Table 1. Definitions of the level of evidence. (Adapted from Sauaia et al. J Trauma Acute Care Surg. 2012; 72(6): 1484-1490).

	Clinical study	Prognostic and epidemiological study	Diagnostic test or criterion	Systematic review & meta-analysis
Level I	Randomized controlled trial with no negative criteria*	Prospective† study with large effect‡ and no negative criteria*	Testing of previously developed diagnostic criteria in consecutive patients (all compared to "gold" standard) and no negative criteria*	Systematic Review or meta-analysis of predominantly **level I** studies and no negative criteria§ for the systematic review/meta-analysis
Level II	• Randomized controlled trial with significant difference and only one negative criterion* • Prospective† comparative study without negative criteria* • Prospective/retrospective† study with large effect‡ and only one negative criterion*	• Prospective† study with less than large effect‡ and no negative criteria* • Untreated controls from randomized controlled trial	Development of diagnostic criteria on consecutive patients (all compared to "gold" standard) and only one negative criterion*	Systematic review/meta-analysis or predominantly **level II** studies and no negative criteria§ for the systematic review/meta-analysis
Level III	• Case-control study without negative criteria* • Prospective† comparative study with only one negative criterion* • Retrospective† comparative study without negative criteria*	• Case-control study without negative criteria* • Prospective/retrospective† study with up to two negative criteria*	Non-consecutive patients (without consistently applied "gold" standard) with up to two negative criteria*	Systematic review/meta-analysis with up to two negative criteria§
Level IV	Prospective/retrospective† study using historical controls or having more than one negative criterion*	Prospective/retrospective† study with up to three negative criteria*	Case-control study with no negative criteria* or other designs with up to three negative criteria	Systematic review/meta-analysis with more than two negative criteria§
Level V	• Case series • Studies with quality worse than level IV	• Case series • Studies with quality worse than level IV	No or poor "gold" standard	

* Negative criteria decreasing level of evidence include: (1) <80% follow up; (2) >20% missing data or missing data not at random without proper use of missing data statistical techniques; (3) limited control of confounding (e.g., mortality comparisons with inadequate risk adjustment); (4) more than minimal bias (selection bias, publication bias, report bias, etc.); (5) heterogeneous populations (e.g., instructions with distinct protocols/patient volume, conditions caused by distinct pathogenic mechanisms); and (6) for RCT only, no blinding or improper randomization; (7) inadequate statistical power: this only applies to studies NOT finding statistical differences and it is defined as power <80% for declaring "failure to detect a significant difference" or power <90% for declaring "bio-equivalence or non-inferiority or comparative effectiveness" or Receiver Operating Characteristic curve <80% or both sensitivity and specificity <80%.

† Prospective versus retrospective: studies with data collected to answer predefined questions are prospective; studies with data collected for questions unrelated to the original question for which the data were gathered are retrospective.

‡ Large effect is defined as: (1) study with large RR (>5 or <0.2), about condition of low-to-moderate morbidity/mortality and (2) study with moderate-to-large RR (2-5 or 0.2-0.5) about condition of high morbidity/mortality.

§ Negative criteria for SR/MS (decreases level of evidence): (1) no or inadequate standard search protocol, (2) more than minor chance of publication bias or publication bias not assessed, (3) moderate heterogeneity of included studies and/or populations (e.g., elective operation and acute operation), (4) predominance of level III or lower studies, and (5) no measures or inappropriate measures of pooled risk (for meta-analysis only).