

ORIGINAL PAPER

NURSING WORKLOAD AND STAFF ALLOCATION IN AN ITALIAN HOSPITAL: A QUALITY IMPROVEMENT INITIATIVE BASED ON NURSING CARE SCORE

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Abstract

Aim: To develop, implement, and evaluate a Nursing Care Score (NCS) system, built into the electronic health record, to optimize nursing workload and staff allocation. *Design:* A quality improvement (QI) initiative with a pre- and post-implementation design was conducted by an interprofessional team in the 33-bed cardio-thoracic unit of a 72-bed hospital in Palermo, Italy. *Methods:* A seven-phase process was used to develop, implement, and evaluate the NCS, which lists 53 nursing work tasks, each assigned a score from 1.5 to 5.0. The nurse-to-patient ratio on all shifts was determined by the NCS. Nurse satisfaction with both the existing system and the NCS workload system was assessed. Descriptive statistics and McNemar's test were used to analyze the data. *Results:* At pre-implementation, 92.5% of nurses reported that the existing system was not effective, 87.5% reported it did not enable them to provide adequate nursing care, and 20.0% believed that workload was fairly distributed. At post-implementation, 75.0% of nurses reported that the NCS system was effective (p = 0.0348), 85.0% reported that the NCS system enabled them to provide adequate care, and 85.0% believed that workload was fairly distributed. An NCS score of 65 ± 5 was found to distribute workload most fairly. *Conclusion:* An automatic electronic operating system to generate a daily workload report based on the NCS was successfully implemented and evaluated. The NCS provided relevant information to guide nurse managers in defining nurse-to-patient ratio and determining staff allocation. Nurses were satisfied with the NCS system. The steps used to develop, implement, and evaluate the NCS system may be transferable to other units and other hospitals.

Keywords: nursing care, nursing workload, nursing care score, staff allocation, patient outcomes.

Introduction

Nursing workload relates to "the amount of performance required to carry out those nursing activities in a specified time period" (Morris et al., 2007). There is no one common definition of nursing workload in the literature, and the lack of a clear definition has been identified as one of the major problems with understanding and measuring nursing workload (Morris et al., 2007). Nursing workload quantifies nursing work in order to manage and allocate nursing staff. Therefore, it is important that any definition of nursing workload be broad enough to include the totality of work activities carried out by nurses.

Corresponding author: Santa Giammona, Department of Nursing Services, Coordinator Nursing Education & Research, IRCCS-ISMETT, 5 Via Tricomi, Palermo, Italy; email: sgiammona@ismett.edu Nursing workload is a fundamental element of establishing the needs of staff in a specific unit (Carmona-Monge et al., 2013). Over the past 30 years, several investigators have developed tools for measuring nursing workload (Gonçalves et al., 2007). Among these tools are many models of the Therapeutic Interventions Scoring System (TISS), of which the Nursing Activities Score (NAS) is the latest version (Miranda et al., 2003). The Therapeutic Interventions Scoring System-28 (TISS-28) is a tool used to assign scores to patients according to severity of illness. In TISS-28, the number of therapeutic interventions, and the amount of nursing time spent on a patient, is related to the severity of the patient's clinical condition. The TISS-28 score is, therefore, an indicator of nursing workload in intensive care unit (ICU) settings (Padilha et al., 2007). NAS was developed as a result of modifications to the TISS-28 with an additional five items, plus 14 sub-items. The

NAS has a reduced scale of 23 items in total, making its application easier, and it has become more widely used. The NAS scale assesses the activities performed and care provided to critically ill patients by nurses. Each item has an assigned score, and the sum of all the scores provides a total that represents the percentage of time a nurse spends in direct care of each patient over a 24-hour period in an ICU unit. In several studies using the NAS scale, it has provided greater accuracy in assessing workload than the TISS-28 (Miranda et al., 2003).

Although nurses are expected to use workload measurement systems to collect data related to the work they perform, the systems in place often add to nurses' workload by requiring them to describe their work (Goossen et al., 2000). This method is inefficient and is often perceived by nurses as an extra task. For example, the NAS has its own specific instructions for use (Miranda et al., 2004 as cited in Gonçalves et al., 2007), and the application of this existing tool adds to the burden of providing care, requires additional activity beyond documenting patient care, and requires nurses to understand both the NAS methodology and software system.

To address this shortcoming, a quality improvement (QI) initiative was undertaken on a cardio-thoracic unit. Prior to the QI initiative, nurse-to-patient ratio on the unit was determined by the criterion of complexity, based solely on continuous monitoring of patients. Nurses were assigned to patients on a ratio of 1:5 for non-monitored patients, and 1:3 for monitored patients, which was not reliable enough to identify the level of complexity of care required by patients and did not take into account nursing workload and degree of intensity. Patients admitted to the cardio-thoracic unit include medical/surgical patients, cardiopulmonary patients, and post cardiacsurgery and thoracic-surgery patients. Each patient admitted from the Operating Room (OR) or transferred from the ICU is monitored for the first 24-48 hours and when hemodynamically stable, the patient is transferred to a non-monitored bed. A monitored bed includes electrocardiography monitoring, pulse oximetry, and non-invasive blood pressure measurement. Not all patients have continuous central venous pressure or invasive arterial blood pressure measurement. Monitored patients may require different specialties and may have different frequencies of measurement of vital signs (i.e., every four hours or every six hours). Not all care of monitored patients is time consuming. Some are independent in terms of walking, bathing, and feeding, and do not require surgical dressing changes. In contrast, non-monitored patients might have tubes and drainages, may require assessment and treatment of pressure ulcers and pain, and may not be able to satisfy even primary needs independently. Therefore, this purely clinical distinction of monitored beds versus non-monitored beds does not always correspond to the actual level of patient care complexity and workload involved with a given patient. Given this discrepancy, some nurses have a high workload and some do not. This situation can result in nurse dissatisfaction and burnout, with negative effects on quality of care and patient satisfaction. O'Brien-Pallas et al. (1997) and O'Brien-Pallas and Baumann (2000) stated that an appropriate system of measuring nursing resource intensity and workload would be a valid system that measures elements of nurses' work that influence nursing workload and patient outcomes.

Aim

In view of the importance of measuring nursing workload to ensure adequate staff to meet patients' care needs in our hospital and to optimize nursing workload and staff allocation, the overall purpose was to identify a method to effectively assess nursing workload for an appropriate and fair distribution of nursing work tasks on the unit. The specific process for capturing workload in hospitals depends on the software that has been implemented and the methodology upon which the software has been based. Thus, one of our goals was to integrate the workload measurement system into the existing patient documentation system, which would save the nurses time that would otherwise be spent on entering data using separate software.

The specific aim of this QI initiative was to develop, implement, and evaluate a Nursing Care Score (NCS) system, built into the actual electronic health record (EHR), which would eliminate the need to enter data on a separate workload system and obviate additional nursing tasks.

Methods

Design

The QI initiative used a pre- and post-implementation design over a 21-month period (July 2013 – March 2015) in the 33-bed cardio-thoracic unit of a 72-bed transplant and specialized procedures hospital in Palermo, Italy. Seven hospital staff members, including four nursing leaders who developed the standards of nursing practice in the institution, formed the interprofessional project team that conducted the QI initiative.

Sample

Forty nurses from the unit participated in both the pre-implementation and post-implementation stages of the QI initiative. 52.5% (21 of 40) of the nurses were female. The mean age was 33.8 ± 4.7 years (range 26–44 years; median = 34 years). The average years of work experience was 6.2 ± 2.7 years (range 3–12 years; median = 7 years).

Data collection

During the QI initiative, the nurse-to-patient ratio on all shifts was determined according to a new workload measurement tool, the NCS, described below. The QI initiative involved the following seven phases.

Phase I: Project sharing with nurses

In early July 2013, an e-mail containing the project's purpose, description, and methodology was sent to the staff nurses. Following this, all project team members met with the nurses to answer any questions raised. These meetings spanned two weeks, with a one-hour session held every day.

Phase II: Identification of nursing work tasks/conditions with high patient care complexity

In late July 2013, the project team members and 52 nurses collaborated to identify a total of 53 nursing work tasks with high patient care complexity (see Table 1), chosen from all the nursing tasks listed in the pre-set electronic nursing notes. Nursing work tasks requiring only minimal nursing care were excluded. The NCS is based on a simple hierarchical classification of nursing work tasks/conditions. Verran (1986) recommends that patient classification instruments should be as concise as possible to limit the amount of nursing time spent in nursing documentation rather than direct patient care.

Phase III: Pre-implementation questionnaire

The two-part pre-implementation questionnaire was completed by 52 nurses over a four-week period from August to September 2013. The first part of the questionnaire was a brief survey that assessed nursing opinions about the adequacy of the nurse-to-patient ratio system based on continuous patient monitoring and the issues this workload system caused for nurses. Nurses responded Yes or No to the following four items: (a) Do you think nurse-to-patient ratio assignments determined by the criterion of complexity based solely on continuous monitoring is effective? (b) Do you agree the "old" system enables you to provide adequate care to your patients? (c) Do you believe the "old" system is able to fairly distribute the workload among nurses during their shifts? (d) Do you think the "old" system enables you to maintain consistent dialogue with your patients?

In the second part of the questionnaire, the nurses rated the relevance of each of the nursing work tasks/conditions with high patient care complexity identified in *Phase II* using a Likert scale of 1 = not relevant to 5 = very relevant. Table 1 shows the mean relevance scores.

Phase IV: Refinement of NCS

In late September 2013, the project team members assigned each nursing work task a final NCS, based on the mean relevance score for each nursing work task calculated from the ratings provided by the nurses. Table 1 shows the assigned NCS. The NCS consists of 53 items that assess the activities performed and care provided to patients by nurses. Each item has an assigned value from 1.5 to 5.0, and the total score is the sum of all the values. The nurses select the items related to the nursing care that each of their patients requires. If the item is not selected, the value will be 0. The total score for each patient represents the amount of the nurse's work the assigned patient accounts for during a particular shift (patient NCS). The sum of the values from the 53 items on the scale can range from a score of 0 to 170. The sum of all patients' scores is then divided by the number of patients present on the unit, in order to obtain the average NCS of the unit. The average NCS is used to assign the nurses to a group of patients in such a way that each nurse has the same average NCS.

Phase V: Implementation of an automatic electronic operating system

Information Technology (IT) support was required to generate an automatic daily workload report. Before the beginning of each shift, all nurses and team leaders for each shift received an e-mail with the NCS of the patients present on the unit. The automatic electronic operating system was fully implemented by the end of October 2013.

Phase VI: Testing of the new nurse-patient assignment system

Project team members developed a checklist to test the efficacy of the NCS system, occasionally observing nurses' documentation of patients' clinical conditions (see Figure 1). Testing of the NCS system was conducted over a four-week period from September to October 2014.

Item number	Nursing Work Tasks/Conditions	mean (± SD)	NCS
1	uncontrolled agitation	4.73 (± 0.86)	5.0
2	disoriented to person, place, and time	$4.65(\pm 0.69)$	5.0
3	restraints	$4.44 (\pm 0.84)$	5.0
4	totally passive mobilization with assistance devices	$4.73(\pm 0.49)$	5.0
5	continuous hemofiltration	$3.67 (\pm 4.50)$	4.5
6	noncompliant	$4.34 (\pm 0.72)$	4.5
7	tracheostomy	$4.45(\pm 0.81)$	4.5
8	complex dressing	$3.75 (\pm 0.92)$	4.0
9	obtunded	$3.65(\pm 1.21)$	4.0
10	insulin drip	$3.79(\pm 0.76)$	4.0
11	transvenous pacemaker	$2.77(\pm 1.61)$	4.0
12	non-invasive mechanical ventilation	$3.87 (\pm 0.92)$	4.0
13	incontinent (gastrointestinal)	$3.89 (\pm 0.79)$	4.0
14	incontinent (genitourinary)	$3.69(\pm 0.97)$	4.0
15	totally dependent for personal hygiene	3.71 (± 1.29)	4.0
16	mobilization with average aid	$3.30 (\pm 0.89)$	3.5
17	anxious	$3.36 (\pm 1.07)$	3.5
18	limited attention span	$3.34 (\pm 0.87)$	3.5
19	responds inappropriately	$4.34 (\pm 0.72)$	3.5
20	pain	$3.65(\pm 0.90)$	3.5
21	febrile	$3.46 (\pm 0.98)$	3.5
22	vital signs every 2 hours	$3.55 (\pm 0.91)$	3.5
23	heparin drip	$3.51 (\pm 0.70)$	3.5
24	ventricular assist device	$3.65(\pm 0.83)$	3.5
25	flexiseal	$3.28 (\pm 0.97)$	3.5
26	bladder irrigation	$3.02 (\pm 1.14)$	3.5
27	intake and output < every 4 hours	$2.83 (\pm 0.92)$	3.0
28	nitroglycerin drip	$3.04 (\pm 0.73)$	3.0
29	blood sample, more than once every shift	$2.89 (\pm 0.77)$	3.0
30	external/transcutaneous pacemaker	$2.87 (\pm 0.88)$	3.0
31	chest tube	2.65 (± 0.63)	3.0
32	fecal bag	3.06 (± 0.82)	3.0
33	depressed	2.81 (± 0.85)	2.5
34	arterial line	2.55 (± 0.73)	2.5
35	mediastinal drainage	2.55 (± 0.73)	2.5
36	enteral nutrition	2.73 (± 0.78)	2.5
37	vital signs every 4 hours	2.53 (± 0.98)	2.5
38	pigtail catheter	2.59 (± 0.67)	2.5
39	parenteral nutrition	2.59 (± 0.67)	2.5
40	nasogastric tube	2.53 (± 0.71)	2.5
41	percutaneous Endoscopic Gastrostomy tube	$2.59 (\pm 0.70)$	2.5
42	feeding tube	2.67 (± 0.71)	2.5
43	"T" tube	2.59 (± 1.03)	2.5
44	medium dressing	2.65 (± 0.94)	2.5
45	partially dependent for personal hygiene	$2.40 (\pm 0.86)$	2.5
46	central venous catheter	$2.22 (\pm 0.96)$	2.0
47	blood sampling every shift (ABG, VBG)	$2.40 (\pm 0.67)$	2.0
48	mobilization with minimal help	2.12 (± 0.78)	2.0
49	Jackson Pratt n°1	2.14 (± 0.61)	2.0
50	Jackson Pratt n°2	$2.14 (\pm 0.61)$	2.0
51	Jackson Pratt n°3	$2.20 (\pm 0.73)$	2.0
52	simple dressing	$1.89 (\pm 0.62)$	2.0
53	vital signs every 8 hours	$1.91 (\pm 0.78)$	1.5

Table 1 Nursing Work Tasks/Conditions with Mean Relevance Scores and Assigned Nursing Care Scores (NCS)

ABG - arterial blood gas, VBG - Venous Blood Gas, SD - standard deviation

Phase VII: Post-implementation questionnaire

In March 2015, 40 of the original 52 nurses completed the post-implementation questionnaire, which was a brief survey to assess nursing opinions about the appropriateness of the new workload measurement system related to nurse-to-patient ratio assignments. Nurses responded Yes or No to the following four items: (a) Do you think the NCS

Name of RN caring for patient:

system is effective? (b) Do you agree the NCS system enables you to provide adequate care to your patients? (c) Do you believe the NCS system is able to fairly distribute the workload among nurses during their shifts? (d) Do you think the NCS system enables you to maintain consistent dialogue with your patients?

	Yes
RN Notes updated before the beginning of each shift (6 a.m., 1 p.m., 8 p.m.)?	
Appropriate Score?	
If NOT, please mark one or more of the following sections that were not appropriately documented:	
Psychosocia	1
Pair	1
Neurologica	1
Cardiovascula	r
Device	e
Pulmonar	7
Gastrointestina	1
Genitourinar	/
Integumentar	/
Mobilization	1
Hygien	•

Name of supervisor:

Figure 1 Audit form to test the efficacy of the Nursing Care Score system

Data analysis

Data were stored in an electronic spreadsheet in Microsoft Excel and analyzed using the Statistical Package for Social Sciences (SPSS) 20.0 for Windows and Stata/MP 13.0 for Windows. Descriptive statistics: mean, standard deviation (SD), median, and range (r) were calculated for nurses' age and years of experience. The McNemar's test was used to verify the potential of the new NCS system and to compare pre- and post-implementation questionnaire data. The level of significance was set at 0.05.

Results

Mean relevance scores for the nursing work tasks obtained in *Phase III* ranged from 1.91 to 4.73. The corresponding assigned NCS ranged from 1.5 to 5.0 by increments of 0.5. One nursing work task was assigned a NCS of 1.5, seven tasks were assigned a NCS of 2.0, thirteen tasks were assigned a NCS of 2.5, six tasks were assigned a NCS of 3.0, eleven tasks were assigned a NCS of 3.5, eight tasks were assigned a NCS of 4.0, three tasks were assigned a NCS of 4.5, and four tasks were assigned a NCS of 5.0.

The response rates obtained from the sample of nurses differed in the pre- and post-implementation phases. The pre-implementation questionnaire questionnaire (Phase III) had a response rate of 100% (n = 52). Since the purpose of the postimplementation questionnaire (Phase VII) was to measure the effect of the NCS system on nurses' workload distribution, it was decided that the sample for the post-implementation questionnaire would consist only of those nurses who had completed the pre-implementation questionnaire. Of the 52 nurses that had completed the pre-implementation

questionnaire in 2013, 76.9% (n = 40) were still working in 2015. All four key questions were answered, and no data were missing.

Pre-implementation questionnaire responses reflected nurses' opinions about the need to identify a method to effectively assess nursing workload for an appropriate and fair distribution of nursing working tasks/clinical conditions. The majority of staff (92.5%; n = 37) agreed that nurse-to-patient ratio assignment determined by the criterion of complexity based solely on continuous patient monitoring was not effective, and 87.5% (n = 35) agreed that the old system was not enabling them to provide adequate nursing care to their patients. Only 20% (n = 8) believed that the old system was able to fairly distribute the workload among nurses during their shifts. A quarter (n = 10) of the nurses claimed that they were able to maintain consistent dialogue with their patients.

The post-implementation questionnaire responses indicated satisfaction with the NCS system. Threequarters (n = 30) of the nurses stated that the NCS system was effective. The majority (85%; n = 34) agreed that the new system enabled them to provide adequate nursing care to their patients, and the same percentage (85%; n = 34) believed that the new system was able to fairly distribute the workload among nurses during their shifts. Similarly, 75% (n = 30) responded that the NCS system enabled them to maintain consistent dialogue with their patients.

The post-implementation responses were examined for differences in proportions from the preimplementation responses (see Table 2). Significant differences were observed when nurses' responses in the pre- and post-implementation questionnaires about effectiveness of the old vs. new systems were compared (McNemar's $X^2 = 4.45$; p = 0.0348). However, there were no significant differences in nurses' responses regarding provision of adequate care under the old and the new systems (McNemar's $X^2 = 0.09$; p = 0.7630). Similarly, no significant differences in nurses' responses were found when the old and the new systems were compared regarding fair distribution of nursing workload (McNemar's X² = 0.33; p = 0.5637). In addition, no significant differences in nurses' responses were discovered regarding nurses' ability to maintain consistent dialogue with their patients when both systems were compared (McNemar's $X^2 = 0.00$; p = 1.0000).

 Table 2 Comparison of Survey Responses Pre- and Post-Implementation of Nursing Care Score (NCS)

Item	Pre-NCS % (n)	Post-NCS % (n)	McNemar X ² (1); p
Workload system is effective			4.45; 0.0348
yes	7.5% (3)	75.0% (30)	
no	92.5% (37)	25.0% (10)	
Workload system enables you to provide appropriate nursing care			0.09; 0.7630
yes	12.5% (5)	85.0% (34)	
no	87.5% (35)	15.0% (6)	
Workload system fairly distributes workload			0.33; 0.5637
yes	20.0% (8)	85.0% (34)	
no	80.0% (32)	15.0% (6)	
Workload system enables you to maintain consistent patient dialogue			0.00; 1.0000
yes	25.0% (10)	75.0% (30)	
no	75.0% (30)	25.0% (10)	

The project team members who tested the efficacy of the NCS system and periodically observed the nurses' documentation of patients' clinical conditions, found that a NCS of 65 ± 5 was optimal in order to fairly distribute workload among nurses on the unit. Based on the NCS, two nurses could be allocated to six patients with a total score of approximately 130 to optimize nursing workload.

Discussion

This QI initiative successfully developed, implemented, and evaluated a NCS system, built into

the actual EHR, which eliminated the need to enter data on a separate workload system and obviated the need for additional nursing tasks. The NCS system, built on the EHR, eliminated the need to use separate software systems; therefore, nurses' tasks did not increase and nurses were only required to pay more attention to documenting patients' needs and clinical conditions. A workload measurement system is critical for identifying nurse-staffing needs for safe patient care and rationalizing nursing resource allocation (Hoi et al., 2010). Daily implementation of the NCS system determines shift-to-shift workforce requirements, generating an average score that is transmitted before the beginning of each shift, which permits the manager or designee to assign the nurses to a group of patients in such a way that each nurse has the same average NCS. Duffield et al. (2009) reported that it is probably not possible to determine perfect staffing systems or nurse-patient ratios if workload is not considered. Analysis of the responses post-implementation questionnaire to the demonstrated an increase in nurses' satisfaction and a sense of gratification for being involved in the development of the NCS system. The development, implementation, and evaluation of the NCS system in the unit optimized nursing workload and provided nurse managers with an adequate tool to define nurse-to-patient ratio and consequently to determine staff allocation. A NCS of 65 ± 5 was found to distribute workload most fairly.

Nursing Implications

The results from this QI initiative have several implications for nursing practice. First, optimal workload distribution may lead in the future to a reduction in stress and burnout syndrome among nurses, and to improvements in job satisfaction, and consequently better retention in the workplace. Second, since resourcing of nursing care is a very real concern for nurse managers across the globe today, understanding the level of the nursing workload is crucial in appropriate resource planning. Resource planning depends on adequate nursing workload allocation, which is associated with lower rates of adverse patient outcomes that are potentially nursing sensitive, such as urinary tract infections, pneumonia, shock, cardiac arrest. upper gastrointestinal bleeding, failure to rescue, and length of hospital stay (Needleman et al., 2002). Furthermore, a higher proportion of registered nurses is associated with positive outcomes, such as lower rates of medication errors and hospital-acquired infections (McGillis Hall et al., 2004).

Recommendations for Future QI Initiatives

Based on the results of this QI initiative, a number of recommendations for future QI initiatives can be made. Patient outcomes, such as infection rates, pressure ulcers, and falls, could be evaluated pre- and post-implementation of the NCS system on other units to verify that the NCS system promotes safety and quality care for patients. In addition, a diffusion of the NCS system to all other units could allow nurse leaders to more easily transfer nursing staff from one unit to another based on the NCS and the unit needs. For example, nurses who call in sick may not need to be replaced by nurses working extra shifts, but by nurses from other units when using the NCS system. A further analysis of expenses related to nursing resources and adverse event rates can be made to verify that the NCS system contributes to institutional cost containment. Moreover, a patient satisfaction evaluation of the pre- and postimplementation of the NCS system on the other units may provide evidence of high levels of patient satisfaction, with a resulting improvement in patient outcomes.

Limitations of study

Due to the fact that this QI initiative was conducted with a small sample from a single Italian cardiothoracic unit, further implementation and evaluation with a larger sample are needed. Since the NCS is a new instrument to measure nursing workload, its use should be expanded to better evaluate its performance. Furthermore, there are few studies in the international literature that allow comparison with the results of other nursing workload measurement tools.

Conclusion

Measuring nursing workload is an important factor in nursing organizations and may positively influence patient outcomes. Appropriate nurse staffing is essential to ensure quality of care. Such staffing will increase patient safety and reduce the risk of adverse events that may occur while staying in the unit. To achieve adequate staffing, tools to measure care needs of patients are necessary. Workload measurement tools guide nurse managers in defining consequently nurse-to-patient ratios and in determining staff allocation. Despite the limitations of this OI initiative, the results allowed us to evaluate the applicability of the NCS system in the unit, and the results showed that the NCS was feasible and provided relevant information on nursing workload.

Post-implementation questionnaire results indicated enhanced nursing satisfaction, as a result of appropriate and fair distribution of nursing work tasks among the nursing staff. The NCS proved to be a valuable tool for measuring workload in the unit. Based on these promising results, NCS performance will be tested in different units in the hospital for broader applicability, and may be transferable to other hospitals.

Ethical aspects and conflict of interest

Since this project was a QI initiative, Institutional Review Board approval was not required. The nurses were informed that their participation in the QI initiative would be entirely voluntary and any request to be exempted from the project would be respected. Patient consent was not required for this QI initiative; data on every patient on the unit was included and confidentiality was maintained. All of the collected data were kept confidentially in a locked area.

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Author contribution

GA, MC, MAB, DS, and AL contributed to the conception and design of the project; SG, MRT, and EAS contributed to the analysis and interpretation of the data; SG and EAS contributed to the drafting and revising of the manuscript; and all authors provided final approval of the manuscript.

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