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## **Appendix 5 (as supplied by the authors): Risk of bias assessment**

Table 1: Risk of bias of included studies for COVID-19 with ARDS

Table 2: Risk of bias of included randomized controlled trials for ARDS

Table 3: Risk of bias of included studies for COVID-19

Table 4: Risk of bias of included cohort studies for SARS

Table 5: Risk of bias of included randomized controlled trial for SARS

Table 6: Risk of bias of included studies for MERS

Table 7: Risk of bias of included cohort studies for influenza

Table 8: Risk of bias of included randomized controlled trial for influenza

Table 9: Risk of bias of included randomized controlled trials for CAP

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**Table 1: Risk of bias of included studies for COVID-19 with ARDS**

<b>Study</b>	<b>From the same population</b>	<b>Assessment of exposure</b>	<b>Outcome not present at start</b>	<b>Adjustment</b>	<b>Assessment of prognostic factors</b>	<b>Assessment of outcome</b>	<b>Adequate follow-up</b>	<b>Co-Interventions similar</b>
Wu 2020	Low	Probably low	Low	Probably low	Probably low	Low	Low	Probably high

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**Table 2: Risk of bias of included randomized controlled trials for ARDS**

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<b>Study</b>	<b>Sequence Generation</b>	<b>Allocation Sequence Concealment</b>	<b>Blinding (Performance bias)</b>	<b>Blinding (Outcome measurement)</b>	<b>Missing Outcome Data</b>	<b>Other Bias</b>	<b>Comments</b>
Steinberg, 2006	Low	Low	Low	Low	Low	Low	None
Meduri, 2007	Low	Low	Low	Low	Low	Probably High	Lack of protocol.
Liu, 2012	Low	Probably low	Low	Low	Low	Probably High	Allocation concealment is not reported and lack of protocol.
Rezk, 2013	High	Probably High	Low	Low	Low	Probably High	Baseline characteristics are imbalance and no detail of random sequence generation or allocation concealment and lack of protocol.
Zhao, 2014	Low	Probably low	Low	Low	Low	Probably High	Lack of protocol.
Tongyoo, 2016	Low	Probably low	Low	Low	Low	High	Discrepancies between the clinical trial registry and the study.
Villar, 2020	Low	Low	Low	Low	Low	Probably Low	This trial was stopped early, however, authors reported stopping roles, less than a 100 events, probability of overestimation of the effect estimate.

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**Table 3: Risk of bias of included studies for COVID-19**

<b>Study</b>	<b>From the same population</b>	<b>Assessment of exposure</b>	<b>Outcome not present at start</b>	<b>Adjustment</b>	<b>Assessment of prognostic factors</b>	<b>Assessment of outcome</b>	<b>Adequate follow-up</b>	<b>Co-Interventions similar</b>
Li 2020	Low	Low	Low	Probably low	Probably low	Low	Probably low	Probably high
Lu 2020	Low	Low	Low	Probably low	Probably low	Low	Probably low	Probably high
Wang 2020	Low	Low	Low	Probably high	Probably low	Low	Probably low	Probably high
Xu 2020	Low	Low	Low	Probably low	Probably low	Low	Probably low	Probably high
Yan 2020	Low	Low	Low	Probably high	Probably low	Low	Probably low	Probably high

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**Table 4: Risk of bias of included cohort studies for SARS**

<b>Study</b>	<b>From the same population</b>	<b>Assessment of exposure</b>	<b>Outcome not present at start</b>	<b>Adjustment</b>	<b>Assessment of prognostic factors</b>	<b>Assessment of outcome</b>	<b>Adequate follow-up</b>	<b>Co-Interventions similar</b>
Lau 2009	Low	Low	Low	Probably low	Low	Low	Low	Probably high
Long 2016	Low	Low	Low	Probably low	Low	Low	Low	Probably high

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**Table 5: Risk of bias of included randomized controlled trial for SARS**

<b>Study</b>	<b>Sequence Generation</b>	<b>Allocation Sequence Concealment</b>	<b>Blinding</b>	<b>Missing Outcome Data</b>	<b>Other Bias</b>
Lee 2004	Probably low	Probably low	Probably low	High	Low

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**Table 6: Risk of bias of included studies for MERS**

<b>Study</b>	<b>From the same population</b>	<b>Assessment of exposure</b>	<b>Outcome not present at start</b>	<b>Adjustment</b>	<b>Assessment of prognostic factors</b>	<b>Assessment of outcome</b>	<b>Adequate follow-up</b>	<b>Co-Interventions similar</b>
Alfaraj 2019	Low	Probably low	Low	Probably high	Probably low	Low	Low	Probably high
Arabi 2018	Low	Probably low	Low	Probably low	Probably low	Low	Probably low	High

**Table 7: Risk of bias of included cohort studies for influenza**

<b>Study</b>	<b>From the same population</b>	<b>Assessment of exposure</b>	<b>Outcome not present at start</b>	<b>Adjustment</b>	<b>Assessment of prognostic factors</b>	<b>Assessment of outcome</b>	<b>Adequate follow-up</b>	<b>Co-Interventions similar</b>
Al-Busaidi 2016	Yes	Yes	Yes	Probably yes	Probably no	Yes	Yes	No
Balaganesakumar 2013	Yes	Probably yes	Yes	Probably yes	Probably yes	Yes	Yes	No
Boudreault 2011	Yes	Yes	Yes	Probably yes	Probably yes	Yes	Yes	Probably no
Brun-Buisson 2011	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Probably no
Cao 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Probably no
Chawla 2013	Yes	Yes	Yes	No	Probably no	Yes	Yes	No
Delaney 2016	Yes	Yes	Yes	Yes	Probably yes	Yes	Yes	Probably yes
Delgado-Rodriguez 2012	Yes	Probably yes	Probably no	Probably yes	Yes	Yes	Yes	No
Han 2011	Yes	Yes	Probably yes	Probably yes	Yes	Probably yes	Yes	No
Jain 2009	Yes	Yes	Yes	No	Probably yes	Yes	Yes	No
Huang 2017	Yes	Yes	Yes	No	Probably no	Yes	Yes	No
Kim 2011	Yes	Yes	Yes	Probably no	Probably yes	Yes	Yes	No
Kinikar 2012	Yes	Yes	Yes	No	Probably yes	Yes	Yes	No
Kudo 2012	Yes	Yes	Yes	No	Probably no	Yes	Yes	No
Lee 2015	Yes	Yes	Yes	Probably yes	Probably yes	Yes	Yes	Probably yes
Li 2012	Yes	Probably no	Yes	No	Probably no	Yes	Yes	No
Li 2017	Yes	Yes	Yes	Yes	Probably yes	Yes	Yes	Yes
Liem 2009	Yes	Yes	Yes	No	Probably yes	Yes	Yes	No
Linko 2011	Yes	Yes	Yes	Probably yes	Probably yes	Yes	Yes	No

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Mady 2012	Yes	No	Yes	No	No	No	Yes	No
Moreno 2018	Yes	Yes	Yes	Yes	Probably yes	Yes	Yes	No
Ono 2016	Yes	Yes	Yes	Yes	Probably yes	Yes	Yes	Probably no
Patel 2013	Yes	Yes	Yes	No	Probably yes	Yes	Yes	Probably no
Sertogullarindan 2011	Yes	Probably yes	Yes	No	Probably no	Yes	Yes	No
Tsai 2020	Yes	Yes	Yes	Probably yes	Probably yes	Yes	Yes	Probably yes
Viasus 2011	Yes	Probably yes	Yes	No	Probably no	Yes	Yes	No
Wu 2012	Yes	No	No	Probably yes	Probably no	Probably yes	Yes	Probably no
Xi 2010	Yes	Yes	Yes	Probably yes	Probably yes	Yes	Yes	Probably no
Yu 2011	Yes	Yes	Yes	Yes	Probably yes	Yes	Yes	Probably no

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**Table 8: Risk of bias of included randomized controlled trial for influenza**

<b>Study</b>	<b>Sequence Generation</b>	<b>Allocation Sequence Concealment</b>	<b>Blinding</b>	<b>Missing Outcome Data</b>	<b>Other Bias</b>
Wirz 2016	Low	Low	Low	Low	Probably low

**Table 9: Risk of bias of included randomized controlled trials for CAP**

<b>Study</b>	<b>Sequence Generation</b>	<b>Allocation Sequence Concealment</b>	<b>Blinding (Performance bias)</b>	<b>Blinding (Outcome measurement)</b>	<b>Missing Outcome Data</b>	<b>Other Bias</b>	<b>Comments</b>
Wagner 1956	High	Probably High	Low	Low	Low	Probably High	Quasi-randomized controlled trial and lack of protocol.
McHardy 1972	Probably Low	Low	Probably High	Probably High	Probably High	Probably High	Lack of blinding, drop-out without explanation and lack of protocol.
Marik 1993	Low	Probably low	Probably High	Probably High	Low	Probably High	Lack of blinding and and lack of protocol.
Confalonieri 2005	Low	Low	Low	Low	Low	High	The trial stopped early and stopping role was a surrogate outcome with less of 50 patients included.
El-Ghamrawy, 2006	Probably High	Probably High	Probably High	Probably Low	Low	Probably High	Lack of information about random sequence generation, lack of protocol (sample size calculation) and blinding pf personal.
Mikami 2007	Probably High	Probably High	Probably High	Probably Low	Low	Probably High	Lack of information about random sequence generation, lack of protocol and blinding pf personal.
Snijders 2010	Low	Low	Low	Low	Low	High	Discrepancy between outcome reported in the registry and the published trial.

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Fernández-Serrano, 2011	Probably High	Probably High	Low	Low	Low	Low	Lack of information about random sequence generation.
Meijvis 2011	Low	Low	Low	Low	Low	High	Discrepancy between outcome reported in the registry and the published trial.
Sabry 2011	Probably High	Probably High	Low	Low	Low	High	Lack of information about random sequence generation and discrepancy between outcome reported in the registry and the published trial.
Nafae 2013	Probably High	Probably High	Probably low	Probably low	Low	Probably High	Lack of information about random sequence generation and lack of protocol.
Blum 2015	Low	Low	Low	Low	Low	Probably High	Only the primary outcome was reported in the registry.
Torres 2015	Low	Low	Low	Low	Low	Probably Low	None
Gang 2016	Low	Probably Low	Probably High	Low	Low	Probably High	Lack of protocol, sample size calculation and blinding in the personal.

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