, plateau pressure and driving pressure, hospital mortality gradually increased. However, the tidal volume within the 6–8 mL/kg of PBW was associated with the lowest hospital mortality (Figure S1).

### **Analgesia and sedation**

The proportion of patients receiving analgesic, sedative, or both did not differ significantly between groups (Table 2). The ratio of midazolam application was much higher in the middle-income group than in the high-income group (Table S3). Daily interruption of sedatives was significantly more common in the high-income group than in the middle-income group (Table 2).

### **Liberation from MV**

Short weaning was more common and prolonged weaning

was less common in the high-income group than in the middle-income group ( $P < 0.05$ , Figure 2D). Kaplan-Meier analyses showed that the probability of weaning was greater in the high-income group than in the middle-income group ( $P = 0.046$ , Figure 3A). Compared with patients in the middle-income group, those in the high-income group had significantly higher median numbers of ventilator-free days within 14 and 28 days (Table 3). Multivariate logistic regression showed that SBT was an independent protection factor associated with hospital mortality (Table 3).

### **Outcomes**

Twenty-eight-day survival was higher in the high-income group than in the middle-income group ( $P = 0.025$ , Figure 3B). However, hospital mortality did not differ between the high-income group (28.5%) and the middle-income group (35.9%,  $P = 0.086$ ). Length of stay in the ICU and in the hospital were comparable between the two groups (Table 3). Univariate analysis showed that patient-level variables associated with hospital

**Table 1** Baseline characteristics and causes of mechanical ventilation

Variables	All (n=483)	High-income (n=291)	Middle-income (n=192)	P value
Age (years)	64.0 (51.0–76.0)	63.0 (50.0–76.0)	64.0 (54.2–75.0)	0.550
Sex (male)	341 (70.6)	206 (70.8)	135 (70.3)	0.910
High (cm)	170.0 (162.0–173.0)	170.0 (163.0–173.0)	168.0 (162.0–173.0)	0.458
Real body weight (kg)	65.0 (60.0–71.5)	66.0 (6.0–72.0)	65.0 (60.0–72.0)	0.117
Predicted body weight (kg)	66.0 (56.9–68.8)	66.0 (56.9–68.8)	64.2 (54.2–68.5)	0.545
APACHE II	19.0 (11.0–25.0)	19.0 (11.0–24.0)	19.0 (11.0–26.0)	0.674
Causes of mechanical ventilation				
Postoperative	150 (31.1)	89 (30.6)	61 (31.8)	0.783
ARDS	135 (28.0)	92 (31.6)	43 (22.4)	0.030
Coma	82 (17.0)	38 (13.1)	44 (22.9)	0.005
Sever sepsis/septic shock	33 (6.8)	20 (6.9)	13 (6.8)	0.965
Pneumonia	27 (5.6)	17 (5.8)	10 (5.2)	0.689
AECOPD	25 (5.2)	16 (5.5)	9 (4.7)	0.694
Congestive heart failure	20 (4.1)	15 (5.2)	5 (2.6)	0.243
Neuromuscular diseases	2 (0.4)	1 (0.3)	1 (0.5)	0.096
Others	9 (1.9)	3 (1.0)	6 (3.1)	0.767

Data are median (IQR) or number (%). APACHE II, Acute Physiology and Chronic Health Evaluation II; AECOPD, acute exacerbation of chronic obstructive pulmonary disease; ARDS, acute respiratory distress syndrome; IQR, interquartile range.

mortality included age, SBT, daily interruption of sedation, the first day of APACHE II, PEEP, tidal volume, plateau pressure, peak pressure, driving pressure, lactic acid, and partial pressure of oxygen to fraction of inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$ ). PEEP was independently associated with in-hospital mortality. PEEP was also correlated with  $\text{PaO}_2/\text{FiO}_2$  ( $r=-0.309$ , 95% CI:  $-0.380$  to  $-0.232$ ,  $P<0.001$ ) and APACHE II score ( $r=0.133$ , 95% CI:  $0.051-0.219$ ,  $P=0.003$ ). Driving pressure, PEEP and SBT were independently associated with in-hospital mortality (Table 4).

## Discussion

In this prospective cross-sectional study, we noted important differences in the management of MV and patient outcomes according to economic variation in China. Patients from high-income provinces had lower tidal volume, plateau and driving pressures; a higher proportion of receiving protective ventilation; shorter weaning; and better survival in the 28 days. This information will help to improve the management of MV, especially in middle-income provinces.

## Patient characteristics and outcomes

We found a somewhat lower proportion of mechanically ventilated patients in ICUs and hospital mortality in this study than in the global data. A system analysis of 18,302 patients from 927 ICUs showed a ventilation rate of 35% in ICU patients and a hospital mortality of 35% in 2010 (3). In the present study, 26.6% of patients received invasive MV and the hospital mortality was 28.5%. However, another survey by Du *et al.* showed a high invasive ventilation rate (68.8%) in patients admitted to 22 Chinese ICUs (11). The most likely explanation is the difference in enrolment criteria and participating ICUs between the two surveys. However, the initial APACHE II scores were comparable (19 vs. 18), which suggests that severity of illness might not be the main reason for the difference between the two Chinese surveys. We found a similar constituent ratio of the main reason for MV between this study and others (1-3), and postoperative respiratory support was the most common reason for invasive MV.

Although patients from high-income and middle-income provinces did not differ in terms of demographics, survival

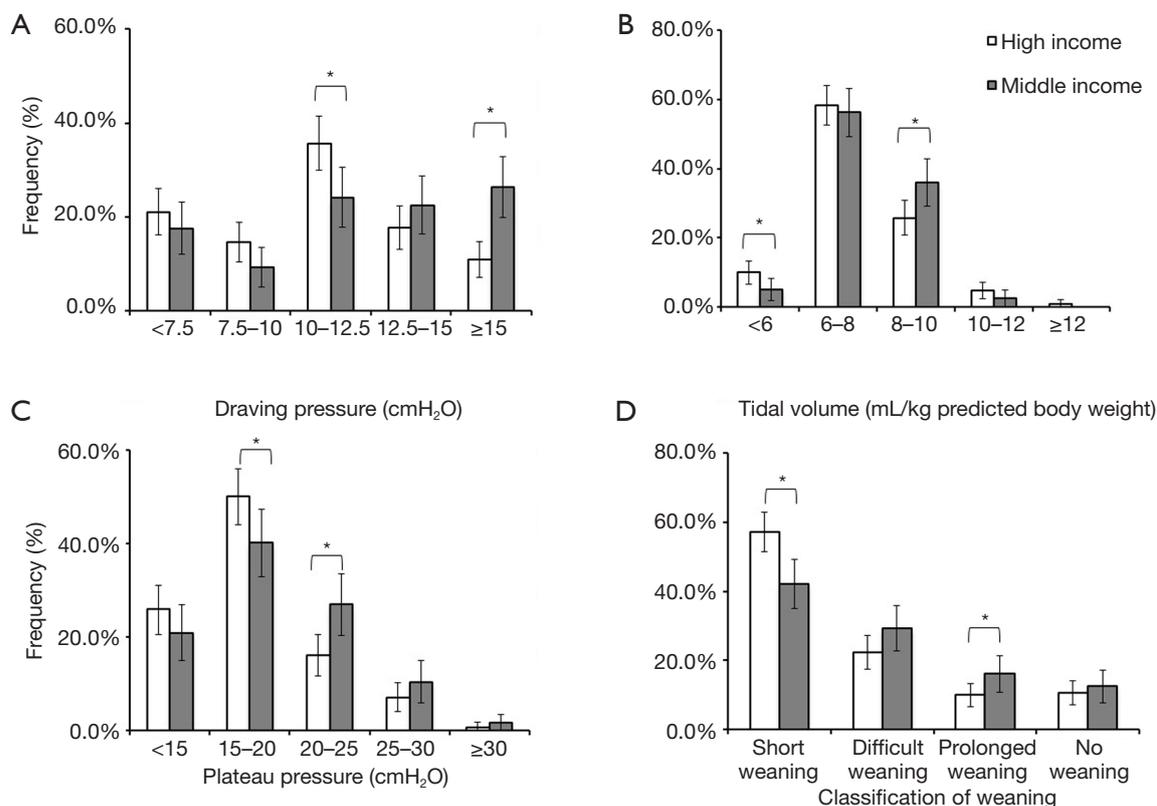
**Table 2** Management of mechanical ventilation of patients with invasive mechanical ventilation

Variables	All (n=483)	High-income (n=291)	Middle-income (n=192)	P value
Ventilation mode				
SIMV + PS	385 (79.7)	235 (80.8)	150 (78.1)	0.482
VCV	7 (1.4)	4 (1.4)	3 (1.6)	1.000
PCV	24 (5.0)	20 (6.9)	4 (2.1)	0.018
BIPAP	28 (5.8)	7 (2.4)	21 (10.9)	0.000
PSV	12 (2.5)	10 (3.4)	2 (1.0)	0.136
Other modes	29 (6.0)	18 (6.2)	11 (5.7)	0.836
Recruitment maneuver	58 (12.0)	30 (10.3)	28 (14.5)	0.157
Breathing patterns				
PEEP (cmH <sub>2</sub> O)	5.0 (5.0–6.0)	5.0 (5.0–7.0)	5.0 (5.0–6.0)	0.543
FiO <sub>2</sub>	0.4 (0.4–0.5)	0.4 (0.4–0.5)	0.4 (0.4–0.5)	0.154
Tidal volume (mL/kg PBW)	7.4 (6.7–8.5)	7.3 (6.7–8.3)	7.7 (6.7–8.9)	0.016
RR (breath/min)	17.0 (15.0–20.0)	17.0 (15.0–20.0)	18.0 (15.0–20.0)	0.857
Ti (second)	1.0 (1.0–1.2)	1.0 (1.0–1.2)	1.0 (1.0–1.3)	0.948
Peak pressure (cmH <sub>2</sub> O)	21.0 (18.0–25.0)	20.0 (18.0–25.0)	22.0 (19.0–28.0)	0.000
Plateau pressure (cmH <sub>2</sub> O)	17.0 (15.0–20.0)	16.0 (15.0–19.0)	18.0 (15.0–20.0)	0.041
Driving pressure (cmH <sub>2</sub> O)	11.0 (8.0–14.0)	11.0 (8.0–13.0)	12.0 (9.0–15.0)	0.045
Receiving protective ventilation <sup>a</sup>	314 (65.0)	207 (71.1)	115 (59.9)	0.014
Sedative	368 (76.2)	219 (75.3)	149 (77.6)	0.553
Analgesic	289 (59.8)	175 (60.1)	114 (59.4)	0.867
Both analgesic and sedative	267 (55.3)	158 (54.3)	109 (56.8)	0.592
Daily interruption of sedation	276 (57.1)	188 (64.6)	88 (45.8)	<0.001
Extubation with SBT	290 (60.0)	184 (63.2)	106 (55.2)	0.078
T piece	142 (29.4)	98 (33.7)	44 (22.9)	0.011
PSV	124 (25.7)	72 (24.7)	52 (27.1)	0.564
CPAP	24 (5.0)	14 (4.8)	10 (5.2)	0.844

Data are median (IQR) or number (%). <sup>a</sup>, tidal volume  $\leq 8$  mL/kg of predicted bodyweight and plateau pressure  $\leq 30$  cmH<sub>2</sub>O. SIMV + PS, synchronized intermittent mandatory ventilation + pressure support ventilation; VCV, volume control ventilation; PCV, pressure support ventilation; BIPAP, bi-level airway pressure ventilation; PSV, pressure support ventilation; PEEP, positive end expiratory pressure; FiO<sub>2</sub>, fraction of inspired oxygen; PBW, predicted body weight; RR, respiratory rate; Ti, inspiratory time; SBT, spontaneous breathing trial; NIV, non-invasive mechanical ventilation; SBT, spontaneous breathing trial; IQR, interquartile range.

within the 28 days was significantly higher in the high-income group than in the middle-income group. Given the comparable ratio of doctors/beds and nurses/beds between the two groups, the shortage of human resources might not be the main reason of the worse survival rate among patients from middle-income provinces when compared

with those from high-income provinces. Although in terms of causes of MV, ARDS was more common in the high-income group and coma was more common in the middle-income group, this difference still cannot be a reasonable explanation for the difference in survival between groups. Part of the potential explanation for that difference might



**Figure 2** Driving pressure (A), tidal volume (B), plateau pressure (C), and classification of weaning (D), by income. Error bars represent 95% CIs; \*,  $P < 0.05$ . No weaning: comprising patients who never experienced any separation attempt. Short weaning: the first attempt resulted in a termination of the weaning process within 1 day (successful separation or early death). Difficult weaning: the weaning was completed after more than 1 day but less than 1 week after the first separation attempt (successful weaning or death). Prolonged weaning: weaning was not terminated 7 days after the first separation attempt (by success or death).

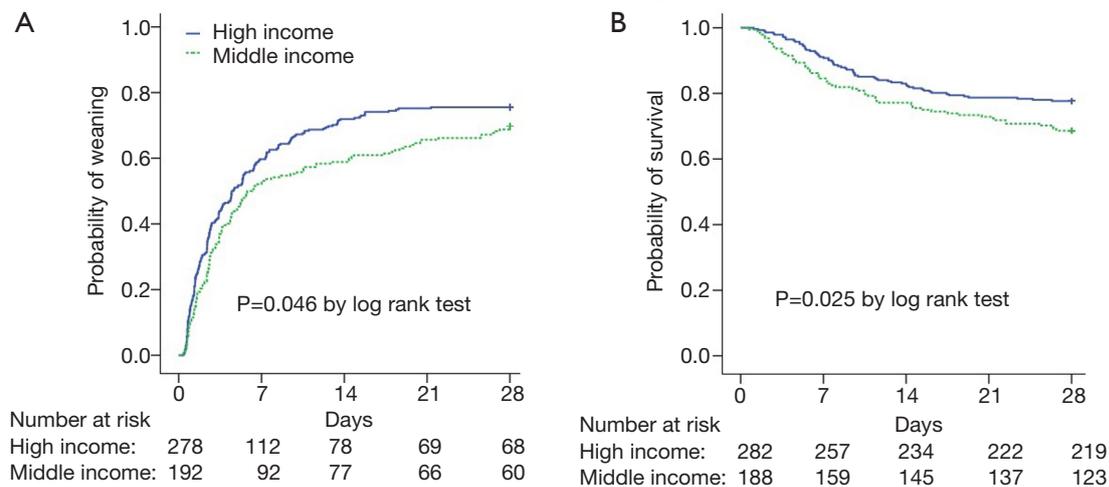
include differences in practices of MV and weaning from ventilation between groups. Other potential explanations might be differences in continuation of further life support care, as the family might not be able to afford the high costs. This might be more prevalent in the middle-income group when compared with the high-income group. However, the present study did not record the withholding and withdrawing populations.

### Management during MV

High-income provinces had a higher proportion of patients receiving protective ventilation (defined as a tidal volume  $\leq 8$  mL/kg of PBW and plateau pressure of  $\leq 30$  cmH<sub>2</sub>O) than middle-income provinces. This might be one of the potential explanations for the better survival of patients from high-income provinces. Tidal volume was

the essential component of lung-protective ventilatory strategies, and low tidal volume may be important in patients with ARDS (12). However, in patients without ARDS, the benefits of low tidal volume remain controversial (13-15). We found that when compared with a tidal volume of 6-8 mL/kg, a higher tidal volume was associated with a worse outcome. The higher tidal volume in the middle-income group than in the high-income group was a potential explanation of the lower survival in the middle-income group.

Higher driving pressure has been associated with poor outcomes in ARDS patients (16). However, driving pressure, which is an attractive method of setting tidal volume, requires normalization to the patient's respiratory system compliance and was questioned in the cohort of patients without ARDS. Within the limits of the ventilatory setting normally used by clinicians, driving pressure was not



**Figure 3** Kaplan-Meier curves of probability of weaning from mechanical ventilation (A) and hospital survival (B), by income. Patients discharged before day 28 were assumed to be alive and off invasive mechanical ventilation on that day.

**Table 3** Outcomes of patients with invasive mechanical ventilation

Outcomes	All (n=483)	High-income (n=291)	Middle-income (n=192)	P value
Successful weaning	366 (75.6)	223 (76.6)	143 (74.5)	0.589
Classification of weaning				
Short weaning	247 (51.1)	166 (57.0)	81 (42.2)	0.001
Difficult weaning	121 (25.1)	65 (22.3)	56 (29.2)	0.107
Prolonged weaning	60 (12.4)	29 (10.0)	31 (16.1)	0.044
No weaning	55 (11.4)	31 (10.7)	24 (12.5)	0.664
Preventative NIV after extubation	33 (6.8)	16 (5.5)	17 (8.9)	0.153
Tracheostomy	45 (9.3)	25 (8.6)	20 (10.4)	0.499
Ventilator-free days, day 14 (days)	8.6 (0–12.1)	8.8 (0–12.3)	8.0 (0–11.6)	0.046
Ventilator-free days, day 28 (days)	22.3 (0–26.1)	22.6 (0–26.2)	21.2 (0–25.6)	0.020
Length of stay in ICU (days)	22.3 (0–26.1)	5.8 (2.5–10.6)	5.7 (2.5–11.4)	0.791
Length of stay in hospital (days)	16.3 (8.2–28.4)	16.4 (9.2–26.9)	15.4 (6.7–29.8)	0.821
ICU mortality	118 (24.4)	70 (24.1)	48 (25.0)	0.813
28-day mortality	123 (25.5)	64 (22.0)	59 (30.7)	0.031
Hospital mortality	152 (31.5)	83 (28.5)	69 (35.9)	0.086

Data are median (IQR) or number (%). No weaning: comprising patients who never experienced any separation attempt. Short weaning: the first attempt resulted in a termination of the weaning process within one day (successful separation or early death). Difficult weaning: the weaning was completed after more than one day but in less than one week after the first separation attempt (successful weaning or death). Prolonged weaning: weaning was still not terminated 7 days after the first separation attempt (by success or death). ICU, intensive care unit; IQR, interquartile range; NIV, non-invasive mechanical ventilation.

**Table 4** Factors associated with hospital mortality (n=448)

Factors	Univariate analysis		Multivariate logistic regression analysis	
	Odds ratio (95% confidence interval)	P value	Odds ratio (95% confidence interval)	P value
Gender <sup>b</sup>	0.751 (0.487–1.159)	0.196	0.911 (0.497–1.667)	0.076
Age <sup>b</sup>	1.014 (1.002–1.027)	0.016	1.013 (0.998–1.030)	0.092
The first day of APACHE II <sup>a</sup>	1.094 (1.067–1.122)	<0.001	1.029 (0.996–1.065)	0.087
Daily interruption of sedation <sup>a</sup>	0.430 (0.285–0.642)	<0.001	0.715 (0.403–1.271)	0.254
PEEP (cmH <sub>2</sub> O) <sup>a</sup>	1.186 (1.086–1.294)	<0.001	1.280 (1.132–1.447)	<0.001 <sup>b</sup>
Tidal volume (mL/kg PBW) <sup>a</sup>				
<6	2.827 (1.395–5.726)	0.004	1.957 (0.795–4.814)	0.144
6–8	1.000 (reference)	–	1.000 (reference)	–
8–10	1.700 (1.080–2.676)	0.022	1.433 (0.788–2.606)	0.238
>10	2.424 (1.104–5.322)	0.027	2.276 (0.747–6.937)	0.148
Plateau pressure (cmH <sub>2</sub> O)	1.123 (1.073–1.176)	<0.001	–	–
Peak pressure (cmH <sub>2</sub> O)	1.083 (1.042–1.127)	<0.001	–	–
Driving pressure (cmH <sub>2</sub> O) <sup>a</sup>	1.065 (1.021–1.111)	0.003	1.084 (1.019–1.153)	0.010 <sup>b</sup>
Blood gas				
pH	0.902 (0.484–1.681)	0.745	–	–
HCO <sub>3</sub> <sup>-a</sup>	0.960 (0.924–0.997)	0.034	0.977 (0.938–1.019)	0.285
Lac <sup>a</sup>	1.093 (1.016–1.176)	0.017	1.045 (0.989–1.105)	0.115
PaO <sub>2</sub>	0.996 (0.992–1.000)	0.077	–	–
PaCO <sub>2</sub>	0.996 (0.976–1.017)	0.714	–	–
PaO <sub>2</sub> /FiO <sub>2</sub> <sup>a</sup>	0.997 (0.996–0.999)	0.002	1.001 (0.999–1.004)	0.278
SBT <sup>a</sup>	0.086 (0.053–0.138)	<0.001	0.118 (0.067–0.206)	<0.001 <sup>b</sup>

<sup>a</sup>, the variables placed in the multivariate logistic regression model; <sup>b</sup>, the significant variables selected by the stepwise method in the multivariate logistic regression. APACHE II, Acute Physiology and Chronic Health Evaluation II; PEEP, positive end expiratory pressure; PBW, predicted body weight; SBT, spontaneous breathing trial; HCO<sub>3</sub><sup>-</sup>, bicarbonate; Lac, lactic acid.

associated with hospital mortality (17). In a heterogeneous population or cohort of patients with MV (28.0% patients with ARDS), we found an association between driving pressure and hospital mortality. Our data supported the idea of altering the mechanical scenario to decrease the driving pressure even in heterogeneous patients (18).

Since the main cause of MV was postoperative respiratory support in the present study, it was no surprise that patients received uniform physiological levels of PEEP in both groups. PEEP is an essential component of lung-protective ventilatory strategies not only in ARDS patients but also in other patients with MV. Observational studies have reported an independent association between

zero PEEP and mortality in a heterogeneous cohort of mechanically ventilated patients (19). In the present study, we found that PEEP was an independent risk factor for hospital mortality. Although high PEEP may cause harm if not necessary, the negative correlation between PEEP and PaO<sub>2</sub>/FiO<sub>2</sub> and the positive correlation between PEEP and the APACHE II score in the present study might suggest that patients with a severe disease and poor oxygenation are more likely to receive higher PEEP.

#### *Analgesia, sedation and liberation from MV*

Patients from high-income provinces had higher numbers

of ventilator-free days within 14 and 28 days and a higher probability of weaning within 28 days than those from middle-income provinces. SBT has been considered an essential step for the decision to extubate (20-23). We found an independent association between SBT and hospital mortality, which suggests that differences in weaning practice partly explained the effect of income on weaning duration. The implementation of sedative and analgesia largely affects weaning duration (24-26). Daily interruption of sedation might relieve continuous deep sedation and decrease the duration of MV (27). The potential explanations of the more common short weaning in patients from high-income provinces include the higher proportion of daily interruption of sedatives than those in patients from middle-income provinces. Other potential explanations included the lower frequency of midazolam used in the high-income group than in the middle-income group. Short weaning has been associated with better outcomes (10); this was another potential explanation of the higher survival rate within the 28 days in patients from high-income provinces. We also found that the proportion of prolonged weaning was higher in patients from the middle-income group; however, the proportion of successful weaning was comparable between groups. These findings implied the delayed weaning in patients from middle-income provinces.

With the exception of 55 (11.4%) patients who never experienced any separation attempt, we classified patients into short, difficult and prolonged weaning based on weaning duration according to the WIND study (10). Our data suggest that the three groups have different weaning outcomes and mortality. Consistent with previous reports, we found that most patients were in the short weaning group, and patients in the prolonged group had the worst survival in 28 days.

Analgesia and sedation are important components of care for the invasive mechanically ventilated patients in the ICU. It is vital to remember that protocols attempting to minimize sedation must first acknowledge the need for adequate pain control (28-30). Consistent with other studies (31,32), we found that only 59.8% of patients with MV received analgesic (no difference between high-income and middle-income groups). Measures to improve the insufficient application of analgesic should be taken in ICUs in China.

### **Limitations**

Our study has several limitations. First, our cohort is a

convenience sample from 20 participating ICUs from nine provinces and therefore might not be representative of actual clinical practice in ICUs in China. Thus, our results could be biased, particularly where specific types of ICUs (e.g., academic ICUs) might be over-represented. Second, the research period (summer) was arbitrarily chosen, which could introduce bias when extrapolating the results to a whole year. However, another study showed that age, severity, the proportion of MV and mortality were not subject to seasonal effects (33). Third, because we only recorded the ventilator parameters during the early phase of MV, the present study was unable to show the graph of the entire MV process and comparison between groups. Fourth, it might not be appropriate to classify groups according to the high and middle incomes of each province in one county according to the 2012 World Bank country classification by GDP per capita. Fifth, inspiration occlusions were not used during the measurement of plateau pressure and driving pressure, and thus the absolute value of the plateau pressure and driving pressure might be slightly overestimated.

### **Conclusions**

This prospective cross-sectional study showed important economic differences in the practice of MV and weaning and in patient outcomes in China. Higher income was associated with a higher proportion of protective ventilation, shorter weaning and better survival in patients with MV. These findings may serve as a current benchmark of the usual care and outcomes of patients with MV in provinces with different income levels in China. They may also indicate a potential for improvement in patient management.

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### Footnote

**Conflicts of Interest:** The authors have no conflicts of interest to declare.

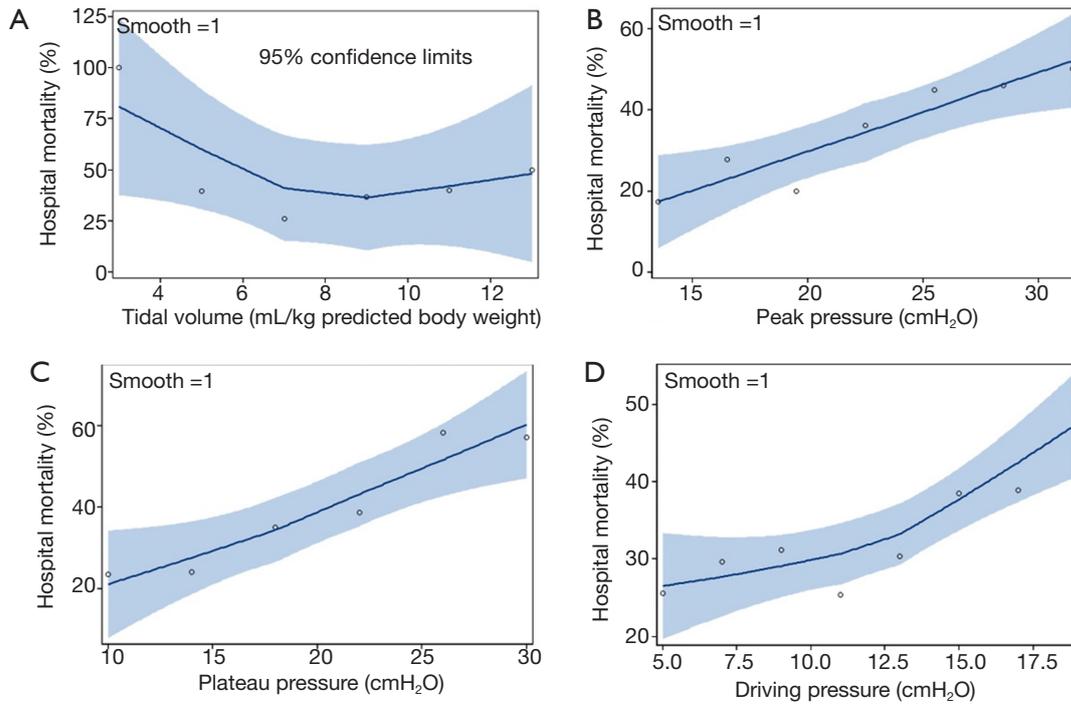
**Ethical Statement:** The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The protocol was approved by the Institutional Ethics Committee of Zhongda Hospital (the core centre, Approval No. 2012ZD11KY09.0).

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**Figure S1** Graphically depiction of the association between hospital mortality and tidal volume (A), peak airway pressure (B), airway platform pressure (C), and driving pressure (D).

**Table S1** Characteristics of participating intensive care unites

Characteristic	All ICUs (n=20)	ICUs from high-income province (n=12)	ICUs from middle-income province (n=8)	P value
University affiliated hospital	16 (80.0)	9 (75.0)	7 (87.5)	0.494
General ICU, n (%)	19 (95.0)	11 (91.7)	8 (100.0)	0.402
Surgical ICU, n (%)	1 (5.0)	1 (8.3)	0 (0)	0.402
Number of ICU beds, n	25 [18–36]	23 [16–36]	25 [18–38]	0.412
Accounting for all hospital beds, %	1.6 (1.1–2.1)	1.7 (1.3–2.4)	1.1 (0.7–1.8)	0.990
Doctor/bed ratio	0.7 (0.5–0.8)	0.7 (0.6–0.8)	0.6 (0.5–0.8)	0.244
Nurse/bed ratio	2.0 (2.0–2.5)	2.0 (2.0–2.5)	2.1 (1.7–2.5)	0.793

Data are median (IQR) or number (%). ICU, intensive care units.

**Table S2** Comorbidities of patients with invasive mechanical ventilation

Comorbidities	All (n=483)	High-income (n=291)	Middle-income (n=192)	P value
Respiratory system				
Smoke	122 (25.3)	70 (24.1)	54 (28.1)	0.339
COPD	26 (5.4)	16 (5.5)	10 (5.2)	1.000
Asthma	8 (1.7)	5 (1.7)	3 (1.6)	1.000
Tumor	9 (1.9)	6 (2.1)	3 (1.6)	0.748
Pulmonary tuberculosis	22 (4.6)	14 (4.8)	8 (4.2)	0.826
Cardiovascular system				
Coronary artery disease	90 (18.6)	58 (19.9)	32 (16.7)	0.367
Hypertension	193 (40.0)	112 (38.5)	81 (42.2)	0.417
Chronic cardiac dysfunction	37 (7.7)	21 (7.2)	16 (8.3)	0.644
History of PCI	26 (5.4)	16 (5.5)	10 (5.2)	0.901
History of cardiosurgery	8 (1.7)	5 (1.7)	3 (1.6)	1000
Diabetes	104 (21.5)	64 (22.0)	40 (20.8)	0.762
Urinary system				
Chronic kidney dysfunction	29 (6.0)	18 (6.2)	12 (6.3)	0.977
Hemodialysis	13 (2.7)	8 (2.7)	5 (2.6)	0.931
Nervous system				
Stroke	73 (15.1)	43 (14.8)	30 (15.6)	0.799
lying in bed $\geq$ 3 months	23 (4.8)	14 (4.8)	9 (4.7)	0.950
Digestive system				
Cirrhosis	8 (1.7)	4 (1.4)	4 (2.1)	0.719
Intestinal obstruction	18 (3.7)	10 (3.4)	8 (4.2)	0.678
Immune system dysfunction	20 (4.1)	13 (4.5)	7 (3.6)	0.657

Data are number (%). APACHE II, Acute Physiology and Chronic Health Evaluation II; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention.

**Table S3** Sedative and analgesic in patients with invasive mechanical ventilation

Sedative and analgesic	All (n=483)	High-income (n=291)	Middle-income (n=192)	P value
Propofol	225 (46.6)	138 (47.4)	87 (45.3)	0.649
Midazolam	94 (19.5)	46 (15.8)	48 (25.0)	0.013
Diazepam	3 (0.6)	2 (0.7)	1 (0.5)	1.000
Dexmedetomidine	121 (25.1)	72 (24.7)	49 (25.5)	0.847
Morphine	142 (29.4)	82 (28.2)	60 (31.3)	0.468
Fentanyl	81 (16.8)	49 (16.8)	32 (16.7)	0.961
Remifentanyl	57 (11.8)	41 (14.1)	16 (8.3)	0.055
Sufentanyl	1 (0.2)	1 (0.3)	0 (0)	1.000