Updates in Covid-19 Treatments: Moving Targets
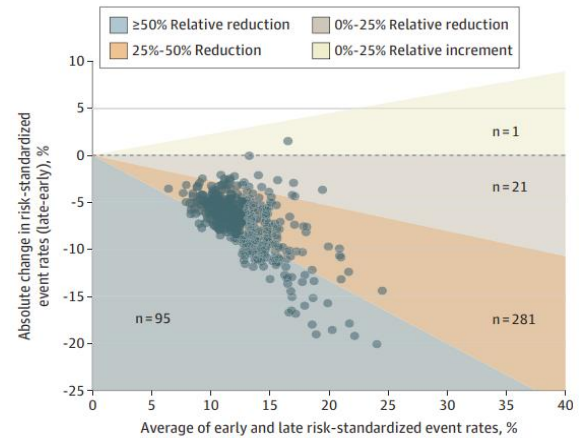
Trends in Covid-19 Care

Context: New cases in the US are down-trending, hopefully indicating progress in combatting the pandemic.

Current: The mortality of patients admitted with Covid-19 also seems to be improving, although huge variability in Covid-19 mortality exists.[1]

Cutting Edge: Standardizing care for Covid-19 patients based on current (and dynamic) evidence may standardize and improve mortality across the US healthcare system.

Anti-inflammatory Agents

Context: Dexamethasone is the 1st treatment to demonstrate mortality benefit.[2]

Current: Tocilizumab is an anti-IL6 receptor that has been shown to potentially reduce LOS and mortality, although the benefit is unclear on meta-analysis.[3]

Cutting edge: Dexamethasone and tocilizumab may work best in conjunction for selected patients.

	Deaths / Patients randomised (%)		Observed−Expected		Ratio of death rates, RR (95% CI)
	Tocilizumab	Usual care	(O−E)*	Var(O−E)	
COR−IMUNO TOCI	7/64 (10.9)	8/67 (11.9)	−0.3	3.3	0.91 (0.31−2.65)
RCT−TCZ−COVID−19	2/60 (3.3)	1/66 (1.5)	0.6	0.7	2.17 (0.22−21.3)
BACC Bay	9/161 (5.6)	(3/82) x2† (3.7)	1.0	2.6	1.51 (0.44−5.13)
COVACTA	58/294 (19.7)	(28/144) x2† (19.4)	0.3	15.3	1.02 (0.62−1.68)
EMPACTA	26/249 (10.4)	(11/128) x2† (8.6)	1.6	7.5	1.23 (0.60−2.52)
REMAP−CAP	98/353 (27.8)	142/402 (35.3)	−14.2	40.8	0.71 (0.52−0.96)
TOCIBRAS	14/65 (21.5)	6/64 (9.4)	3.9	4.3	2.51 (0.97−6.50)
Subtotal: 7 trials	214/1246 (17.2)	241/1307 (18.4)	−7.2	74.5	0.91 (0.72−1.14)
RECOVERY	596/2022 (29.5)	694/2094 (33.1)	−48.2	316.0	0.86 (0.77−0.96)
All trials	810/3268 (24.8)	935/3401 (27.5)	−55.4	390.5	0.87 (0.79−0.96) p=0.005

Heterogeneity between RECOVERY and previous trials: χ^2_1=0.2

Remdesivir

Context: Early studies of the anti-viral remdesivir demonstrated quicker recovery but not improved mortality.

Current: A well-powered (1,062 patients) pragmatic study found reduced time for recovery (10 days vs. 15 days, p<0.001) and trend toward reduced mortality with HR of 0.55 ((5% CI 0.36-0.83) at 15 days and 0.73 (95% CI 0.52-1.03) at 29 days.[4]

Cutting Edge: Remdesivir seems to be most effective for those with <10 days of symptoms and requiring oxygen but not on mechanical ventilation.

Convalescent Plasma

Context: The utility of convalescent plasma for conveying passive immunity to Covid-19 remains unclear.

Current: Recent trials suggest potential benefit with high titers of anti-SARS-CoV2 antibodies.[4]

Cutting Edge: Hight titer plasma is potentially beneficial if given within 3 days of symptoms or hospitalization.

References:
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2.   RECOVERY Collaborative Group. Dexamethasone in Hospitalized Patients with Covid-19. NEJM. 2021;384(8):693-704.
3.   RECOVERY Collaborative Group. Tocilizumab in patients admitted to hospital with Covid-19: preliminary results of 5 randomised, controlled, open-label, platform trial. Posted 2/11/21 on MedRxiv: https://www.medrxiv.org/content/10.1101/2021.02.11.21249258v1%20
4.   ACTT-1 Study Group. Remdesivir for the Treatment of Covid-19 – Final Report. NEJM. 2020;383(19):1813-1826,
5.   MJ Joyner, et al. Convalescent Plasma Antibody Levels and the Risk of Death from Covid-19. NEJM, Published on-line ahead of print January 13, 2021. DOI: 10.1056/NEJMoa2031893