Supplementary Material for the 2024 Clinical Practice Guideline Update by the

Infectious Diseases Society of America on Complicated Intra-abdominal Infections: Risk

Assessment in Adults and Children

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METHODS

Panel formation and conflicts of interest

The chair of the guideline panel was selected by the leadership of IDSA. Fifteen additional panelists comprised the full panel. The panel included clinicians with expertise in infectious diseases, pediatric infectious diseases, surgery, emergency medicine, microbiology, and pharmacology. Panelists were diverse in gender, geographic distribution, and years of clinical experience. Guideline methodologists oversaw all methodological aspects of the guideline development and identified and summarized the scientific evidence for each clinical question. IDSA staff oversaw all administrative and logistic issues related to the guideline panel.

All members of the expert panel complied with the IDSA policy on conflict of interest (COI), which requires disclosure of any financial, intellectual, or other interest that might be construed as constituting an actual, potential, or apparent conflict. Evaluation of such relationships as potential conflicts of

interest was determined by a review process which included assessment by the Standards and Practice Guideline Committee (SPGC) Chair, the SPGC liaison to the Guideline panel and the Board of Directors liaison to the SPGC, and if necessary, the Conflicts of Interests Task Force of the Board. This assessment of disclosed relationships for possible COI was based on the relative weight of the financial relationship (i.e., monetary amount) and the relevance of the relationship (i.e., the degree to which an independent observer might reasonably interpret an association as related to the topic or recommendation of consideration). The reader of these guidelines should be mindful of this when the list of disclosures is reviewed. See the Notes section at the end of this guideline for the disclosures reported to IDSA.

Practice recommendations

Clinical Practice Guidelines are statements that include recommendations intended to optimize patient care by assisting practitioners and patients in making shared decisions about appropriate health care for specific clinical circumstances. These are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options [IOM 2011]. The "IDSA Handbook on Clinical Practice Guideline Development" provides more detailed information on the processes followed throughout the development of this guideline [IDSA CPG Handbook].

Review and approval process

Feedback was obtained from five external individual peer expert reviewers as well as the endorsing organizations. The IDSA Standards and Practice Guidelines Subcommittee (SPGS) and Board of Directors reviewed and approved the guideline prior to publication.

Process for updating

IDSA guidelines are regularly reviewed for currency. The need for updates to the guideline is determined by a scan of current literature and the likelihood that any new data would impact the recommendations. Any changes to the guideline will be submitted for review and approval to the appropriate Committees and Board of IDSA.

Clinical questions

Each clinical question was formatted according to the PICO style: Patient/Population (P), Intervention/Indicator (I), Comparator/Control (C), Outcome (O). For each PICO question, outcomes of interest were identified a priori and rated for their relative importance for decision-making.

Literature search

A medical librarian designed the literature searches and MeSH terms for Ovid Medline, Embase, and Cochrane Library. Searches were limited to studies published in English. The initial formal literature searches were performed in July to November 2018, and updated literature searches were conducted in March 2021 and October 2022. To supplement the electronic searches, reference lists of related articles and guidelines were reviewed for relevance.

MEDLINE

#1 exp *Intraabdominal Infections/

#2 ((intraabdom?n* or abdom?n* or appendix or appendectom* or appendic* or peritonitis* or typhlitis* or diverticul* or subdiaphragmat* or subphren* or sub-diaphragmat* or sub-phren* or peritoneal* or pericolon* or peri-colon* or periappendic* or phlegmon*) adj2 (complicat* or infect* or candidias* or bacteremia* or abscess* or abcess* or sepsis or septic or shock*)).ti,kf.

```
#3 ((intraabdom?n* or abdom?n* or appendix or appendectom* or appendic* or peritonitis* or
typhlitis* or diverticul* or subdiaphragmat* or subphren* or sub-diaphragmat* or sub-phren*
or peritoneal* or pericolon* or peri-colon* or periappendic* or phlegmon*) adj2 (complicat* or
infect* or candidias* or bacteremia* or abscess* or abcess* or sepsis or septic or shock*)).ab.
/freq=2
#4 or/1-3
#5 exp *mortality/
#6 (survival* or mortalit* or death*).ti,kf.
#7 (survival* or mortalit* or death*).ab. /freq=4
#8 (mortalit* adj5 (risk* or predictor* or complic* or rate* or prognos*)).ab. /freq=2
#9 (((surgic* adj2 infection*) or SSI) and (risk* or survival* or mortalit* or death*)).ab. /freq=2
#10 (risk* adj1 (factor* or assessment* or stratific* or ratio?)).tw,kf.
#11 or/5-10
#12 4 and 11
#13 exp *Intraabdominal Infections/mo
#14 Intraabdominal Infections/mo
#15 ((intraabdom?n* or abdom?n*) adj2 (complic* or infect* or abscess* or abcess*) adj3
(mortalit* or death*)).tw,kf.
#16 exp *Cholecystitis/mo
#17 ((cholecystit* or ((gallbladder* or gall-bladder*) adj1 (infection* or empyema*))) adj5
(mortalit* or death*)).tw,kf.
#18 exp *Cholangitis/mo
#19 (cholangit* adj5 (mortalit* or death*)).tw,kf.
#20 *Pancreatitis, Acute Necrotizing/mo
#21 (pancreatit* adj1 necrotiz* adj5 (mortalit* or death*)).tw,kf.
#22 *Peptic Ulcer Perforation/mo
#23 ((peptic or stomach* or gastric* or jejun* or duoden* or bowel* or gastrointestin* or
intestin* or luminal* or lumen*) adj1 ulcer* adj2 perforat* adj5 (mortalit* or death*)).tw,kf.
#24 *Intestinal Perforation/mo
#25 (intestin* adj2 perforat* adj5 (mortalit* or death*)).tw,kf.
#26 or/13-25
#27 "severity of illness index"/
#28 *APACHE/
#29 *Injury Severity Score/
#30 *sickness impact profile/
#31 (AGS or PATI or WSES or SOFA or ASA or MPI or MODS or SAPS-II or PRISM or ISS or Hinchey
or ((injur* or sepsis*) adj1 severit* adj1 (score* or index*)) or (((((appendicit* or cholangit*)
adj2 grading) or (abdom?n* adj1 trauma*)) adj1 (system* or score* or index*)) or ((Apache adj2
```

(II or III)) or (Charlson adj1 comorbid* adj1 index*)))).ti,kf.

#32 (AGS or PATI or WSES or SOFA or ASA or MPI or MODS or SAPS-II or PRISM or ISS or Hinchey or ((injur* or sepsis*) adj1 severit* adj1 (score* or index*)) or (((((appendicit* or cholangit*) adj2 grading) or (abdom?n* adj1 trauma*)) adj1 (system* or score* or index*)) or ((Apache adj2 (II or III)) or (Charlson adj1 comorbid* adj1 index*)))).ab. /freq=3

#33 or/27-32

#34 4 and 33

#35 34 and ((risk* or survival* or mortalit* or death*).hw,tw,kf. or mo.fs.)

#36 12 or 26 or 35

#37 Animals/ not (Animals/ and Humans/)

#38 ((animal or animals or canine* or cat or cats or dog or dogs or feline or hamster* or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep*) not (human* or patient*)).ti,kf.

#39 36 not (37 or 38)

#40 limit 39 to (comment or editorial or letter or case reports or congress or clinical conference or consensus development conference or consensus development conference, nih)

#41 39 not 40

#42 limit 41 to english

#43 42 and (prognosis/ or Observational Study/ or exp Cohort Studies/ or case-control studies/ or multicenter study/ or cross-sectional study/ or odds ratio/)

#44 42 and (observational or prospectiv* or retrospectiv* or longitudinal* or follow-up stud* or cohort* or case control* or prognosis).tw,kf.

#45 43 or 44

#46 remove duplicates from 45

#47 limit 46 to yr="2010 -Current"

EMBASE

#1 exp *abdominal infection/

#2 ((intraabdom?n* or abdom?n* or appendix or appendectom* or appendic* or peritonitis* or typhlitis* or diverticul* or subdiaphragmat* or subphren* or sub-diaphragmat* or sub-phren* or peritoneal* or pericolon* or peri-colon* or periappendic* or phlegmon*) adj2 (complicat* or infect* or candidias* or bacteremia* or abscess* or abcess* or sepsis or septic or shock*)).ti,kw,kf.

#3 ((intraabdom?n* or abdom?n* or appendix or appendectom* or appendic* or peritonitis* or typhlitis* or diverticul* or subdiaphragmat* or subphren* or sub-diaphragmat* or sub-phren* or peritoneal* or pericolon* or peri-colon* or periappendic* or phlegmon*) adj2 (complicat* or infect* or candidias* or bacteremia* or abscess* or abcess* or sepsis or septic or shock*)).ab. /freq=2

#4 *acute cholecystitis/

#5 exp *cholangitis/co, su

#6 *acute hemorrhagic pancreatitis/co, su

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#7 *ulcer perforation/co, su
#8 exp *intestine perforation/
#9 or/1-8
#10 exp *mortality/
#11 mortality risk/
#12 (survival* or mortalit* or death*).ti,kw,kf.
#13 (survival* or mortalit* or death*).ab. /freq=4
#14 (mortalit* adj5 (risk* or predictor* or complic* or rate* or prognos*)).ab. /freq=2
#15 (((surgic* adj2 infection*) or SSI) and (risk* or survival* or mortalit* or death*)).ab. /freq=2
#16 (risk* adj1 (factor* or assessment* or stratific* or ratio?)).tw,kw,kf.
#17 or/10-16
#18 9 and 17
#19 ((intraabdom?n* or abdom?n*) adj2 (complic* or infect* or abscess* or abcess*) adj3
(mortalit* or death*)).tw,kw,kf.
#20 ((cholecystit* or ((gallbladder* or gall-bladder*) adj1 (infection* or empyema*))) adj5
(mortalit* or death*)).tw,kw,kf.
#21 (cholangit* adj5 (mortalit* or death*)).tw,kw,kf.
#22 (pancreatit* adj1 necrotiz* adj5 (mortalit* or death*)).tw,kw,kf.
#23 ((peptic or stomach* or gastric* or jejun* or duoden* or bowel* or gastrointestin* or
intestin* or luminal* or lumen*) adj1 ulcer* adj2 perforat* adj5 (mortalit* or death*)).tw,kw,kf.
#24 (intestin* adj2 perforat* adj5 (mortalit* or death*)).tw,kw,kf.
#25 or/19-24
#26 *"severity of illness index"/
#27 *apache/
#28 exp *injury scale/
#29 *sickness impact profile/
#30 (AGS or PATI or WSES or SOFA or ASA or MPI or MODS or SAPS-II or PRISM or ISS or Hinchey
or ((injur* or sepsis*) adj1 severit* adj1 (score* or index*)) or (((((appendicit* or cholangit*)
adj2 grading) or (abdom?n* adj1 trauma*)) adj1 (system* or score* or index*)) or ((Apache adj2
(II or III)) or (Charlson adj1 comorbid* adj1 index*)))).ti,kw,kf.
#31 (AGS or PATI or WSES or SOFA or ASA or MPI or MODS or SAPS-II or PRISM or ISS or Hinchey
or ((injur* or sepsis*) adj1 severit* adj1 (score* or index*)) or (((((appendicit* or cholangit*)
adj2 grading) or (abdom?n* adj1 trauma*)) adj1 (system* or score* or index*)) or ((Apache adj2
(II or III)) or (Charlson adj1 comorbid* adj1 index*)))).ab. /freq=3
#32 or/26-31
#33 9 and 32
#34 33 and (risk* or survival* or mortalit* or death*).hw,tw,kw,kf.
#35 18 or 25 or 34
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#36 (exp animal/ or exp juvenile animal/ or adult animal/ or animal cell/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not human/

#37 ((animal or animals or canine* or cat or cats or dog or dogs or feline or hamster* or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep*) not (human* or patient*)).ti,kw,kf.

#38 35 not (36 or 37)

#39 limit 38 to (books or "book review" or chapter or conference abstract or conference paper or "conference review" or editorial or letter or note)

#40 38 not 39

#41 limit 40 to english

#42 limit 41 to "prognosis (best balance of sensitivity and specificity)"

#43 41 and (prognosis/ or cohort analysis/ or case-control study/ or multicenter study/ or cross-sectional study/)

#44 41 and (observational or prospectiv* or retrospectiv* or longitudinal* or follow-up stud* or cohort* or case control* or prognosis).tw,kw,kf.

#45 42 or 43 or 44

#46 remove duplicates from 45

#47 limit 46 to yr="2010 -Current"

COCHRANE

#1 ((intraabdom?n* or abdom?n* or appendix or appendectom* or appendic* or peritonitis* or typhlitis* or diverticul* or subdiaphragmat* or subphren* or sub-diaphragmat* or sub-phren* or peritoneal* or pericolon* or peri-colon* or periappendic* or phlegmon*) NEAR/2 (complicat* or infect* or candidias* or bacteremia* or abscess* or abcess* or sepsis or septic or shock*)):ti,ab,kw

#2 (survival* or mortalit* or death*):ti,ab,kw

#3 (((surgic* NEAR/2 infection*) or SSI) and (risk* or survival* or mortalit* or death*)):ti,ab,kw

#4 (risk* NEAR/1 (factor* or assessment* or stratific* or ratio?)):ti,ab,kw

#5 #2 OR #3 OR #4

#6 #1 AND #5

#7 ((intraabdom?n* or abdom?n*) NEAR/2 (complic* or infect* or abscess* or abcess*) NEAR/3 (mortalit* or death*)):ti,ab,kw

#8 ((cholecystit* or ((gallbladder* or gall-bladder*) NEAR/1 (infection* or empyema*))) NEAR/5 (mortalit* or death*)):ti,ab,kw

#9 (cholangit* NEAR/5 (mortalit* or death*)):ti,ab,kw

#10 (pancreatit* NEAR/1 necrotiz* NEAR/5 (mortalit* or death*)):ti,ab,kw

#11 ((peptic or stomach* or gastric* or jejun* or duoden* or bowel* or gastrointestin* or intestin* or luminal* or lumen*) NEAR/1 ulcer* NEAR/2 perforat* NEAR/5 (mortalit* or death*)):ti,ab,kw

#12 (intestin* NEAR/2 perforat* NEAR/5 (mortalit* or death*)):ti,ab,kw

#13 #7 OR #8 OR #9 OR #10 OR #11 OR #12

#14 (AGS or PATI or WSES or SOFA or ASA or MPI or MODS or SAPS-II or PRISM or ISS or Hinchey or ((injur* or sepsis*) near/1 severit* near/1 (score* or index*)) or (((((appendicit* or cholangit*) near/2 grading) or (abdom?n* near/1 trauma*)) near/1 (system* or score* or index*)) or ((Apache near/2 (II or III)) or (Charlson near/1 comorbid* near/1 index*)))):ti,ab,kw

#15 #14 and (risk* or survival* or mortalit* or death*):ti,ab,kw

#16 #1 AND #15

#17 #6 OR #13 OR #16

#18 #17 in Cochrane Reviews, Cochrane Protocols, Clinical Answers, Special collections #19 #17 in Cochrane Reviews, Cochrane Protocols, Clinical Answers, Special collections with Cochrane Library publication date from Jan 2010 to Oct 2022

#20 #17 in Cochrane Reviews, Cochrane Protocols, Clinical Answers, Special collections

Study selection

Titles and abstracts were screened in duplicate for all identified citations using Rayyan [Ouzzani 2016]. All potentially relevant citations were subjected to a full-text review, using predefined inclusion and exclusion criteria tailored to meet the specific population, intervention, and comparator of each clinical question. The steps of the literature selection process were supervised and reviewed by a guideline methodologist for the final selection of the relevant articles.

The following eligibility criteria were used:

Inclusion criteria:

- Patient population- Adults and children with complicated intra-abdominal infection (cIAI; infection extended beyond visceral organ)
- Intervention- Scoring tool
- Outcomes- Mortality (prediction of)
- Study design- Observational studies reporting on mortality (30±2-day or in-hospital), includes at least 100 patients in study, all risk factors must be available within 24 hours of hospital or ICU admission

Exclusion criteria:

- Patient population- Patients with peritoneal dialysis-related peritonitis, cirrhosis-associated spontaneous peritonitis
- Outcomes- Mortality related to surgical approach to source control
- Study design- Systematic reviews (only primary studies are included), studies reporting
 univariate analyses only, abstracts and conference proceedings, letters to the editor, editorials,
 and review articles

Data extraction and analysis

A guideline methodologist in conjunction with panelists extracted the data for each pre-determined patient-important outcome. If a relevant publication was missing raw data for an outcome prioritized by the panel, an attempt was made to contact the author(s) for the missing data. Where applicable, data were pooled using random-effects model (fixed effects model for pooling of rates) using RevMan [RevMan].

Evidence to decision

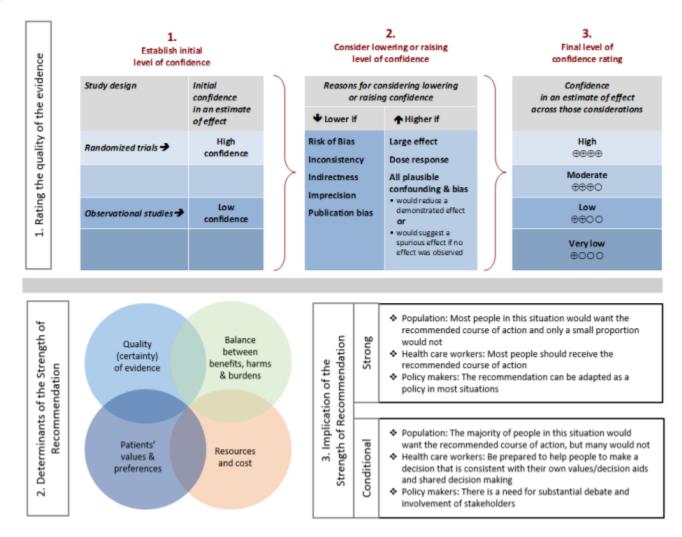
Guideline methodologists prepared the evidence summaries for each question and assessed the risk of bias and the certainty of evidence. Risk of bias was assessed by using the QUIPS tool for studies addressing risk/prognostic factors [Hayden 2013] and the QUADAS-2 tool for diagnostic test accuracy studies [Whiting 2011]. The certainty of evidence was determined first for each critical and important outcome and then for each recommendation using the GRADE approach for rating the confidence in the evidence [Guyatt 2008, GRADE Handbook]. Evidence profiles were developed using the GRADEpro Guideline Development Tool [Guyatt 2008] and reviewed by panel members responsible for each PICO.

The Evidence to Decision framework [GRADEpro] was used to translate the evidence summaries into practice recommendations. All recommendations were labeled as either "strong" or "conditional" according to the GRADE approach [IDSA CPG Handbook]. The words "we recommend" indicate strong recommendations and "we suggest" indicate conditional recommendations. Supplementary Figure 1 provides the suggested interpretation of strong and conditional recommendations for patients, clinicians, and healthcare policymakers. For recommendations where the comparator treatment or tests are not formally stated, the comparison of interest is implicitly referred to as "not using the intervention" (either not using a specific treatment or a diagnostic test).

All members of the panel participated in the preparation of the draft guideline and approved the recommendations.

TABLES AND FIGURES

Supplementary Figure 1. Approach and implications to rating the quality of evidence and strength of recommendations using GRADE methodology (unrestricted use of figure granted by the U.S. GRADE Network)



Supplementary Table 3. GRADE Evidence Profile: Which severity of illness score for risk stratification calculated within 24 hours of hospital or ICU admission best predicts 30-day or in-hospital mortality?

Outcome	No. of	2 "			Certainty	Assessment				Effect		
(risk factor)	Studies	Studies	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Effect measure	Adjusted effect estimate	95% CI	Certainty
APACHE II (OR, Per Point)	6	Karvellas 2019, Lichtenst ern 2015, Pan 2021, Politano 2011, Tartaglia 2015, Tellor 2015	observational study	serious a	serious ^b	not serious	not serious	Publication bias suspected	OR	1.07	1.00- 1.15	⊕○○○ VERY LOW
APACHE II (HR, Per Point)	1	Ozdogan 2015	observational study	not serious	not serious	not serious	not serious	Publication bias suspected	HR	1.16	1.07- 1.26	⊕⊕⊕⊖ MODERATE
APACHE II (OR, Cutoff)	4	Guilbart 2016, Li 2017, Morais 2018, Wu 2016	observational study	serious ^a	not serious	not serious	serious °	Publication bias suspected	OR	Not pooled	N/A	ФФОО LOW
APACHE II (RR, Cutoff)	1	Buck 2012	observational study	not serious	not serious	not serious	serious ^c	Publication bias suspected	RR	31.60	1.80- 554.8 3	⊕⊕⊖⊖ Low
SAPS II (OR, Per Point)	3	De Waele 2014, Dupont 2011,	observational study	not serious	not serious	not serious	not serious	Publication bias suspected	OR	1.06	1.03- 1.08	⊕⊕⊕⊖ MODERATE

		Maseda 2019										
SAPS II (OR, Cutoff)	2	Alqarni 2018, Suarez de la Rica 2015	observational study	not serious	not serious	not serious	not serious	Publication bias suspected	OR	5.00	2.89- 8.65	⊕⊕⊕⊖ MODERATE
SOFA (OR, Per Point)	4	Augustin 2020, Dupont 2011, Pupelis 2014, Sim 2020	observational study	not serious	not serious	not serious	not serious	Publication bias suspected	OR	1.30	1.21- 1.41	⊕⊕⊕○ MODERATE
SOFA (HR, Per Point)	2	Luo 2022, Montrave rs 2016	observational study	not serious	not serious	not serious	not serious	Publication bias suspected	HR	1.29	1.20- 1.39	⊕⊕⊕⊖ MODERATE
SOFA (OR, Cutoff)	3	Nugraha 2022, Suarez de la Rica 2015, Wu 2016	observational study	not serious	not serious	not serious	not serious	Publication bias suspected	OR	Not pooled	N/A	⊕⊕⊕○ MODERATE
SOFA (HR, Cutoff)	1	Roger 2022	observational study	not serious	not serious	not serious	serious °	Publication bias suspected	HR	6.14	1.40- 26.93	\bigoplus_{LOW}
ASA (OR, Per Point)	3	Moller 2012, Pupelis 2014, Sim 2020	observational study	not serious	not serious	not serious	serious ^d	Publication bias suspected	OR	1.76	0.92- 3.40	⊕⊕⊖ Low
ASA (OR, Cutoff)	3	Bensigno r 2018, Faes 2021,	observational study	not serious	not serious	not serious	not serious	Publication bias suspected	OR	Not pooled	N/A	⊕⊕⊕○ MODERATE

		Tartaglia 2021										
ASA (RR, Cutoff)	1	Buck 2012	observational study	not serious	not serious	not serious	not serious	Publication bias suspected	RR	21.5	3.10- 149.1 2	⊕⊕⊕○ MODERATE
WSES (OR, Per Point)	2	Abdel- Kader 2019, Sartelli 2015	observational study	serious a	not serious	not serious	not serious	Publication bias suspected	OR	1.78	1.73- 1.84	ФФОО

- a. According to QUIPS
- b. Inconsistent results (95% CIs on opposite sides of the null and not overlapping)
- c. Imprecise results (wide 95% CIs)
- d. Imprecise results (95% CI of the pooled point estimate crosses the null)

Forest Plots. Severity of illness scoring system [obtained or calculated] within 24 hours of hospital or ICU admission, 30-day or in-hospital mortality from studies with multivariate analysis

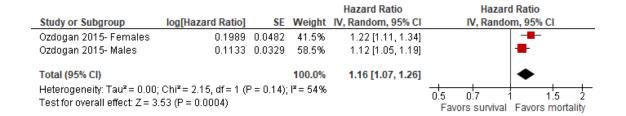
Supplementary Figure 2. APACHE II as a Predictor of Mortality

a) OR, Per Point

				Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Karvellas 2019	0.1222	0.0326	16.9%	1.13 [1.06, 1.20]	
Lichtenstern 2015	0.003	0.0118	19.4%	1.00 [0.98, 1.03]	+
Pan 2021	0.1906	0.0304	17.2%	1.21 [1.14, 1.28]	_ -
Politano 2011	0.0421	0.0194	18.7%	1.04 [1.00, 1.08]	
Tartaglia 2021	0.1655	0.0596	12.5%	1.18 [1.05, 1.33]	_
Tellor 2015*	-0.0726	0.0421	15.3%	0.93 [0.86, 1.01]	
Total (95% CI)			100.0%	1.07 [1.00, 1.15]	•
Heterogeneity: Tau² : Test for overall effect	•		P < 0.000	01); I² = 90%	0.85 1 1.1 1.2 Favors survival Favors mortality

^{*}Tellor 2015 used a modified APACHE II score that didn't include Glasgow coma scale.

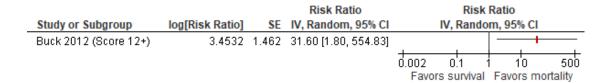
b) HR, Per Point



c) OR Cutoff

			Odds Ratio	Odds	Ratio
Study or Subgroup	log[Odds Ratio]	SE	IV, Random, 95% CI	IV, Rando	m, 95% CI
Guilbart 2016 (Score 8+)	2.5096	0.6269	12.30 [3.60, 42.03]		
Wu 2016 (Score 12+)	0.7481	0.4873	2.11 [0.81, 5.49]	•	 -
Morais 2018 (Score 19+)	1.0494	0.5	2.86 [1.07, 7.61]		
Li 2017 (Score 21+)	2.2513	1.1	9.50 [1.10, 82.04]		
				0.01 0.1	10 100
				Favors survival	Favors mortality

d) RR, Cutoff



Other

Though an OR was not reported by the authors, APACHE II was identified as an independent predictor of mortality in a retrospective study of 544 patients as determined by LASSO multivariate regression analysis of 37 variables [Huang 2021].

e) AUCs

				AUC	AUC		
Study or Subgroup	log[AUC]	SE	Weight	IV, Random, 95% CI	IV, Random, 9	5% CI	
Buck 2012	-0.2744	0.0347	16.0%	0.76 [0.71, 0.81]			
Huang 2021 (study cohort)	-0.1625	0.0183	17.5%	0.85 [0.82, 0.88]	-		
Huang 2021 (validation cohort)	-0.1985	0.019	17.5%	0.82 [0.79, 0.85]	-		
Ozdogan 2015	-0.0619	0.0222	17.2%	0.94 [0.90, 0.98]			
Pan 2021	-0.2107	0.0461	14.6%	0.81 [0.74, 0.89]			
Posadas-Calleja 2018	-0.3285	0.0217	17.2%	0.72 [0.69, 0.75]	-		
Total (95% CI)			100.0%	0.81 [0.75, 0.88]	•		
Heterogeneity: Tau² = 0.01; Chi²:	= 82.33, df = 5 (P <	0.00001);	6	 	- 1 ₅	
Test for overall effect: Z = 5.15 (P					0.5 0.7 1 Discrimination (0-1) N/A	1.5	2

One additional study [Lebedev 2021] reported an AUC of 0.84 for APACHE II but 95% CI was not provided.

Supplementary Figure 3. SAPS II as a Predictor of Mortality

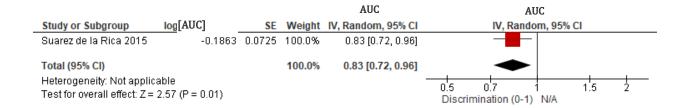
a) OR, Per Point

				Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI
De Waele 2014	0.0583	0.0048	40.6%	1.06 [1.05, 1.07]	-
Dupont 2011	0.0296	0.01	32.9%	1.03 [1.01, 1.05]	
Maseda 2019	0.077	0.014	26.6%	1.08 [1.05, 1.11]	
Total (95% CI)			100.0%	1.06 [1.03, 1.08]	•
Heterogeneity: Tau ^z = Test for overall effect:			= 0.009);	l² = 79%	0.85 0.9 1 1.1 1.2 Favours survival Favours mortality

b) OR, Cutoff

				Odds Ratio	Odds Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
Alqarni 2018 (Score 48+)	1.5644	0.2895	93.6%	4.78 [2.71, 8.43]	-	
Suarez., 2015 (Score 47+)	2.2565	1.1084	6.4%	9.55 [1.09, 83.84]	•	_
Total (95% CI)			100.0%	5.00 [2.89, 8.65]	•	
Heterogeneity: Tau² = 0.00; 0 Test for overall effect: Z = 5.7	' '	P = 0.55)	; I² = 0%		0.005 0.1 1 10 Favours survival Favours mo	200 rtality

c) AUC



Supplementary Figure 4. SOFA as a Predictor of Mortality

a) OR, Per Point

				Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Augustin 2020	0.3221	0.0464	35.9%	1.38 [1.26, 1.51]	-
Dupont 2011	0.1655	0.0596	27.1%	1.18 [1.05, 1.33]	
Pupelis 2014	0.3646	0.1612	5.5%	1.44 [1.05, 1.97]	
Sim 2020	0.2662	0.0527	31.4%	1.30 [1.18, 1.45]	
Total (95% CI)			100.0%	1.30 [1.21, 1.41]	•
Heterogeneity: Tau ² = Test for overall effect:		•	= 0.20); l²	²= 36%	0.5 0.7 1 1.5 2 Favors survival Favors mortality

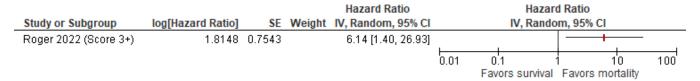
b) HR, Per Point

				Hazard Ratio	Hazar	d Ratio	
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% CI	IV, Rando	m, 95% CI	
Luo 2022	0.2546	0.0542	47.1%	1.29 [1.16, 1.43]		-	
Montravers 2016	0.2554	0.0511	52.9%	1.29 [1.17, 1.43]		-	
Total (95% CI)			100.0%	1.29 [1.20, 1.39]		•	
Heterogeneity: Tau² = Test for overall effect:		•	0.99); l²=	0%	0.5 0.7 Favors survival	1 1.5 Favors mortality	+ 2 V

c) OR, Cutoff

Study or Subgroup	log[Odds Ratio]	SE	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
Wu 2016 (Score 4+)	0.184	0.4558	1.20 [0.49, 2.94]	
Suarez (Score 7+)	2.0968	0.8021	8.14 [1.69, 39.21]	
Nugraha 2022 (Score 3+)	2.4965	0.767	12.14 [2.70, 54.59]	-
				0.01 0.1 1 10 100 Favors survival Favors mortality

d) HR, Cutoff



Other

Though an OR was not reported by the authors, SOFA was not an independent predictor of mortality in a retrospective study of 544 patients as determined by LASSO multivariate regression analysis of 37 variables [Huang 2021].

e) AUCs

				AUC	AU	ıc	
Study or Subgroup	log [AUC]	SE	Weight	IV, Random, 95% CI	IV, Rando	m, 95% CI	
Huang 2021 (study cohort)	-0.1863	0.0188	19.3%	0.83 [0.80, 0.86]	-		
Huang 2021 (validation cohort)	-0.1863	0.0188	19.3%	0.83 [0.80, 0.86]	+		
Pawar 2022	-0.2614	0.0414	16.7%	0.77 [0.71, 0.84]	-		
Pieroni 2022	-0.462	0.0422	16.6%	0.63 [0.58, 0.68]			
Posadas-Calleja 2018	-0.3285	0.0292	18.3%	0.72 [0.68, 0.76]	-		
Suarez de la Rica 2015	-0.3567	0.0959	9.7%	0.70 [0.58, 0.84]			
Total (95% CI)			100.0%	0.75 [0.69, 0.81]	•		
Heterogeneity: Tau² = 0.01; Chi²:	= 54.61, df = 5 (P <	0.00001);	6	0.5 0.7 1	1.5	+
Test for overall effect: Z = 6.95 (P	< 0.00001)				Discrimination (0-1)		. 2

Supplementary Figure 5. ASA as a Predictor of Mortality

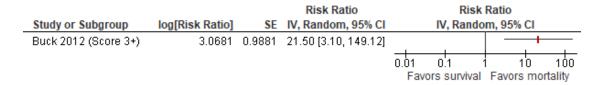
a) OR, Per Point

				Odds Ratio		Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI
Moller 2012	0.4574	0.2489	73.5%	1.58 [0.97, 2.57]		-
Pupelis 2014	2.3571	1.2129	7.2%	10.56 [0.98, 113.79]		-
Sim 2020	0.3221	0.7	19.3%	1.38 [0.35, 5.44]		- •
Total (95% CI)			100.0%	1.76 [0.92, 3.40]		•
Heterogeneity: Tau² : Test for overall effect			= 0.30); P	²= 18%	0.001	0.1 1 10 1000 Favors survival Favors mortality

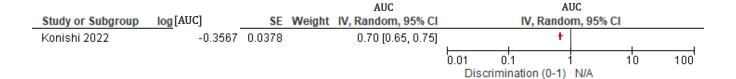
b) OR, Cutoff

				Odds Ratio	Odds	Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Rando	m, 95% CI	
Bensignor 2018 (Score 3+)	1.0116	0.4816		2.75 [1.07, 7.07]			
Faes 2021 (Score 4)	1.7492	0.4089		5.75 [2.58, 12.82]			
Tartaglia 2021 (Score 4)	2.0618	0.6543		7.86 [2.18, 28.34]			
					0.01 0.1	1 10	100
					Favors survival	Favors more	tality

c) RR, Cutoff



d) AUC

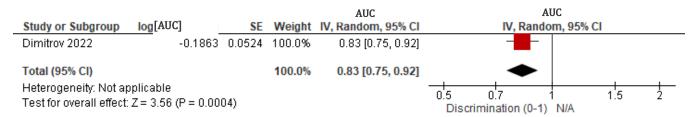


Supplementary Figure 6. WSES as a Predictor of Mortality

a) OR, Per Point

				Odds Ratio		Odds	Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Rando	m, 95% CI	
Abdel-Kader 2019	0.5766	0.0235	48.5%	1.78 [1.70, 1.86]				
Sartelli 2015	0.5789	0.0228	51.5%	1.78 [1.71, 1.87]			•	
Total (95% CI)			100.0%	1.78 [1.73, 1.84]			1	
Heterogeneity: Tau² = Test for overall effect:			= 0.94); l²	² = 0%	0.01	0.1 Favors survival	10 Favors mortality	100

b) AUC



One additional study [Lebedev 2021] reported an AUC of 0.88 for ASA but 95% CI was not provided.

Supplementary Table 4. Other Independent Risk Factors for Mortality (Multivariate Analysis Only)

	Condition	No. of studies	Total No. of subjects	Mortality rate (%)	Odds ratio	95% CI	References
Non-	-modifiable factors			•			
1	Age >65 years	5	7,525	16.7	2.85	2.23-3.64	Claridge 2014, Maseda 2019, Moller 2012, Posadas-Calleja 2018, Sartelli 2019
2	Cancer	4	7,562	18.7	2.39	1.58-3.61	De Waele 2014, Kang 2011, Moller 2012, Sartelli 2019,
3	Co-morbidity	2	7,573	7.4	2.60	2.31-2.93	Gross 2018, Posadas-Calleja 2018
4	Immunosuppression	4	9,873	9.7	2.94	1.94-4.48	Politano 2011, Sartelli 2015, Sartelli 2014, Zhang 2018
5	Liver disease	4	7,013	26.9	2.38	1.80-4.42	Blot 2019, De Waele 2014, Kang 2011, Moller 2012
6	Central nervous system dysfunction	3	4,999	9.7	4.45	2.47-8.03	Posadas-Calleja 2018, Sartelli 2019, Schneider 2016
7	Generalized vs. focal peritonitis	3	3,529	22.5	2.88	1.46-5.70	Blot 2019, Guilbart 2016, Sallinen 2015
8	ICU care	4	5,444	10.2	3.56	1.40-9.06	Politano 2011, Sartelli 2014, Zhang 2018, Yildiz 2018
9	Small bowel vs. colonic perforation	2	2,089	10.8	3.00	1.77-5.08	Bensignor 2018, Sartelli 2014

10	Sarcopenia	1	287	19.9	2.10	1.10-4.00	Ji 2018
11	Visceral obesity	1	287	19.9	1.70	1.00-2.89	Ji 2018
12	Pittsburg bacteremia score	1	365	11.5	1.29	1.11-1.50	Kang 2011
13	Serum procalcitonin >100 ng/mL	1	121	18.2	11.28	1.80-70.20	Suarez de la Rica 2015
14	Prolonged activated partial thromboplastin time	1	138	31.9	1.07	1.02-1.11	Xu 2019
15	Prior antibiotic treatment	1	2,756	9.5	1.38	1.05-1.78	Zhang 2018
16	Need for urgent surgery	1	343	31.5	2.71	1.53-4.80	Alqarni 2018
Pote	ntially modifiable factors	•				•	
1	Catheter-related blood stream infection	1	323	8.7	6.16	2.30-16.51	Claridge 2014
2	Cardiovascular dysfunction	5	7,910	16.0	2.78	2.03-3.82	Blot 2019, Claridge 2014, Posadas-Calleja 2018, Sartelli 2019, Schneider 2016
3	Peripheral vascular disease	1	226	23.9	2.10	1.07-4.12	Abaziou 2020
4	Renal dysfunction	10	16,965	13.2	3.02	2.23-4.08	Abaziou 2020, De Waele 2014, Gross 2018, Lichtenstern 2015, Moller 2012, Patel 2019, Politano 2011, Posadas- Calleja 2018, Sartelli 2019, Schneider 2016
5	Respiratory dysfunction	4	8,503	8.8	2.09	1.49-2.93	Posadas-Calleja 2018, Sartelli 2019, Schneider 2016, Zhang 2018

6	Hypothermia	1	1,052	18.3	1.60	1.08-2.36	Posadas-Calleja 2018
7	Sepsis	3	7,486	16.2	3.99	2.58-6.17	Blot 2019, Kang 2011, Sartelli 2015
8	Shock	5	5,818	26.6	2.42	1.34-4.39	Blot 2019, Li 2017, Moller 2012, Patel 2019, Sim 2020
9	Serum lactate >4 mmol/L	2	3,258	9.2	4.14	2.71-6.33	Sartelli 2019, Suarez de la Rica 2015
10	Hypalbuminemia	1	810	1.7	4.90	2.80-8.40	Schneider 2016
11	Malnutrition	1	2,588	29.1	2.05	1.33-3.15	Blot 2019
12	Intra-abdominal culture	1	41,495	4.7	0.85	0.77-0.95	Tsuchiya 2019
13	Candida present	2	656	13.4	2.77	1.60-4.79	Maseda 2019, Montravers 2016
14	Clostridial infection	1	323	8.7	13.03	3.09-54.89	Claridge 2014
15	Enterococcal infection	1	160	47.5	2.24	1.06-4.74	Dupont 2011
16	Multi-resistant organism	3	5,504	19.8	1.59	1.25-2.02	Blot 2019, Dupont 2011, Zhang 2018
17	Open vs. percutaneous drainage	1	686	12.4	2.04	1.13-3.67	Politano 2011
18	Delayed initial source control >24h	5	9,485	15.1	2.80	1.83-4.28	Karvellas 2019, Moller 2012, Patel 2019, Sartelli 2014, Sartelli 2015
19	Inadequate source control	3	2,833	29.6	4.94	3.90-6.25	Blot 2019, Tellor 2015, De Pascale 2019
20	Inappropriate antimicrobial therapy	5	1,149	28.5	2.94	1.81-4.77	Augustin 2020, Alqarni 2018, De Pascale 2019, Guilbart 2016, Tellor 2015

Supplementary Table 1. Characteristics of included studies

Author, year of publication	Location, years of data collection	Study design	Number of patients and age	Population included	Scoring system(s)	Mortality
Abdel-Kader 2019	UAE 2014-2016	Retrospective cohort study	100 adults with cIAI Median age 32 years (range 18-75)	Adults with cIAI who had undergone interventional drainage or surgery for disease management	WSES	Presumably in-hospital mortality: 1%
Alqarni 2018	France 1999-2014	Retrospective cohort study	343 ICU patients with postoperative IAI Median 62 years	Post-operative intra-abdominal infections admitted to ICU	SAPS II	All-cause ICU mortality: 31.5%; All-cause hospital mortality: 33.2%
Augustin 2020	France 1998-2012, divided into two 6-year periods	Retrospective cohort study (data collected prospectively)	251 adults with postoperative peritonitis Mean age for first period 64 years, mean age for second period 62 years	Adults with postoperative peritonitis requiring admission to the ICU	SOFA	ICU mortality: 31.2%; Hospital mortality: 40.2%
Bensignor 2018	France 2004-2013	Multicenter, retrospective cohort study	191 patients with postoperative peritonitis Mean age 61 years	Patients with postoperative peritonitis undergoing relaparotomy	ASA	Overall mortality: 14.1%
Buck 2012	Denmark 2008-2009	Multicenter, retrospective study	117 adults surgically treated for perforated peptic ulcer Median age 70 years (range 25-92)	Adults with surgically treated perforated peptic ulcer	APACHE II, ASA	30-day mortality: 17.1%
De Waele 2014	75 countries Study day in 2007	Multicenter 1-day point prevalence study	1,392 adults with IAI Mean age 62 years	Adults with IAI (diagnosed using International Sepsis Forum criteria)	SAPS II	ICU mortality: 20.4%; Hospital mortality: 36.3%
Dimitrov 2022	Bulgaria 2017-2019	Retrospective study	110 adults with cIAIs Mean age 61 years	Adults who were operated on for clAls	WSES	In-hospital mortality: 22.7%
Dupont 2011	France 1997-2007	Retrospective cohort study	160 elderly patients with severe IAI Mean age 82 years	Elderly ICU patients (≥75 years) with severe IAI	SAPS II, SOFA	ICU mortality: 47.5%
Faes 2021	Switzerland 2016-2020	Prospective cohort study	203 patients Median age 70 years	Patients who had damage-control surgery for severe intra-abdominal sepsis	ASA	In-hospital mortality: 26%
Guilbart 2016	France 2009-2011	Prospective cohort study	310 patients with cIAI (both community- acquired and healthcare-associated) Mean age 60 years (range 17-97)	Patients with cIAI	APACHE II	Observed mortality: 10%
Huang 2021	China 2017-2018	Multicenter retrospective study	544 adults with cIAI Median age 65 years	Adults diagnosed with cIAI	APACHE II, SOFA	In-hospital mortality: 18.9%
Karvellas 2019	Canada, USA, and Saudi Arabia 1996-2015	Multicenter retrospective cohort study	196 adults with acute cholecystitis- associated septic shock Mean age 69.9 years	Cholecystitis-associated septic shock	APACHE II	In-hospital mortality: 37%
Konishi 2022	Japan 2016-2017	Retrospective cohort study (data from administrative claims data from >1,200 hospitals in Japan)	3,465 adults Mean age 62.9 years	Patients with gastroduodenal ulcer perforation who underwent surgical repair (in a validation cohort)	ASA	In-hospital mortality: 4.6%

Lebedev 2021	Russia	Retrospective cohort	352 patients	Patients with secondary diffuse	WSES, APACHE II	Mortality: 16.7%
Lebeuev 2021	Unclear	study	Mean age 55.8 years	peritonitis	WSES, APACHE II	Mortality. 16.7 %
Li 2017	Taiwan 2008-2012	Retrospective cohort study	133 adults hospitalized with perforated peptic ulcer and subsequent growth of Candida Age (unclear if mean or median) of those without postoperative antifungal therapy 63 years (range 27-89), those with postoperative antifungal therapy 70 years (38-88)	Adults with community-acquired perforated peptic ulcer-associated peritonitis with <i>Candida</i> isolated	APACHE II	30-day mortality: 12%
Lichtenstern 2015	Germany	Retrospective cohort study	283 patients with sepsis due to peritonitis	ICU patients with sepsis due to peritonitis (complicated peritonitis)	APACHE II	Overall mortality: 41.3%; 28-day mortality: 29.3%
2013	2005-2008	Study	Mean age 64 years	pentonitis (complicated pentonitis)		20-day mortanty. 29.5%
Luo 2022	China	Retrospective review	476 patients	Patients with IAI (community- and healthcare-acquired) admitted to the	SOFA	28-day mortality: 16%
	2011-2018		Median age 60.5 years 345 adults with non-postoperative/non-	ICU		
Maseda 2019	Spain 2014-2015	Multicenter, prospective cohort study	nosocomial IAI Mean age for healthcare-associated infections 72.5 years, for community-acquired infections 62.3 years, and for immunocompromised 61.0 years	Adults with non-postoperative and non-nosocomial IAIs (healthcare-associated or community-acquired) in the ICU after surgical treatment for infection control	SAPS II	ICU mortality: 8.1%; 30-day mortality: 14.5%
Moller 2012	Denmark 2003-2009	Retrospective cohort study (data collected prospectively)	2,668 patients surgically treated for perforated peptic ulcer Median age 70.9 years (range 16.2-104.2)	Patients with gastric or duodenal perforated peptic ulcer patients who underwent surgery	ASA	30-day mortality: 26.5%
Montravers 2016	France 1999-2011	Retrospective cohort study (data collected prospectively)	311 patients with healthcare- associated IAI (data provided for 302 patients) Median age of all groups (de- escalation, no de-escalation, escalation, and no change) ranged from 61-70 years across groups	Patients admitted for the management of healthcare-associated IAI who survived >3 days following their diagnosis, remained in the ICU for >3 days, and did not undergo early reoperation during the first 3 days	SOFA	ICU mortality: 28.8%; Hospital mortality: 30.1%
Morais 2018	Portugal 2009-2017	Retrospective cohort study	101 patients submitted to laparostomy Median age 64 years (range 22-88)	Patients with open abdomen	APACHE II	Global in-hospital mortality: 62.4%
Nugraha 2022	Indonesia 2020-2021	Retrospective cohort study	265 patients Mean age 42.6 years	Adults diagnosed with cIAI or suffering from secondary/tertiary peritonitis or intra-abdominal abscess who underwent source control surgery during hospitalization	SOFA	Mortality "during treatment": 34.7%
Ozdogan 2015	Turkey 2010-2013	Retrospective cohort study	103 adults with cIAI admitted to ICU Mean age 64 years	ICU adults with cIAI sepsis	APACHE II	Overall mortality: 50.5%
Pan 2021	China 2012-2019	Retrospective review	282 patients Mean age 57 years	Patients with intra-abdominal infection	APACHE II	Mortality: 22.7%

Pawar 2022	USA 2008-2018	Retrospective review	478 patients with cholangitis/cholecystitis; 396 patients with peritonitis Median age of total cohort 70 years (IQR 57-82)	Subset of adult ICU patients with cholangitis/cholecystitis, from a broader cohort of patients with various types of infections	SOFA	Mortality: 10.3% for cholecystitis/cholangitis; 20% for peritonitis
Pieroni 2022	USA 2014-2015	Retrospective review of multicenter ICU database (335 ICUs across 208 hospitals)	544 abdominal sepsis admissions, from a bigger cohort of sepsis admissions Mean age for abdominal sepsis group 67 years	Adults in medical ICU, surgical ICU, and medical-surgical ICU with an ICU stay >72 hours	SOFA	In-hospital mortality for abdominal sepsis: 18.9%
Politano 2011	USA 13-year period; years not stated	Retrospective cohort study (data collected prospectively)	686 patients with IAI requiring an intervention after an index operation Mean age in percutaneous drainage group 52.9 years, mean age in surgical drainage group 52.3 years	Patients with postoperative IAI requiring intervention	APACHE II	Presumably in-hospital mortality: 6.7%
Posadas-Calleja 2018	Canada 2005-2010	Multicenter retrospective cohort study (data collected prospectively)	905 patients with intra-abdominal sepsis Mean age 64 years	Patients with intra-abdominal sepsis (met ≥2 SIRS criteria)	APACHE II, SOFA	Overall ICU mortality: 21.3%
Pupelis 2014	Belgium 2010-2012	Retrospective cohort study	222 patients with secondary peritonitis Mean/Median (unclear which) age 65 years	Patients admitted to the SICU with secondary peritonitis (either localized or diffuse)	SOFA, ASA	ICU mortality: 9.9%; Hospital mortality: 14.9%
Roger 2022	France 2018-2019	Multicenter, prospective observational study	205 patients Mean age 56 years	Adults diagnosed with community- acquired IAI	SOFA	28-day mortality: 7%
Sartelli 2015	2014-2015 54 countries worldwide	Multicenter prospective study	4,533 adults with cIAI sepsis Mean age 51.2 years (range 18-99)	Adults with cIAI who had surgical management or interventional radiological drainage	WSES	Overall mortality: 9.2%
Sim 2020	Korea 2013-2018	Retrospective cohort study	239 adults who underwent emergency gastrointestinal surgery Mean/Median (unclear which) for culture positive 76 years, for culture negative 70 years	Adults with sepsis or septic shock who underwent emergency cIAI surgery and needed postoperative ICU care	SOFA, ASA	In-hospital mortality: 18%; 30-day mortality: 15.1%
Suarez de la Rica 2015	Spain 2012-2013	Multicenter, retrospective cohort study (data collected prospectively)	121 adults with cIAI Mean 65.6 years (range 18-96)	Adults with cIAI admitted to the SICU for ≥48 hours in 4 Spanish hospitals	SAPS II, SOFA	Intra-SCCU mortality: 11.6% Overall mortality (28 days from SCCU admission): 18.2%
Tartaglia 2021	Italy 2010-2019	Retrospective review	113 patients Mean age 68.1 years	Patients admitted with abdominal sepsis requiring open abdomen	APACHE II, ASA	In-hospital mortality (during treatment or within 30 days of treatment): 43.4%
Tellor 2015	USA 2005-2011	Retrospective cohort study	108 patients with IAI BSI Median age 60 years	Patients with severe sepsis because of cIAI	Modified APACHE II that didn't include Glasgow coma scale	Overall mortality: 27.8%
Wu 2016	China 2013-2014	Retrospective study (data collected prospectively)	267 adults with IAI Mean age 49.5 years	Adults >18 years with IAI	APACHE II, SOFA	ICU mortality: 7.87%; 28-day mortality: 9.0%

Supplementary Table 2a. Risk of bias for included studies evaluating APACHE II

			J	Risk o	of bias do	mains				
		D1	D2	D3	D4	D5	D6	Overall		
	Buck 2012	+	+	+	+	+	-	+		
	Guilbart 2016	+	+	-	+	-	-	-		
	Karvellas 2019	+	-	+	+	+	-	+		
	Huang 2021	+	+	+	+	+	+	+		
	Lebedev 2021	+	+	+	-	+	-	+		
	Li 2017	+	-	+	+	+	-	+		
	Lichtenstern 2015	+	+	+	+	+	X	-		
Study	Morais 2018	-	+	+	+	+	+	+		
	Ozdogan 2015	+	+	+	-	+	-	+		
	Pan 2021	+	+	+	+	+	+	+		
	Politano 2011	+	+	+	+	+	+	+		
	Posadas-Calleja 2018	+	+	+	+	+	+	+		
	Tartaglia 2021	-	+	+	+	+	+	+		
	Tellor 2015	+	+	-	+	+	+	+		
	Wu 2016	+	+	+	+	+	+	+		
		Domains: D1: Bias due to participation. D2: Bias due to attrition. D3: Bias due to prognostic factor measurement. D4: Bias due to outcome measurement. D5: Bias due to confounding. D6: Bias in statistical analysis and reporting.								

Supplementary Table 2b. Risk of bias for included studies evaluating ASA

Risk of bias domains D1 D2 D3 D4 D6 Overall D5 + + + ++ + + Buck 2012 Ŧ \oplus \oplus \bigcirc \oplus lacksquare \oplus Bensignor 2018 \oplus \oplus \oplus lacktriangledown \oplus \bigoplus \oplus Faes 2021 Ŧ \oplus Ŧ \oplus \oplus + \pm Konishi 2022 Study Ŧ \oplus lacktriangledown \bigcirc \oplus \oplus +Moller 2012 Ŧ \oplus Ŧ \bigcirc Ŧ \oplus E Pupelis 2014 Ŧ \oplus \bigcirc + \oplus \bigcirc (+)Sim 2020 **+** Ŧ Ŧ -+ + + Tartaglia 2021

Domains:

D1: Bias due to participation.

D2: Bias due to attrition.

D3: Bias due to prognostic factor measurement.

D4: Bias due to outcome measurement.

D5: Bias due to confounding.

D6: Bias in statistical analysis and reporting.

Judgement

Moderate

+ Low

Supplementary Table 2c. Risk of bias for included studies evaluating SAPS II

Risk of bias domains D1 D2 D3 D4 D5 D6 Overall lacktriangleŦ Ŧ Ŧ Ŧ + Alqarni 2018 Ŧ \bigoplus \bigcirc Ŧ Ŧ E +De Waele 2014 Study Ŧ Ŧ Ŧ \oplus Ŧ \pm Dupont 2011 \pm lacktriangleŦ Ŧ Image: Control of the \bigoplus Ŧ Maseda 2019 Ŧ +E \bigcirc + +Suarez de la Rica 2015

Domains:

D1: Bias due to participation.

D2: Bias due to attrition.

D3: Bias due to prognostic factor measurement.
D4: Bias due to outcome measurement.

D5: Bias due to confounding.

D6: Bias in statistical analysis and reporting.

Judgement

Moderate

Low

Supplementary Table 2d. Risk of bias for included studies evaluating SOFA

		Risk of bias domains									
		D1	D2	D3	D4	D5	D6	Overall			
	Augustin 2020	+	+	+	+	+	+	+			
	Dupont 2011	+	+	+	+	+	+	+			
	Huang 2021	+	+	+	+	+	+	+			
	Luo 2022	+	+	+	+	+	+	+			
	Montravers 2016	+	+	+	+	+	+	+			
	Nugraha 2022	+	+	+	+	-	+	+			
Study	Pawar 2022	+	+	X	+	+	+	-			
ß	Pieroni 2022	+	+	+	+	+	+	+			
	Posadas-Calleja 2018	+	+	+	+	+	+	+			
	Pupelis 2014	+	+	+	+	+	+	+			
	Roger 2022	+	+	+	+	+	+	+			
	Sim 2020	+	+	+	+	+	+	+			
	Suarez de la Rica 2015	+	+	+	+	-	+	+			
	Wu 2016	+	+	+	+	+	+	+			
		Domains: D1: Bias due to participation. D2: Bias due to attrition. D3: Bias due to prognostic factor measurement. D4: Bias due to outcome measurement. D5: Bias due to confounding. D6: Bias in statistical analysis and reporting. Judgement High Moderat Low									

Supplementary Table 2e. Risk of bias for included studies evaluating WSES

Risk of bias domains

		There of blue definants							
		D1	D2	D3	D4	D5	D6	Overall	
Study	Abdel-Kader 2019	+	+	+	+	X	+	-	
	Dimitrov 2022	+	+	+	+	+	+	+	
	Lebedev 2021	+	+	+	-	+	-	+	
	Sartelli 2015	+	+	+	+	+	+	+	

Domains:

D1: Bias due to participation.
D2: Bias due to attrition.
D3: Bias due to prognostic factor measurement.
D4: Bias due to outcome measurement.

D5: Bias due to confounding.
D6: Bias in statistical analysis and reporting.

Judgement

High

Moderate

Low

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