# Impact of Colonization by Multidrug Resistant Bacteria on Graft Survival, Risk of Infection, and Mortality in Recipients of Solid Organ Transplant:

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POSTER

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Systematic Review and Meta-analysis

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#### BACKGROUND

- Colonization with multidrug resistant (MDR) in solid organ transplant (SOT) recipients increases the risk of post-transplant bacterial infection.
- The impact of MDR colonization on graft survival and mortality is not well established.
- This systematic review will identify and summarise the evidence behind the impact of MDR colonization on SOT recipients' mortality or graft failure or re-transplantation in addition to the risk of infection.

#### METHODS

- A search was executed by an expert on PROSPERO, OVID librarian Medline, Ovid EMBASE, Library, Cochrane ProQuest Dissertations and Theses Global and SCOPUS, from inception until October 26, 2021. Protocol was registered in PROSPERO 2022-CRD42022290011.
- Pairs of reviewers screened abstracts and full text studies for inclusion and extracted data independently.
- Data from studies on adult SOT recipients colonized MRSA, VRE, ESBL or AmpC producing bacteria, CRE, or MDR Pseudomonas were included and compared to non-colonized SOT recipients.
- We used RevMan to conduct a metaanalysis using the random effects models to calculate the pooled risk ratio (RR) with 95% confidence interval (CI) for the incidence of infection, mortality, or graft loss (GL).
- Statistical heterogeneity was determined using the I2 statistic.

# RESULTS

Organ	VRE (# of study)	MRSA	CRE	MDR PsA	ESBL
Liver	See graphs below	See graphs below	See graphs below	Infection (1), col 6/22 vs non-col 3/154; RR=14, 95%CI 3.77,51.99; p<0.001.	Infection (5), col 78/274 vs non-col 65/1729; RR=6.79; 95%CI 3.41,13.52, p<0.001; I2(73%).
Kidney		Mortality or graft loss (1) col 0/28 vs non-col 0/56.	Infection (1) col 64/309 vs non-col 54/453; RR= 1.74, 95%CI: 1.25, 2.42; p <0.001.		Infection (1) col 50/74 vs non-col 75/318; RR= 2.86, 95%CI: 2.22,3.69; p <0.001.
Lung		Infection (1), col 12/38 vs non-col 12/461; RR= 12.13, 95%CI: 5.85, 25.14; p <0.001.		Mortality or graft loss (1) col 2/25 vs 1/19; RR=1.52 [95%CI 0.15, 15.55]; p=0.72.	
Intestine or MVT	Infection (1) col 8/22 vs non-col 1/23; RR=8.36; 95%Cl 1.14,61.49, p=0.04		Infection (1), col 4/6 vs 2/39; RR=13, 95%Cl 3.01,56.18; p<0.001.		

### Liver Transplant: Risk of Infection

**VRE** colonization

# MRSA colonization

Heterogeneity:  $Tau^2 = 0.71$ ;  $Chl^2 = 117.80$ , df = 11 (P < 0.00001);  $l^2 = 91\%$  Test for overall effect: Z = 3.98 (P < 0.0001)

	Colon	zed	Non colo	nized		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M–H, Random, 95% CI	M–H, Random, 95% CI
3.7.2 Liver							
Bert 2000 - MRSA Infection liver (1)	7	8	8	79	11.1%	8.64 [4.26, 17.53]	
Bert 2005 - MRSA Infection liver (2)	15	19	48	304	15.6X	5.00 [3.53, 7.08]	-
Desal 2003 - MRSA Infection Liver	11	35	11	122	10.6%	3.49 [1.65, 7.35]	<del></del>
Hashimoto 2008 – MRSA infection Liver (3)	16	61	9	181	10.4%	5.28 [2.46, 11.32]	_ <del>-</del>
Kim 2015 – MRSA infection Liver (4)	9	21	10	121	10.3%	5.19 [2.40, 11.22]	_ <del>-</del>
Russell 2008 – MRSA Infection Liver	16	47	29	659	13.3X	7.74 [4.54, 13.19]	
Singh 2000 – MRSA infection Liver (5)	14	30	5	21	9.4%	1.96 [0.83, 4.61]	<del>  • -</del>
Woeste 2005 - MRSA Infection Liver	4	12	12	54	8.5%	1.50 [0.58, 3.85]	<del>-   • -</del>
Subtotal (95% CI)		233		1541	89.2%	4.50 [3.09, 6.55]	•
Total events	92		132				

		CI	RE	CO	lon	ization	
Sanda - Sala	Colon		Non colo		14-1-ba	Risk Ratio	Risk Ratio
Study or Subgroup	Events	iotai	Events	rotai	Weight	M–H, Random, 95% CI	M-H, Random, 95% CI
3.5.1 Liver							
Chen 2020 – CRE Infection liver	13	65	13	322	10.8%	4.95 [2.41, 10.19]	
Freire 2017 – CRE Infection Liver (1)	36	114	3	248	9.9%	26.11 [8.21, 83.00]	-
Glannella 2019 - CRE Infection Liver (2)	51	147	6	406	10.6%	23.48 [10.29, 53.55]	
Lubbert 2014 – CRE Infection Liver	8	9	0	18	6.0%	32.30 [2.07, 503.97]	
Macesic 2018 - CRE Infection Liver (3)	3	25	0	103	5.7%	28.00 [1.49, 525.35]	
Mazza 2017 - CRE Infection Liver (4)	8	20	44	290	10.9%	2.64 [1.44, 4.81]	_ <del></del>
Subtotal (95% CI)		380		1387	53.9%	11.31 [3.67, 34.79]	
Total events	119		66				
Heterogeneity: $Tau^2 = 1.43$ ; $Chi^2 = 33.53$ , Test for overall effect: $Z = 4.23$ (P < 0.000	_	< 0.00	(001); ř =	85%			

#### Liver Transplant: Risk of Mortality or Graft Loss

#### **VRE** colonization

	Coloni	zed	Non colo	nized		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M–H, Random, 95% CI
2.4.1 Liver							
Banach 2016 – VRE death liver (1)	4	27	1	34	5.6X	5.04 [0.60, 42.48]	<del>                                     </del>
Ejtehadi 2021 – VRE Death Liver (2)	3	51	78	702	15.2%	0.53 [0.17, 1.62]	
Kim 2015 – VRE Death Liver (3)	10	58	13	84	23.6%	1.11 [0.52, 2.37]	<del>-</del>
McNell 2006 – VRE Death Liver (4)	5	22	6	98	15.6%	3.71 [1.24, 11.07]	_ <del>-</del>
Russell 2008 – VRE Death Liver Subtotal (95% CI)	46	103 261	167	603 1521	40.0% 100.0%	1.61 [1.26, 2.07] 1.51 [0.88, 2.60]	
Total events Heterogeneity: $Tau^2 = 0.17$ ; $Chi^2 = 6$ . Test for overall effect: $Z = 1.51$ (P = 0	-	4 (P =	265 0.08); ř =	51 <b>%</b>			
Total (95% CI)		261		1521	100.0%	1.51 [0.88, 2.60]	•
Total events	68		265				
Heterogeneity: $Tau^2 = 0.17$ ; $Chi^2 = 8$ . Test for overall effect: $Z = 1.51$ (P = ( Test for subgroup differences: Not app	).13)	4 (P =	0.08); l² =	51 <b>%</b>			0.01 0.1 1 10 Non-Colonized Colonized

#### MRSA colonization

		zed	Non colo			Risk Ratio	Risk Ratio
tudy or Subgroup	Events	Total	Events	Total	Weight	M–H, Random, 95% CI	M–H, Random, 95% CI
.5.1 Liver							
esal 2003 – MRSA Death Liver (1)	11	35	24	122	25.5%	1.60 [0.87, 2.93]	+-
lm 2015 – MRSA Death Liver (2)	4	10	10	121	15.5%	4.84 [1.85, 12.69]	_ <del></del>
ussell 2008 – MRSA Death Liver	18	47	196	659	34.3%	1.29 [0.88, 1.89]	<del> -</del>
akemura 2019 – MRSA Death Liver (3)	4	14	12	92	15.2%	2.19 [0.82, 5.85]	+-
oeste 2005 – MRSA Death Liver (4)	3	12	4	54	9.5%	3.38 [0.87, 13.15]	<del>  • • • • • • • • • • • • • • • • • • •</del>
ubtotal (95% CI)		118		1048	100.0%	1.98 [1.24, 3.18]	•
otal events	40		246				

#### CRF colonization

	Coloni	zed	Non colo	nized		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
2.6.2 Liver							
reire 2017 – CRE Death Liver (1)	76	182	57	204	38.4%	1.49 [1.13, 1.98]	-
ubbert 2014 – CRE Death Liver (2)	7	9	2	18	28.2%	7.00 [1.81, 27.07]	
Mazza 2017 – CRE Death Liver (3)	6	20	10	290	33.3%	8.70 [3.52, 21.51]	
Subtotal (95% CI)		211		512	100.0%	4.16 [1.06, 16.26]	
Fotal events	89		69				
Heterogeneity: $Tau^2 = 1.24$ ; $Chl^2 = 17.2$	3. df = 2 (P)	= 0.00	$02$ ): $t^2 = 6$	8%			

# Figure 1 PRISMA flow chart 5774 Citations 3560 Non-duplicate Citations Screened Inclusion/Exclusion 2940 Articles Excluded Criteria Applied After Title/Abstract Screen 620 Articles Retrieved **1585 Articles Excluded After** Inclusion/Exclusion Criteria Applied Full Text Screen 35 Articles

#### CONCLUSION

Included in Meta

analysis

While colonization with VRE in liver transplant was not associated with increase mortality, CRE or MRSA colonization were associated with almost 4- or 2-fold increased risk of death, respectively. These data should be taken into account when stratifying the risk of transplant.

# GL: Graft loss;

Abbreviations:

MDR: Multi Drug resistant; MRSA:Methicillin Staphylococcus aureus; VRE Vancomycin-resistant Enterococci; ESBL: Extended-spectrum betalactamase; CRE: carbapenem colonized; CI: Confidence inter-Tx: transplant. MVT: multi-viscera transplant



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