Epidemiology of weaning outcome according to a new definition.

The WIND study

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At a Glance Commentary

Scientific Knowledge on the Subject:

Despite the importance of the weaning period during mechanical ventilation, our knowledge of the separation process from mechanical ventilation as it is currently performed and the complications associated with its prolongation are poorly described.

What This Study Adds to the Field:

The WIND classification is based on the duration of ventilation after the first separation attempt. This classification shows that prolongation of weaning have a direct and immediate impact on morbidity and mortality, by contrast with previous reports using the International Consensus Conference classification. The first separation attempt is a major milestone, and each additional day without a weaning success after this first attempt is associated with an increased crude mortality.

Abstract

Rationale:

The weaning process concerns all patients receiving mechanical ventilation. A previous classification into simple, prolonged and difficult weaning ignored weaning failure and presupposed the use of spontaneous breathing trials.

Objectives:

To describe the weaning process defined as starting with any attempt at separation from mechanical ventilation and its prognosis, according to a new operational classification working for all patients under ventilation.

Methods:

Multinational prospective multicenter observational study over three months of all patients receiving mechanical ventilation in 36 intensive care units, with daily collection of ventilation and weaning modalities. Pragmatic definitions of separation attempt and weaning success allowed to allocate patients in four groups.

Measurements and main results:

2729 patients were enrolled. Whereas half of them could not be classified using the previous definition, 99% entered the groups based on our new definition as follows: 24% never started a weaning process, 57% had a weaning process of less than 24 hours (group 1), 10% had a difficult weaning of more than one day and less than one week (group 2) and 9% had a prolonged weaning duration of one week or more (group 3). Duration of ventilation, ICU stay and mortality (6%, 17% and 29% for respectively the three groups) all significantly increased from one group to the next. The unadjusted risk of dying was 19% after the 1st separation attempt and rose to 37% after 10 days.

Conclusion:

A new classification allows categorizing all weaning situations. Every additional day without a weaning success after the first separation attempt increases the risk of dying.

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Key words: Mechanical ventilation. Weaning. Separation Attempt. Outcome.

GLOSSARY

International Consensus Conference

- International Consensus Conference weaning groups:
    - Group 1 (simple weaning): successful extubation after the first spontaneous breathing trial (SBT)
    - Group 2 (difficult weaning): successful extubation after two to three SBTs and taking less than 7 days
    - Group 3 (prolonged weaning): successful extubation after more than three SBTs or taking more than seven days
- International Consensus Conference weaning success and failure definitions:
    - Weaning success is defined as extubation not requiring reinstitution of ventilatory support in the 48 h following extubation.
    - Weaning failure is defined as one of the followings:1) failed SBT; 2) reintubation and/or resumption of ventilator support in the 48h following extubation; or 3) death within 48 h following extubation.

WIND study

• Weaning: the start of weaning is the first attempt at separating the patient from the ventilator, whatever its modality. Weaning is terminated when the patient is successfully separated from the ventilator (see below). *Weaning does not include the possible gradual reduction of support that may have occurred before*.

• Spontaneous Breathing trial (SBT): test of spontaneous ventilation without or with "minimal" level of support (pressure support and or PEEP and/or CPAP)

• Separation attempt

- For intubated patients: SBT with or without extubation, or an extubation directly performed without identified SBT (whatever the type: planned or unplanned extubation)
- For tracheotomized patients: 24 hours or more with spontaneous ventilation through tracheostomy without any mechanical ventilation

• Successful weaning (or successful separation)

- Intubated patients: extubation without death or reintubation within the next seven days following extubation (whether post-extubation NIV was used or not), or ICU discharge without invasive mechanical ventilation within 7 days, whichever comes first.
- Tracheotomized patients: spontaneous ventilation through tracheostomy without any mechanical ventilation during seven consecutive days or ICU discharge with spontaneous breathing, whichever comes first.

- WIND Groups

  - Group no weaning: patients never experienced any separation attempt
  - Group 1 (short weaning): the first separation attempt resulted in a termination of the weaning process within 24 h (successful separation or early death)
  - Group 2 (difficult weaning): weaning was terminated after more than one day but in less than one week after the first separation attempt (successful separation or death).
  - Group 3 (prolonged weaning): weaning was still not terminated 7 days after the first separation attempt (by success or death).

Introduction

Mechanical ventilation is used daily as a life-saving technique in intensive-care units (ICUs). Its application, however, is associated with serious complications and costs, often directly linked to the duration of ventilation (1, 2). Likewise extubation failure contributes to impaired outcome: longer length of ventilation, longer length of stay in the ICU and in the hospital and is associated with higher mortality (3, 4). Therefore weaning from mechanical ventilation represents a crucial step for every patient (5–7) and aiming to shorten duration of ventilation is fundamental (8–10). Despite the importance of this period, the weaning process is not rigorously defined, with wide variations in definitions and practices, thus making epidemiological studies difficult to conduct and interpret. In addition, the specific impact of weaning difficulties is still poorly understood. This is an important problem since general recommendations regarding the entire weaning process may encompass completely different causes and consequences of its prolongation and therefore may be totally inappropriate for individual patients. A relatively simple classification may help to differentiate the various situations; in 2007, an International Consensus Conference (ICC) on weaning from mechanical ventilation (5), proposed a classification in three different groups (ICC-groups), based on number, timing and results of spontaneous breathing trials (SBTs, defined as a T-piece trial or a low-level pressure support $\leq$8 cmH_2O) as well as extubation outcomes. This approach, though useful to illustrate the different problems associated with these three groups, was not initially proposed as an operational tool for prognostication. In this regard, its major shortcoming was that it only considered patients who were ultimately weaned. In addition, the use of well identified SBT is not a universal practice and some patients are weaned without SBT. These patients cannot be classified in any of these three ICC-groups. To our knowledge, six studies applied this classification using different adaptations of the initial description (11–16) but mostly on a small number of patients or in single center (12–16), or trying to retrospectively classify patients from an ICU database (11, 12). The different designs and the limitations in the definitions may have explained

differences among the studies and some surprising findings. For instance previous studies have been unable to find a different prognosis associated with simple and difficult weaning (11, 12). Prospective data concerning the weaning process as it is currently performed and its associated mortality in a large population of ICU patients are therefore lacking.

We thus designed a multicentre multinational prospective observational study, the Weaning accordIng to New Definition (WIND) study, in a large population of patients receiving invasive mechanical ventilation to obtain a comprehensive view of weaning trajectories including weaning prolongation and its associated prognosis. We defined the start of weaning as the first attempt at separating the patients from the ventilator, whatever its modality, and did not try to describe the possible gradual reduction of support that may have occurred before. We propose a modification of the ICC classification (5) that could better fit daily ICU practice and could be operational for every patient under invasive mechanical ventilation in various environments. Such a classification may be useful for epidemiological studies, quality improvement projects and benchmarking, health-economics calculations, for conducting trials and for guidelines and recommendations. Some of the results of this study have been previously reported in the form of abstracts (17, 18).

Patients and Methods

A full version of the Methods is in the electronic supplement.

This prospective multicentre observational study was endorsed by the Réseau Européen de Recherche en Ventilation Artificielle (REVA network) and included patients admitted in 36 intensive care units in France (N=29), Spain (N=6) and Switzerland (N=1) over a twelve weeks period (April 2013 to June 2013). All patients newly admitted during this period and requiring intubation for ventilation were enrolled at the date of intubation and followed until ICU discharge or day 60, whichever came first.

Ethical and legal aspects

This study was approved by the French Intensive Care Society (Société de Reanimation de Langue Française-SRLF) ethics committee with a waiver of consent, and as of April 9, 2013 by the Commission Nationale de l'Informatique et des Libertés (CNIL), the French independent administrative authority that operates in accordance with the data protection legislation. For the centers in Switzerland and Spain, local ethics committee approval was obtained.

Data collection

Investigators had first to answer a questionnaire about their centers, including the use of sedation and weaning protocols. Participating investigators collected daily ventilation parameters and weaning strategies. Investigators recorded the weaning modalities including performance of SBTs, and if so the technique used. Data collection was continued until ICU discharge or day 60 whichever occurred first.

Weaning classification according to the International Consensus Conference

We first applied the ICC classification (5). Three weaning groups were defined based on number, timing and results of SBTs as well as extubation outcomes: simple weaning (ICC-Group 1) was defined by a successful extubation after the first SBT; difficult weaning (ICC-Group 2) was defined by a successful extubation after two to three SBTs and taking less than 7 days; prolonged weaning (ICC-Group 3) was defined by a successful extubation after more than three SBTs or by more than seven days.

The new WIND definition and classification

After observing the variety of practices and in order to cover the range of clinical situations encountered, we proposed an evolution of the ICC classification (see electronic supplement for the methods). This “WIND classification” defined the start of weaning as any kind of separation attempt (without accounting for the previous reduction in the ventilation support), computed the duration of this process and its prognosis, and proposed the following definitions:

For intubated patients

- Separation attempt from mechanical ventilation: a SBT with or without extubation, or an extubation directly performed without identified SBT (whatever the type: planned or unplanned extubation)
- Successful weaning or separation: extubation without death or reintubation within the next seven days whether post-extubation NIV was used or not, or ICU discharge without invasive mechanical ventilation within 7 days, whichever comes first. The date of the successful weaning was counted retrospectively to the actual day of extubation after the patient have completed 7 days without reintubation (or was discharged earlier without reintubation)

For tracheostomized patients

- Separation attempt from mechanical ventilation: 24 hours or more with spontaneous ventilation through tracheostomy without any mechanical ventilation.
- Successful weaning or separation: spontaneous ventilation through tracheostomy without any mechanical ventilation during seven consecutive days or discharged with spontaneous breathing, whichever comes first.

The whole population was then classified into four mutually exclusive groups, based on the duration of the weaning process (i.e. delay between the first separation attempt and weaning termination):

- Group “no weaning”, comprising patients who never experienced any separation attempt.
- Group 1 (short weaning): the first attempt resulted in a termination of the weaning process within one day (successful separation or early death)
- Group 2 (difficult weaning): the weaning was completed after more than one day but in less than one week after the first separation attempt (successful separation or death).
- Group 3 (prolonged weaning): weaning was still not terminated 7 days after the first separation attempt (by successful separation or death).

This last group was further split in *Group 3a* (prolonged weaning leading to a successful weaning after seven days or more after the first attempt) and *Group 3b* (prolonged weaning without success).

Outcome according to the WIND definition:

Ventilator free days were calculated as the number of days without invasive ventilation to day 28. Non survivors were considered to have a ventilator free days value of 0. We assessed the crude mortality rate of each group. We also calculated the daily risk of dying for patients still not having a successful weaning each day after the first separation attempt.

Use of sedation and weaning protocols, and use of SBT

We assessed the association between the presence of protocols for sedation or for weaning and the likelihood of having a short phase of separation or short weaning. We also compared patients whose first separation attempt was a SBT to patients who had another type of first separation attempt.

Statistical analysis:

Descriptive statistics included frequency (percentages) for categorical variables, mean and standard deviation or median and interquartile ranges (IQR) for continuous variables. Comparisons of proportions were made using Chi2 or exact Fisher tests and continuous variables were compared using Student t-test or Wilcoxon rank sum test when two groups were compared and analysis of variance or Kruskal-Wallis tests when more than two groups were compared. We performed a multivariable analysis of factors associated with simple weaning by means of a logistic regression, forcing both sedation and weaning protocols in the final model. Last, we performed a multivariable logistic regression to assess factors associated with the use of a SBT before a planned extubation.

Results:

1. **ICU and patients characteristics**

A total of 36 units participated with a median [interquartile range] number of beds of 12 [10-17] and 740 [498-901] admissions per year including a median of 324 [222-462] intubated patients. Most of these centers used a sedation protocol (57%) and 43% had a weaning protocol. Over the three studied months, a total of 2729 patients met the inclusion criteria which represented 71 [43-106] patients per unit. Among them, 20 patients were excluded since the main reason for mechanical ventilation was a tracheostomy for oro-tracheal obstruction, and thus were not concerned by the weaning process. The final cohort comprised therefore 2709 patients whose main characteristics are detailed in Table 1. A majority (66.9%) were discharged alive from the ICU and weaned from mechanical ventilation; 125 (4.6%) were still alive but not fully weaned at discharge or at day 60, and the ICU mortality of the total cohort was 28.5%.

2. Classifications and characteristics of the groups

Applying the ICC classification to our cohort (n=2709), only 1379 (51.0%) patients could be classified: 1016 (37.5%) did not have a SBT, 735 (27.1%) were never extubated, 337 (12.4%) had an extubation without SBT, 1070 (39.5%) never met successful weaning criteria of the ICC (comprising 170 patients still under NIV 48 hours after extubation); 786 (29.0%) had no SBT nor weaning success. Among the classified patients, 962 (69.8%) belonged to ICC-group 1, 308 (22.3%) to ICC-group 2, and 109 (7.9%) to ICC-group 3.

The new WIND classification allowed describing the distribution and mortality of the whole cohort as follows (Figures 1&2):

- Group no weaning comprised 658 (24.3%) patients who never had any separation attempt.
- Group 1 comprised 1543 patients (57.0%) whose weaning was terminated within 24 hours following the 1st separation attempt. Most had a successful weaning (94.5%) but 82 patients (5.3%) died and 2 patients (0.2%) were transferred before weaning success in the 24 hours following the first separation attempt.

- Group 2 comprised 273 patients (10.1%) whose weaning was terminated between 2 and 6 days after the 1st separation attempt. Among these patients, 83.5% had a successful weaning, 15.4% died and 1.1% were transferred before weaning success.
- Group 3 comprised 235 (8.7%) patients who did not have a separation attempt leading to weaning success one week after their first separation attempt. This group had a death rate of 29.8%. Of this group, 145 (61.7%) patients finally had a successful weaning (group 3a), and 90 (38.3%) patients were never weaned (group 3b) because they died (74.4%), were transferred under mechanical ventilation (13.3%) or were still under mechanical ventilation at day 60 (13.3%). Patients' baseline characteristics and outcomes in the groups are described in Table 2 and Table E1 and differences between the ICC and the WIND classifications are described in Table E2. Patients from group 1 significantly differed from patients of groups 2 and 3 by being younger and with lower admission SOFA score ($p<0.001$ for each comparison, Chi2 tests). No evidence of any differences in baseline characteristic between patients of groups 2 and 3 was observed. Outcomes were significantly different across the 3 groups: length of ICU stay, ventilator free days (Figure 3 & Figure E1) and mortality were significantly different between all groups ($p<0.001$ for each comparison, Chi2 tests) (Table 2).

3. Factors associated with a short weaning duration

A total of 1812 patients had at least one separation attempt and did not have any withholding/withdrawing decisions, comprising 1413 who had a short weaning (group 1) and 399 patient who had a longer weaning (groups 2 and 3) (Table 3). Among these patients, 995 (54.9%) were managed in a center using a sedation protocol, and 653 (36.0%) were managed in a center using a weaning protocol. In a multivariable analysis, younger age, lower SOFA score at admission, shorter duration of mechanical ventilation before the 1st separation attempt and admission for planned surgery were associated with a short weaning whereas being in a unit using a protocol for sedation or for weaning did not influence this proportion (Table 3)

4. Mortality over time

Crude mortality of the patients remaining on mechanical ventilation was calculated on a daily basis after the 1st separation attempt for patients still present but not successfully weaned at each specific day. Each additional day was associated with a progressively increasing mortality, from 19.0% in patients not weaned one day after the 1st attempt to 36.8% in patients still present in the ICU and not successfully weaned 10 days after the 1st attempt (Figure 4).

5. Extubation modalities

The 2051 patients in the 3 weaning groups underwent a total of 2172 extubations : most of them occurred after a SBT success (77.9%), but 13.7% were performed without any SBT, 7.6% were unplanned extubations and 0.8% were performed after a SBT failure. Physicians performed a total of 2904 SBT, almost equally distributed between T-piece ventilation (49.9%) and low PSV trials (47.5%); A few (2.7%) used other type of trials with low support or low PEEP. All these results are detailed in Table 4 and Table E3.

The 2051 patients who had at least one separation attempt comprised 1669 patients whose first separation attempt was a SBT and 382 who had another type of first separation attempt (Table E4). We identified three types of patients who were extubated without SBT: 1) patients with unplanned extubation; 2) patients with (withholding/withdrawal) who were accordingly extubated without probability of success assessment; 3) patients probably assumed by their physician to have a high likelihood of weaning success. After excluding patients with a decision of withholding/withdrawal (N=95) and patients with a unplanned extubation as a first separation attempt (N=124), we compared patients who had a planned extubation with or without SBT as first separation attempt (Table 5). In a multivariate analysis restricted to these patients, younger age, lower SOFA at admission, admission for planned or emergent surgery were associated with performing a first separation attempt without SBT (Table 5). Use of a weaning protocol was not associated with use of SBT.

Discussion

To our knowledge, the WIND study is the largest prospective observational study offering a daily systematic description of the weaning process after the first separation attempt, and the outcome associated with the prolongation of the weaning process. We found several new and relevant results: 1) The ICC definition on weaning from mechanical ventilation could not classify almost half of invasively ventilated patients from this mixed medical and surgical ICU population (5). The WIND classification, based on the concept of separation attempts, an evolution of the weaning success definition, and mainly on the duration of the weaning process after a first attempt, allowed to classify all patients; 2) These groups based on weaning duration have gradually increasing morbidity, length of stay and mortality, by contrast with previous reports using the ICC classification (11, 13–16); 3) Each additional day without a weaning success after the first attempt was associated with an increased crude mortality; 4) The use of protocols for sedation and weaning were not associated with a higher rate of short weaning; 5) SBT were equally distributed between T-piece and low PSV and both modalities led to a successful weaning rate of approximately 50% (Table 3); 6) A small number of patients are intentionally extubated without SBT and are less severe than the patients extubated after a SBT.

The classification proposed in 2007 by the ICC (5), based on expert opinion, failed to allocate one half of the invasively ventilated patients included in the present cohort, for two main reasons: First, only successfully weaned patients could enter this classification. Many patients of the present cohort were never eventually weaned either because they died before entering the weaning process (21%), had an unsuccessful weaning process or were discharged to another unit or a weaning center under mechanical ventilation (3%) and/or with a tracheostomy (3%). Moreover, the ICC classification did not specify how to classify tracheostomized patients and gave an unclear definition of patients receiving noninvasive ventilation 48h after extubation as a “weaning in

progress" group. Secondly, the ICC classification was based on the performance of SBTs whereas a substantial number of patients were weaned after a planned extubation time without any SBT or after unplanned extubation (10.7% and 5.9% respectively). The six published studies which used the 2007 ICC so far also evidenced a very high rate of patients who could not be classified, ranging from 40 to 75% (11–16). Even though none of these studies discussed the applicability of the 2007 classification, several authors did not precisely follow ICC-groups definitions: only 2 groups strictly applied the classification proposed in 2007 (14, 15).

We propose to modify the ICC classification to overcome these issues. The new WIND classification is operational for daily clinical practice, allows a straightforward epidemiological description, and accounts for all the patients receiving invasive ventilation. Because we considered all types of extubation with or without SBT, the first main change was the definition of "separation attempts" that brought together all the situations leading to extubation: a formal SBT as well as an extubation without SBT. In a study where patients were extubated without SBT, the rate of failure with reintubation in the next 48 hours was as high as 39.3% (19). Nevertheless, a recent study found the same rate of successful extubation with or without using a SBT in a mixed medical and surgical population of patients (20). Our data suggest, however, that they may not be the same group of patients. The fact that this was not associated with weaning protocols may also suggest that it is more driven by individual patient characteristics than by ICU policy. Furthermore we also considered unplanned extubation as a separation attempt (leading to successful weaning in most of the cases). In addition, we also took into account tracheostomized patients in the WIND classification since almost 5% of the patients included in the cohort had a tracheostomy at any point of their ICU stay.

The second main change was the weaning success definition: in the ICC, a delay of 48h without any form of mechanical ventilation (invasive or not) was retained. We chose a seven day delay whatever the use or noninvasive ventilation or not. Time after which extubation is considered as a

success remains a subject of debate and is further complicated by the use of non-invasive ventilation, which may prolong the time to reintubation (4, 21).

Distribution of the weaning groups

The WIND classification strongly discriminated three weaning groups with very different weaning trajectories and prognosis using the weaning time span. Defining groups by the delay between the first separation attempt and the outcome (weaning success or death) makes the classification easy and appears to be of paramount importance for the prognosis. The short weaning group gathered patients that could be successfully weaned early or either died immediately after extubation without reintubation (90% of them with do not reintubate orders, Table 2). This group 1 accounted for most of the patients included (57.0 % of the whole cohort, 75.2 % of the weaning cohort). Almost 25% of the patients entering the weaning process were allocated to group 2 (difficult weaning) and 3 (prolonged weaning) with an almost equal distribution. This result could justify future studies to better understand the pathophysiological process leading to difficult weaning in order to apply strategies to reduce the number of patients transiting to the prolonged weaning group. By contrast with previous reports we found a very different outcome of these two groups (11, 13–15), thus bringing an important predictive validity of the classification. Indeed, duration of ventilation, of ICU stay and mortality all differ among the groups. As found in previous reports , the total length of mechanical ventilation raised from group 1 to 3 (11–16), nevertheless, in this cohort, the difference between group 2 and 3 was mainly due to the length of mechanical ventilation after the first separation attempt: surprisingly, the length of ventilation before the first separation attempt did not differ between group 2 and group 3, emphasizing the importance of what happens after the first separation attempt and shining a new light on the mortality related to the duration of mechanical ventilation. This support the finding that after a first separation attempt, each additional day before the eventual weaning increased the risk of death. Our results suggest that the three groups are very different and have different outcomes. Including the three groups in randomized controlled trials, however, have often produced results heavily driven by group 1, and lead to recommendations

potentially non applicable to other patients. Patients in the group 3 represent a population with special needs, prolonged hospitalization and high resource consumption whose specific organizational consequences need to be better analyzed (22).

Mortality over time

Because patients that died early after extubation or who failed weaning were excluded from the ICC definition, ICU mortality reported in previous weaning cohort studies was very low, especially in ICC-groups 1 and 2 (from 0 to 7% in a general population (11, 12, 14, 15) to 12% in a COPD cohort (13) and did not match with clinical reality. Including those patients in our cohort resulted in a more usual case mix and highlighted differences between the three weaning groups. The daily data collection allowed to describe the risk of death associated with the duration of the weaning process. We have shown that each additional day of mechanical ventilation after failure of the first attempt is associated with an increasing risk of death, with a kind of plateau between day 2 and day 6. We believe this represents useful information for clinicians. In contrast, Peñuelas et al., based on a different population and classification definitions, found higher mortality only for weaning lasting more than seven days (11).

Strengths and weaknesses

This study comprises the largest prospective cohort with daily collection of weaning assessment, extubation outcome and was especially designed for this purpose. The simple definitions of "separation attempt" and "successful weaning" allowed classification of the whole cohort and overcame most of the ICC issues, meeting daily clinical practice needs. Beyond limitations inherent to the observational design of the WIND study, it should be noted that only European ICUs participated (half of them located in university hospital) and our conclusions may not apply worldwide. We believe, however, that the type of classification proposed is operational to be adopted worldwide. Apart from mechanical ventilation settings, only few clinical data were collected and patients were not followed-up after ICU discharge in order to reduce investigators

workload. Although this limited the possibilities of performing additional analyses and adjustments, it also resulted in a high quality dataset without missing data.

Conclusions

The first separation attempt is a major milestone in the ventilated patients' ICU course. The proposed new definitions of separation attempts and successful weaning allow the classification of all patients in meaningful groups. This is relevant to optimize the weaning process and to design and conduct future research in this field. The three weaning groups defined by the delay between the first separation attempt and the weaning termination generate groups with very different morbidity and mortality. Mortality start to increase after the first unsuccessful separation attempt.

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Figure legends

Figure 1: Patients flowchart and classification

This figure shows the flowchart of the patients receiving mechanical ventilation in the participating units during the study. Groups' classification is briefly defined and the number and percentage of patients constituting each group are shown.

As defined in the manuscript:

For intubated patients

- Separation attempt from mechanical ventilation: a SBT with or without extubation, or an extubation directly performed without identified SBT (whatever the type: planned or unplanned extubation)
- Successful weaning: extubation without death or reintubation within the next seven days whether post-extubation NIV was used or not, or ICU discharge without mechanical ventilation within 7 days, whichever comes first.

For tracheostomized patients

- Separation attempt from mechanical ventilation: a whole day or a period of several consecutive days with spontaneous ventilation through tracheostomy without any mechanical ventilation.
- Successful weaning: spontaneous ventilation through tracheostomy without any mechanical ventilation during seven consecutive days or discharged with spontaneous breathing, whichever comes first.

Abbreviation: SA: Separation Attempt

Figure 2: Group definitions and mortality

This figure shows the group classification according to the number of days between the first separation attempt and the weaning termination. Groups' number, total duration of mechanical ventilation, number of days between the first separation attempt and the weaning success and mortality are displayed

*: median duration of mechanical ventilation (days)

**: median number of days between the first separation attempt and the weaning success (patients who never had a weaning success are excluded from this calculation)

Figure 3. Distribution of Ventilator free days at day 28 according to weaning groups

This figure shows for each group and for the whole population, the proportion of patients achieving each number of ventilator free days from 27 to 0. Ventilator free days are defined by 28 minus the total number of days with Invasive Mechanical Ventilation. Non survivors were considered as having 0 Ventilator free days.

Figure 4: Daily probability of death after the first failed separation attempt for patients still in the ICU without weaning success

This figure shows the probability of death in patients still present but not weaned each day after the first separation attempt.

The corresponding table attached shows the distribution of these patients in the 3 weaning groups each day after the first separation attempt

TABLES

TABLE 1: Wind study population characteristics

	N=2709 included patients
Baseline characteristics	N (%) or mean ±SD or median [IQR]
Age, years	61 ±16
Sex ratio M/F	1.90
SAPS II at admission, points	52±21
SOFA at admission, points	7.9 ±4.2
SOFA at day 3 (n=2225) , points	5.8 ±4.6
Admission type, n (%)	
Medical	2042 (75.4%)
Planned / Unplanned surgery	283 (10.5%) / 384 (14.2%)
- Abdominal	- 203 (30.4%)
- Cardiac	- 157 (23.5%)
- Vascular	- 57 (8.5%)
- Neuro	- 54 (8.1%)
- Urologic	- 49 (7.3%)
- Trauma	- 49 (7.3%)
- Thoracic	- 33 (4.9%)
- Head & Neck	- 24 (3.6%)
- Others	- 41 (6.1%)
Outcome	
Total number of days of invasive MV, days	4 [2;9]
Ventilator free days[1], days	21 [0;26]
Delay from intubation to 1st SA, days	3 [2;7]
Length of stay in the ICU, days	6 [3;13]
Length of stay in the ICU in survivors, days	7 [4;14]
Status at ICU discharge (or day 60)	
Dead	771 (28.5%)

Alive and weaned	
- Spontaneous breathing	1700 (62.8%)
- NIV	65 (2.4%)
- Tracheostomy (permanent spontaneous breathing)	48 (1.8%)
Alive and not weaned	
- Intubation	88 (3.3%)
- Tracheostomy with mechanical ventilation	37 (1.4%)

Abbreviations: SAPS II: Simplified Acute Physiology Score II; SOFA: Sequential Organ Failure Assessment; MV: mechanical ventilation; SA: separation attempt; ICU: intensive care unit; NIV: noninvasive ventilation; SD: standard deviation; IQR: interquartile range

[1] Ventilator free days were defined by 28 minus the total number of days with Invasive Mechanical Ventilation. Non survivors were considered as having 0 ventilator free days.

TABLE 2: Characteristics of the population according to the weaning group (WIND classification)

	Group 1 N=1543	Group 2 N=273	Group 3 N=235	p-value [1]	G NW N=658
Age, y	59±17	65±15	65±13	<0.001	64±15
Sex ratio M/F	1.9	2.1	1.9	0.91	1.9
SAPS II at admission, points	45±17	51±18	53±18	<0.001	68±23
SOFA at admission, points	6.6±3.6	8.0±3.3	8.1±3.7	<0.001	11±4.3
SOFA at day 3, points	4.3±3.8	6.7±4.0	6.8±3.7	<0.001	10.4±5.1
Admission type					
Medical	1084 (70.3%)	220 (80.6%)	185 (78.7%)	<0.001	553 (84%)
Planned surgery	234 (15.2%)	10 (3.7%)	18 (7.7%)		21 (3.2%)
Emergent surgery	225 (14.6%)	43 (15.8%)	32 (13.6%)		84 (13%)
Type of surgery					
Cardiac	129 (8.4%)	8 (2.9%)	10 (4.3%)		10 (1.5%)
Abdominal	125 (8.1%)	24 (8.8%)	14 (6.0%)		40 (6%)
Vascular	37 (2.4%)	2 (0.7%)	9 (3.8%)		9 (1.4%)
Neuro	23 (1.5%)	7 (2.6%)	5 (2.1%)		19 (2.9%)
Urologic	40 (2.6%)	1 (0.4%)	1 (0.4%)		7 (1%)
Thoracic	17 (1.1%)	3 (1.1%)	6 (2.6%)		7 (1%)
Trauma	37 (2.4%)	6 (2.2%)	2 (0.9%)		4 (0.6%)
Head & Neck	17 (1.1%)	2 (0.7%)	0 (0.0%)		5 (0.8%)
Others	34 (2.2%)	0 (0.0%)	3 (1.3%)		4 (0.6%)
Total number of days of invasive MV, days	3 [2;6]	9 [6;13]	19 [15;31]	<0.001	3 [2;7]
Ventilator free days[2], days	25 [22;26]	18 [9;21]	0 [0;12]	<0.001	0 [0;0]
Delay from intubation to 1st SA	3 [2;5]	6 [3;10]	6 [3;10]	<0.001	-
Length of stay in the ICU, days	5 [3;9]	14 [8;25]	31 [20;46]	<0.001	3 [2;8]
Length of stay in the ICU in survivors, days	5 [3;9]	15 [9;25]	37 [23;52]	<0.001	8 [2;31]

Status at ICU discharge (or D60)					
Dead	90 (5.8%)	45 (16.5%)	70 (29.8%)	<0.001	566 (86%)
Alive and weaned[3]					
- Spontaneous breathing	1449 (93.9%)	224 (82.0%)	140 (59.6%)		0 (0%)
- NIV	1394 (90.3%)	210 (76.9%)	96 (40.9%)		0 (0%)
- Tracheostomy	44 (2.9%)	11 (4.0%)	10 (4.3%)		0 (0%)
	11 (0.7%)	3 (1.1%)	34 (14.5%)		0 (0%)
Alive and under invasive mechanical ventilation[3]	4 (0.3%)	4 (1.5%)	25 (10.6%)		92 (14%)
- Tube	2 (0.1%)	2 (0.7%)	5 (2.1%)		79 (12.0%)
- Tracheostomy	2 (0.1%)	2 (0.7%)	20 (8.5%)		13 (2.0%)
Decision of withholding or withdrawing invasive MV:					
- Total	130 (8.4%)	46 (16.9%)	63 (26.8%)	<0.001	117 (17.8%)
- Among deceased patients	81 (90.0%)	30 (66.7%)	42 (60.0%)	<0.001	113 (20.0%)
- Among survivors	49 (3.4%)	16 (7.0%)	21 (12.7%)	<0.001	4 (4.4%)

Abbreviations: MV: mechanical ventilation; SA: separation attempt; ICU: intensive care unit; NIV: noninvasive ventilation; SD: standard deviation; IQR: interquartile range

[1]Overall comparison between the group 1, group 2 and group 3. Chi2 test, ANOVA or Kruskal-Wallis tests were used

[2]Ventilator free days were defined by 28 minus the total number of days with Invasive Mechanical Ventilation. Non survivors were considered as having 0 Ventilator free days.

[3]No statistical test to compare status at ICU discharge between groups were performed as weaning entered in the groups definition

Table 3: Factors associated with a short weaning in patients with no decision of withholding/withdrawal. Bivariate and multivariate analysis

	Patients with a short weaning (N=1413)	Patients with a longer weaning (N=399)	Bivariate analysis p-value [1]	Multivariate analysis OR, 95% IC	p-value
Age, years	58±17	65±14	<0.001	0.98, 0.97-0.99	<0.001
SAPS II at admission, points	44±16	50±18	<0.001		
SOFA at admission, points	6.4±3.5	7.9±3.5	<0.001	0.94, 0.91-0.97	0.003
Admission: - Medical - Planned surgery - Unplanned surgery	 - 968 (68.5) - 231 (16.4) - 214 (15.2)	 - 312 (78.2) - 25 (6.3) - 62 (15.5)	 <0.001 <0.001 0.91	 2.27, 1.12-4.78	 0.024
Reintubation	19 (1.3)	181 (45.4)	<0.001		
Sedation protocol	735 (52.0)	260 (65.2)	<0.001	0.72; 0.39-1.32	0.576
Weaning protocol	513 (36.3)	140 (35.0)	0.76	0.84, 0.65-1.09	0.198
Total number of days of invasive MV, days Ventilator free days[2], days	3 [2;5] 25 [23;26]	12 [8;19] 15[2;20]	<0.001 <0.001		
Delay from intubation to 1st SA, days Length of stay in the ICU, days	3 [1;5] 5 [3;9]	6 [3;10] 21 [12;38]	<0.001 <0.001	0.92, 0.91-0.94	<0.001

Length of stay in the ICU in survivors, days	5 [3;9]	22 [12;40]	<0.001		
Death	9 (0.6)	43 (10.8)	<0.001		

Data are presented as mean ±SD, **median [IQR] or N (%)**

Abbreviations: SAPS II: Simplified Acute Physiology Score II; SOFA: Sequential Organ Failure Assessment; MV: mechanical ventilation; SA: separation attempt; ICU: intensive care unit; NIV: noninvasive ventilation; SD: standard deviation; IQR: interquartile range

[1]Comparison between the patients with a short weaning vs patients with a longer weaning (Student-test, Wilcoxon test or Chi2 test)

[2] Ventilator free days are defined by 28 minus the total number of days with Invasive Mechanical Ventilation. Non survivors were considered as having 0 Ventilator free days.

TABLE 4: Characteristics of the weaning process for the whole cohort of the 2709 included patients

Patients characteristics (N=2709)	
Patients with	
0 SA[1]	658 (24.3%)
1 SA[1]	1398 (51.6%)
2 or more SA[1]	653 (24.1%)
Patients with	
0 SBT[2]	1016 (37.5%)
1 SBT [2]	1112 (41%)
2 or more SBT[2]	581 (21.4%)
Patients with extubation following a SBT success	1565 (57.8%)
Patients with planned extubation without SBT	290 (10.7%)
Patients with unplanned extubation[3]	161 (5.9%)
Delay from inclusion to first SA, days	3 [2;7]
Patients tracheotomized	112 (4.1%)
Patients reintubated	240 (8.8%)
Patients receiving post extubation NIV	308 (11.4%)
Patient with do not reintubate order	356 (13.1%)
SA characteristics (N=3471)	
Type of SA	
T-tube	1448 (41.7%)
Low PSV	1379 (39.7%)
Other SBT	77 (2.2%)
Planned extubation without SBT	298 (8.6%)
Unplanned extubation	166 (4.8%)
Planned extubation despite SBT failure	17 (0.5%)
Continuous period of spontaneous breathing during tracheostomy	86 (2.5%)

SBT characteristics (N=2904)	
SBT success followed by **planned** extubation (within 24h)	1691 (58.2%)
T-tube success followed by planned extubation	812 (56.1%)
Low PSV success followed by planned extubation	827 (60.0%)
"other types" of SBT success followed by planned extubation	52 (67.5%)
SBT success followed by **successful** extubation (within 24h)	1457 (50.1%)
T-tube success followed by successful weaning[4]	688 (47.5%)
Low PSV success followed by successful weaning[4]	729 (52.9%)
"other types" success followed by successful weaning[4]	40 (51.9%)
Extubations characteristics (N=2172)	
Extubation with SBT success, n (%)	1691 (77.9%)
Extubation despite SBT failure, n (%)	17 (0.8%)
Planned Extubation without SBT, n (%)	298 (13.7%)
Unplanned extubation	166 (7.6%)
Delay from inclusion to 1st extubation, d (N=1974)	4 [2;7]
Successful extubation, n (%)	1772 (81.6%)
Delay from inclusion to first successful extubation, d (N=1772)	3 [2;8]
Delay from inclusion to first unplanned extubation, d	4 [2;8]
Successful unplanned extubation, n	113 (5.2%) [68% of the unplanned extubations]

Data are presented as N (%) or median [IQR]

Abbreviations: SA: separation attempt; SBT: spontaneous breathing trial; LPSV: Low Level Pressure Support Ventilation;

Of note: The number of patients having 1 separation attempt is lower than the number of patients in group 1 because as defined in the manuscript, patients having a SBT but extubated the day after (within the 24h of the first SBT) where classified in group 1 despite having 2 separation attempt (the SBT at day1 and the extubation at day 2).

On the opposite, some patients in group 2 had only 1 separation attempt: if a patient had an extubation as first separation attempt and then died between day 2 and day 7 without being reintubated, he was classified in group 2 (weaning terminated between 2 and 7 days after the 1st separation attempt)

[1]As defined in the manuscript:

- For an intubated patient, a separation attempt was defined as a SBT with or without extubation, or an extubation directly performed without identified SBT (whatever the type: planned, unplanned extubation)
- For a tracheostomized patient, a separation attempt was defined as a period of consecutive days (at least 1 day) with complete spontaneous ventilation through tracheostomy without any mechanical ventilation.

[2]A SBT was defined as a T-piece trial, a low-level pressure support ≤8 cmH_2O and a PEEP≤5cmH_20 or another type trial considered as the treating physician as an SBT

[3] 5 patients had 2 unplanned extubations

[4] As defined in the manuscript:

- For an intubated patient, successful weaning was defined as an extubation without death or reintubation within the next seven days whether post-extubation NIV was used or not, or ICU discharge without MV within 7 days, whichever comes first.
- For a tracheostomized patient, a successful weaning was defined as spontaneous ventilation through tracheostomy without any mechanical ventilation during seven consecutive days or discharged with spontaneous breathing, whichever comes first.

Table 5: Factors associated with extubation following or not a SBT in patients with planned extubation and with no decision of withholding/withdrawal. Bivariate and multivariate analysis

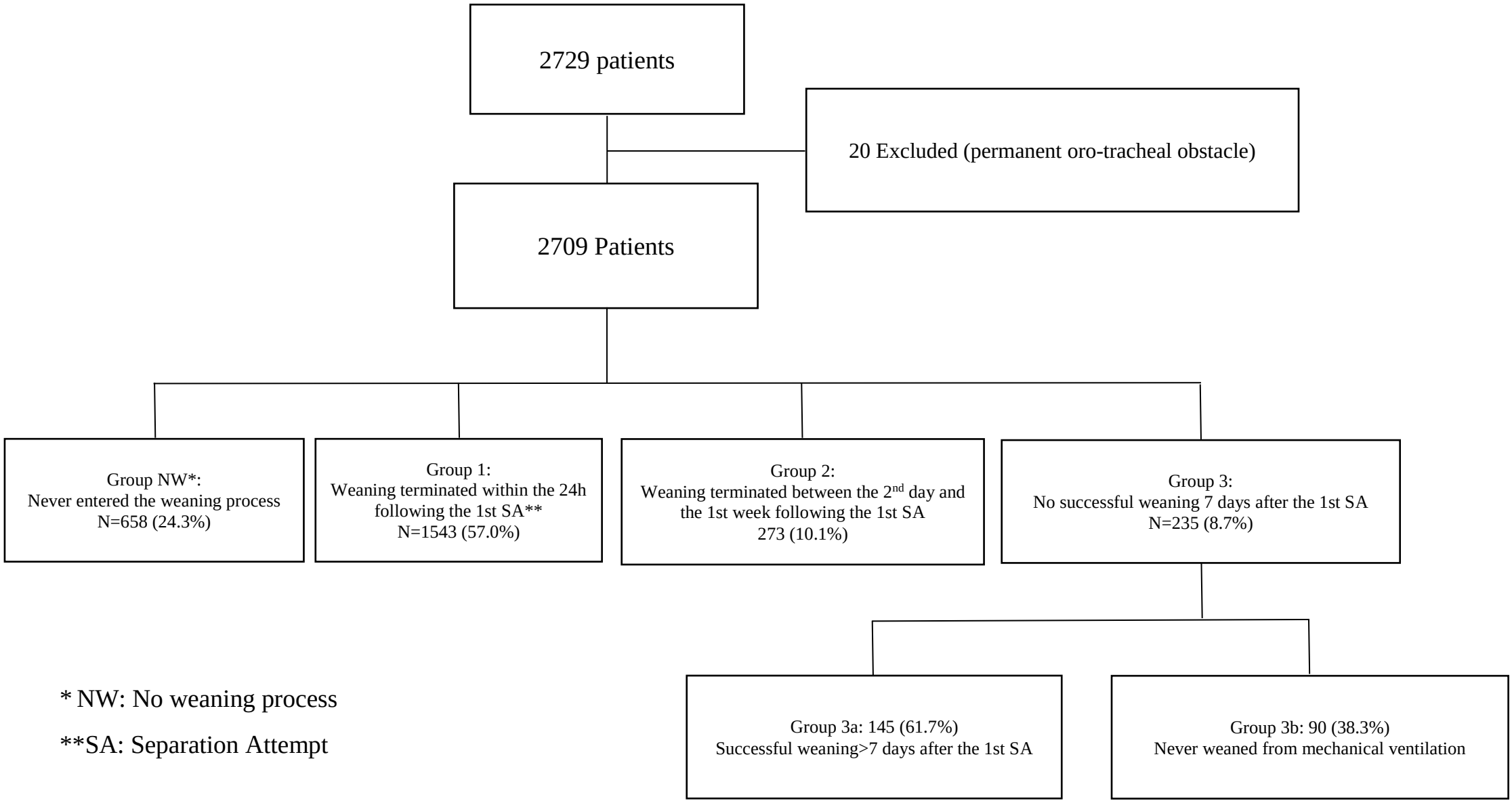
	Patients with planned extubation **without** SBT N=177	Patients with planned extubation **after** a SBT N=1489	Bivariate analysis p-value [1]	Multivariate analysis OR, 95% IC	p-value
Age, y	53±16	61±16	<0.001	0.97, 0.97-0.98	<0.001
SAPS II at admission, points	41±16	46±17	<0.001		
SOFA at admission, points	5.9±3.2	6.7±3.5	<0.001	0.95, 0.90-0.99	0.044
Admission: - Medical - Surgery (planned or unplanned)	 - 107 (60.5) - 70 (39.5)	 - 1056 (70.9) - 433 (29.1)	0.004	 1.69, 1.20-2.39	 0.003
Reintubations	11 (6.3)	148 (11.7)	0.11		
Total number of days of invasive MV, days	2 [1;6]	4 [2;9]	<0.001		
Delay from intubation to 1st SA, days	2 [1;5]	3 [2;6]	<0.001		
Length of stay in the ICU, days	4 [3;12]	7 [4;13]	<0.001		
Death, n (%)	5 (2.8)	41 (2.8)	0.85		

Data are presented as mean ±SD, median [IQR] or N (%)

Abbreviations: SAPS II: Simplified Acute Physiology Score II; SOFA: Sequential Organ Failure Assessment; MV: mechanical ventilation; SA: separation attempt; ICU: intensive care unit; NIV: noninvasive ventilation; SD: standard deviation; IQR: interquartile range

[1]Comparison between the patients with a short weaning vs patients with a longer weaning (Student-test, Wilcoxon test, Chi2 test or fisher test)

Figure 1: Patients flowchart and classification



* NW: No weaning process

**SA: Separation Attempt

Figure 2

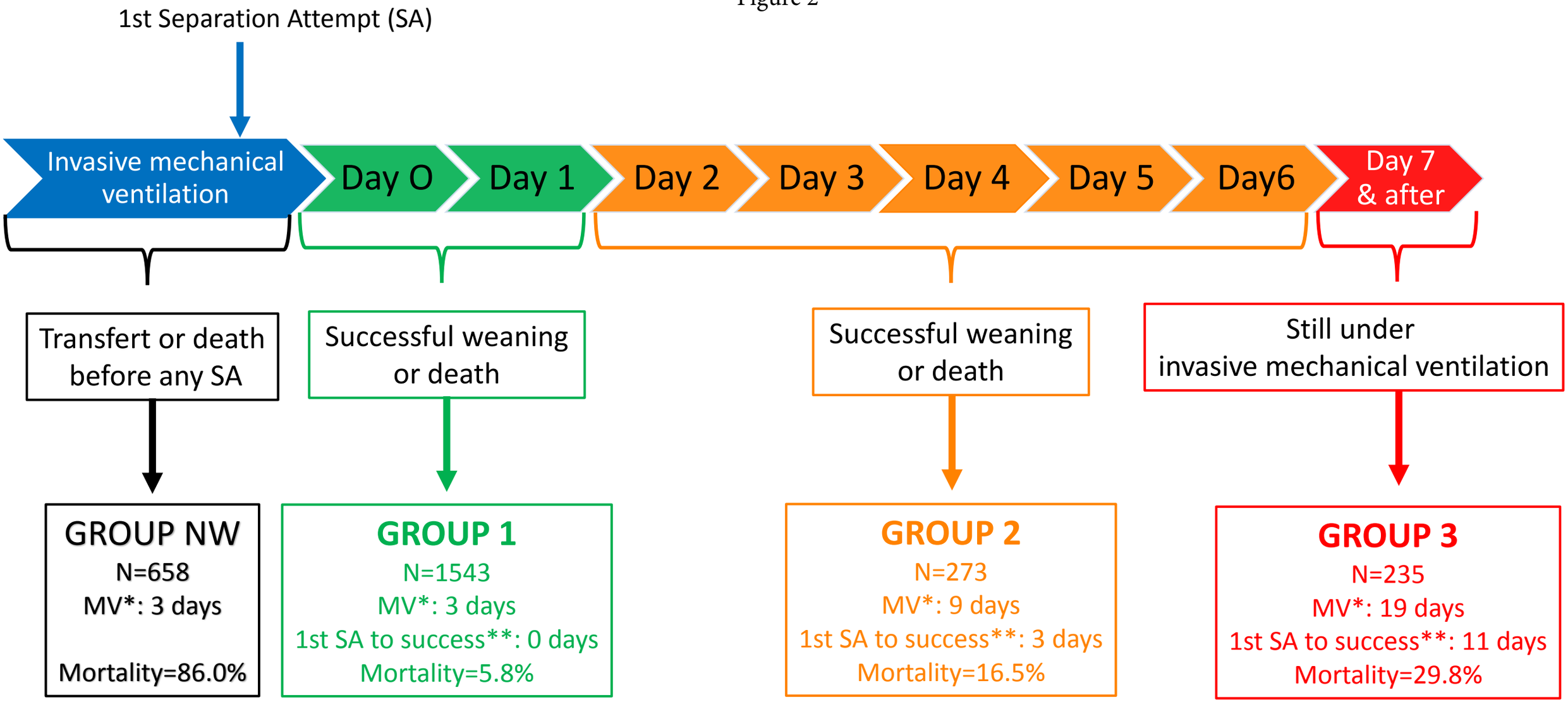
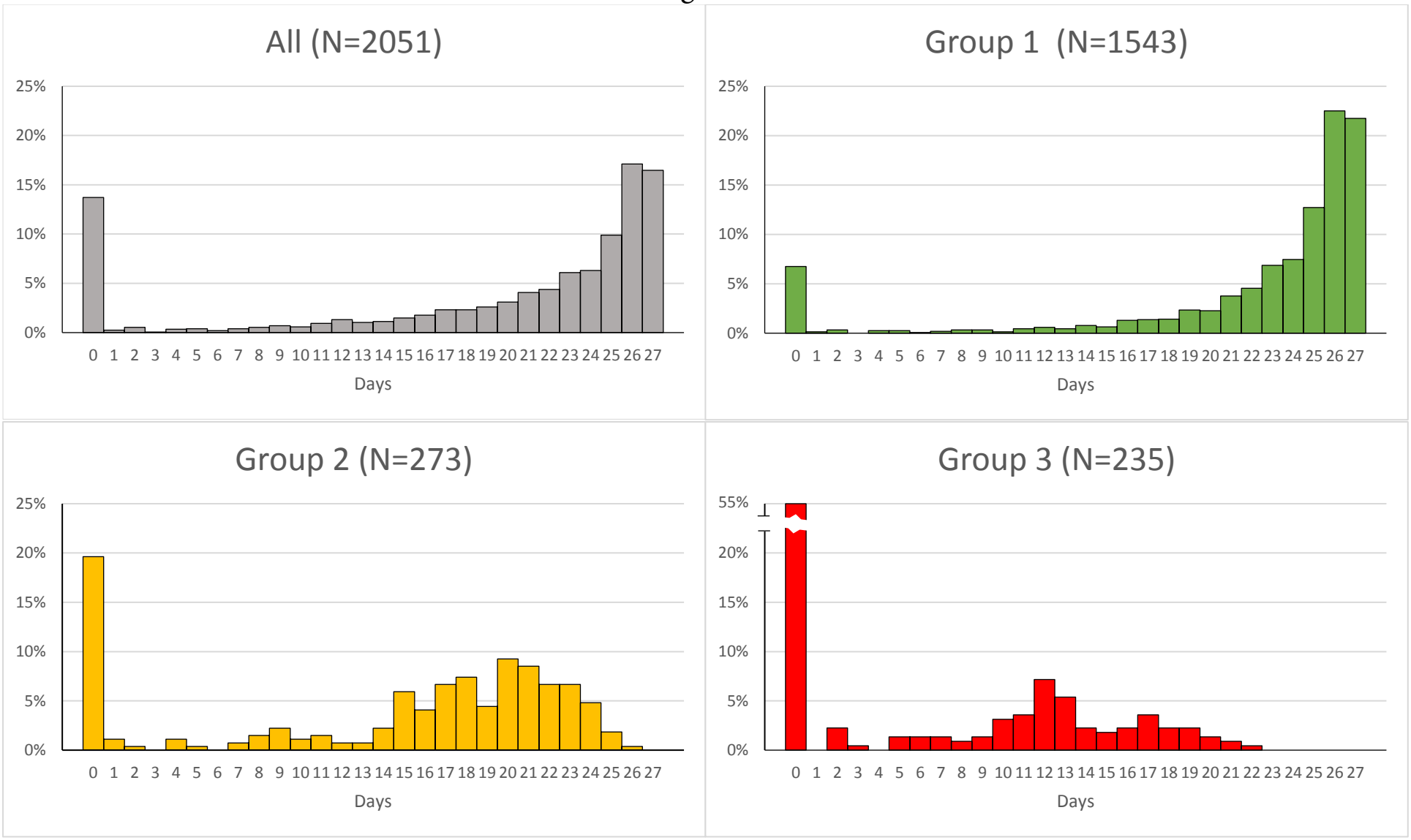
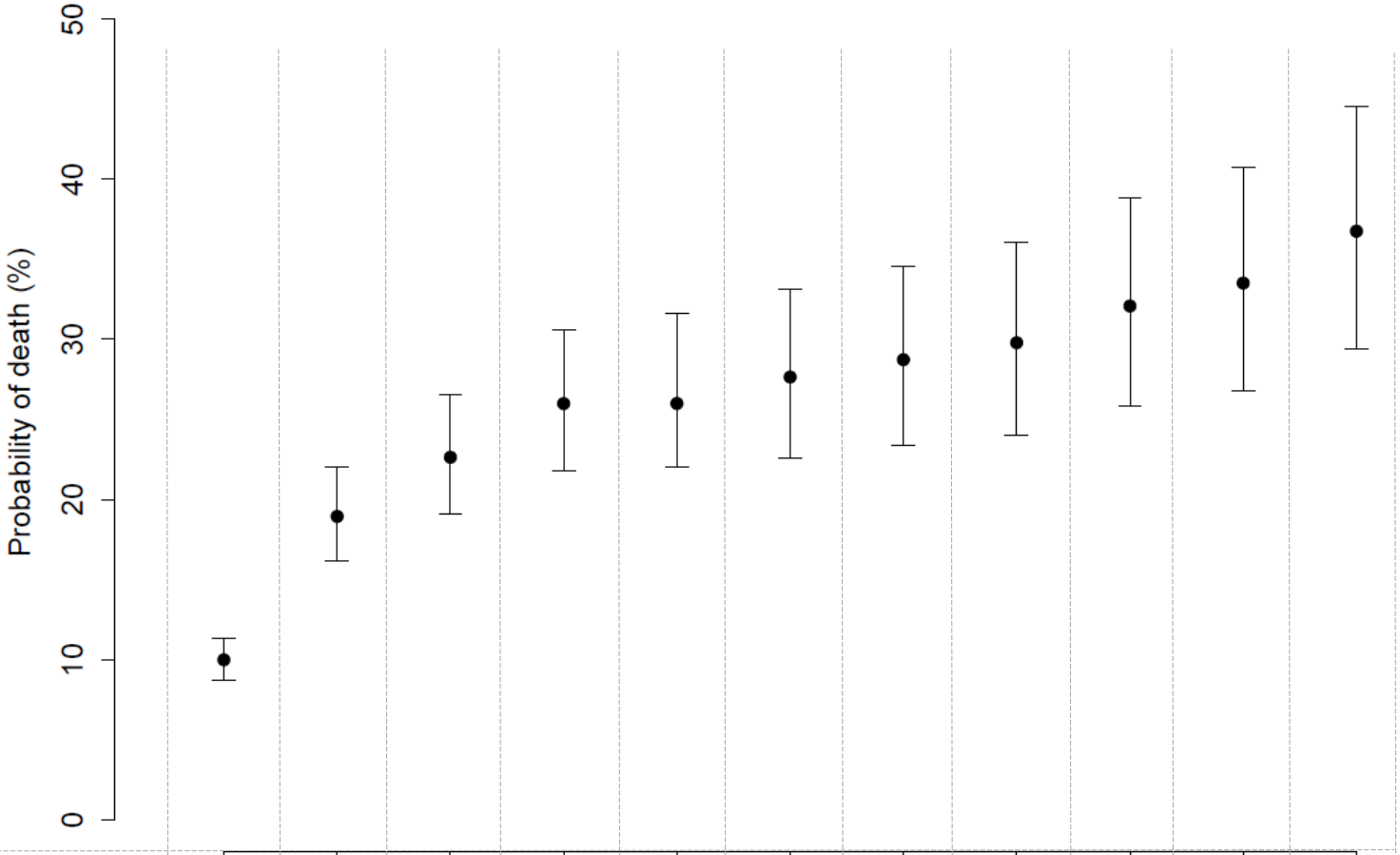

1st Separation Attempt (SA)
Invasive mechanical ventilation
Day O
Day 1
Day 2
Day 3
Day 4
Day 5
Day6
Day 7 & after
Transfert or death before any SA
Successful weaning or death
Successful weaning or death
Still under invasive mechanical ventilation
GROUP NW
N=658
MV*: 3 days
Mortality=86.0%
GROUP 1
N=1543
MV*: 3 days
1st SA to success**: 0 days
Mortality=5.8%
GROUP 2
N=273
MV*: 9 days
1st SA to success**: 3 days
Mortality=16.5%
GROUP 3
N=235
MV*: 19 days
1st SA to success**: 11 days
Mortality=29.8%

Figure 3


All (N=2051)
Group 1 (N=1543)
Group 2 (N=273)
Group 3 (N=235)
25%
20%
15%
10%
5%
0%
55%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27
Days



Days after the 1st SA	0	1	2	3	4	5	6	7	8	9	10
Nb at risk*, N	2051	723	508	404	342	293	268	235	212	188	166
Group 1, N (%)	1543 (75.2)	215 (29.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Group 2, N (%)	273 (13.3)	273 (37.8)	273 (53.7)	169 (41.8)	107 (31.3)	58 (19.8)	33 (12.3)	0 (0)	0 (0)	0 (0)	0 (0)
Group 3, N (%)	235 (11.5)	235 (32.5)	235 (46.3)	235 (58.2)	235 (68.7)	235 (80.2)	235 (87.7)	235 (100)	212 (100)	188 (100)	166 (100)

Figure 4

Electronic supplement

Epidemiology of weaning outcome according to a new definition.

The WIND study

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Methods

Patients and Methods

This prospective multicentre observational study was endorsed by the Réseau Européen de Recherche en Ventilation Artificielle (REVA network) and included patients admitted in 36 intensive care units in France (N=29), Spain (N=6) and Switzerland (N=1) over a twelve weeks period (April 2013 to June 2013). All patients newly admitted during this period and requiring intubation for mechanical ventilation (MV) were enrolled at the date of intubation and followed until ICU discharge or day 60, whichever came first.

Ethical and legal aspects

This study was approved by the French Intensive Care Society (Société de Reanimation de Langue Française-SRLF) ethics committee with a waiver of consent, and as of April 9, 2013 by the Commission Nationale de l'Informatique et des Libertés (CNIL), the French independent administrative authority that operates in accordance with the data protection legislation. For the centers in Switzerland and Spain, local ethics committee approval was obtained. All patients or surrogates were informed of their inclusion in this prospective study, and of the possibility to withdraw their data.

Data collection

Investigators had first to answer a questionnaire about their centres, including the use of sedation and weaning protocols. Participating investigators collected daily ventilation parameters and weaning strategies. Investigators recorded the weaning modalities including performance of spontaneous breathing trials (SBTs), and if so the technique used (i.e., T-piece, Low Level Pressure Support Ventilation with PSV $\leq$8 cm H_2O and low positive end-expiratory pressure (PEEP $\leq$5 cm H_2O), or other methods); results of SBT; extubation circumstances (i.e., planned, following a SBT or not, or self-extubation and reintubation, as

well as ICU outcome (length of MV, survival). Data collection was continued until ICU discharge or day 60 whichever occurred first.

Quality control

Collected data were directly downloaded as electronic files from the WIND website hosting. The electronic case report form (CRF) and the database were verified by the coordinator investigator (GB). When inconsistencies were detected, queries were sent to the investigators in order to cross-check data and solve inconsistencies. Double entries were not possible. We followed the STROBE (Strengthening The Reporting of Observational studies in Epidemiology) statement guidelines for observational cohort studies (1).

Weaning classification according to the International Consensus Conference (ICC)

We first applied the ICC classification (2), which defined weaning success as an extubation after a SBT and the absence of ventilator support (reintubation or noninvasive ventilation [NIV]) or death 48h following the extubation. Three weaning groups were defined based on number, timing and results of SBTs as well as extubation outcomes: simple weaning (ICC-Group 1) was defined by a successful extubation after the first SBT; difficult weaning (ICC-Group 2) was defined by a successful extubation after two to three SBTs and taking less than 7 days from the first SBT; prolonged weaning (ICC-Group 3) was defined by a successful extubation after more than three SBTs or by a weaning taking more than seven or more days after the first SBT.

The new WIND definition and classification

After observing the variety of practices and in order to cover the range of clinical situations encountered, we proposed an evolution of the ICC classification. This “WIND classification”, defined the start of weaning as any kind of separation attempt, computed the duration of this process and its prognosis, and proposed the following definitions:

For intubated patients

- Separation attempt from MV: a SBT with or without extubation, or an extubation directly performed without identified SBT (whatever the type: planned, accidental or self extubation)
- Successful weaning: extubation without death or reintubation within the next seven days whether post-extubation NIV was used or not, or ICU discharge without MV within 7 days, whichever comes first.

For tracheostomized patients

- Separation attempt from MV: a whole day or a period of several consecutive days with spontaneous ventilation through tracheostomy without any mechanical ventilation.
- Successful weaning: spontaneous ventilation through tracheostomy without any mechanical ventilation during seven consecutive days or discharged with spontaneous breathing, whichever comes first.

Using the separation attempt and the successful weaning definitions, the whole population was then classified into four mutually exclusive groups, based on the duration of the weaning process (i.e. delay between the first separation attempt and weaning termination):

- Group no weaning, comprising patients who never experienced any separation attempt.
- Group 1 (short weaning): the first attempt resulted in a termination of the weaning process within one day (successful separation or early death).
- Group 2 (difficult weaning): the separation was completed after more than one day but in less than one week after the first separation attempt (successful weaning or death).
- Group 3 (prolonged weaning): weaning was still not terminated 7 days after the first separation attempt (by success or death).

This last group was further split in two subgroups: *Group 3a* (prolonged weaning leading to a weaning success): successful weaning after seven days or more after the first attempt; *Group 3b* (prolonged weaning without success).

"The new WIND definition and classification".

The new "WIND classification", an evolution of the ICC classification, was elaborated after the first results of the study describing various clinical practice, in particular concerning lack of use of SBT, use of NIV, the presence of tracheostomised patients, etc. The steering committee met (GaB, TP, FS, JCR, JM, AM and LB) to formulate proposal which would allow to classify all patients. The goal was to take into account the variety of clinical practice and to maximize the number of patients classified. We therefore proposed a priori simplified and pragmatic definitions based on the duration of the process that could be operational in any institution.

We considered useful to clearly identify patients with no separation attempt from patients who entered the weaning process, including those for which a weaning of MV was unsuccessful or leading to death. This allowed to classify all the patients, which may be important for future research and quality improvement programs about weaning from MV.

An important change was the definition of “separation attempts” that brought together all the situations leading to extubation: a formal SBT as well as an extubation without SBT. Indeed, clinicians may not want to perform SBT before extubation when the likelihood of success is very high, such as scheduled post-operative conditions or non-complicated drug overdose with coma.

We modified the definition of the weaning success to seven days, to take into account the frequent use of noninvasive ventilation that may prolong the time before reintubation. Post-extubation noninvasive ventilation is widely used and could actually modify post-extubation

evolution, with the possibility to increase the time at which success or failure can be defined, leading several authors to propose a delay of seven days to define extubation success (3, 4). Weaning definitions in tracheostomized patients raised specific issues: these patients were not defined in the ICC groups and have been often excluded from the weaning studies (5, 6). Previous studies defined weaning success in tracheostomized patients as spontaneous breathing trough the tracheal cannula or directly through the tracheostoma for 48 hours (7, 8) to five days (9). We here used a time threshold of seven days to be consistent with the extubation success definition and with the consensus conference on the management of patients requiring prolonged mechanical ventilation (10).

We then tested whether these definitions could be applied and further discussed all ambiguous cases. The final model was then applied and the results analyzed.

Use of sedation and weaning protocols, and use of SBT

We assessed the association between the presence of protocols for sedation or for weaning and the likelihood of having a short phase of separation or short weaning. For this analysis, patients with limitations decisions were excluded in order not to consider patients who had an end of life extubation as having a short weaning.

We compared patients whose first separation attempt was a SBT to patients who had another type of first separation attempt. We restricted the group of patients without SBT to those who had a planned extubation without SBT and no limitation decision (e-table 4).

Statistical analysis:

Descriptive statistics included frequency (percentages) for categorical variables, mean and standard deviation or median and interquartile ranges (IQR) for continuous variables. Comparisons of proportions were made using Chi2 or exact Fisher tests and continuous variables were compared using Student t-test or Wilcoxon rank sum test as appropriate.

We performed a multivariable analysis of factors associated with simple weaning by means of a logistic regression, forcing both sedation and weaning protocols in the final model. Last, we performed a multivariable logistic regression to assess factors associated with the use of a SBT before a planned extubation.

All statistical tests were two-sided. Two-sided P values of 0.05 or less were considered statistically significant. Statistical analyses were performed with R 3.2.3 (http://www.R-project.org) software packages.

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E-TABLES

TABLE E1: Characteristics of the group 3 including comparison between group 3a and group 3b

	G3 (All) N=235	G3a N=145	G3b N=90
Age, years	65±13	64 ±14	67±12
Sex M/F	1.9	2.0	1.8
SAPS II at admission, points	53±18	52 ±19	55±17
SOFA at admission, points	8.1±3.7	7.7±3.5	8.8±4.0
SOFA at Day 3	6.8±3.7	6.3±3.6	7.4±3.6
Admission type			
Medical	185 (78.7%)	116 (80.0%)	69 (76.7%)
Planned surgery	18 (7.7%)	10 (6.9%)	8 (8.9%)
Unplanned surgery	32 (13.6%)	19 (13.1%)	13 (14.4%)
Cardiac	10 (4.3%)	3 (2.1%)	7 (7.8%)
Abdominal	14 (6.0%)	8 (5.5%)	6 (6.7%)
Vascular	9 (3.8%)	6 (4.1%)	3 (3.3%)
Neuro	5 (2.1%)	5 (3.5%)	0 (0%)
Urologic	1 (0.4%)	1 (0.7%)	0
Thoracic	6 (2.6%)	2 (1.4%)	4 (4.4%)
Trauma	2 (0.9%)	2 (1.4%)	0 (0%)
Head & Neck	0 (0.0%)	0 (0%)	0 (0%)
Others	3 (1.3%)	2 (1.4%)	1 (1.1%)
Total number of days of invasive MV, days	19 [15;31]	17 [14;28]	23 [16;38]
Ventilator free days[1], days	0 [0;12]	11 [0;14]	0 [0;0]
Delay from intubation to 1st SA	6 [3;10]	7 [3;10]	6 [3;10]
Length of stay in the ICU, days	31 [20;46]	34 [22;47]	28 [17;42]
Length of stay in the ICU in survivors, days	37 [23;52]	34 [21;47]	56 [33;60]
Status at ICU discharge (or D60)			
Dead	70 (29.8%)	3 (2.1%)	67 (74.4%)
Alive and weaned	140 (59.6%)	140 (96.6%)	0 (0%)
- Spontaneous breathing	96 (40.9%)	96 (66.2%)	0 (0%)
- NIV	10 (4.3%)	10 (6.9%)	0 (0%)
- Tracheostomy (permanent spontaneous breathing)	34 (14.5%)	34 (23.4%)	0 (0%)
Alive and Invasive ventilation	25 (10.6%)	2 (1.4%)	29 (30.2%)
- Tube	5 (2.1%)	0 (0%)	9 (9.4%)
- Tracheostomy with mechanical ventilation	20 (8.5%)	2 (1.4%)	20 (20.8%)
Decision of withholding or withdrawing invasive MV:			
- Total	63 (26.8%)	23 (16.0%)	40 (41.7%)
- Among deceased patients	42 (60.0%)	3 (100%)	39 (58.2%)
- Among survivors	21 (12.7%)	20 (14.1%)	1 (3.5%)

Abbreviations: MV: mechanical ventilation; SA: separation attempt; ICU: intensive care unit; NIV: noninvasive ventilation; SD: standard deviation; IQR: interquartile range

[1]Ventilation free days (VFD) = 28 minus the total number of days with Invasive MV

TABLE E2: Comparison consensus conference classifications and the new WIND classification

Consensus / Wind Conference Classification	1	2	3	Not classified	TOTAL	Agreement (%)
NW	0	0	0	658	658	NA
1	945	156	3	442	1543	61.2%
2	5	141	46	81	273	51.6%
3	12	11	60	152	235	25.5%
TOTAL (N)	962	308	109	1330	2709	
Agreement (%)	98.2%	45.8%	55.0%	NA		42.3 %

For each line and each column, agreement was calculated as follow:

$$\frac{\textit{Number of patients classified in the same group in the 2 classifications}}{\textit{Total number of patients of the line or column}}$$

TABLE E3: Characteristics of separation attempt and weaning according to the weaning group, data are presented as mean ±SD, median [IQR] or N (%)

	GO N=658	G1 N=1543	G2 N=273	G3		
				All N=235	G3a N=145	G3b N=90
Total Number of SA		1769*	766	936	638	298
Number of SA per patient		1 [1;1]	3 [2;3]	3 [2;5]	4 [2;5]	2 [1;4]
Type of SA, n (%):						
T-tube		662 (37.4%)	399 (52.1%)	387 (41.3%)	270 (42.3%)	117 (39.3%)
LPSV		702 (39.7%)	291 (38.0%)	386 (41.4%)	244 (38.2%)	142 (47.7%)
Extubation without SBT		237 (13.4%)	24 (3.1%)	37 (4.0%)	23 (3.6%)	14 (4.7%)
Self extubation		109 (6.2%)	22 (2.9%)	35 (3.7%)	22 (3.4%)	13 (4.4%)
Planned extubation despite SBT failure		9 (0.5%)	6 (0.8%)	2 (0.2%)	0 (0%)	2 (0.7%)
Other type of SBT		36 (2.0%)	14 (1.9%)	27 (2.9%)	18 (2.8%)	9 (3.0%)
Continuous period of spontaneous breathing during tracheostomy		14 (0.8%)	10 (1.3%)	62 (6.6%)	61 (9.6%)	1 (0.3%)
Total Number of extubations		1542**	325	305	218	87
Number of extubations per patient		1 [1;1]	1 [1;1]	1 [1;2]	2 [1;2]	1 [0;1]
No of days with invasive MV	3 [2;7]	3 [2;6]	9 [6;13]	19 [15;31]	17 [14;28]	23 [16;38]
Delay from intubation to first weaning attempt, days		3 [2;5]	6 [3;10]	6 [3;10]	7 [3;10]	6 [3;10]
Delay from intubation to first successful extubation, days		3 [2;5]	9 [7;13]	16 [12;22]	16 [12;22]	
No of patients with pressure support before first SBT or first extubation, n		973 (63.1%)	215 (78.8%)	179 (76.2%)	111 (76.6%)	68 (75.6%)
Pressure support before first SBT or first extubation, days		1 [0;2]	2 [1;4]	2 [1;4]	2 [1;4]	2 [1;4]
Patients with planned extubation after SBT success, n		1179 (76.4%)	226 (82.8%)	160 (68.1%)	115 (79.3%)	45 (50.0%)
Patients with self extubation, n		107 (6.9%)	21 (7.7%)	33 (14.0%)	21 (14.5%)	12 (13.3%)
Patients with self extubation only (i.e. no planned extubation)		103 (6.7%)	10 (3.7%)	11 (4.7%)	3 (2.1%)	8 (8.9%)
Patients with reintubation, n		0	70 (25.6%)	148 (63.0%)	94 (64.8%)	54 (60.0%)
Patients receiving post extubation NIV, n		202 (13.1%)	47 (17.2%)	59 (25.1%)	39 (26.9%)	20 (22.2%)
Patient with do not reintubate order, n	117 (17.8%)	130 (8.4%)	46 (16.8%)	63 (26.8%)	23 (15.9%)	40 (44.4%)

Abbreviations: SA: separation attempt; LPSV: Low Level Pressure Support Ventilation; SBT: Spontaneous Breathing Trial; MV: mechanical ventilation; NIV: noninvasive ventilation; SD: standard deviation; IQR: interquartile range

* More SA than patients because of possibility of several SA in 24h

** 17 patients were never extubated : one died after the 1st SA, 14 were tracheotomised before any SA and then were weaned, 2 were discharged with invasive MV within 24h after their 1st SA

Table E4: Type separation attempt among the 382 patients whose first separation attempt was not a SBT

Type of separation attempt	N (%)
Planned extubation without SBT	252 (55.6%)
Self-extubations	124 (27.3%),
Separation attempt while tracheostomized	30 (6.6%)
SBT after their first Separation attempt	48 (10.6%)
Total	454 (100%)

Figure E1: Distribution of Ventilator free days at day 28 according to weaning groups (absolute numbers)
This figure shows for each group and for the whole population, the number of patients achieving each number of ventilator free days from 27 to 0. Ventilator free days are defined by 28 minus the total number of days with Invasive Mechanical Ventilation. Non survivors were considered as having 0 Ventilator free days.