A Prospective, Controlled Trial of a Protocol-based Strategy to Discontinue Mechanical Ventilation

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Weaning protocols can improve outcomes, but their efficacy may vary with patient and staff characteristics. In this prospective, controlled trial, we compared protocol-based weaning to usual, physician-directed weaning in a closed medical intensive care unit (ICU) with high physician staffing levels and structured, system-based rounds. Adult patients requiring mechanical ventilation for more than 24 hours were assigned to usual care (UC) or protocol weaning based on their hospital identification number. Patients assigned to UC (n = 145) were managed at their physicians' discretion. Patients assigned to protocol (n = 154) underwent daily screening and a spontaneous breathing trial by respiratory and nursing staff without physician intervention. There were no significant baseline differences in patient characteristics between groups. The proportion of patients (protocol vs. UC) who successfully discontinued mechanical ventilation (74.7% vs. 75.2%, p = 0.92), duration of mechanical ventilation (median [interquartile range]: 60.4 hours [28.6–167.0 hours] vs. 68.0 hours [27.1–169.3 hours], p = 0.61), ICU (25.3% vs. 28.3%) and hospital mortality (36.4% vs. 33.1%), ICU length of stay (115 vs. 146 hours), and rates of reinstituting mechanical ventilation (10.3% vs. 9.0%) was similar. We conclude that protocol-directed weaning may be unnecessary in a closed ICU with generous physician staffing and structured rounds.

Keywords: ventilator weaning; respirator, artificial; critical care; nursing care

Several recent randomized trials and prospective case series have found that protocols directed by nursing and respiratory care staff can expedite the discontinuation of mechanical ventilation (1–12). Because mechanical ventilation commonly necessitates intensive care unit (ICU) care, these findings could improve both patient outcomes and resource use. A recent evidence-based report recommended more widespread use of such protocols to expedite discontinuation of mechanical ventilation in ICU patients (13), based on a small number of prospective, randomized trials (3, 5, 6).

However, although the outcome benefits of protocols have received wide attention, their limitations are less often acknowledged. Protocols demand substantial resources to design, implement, promote, and sustain their use, without which they may be rapidly abandoned (14). Structural changes such as administratively closed ICUs (15), higher levels of intensivist physician staffing (16), or checklists to make rounds more systematic (17) may also improve clinical outcomes of critically ill patients. It is not known whether weaning protocols retain their ability to speed weaning when such structural changes are in place. If protocols speed the discontinuation of mechanical ventilation only by enforcing daily attention to patients' readiness to breathe unassisted, they may be unnecessary in ICUs in which other structural or practice patterns encourage the same degree of vigilance.

Therefore, the primary objective of this clinical trial was to evaluate whether a protocol for discontinuation of mechanical ventilation, based on a strategy previously shown to be effective (3), accelerates discontinuation of mechanical ventilation compared with usual care (UC) in a closed, academic intensivist–run medical ICU with high physician staffing levels and structured, system-based rounds. Some of these results have been presented in abstract form (18).

METHODS

Detailed methods are available in an online supplement. The medical ICU is a closed 14-bed unit staffed by 2 attendings and 10 M.D. trainees. The physicians work in two teams of six, each team caring for half the patients. All attend structured daily bedside rounds lasting approximately 3 hours. Presentations on rounds are based on a printed template covering each major physiologic system, which is completed by the house staff daily (*see* online supplement). Most physicians remain in the ICU for the workday, and three house officers stay overnight. The nurse (all registered nurses) to patient ratio is 1:2, plus one to two additional senior nurses and one to two respiratory therapists. The staff is experienced with numerous protocols guiding nonventilatory care and has used ventilator protocols in patients enrolled in the Acute Respiratory Distress Syndrome Network studies (19).

All patients requiring invasive ventilation for 24 hours or more from April 2000 to July 2001 were eligible. Previous participants, those enrolled in other studies that controlled weaning (such as the ARDS Network studies) or transferred from other facilities already intubated, were excluded. The institutional review board waived the requirement for informed consent.

Patients were assigned to a study group by their hospital numbers (odd versus even). The protocol wean (PW) was based on one previously shown to reduce duration of ventilation (3). This consisted of a daily screen for readiness, followed by measurement of the ratio of respiratory frequency to mean V_T (f/V_T) in patients passing the screen. If f/V_T was 105 or less, a spontaneous breathing trial (SBT) was then attempted on continuous positive airway pressure (CPAP), with 5 cm H_2O pressure support added if the endotracheal tube was 7 mm or less. Physicians were told whether the SBT was tolerated for 1 hour. If not, the patient was rested on mechanical ventilation until the next morning (Table 1). Physicians could also extubate PW patients based on their clinical judgment. Staff were trained in the protocol, which was piloted during a 2-month run-in period. For patients randomized to UC, discontinuation of ventilation was left entirely to the discretion of the physicians. No scheduled screening was performed by ancillary staff, although an f/V_T determination could be requested or measured by the attending at the bedside. Physicians specified each ventilator setting or the beginning and end of a SBT with an individual order. Routine care included a sedation protocol titrating midazolam and/or fentanyl to a behavioral goal.

The ICU fellow documented the reason for intubation and presence of chronic respiratory disease on case report forms. A study coordinator contemporaneously reviewed and reinforced staff compliance.

Data on weaning methods were not collected contemporaneously on patients in the UC arm. After completion of the study, a random sample of 50 patient charts in this group was reviewed to extract data

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TABLE 1. FAILURE CRITERIA FOR SCREENING FOR SPONTANEOUS BREATHING TRIAL AND FOR THE TRIAL ITSELF

Screening for f/VT
- Patient is not advanced to f/VT measurement if any of the following are present:
  - Known or suspected increased intracranial pressure
  - Unstable coronary artery disease
  - Heart rate ⩾ 140 bpm
  - Wean screen prohibited by physician
  - $Sp_{O_2} < 92\%$
  - PEEP > 5 cm H_2O
  - $F_{I_{O_2}} > 0.5$
  - Receiving paralytics
  - Absent cough and gag reflex
  - Unresponsive to noxious stimuli

SBT (performed if screen for f/VT passed and f/VT < 106)
- Patient is returned to ventilator if within 1 hr of initiating SBT any of the following occur:
  - Heart rate > 20 bpm above rate before initiating SBT, persisting for > 5 min
  - Systolic blood pressure < 90 torr (12 kPa) or > 30 torr (4 kPa) change after initiating SBT, persisting > 5 min
  - Chest pain or ECG changes (ischemia or new arrhythmia)
  - $Sp_{O_2} < 88\%$ or $Pa_{O_2} < 60$ torr (8 kPa), persisting > 5 min
  - Marked distress, dyspnea, or agitation

Definition of abbreviations: f/VT = frequency to mean VT; PEEP = positive end-expiratory pressure; SBT = spontaneous breathing trial; Sp_{O_2} = pulse oximetric measurement of arterial oxygen saturation.

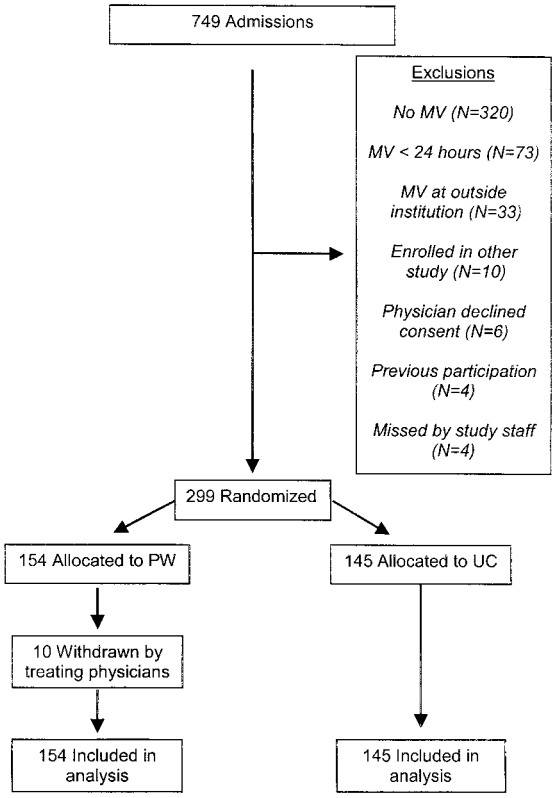

Figure 1. Patient-flow diagram. MV = mechanical ventilation; PW = protocol-directed MV discontinuation; UC = usual care (traditional, physician-directed MV discontinuation).

on weaning methods. Because measurement of f/VT was not routinely performed or documented in the UC group, these data are unavailable.

Data are presented as mean ± SD, median (interquartile range), or proportions, as appropriate. The primary outcome was duration of ventilation, defined as the time from intubation to the beginning of the SBT that ended with successful discontinuation of mechanical ventilation. Patients were considered to have successfully weaned if they were able to breathe unassisted for 48 hours. Compliance with the protocol was evaluated by review of the weaning documentation form used by the therapists and nurses and chart review. Analyses were based on intention to treat, with χ^2 tests or Fisher's exact tests and *t* tests or Wilcoxon-rank sum tests, as appropriate. Multivariable linear regression evaluated the sensitivity of results to imbalances in patient baseline characteristics; p values of more than 0.05 were considered nonsignificant. The sample size provided 82% power (assuming two-sided type I error = 0.05) to detect a 1-day difference in mechanical ventilation duration. Computations were performed using STATA 7.0 (StataCorp LP, College Station, TX).

RESULTS

During the study period, there were 749 admissions to this ICU, of which 356 (47.5%) required invasive mechanical ventilation for at least 24 hours and hence were eligible to participate. Among the excluded patients, 320 were not intubated or ventilated, and 73 were extubated or died in less than 24 hours. Fifty-three patients who were intubated and ventilated for more than 24 hours were excluded for the reasons shown in Figure 1 (33 because of having been transferred from another institution already intubated). Four other potential subjects were missed. Two hundred ninety-nine patients were enrolled. One hundred fifty-four were assigned to the protocol strategy, and 145 to usual physician-directed weaning. Baseline characteristics of the participants are shown in Table 2. There were no significant differences between treatment groups in regards to age, sex, ethnicity, severity of illness on ICU admission (Simplified Acute Physiology Score II score), oxygenation ($Pa_{O_2}/F_{I_{O_2}}$), or presence of chronic respiratory disease. Patients assigned to PW were less likely to be admitted from another ICU (7.1% vs. 12.4%) or hospital (2.0% vs. 5.5%) or nursing home (1.3% vs. 2.1%) and were more likely to have pneumonia/acute lung injury on initiating mechanical ventilation (33.2% vs. 21.4%), although overall differences between groups in source of admission and reason for initiating mechanical ventilation were not significant (p = 0.27 and p = 0.29, respectively).

Compliance with the protocol was high among the 154 patients assigned to PW. Screening was performed on 743 of 863 patient-days (86.1%) of mechanical ventilation, with 130 patients (84.4%) screened every day when they were on mechanical ventilation. Of the 406 patient-days on which all the screening criteria were passed, 343 (84.5%) were followed by a 1-minute chronic obstructive pulmonary disease trial. Among the 223 patient-days on which f/VT was 105 or less, patients were advanced to a SBT in 88.3% of cases. Ten patients were withdrawn from the PW by their treating physicians, with three (30%) of them dying before ICU discharge.

In the intention-to-treat analyses, there was no difference between groups (PW vs. UC) in the number of patients who successfully discontinued mechanical ventilation before ICU discharge (115 [74.7%] vs. 109 [75.2%], p = 0.92) or their duration of mechanical ventilation (median [interquartile range]: 60.4 hours [28.6–167.0 hours] vs. 68.0 hours [27.1–169.3 hours], p = 0.61; Figure 2). There was no significant advantage to the protocol-based strategy in reducing the time to discontinuing mechanical ventilation even after adjusting for differences in the source of admission and reason for initiating mechanical ventilation at baseline (multivariable linear regression model: reduction in me-

TABLE 2. BASELINE PATIENT CHARACTERISTICS BY GROUP

Characteristic	PW (*n = 154*)	UC (*n = 145*)	p Value
Age, yr, mean ± SD	52.2 ± 7.6	54.5 ± 16.7	0.52
Female, %	52.6	53.1	0.93
Ethnicity, %			
African American	68.8	62.8	0.31
White	26.6	34.5	
Asian	2.6	0.7	
Other	2.0	2.1	
Source of admission, %			
Emergency department	52.0	47.6	0.27
In-patient floor	28.6	22.8	
Other ICU	7.1	12.4	
Intermediate care unit	6.5	4.8	
Other hospital	2.0	5.5	
Nursing home	1.3	2.1	
Other	2.6	4.8	
Reasons for initiating mechanical ventilation, %			
Cardiopulmonary arrest	11.0	12.4	0.29
Pneumonia/acute lung injury	33.2	21.4	
COPD/asthma exacerbation without infiltrates on chest X-ray	9.7	10.3	
Cardiogenic pulmonary edema	5.2	4.1	
Neurologic emergency	16.9	19.3	
Other	24.0	32.4	
SAPS II score, mean ± SD	51.9 ± 18.5	51.2 ± 16.0	0.72
SAPS II predicted hospital mortality, %	50.5	48.8	0.77
Pa_{O_2}/Fi_{O_2}, first 24 hr of ICU stay, median (IQR)*	148 (94–238)	157 (92–228)	0.64
Chronic respiratory disease, %	25.3	31.0	0.27

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; ICU = intensive care unit; IQR = interquartile range; PW = protocol wean; SAPS II = Simplified Acute Physiology Score II; UC = usual care.

* Recorded in patients who required mechanical ventilation within the first 24 hours of ICU stay (UC: 133/154, PW: 129/145).

chanical ventilation time in the PW group = 0.84 hours, p = 0.26). The duration of the SBT preceding successful discontinuation of mechanical ventilation was longer among patients assigned to PW compared with UC (median, 3.0 vs. 1.6 hours, $p < 0.01$; Table 3). There were no significant differences (PW vs. UC) in the number of patients requiring reinstitution of mechanical ventilation (either within or after 48 hours), ICU length of stay, location after ICU discharge, and hospital mortality.

Among the 50 patients in the UC group whose charts were randomly selected for review, 34 (68%) were weaned, and 1 was discharged on mechanical ventilation. Fourteen of these 34 patients (41%) were successfully weaned using intermittent T-piece trials. Fourteen were weaned using pressure support, four (12%) by both pressure support and T-piece trials (changing mode after failure to progress), and two patients were weaned using intermittent mandatory ventilation. Sixty-five percent of the successfully weaned patients were extubated after their first SBT (either CPAP or T-piece), 15% after their second, and the remainder required three or more SBTs before successful weaning. Mean ± SD pulse oximetric measurement of arterial oxygen saturation at the initiation of the SBT was 97 ± 2.1%. Six patients, including three with an endotracheal tube larger than 7 mm, had their SBT on low levels of pressure support immediately preceding extubation. Four patients underwent a SBT while on vasopressors. For comparison, among the patients in the PW group who were weaned, 54% required only one SBT, 19.5% required two, and the remainder required three or more. Mean oxygen saturation at the initiation of the SBT was 97 ± 2.4%.

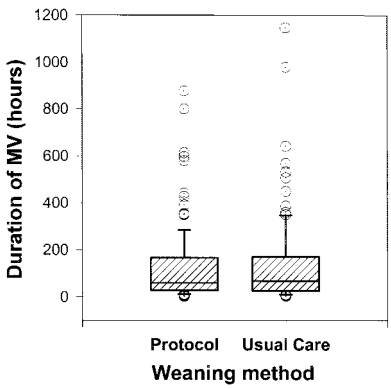

Figure 2. Duration of mechanical ventilation, by treatment group, among patients who discontinued mechanical ventilation before ICU discharge. The *horizontal line* is the median. The *box* denotes 25–75th percentile, and *whiskers* denote 10% and 90% confidence limits. Protocol group, n = 115; traditional group, n = 109; p = 0.61 by Wilcoxon rank sum.

DISCUSSION

We could not document any improvement in clinical outcomes with the use of a nursing/respiratory therapy-driven protocol for discontinuing mechanical ventilation. The protocol we used was similar to that previously shown to speed weaning in medical and coronary ICU patients (3). Our protocol was more aggressive in a few respects. First, patients could be advanced to a f/VT determination even if they were still on vasopressors. Second, we did not require a physician order to begin a SBT. Finally, we required only 1 hour of spontaneous breathing before discontinuing mechanical ventilation, based on a report that as little as 30 minutes of a SBT may be sufficient to identify patients likely to breathe unassisted (20).

A protocol will be ineffective if it is not followed. Poor compliance with study procedures has been noted in a previous investigation in which a protocol shown to be effective in shortening mechanical ventilation duration in one setting was not effective elsewhere (14). In this investigation, we documented rates of

TABLE 3. SECONDARY OUTCOMES BY GROUP

Outcome	Group		p Value
	PW	UC	
Duration of SBT, hr, median (IQR)	3.0 (1.3–5.6)	1.6 (0–3.9)	< 0.01
Reinstitution of mechanical ventilation, n (%)			
⩽ 48 hr	9 (5.8)	10 (6.9)	0.71
> 48 hr	7 (4.6)	3 (2.1)	0.23
ICU length of stay, hr, median (IQR)	115 (67–259)	146 (81–291)	0.10
Location after ICU discharge, n (%)			
In-patient floor	84 (54.6)	80 (55.2)	0.32
Died	39 (25.3)	41 (28.3)	
Intermediate care unit	15 (9.7)	9 (6.2)	
Home	4 (2.6)	8 (5.5)	
Other ICU	5 (3.4)	2 (1.4)	
Other hospital	3 (2.0)	2 (1.4)	
Chronic ventilator unit	3 (2.0)	0 (0.0)	
Other	1 (0.6)	3 (2.1)	
Hospital deaths, n (%)	56 (36.4)	48 (33.1)	0.55

Definition of abbreviations: ICU = intensive care unit; IQR = interquartile range; PW = protocol-directed discontinuation of mechanical ventilation; SBT = spontaneous breathing trial; UC = traditional physician-directed discontinuation of mechanical ventilation.

compliance with the study procedures in the intervention group, which compare favorably with similar studies. In other studies of weaning protocols, compliance with the screening step ranged from 60 (5) to 95% (3). The compliance with the SBT step in eligible patients also varied widely in other studies from 10–81% (14). In this study, we cannot distinguish weaning steps that were omitted because of simple oversight from steps that were omitted because of clinical judgment (e.g., a patient undergoing a procedure). Moreover, in this study, only 10 (3.3%) enrolled patients were withdrawn by treating physicians. Thus, we do not believe that inadequate compliance to study procedures explains the difference between this study and others addressing the same question.

A protocol may not be needed if it merely codifies a set of behaviors that are already in use. It is possible that the house staff and attendings had already incorporated some strategies that have been shown to speed weaning into their regular practice. Although we did not prospectively record physicians' approaches to discontinuing mechanical ventilation in the UC group, our chart review found that patients in UC were weaned by a variety of methods. Therefore, it is unlikely that the use of once-daily T-piece trials was an essential element of expeditious weaning. We also did not find evidence of a notably aggressive style of weaning in the UC group, as few of these patients were weaned while on vasopressors or were extubated directly from low levels of pressure support, and arterial oxygen saturation was well above minimum acceptable levels at the beginning of SBTs.

What factors then may have allowed physicians to function as well as the protocol? We believe one simple but important factor is the amount of attention that can be provided to assess patients' readiness to breathe unassisted. Unstable, critically ill patients demand physician attention, and thus, it is nearly unavoidable that stable patients (e.g., those needing only mechanical ventilation discontinuation) fall to a lower priority. When physician availability is a limiting factor in weaning, a protocol can fill that gap. However, when more physicians are available, there may be little chance for a weaning protocol to improve care. To help us further explore this possibility, the authors of previous clinical trials that evaluated protocols for weaning generously provided information to allow us to compare physician staffing levels across studies. We considered the number of ICU beds, the number of physicians assigned to the ICU, and the average number of hours they were present in the ICU each day (during the day and overnight) to calculate the number of physician-hours per bed per day in each of the studies. Compared with approximately 9.5 physician-hours/bed/day in this study, physician staffing was considerably less in the three previous randomized clinical trials: 3.5 physician-hours/bed/day (personal communication, E.W. Ely, M.D., M.P.H.) (3), 4.0 physician-hours/bed/day (personal communication, M.H. Kollef, M.D.) (5), and 4.7 physician-hours/bed/day (personal communication, G. Marelich, M.D.) (6). Although the optimal level of physician staffing for critically ill patients is not known, we speculate that the twofold to threefold increased levels of physician staffing in our ICU may have allowed more timely discontinuation of mechanical ventilation in patients ready to breathe unassisted, rendering the protocol unnecessary. This explanation is supported by results of recent studies reporting an inverse relationship between workload and patient outcomes in ICU and other healthcare settings (16, 21–23).

Another potential explanation is our use of a printed rounding template that covers each of the physiologic systems and then becomes the house staff progress note (reprinted in the online supplement). Similar templates were not in use during other randomized, controlled trials of weaning protocols (3, 5, 6) (personal communications, E. Haponik, M.D.; M.H. Kollef, M.D.; and S. Murin, M.D.). Although the template does not specifically address weaning, it may have helped prompt the team to address ventilator issues each day. In support of this explanation, the use of a simple checklist on rounds was recently shown to reduce the length of stay in a surgical/oncologic ICU (17).

Our findings might suggest that protocol-directed weaning would reduce needs for costly physician staff time. Protocols generally address focused and specific problems that are common, formulaic, and relatively straightforward. However, adequate numbers of skilled and sentient staff can promptly recognize and treat multiple subtle or complicated issues that may not be suitable for management by protocol. Adequate nursing staff, like protocols, have been shown to improve ICU outcomes, including discontinuation of mechanical ventilation and mortality (16, 21–24). In this study, the observed hospital mortality rates of 36.4% and 33.1% in PW and UC groups compare favorably with the mortality rates predicted by their Simplified Acute

Physiology Score II severity of illness score on ICU admission (50.5%, p = 0.02, and 48.8%, p = 0.008, respectively; p values for observed vs. predicted in each group). Intensivist-led or closed ICUs have been shown to improve ICU mortality (15, 16). For these reasons, we do not believe that ICU protocols can substitute for qualified physician and nursing staff. Greater staffing levels are expensive. However, costs of insufficient staff, although hidden to hospital administrators, may be greater.

Our study has several potential limitations. As in other similar unblinded studies (3, 5, 6, 9), it is possible that some physicians, nurses, or respiratory therapists may have changed their UC ventilator management practice because they knew the study was underway (Hawthorne effect). If they reverted to less salutary practice after the trial period ended, the effectiveness of the protocol during a more typical period might have been obscured.

Our allocation process by even or odd medical record number was only quasirandomized and therefore potentially subject to selection bias. Medical record numbers are assigned administratively by a computer in order of a patient's first contact with our medical system, without regard to age, sex, race, diagnoses, ICU admission, etc. This system allowed patients to be assigned to a group immediately on admission without intervention by the investigators and contributed to there being few patients who were inadvertently overlooked (just 4 of 749 admissions, 0.5%). The small number of subjects (six) who were excluded by their treating physicians also suggests that there was no bias to the treatment assignments.

There was a clinically unimportant but significantly longer interval between the initiation of the final SBT and extubation in the patients weaned by protocol. We believe we understand why this occurred. In PW patients who successfully completed 1 hour of a SBT, nurses were often reluctant to interrupt attending physician rounds (generally from 8–11 A.M.) for an order to discontinue mechanical ventilation. Physicians on rounds, if interrupted, were also likely to postpone a decision if that patient had not yet been reviewed by the team. In contrast, physicians were likely to review and promptly act on the results of a SBT that they had initiated in patients assigned to UC.

Finally, our data on the UC group are limited by the retrospective chart review. It is difficult to infer the factors motivating physicians in that group, and the influence of staffing levels, the rounding template, or other factors remains speculative and subject to prospective confirmation.

Conclusions

In summary, in contrast to previous reports, weaning by nursing and respiratory therapy according to a protocol did not reduce duration of mechanical ventilation, length of stay, or mortality compared with weaning by physicians. We speculate that this lack of benefit may have been due to the high levels of physician staffing in our intensivist-run closed ICU or the use of a template on rounds to promote daily discussion of mechanical ventilation on each patient. Protocols, which are laborious to design and implement, do not necessarily improve patient care and should be tested in the setting in which they are to be applied. The most cost-effective ICU physician staffing level is unknown and will vary among ICUs. However, intensivists inarguably should be attentive to weaning. This attention may be promoted by a weaning protocol, structured rounds, additional staffing, or other tools to ensure that the ability to breathe is recognized promptly.

Conflict of Interest Statement: J.A.K. has no declared conflict of interest; D.M. has no declared conflict of interest; C.R. has no declared conflict of interest; C.S.R. has no declared conflict of interest; H.E.F. has no declared conflict of interest.

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