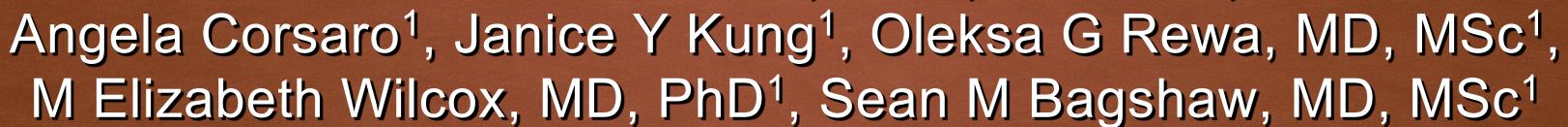# Association Between Acute Kidney Injury, Delirium, & Outcomes in Patients with Critical Illness: A Systematic Review & Meta-Analysis

Prit Kusirisin, MD, PhD[1,2],
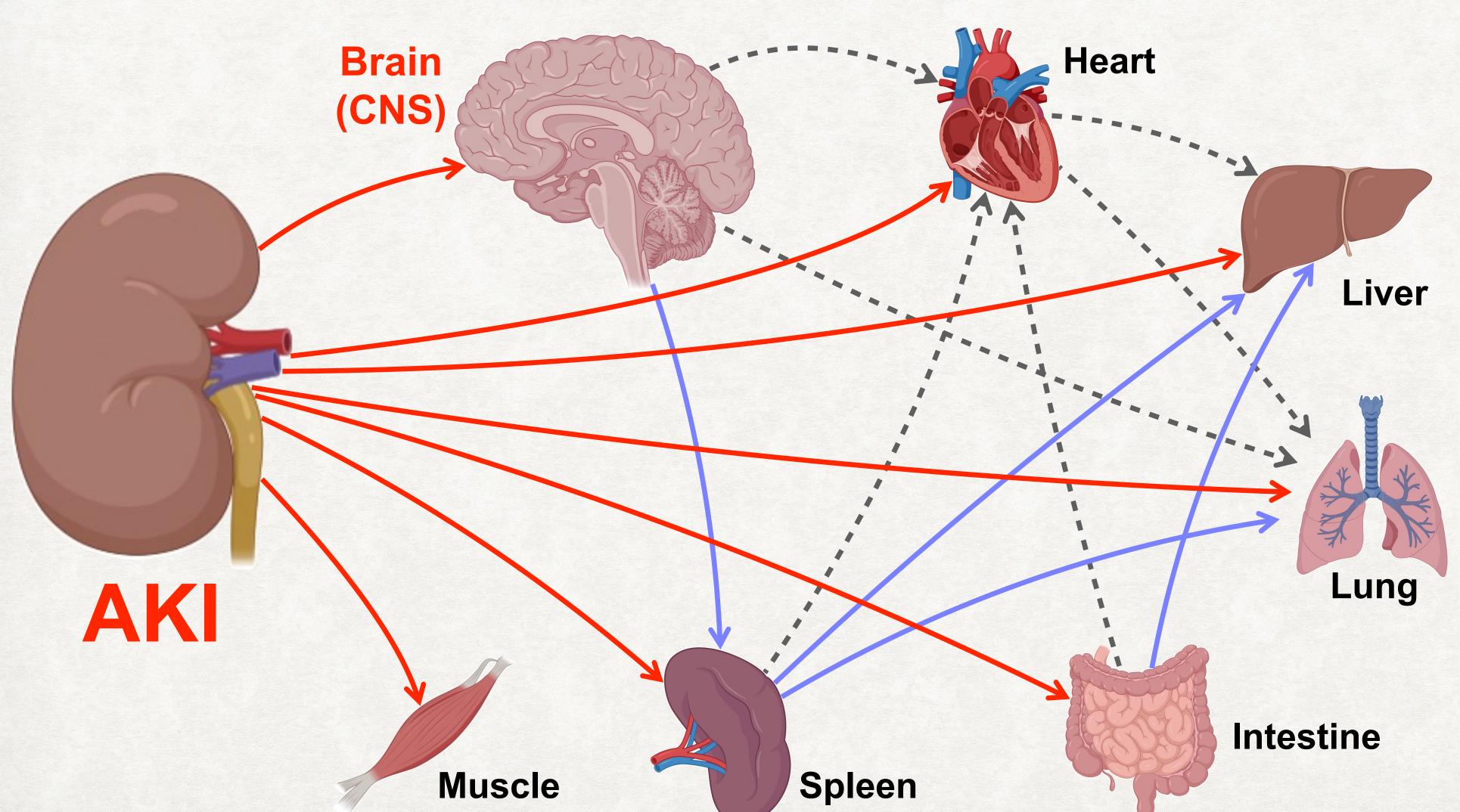Angela Corsaro[1], Janice Y Kung[1], Oleksa G Rewa, MD, MSc[1],
M Elizabeth Wilcox, MD, PhD[1], Sean M Bagshaw, MD, MSc[1]

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NEPHRO MED CMU

AK CRRT 2025

6TH ASIA PACIFIC AKI CRRT

October 2 - 4, 2025
Eastin Grand Hotel Phayathai
Bangkok, Thailand

ORGANIZED BY: CRRT, INC.
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OPTIMIZING AKI CARE:
BRIDGING GAPS ACROSS DIVERSE SETTINGS

Introduction:
AKI & Delirium in Critically Ill Patients

CNS, central nervous system;
DAMPs, damage-associated molecular patterns; PAMPs, pathogen-associated molecular patterns

Proposed Mechanisms of AKI-Associated Delirium & Potential Cellular Drivers of Delirium

Impaired clearance of toxins & drugs including sedatives

Electrolyte imbalances

Acute kidney injury

↑ vascular permeability

Inflammation

↓ central dopamine turnover

Fluid accumulation

Disruption of BBB

CNS

Periphery

Blood endotoxin/cytokines

Cytokine release

Cerebral edema

BBB activation

Microglial activation

Hippocampal injury

Brain cytokines

TNF-α IL-6 IL-1α IL-1β

Delirium

Neuronal dysfunction & injury

Astrocyte activation

BBB

Blood vessel

Knowledge gap (review question)
No systematic evaluation describing clinical association between AKI & delirium among critically ill patients

Objective
To perform systematic review describing association between AKI & delirium among patients with critical illness

BBB, blood-brain barrier; IL, interleukin; TNF, tumor necrosis factor

Pang H, et al. Crit Care. 2022;26(1):258.

Methods

- **Study registration:** PROSPERO on March 25, 2025 (CRD420251001864)
- **Searching**
  - **Databases:** Ovid MEDLINE, Ovid Embase, CINAHL, Scopus, Web of Science Core Collection, Cochrane library, Google scholar
  - **Keywords:** acute kidney injury, renal replacement therapy (RRT), critical care, critical illness, intensive care, intensive care units, delirium
- 2 reviewers independently screened, selected, extracted studies, & assessed risk of bias using web-based tool Covidence

- **Inclusion criteria**
  - Clinical trial or observational cohort
  - Study reports occurrences of both AKI & delirium, using validated definitions
  - Study focused on population admitted to critical care or intensive care unit (ICU)
  - Published between January 2000 to January 2025
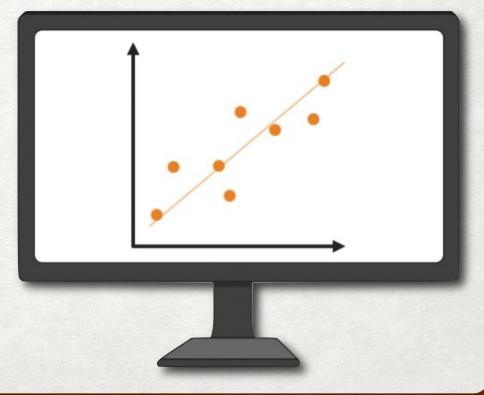 - Published in English language
- **Exclusion criteria**
  - Case reports or case series
  - Pre-clinical or experimental studies

Methods

Population	Critically ill patients with AKI
Comparison	**Develop delirium** vs **Do not develop delirium**
Outcomes	• **Primary:** proportion of de novo delirium • **Secondary:** • Odds of delirium stratified by AKI severity • In-hospital mortality • Use of organ support: RRT, mechanical ventilation (MV), vasopressor • Length of ICU & hospital stay
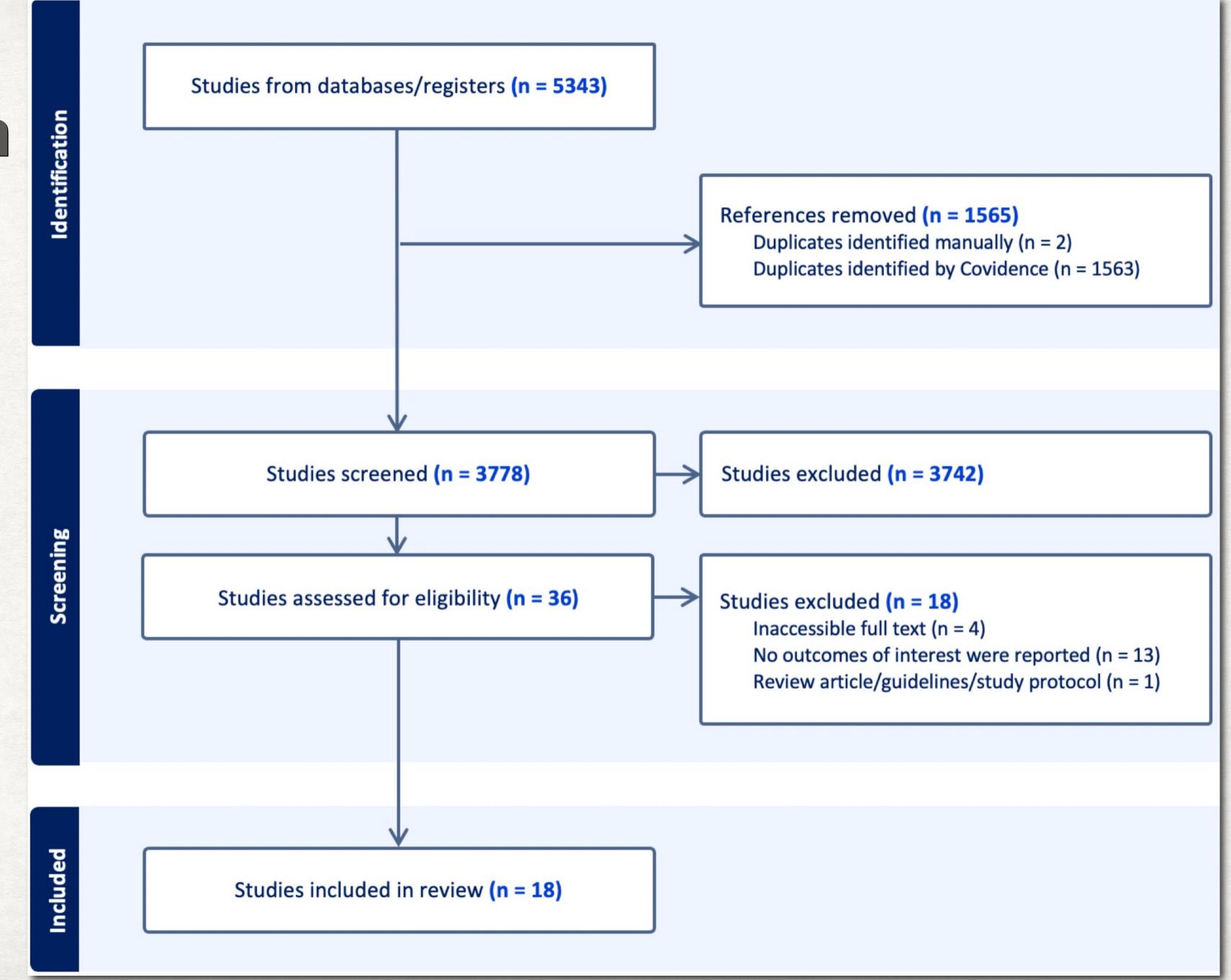
- **Qualitative synthesis:** summary characteristics of included studies

- **Quantitative synthesis**
  - **Dichotomous outcomes:** pooled proportion, risk ratio (RR), or odds ratio (OR), with 95% CI
  - **Continuous outcomes:** weighted mean differences (WMD), with 95% CI
  - **Pooled meta-analysis:** DerSimonian-Laird random-effects model
  - **Statistical heterogeneity:** visual inspection, Q test <0.10, I2 statistic >50%
  - **Publication bias:** funnel plot (if >10 studies per outcomes)
  - **Statistical significance:** p <0.05
  - **Strength of evidence:** GRADE tool

**STATA
statistical software,
version 17**
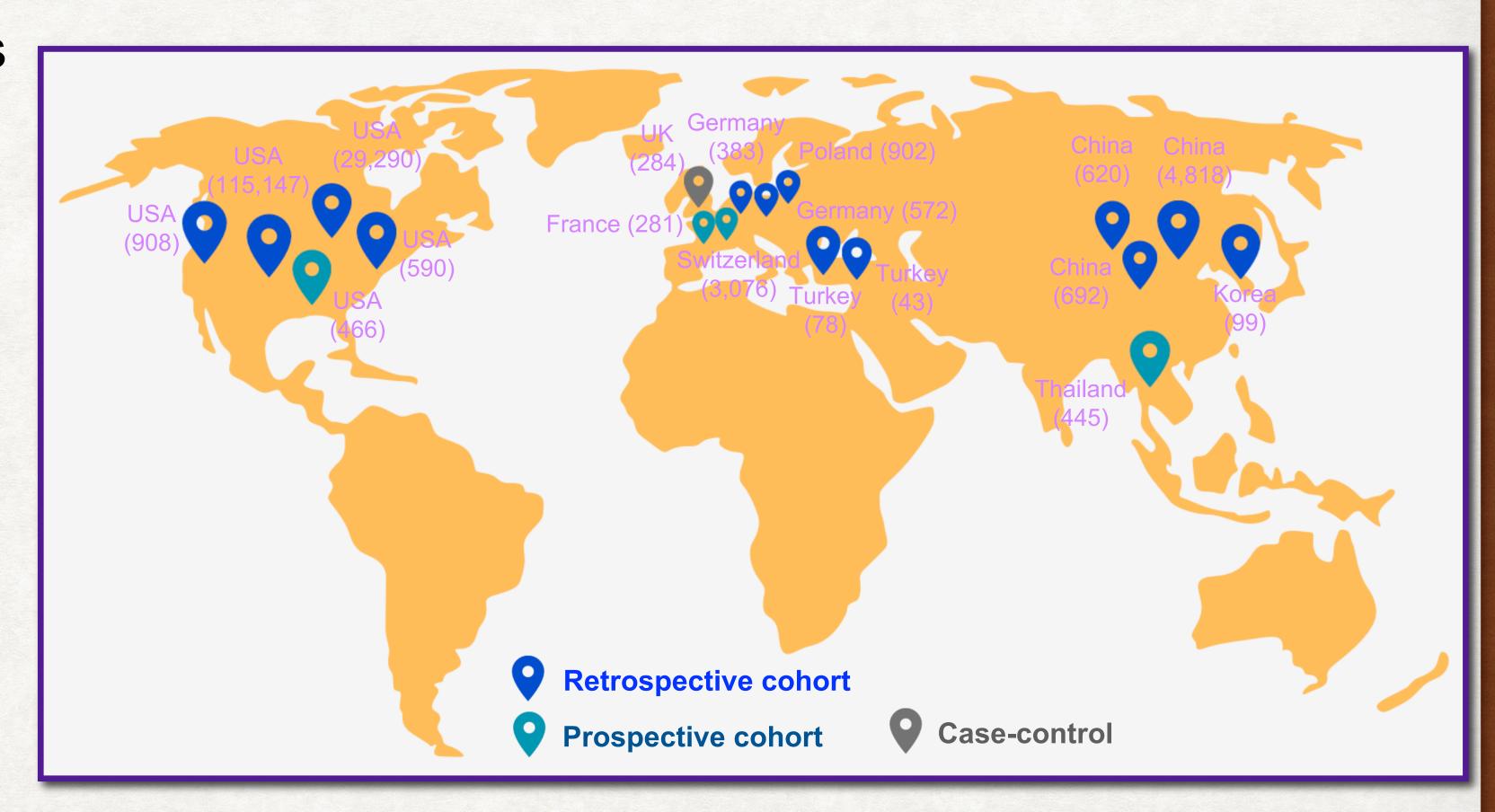
Results: PRISMA Diagram

- Search complete on March 25, 2025

- Included 18 observational studies

- Study quality
  - Using Newcastle-Ottawa Scale
  - Moderate quality (mean 6.7±1.3, range of 4-8)

Identification

Studies from databases/registers **(n = 5343)**

References removed **(n = 1565)**
Duplicates identified manually (n = 2)
Duplicates identified by Covidence (n = 1563)

Screening

Studies screened **(n = 3778)**

Studies excluded **(n = 3742)**

Studies assessed for eligibility **(n = 36)**

Studies excluded **(n = 18)**
Inaccessible full text (n = 4)
No outcomes of interest were reported (n = 13)
Review article/guidelines/study protocol (n = 1)

Included

Studies included in review **(n = 18)**

Characteristics of Included Studies

- 18 studies ≈ 158,694 patients

- **Population setting**
  - Surgical ICU (10), medical ICU (1), cardiac ICU (1), mixed ICU (5), pediatric ICU (1)

- **Definition**
  - **AKI**
    - KDIGO (8), AKIN (1), N/A (9)
  - **Delirium**
    - CAM-ICU (12), DSM (2), CAPD (1), NuDesc (1), N/A (1)

USA (29,290)
UK (284)
Germany (383)
Poland (902)
China (620)
China (4,818)
USA (115,147)
USA (908)
France (281)
Germany (572)
USA (590)
Switzerland (3,076)
USA (466)
Turkey (78)
Turkey (43)
China (692)
Korea (99)
Thailand (445)

Retrospective cohort
Prospective cohort
Case-control

Primary Outcome

Proportion of Delirium

Study	Proportion (95% CI)	% Weight
Chen et al, 2024	0.24 (0.22, 0.25)	5.59
Jackel et al, 2021	0.60 (0.55, 0.65)	5.56
Kalyoncuoglu et al, 2020	0.22 (0.14, 0.32)	5.47
Kotfis et al, 2020	0.13 (0.11, 0.15)	5.59
Koth et al, 2022	0.69 (0.66, 0.72)	5.58
Lescot et al, 2013	0.10 (0.07, 0.14)	5.58
Lin et al, 2023	0.32 (0.28, 0.35)	5.58
Marquetand et al, 2021	0.42 (0.40, 0.44)	5.59
Mungan et al, 2020	0.23 (0.13, 0.38)	5.36
Pauley et al, 2015	0.20 (0.17, 0.24)	5.58
Rustenbach et al, 2024	0.17 (0.14, 0.20)	5.58
Shin et al, 2018	0.40 (0.31, 0.50)	5.46
Siew et al, 2017	0.82 (0.78, 0.85)	5.58
Singh et al, 2020	0.50 (0.49, 0.51)	5.60
Tian et al, 2020	0.15 (0.12, 0.18)	5.58
Trongtrakul et al, 2016	0.12 (0.10, 0.16)	5.58
Wan et al, 2020	0.50 (0.44, 0.56)	5.54
Yang et al, 2023	0.01 (0.01, 0.01)	5.60
Overall ($I^2 = 99.95\%$, p = 0.00)	0.32 (0.18, 0.47)	100.00

Proportion of delirium

Proportion of delirium among patients with AKI
32% (95% CI, 18-47)

A. Odds for delirium stratified by AKI stage 1

Study	Odds ratio with 95% CI	Weight (%)
Kotfis et al, 2020	3.30 [-12.22, 18.82]	0.78
Koth et al, 2022	1.04 [-0.90, 2.98]	49.63
Siew et al, 2017	1.13 [-1.22, 3.48]	33.78
Tian et al, 2020	1.66 [-2.30, 5.62]	11.92
Wan et al, 2020	1.28 [-5.64, 8.20]	3.90
Overall	1.68 [1.15, 2.43]	

$H^2 = 1.00$

Patients without delirium   Patients with delirium

Stratified by AKI stage 1
OR 1.68 (95% CI, 1.15-2.43;
p = 1.00, $I^2 = 0\%$; low certainty)

B. Odds for delirium stratified by AKI stage 2

Study	Odds ratio with 95% CI	Weight (%)
Kotfis et al, 2020	5.30 [-41.29, 51.89]	0.21
Koth et al, 2022	1.14 [-1.23, 3.51]	81.22
Siew et al, 2017	1.55 [-4.06, 7.16]	14.54
Tian et al, 2020	1.24 [-12.81, 15.29]	2.31
Wan et al, 2020	1.44 [-14.87, 17.75]	1.72
Overall	2.13 [1.06, 4.63]	

$H^2 = 1.00$

Patients without delirium   Patients with delirium

Stratified by AKI stage 2
OR 2.13 (95% CI, 1.06-4.63;
p = 1.00, $I^2 = 0\%$; low certainty)

C. Odds for delirium stratified by AKI stage 3

Study	Odds ratio with 95% CI	Weight (%)
Kotfis et al, 2020	12.60 [-10.92, 36.12]	0.43
Koth et al, 2022	1.00 [-0.96, 2.96]	62.13
Lin et al, 2023	2.66 [-1.26, 6.58]	15.53
Siew et al, 2017	2.56 [-1.36, 6.48]	15.53
Tian et al, 2020	4.31 [-3.53, 12.15]	3.88
Wan et al, 2020	5.40 [-4.40, 15.20]	2.49
Overall	4.76 [2.27, 12.29]	

$H^2 = 1.00$

Patients without delirium   Patients with delirium

Stratified by AKI stage 3
OR 4.76 (95% CI, 2.27-12.29;
p = 0.75, $I^2 = 0\%$; low certainty)

Secondary Outcomes

Mortality

Study	Delirium Events	Total	No delirium Events	Total	Risk ratio with 95% CI	Weight (%)
Jackel et al, 2021	50	230	12	153	2.46 [1.35, 4.47]	11.55
Kalyoncuoglu et al, 2020	13	17	13	61	2.47 [1.30, 4.68]	11.10
Koth et al, 2022	28	629	2	279	5.99 [1.44, 24.96]	5.00
Lescot et al, 2013	9	28	30	253	2.29 [1.18, 4.45]	10.89
Lin et al, 2023	19	220	20	472	1.96 [1.06, 3.59]	11.45
Mungan et al, 2020	1	10	0	33	8.50 [0.37, 194.86]	1.38
Pauley et al, 2015	39	120	24	470	5.05 [3.14, 8.13]	12.89
Shin et al, 2018	14	40	3	59	5.36 [1.63, 17.65]	6.32
Trongtrakul et al, 2016	159	55	286	390	1.76 [1.56, 1.98]	15.81
Wan et al, 2020	32	142	44	142	0.78 [0.52, 1.17]	13.62
Overall					2.36 [1.61, 3.47]	

In-hospital mortality
RR 2.36 (95% CI, 1.61-3.47; p <0.01, I² = 79%; moderate certainty)

Receipt of Renal Replacement Therapy

Study	Delirium Events	Total	No delirium Events	Total	Risk ratio with 95% CI	Weight (%)
Chen et al, 2024	149	1,133	130	3,685	3.41 [2.72, 4.28]	21.25
Jackel et al, 2021	34	230	18	153	1.22 [0.71, 2.10]	17.68
Koth et al, 2022	26	629	3	279	3.73 [1.14, 12.23]	9.87
Lescot et al, 2013	6	28	4	253	11.34 [3.37, 38.16]	9.63
Pauley et al, 2015	12	120	4	470	10.77 [3.53, 32.85]	10.56
Rustenbach et al, 2024	20	98	46	474	1.92 [1.18, 3.11]	18.38
Shin et al, 2018	11	40	6	59	2.34 [0.93, 5.89]	12.63
Overall					3.12 [1.89, 5.15]	

Receipt of RRT
RR 3.12 (95% CI, 1.89-5.15; p <0.01, I² = 76%; moderate certainty)
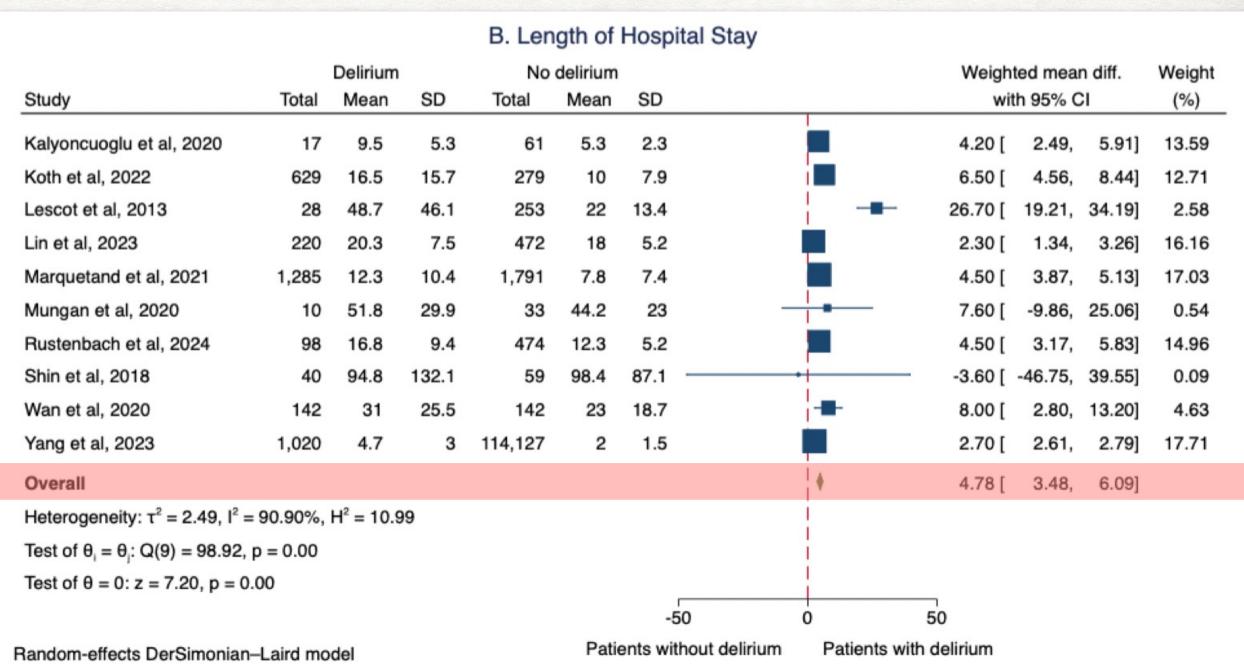
Receipt of Mechanical Ventilation

Study	Delirium Events	Total	No delirium Events	Total	Risk ratio with 95% CI	Weight (%)
Chen et al, 2024	676	1,133	855	3,685	1.98 [1.82, 2.16]	10.50
Jackel et al, 2021	193	230	62	153	1.58 [1.25, 2.00]	10.11
Koth et al, 2022	320	629	20	279	5.04 [3.27, 7.77]	9.15
Lin et al, 2023	220	220	472	472	1.00 [0.89, 1.12]	10.45
Marquetand et al, 2021	208	1,285	24	1,791	10.54 [6.94, 15.99]	9.24
Pauley et al, 2015	77	120	86	470	2.53 [1.95, 3.28]	10.00
Singh et al, 2020	7,550	14,645	9,950	14,645	0.84 [0.82, 0.86]	10.56
Tian et al, 2020	93	93	527	527	1.00 [0.86, 1.17]	10.36
Wan et al, 2020	113	142	96	142	1.10 [0.89, 1.35]	10.20
Yang et al, 2023	27	1,020	510	114,127	5.80 [3.96, 8.50]	9.43
Overall					2.08 [1.46, 2.98]	

Receipt of MV
RR 2.08 (95% CI, 1.46-2.98; p <0.01, I² = 99%; low certainty)

Receipt of Vasopressors

Study	Delirium Events	Total	No delirium Events	Total	Risk ratio with 95% CI	Weight (%)
Chen et al, 2024	949	1,133	1,771	3,685	1.40 [1.32, 1.49]	34.71
Jackel et al, 2021	158	230	41	153	1.93 [1.43, 2.59]	26.00
Pauley et al, 2015	48	120	68	470	2.26 [1.63, 3.13]	24.66
Shin et al, 2018	13	40	22	59	0.90 [0.50, 1.63]	14.63
Overall					1.61 [1.20, 2.16]	

Heterogeneity: τ² = 0.06, I² = 78.68%, H² = 4.69
Test of θᵢ = θⱼ: Q(3) = 14.07, p = 0.00
Test of θ = 0: z =

Random-effects D

Receipt of vasoactive support
RR 1.61 (95% CI, 1.20-2.16; p <0.01, I² = 79%; low certainty)

Secondary Outcomes: Length of Stay

Length of ICU stay
WMD 3.54 days
(95% CI, 1.20-5.87; p <0.01, I² = 99%; moderate certainty)

Length of hospital stay
WMD 4.78 days
(95% CI, 3.48-6.09; p <0.01, I² = 91%; moderate certainty)

Discussion

- **Key findings**
  - Common incidence of delirium (32%) among critically ill patients with AKI
  - Stepwise ↑ risk of developing delirium with worsening AKI stage
  - Delirium associated with ↑ risk of mortality, ↑ receipt of RRT, MV, & vasoactive therapy, as well as longer ICU & hospital stays
- Offer new insights by comprehensively synthesizing current evidence on the association between AKI & delirium in critically ill patients

- **Limitation**
  - Quality & heterogeneity of included studies
    - Diverse populations
    - Varying definitions of AKI & delirium
    - Regional disparities in healthcare systems & AKI management
  - Absence of clear time points for delirium onset relative to AKI, which limits interpretation of causality
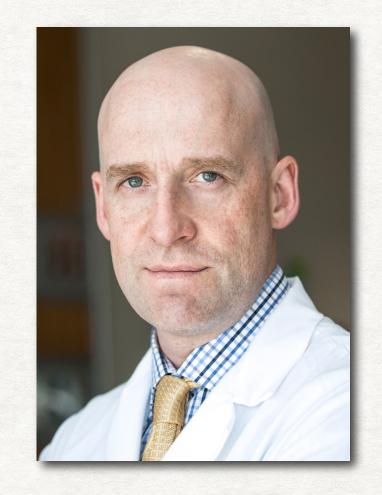- **Clinical application**
  - ↑ awareness of incident delirium
  - Early detection & management of AKI to mitigate the risk of kidney-brain crosstalk

Conclusion

- Delirium is common among critically ill patients with AKI & is associated with worse clinical outcomes & greater health resource use.

- Strategies to improve the recognition & monitoring of delirium may enhance ICU care & mitigate adverse patient outcomes.

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Thank You for Your Attention