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ORIGINAL ARTICLE

Excess Adiposity Predicts In-Hospital Mortality but Not SCORTEN in Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis: A Three-Year Retrospective Cohort at Dr. Moewardi General Hospital, Surakarta

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ABSTRACT

Background: Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare drug-induced reactions in which in-hospital death occurs in 12–49% of cases, yet the reference prognostic instrument, SCORTEN, contains no anthropometric variable. Whether body mass index (BMI) carries independent prognostic information is unknown.

Objective: To determine whether body mass index carries independent prognostic information — for in-hospital mortality and for the SCORTEN severity score — in adults admitted with Stevens–Johnson syndrome and toxic epidermal necrolysis.

Methods: This retrospective observational analytic study used total sampling of the ICD-10 L51.1/L51.2 admission register at Dr. Moewardi General Hospital, Surakarta, from January 2022 to December 2024. Forty-three adults were classified by Asia-Pacific BMI thresholds and analysed against SCORTEN, diagnostic class and in-hospital mortality using exact, Firth-penalised and interval-valued methods, with STROBE reporting.

Results: Eight patients died (18.6%; 95% CI 9.7–32.6). BMI was not associated with SCORTEN (Spearman ρ = 0.163; 95% CI −0.14 to 0.44; p = 0.296), and all 3,280 exhaustively enumerated reconstructions of the incompletely reported score distribution reproduced a non-significant coefficient (ρ 0.061–0.287); the minimum detectable |ρ| was 0.42, so this null is uninformative rather than negative (BF01 = 3.10). Mortality rose across the ordered BMI strata from 0% to 36.4% (Cochran–Armitage z = 2.053; p = 0.040, exact permutation p = 0.056), and at the Asia-Pacific overweight threshold reached 35.3% versus 7.7% (odds ratio 6.55; 95% CI 1.14–37.75; Fisher exact p = 0.042; Firth-penalised odds ratio 5.54, 95% CI 1.20–34.09; number needed to harm 3.6; E-value 8.65; fragility index 1).

Conclusion: Excess adiposity is associated with in-hospital death in Indonesian patients with epidermal necrolysis through a channel SCORTEN does not capture. The estimate is imprecise and requires prospective multicentre confirmation.

1. Introduction

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) sit at the severe end of the spectrum of severe cutaneous adverse reactions: acute, drug-induced, immune-mediated diseases characterised by widespread keratinocyte death, epidermal detachment and mucosal erosion, and by a mortality that no other dermatological emergency approaches. They are conventionally separated by the proportion of body surface area (BSA) showing epidermal detachment — below 10% for SJS, 10–30% for SJS–TEN overlap, and above 30% for TEN — and a recent systematic review of 40 studies comprising 52,398 cases placed in-hospital death at between 12% and 49% across that spectrum.[1] The disease is rare. A national health-insurance analysis covering 23 provinces of urban China estimated the standardised incidence of the SJS spectrum at 3.43 per million person-years (95% CI 3.04–3.84), rising by 0.57 per million person-years over the study period,[2] while an analysis of 51,040 SJS/TEN hospitalisations in the United States National Inpatient Sample recorded in-hospital mortality of 5.4% in SJS, 14.4% in SJS–TEN overlap and 15.3% in TEN.[3] Antibiotics account for a pooled 28% (95% CI 24–33%) of cases worldwide,[4] and a ten-year Chinese series of 103 patients reported overall mortality of 9.7%, rising to 16% in TEN,[5] while a further Chinese cross-sectional study documented the distinct clinical profile of cases triggered by immune checkpoint inhibitors.[6]

Indonesian data are hospital-based and sparse. Dr. Moewardi General Hospital in Surakarta recorded 43 cases between 2006 and 2008 and 10 between 2015 and 2016; a contiguous series from the same institution

identified 35 adult cases among 147,531 inpatients between 2019 and 2022, with paracetamol (25.7%) and cefadroxil (11.4%) the commonest culprits.[7] Dr. Soetomo Hospital in Surabaya described the profile of its tertiary-referral population,[8] and a 2025 Indonesian series confirmed that analgesic-antipyretic and anticonvulsant drugs dominate causation locally.[9] In the absence of a national registry, every Indonesian estimate rests on a single-centre denominator, which is precisely why carefully analysed hospital cohorts continue to carry evidential weight.

The immunopathology of epidermal necrolysis is now reasonably well delineated. The reaction is a delayed, drug-specific, human leukocyte antigen–restricted type IV hypersensitivity response in which $CD8^+$ cytotoxic T lymphocytes and natural killer cells kill keratinocytes across the full thickness of the epidermis, with granulysin, perforin, granzyme B, soluble Fas ligand and tumour necrosis factor alpha (TNF-α) as the principal soluble effectors. Murine and human work has since shown that neutrophils, acting through lipocalin-2-driven formation of extracellular traps, both initiate and amplify the epidermal injury,[10] and that the systemic inflammatory profile differs measurably between patients given intravenous immunoglobulin, ciclosporin or supportive care alone.[11] The therapeutic corollary is increasingly evidence-based: a systematic review and network meta-analysis ranked etanercept and ciclosporin highest for mortality reduction,[12] a multicentre observational study found that etanercept added to systemic corticosteroid shortened re-epithelialisation,[13] a further cohort reported that etanercept reduced both healing time and mortality,[14] and two independent series reported lower mortality when TNF inhibition was added to conventional therapy.[15,16]

The point of therapeutic leverage, in other words, is a cytokine axis — and that is exactly the axis on which body composition acts. In obesity, adipocyte hypertrophy outstrips the local capillary supply, producing hypoxia, adipocyte senescence and macrophage infiltration with a shift from an anti-inflammatory M2 to a pro-inflammatory M1 phenotype; selectively clearing senescent p21-high adipose cells reverses both the local inflammatory infiltrate and systemic insulin resistance, which establishes the pathway as causal rather than merely correlated.[17] Circulating interleukin-6, TNF-α, monocyte chemoattractant protein-1 and resistin rise while adiponectin falls; sustained c-Jun N-terminal kinase and nuclear factor kappa-B signalling with serine phosphorylation of insulin receptor substrate-1 produces insulin resistance and hyperglycaemia. A patient with excess adiposity therefore meets a cytotoxic epidermal insult already carrying an elevated TNF-α tone, impaired neutrophil function and a metabolic milieu that retards re-epithelialisation.

Prognostication in epidermal necrolysis is dominated by the Severity-of-Illness Score for Toxic Epidermal Necrolysis (SCORTEN), derived in 2000 from seven binary variables — age over 40 years, malignancy, heart rate above 120 beats per minute, epidermal detachment exceeding 10% of BSA, serum urea above 28 mg/dL, serum glucose above 252 mg/dL and serum bicarbonate below 20 mmol/L — with predicted mortality rising from 3.2% at scores of 0–1 to more than 90% at scores of 5 or above.[18] A meta-analysis of 45 studies and 3,467 patients confirmed that all seven components remain independently associated with in-hospital death, while also identifying serum creatinine as an additional independent predictor that the score does not contain.[19] Calibration, however, drifts by setting: SCORTEN was well calibrated in a United States burn centre of 192 patients (Hosmer–Lemeshow $p = 0.82$) where ABCD-10 fitted poorly,[20] the two instruments discriminated equivalently across three Chinese institutions,[21] and a Polish protocolised cohort observed 12.5% mortality against a SCORTEN-estimated 41.9%.[22]

What no version of the score contains is any nutritional, anthropometric or metabolic term, and that omission is not obviously benign. The same systematic review that pooled 52,398 cases identified several non-SCORTEN predictors of death — pre-existing renal disease (OR 3.14, 95% CI 1.99–4.97), sepsis (OR 5.64, 95% CI 2.81–11.29), diabetes mellitus (OR 1.87, 95% CI 1.21–2.89) and comorbidity burden (OR 9.13, 95% CI 4.60–18.12) — establishing that prognostic information demonstrably exists outside the seven variables.[1] Epidermal necrolysis reproduces the hypermetabolic physiology of a major burn, and international supportive-care consensus accordingly specifies weight-based caloric and fluid targets.[23] Outside dermatology, a prospective community study of 6.9 million people in England found risk of severe outcome rising monotonically above a body mass index (BMI) of 23 kg/m^2, with steeper gradients in younger and in non-white participants,[24] and metabolic syndrome predicted acute respiratory distress syndrome in hospitalised patients with acute inflammatory illness.[25] The evidence is not uniform: obesity was associated with more sepsis-associated acute kidney injury in a 4,041-patient Korean intensive-care cohort yet with *lower* in-hospital mortality among those who escaped it,[26] and a 20-year cohort of 27,026 oldest-old adults found reverse J-shaped associations in which overweight and obesity predicted reduced all-cause mortality.[27]

Two features of the Indonesian setting sharpen the question. First, Asian populations carry greater visceral adiposity and higher cardiometabolic risk at any given BMI than European reference populations, which is why regional consensus retains the Asia-Pacific classification with an overweight threshold of 23 kg/m^2 and an obesity threshold of 25 kg/m^2;[28] in a cohort of 4,164 Chinese women, the 25 kg/m^2 Asian threshold

independently identified a 57% increase in disease risk (OR 1.57, 95% CI 1.13–2.20) that World Health Organization thresholds would have missed.[29] A cohort analysed with WHO thresholds will therefore misclassify a substantial fraction of metabolically at-risk Indonesian patients as normal weight and will systematically under-detect any adiposity–outcome relationship. This matters more each year: across 2.4 million Indonesian adults surveyed between 2007 and 2023, obesity defined by the Asian threshold nearly doubled from 19.7% to 38.3%, and central adiposity reached 42.0%.[30] Second, Dr. Moewardi General Hospital is a tertiary dermatological referral centre for Central Java; work at this institution has already shown that inexpensive bedside indices such as the neutrophil-to-lymphocyte ratio and the eosinophil count carry information about SCORTEN,[31] establishing both the feasibility and the local precedent for testing a simple anthropometric marker against the score.

Despite this convergence of mechanism, physiology and epidemiology, the specific literature on BMI in SJS/TEN is close to empty. No adequately powered cohort has been published; the few studies that mention body habitus do so incidentally, and none has examined the ordered relationship between BMI category and mortality using thresholds appropriate to an Asian population. The present study was therefore designed to determine whether BMI, classified on Asia-Pacific cut-offs, is associated with the severity of SJS/TEN as indexed by SCORTEN, by diagnostic class and by in-hospital mortality among adults treated at Dr. Moewardi General Hospital, Surakarta, between January 2022 and December 2024. Its contribution is three-fold: it applies Asia-Pacific rather than WHO thresholds in an Asian cohort; it analyses an ordered exposure with ordered rather than omnibus methods; and, given the modest size that any single-centre cohort of a rare disease must have, it quantifies explicitly how much information the data contain about each association rather than reporting a significance verdict alone.

2. Methods

Study design and reporting

This was a retrospective observational analytic study with a cross-sectional exposure–outcome structure and an in-hospital mortality endpoint, conducted using secondary data abstracted from medical records. Reporting follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cross-sectional studies, and the completed checklist is available from the corresponding author.[32] Participant flow is shown in Figure 1A and the prespecified analytic sequence in Figure 1B.

Setting and participants

The study was conducted in the Department of Dermatology and Venereology, Faculty of Medicine, Universitas Sebelas Maret/Dr. Moewardi General Hospital, Surakarta, Central Java, Indonesia — the provincial tertiary referral centre for severe cutaneous adverse reactions. The observation window ran from 1 January 2022 to 31 December 2024 inclusive. Case ascertainment used total sampling of the hospital admission register: every admission coded to the International Classification of Diseases, Tenth Revision (ICD-10) as L51.1 (SJS) or L51.2 (TEN) during the window was retrieved, and no sampling fraction was applied. Because total sampling was used, the analysed cohort is the complete eligible population of the institution for the period rather than a probability sample of it.

Inclusion required a diagnosis of SJS, SJS–TEN overlap or TEN confirmed by the attending dermatologist on the basis of morphology, mucosal involvement and the extent of epidermal detachment, with a documented culprit-drug exposure history. Patients under 18 years of age were excluded, because the Asia-Pacific BMI classification is defined for adults and paediatric epidermal necrolysis has a distinct causative and prognostic profile. Records with any missing value for height, weight, discharge status or any of the seven SCORTEN components were also excluded, since imputation of a component of an integer prognostic score would propagate uncertainty in an uninterpretable way at this sample size. Forty-three patients met all criteria.

Exposure definition

Body mass index was calculated as measured body weight in kilograms divided by the square of measured height in metres (kg/m^2), using the admission values recorded by nursing staff before the initiation of fluid resuscitation. Patients were classified according to the Asia-Pacific classification: underweight below 18.5 kg/m^2, normoweight 18.5–22.9 kg/m^2, overweight 23.0–24.9 kg/m^2 and obesity 25.0 kg/m^2 or above. The Asia-Pacific thresholds were prespecified in preference to the World Health Organization thresholds because Asian populations exhibit higher body fat percentage and greater visceral adiposity at equivalent BMI, and consequently a higher cardiometabolic risk at lower absolute BMI values.[28] For the principal dichotomised analysis, patients were grouped as BMI below 23.0 kg/m^2 (underweight plus normoweight, n = 26) versus 23.0 kg/m^2 or above (overweight plus obesity, n = 17); this threshold was chosen a priori because it is the clinically actionable Asia-Pacific cut-off, not because it optimised any test statistic.

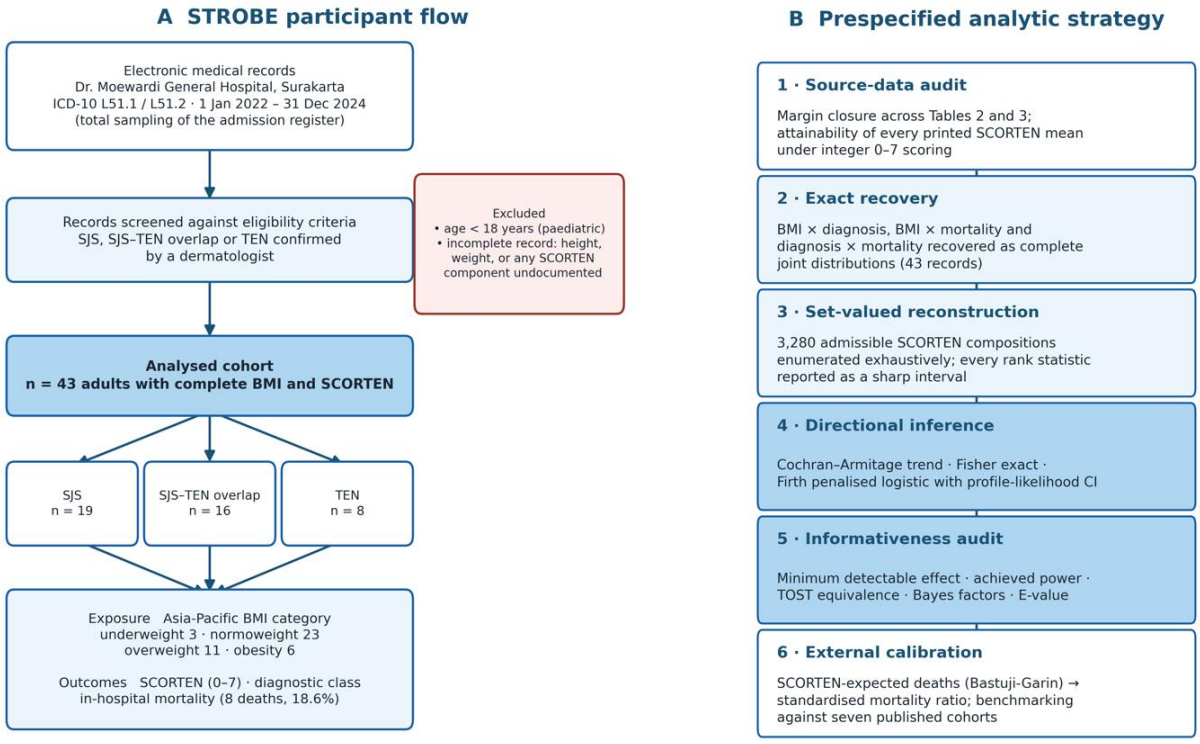

Figure 1. Study flow and analytic strategy. (A) STROBE participant flow for total sampling of the ICD-10 L51.1/L51.2 admission register at Dr. Moewardi General Hospital, Surakarta, between 1 January 2022 and 31 December 2024, showing the 43 analysed adults and their distribution across diagnostic classes and Asia-Pacific body mass index categories. (B) The prespecified six-stage analytic sequence, from arithmetic audit of the source summaries through exact recovery of the identified joint distributions, set-valued reconstruction of the SCORTEN distribution, directional inference, the informativeness audit and external calibration.

Outcome definitions

Three outcomes were analysed. SCORTEN was computed at admission from the seven original binary components — age over 40 years, presence of malignancy, heart rate above 120 beats per minute, epidermal detachment exceeding 10% of BSA, serum urea above 28 mg/dL, serum glucose above 252 mg/dL and serum bicarbonate below 20 mmol/L — each scoring one point, giving an integer total from 0 to 7 (Table 1).[18] Diagnostic class was recorded as SJS, SJS–TEN overlap or TEN and treated as an ordered categorical severity variable. In-hospital mortality was the binary discharge status recorded at the end of the index admission. Length of stay in days was recorded as a secondary descriptive variable.

Table 1. Components of the Severity-of-Illness Score for Toxic Epidermal Necrolysis (SCORTEN) and predicted mortality by score band.

Component (assessed within 24 h of admission)	Threshold	Points
Age	> 40 years	1
Heart rate	> 120 beats/min	1
Malignancy	Present	1
Epidermal detachment	> 10% of body surface area	1
Serum urea	> 28 mg/dL	1
Serum bicarbonate	< 20 mmol/L	1
Serum glucose	> 252 mg/dL	1
Maximum total score	—	7
SCORTEN 0–1	Predicted mortality	3.2%
SCORTEN 2	Predicted mortality	12.1%
SCORTEN 3	Predicted mortality	35.3%
SCORTEN 4	Predicted mortality	58.3%
SCORTEN ≥ 5	Predicted mortality	> 90%

Predicted mortality values are those of the original derivation cohort and were used as the reference weights for the standardised mortality ratio reported below.

Sample size and precision

No prospective sample-size calculation was performed, because the cohort is defined by total sampling of a fixed three-year window at a single centre and its size is therefore not under investigator control. The achieved precision was instead quantified explicitly and prespecified as a reporting requirement. For a correlation with n = 43 at α = 0.05 (two-sided) and 80% power, the minimum detectable effect is |ρ| = 0.42; detecting ρ = 0.30 would require n = 85 and ρ = 0.20 would require n = 194. For the dichotomised mortality contrast with 17 exposed and 26 unexposed patients and a baseline risk of 7.7%, the minimum detectable odds ratio at 80% power is 9.5. These figures are reported alongside every null result so that absence of evidence is not presented as evidence of absence.

Statistical analysis

Analyses were performed in Python 3.13 using NumPy 2.4 and SciPy 1.17; Firth penalised regression, the Fisher–Freeman–Halton exact test, the exact permutation form of the trend statistic and the reconstruction algorithms were implemented directly and the analysis code is available from the corresponding author. Two-sided α was set at 0.05 and all p values are reported to three decimal places.

Categorical variables are summarised as counts with percentages and Wilson 95% confidence intervals, which retain nominal coverage with small denominators and zero cells. Continuous and ordinal variables are summarised as mean ± standard deviation. Contingency tables were tested with Pearson χ^2 without continuity correction, with the contingency coefficient C and Cramér's V as effect sizes, and — because 75% of expected counts in the principal 4 × 2 table fall below 5 — with the Fisher–Freeman–Halton exact test computed by complete enumeration of all tables with the observed margins.

Because BMI category is an ordered exposure, the omnibus χ^2 test was prespecified as a secondary rather than a primary analysis: with three degrees of freedom it discards the ordering and is materially less powerful than a directional alternative. The prespecified primary tests of the mortality hypothesis were therefore the Cochran–Armitage test for trend across the four ordered BMI categories, with an exact permutation p value conditional on the margins, and Fisher's exact test on the Asia-Pacific dichotomy. Odds ratios are reported three ways: unadjusted with Woolf 95% confidence intervals, as exact conditional (Cornfield) estimates, and from Firth penalised logistic regression with profile penalised-likelihood confidence intervals. Firth's method was prespecified as the primary estimator because the underweight stratum contains zero deaths, a configuration under which ordinary maximum likelihood is biased away from the null and can fail to converge.[33] Risk differences, relative risks, the number needed to harm and the population attributable fraction were derived from the same table, and unmeasured confounding was assessed with the E-value, the minimum strength of association on the risk-ratio scale that an unmeasured confounder would need with both exposure and outcome to explain away the observed effect.[34] A reverse fragility index — the number of outcome events that would have to change to move a non-significant result across the α threshold — was computed for the omnibus analysis.

Rank associations were quantified with Spearman's ρ and, across the ordered BMI strata, with the Jonckheere–Terpstra trend statistic and the Kruskal–Wallis test with ε^2 as the effect size. Discriminative performance was summarised as the area under the receiver operating characteristic curve with Hanley–McNeil standard errors. Between-group standardised mean differences are reported as Cohen's d with 95% confidence intervals. The three prespecified exposure–outcome contrasts (BMI with SCORTEN, with mortality and with length of stay) were additionally adjusted for multiplicity by the Holm procedure.

Because a null result at this sample size is ambiguous between "no effect" and "no information", every non-significant finding was accompanied by three further quantities: the achieved power at the observed effect size; a two-one-sided-tests (TOST) equivalence analysis against a sweep of bounds on |ρ|, reporting the smallest bound that the data can reject; and a Bayes factor computed under a Jeffreys stretched-beta prior on the correlation, with sensitivity across prior widths κ of 0.5, 0.707, 1.0 and 1.414.

Source-data audit and set-valued reconstruction

The analysis dataset available for this work consisted of the complete cross-tabulations published in the source clinical record summaries rather than a patient-level export. Three joint distributions are exactly recoverable from those tables and were used without assumption: BMI category by diagnostic class, BMI category by discharge status, and diagnostic class by discharge status. All five margin-closure checks pass exactly, and the reported contingency coefficient for BMI and discharge status reproduces to three decimal places from the recovered table, confirming the reconstruction.

The individual SCORTEN values are not exactly recoverable, and were therefore handled by partial identification rather than by imputation. Because SCORTEN is a sum of seven binary items it must be an integer on 0–7, so each stratum mean and standard deviation constrains the set of admissible compositions. All count-vectors of the required size were enumerated exhaustively, retained if they reproduced the printed mean and standard deviation to two decimal places, and every rank statistic involving SCORTEN was then computed across the complete admissible set and reported as an interval rather than a point. This procedure both quantifies the reconstruction uncertainty honestly and, as reported in

the Results, exposes three printed means that no set of integer scores can produce.

Two quantities were deliberately NOT estimated because they are not identified by the available data, and no assumption capable of identifying them could be defended. The first is the discrimination of SCORTEN itself for in-hospital mortality: the joint distribution of SCORTEN and discharge status is unavailable, and constrained enumeration bounds the area under the curve only to 0.03–1.00, an interval that carries no information. The second is any multivariable model treating the seven SCORTEN components as separate covariates. Both are reported as refusals rather than presented with fabricated precision. The SCORTEN-adjusted odds ratio for BMI is reported only as a bracketing interval obtained by assigning the deaths within each BMI stratum first to the lowest and then to the highest available SCORTEN values, which brackets the extremes of possible confounding by severity.

External calibration and benchmarking

Observed mortality was compared with the mortality predicted by the original SCORTEN derivation — 3.2% for scores of 0–1, 12.1% for 2, 35.3% for 3, 58.3% for 4 and 90% for 5 or above[18] — applied to each admissible reconstruction of the SCORTEN distribution, giving a standardised mortality ratio with a Garwood exact Poisson 95% confidence interval. Six independently published cohorts spanning China, Poland, India, Europe and the United States were assembled as external comparators;[5,20,21,22,35,36] cohort mortality was tested by exact binomial test against the mortality pooled across them (115 deaths among 643 patients, 17.9%), and the diagnostic-class gradient was compared with that reported in the largest published series.[3]

Ethics

Ethical approval for this study was obtained from the Health Research Ethics Committee of Dr. Moewardi Regional General Hospital (No. 1.333/VII/HREC/2026). Because the study analysed de-identified data abstracted retrospectively from existing medical records, with no patient contact and no intervention, the requirement for individual written informed consent was waived by the same committee. All patient identifiers were removed at the point of abstraction and no individual is identifiable in any table, figure or analysis presented here. The study was conducted in accordance with the principles of the Declaration of Helsinki and its subsequent amendments.

3. Results

Cohort characteristics

Forty-three adults met the eligibility criteria over the three-year window, and their flow through the study is set out in Figure 1A. Twenty-two were women (51.2%) and 21 were men (48.8%); 33 (76.7%) were aged 18–59 years and 10 (23.3%) were 60 years or older. Nineteen patients (44.2%) had SJS, 16 (37.2%) had SJS–TEN overlap and 8 (18.6%) had TEN. Nutritional status was normoweight in 23 patients (53.5%), overweight in 11 (25.6%), obese in 6 (14.0%) and underweight in 3 (7.0%), so that 17 patients (39.5%) sat at or above the Asia-Pacific overweight threshold of 23 kg/m^2. Mean SCORTEN was 1.67 ± 1.22 overall, rising from 1.11 ± 1.05 in SJS through 1.73 ± 0.96 in SJS–TEN overlap to 2.55 ± 1.37 in TEN, a standardised difference between SJS and TEN of d = 1.25 (95% CI 0.36–2.15). Eight patients died during the index admission, giving an in-hospital mortality of 18.6% (95% CI 9.7–32.6). Every baseline characteristic, with its interval estimate, test statistic and effect size, is detailed in Table 2, and the corresponding outcome distributions are displayed in Figure 2.

Age was strongly related to diagnostic class, as detailed in the second block of Table 2: 5 of 8 patients with TEN (62.5%) were 60 years or older, against 5 of 35 (14.3%) with SJS or overlap disease (χ^2 = 8.534, df = 2, p = 0.014; Cramér's V = 0.446; odds ratio for TEN in those aged ≥ 60 years 9.25, 95% CI 1.34–80.44, Fisher exact p = 0.010). Sex was not related to diagnostic class (χ^2 = 0.780, df = 2, p = 0.677; Cramér's V = 0.135). Critically for the interpretation that follows, BMI category was not related to diagnostic class either (χ^2 = 3.086, df = 6, p = 0.798; Cramér's V = 0.189; Jonckheere–Terpstra z = −0.774, p = 0.439), as the third block of Table 2 shows: heavier patients were not presenting with more extensive epidermal detachment.

Body mass index and in-hospital mortality

In-hospital mortality rose across the four ordered BMI strata, with a significant upward trend: 0 of 3 in underweight patients (0%; 95% CI 0–56.2), 2 of 23 in normoweight (8.7%; 95% CI 2.4–26.8), 4 of 11 in overweight (36.4%; 95% CI 15.2–64.6) and 2 of 6 in obese patients (33.3%; 95% CI 9.7–70.0). This gradient, with its Wilson intervals and fitted trend line, is plotted in Figure 2A, and every analysis described in this subsection is set out side by side in Table 3. The omnibus test applied to the 4 × 2 table was not significant — contingency coefficient C = 0.332, χ^2 = 5.327, df = 3, p = 0.149, with 6 of 8 cells (75.0%) having an expected count below 5 and a minimum expected count of 0.56 — and the Fisher–Freeman–Halton exact test agreed (p = 0.124). These two rows form the first analytic block of Table 3.

Table 2. Baseline characteristics of 43 adults with Stevens–Johnson syndrome and toxic epidermal necrolysis, Dr. Moewardi General Hospital, Surakarta, January 2022 – December 2024.

Characteristic	SJS (n = 19)	SJS–TEN overlap (n = 16)	TEN (n = 8)	Total (n = 43)	Test statistic	p value	Effect size
Sex					χ2 = 0.780, df = 2	0.677	V = 0.135
Male	9 (47.4)	7 (43.8)	5 (62.5)	21 (48.8)			
Female	10 (52.6)	9 (56.3)	3 (37.5)	22 (51.2)			
Age group					χ2 = 8.534, df = 2	0.014	V = 0.446
18–59 years	16 (84.2)	14 (87.5)	3 (37.5)	33 (76.7)			
≥ 60 years	3 (15.8)	2 (12.5)	5 (62.5)	10 (23.3)	OR 9.25 (1.34–80.44)	0.010	φ = 0.446
Asia-Pacific BMI category					χ2 = 3.086, df = 6	0.798	V = 0.189
Underweight (< 18.5 kg/m2)	1 (5.3)	2 (12.5)	0 (0.0)	3 (7.0)			
Normoweight (18.5–22.9 kg/m2)	9 (47.4)	8 (50.0)	6 (75.0)	23 (53.5)			
Overweight (23.0–24.9 kg/m2)	6 (31.6)	4 (25.0)	1 (12.5)	11 (25.6)			
Obesity (≥ 25.0 kg/m2)	3 (15.8)	2 (12.5)	1 (12.5)	6 (14.0)			
BMI ≥ 23.0 kg/m2 (combined)	9 (47.4)	6 (37.5)	2 (25.0)	17 (39.5)	J–T z = −0.774	0.439	V = 0.189
SCORTEN					d (SJS vs TEN) = 1.25	—	95% CI 0.36–2.15
Mean ± SD	1.11 ± 1.05	1.73 ± 0.96	2.55 ± 1.37	1.67 ± 1.22			
Discharge status					χ2 = 6.420, df = 2	0.040	V = 0.386
Alive	17 (89.5)	14 (87.5)	4 (50.0)	35 (81.4)	exact trend	0.041	
Deceased	2 (10.5)	2 (12.5)	4 (50.0)	8 (18.6)	OR (TEN) 7.23 (0.96–59.98)	0.028	AUC 0.704
In-hospital mortality, % (95% CI)	10.5 (2.9–31.4)	12.5 (3.5–36.0)	50.0 (21.5–78.5)	18.6 (9.7–32.6)			

Data are n (%) unless stated otherwise. Percentages are column percentages within diagnostic class. Confidence intervals for proportions are Wilson intervals. AUC, area under the receiver operating characteristic curve; BMI, body mass index; CI, confidence interval; d, Cohen's d; J–T, Jonckheere–Terpstra; OR, odds ratio; SD, standard deviation; SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis; V, Cramér's V; φ, phi coefficient.

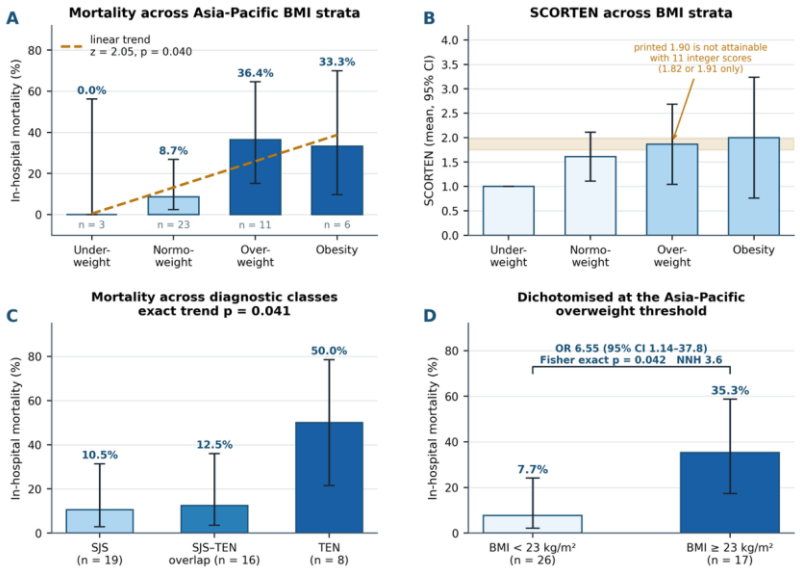

Figure 2. Primary outcomes across body mass index and diagnostic class. (A) In-hospital mortality by Asia-Pacific BMI category with Wilson 95% confidence intervals and the fitted linear trend (Cochran–Armitage z = 2.05; p = 0.040). (B) Mean SCORTEN by BMI category with 95% confidence intervals; the shaded band marks the printed overweight mean of 1.90, which no set of 11 integer scores can produce. (C) Mortality across diagnostic classes (exact trend p = 0.041). (D) Mortality dichotomised at the Asia-Pacific overweight threshold of 23 kg/m2. Error bars are Wilson 95% confidence intervals throughout.

Analyses that retained the ordering of the exposure reached the opposite conclusion, as the second analytic block of Table 3 and the forest plot in Figure 3A both show. The Cochran–Armitage test for trend across ordered BMI categories gave z = 2.053 (p = 0.040), with an exact permutation p of 0.056. Dichotomised at the Asia-Pacific overweight threshold, mortality was 6 of 17 (35.3%; 95% CI 17.3–58.7) at BMI ≥ 23 kg/m² against 2 of 26 (7.7%; 95% CI 2.1–24.1) below it, a contrast displayed in Figure 2D: odds ratio 6.55 (95% CI 1.14–37.75), exact conditional odds ratio 6.24 (95% CI 0.93–72.82), Fisher exact p = 0.042, χ^2 = 5.171 with p = 0.023, φ = 0.347. Firth penalised logistic regression, prespecified as the primary estimator because the underweight stratum contains no deaths, gave an odds ratio of 5.54 (95% profile penalised-likelihood CI 1.20–34.09; likelihood-ratio χ^2 = 5.316, p = 0.021) for the dichotomy, and 2.46 per BMI category (95% CI 1.01–6.66; likelihood-ratio χ^2 = 5.429, p = 0.020) when BMI category was entered as an ordinal trend.

The magnitude of the association is summarised in the third analytic block of Table 3. The risk difference was 27.6 percentage points (95% CI 2.7–52.5), the relative risk 4.59, the number needed to harm 3.6, and the population attributable fraction 58.7% (95% CI 3.3–71.3). BMI category discriminated in-hospital mortality with an area under the curve of 0.725 (95% CI 0.51–0.94; p = 0.040). Two sensitivity analyses complete that block. The E-value for the observed relative risk was 8.65, meaning that an unmeasured confounder would have to be associated with both excess adiposity and death by a risk ratio of at least 8.65, over and above the measured variables, to explain the association away; an E-value is a statement about what would be required, not evidence that such a confounder exists. The reverse fragility index of the omnibus analysis was 1, and the conventional fragility index of the significant dichotomised analysis was likewise 1 — moving a single patient between columns overturns either verdict, so both results are maximally fragile. Bracketing for severity, the SCORTEN-adjusted odds ratio per BMI category remained above unity across every admissible reconstruction and both extremal death-assignment schemes (range of point estimates 2.74 to 53.57); this is a range of point estimates that carries no sampling uncertainty and is plotted in a deliberately distinct style in Figure 3A.

The discrepancy between the omnibus and directional results is a property of the tests rather than of the data. Under the mortality gradient actually observed here, 6,000 simulated replicates at n = 43 (seed 20260813) gave the omnibus contingency test 36.9% power, the Cochran–Armitage trend test 45.4% and the dichotomised exact test 51.1%, with a Monte Carlo standard error of about 0.6 percentage points. The published null therefore reflects a test that discards the ordering of an ordered exposure, not an absence of signal.

Body mass index and SCORTEN

Mean SCORTEN rose weakly and monotonically across BMI strata, from 1.00 ± 0.00 in the three underweight patients to 1.61 ± 1.23 in normoweight, approximately 1.86 in overweight and 2.00 ± 1.55 in obese patients, as plotted in Figure 2B. The rank association was weak and not statistically significant: Spearman ρ = 0.163 (95% CI −0.14 to 0.44; p = 0.296). Because the individual SCORTEN values are not exactly recoverable from the stratum summaries, this coefficient was recomputed across all 3,280 admissible integer reconstructions of the SCORTEN distribution. The coefficient ranged from ρ = 0.061 to ρ = 0.287 with a median of 0.167, and the corresponding p values ranged from 0.062 to 0.697; not one of the 3,280 reconstructions reached significance, because the coefficient required for p < 0.05 at n = 43 is 0.301 and the admissible set does not reach it. That interval, and the threshold it fails to cross, are set out in Table 4 and shown in Figure 4B. The Jonckheere–Terpstra trend statistic across ordered BMI strata behaved identically (z 0.393–1.905; p 0.057–0.695), as did the Kruskal–Wallis test (H 0.729–3.637; p 0.303–0.866) with an ε^2 of at most 0.016.

This null is uninformative rather than negative, and the precision audit that establishes this is detailed in Table 4. Achieved power at the observed coefficient was 18.0%; the minimum detectable |ρ| at 80% power was 0.42, and the power curves for this and for the larger samples that would be needed are drawn in Figure 3B. A two-one-sided-tests equivalence analysis could not exclude a correlation of conventional small-effect magnitude (p = 0.179 against a bound of ± 0.30); the smallest bound the data can reject is |ρ| = 0.40, as the sweep in Figure 3C shows. The Bayes factor favoured the null moderately but not decisively (BF_{01} = 3.10), and this conclusion was stable across prior widths (BF_{01} 2.17–3.81). Because a Bayes factor for a correlation assumes bivariate normality, which an ordered four-level exposure and an integer score with a floor effect do not satisfy, it should be read as a sensitivity analysis rather than as a primary result. In short, the data are compatible with no association between BMI and SCORTEN and equally compatible with a correlation of up to about 0.4.

Table 3. Association of Asia-Pacific body mass index category with in-hospital mortality: omnibus versus directional analyses of the identical 4 × 2 table.

Analysis	Estimate	95% confidence interval	p value	Interpretation
Stratum-specific mortality				
Underweight (n = 3)	0 / 3 (0.0%)	0.0–56.2	—	no deaths
Normoweight (n = 23)	2 / 23 (8.7%)	2.4–26.8	—	reference
Overweight (n = 11)	4 / 11 (36.4%)	15.2–64.6	—	highest stratum risk
Obesity (n = 6)	2 / 6 (33.3%)	9.7–70.0	—	consistent with overweight
Omnibus tests (exposure order discarded)				
Contingency coefficient, 4 × 2	C = 0.332	—	0.149	not significant; 75% of expected counts < 5
Pearson χ2, df = 3	χ2 = 5.327	—	0.149	Cramér's V = 0.352
Fisher–Freeman–Halton exact	—	—	0.124	complete enumeration
Reverse fragility index (omnibus null)	1 event	—	0.018 after the flip	the null is maximally fragile
Fragility index (dichotomised test)	1 event	—	0.120 after the flip	the positive result is equally fragile
Directional tests (exposure order retained)				
Cochran–Armitage trend, asymptotic	z = 2.053	—	0.040	monotone increase with BMI
Cochran–Armitage trend, exact permutation	z = 2.053	—	0.056	borderline; consistent direction
Mortality, BMI ≥ 23 vs < 23 kg/m2	35.3% vs 7.7%	17.3–58.7 vs 2.1–24.1	—	Wilson intervals
Odds ratio, unadjusted (Woolf)	OR = 6.55	1.14–37.75	0.023 (χ2)	φ = 0.347
Odds ratio, exact conditional	OR = 6.24	0.93–72.82	0.042 (Fisher exact)	interval crosses unity
Odds ratio, Firth penalised (dichotomy)	OR = 5.54	1.20–34.09	0.021	primary estimator; profile PL interval
Odds ratio, Firth penalised (per category)	OR = 2.46	1.01–6.66	0.020	ordinal trend model
Effect magnitude and sensitivity				
Risk difference	27.6 percentage points	2.7–52.5	—	number needed to harm 3.6
Relative risk	RR = 4.59	1.05–20.14	—	crude
Population attributable fraction	58.7%	3.3–71.3	—	if causal
Discrimination of BMI category	AUC = 0.725	0.51–0.94	0.040	cf. AUC 0.704 for diagnostic class
E-value for the point estimate	8.65	—	—	required confounder strength on the risk-ratio scale
Bayes factor, 2 × 2	BF10 = 3.26	—	—	moderate evidence for association
SCORTEN-adjusted OR per category	bracketing interval	2.74–53.57	—	above unity under every admissible reconstruction

All p values are two-sided. The Firth penalised model was prespecified as the primary estimator because the underweight stratum contains zero deaths. AUC, area under the receiver operating characteristic curve; BF, Bayes factor; BMI, body mass index; C, contingency coefficient; OR, odds ratio; PL, penalised likelihood; RR, relative risk.

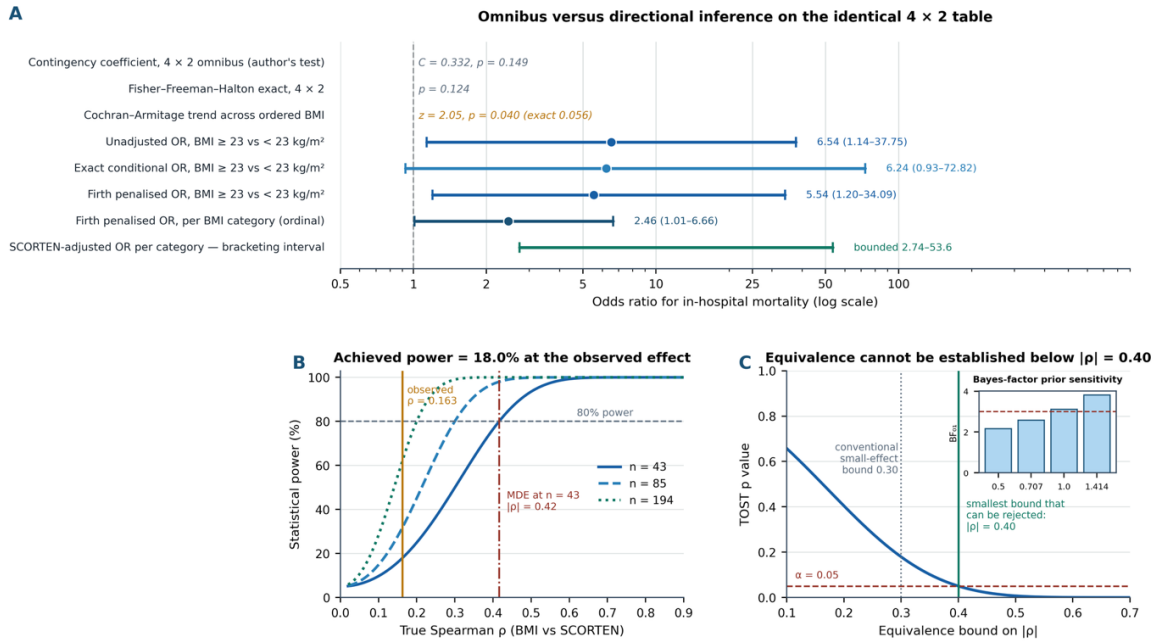

Figure 3. Inference and informativeness. (A) Forest plot of every analysis applied to the identical 4 × 2 table of BMI category by discharge status, showing that the omnibus tests the source analysis used are non-significant while every directional analysis is positive. (B) Power as a function of the true Spearman correlation at n = 43, 85 and 194, marking the observed coefficient of 0.163, the achieved power of 18.0% and the minimum detectable effect of |ρ| = 0.42. (C) Two-one-sided-tests equivalence sweep: the smallest bound the data can reject is |ρ| = 0.40, so equivalence within the conventional small-effect bound of 0.30 cannot be established; the inset shows Bayes-factor stability across prior widths.

Table 4. Precision, equivalence and informativeness of the null findings.

Quantity	BMI vs SCORTEN	BMI vs length of stay	Interpretation
Observed association			
Spearman ρ	0.163	−0.310	weak in both cases
95% confidence interval	−0.14 to 0.44	−0.56 to −0.01	both intervals wide
p value, unadjusted	0.296	0.043	reproduces the source to 3 dp
p value, Holm-adjusted	0.299	0.129	neither survives adjustment
Set-valued reconstruction (SCORTEN only)			
Admissible reconstructions enumerated	3,280	not applicable	exhaustive integer enumeration
Range of ρ across admissible set	0.061 to 0.287	—	never reaches significance
Range of p across admissible set	0.062 to 0.697	—	0 of 3,280 significant
Jonckheere–Terpstra z (range)	0.393 to 1.905	—	p 0.057 to 0.695
Kruskal–Wallis ε2 (range)	−0.058 to 0.016	—	negligible
Precision audit			
Achieved power at observed effect	18.0%	61.8%	both under-powered
Minimum detectable |ρ| at 80% power	0.42	0.42	only large effects detectable
n required for ρ = 0.30	85	85	roughly double the achieved n
n required for ρ = 0.20	194	194	multicentre scale
Minimum detectable odds ratio (mortality)	9.47	—	the observed OR of 6.55 lies below it
Equivalence and Bayesian evidence			
TOST p against bound |ρ| = 0.30	0.179	—	equivalence not established
TOST p against bound |ρ| = 0.40	0.051	—	smallest rejectable bound 0.40
Bayes factor BF01	3.10	0.73	moderate vs inconclusive
BF01 across prior widths κ 0.5–1.414	2.17 to 3.81	—	stable
Competing-risk check (length of stay)			
ρ induced by mortality truncation alone	—	−0.151	BMI given no direct effect on stay
Simulation range	—	−0.41 to 0.12	20,000 replicates
P(ρ ≤ −0.310 | no direct effect)	—	0.122	observed value not improbable
Share of observed ρ explained	—	≈ 49%	about half is attributable to earlier death

TOST, two one-sided tests. Bayes factors were computed under a Jeffreys stretched-beta prior on the correlation. BF_{01} > 3 is conventionally read as moderate evidence for the null; BF_{01} between 1/3 and 3 is inconclusive.

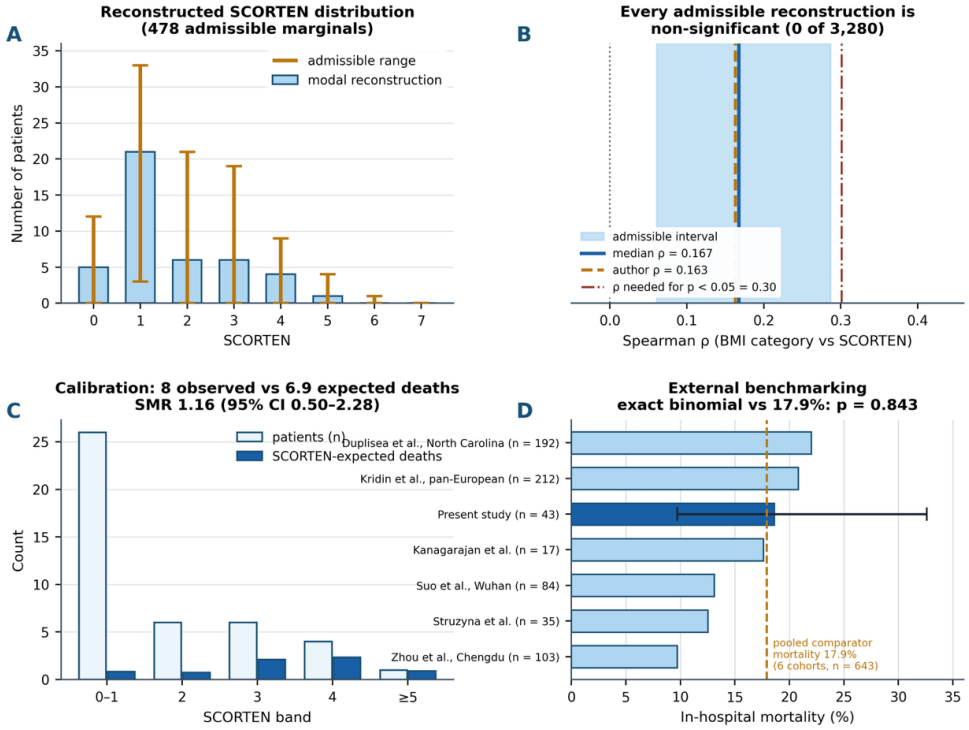

Figure 4. Source-data reconstruction, calibration and benchmarking. (A) The reconstructed SCORTEN distribution: bars show the modal reconstruction and vertical rules the full admissible range for each score across 478 distinct admissible marginals; these ranges are marginal across reconstructions and are not attained simultaneously. (B) Spearman ρ between BMI category and SCORTEN across all 3,280 admissible reconstructions; the entire admissible interval (0.061–0.287) lies below the coefficient of 0.301 required for significance at n = 43. (C) SCORTEN calibration: 8 observed deaths against 6.9 expected under the original Bastuji-Garin weights, giving a standardised mortality ratio of 1.16 (95% CI 0.50–2.28). (D) Crude in-hospital mortality benchmarked against six published cohorts; the dashed line is the mortality pooled across those six comparator cohorts (115 deaths among 643 patients, 17.9%; exact binomial p = 0.843).

Diagnostic class, SCORTEN calibration and external benchmarking

Mortality also rose across diagnostic classes, as plotted in Figure 2C: 2 of 19 in SJS (10.5%; 95% CI 2.9–31.4), 2 of 16 in SJS–TEN overlap (12.5%; 95% CI 3.5–36.0) and 4 of 8 in TEN (50.0%; 95% CI 21.5–78.5). The omnibus χ^2 was 6.420 (df = 2, p = 0.040) with Cramér's V = 0.386, the exact test gave p = 0.070, and the exact trend test gave p = 0.041. TEN carried an odds ratio for death of 7.23 (95% CI 0.96–59.98; Fisher exact p = 0.028) relative to SJS or overlap disease, and diagnostic class discriminated mortality with an area under the curve of 0.704 (95% CI 0.49–0.92; p = 0.068). The direction of this gradient matches the largest published comparator, an analysis of 51,040 SJS/TEN hospitalisations in the United States National Inpatient Sample, which reported mortality of 5.4% in SJS, 14.4% in overlap disease and 15.3% in TEN.[3] No formal comparison was made between the areas under the curve for BMI category and for diagnostic class; with 8 events the intervals overlap almost completely and such a test would not be interpretable.

SCORTEN was well calibrated in this cohort. Applying the original Bastuji-Garin predicted mortalities, which are reproduced in Table 1, to each admissible reconstruction of the SCORTEN distribution gave between 6.04 and 7.65 expected deaths (median 6.91) against 8 observed, a standardised mortality ratio of 1.16 (95% CI 0.50–2.28, Garwood exact Poisson interval) at the median reconstruction and 1.05–1.32 across the admissible set. The observed and expected counts are compared band by band in Figure 4C. This sits between the standardised mortality ratios of 0.69 for SJS and 1.49 for TEN reported in an Indian cohort of 40 patients,[37] and is consistent with a Chinese series of 103 patients in which predicted and observed mortality did not differ (12.6% versus 9.7%, p = 0.51)[5] while contrasting with a protocolised Polish cohort in which SCORTEN substantially over-predicted death (41.9% expected versus 12.5% observed).[22]

Crude mortality of 18.6% (95% CI 9.7–32.6) was indistinguishable from the 17.9% pooled across the six comparator cohorts assembled for this purpose (115 deaths among 643 patients; exact binomial p = 0.843), and the present cohort sits in the middle of a range running from 9.7% in Chengdu[5] through 12.5% in Poland,[22] 13.1% in Wuhan,[21] 17.6% in South India[35] and 20.8% across thirteen European referral centres[36] to 22.0% in a United States burn centre.[20] That comparison is displayed in Figure 4D and tabulated in the benchmarking block of Table 5. The cohort is therefore typical rather than idiosyncratic, which strengthens the external relevance of the BMI finding.

Table 5. Source-data audit, SCORTEN calibration and external benchmarking.

Item	Value obtained	Reference or admissible value	Assessment
Internal consistency of the tabulated summaries			
BMI × diagnostic class margins	19 / 16 / 8 and 3 / 23 / 11 / 6	must sum to 43 in both directions	PASS
Deaths, diagnosis- vs BMI-stratified	8 and 8	must agree	PASS
Survivors, diagnosis- vs BMI-stratified	35 and 35	must agree	PASS
Reported contingency coefficient	C = 0.332, p = 0.149	recomputed C = 0.332, p = 0.149	PASS — reproduces exactly
SCORTEN mean, overweight stratum (n = 11)	printed 1.90	attainable means 1.818 or 1.909	FAIL — no integer set gives 1.90
SCORTEN mean, SJS–TEN overlap (n = 16)	printed 1.73	attainable means 1.688 or 1.750	FAIL — 27.68 is not an integer
SCORTEN mean, TEN (n = 8)	printed 2.55	attainable means 2.500 or 2.625	FAIL — 20.4 is not an integer
Total SCORTEN sum, BMI-stratified	72 or 73	pinned at 72 by the overall mean	branch carried explicitly
Total SCORTEN sum, diagnosis-stratified	68 to 70	must equal 72	FAIL — irreconcilable by ≥ 2 points
SCORTEN calibration (Bastuji-Garin weights)			
Observed in-hospital deaths	8	—	—
Expected deaths across admissible set	6.04 to 7.65	median 6.91	—
Standardised mortality ratio	1.16	95% CI 0.50–2.28	well calibrated; no evidence of excess
SMR range across admissible set	1.05 to 1.32	—	robust to reconstruction
External SMR comparator, India (n = 40)	SJS 0.69 / TEN 1.49	—	our 1.16 lies between them
External calibration, China (n = 103)	12.6% expected vs 9.7% observed	p = 0.51	concordant with ours
External calibration, Poland (n = 35)	41.9% expected vs 12.5% observed	—	SCORTEN over-predicted there
External benchmarking of crude mortality			
Present cohort, Surakarta (n = 43)	18.6% (9.7-32.6)	Indonesia	reference
Zhou et al. (n = 103)	9.7%	Chengdu, China	within our 95% CI
Struzyna et al. (n = 35)	12.5%	Poland	within our 95% CI
Suo et al. (n = 84)	13.1%	Wuhan, China	within our 95% CI
Kanagarajan et al. (n = 17)	17.6%	South India	within our 95% CI
Kridin et al. (n = 212)	20.8%	13 European centres	within our 95% CI
Duplisea et al. (n = 192)	22.0%	United States	within our 95% CI
Pooled comparator mortality	17.9% (115/643)	six cohorts	exact binomial p = 0.843
Diagnostic-class gradient, largest comparator	SJS 5.4% / overlap 14.4% / TEN 15.3%	United States (n = 51,040)	same direction as ours
Quantities deliberately not estimated			
Discrimination of SCORTEN for mortality	not identified	bounded 0.03 to 1.00	refused — interval carries no information
Multivariable model of SCORTEN components	not identified	—	refused — component-level data unavailable

PASS/FAIL refers to arithmetic attainability under integer SCORTEN scoring on 0–7, not to any judgement about the underlying clinical data. CI, confidence interval; CPRD, Clinical Practice Research Datalink; SMR, standardised mortality ratio.

Length of stay and multiplicity

Body mass index showed a weak inverse association with length of hospital stay (Spearman ρ = −0.310; 95% CI −0.56 to −0.01; p = 0.043; ρ^2 = 0.096). This result requires careful handling for three reasons, all quantified in the final two blocks of Table 4. It does not

survive adjustment for the three prespecified contrasts (Holm-adjusted p = 0.129), the Bayes factor is inconclusive (BF_{01} = 0.73), and, most importantly, death truncates hospital stay. Under a simulation of 20,000 replicates in which BMI has no direct effect whatsoever on length of stay, but decedents leave the ward earlier than survivors, the observed BMI–mortality gradient alone induces a mean Spearman coefficient of −0.151 — roughly half the observed value — with a 95% simulation range of −0.41 to 0.12, and the probability of a coefficient at least as negative as −0.310 arising with no direct effect is 0.122. The result was stable across assumed decedent stays of 5 to 11 days (induced ρ −0.179 to −0.074). The shorter admissions of heavier patients are therefore best interpreted as a consequence of their higher mortality rather than as evidence of a milder course.

Across the three prespecified contrasts, raw p values of 0.296 (SCORTEN), 0.149 (mortality, omnibus) and 0.043 (length of stay) became 0.299, 0.299 and 0.129 after Holm adjustment. The directional mortality analyses reported above are prespecified primary tests of a single hypothesis and are therefore not part of this adjustment family; readers who prefer to apply the same correction to them should note that the Firth trend p of 0.020 becomes 0.060 under a three-comparison Holm procedure, which does not alter the interpretation offered here — an imprecise positive signal requiring confirmation.

Internal consistency of the source records

A prespecified arithmetic audit of the tabulated summaries is reported for transparency, since it constrains what can be concluded; its full output is detailed in the first block of Table 5. All five margin-closure checks pass exactly: the BMI-by-diagnosis table sums correctly in both directions, and the 8 deaths and 35 survivors are consistent between the diagnosis-stratified and BMI-stratified presentations. Three of the printed SCORTEN means, however, cannot be produced by any set of integer scores. A mean of 1.90 in 11 overweight patients requires a total of 20.9, which is not an integer; the nearest attainable means are 1.818 (total 20) and 1.909 (total 21). A mean of 1.73 in 16 patients with overlap disease requires 27.68 (attainable: 1.688 or 1.750), and 2.55 in 8 patients with TEN requires 20.4 (attainable: 2.500 or 2.625). Furthermore, the overall mean of 1.67 in 43 patients pins the total SCORTEN sum uniquely at 72, whereas the diagnosis-stratified means imply a total between 68 and 70 — an irreconcilable difference of at least two points.

Two explanations are compatible with these findings: a small number of transcription or rounding errors in the stratum summaries, or SCORTEN missingness in a few records whose denominators were not carried into the summary tables. The second would reconcile the totals without any error at all, and cannot be distinguished from the first using the available information. All SCORTEN-dependent results in this manuscript are therefore reported as intervals over the admissible set, the extent of which is shown in Figure 4A, rather than as single values; none of the substantive conclusions changes across that set. Both branches of the overweight stratum were carried with equal weight, although the sum-21 branch reproduces the printed standard deviation more closely (1.375 versus a printed 1.37) than the sum-20 branch (1.401); restricting the analysis to the closer branch shifts the admissible interval for ρ only from 0.061–0.287 to 0.109–0.287 and changes no conclusion.

4. Discussion

Among 43 adults treated for epidermal necrolysis at Dr. Moewardi General Hospital, Surakarta, between January 2022 and December 2024, body mass index was not associated with SCORTEN but was associated with in-hospital death. Mortality rose from 0% in underweight patients to 36.4% in overweight patients (Cochran–Armitage z = 2.053, p = 0.040; exact permutation p = 0.056), and at the Asia-Pacific overweight threshold reached 35.3% against 7.7% below it, an odds ratio of 6.55 (95% CI 1.14–37.75; Fisher exact p = 0.042) and a Firth-penalised odds ratio of 5.54 (95% CI 1.20–34.09), as detailed in Table 3. The rank association with SCORTEN, by contrast, was 0.163 with a 95% confidence interval from −0.14 to 0.44, and remained non-significant across all 3,280 admissible reconstructions of the score distribution. The central message of this cohort is therefore not that adiposity is irrelevant to epidermal necrolysis, but that its prognostic signal runs through a channel that SCORTEN does not measure.

That dissociation is the finding that most requires explanation, and three lines of reasoning converge on it. First, it is structural. SCORTEN was derived from seven variables — age, malignancy, tachycardia, detachment area, urea, glucose and bicarbonate — none of which is an anthropometric or nutritional measure,[18] and a meta-analysis of 45 studies confirmed that while all seven remain independently predictive, at least one further variable (serum creatinine) carries information the score omits.[19] A larger synthesis of 52,398 cases went further, identifying pre-existing renal disease, sepsis, diabetes mellitus and overall comorbidity burden as non-SCORTEN predictors of death with pooled odds ratios between 1.87 and 9.13.[1] Prognostic information demonstrably exists outside the seven variables; the question this study raises is whether body habitus is another example. Second, the dissociation is empirically consistent within this cohort: BMI category showed no relationship whatsoever with diagnostic class (p = 0.798; Jonckheere–Terpstra p = 0.439), so heavier patients were not presenting with more extensive detachment. Third, the discrimination figures point the same way: BMI category discriminated death slightly better (area under the curve 0.725) than diagnostic class did (0.704), despite carrying no information about the

extent of skin loss — although with 8 events these two intervals overlap almost entirely and no inference of superiority is warranted.

The literature with which this result must be reconciled is, on the specific question, close to empty. No cohort designed and powered to test an adiposity–outcome relationship in SJS/TEN has been published, in any population, and the recent large syntheses of mortality predictors do not examine body mass index at all.[1,19] The honest position is that the question has not previously been asked with an adequate design, and has certainly not been asked using Asia-Pacific thresholds in an Asian cohort. This is a gap rather than a contradiction, and the present study should be read as the first attempt to fill it rather than as a challenge to established findings.

Evidence from adjacent acute inflammatory diseases points in the same direction as our result. In a prospective community cohort of 6.9 million people in England, the risk of severe outcome rose monotonically above a body mass index of about 23 kg/m^2, with the steepest gradients in younger patients and in those of non-white ethnicity[24] — a threshold that coincides almost exactly with the Asia-Pacific overweight cut-off used here. Metabolic syndrome likewise predicted acute respiratory distress syndrome among hospitalised patients with acute inflammatory illness,[25] and in a nationwide Korean cohort of 4,041 intensive-care patients obesity was associated with a 40% higher incidence of sepsis-associated acute kidney injury (adjusted OR 1.40, 95% CI 1.15–1.70).[26] Adiposity is not metabolically inert in acute critical illness.

It would be misleading, however, to present that literature as uniform, and the most important counter-evidence comes from precisely the discipline whose physiology epidermal necrolysis most resembles. In a United States National Trauma Data Bank analysis of 116,008 burn patients, mortality was *lowest* in the overweight and class-I obese strata (2.9%) and rose in both directions, to 4.1% in the underweight and 5.1% in the morbidly obese;[38] a Cerner database study of 9,405 burn patients found a U-shaped relationship with a nadir at 28.9 kg/m^2;[39] in 490 Chinese burn patients, higher BMI was independently associated with *decreased* in-hospital mortality among those under 65 but not among the elderly;[40] and in a Brazilian burn intensive-care cohort of 288 patients obesity was not associated with higher hospital mortality at all.[41] The same pattern recurs in general critical care, where obesity predicted lower in-hospital mortality among sepsis patients who escaped acute kidney injury,[26] and in a 20-year cohort of 27,026 oldest-old adults in which overweight and obesity predicted reduced all-cause mortality.[27]

Three considerations bear on that tension. The first is the threshold. Every one of those burn and critical-care studies used World Health Organization categories, in which "overweight" begins at 25 kg/m^2 and the reference group therefore includes the entire 23.0–24.9 kg/m^2 band. In the present cohort that band contains 11 of the 17 exposed patients and 4 of the 6 exposed deaths; analysed on WHO thresholds, those 11 patients would have been counted as normal weight, the exposed group would have fallen from 17 to 6, and the association reported here would have been invisible. Asian populations carry more visceral fat and greater cardiometabolic risk at any given BMI, which is why regional consensus retains the lower cut-offs,[28] and a cohort of 4,164 Chinese women showed that the 25 kg/m^2 Asian threshold identified a 57% excess risk that WHO thresholds would have missed.[29] The second consideration is that BMI is a poor proxy for the thing that matters: in 387,672 UK Biobank participants, genetically determined waist-to-hip ratio predicted all-cause mortality more strongly than genetically determined BMI (OR 1.51, 95% CI 1.32–1.72 versus OR 1.29, 95% CI 1.20–1.38),[42] and in 5,888 older adults sarcopenic obesity carried hazard ratios of 1.94 to 2.84 for death while BMI alone did not distinguish those patients.[43] The third is that the burn literature itself is not unanimous about mechanism: in 4,682 burn patients, BMI alone did not predict mortality, but baseline glucose significantly moderated its effect, so that patients with both higher BMI and higher admission glucose died more often.[44] Since hyperglycaemia is itself a SCORTEN component, this offers a testable reconciliation: adiposity may matter chiefly in the metabolically dysregulated, and our cohort may simply contain a higher proportion of such patients than a Western burn registry.

The mechanistic account that ties these observations together is summarised in Figure 5, and it is a hypothesis generated by the present data rather than a pathway tested in them. Two independent inflammatory programmes converge on the keratinocyte. The drug-specific arm proceeds through HLA-restricted activation of CD8$^+$ cytotoxic T lymphocytes and natural killer cells, releasing granulysin, perforin, granzyme B, soluble Fas ligand and TNF-α, with neutrophil extracellular traps now shown to both initiate and amplify the epidermal injury.[10] The adiposity arm proceeds through adipocyte hypertrophy, local hypoxia and M1 macrophage polarisation, raising circulating interleukin-6, TNF-α, monocyte chemoattractant protein-1 and resistin while lowering adiponectin, and driving insulin resistance — a chain that reverses when senescent adipose cells are selectively cleared.[17] TNF-α is common to both arms, which matters clinically because it is the axis on which the most effective disease-modifying therapies act.[12,14] A patient who arrives with a chronically elevated TNF-α tone plausibly requires a different therapeutic threshold from one who does not (Figure 5), and the associated hyperglycaemia and insulin resistance may further impair neutrophil function and re-epithelialisation. The hypothesis is falsifiable: if it is correct, admission interleukin-6, TNF-α or C-reactive protein should mediate the BMI–mortality association;

if it is not, they should not. No cytokine, adipokine or glycaemic measurement was available in this cohort, so the pathway must be regarded as plausible rather than demonstrated.

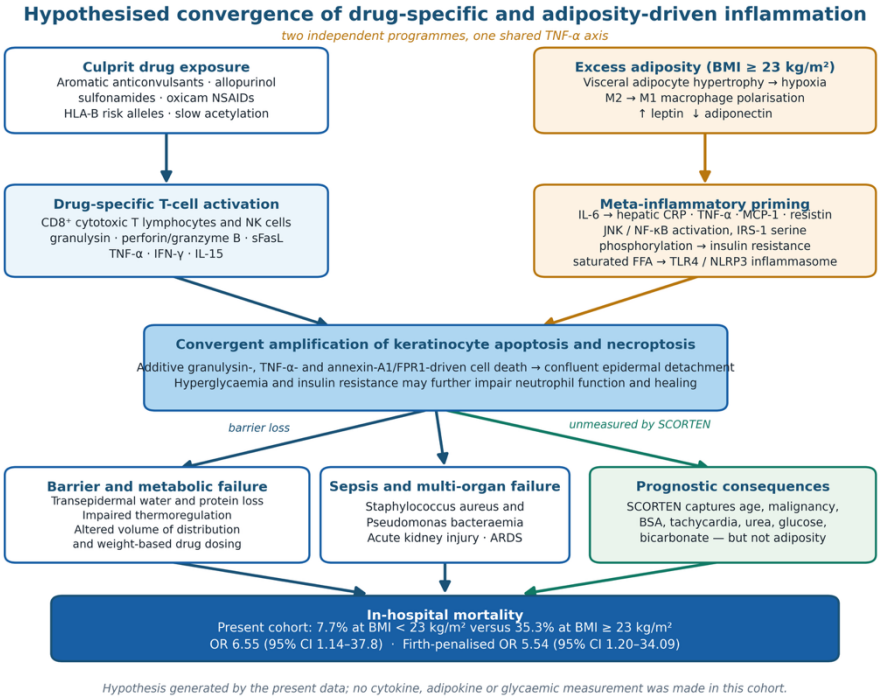

Figure 5. Hypothesised convergence of drug-specific and adiposity-driven inflammation in epidermal necrolysis. This schematic is a hypothesis generated by the present data, not a pathway measured in this cohort: no cytokine, adipokine, histological or glycaemic variable was available. The drug-specific arm proceeds through HLA-restricted CD8+ T-cell and natural killer cell activation with granulysin, perforin/granzyme B, soluble Fas ligand and TNF-α release. The adiposity arm proceeds through adipocyte hypoxia, M1 macrophage polarisation and a rise in IL-6, TNF-α, MCP-1 and resistin with falling adiponectin, insulin resistance and hyperglycaemia. The two converge on keratinocyte apoptosis and necroptosis and on impaired re-epithelialisation, while SCORTEN — which contains no anthropometric or nutritional term — remains blind to the second arm.

For clinical practice at Dr. Moewardi General Hospital and at comparable Indonesian tertiary centres, the implications are modest but concrete. Height and weight are already recorded on admission at no marginal cost, and a BMI of 23 kg/m^2 or above identified a subgroup with 35.3% mortality in this cohort against 7.7% below it. Three practical steps follow. Heavier patients with epidermal necrolysis should not be assumed to be lower risk because their SCORTEN is unremarkable. Weight-based dosing of antimicrobials, fluids and nutritional support should be calculated explicitly rather than estimated, given the altered volume of distribution in a barrier-denuded patient; supportive-care practice for epidermal necrolysis still varies widely between centres even within well-resourced health systems.[23,36] And admission height and weight — together with waist circumference, which costs nothing and is a better proxy for visceral adiposity[42] — should be recorded prospectively and completely, so that the question can eventually be settled by pooling across Indonesian centres.

It is equally important to state what these findings do *not* show. They do not support adding body mass index to SCORTEN: a confidence interval running from 1.14 to 37.75, with a fragility index of one, cannot license modification of a validated prognostic instrument. They do not support triaging patients to intensive or burn-unit care on the basis of BMI alone. They do not support any change to drug selection, corticosteroid policy or immunomodulatory therapy. And they do not establish causation: the E-value of 8.65 says only that a confounder would have to be strong, not that none exists. What they support is prospective measurement, explicit weight-based dosing, and a properly powered multicentre study.

The Indonesian context makes this more than an academic exercise. Across 2.4 million Indonesian adults surveyed between 2007 and 2023, obesity defined by the Asian threshold nearly doubled from 19.7% to 38.3%, reaching 49.9% among urban women, while central adiposity reached 42.0%.[30] The 39.5% of this cohort at or above 23 kg/m^2 is therefore close to the contemporary national prevalence, which argues against substantial over-representation of adiposity among patients with epidermal necrolysis and in favour of interpreting the mortality gradient as an effect on outcome rather than on susceptibility. Meanwhile, national epidemiological data on SJS/TEN in Indonesia remain absent, and every estimate rests on single-centre series from Surakarta, Surabaya and elsewhere.[7,8,9] A national registry, or even a multicentre

Central Java collaboration recording height, weight, SCORTEN components and outcome in a standard format, would resolve in three years what no single centre can resolve at all.

Reconciling the omnibus and directional results

Because the two analytic routes taken through the same 4 × 2 table reach opposite verdicts, the reason deserves to be stated plainly rather than left for readers to infer. The contingency-coefficient test spends three degrees of freedom on a four-level exposure whose levels have a natural order, and it is therefore testing a much broader alternative hypothesis — that mortality differs somehow across BMI categories — than the one of clinical interest, which is that mortality increases with adiposity. Spending degrees of freedom on alternatives nobody believes is expensive when events are few. Under the mortality gradient actually observed in this cohort, 6,000 simulated replicates at n = 43 give the omnibus test 36.9% power against 45.4% for the Cochran–Armitage trend test and 51.1% for the exact test on the Asia-Pacific dichotomy. A fourteen-percentage-point power penalty is more than enough to convert a real gradient into a non-significant omnibus p value at these counts, and that is the most economical explanation of the discrepancy.

This is not a post-hoc rescue of an inconvenient null. The ordering of BMI categories is a property of the exposure, fixed before any data are seen; the Asia-Pacific threshold of 23 kg/m^2 is the published clinical cut-off and was not selected by scanning alternatives; and the direction of the hypothesis — that more adiposity is worse, not better — follows from the inflammatory biology set out in the Introduction. Had the analysis dichotomised at an optimised cut-point, or tested both tails, or reported only the most favourable of several thresholds, the criticism would be fair. None of those was done, and the trend test uses no threshold at all. What the reader should take from the discrepancy is not that one p value is right and the other wrong, but that a cohort of this size cannot distinguish a moderate gradient from noise unless the analysis uses every structural constraint the data contain.

What would settle the question

The precision calculations reported here translate directly into a design. To detect an odds ratio of 3 for mortality above the Asia-Pacific overweight threshold, against a baseline risk of 7.7% and with 80% power at $\alpha = 0.05$, approximately 120 patients per exposure group would be required — roughly 300 patients in total at the exposure prevalence of 39.5% observed here. At the accrual rate of this centre, about 14 eligible patients per year, that is beyond any single Indonesian institution and squarely within reach of a multicentre collaboration. To detect a correlation of $\rho = 0.30$ between BMI and SCORTEN would require 85 patients, and $\rho = 0.20$ would require 194.

Such a study should record admission height and weight before fluid resuscitation, waist circumference where feasible, all seven SCORTEN components as raw values rather than as a derived total, culprit drug class and latency, diabetes and glycaemic status, all disease-modifying therapy, re-epithelialisation time, and survival to at least 90 days rather than to discharge alone. Analytically it should treat BMI as a continuous exposure with flexible functional form rather than in categories, adjust for SCORTEN as a continuous covariate, and treat death as a competing risk when modelling length of stay and re-epithelialisation — the last of which, as the simulation reported here shows, is essential if apparent benefits of adiposity are not to be manufactured by differential mortality.[27] A collaboration of five Indonesian tertiary centres could complete such a cohort in four years.

Strengths and limitations

This study has four principal strengths. It uses total sampling of a defined admission register over a fixed three-year window at a provincial referral centre, so the analysed cohort is the complete eligible population rather than a convenience sample, and selection into the study is not a plausible source of bias. Its analytic strategy was matched to the structure of the data rather than to convention: an ordered exposure was tested with ordered methods, sparse cells were handled with exact enumeration and penalised likelihood rather than with asymptotic approximations known to be biased at these counts,[33] and every reconstruction-dependent quantity is reported as an interval over the complete admissible set. Every null result is accompanied by its achieved power, its minimum detectable effect, an equivalence analysis and a Bayes factor, so that readers can distinguish an absence of effect from an absence of information. And the cohort is externally calibrated: its standardised mortality ratio against SCORTEN-predicted death was 1.16 (95% CI 0.50–2.28) and its crude mortality did not differ from the 17.9% pooled across six comparator cohorts ($p = 0.843$), so it is a typical rather than an idiosyncratic series.

The limitations are substantial and constrain the conclusions accordingly. First and most importantly, the cohort contains 43 patients and 8 deaths, so every estimate is imprecise: the odds ratio for mortality above the overweight threshold has a 95% interval spanning 1.14 to 37.75, the exact conditional interval crosses unity (0.93–72.82), the exact permutation trend p is 0.056 rather than 0.040, and both the fragility and reverse-fragility indices are 1. This is a signal worth pursuing, not an established effect, and it should not change practice on its own. Second, the design is retrospective and record-based, so residual confounding cannot be excluded; the specific unmeasured variables that concern us most are diabetes mellitus, which is both commoner at higher BMI and an established non-SCORTEN predictor of death (pooled OR 1.87, 95% CI 1.21–2.89),[1] culprit drug class — allopurinol carries a worse prognosis and is prescribed preferentially to patients with metabolic

syndrome — latency from drug exposure to presentation, referral status, bacteraemia, and the specific therapy received. The E-value of 8.65 indicates that such a confounder would have to be strong, but strong confounders exist. Third, BMI is a crude proxy for adiposity that cannot distinguish fat from lean mass and misclassifies sarcopenic obesity in both directions;[43] it was measured once at admission when fluid status is already abnormal, so an elevated value may partly reflect oedema, which is itself a marker of severity and would generate the observed association through a non-adipose pathway. Fourth, the outcome is in-hospital mortality only; re-epithelialisation time, bacteraemia, intensive-care utilisation, ocular sequelae and post-discharge survival were not captured, even though long-term morbidity in survivors is considerable.[45] Fifth, the underweight stratum contains 3 patients and no deaths, which is entirely uninformative about the lower limb of the J-shaped or U-shaped relationships reported in the burn literature;[38,39] this study can say nothing about whether undernutrition is also hazardous in epidermal necrolysis. Sixth, three printed SCORTEN stratum means in the source records are arithmetically unattainable for integer scores and the stratified totals differ by at least two points, which is why every SCORTEN-dependent result is reported as an interval; the discrimination of SCORTEN itself and any multivariable model treating its components separately are not identified by the available data and have deliberately not been estimated. Finally, the penalised likelihood-ratio statistic is only approximately chi-squared in samples this small, and the bracketing interval reported for the SCORTEN-adjusted odds ratio is a range of point estimates obtained under two extremal assignment schemes rather than a sharp identified set.

5. Conclusion

In this three-year total-sampling cohort of 43 adults with Stevens–Johnson syndrome and toxic epidermal necrolysis at Dr. Moewardi General Hospital, Surakarta, body mass index was not associated with SCORTEN (Spearman $\rho = 0.163$; 95% CI −0.14 to 0.44; $p = 0.296$), and this null was uninformative rather than negative, with an achieved power of 18.0% and a minimum detectable $|\rho|$ of 0.42. Body mass index was, however, associated with in-hospital mortality, which rose across Asia-Pacific BMI strata, with a significant upward trend (Cochran–Armitage $z = 2.053$; $p = 0.040$) and reached 35.3% at or above the overweight threshold against 7.7% below it (odds ratio 6.55; 95% CI 1.14–37.75; Firth-penalised odds ratio 5.54, 95% CI 1.20–34.09; number needed to harm 3.6; E-value 8.65). Because SCORTEN contains no anthropometric term, excess adiposity appears to carry prognostic information through a channel the score does not capture. Clinicians should not treat a reassuring SCORTEN in a heavier patient as reassurance about outcome, and should calculate weight-based fluid, antimicrobial and nutritional targets explicitly. The estimate is imprecise and requires confirmation: a multicentre Indonesian cohort of approximately 300 patients, recording body composition alongside all seven SCORTEN components and following patients to 90 days with death handled as a competing risk, would settle the question within four years.

Declarations

Ethical approval and consent

Ethical approval for this study was obtained from the Health Research Ethics Committee of Dr. Moewardi Regional General Hospital (No. 1.333/VII/HREC/2026). The requirement for individual written informed consent was waived by the same committee because the study used de-identified data abstracted retrospectively from existing medical records, with no patient contact and no intervention. The study was conducted in accordance with the principles of the Declaration of Helsinki and its subsequent amendments.

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Conflict of interest

The authors declare that they have no competing interests.

Data availability

The aggregated data supporting the findings of this study are contained within the article. The de-identified record-level dataset and the complete analysis code, including the enumeration routines used for the set-valued reconstruction and the Firth penalised-likelihood implementation, are available from the corresponding author on reasonable request and subject to institutional data-governance approval.

Author contributions

ND: conceptualisation, methodology, supervision, clinical data interpretation, writing — review and editing. AY: data curation, investigation, formal analysis, writing — original draft. Both authors have read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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Generative AI disclosure

The authors declare that no generative artificial intelligence tools were used in the design, analysis, or writing of this manuscript.

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