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Prospective Comparison of the Alvarado Score and CT Scan in the Evaluation of Suspected Appendicitis: A Proposed Algorithm to Guide CT Use

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BACKGROUND: Although computed tomography (CT) has reduced negative appendectomy rates, its radiation risk remains a concern. We compared the performance statistics of the Alvarado Score (AS) with those of CT scan in the evaluation of suspected appendicitis, with the aim of identifying a subset of patients who will benefit from CT evaluation.

STUDY DESIGN: We performed prospective data collection on 350 consecutive patients with suspected appendicitis who were evaluated with CT scans. The AS for each patient was scored at admission and correlated with eventual histology and CT findings. The sensitivity, specificity, and positive likelihood ratios were determined for various AS and for CT scan. The AS ranges that benefitted most from CT evaluation were determined by comparing the positive likelihood ratios of CT scan with each of the AS cutoff values.

RESULTS: The study included 134 males (38.3%) and 216 females (61.7%). The overall prevalence of appendicitis was 44.3% in the total study population; 37.5% in females and 55.2% in males. There were 168 patients (48%) who underwent surgery, with a negative appendectomy rate of 7.7%. Positive likelihood ratio of disease was significantly greater than 1 only in patients with an AS of 4 and above. An AS of 7 and above in males and 9 and above in females has a positive likelihood ratio comparable to that of CT scan.

CONCLUSIONS: Evaluation by CT is beneficial mainly in patients with AS of 6 and below in males and 8 and below in females. We propose an objective management algorithm with the AS guiding subsequent evaluation. (J Am Coll Surg 2015;220:218–224. © 2015 by the American College of Surgeons. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license [http://creativecommons.org/licenses/by-nc-nd/3.0/].)

Acute appendicitis is one of the most common causes of acute abdominal pain requiring surgical intervention, with a lifetime risk of 8.6% for males and 6.7% for females.[1,2] Historically, negative appendectomy rates of more than 20% were considered the norm. However, this is no longer acceptable because even though complication rates in the setting of negative appendectomy are low, conditions such as incisional hernias, intestinal obstruction secondary to adhesions, and stump leakages can result in significant morbidity.

Computed tomography (CT) scan has emerged as the dominant imaging modality for evaluation of suspected appendicitis in adults.[3] It has decreased negative appendectomy rates to less than 10%.[4-6] However, the radiation exposure with CT poses a concern, particularly in appendicitis, which occurs predominantly in young patients most susceptible to the adverse effects of radiation.[7,8] Available literature has estimated that at least 25% of CT scans are not clinically warranted and may pose more harm than benefit.[9] Rules for clinical decisions guiding CT use are therefore essential to minimize unnecessary CT scans.[9] We previously proposed a management algorithm for suspected appendicitis with the Alvarado

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Table 1. The Alvarado Scoring System

Mnemonic (MANTRELS)	Value
Symptom	
Migration	1
Anorexia-acetone	1
Nausea-vomiting	1
Signs	
Tenderness in right lower quadrant	2
Rebound pain	1
Elevation of temperature >37.3°C	1
Laboratory	
Leukocytosis	2
Shift to the left	1
Total score	10

score (AS) (Table 1) guiding CT use.[10] This algorithm was, however, developed based on retrospective data with its antecedent limitations.

This study aimed to compare the performance statistics of the AS with CT scan in the evaluation of suspected appendicitis. Thereafter, we attempt to use the AS to stratify patients with suspected appendicitis into subgroups that might benefit from CT evaluation. An objective algorithm for the management of suspected appendicitis guided by the AS is then proposed.

METHODS

We performed an analysis of prospectively collected data from 450 consecutive patients with suspected appendicitis, admitted to the General Surgery Department at Singapore General Hospital. The study ran from August 2013 to March 2014, and only patients who underwent CT evaluation were included in the final analysis. Decision for CT evaluation was left to the discretion of the attending surgeon during the initial assessment. Patient demographics, presenting signs and symptoms, and relevant laboratory values were prospectively collected and recorded in a standardized data collection sheet. The AS of each patient was scored by the attending surgeon at the point of admission, before the decision was made for CT evaluation, and it was recorded in the clinical chart. Computed tomography findings, surgical findings, and histologic results were recorded for each patient when applicable. Study data were collected and managed using the REDCap electronic data capture tools hosted at Singapore General Hospital. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies.[11]

In order to ensure short-term follow-up, all patients were reviewed in person by a clinician outpatient at least once within 2 weeks from discharge. Subsequent follow-up visits were determined based on clinical indication. Patients discharged without surgery were treated with antibiotics only if they were diagnosed with conditions that warranted therapy. Empirical treatment with antibiotics was not practiced. Repeat admissions for patients discharged without surgery were identified by a search of the National Electronic Health Record database in Singapore, a database that captures the admission information of every person in Singapore who has visited the public health care system. A case of missed diagnosis was defined as readmission within 2 weeks from initial discharge, with eventual surgery showing acute appendicitis on histology.

Appendicitis was considered present when patients who had undergone surgery had a final histology showing acute appendicitis. A case was considered to be a negative appendectomy when a patient had undergone surgery with the clinical impression of acute appendicitis but had no features of appendicitis in histology. Patients who did not undergo surgery were considered not to have appendicitis if they did not re-present within 2 weeks from initial discharge with acute appendicitis. Computed tomography scans were read by the radiologist on duty when the scans were ordered, and findings were categorized into 3 groups: positive for acute appendicitis, negative for acute appendicitis, and equivocal findings.

Sensitivity, specificity, positive and negative predictive values, and likelihood ratios were estimated for each of the cut off AS scores ranging from 2 to 10, using histology results as the gold standard. Scores of zero and 1 were omitted because there were no patients with such scores. The same diagnostic performance measures were calculated for CT scan using the same gold standard. Equivocal CT scans were considered positive for acute appendicitis in the calculations above. This method of classifying equivocal scans was chosen because in our institution, most surgeons would offer a diagnostic laparoscopy for patients who present with suspected appendicitis and an equivocal CT scan. Because we were concerned that classification in this manner may influence the eventual findings, we repeated the above statistical analysis first by excluding and thereafter by classifying these equivocal cases as negative for acute appendicitis separately. It is our institution's practice to remove all appendixes even if there were no macroscopic features of acute appendicitis intraoperatively. This is guided by existing data, which revealed that up to 33% of macroscopically normal appendixes have features of inflammation on histology.[12]

The range of AS for which patients were least likely to benefit from CT evaluation was determined by identifying AS ranges that had positive likelihood ratios not

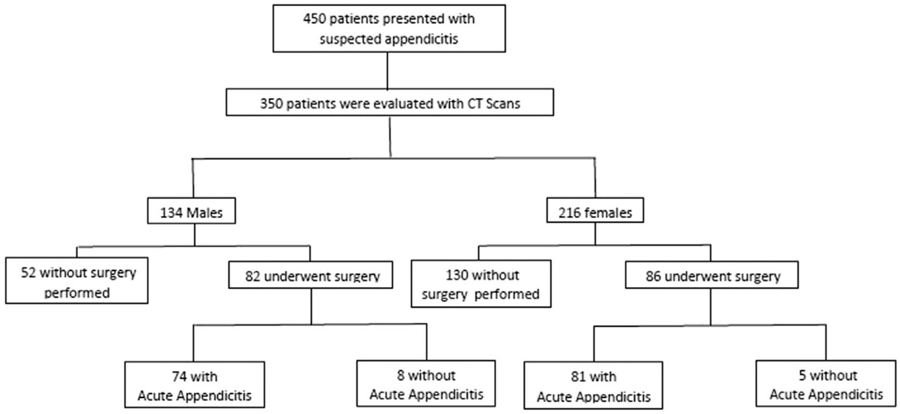

Figure 1. Management course and outcomes of study cohort.

significantly different from those of CT scans. Likelihood ratios were selected as the parameter for comparison because they were independent of disease prevalence and depended only on the intrinsic ability of the diagnostic test to distinguish between diseased and nondiseased individuals. The pairwise comparisons of predictive values and likelihood ratios are based on the methods described by Moskowitz and Pepe (2006)[13] and Nofuentes and Castillon (2007),[14] respectively. The above statistics were subanalyzed by sex because the performance of the AS has been shown to vary according to sex.[15] Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) Version 17. Performance measures, including sensitivity, specificity, positive and negative predictive values, and diagnostic likelihood ratios were calculated and compared using the BDT comparator program.[16] A p value of less than 0.05 was considered to indicate statistical significance.

The study was carried out under the approval of the Centralized Institutional Review Board of the Singapore Health Services.

RESULTS

There were 450 patients admitted for suspected appendicitis from August 2013 to March 2014. One hundred patients were not evaluated with CT scans and were excluded from the study. Altogether, 350 patients underwent CT evaluation. There were no cases of missed diagnosis in these patients, who were all evaluated with CT scans.

There were 134 males (38.3%) and 216 females (61.7%). The overall median age of the patients was 33 years (range 15 to 82 years): 32 years for males and 33 years for females. Among the 350 patients who presented with suspected appendicitis and were evaluated with CT scans, the overall prevalence of appendicitis was 44.3% in the total study population; 37.5% in females and 55.2% in males (Fig. 1).

Nineteen (5.4%) of the CT scans were deemed equivocal, 11 in females and 8 in males. Surgery was performed for 168 patients (48%), of whom 40, 126, and 2 underwent open appendectomy, laparoscopic appendectomy, and laparotomy, respectively. The overall negative appendectomy rate was 7.7%.

The number of patients within each AS cut off category is illustrated in Table 2. The sensitivity, specificity, positive and negative predictive values, and positive likelihood ratio of the various AS cut-off values compared with CT scan are illustrated in Table 3. Sub-analysis of the positive likelihood ratios of the various AS values stratified by sex and compared with CT scan are illustrated in Table 4.

Alvarado Scores of 7 and above in males (AS $\geq$ 7, p = 0.513; AS $\geq$ 8, p = 0.442; AS $\geq$ 9, p = 0.398; AS $\geq$ 10, p = 0.896) and 9 and above in females (AS $\geq$ 9, p = 0.513; AS $\geq$ 10, p = 0.638) have positive likelihood ratios comparable to those of CT scan. Analysis after excluding equivocal scans or after classifying equivocal

Table 2. Number of Patients within Each Alvarado Score Category Cut Off with Sex Stratification

	Sex	
Alvarado Score	Male, n	Female, n
≥2	134	216
≥3	127	203
≥4	120	187
≥5	101	156
≥6	72	123
≥7	37	73
≥8	17	40
≥9	5	11
≥10	1	3

Table 3. Performance Statistics of Alvarado Score Cut Off Values and Results from Pairwise Comparison of these Statistics with that of CT Scan

	Sensitivity, %	p Value*	Specificity, %	p Value*	Positive predictive value, %	p Value*	Negative predictive value, %	p Value*	Positive likelihood ratio	p Value*
CT scan	98.7 (95.4–99.8)		88.5 (83.2–92.7)		87.4 (81.6–92.0)		98.8 (95.8–99.9)		8.570 (5.782–12.701)	
Alvarado Score										
≥2	100.0 (97.6–100.0)	0.479	0 (0.0–1.9)	<0.001	44.8 (39.5–50.2)	<0.001	50.0 (0.0–100.0)	0.664	1.00 (0.995–1.005)	<0.001
≥3	96.7 (92.6–98.9)	0.449	7.9 (4.5–12.6)	<0.001	46.0 (40.5–51.6)	<0.001	75.0 (50.9–91.3)	0.032	1.05 (0.998–1.10)	<0.001
≥4	94.2 (89.2–97.3)	0.070	17.8 (12.7–23.9)	<0.001	48.2 (42.4–54.0)	<0.001	79.1 (64.0–90.0)	0.004	1.14 (1.06–1.24)	<0.001
≥5	85.1 (78.4–90.3)	<0.001	36.5 (29.6–43.7)	<0.001	52.2 (45.8–58.5)	<0.001	75.3 (65.2–83.6)	<0.001	1.34 (1.18–1.52)	<0.001
≥6	74.7 (67.0–81.3)	<0.001	60.2 (52.9–67.2)	<0.001	60.4 (53.1–67.4)	<0.001	74.7 (67.0–81.3)	<0.001	1.88 (1.55–2.29)	<0.001
≥7	47.1 (39.0–55.3)	<0.001	81.7 (75.4–86.9)	0.086	67.6 (57.9–76.3)	<0.001	65.5 (59.4–71.5)	<0.001	2.57 (1.82–3.62)	<0.001
≥8	26.5 (19.7–34.1)	<0.001	92.1 (87.4–95.5)	0.265	73.2 (59.7–84.2)	0.023	60.7 (54.8–66.3)	<0.001	3.37 (1.94–5.85)	0.004
≥9	8.4 (4.5–13.9)	<0.001	99.0 (96.3–99.9)	<0.001	86.7 (59.5–98.3)	0.931	57.1 (51.6–62.4)	<0.001	8.01 (1.84–35.0)	0.928
≥10	1.9 (0.4–5.6)	<0.001	100 (98.1–100.0)	<0.001	96.8 (27.8–100.0)	0.336	55.7 (50.3–61.0)	<0.001	37.0 (0.0690–20000)	0.526

*p Values are from pairwise comparison test statistics for the respective performance parameter.

scans as negative for acute appendicitis did not change these conclusions (data not shown).

DISCUSSION

Computed tomography scan has emerged as the dominant imaging modality for evaluation of suspected appendicitis in adults.[3] However, in view of its cost, radiation risk, and the potential delay in therapeutic intervention, CT scans should be reserved for clinically equivocal cases.[17-21] A single CT abdomen pelvis exposes a patient to 14 mSv of ionizing radiation, which adds an additional cancer risk of up to 0.2% for an individual of 30 years of age.[22,23] We previously proposed a management algorithm guiding CT use for suspected appendicitis based on the AS.[10] This was, however, derived from retrospective data with its antecedent limitations. So, we aimed to compare the performance statistics of the AS with CT scan in the evaluation of suspected appendicitis. The eventual objective was to identify AS ranges that will benefit from CT evaluation. Thereafter, we propose an objective management algorithm, with AS guiding subsequent evaluation and management.

Our data indicate that CT evaluation has value mainly in male patients with AS of 6 and below and female patients with AS 8 or less; the positive likelihood ratio of CT was significantly superior to the positive likelihood ratio of the AS within these score ranges (Table 4). Males with AS of 7 and above and females with AS of 9 and above are unlikely to benefit from CT evaluation because the positive likelihood ratios of the AS within these score ranges were not significantly different from those of CT scan (Table 4). So, males with an AS of 7 to 10 and females with AS of 9 to 10 can be counselled for surgery (diagnostic laparoscopy with possible appendectomy) without further imaging evaluation.

Based on these findings, we propose an algorithm for the management of suspected appendicitis with the AS as a stratification tool (Fig. 2). Patients with an AS of 3 and below are discharged and followed up as outpatients. These patients have a low likelihood of acute appendicitis because their positive likelihood ratios are not significantly greater than 1 (includes 1 in their confidence interval). Using an AS cut off value of 3 and below to exclude acute appendicitis has an overall sensitivity of 94.2% (Table 3).

Differences in sex dictate further management for patients with AS of 4 and above. Males with an AS ranging from 4 to 6 and females with an AS ranging from 4 to 8 are subjected to CT evaluation. Within these score ranges, the positive likelihood ratio of CT scan clearly outperforms that of the AS (Table 4). Diagnostic laparoscopy

Table 4. Diagnostic Likelihood Ratio with 95% Confidence Interval for a Positive Test of Acute Appendicitis Using Different Alvarado Score Cut Off Values Stratified by Sex, and Results from Pairwise Comparison of these Likelihood Ratios with that of a Positive Test for CT Scan

	Male				Female			
	Sensitivity	**Specificity**	**Positive likelihood ratio**	**p Value***	**Sensitivity**	**Specificity**	**Positive likelihood ratio**	**p Value***
CT scan	98.6 (92.7–100)	83.1 (71.0–91.6)	5.82 (3.31–10.2)		98.8 (93.3–100.0)	90.9 (84.7–95.2)	10.864 (6.331–18.643)	
Alvarado Score								
≥2	100 (95.1–100.0)	0.0 (0.0–6.1)	1.00 (0.987–1.01)	<0.001	100.0 (95.5–100.0)	0.0 (0.0–2.8)	1.00 (0.991–1.01)	<0.001
≥3	97.3 (90.6–99.7)	8.5 (2.8–18.7)	1.06 (0.975–1.16)	<0.001	96.3 (89.6–99.2)	7.6 (3.7–13.5)	1.04 (0.976–1.11)	<0.001
≥4	94.6 (86.7–98.5)	16.9 (8.4–29.0)	1.14 (1.00–1.29)	<0.001	93.8 (86.2–98.0)	18.2 (12.0–25.8)	1.15 (1.04–1.26)	<0.001
≥5	86.5 (76.5–93.3)	39.0 (26.5–52.6)	1.42 (1.13 − 1.77)	<0.001	84.0 (74.1–91.2)	35.6 (27.5–44.4)	1.30 (1.11–1.53)	<0.001
≥6	70.3 (58.5–80.3)	66.1 (52.6–77.9)	2.07 (1.41–3.05)	0.003	79.0 (68.5–87.3)	57.6 (48.7–66.1)	1.86 (1.48–2.34)	<0.001
≥7	41.9 (30.5–53.9)	89.8 (79.2–96.2)	4.12 (1.84–9.21)	0.513	51.9 (40.5–63.1)	78.0 (70.0–84.8)	2.36 (1.61–3.47)	<0.001
≥8	21.6 (12.9–32.7)	98.3 (90.9–100.0)	12.8 (1.74–93.4)	0.442	30.9 (21.1–42.1)	89.4 (82.8–94.1)	2.91 (1.61–5.27)	<0.001
≥9	6.8 (2.2–15.1)	100.0 (93.9–100.0)	39.9 (0.0770–20700)	0.398	9.9 (4.4–18.5)	98.5 (94.6–99.8)	6.52 (1.42–29.9)	0.513
≥10	1.4 (0.0–7.3)	100.0 (93.9–100.0)	7.99 (0.0120–5270)	0.896	2.5 (0.3–8.6)	100.0 (97.2–100.0)	32.6 (0.057–18600)	0.638

*p Values are from pairwise comparison test statistics for the respective performance parameter.

without further imaging evaluation is offered for male patients with an AS of 7 to 10 and females with an AS of 9 and 10. The criteria for surgery without further imaging evaluation are more stringent in females than in males because the AS is known to over-predict the probability of acute appendicitis in females.[15] This is further supported by our data, which indicate that the positive likelihood ratio of the AS in females is not significantly different from that of CT scan only with an AS of 9 ($p = 0.513$) and 10 ($p = 0.638$). These findings are congruent with sentiments from practicing surgeons, who are usually more willing to offer surgery without further imaging evaluation in males with suspected appendicitis because there are no gynecologic conditions to mimic their presenting signs and symptoms.[24] Using our proposed algorithm would have reduced CT use to approximately 70%, with an estimated 90 fewer CT scans performed over a short duration of 7 months. This reduction in CT use will prove to be significant in the long run in view of the high incidence of suspected acute appendicitis.

To the best of our knowledge, there have only been 2 previous studies evaluating the use of the AS as a stratification tool for CT evaluation in suspected appendicitis.[10,25] Both studies were, however, performed in retrospective settings and therefore had their antecedent limitations in terms of the accuracy of medical records. This is the only study based on prospective data that evaluates the usefulness of the AS in identifying a subset of patients who benefit from CT evaluation. Our study is also the first to compare the estimates of performance measures of the AS with that of CT scan as a diagnostic test, using sound statistical methodology to determine the range of AS values that clearly benefit from CT evaluation. The statistical methodology used to compare the likelihood ratio estimates took into account the paired design in our data, increasing the overall power of our study.

There are several limitation of our study. First, our definition of acute appendicitis comprised only those who had undergone surgery with histologic confirmation of acute appendicitis. This may have misclassified patients with acute appendicitis, who declined or were not offered surgery due to a missed diagnosis. Review of patient records did not reveal any patient who declined when offered surgery. We also attempted to minimize initial misclassification of missed diagnoses (ie, patients with acute appendicitis classified as no acute appendicitis) by identifying patients with repeat admissions to any public health care institution (within 2 weeks from discharge) as a surrogate of an initial missed diagnosis. No cases of missed diagnosis were identified during the study. Furthermore, our institution did not practice empirical antibiotics treatment in cases of suspected appendicitis.

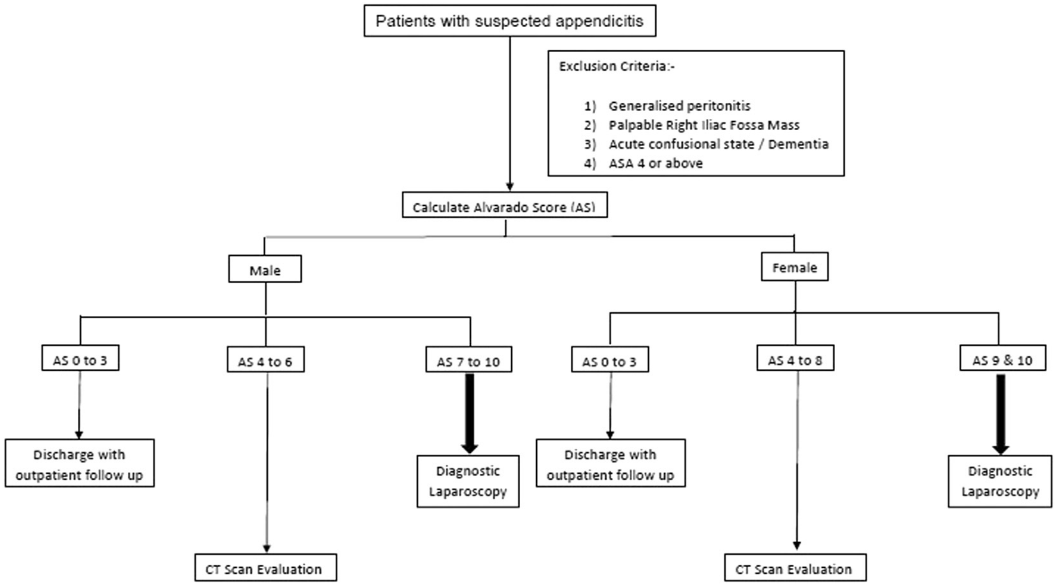

Figure 2. Proposed management algorithm for suspected appendicitis.

This would have minimized the misclassification of acute appendicitis patients who did not undergo surgery due to antibiotic treatment. We acknowledge that the use of the National Electronic Health Record database to identify cases of missed diagnosis has the limitation of missing patients who re-presented with acute appendicitis to the private sector. However, the number of cases missed is unlikely to be significant; Singapore health care statistics indicate that 80% of patients seek hospitalization in the public sector.

Second, there were relatively few patients with an AS of 9 and above (5 male and 11 female patients). This is not surprising because such obvious cases usually warrant surgical exploration without further CT evaluation, which was an inclusion criterion in our study. The small number of patients with an AS of 9 and 10 may lead to a type II error during comparison of performance measures for these score values with CT scans. This is a limitation that may be overcome only by performing a study in which CT evaluation is performed uniformly in all cases, even in those with obvious clinical features of acute appendicitis. Even then, a large study population would be required because the prevalence of those with an AS of 9 and above in our study was less than 5%. Such a study design may pose ethical concerns for CT scans; though noninvasive, they are not without accompanying risks. Subjecting patients with an obvious clinical diagnosis of acute appendicitis to CT evaluation may not be justified. Among the 100 patients without CT evaluation who were excluded from our study, 15 had AS of 9 and above. All 15 patients underwent surgery without any negative appendectomies. This concurs with our study findings that CT scans are unnecessary in those with an AS of 9 and 10.

CONCLUSIONS

An AS of 7 and above in males and 9 and above in females had positive likelihood ratios not significantly different from those of CT scan. These patients (males with AS 7 and above, females with AS 9 and above) are least likely to benefit from CT evaluation. Evaluation by CT is of value mainly in patients with AS of 6 or less in males and 8 or less in females. We propose an objective management algorithm with the AS guiding subsequent evaluation and management.

Author Contributions

Study conception and design: Tan, Acharyya, Ong
Acquisition of data: Tan, Goh, Chan, Wong
Analysis and interpretation of data: Tan, Acharyya, Ooi
Drafting of manuscript: Tan, Acharyya, Ooi, Ong
Critical revision: Chan, Wong, Ooi, Ong

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