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Toward Optimizing Pertussis Detection During Outbreaks: A Comparison of National and High Epidemic Area Case Definitions in Narathiwat, Thailand, 2024

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Abstract

Pertussis remains a significant public health challenge in low-vaccination areas. This study described the characteristics of cases meeting the Narathiwat and national definitions and cases confirmed by reverse transcription polymerase chain reaction (RT-PCR) during the epidemic. It also assessed diagnostic accuracy of the definitions. A cross-sectional analysis utilized data from the Narathiwat Emergency Operations Center during September 2023 to May 2024. For the Narathiwat definition, a suspected case was a person with a cough lasting ≥1 week plus at least one symptom (i.e., paroxysmal cough, post-tussive vomiting, inspiratory whooping, or apnea), while the national definition required cough lasting ≥2 weeks. Among 486 cases, 171 met the Narathiwat definition, 107 met the national definition, and 208 met neither. RT-PCR confirmed cases were 47.9%, 57.9% and 30.8% among cases meeting the Narathiwat, national, and neither definitions, respectively. Timeliness of pertussis detection had a median of 9 days (interquartile range (IQR) 7.8–10 days) for the Narathiwat definition and 16 days (IQR 15–21 days) for the national definition. Paroxysmal cough had the highest detection rate by RT-PCR (84.6%) and was more common among RT-PCR positive cases compared to RT-PCR negative cases. The Narathiwat definition had a sensitivity of 39.4% and a positive predictive value (PPV) of 48.0%. The national definition had a lower sensitivity, 29.8%, but a higher PPV, 57.9%. A proposed alternative definition (cough ≥1 week, accompanied by paroxysmal cough) achieved a sensitivity of 37.5% and a PPV of 49.1%. Modifying the definition improved early outbreak detection during epidemics.

Keywords: pertussis, case definition, sensitivity, PPV, outbreak, low vaccine coverage

Introduction

Pertussis, also known as whooping cough, is a highly contagious bacterial infection caused by *Bordetella pertussis*. Despite widespread vaccination efforts, pertussis remains a significant global public health concern, particularly affecting infants who are incompletely vaccinated and lack sufficient herd immunity.[1] The disease typically manifests with catarrhal stage that can escalate to severe paroxysmal cough, marked by a characteristic “whoop” sound, and transmission primarily occurs through respiratory droplets expelled during coughing or sneezing.[2]

The World Health Organization (WHO) recommends clinical and laboratory case definitions for pertussis diagnosis. The clinical definition involves a prolonged cough (≥2 weeks) with characteristic symptoms, while the laboratory definition confirms the diagnosis through methods such as reverse transcription polymerase chain reaction (RT-PCR) or serology.[3] In Thailand, Narathiwat is a province with unique public health challenges, including a consistently low diphtheria-tetanus-pertussis (DTP) vaccine coverage rate, which has remained below 90% for years.[4,5] This low vaccination rate has contributed to the province’s

heightened vulnerability to pertussis outbreaks and rapid transmission, distinguishing it from other regions in Thailand. The most recent large pertussis outbreak occurred between September 2023 and May 2024. However, the Thailand national clinical case definition (national definition), which requires a cough lasting ≥2 weeks [6], posed limitations in this high-risk context by delaying case detection and hindering timely identification and containment of pertussis cases during the outbreak. In response to these challenges, the Narathiwat Provincial Public Health Office activated the Emergency Operations Center (EOC) on 25 Oct 2023, to strengthen outbreak response efforts. Unlike the routine outbreak response system, which is generally slower and may not fully mobilize resources in high-risk settings, the EOC facilitated a coordinated and rapid response to manage the potential epidemic.

One of the key responses was to modify the surveillance clinical case definition for suspected pertussis cases, adopting the Narathiwat definition to address the specific needs of the local outbreak. The Narathiwat definition, which includes clinical suspected cases with a cough lasting ≥1 week. Both factors were critical for effective outbreak management. During the outbreak, it was observed that some suspected cases met the national definition because they were detected during the period when they had a cough lasting ≥2 weeks. RT-PCR testing was conducted for all cases meeting either definition. Moreover, some individuals who did not meet any definition underwent RT-PCR testing due to physicians' suspicion or because they were identified as high-risk contacts (HRC) through contact tracing.

Thus, this study aimed to: (1) describe the characteristics of individuals meeting the Narathiwat definition, the national definition, and RT-PCR positive pertussis cases during the epidemic; (2) assess the clinical manifestations of RT-PCR positive and negative cases; and (3) evaluate the diagnostic accuracy of the Narathiwat, national, and alternative pertussis case definitions.

Methods

This descriptive cross-sectional study was conducted using secondary data to examine characteristics, signs or symptoms, and diagnostic accuracy among individuals who underwent RT-PCR testing during the pertussis outbreak in Narathiwat Province, which occurred between September 2023 and May 2024. The RT-PCR testing database included individuals meeting the suspected pertussis case definition under one of the two definitions, and others who did not meet any definition, but were tested based on clinical suspicion by physicians or because they were identified as HRC through contact tracing. Cases meeting the Narathiwat definition were defined as individuals with a cough lasting ≥1 week (detected cases with a cough duration of 7 to 13 days) combined with at least one sign or symptom (paroxysmal cough, post-tussive vomiting, inspiratory whooping, or apnea). In contrast, cases meeting the national definition required a cough lasting ≥2 weeks (detected cases with 14 or more days of cough duration) combined with at least one of the same signs or symptoms. The cases meeting the two definitions in this analysis did not overlap each other, as cases were categorized based on the timing of detection, specifically the cough duration at diagnosis. The clinical data of the two groups were collected only at the time of case detection and were not followed up throughout the course of illness. Therefore, the Narathiwat and national definitions' cases were treated as independent groups. An RT-PCR positive case was defined as an individual who tested positive for *Bordetella pertussis* using RT-PCR, regardless of whether they met a clinical case definition.

Data were retrieved from line listings of pertussis cases recorded by the EOC using Microsoft Excel 2016.[7] Variables included gender, age group, case type, DTP vaccination status, clinical signs or symptoms, and RT-PCR test results. Case types included index cases, which were the initial cases identified in an outbreak; HRC, referring to individuals identified through contact tracing, such as household members or those in close contact with RT-PCR positive pertussis cases at a distance of less than one meter for at least five minutes without wearing a mask; and active case finding, involving cases identified through proactive surveillance. DTP vaccination status was categorized as completely vaccinated, incompletely vaccinated, or never vaccinated. Signs or symptoms recorded were paroxysmal cough, inspiratory whoop, post-tussive vomiting, and apnea. These symptoms were assessed at the time individuals met the definition (7–13 days of cough duration), but were not reassessed later when cases might meet the national definition (14 or more days of cough duration). RT-PCR testing was conducted using nasopharyngeal swabs collected with Dacron or rayon swabs, which were placed in sterile tubes. Samples were either sent immediately or stored at –10°C for no more than 48 hours before being transported within two hours in temperature-controlled containers to the Regional Medical Sciences Center 12, Songkhla Province, Thailand. RT-PCR test results were reported as positive, inconclusive, or negative for pertussis (no cycle threshold reported). Only cases with positive results were considered as RT-PCR positive pertussis cases.

The data were checked for completeness and accuracy, cleaned, and analyzed using R version 4.2.1.[8] The analysis addressed the following study objectives:

The first objective described demographic factors (gender, age group), case type, DTP vaccination status, and clinical signs or symptoms among the three groups: cases meeting the Narathiwat definition, cases meeting the national definition, and all RT-PCR positive cases (confirmed cases). Additionally, timeliness of pertussis detection, defined as the time from symptom onset to positive RT-PCR confirmation, was calculated separately for cases meeting the Narathiwat definition and the national definition. The results were presented as frequencies, percentages, median, and interquartile range (IQR). Chi-squared test or Fisher's exact test (p <0.05) were used to compare the frequencies for between groups. The second objective involved assessing clinical manifestations of RT-PCR positive and negative cases. This analysis included pertussis related signs or symptoms, such as paroxysmal cough, post-tussive vomiting, inspiratory whooping, and apnea. The odds ratios (OR) and p-values were calculated to assess the association between those clinical symptoms and RT-PCR positivity. The third objective was to evaluate the diagnostic accuracy of the Narathiwat definition and the national definition for pertussis detection, using RT-PCR for pertussis results as the reference standard. Additionally, alternative definitions combining cough duration with statistically significant symptoms (p <0.05), identified through univariable logistic regression analysis, were proposed and assessed using standard 2x2 table formulas to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and 95% confidence intervals (CI).[9]

		Reference standard (RT-PCR for pertussis)	
		Positive	Negative
Meeting the case definition	Yes	A	B
	No	C	D

Sensitivity = A/(A+C),
Specificity = D/(B+D),
Positive predictive value (PPV) = A/(A+B) ,
Negative predictive value (NPV) = D/(C+D)

From the 2x2 table, cases were categorized as follows: those meeting the case definition who tested positive (A: true positive) or negative (B: false positive), and those not meeting the case definition who tested positive (C: false negative) or negative (D: true negative). Cells C and D included individuals who underwent RT-PCR testing despite not meeting both clinical suspected case definitions. Those individuals were tested either based on physicians' suspicion of pertussis or identified as HRC through contact tracing.

Ethics

Ethical clearance was omitted as this investigation was conducted under EOC outbreak management. Data collection was part of the investigation, with participants informed of objectives and benefits beforehand. Responses were recorded on forms without audio, ensuring anonymity by excluding full names and addresses. All documents were securely stored, and accessible only to the principal investigator, who oversaw data disposal post-publication.

Results

A total of 486 cases were analyzed, including 171 cases that met the Narathiwat definition, 107 cases that met the national definition, and 208 cases that did not meet either definition. All 486 cases underwent RT-PCR testing. For the 208 cases who did not meet either definition, 171 were tested based on physicians' suspicion of pertussis (with a 27.8% positive rate), while 37 were identified as high-risk contacts through contact tracing (with a 59.5% positive rate). Following RT-PCR, confirmed cases were 47.9% (82/171), 57.9% (62/107) and 30.8% (64/208) among cases meeting the Narathiwat, national, and neither definitions, respectively. Timeliness of pertussis detection had a median of 9 days (IQR 7.8–10 days) for cases meeting the Narathiwat definition and a median of 16 days (IQR 15–21 days) for cases meeting the national definition. Of the RT-PCR positive cases, 53.4% were female and 46.6% male. Cases meeting the Narathiwat definition comprised 51.5% female and 48.5% male, while those under the national definition had 58.0% female and 42.0% male (p 0.57). The majority of cases fell in the 0–1 year age group, accounting for 49.0% of RT-PCR positive cases, 46.8% of those meeting the Narathiwat definition, and 39.3% of those under the national definition (p 0.15). Paroxysmal cough was present in 84.6% of RT-PCR positive cases, 93.0% under the Narathiwat definition, and 94.4% under the national definition (p 0.01); inspiratory whoop in 30.8%, 42.1%, and 43.0%, respectively (p 0.03); and post-tussive vomiting in 62.5%, 63.2%, and 72.9%, respectively (p 0.15) (Table 1).

Table 1. Characteristics of RT-PCR positive cases and cases meeting Narathiwat and national definitions

Variables		Frequency, n (%)			*P*-value
		RT-PCR positive cases (n=208)	Cases meeting the Narathiwat definition (n=171)	Cases meeting the national definition (n=107)	
Gender					
Female		111 (53.4)	88 (51.5)	62 (58.0)	0.57
Male		97 (46.6)	83 (48.5)	45 (42.0)	
Age group (years)					
0–1		102 (49.0)	80 (46.8)	42 (39.3)	0.15
2–3		49 (23.6)	34 (19.9)	35 (32.7)	
4–5		19 (9.1)	25 (14.6)	9 (8.4)	
≥6		38 (18.3)	32 (18.7)	21 (19.6)	
Type of case					
Index		179 (86.1)	159 (93.0)	101 (94.4)	0.03
Active case finding		8 (3.8)	5 (2.9)	2 (1.9)	
High-risk contact		21 (10.1)	7 (4.1)	4 (3.7)	
DTP vaccination status					
Never		153 (73.6)	93 (54.4)	77 (71.9)	0.01
Incomplete		36 (17.3)	56 (32.8)	20 (18.7)	
Complete		4 (1.9)	11 (6.4)	5 (4.7)	
Unknown		15 (7.2)	11 (6.4)	5 (4.7)	
Sign or symptom					
Paroxysmal cough	Yes	176 (84.6)	159 (93.0)	101 (94.4)	0.01
	No	32 (15.4)	12 (7.0)	6 (5.6)	
Inspiratory whooping	Yes	64 (30.8)	72 (42.1)	46 (43.0)	0.03
	No	144 (69.2)	99 (57.9)	61 (57.0)	
Post-tussive vomiting	Yes	130 (62.5)	108 (63.2)	78 (72.9)	0.15
	No	78 (37.5)	63 (36.8)	29 (27.1)	

P-values were calculated using the chi-squared test or Fisher's exact test, as appropriate.

The distribution of RT-PCR positive cases based on various clinical case criteria showed distinct differences. Among RT-PCR positive cases (n=208) with cough lasting ≥1 week, 82 had combined at least one sign or symptom (OR 1.38, 95% CI 0.95–2.01, p 0.09), 78 had paroxysmal cough (OR 1.46, 95% CI 1.00–2.14, p 0.05), 54 had post-tussive vomiting (OR 1.45, 95% CI 0.95–2.23, p 0.09), and 30 had inspiratory whooping (OR 0.95, 95% CI 0.57–1.57, p 0.83). Among RT-PCR positive cases with cough lasting ≥2 weeks, 62 had combined at least one sign or symptom (OR 2.20, 95% CI 1.42–3.40, p ≤0.01), 60 had paroxysmal cough (OR 2.34, 95% CI 1.10–3.66, p <0.01), 48 had post-tussive vomiting (OR 2.48, 95% CI 1.51–4.10, p <0.01), and 24 had inspiratory whooping (OR 1.51, 95% CI 0.83–2.79, p 0.18). Paroxysmal cough was significantly more common among RT-PCR positive cases compared to RT-PCR negative cases for both cough duration categories (p 0.05 for ≥1 week, p <0.01 for ≥2 weeks (Table 2).

Table 2. Distribution of RT-PCR positive cases based on various clinical case criteria

Clinical case criteria		Frequency, n (%)		OR (95% CI)	*P*-value
Cough duration*	Combine with sign or symptom	RT-PCR positive (n=208)	RT-PCR negative (n=278)		
Cough lasting ≥1 week	At least one sign or symptom	82	89	1.38 (0.95–2.01)	0.09
	Paroxysmal cough	78	81	1.46 (1.00–2.14)	0.05
	Post-tussive vomiting	54	54	1.45 (0.95–2.23)	0.09
	Inspiratory whooping	30	42	0.95 (0.57–1.57)	0.83
	Apnea	2	2	1.33 (0.19–9.59)	0.77
Cough lasting ≥2 weeks	At least one sign or symptom	62	45	2.20 (1.42–3.40)	<0.01
	Paroxysmal cough	60	41	2.34 (1.10–3.66)	<0.01
	Post-tussive vomiting	48	30	2.48 (1.51–4.10)	<0.01
	Inspiratory whooping	24	22	1.51 (0.83–2.79)	0.18
	Apnea	1	0	NA	0.23

**Cough duration: 1) cough ≥1 week: detects cases with 7 to 13 days of cough duration, 2) cough ≥2 weeks: detects cases with 14 or more days of cough duration. P-values and odds ratios were calculated using univariable logistic regression analysis. NA: not applicable, OR: odds ratio, CI: confidence interval.*

The diagnostic accuracy of the Narathiwat and national definitions demonstrated key differences, particularly in sensitivity and PPV. The Narathiwat definition showed higher sensitivity (39.4%; 95% CI 32.7–46.4) compared to the national definition (29.8%; 95% CI 23.7–36.5). However, its PPV was lower at 48.0% (95% CI 40.3–55.7), compared to 57.9% (95% CI 48.0–67.4) for the national definition. Among alternative definitions, definition A (cough ≥1 week, accompanied by paroxysmal cough) demonstrated a sensitivity of 37.5% (95% CI 30.9–44.5) and a PPV of 49.1% (95% CI 41.1–57.1), which was comparable to the Narathiwat definition (Table 3).

Table 3. Diagnostic accuracy of clinical case definitions for pertussis compared to RT-PCR testing results as the reference standard

Clinical case definitions*	Number of cases in cell				Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)
	TP	FP	FN	TN				
Narathiwat definition: Cough ≥1 week +at least one sign or symptom†	82	89	126	189	39.4 (32.7–46.4)	68.0 (62.2–73.4)	48.0 (40.3–55.7)	60.0 (54.4-65.5)
National definition: Cough ≥2 weeks +at least one sign or symptom†	62	45	146	233	29.8 (23.7–36.5)	83.8 (78.9–87.9)	57.9 (48.0–67.4)	61.5 (56.4-66.4)
Alternative definition								
(A) cough ≥1 week +paroxysmal cough	78	81	130	197	37.5 (30.9–44.5)	70.9 (65.1–76.1)	49.1 (41.1–57.1)	60.2 (54.7-65.6)
(B) cough ≥2 weeks +paroxysmal cough	60	41	148	237	28.8 (22.8–35.5)	85.3 (80.5–89.2)	59.4 (49.2–69.1)	61.6 (56.4-66.4)
(C) cough ≥1 week +post-tussive vomiting	54	54	154	224	26.0 (20.1–32.5)	80.6 (75.4–85.1)	50.0 (40.2–59.8)	59.3 (54.1-64.3)
(D) cough ≥2 weeks +post-tussive vomiting	18	10	190	268	8.7 (5.2–47.3)	96.4 (93.5–98.3)	64.3 (44.1–81.4)	58.5 (53.9-63.1)
(E) cough ≥1 week +inspiratory whooping	30	42	178	236	14.4 (9.9–19.9)	84.9 (80.1–88.9)	41.7 (30.2–53.9)	57.0 (52.1-61.8)
(F) cough ≥2 weeks +inspiratory whooping	12	5	196	273	5.8 (3.0–9.9)	98.2 (95.9–99.4)	70.6 (44.0–89.7)	58.2 (53.6-62.7)

**Cough duration in clinical case definitions: 1) cough ≥1 week: detects cases with 7 to 13 days of cough duration, 2) cough ≥2 weeks: detects cases with 14 or more days of cough duration. †The signs and symptoms include paroxysmal cough, post-tussive vomiting, inspiratory whooping, and apnea. (A)–(F) represent the alternative case definitions assessed for diagnostic accuracy. TP: true positive. FP: false positive. FN: false negative. TN: true negative. PPV: positive predictive value, NPV: negative predictive value.*

Discussion

This study assessed the diagnostic performance of pertussis case definitions in a low-vaccination setting, comparing the Narathiwat and national definitions in detecting RT-PCR confirmed cases. The findings have highlighted differences in sensitivity and PPV between the two definitions, with alternative criteria also evaluated to improve detection. Notably, a significant proportion of cases did not meet either definition, emphasizing the challenges in clinical diagnosis. The results underscore the importance of standardized case definitions in outbreak settings and suggest the need for optimized criteria to enhance early detection and intervention.

Paroxysmal cough had the highest positive detection rate by RT-PCR (84.6%) and was significantly more common among RT-PCR positive cases compared to RT-PCR negative cases for both cough duration categories. This finding has reinforced paroxysmal cough's diagnostic value as recommended by the WHO and the US Centers for Disease Control and Prevention.[10] Studies have consistently emphasized the high prevalence of paroxysmal cough in confirmed pertussis cases, supporting its inclusion in case definitions.[11–13]

Post-tussive vomiting was more commonly observed in cases with a longer cough duration (≥2 weeks) (OR 2.48, 95% CI 1.51–4.10, p <0.01) compared to those with a shorter cough duration (≥1 week) (OR 1.45, 95% CI 0.95–2.23, p 0.09). Similarly, inspiratory whooping was more frequently observed in cases with a longer cough duration (OR 1.51, 95% CI 0.83–2.79, p 0.18) compared to a shorter cough duration (OR 0.95, 95% CI 0.57–1.57, p 0.83). These findings may reflect differences in cough duration and symptom reporting. They have aligned with evidence suggesting that symptoms such as post-tussive vomiting and inspiratory whooping often intensify after two weeks of coughing.[14–16] In contrast, apnea showed no significant association with any clinical case criteria, reflecting its limited diagnostic value in this context. However, previous research has highlighted that, although inspiratory whooping and apnea are less commonly observed, they can still aid in confirming the diagnosis in certain cases.[17]

The diagnostic performance of pertussis case definitions have highlighted their strengths and limitations in the contexts of outbreak detection versus routine surveillance. The Narathiwat definition, requiring ≥1 week of cough with at least one sign or symptom, achieved higher sensitivity (39.4%) than the national definition, which requires ≥2 weeks of cough with at least one sign or symptom (29.8%). This higher sensitivity allows for earlier detection, which has been supported by previous studies.[13] Additionally, the median time for pertussis detection according to the Narathiwat definition was nine days (IQR 7.8–10 days), which aligned with research on the optimal timing of specimen collection, suggesting that modified case definitions could help detect cases earlier and allow for more timely interventions.[18] However, the national definition demonstrated superior specificity (83.8% versus 68.0%) and PPV (57.9% versus 48.0%), making it more effective for identifying true cases while minimizing false positives in routine surveillance.[12] Alternative definitions, such as cough ≥1 week combined with paroxysmal cough, can increase specificity and PPV while still maintaining similar sensitivity compared to the definition of >1 weeks of cough with at least one sign or symptom. This aligned with studies which have suggested that including paroxysmal cough as a criterion can improve the balance of diagnostic accuracy by enhancing specificity, and PPV. Such an approach provides a more effective way to identify true pertussis cases while minimizing false positives and negatives.[19]

The relatively low RT-PCR positive rate of 27.8% among cases identified based solely on physicians' suspicion without meeting any case definition highlights the limitations of relying on clinical judgment alone, especially in outbreak settings where escalating laboratory costs pose additional challenges. However, the WHO and European Union consider physicians' suspicion as a valid component of case definitions.[3,10] This approach may be less effective in high-prevalence settings like Narathiwat. To address this during the epidemic, the EOC implemented regular clinician training and follow-ups to ensure consistent application of the Narathiwat definition across hospitals and community settings, improving diagnostic accuracy and outbreak management.

Limitations

During the outbreak, case definitions were based on patients visiting the hospital or being identified through investigations. Symptom data were recorded only at the time of investigation, preventing tracking of new or changing symptoms. This study relied on secondary data, and the completeness and accuracy of certain variables, especially clinical symptoms, could not be fully verified. Variability in symptom reporting may have affected case classification. Therefore, cases meeting the Narathiwat definition (7–13 days of cough) and the national definition (≥14 days of cough) were analyzed separately

Recommendations

To improve pertussis detection and response, case definitions with high sensitivity, such as the Narathiwat definition (≥1 week of cough with one sign or symptom), should be prioritized during outbreaks in high-prevalence and widespread epidemic areas to enable early detection and timely intervention. Alternative definitions, such as cough ≥1 week combined with paroxysmal cough, offer a better balance of sensitivity (37.5%) and PPV (49.1%), enhancing diagnostic accuracy while minimizing false positives. For routine surveillance in non-outbreak settings, the national definition (≥2 weeks of cough with one sign or symptom) is more appropriate due to its higher specificity (83.8%). Regular clinician training and consistent follow-up measures are vital to ensure the standardized application of case definitions, thereby reducing unnecessary laboratory testing costs and maintaining efficiency.

Conclusion

This study compared the characteristics of cases meeting the Narathiwat definition, national definition, and RT-PCR positive pertussis cases, focusing on demographics, vaccination status, and clinical signs. Paroxysmal cough, present in 84.6% of RT-PCR positive cases, was significantly more common among RT-PCR positive cases compared to RT-PCR negative cases, reinforcing its diagnostic value. The Narathiwat definition, with higher sensitivity (39.4%), detected earlier cases (≥1 week of cough), than the national definition, with higher specificity (83.8%). Additionally, the median time for pertussis detection was nine days (IQR 7.8–10 days) according to the Narathiwat definition, suggesting that modified case definitions could help to detect cases earlier and allow for more timely interventions. Alternative definitions, like cough ≥1 week plus paroxysmal cough, offered a balanced sensitivity (37.5%) and PPV (49.1%). Periodic reviews of case definitions, clinician training, and consistent application are crucial for improving pertussis detection, resource allocation, and outbreak response.

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Conflicts of Interests

The author declares no conflicts of interest related to this work.

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