DCCM COVID-19 Town Hall

May 6, 2020

Welcome/Ground Rules

- Welcome
- Webinar Format
  - Host and panelists
  - Audience participation/Chat

Agenda

- COVID-19 Dashboard
- Emerging COVID literature
  - Epidemiology and outcomes data
  - Use of systemic corticosteroids
- Questions

COVID-19 Dashboard

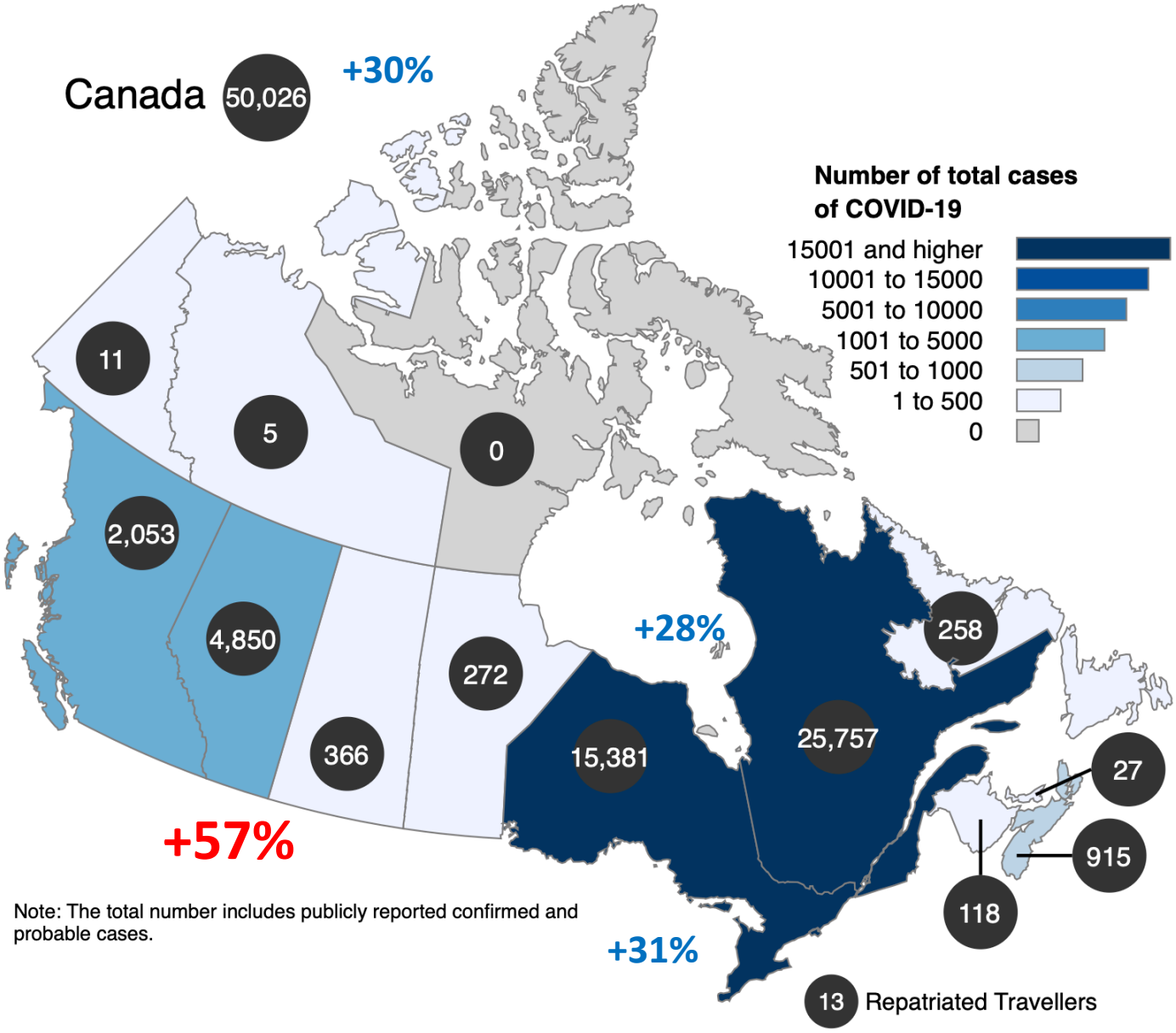
Dan Niven

Sources of Information up to May 5:

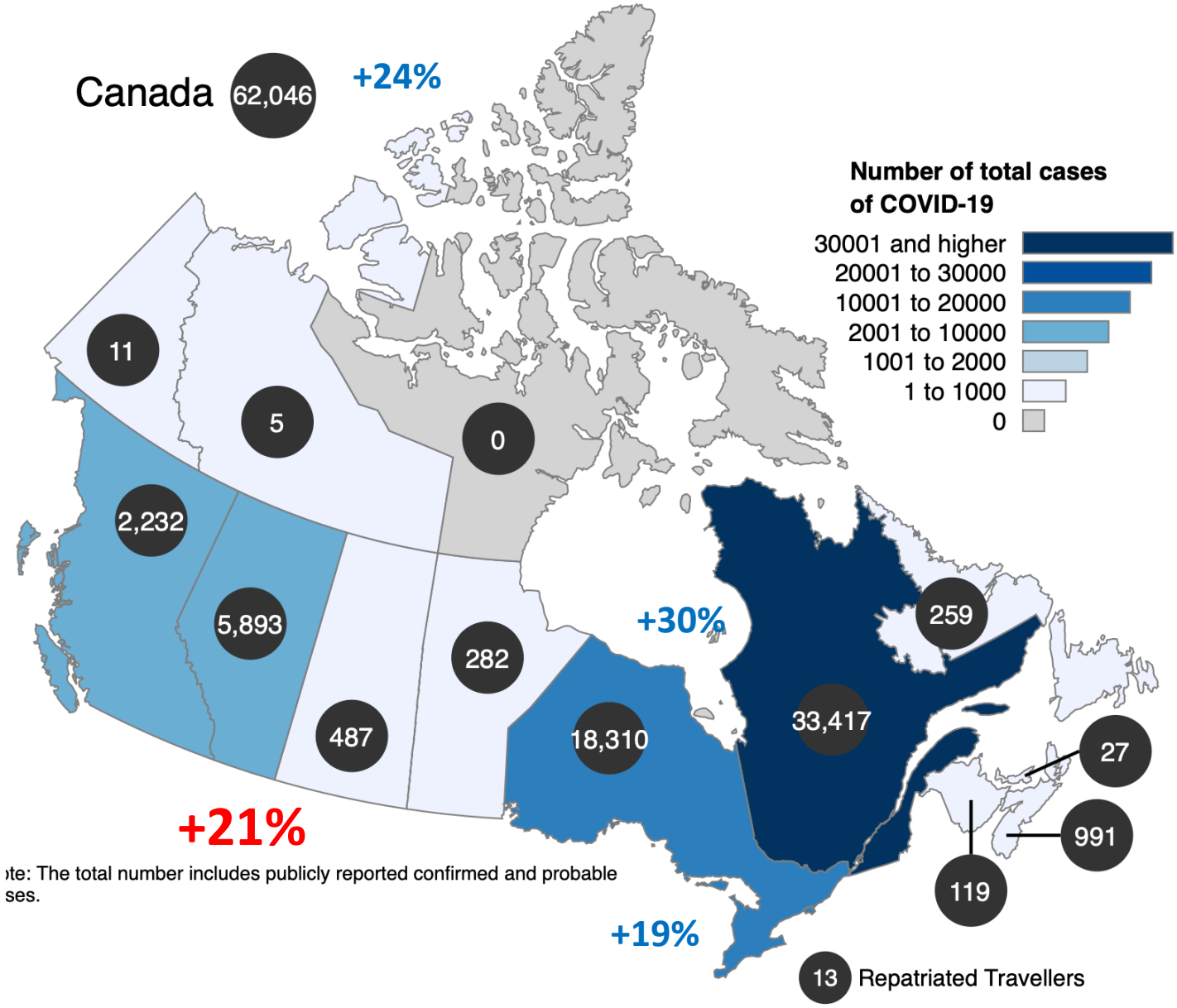
https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection.html#a1

https://www.alberta.ca/covid-19-alberta-data.aspx

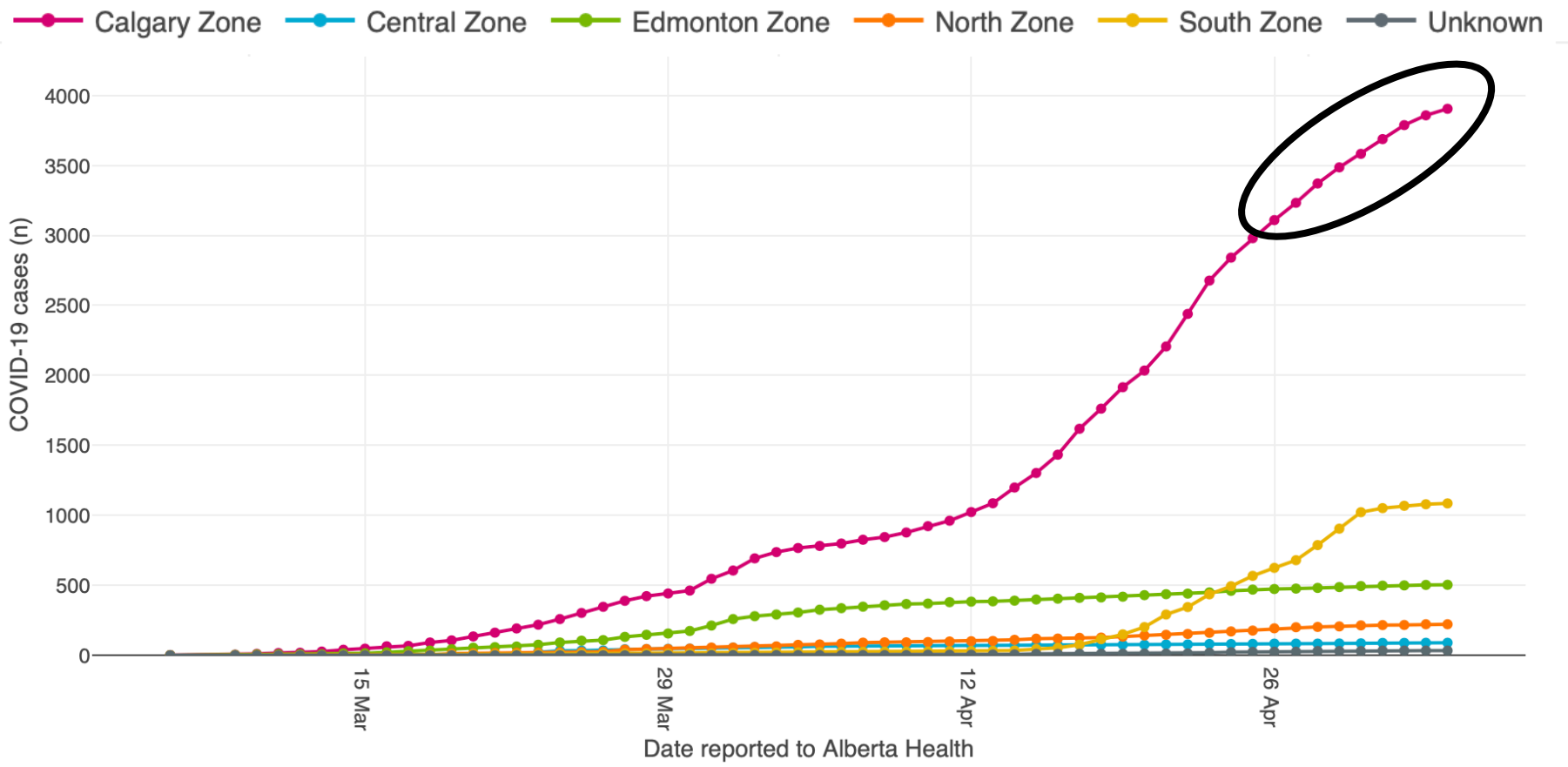
APRIL 28


Canada 50,026
+30%
Number of total cases of COVID-19
15001 and higher
10001 to 15000
5001 to 10000
1001 to 5000
501 to 1000
1 to 500
0
11
5
0
2,053
4,850
272
366
+28%
258
25,757
15,381
27
915
118
+57%
+31%
13 Repatriated Travellers
Note: The total number includes publicly reported confirmed and probable cases.

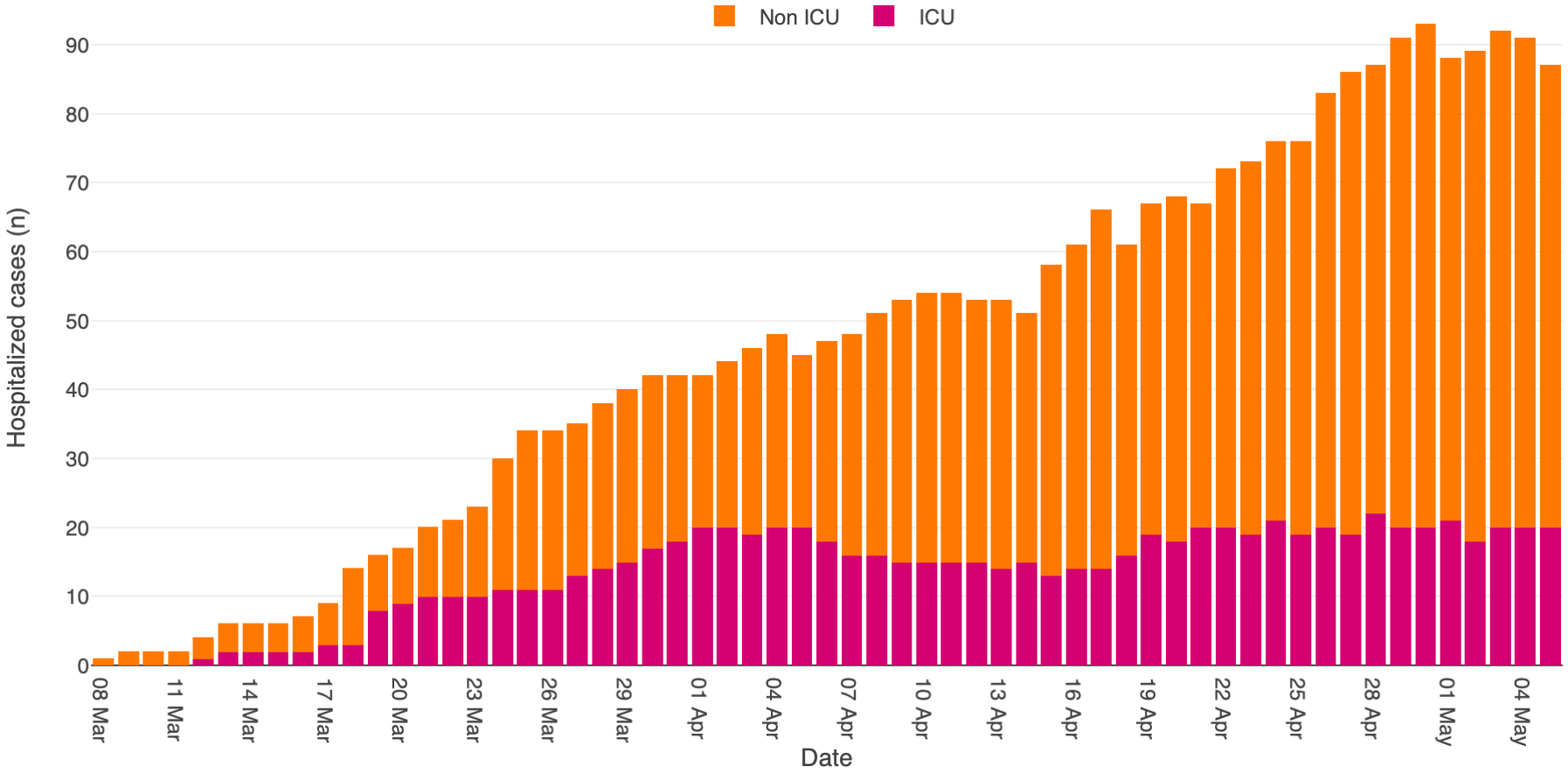
May 6


Canada 62,046
+24%
Number of total cases of COVID-19
30001 and higher
20001 to 30000
10001 to 20000
2001 to 10000
1001 to 2000
1 to 1000
0
11
5
0
2,232
5,893
487
282
+30%
259
33,417
18,310
27
991
119
+21%
+19%
13 Repatriated Travellers
ote: The total number includes publicly reported confirmed and probable
ses.

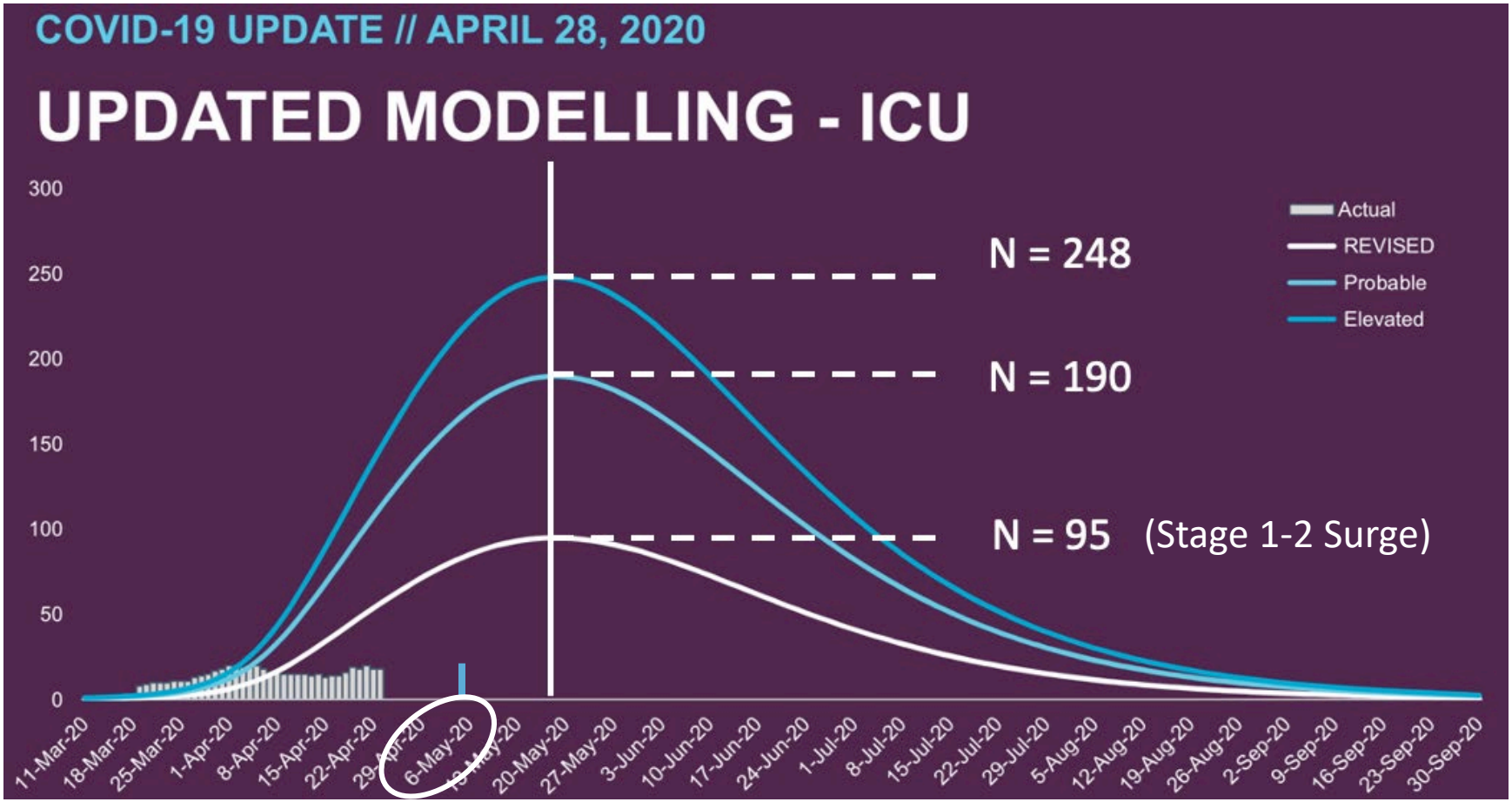
Alberta – Slowed Growth Even in Calgary and South Zones



67 Hospitalized Non-ICU, 20 in ICU



Actual < Revised 'Low' Model



May 5, N = 20 COVID Patients in Alberta ICUs

COVID-19 Critical Care Literature Update: Epidemiology & Outcomes

Dan Niven

Research

JAMA | Original Investigation

Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area

Safiya Richardson, MD, MPH; Jamie S. Hirsch, MD, MA, MSB; Mangala Narasimhan, DO; James M. Crawford, MD, PhD; Thomas McGinn, MD, MPH; Karina W. Davidson, PhD, MASc; and the Northwell COVID-19 Research Consortium

Richardson et al. *JAMA* 2020

- Case series of 5700 patients admitted to 12 hospitals in state of New York between March 1 and April 4
- SARS-CoV-2 confirmed by RT-PCR on NP swab

- Of 5700 patients
  - **3066 remain in hospital at time of publication**
  - **2634 discharged or died**

JAMA. doi:10.1001/jama.2020.6775

Richardson et al. *JAMA* 2020

- Median age 63y, 60% male, 57% HTN, 34% DM, 42% obese

- **Outcomes (among discharged or died, n = 2634)**
  - **Overall Mortality**: 553/2634 = **21%**
  - ICU Admission: 373/2634 = 14%
  - Invasive ventilation in ICU: 320/373 = 86%

JAMA. doi:10.1001/jama.2020.6775

Richardson et al. *JAMA* 2020

- **Outcomes among the 373 patients admitted to ICU**
- **Total deaths: n = 291, 78%**
- **Total deaths by age**
  - 18 – 65y: 109/171 = 64%
  - > 65y: 182/200 = 91%

- **Invasive mechanical ventilation: n = 320**
  - **Total deaths**: n = 282, **88%**
  - 18 – 65y: 107/140: 76%
  - >65y: 175/180: 95%

JAMA. doi:10.1001/jama.2020.6775

Richardson et al. *JAMA* 2020
Correction…

Among the 2634 patients who were discharged or had died at the study end point, during hospitalization, 373 (14.2%) were treated in the ICU, 320 (12.2%) received invasive mechanical ventilation, 81 (3.2%) were treated with kidney replacement therapy, and 553 (21%) died (**Table 5**). As of April 4, 2020, for patients requiring mechanical ventilation (n = 1151, 20.2%), 38 (3.3%) were discharged alive, 282 (24.5%) died, and 831 (72.2%) remained in hospital. Mortal-

?

JAMA. doi:10.1001/jama.2020.6775

Richardson et al. *JAMA* 2020

- **Limitations:**
- There are **3,066 patients still in hospital** including in ICU, and including those on a ventilator…
  - It's possible these are patients **who are more likely to survive and current mortality estimates are overestimates within this cohort…**

- We **have a paucity of data on the 373 patients admitted to ICUs** and even less on the 320 patients invasively ventilated…

JAMA. doi:10.1001/jama.2020.6775

Understanding pathways to death in patients with COVID-19

- **Highly variable reported case fatality rates** for COVID-19 – cause of death is important

- Propose **3 important characteristics of the dying process** in COVID-19
  - Predominant terminal organ failure (e.g. die on ECMO)
  - Proportionality of care (some limitation on life support)
  - Involvement of COVID-19 in the dying process (die with COVID-19 not due to COVID-19)

Lancet Resp Med 2020 Published online April 6 2020

icnarc intensive care national audit & research centre

25 years and counting...

Napier House
24 High Holborn
London WC1V 6AZ
email: COVID-19@icnarc.org
www.icnarc.org

ICNARC report on COVID-19 in critical care

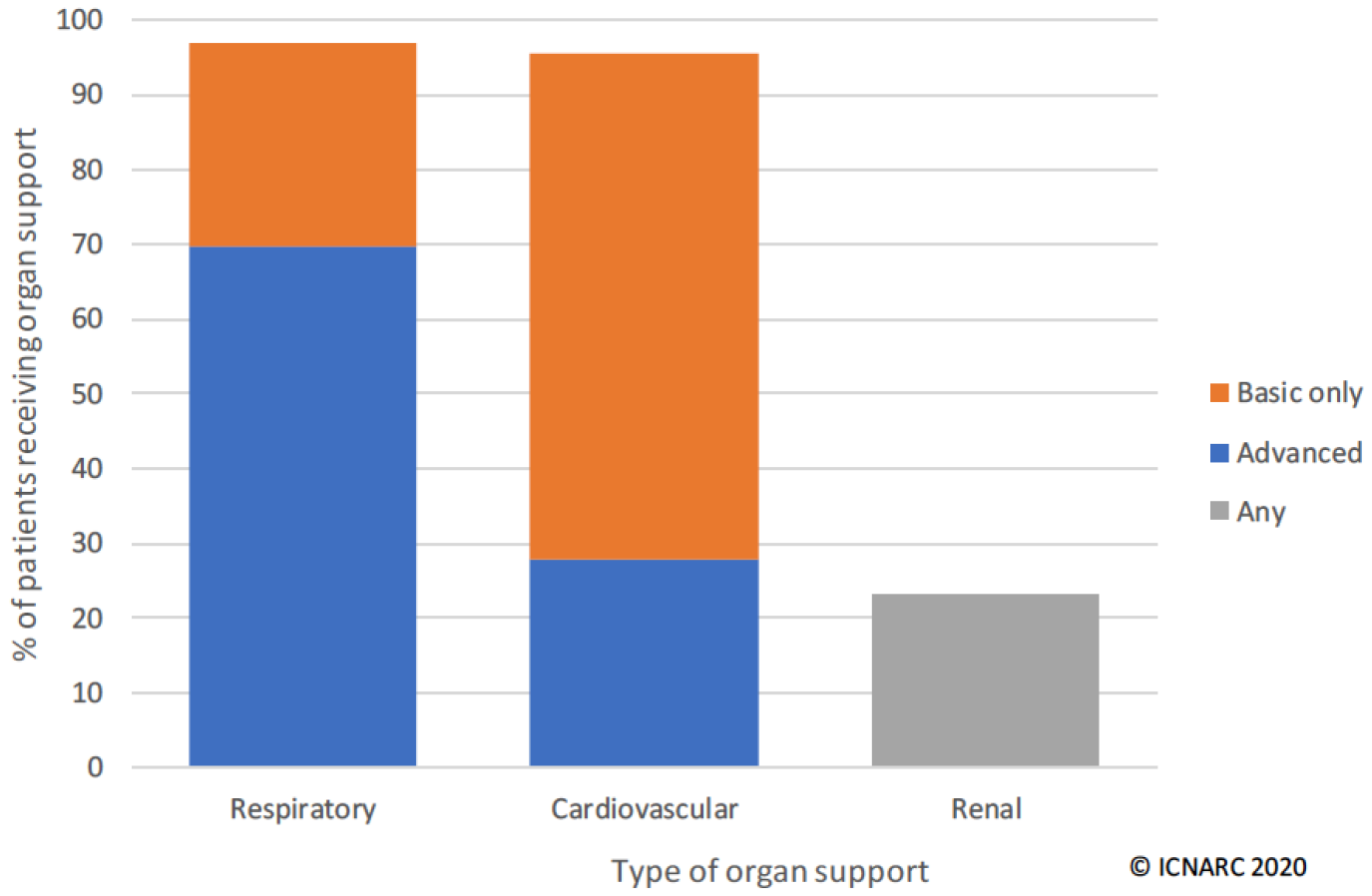
01 May 2020

- One of (if not the…) **best source of data on critically ill COVID-19 patients** to date
- **7,542 patients with COVID-19 from 254 adult ICUs** in England, Wales, and Northern Ireland
- **5,139 patients with outcome data** reported

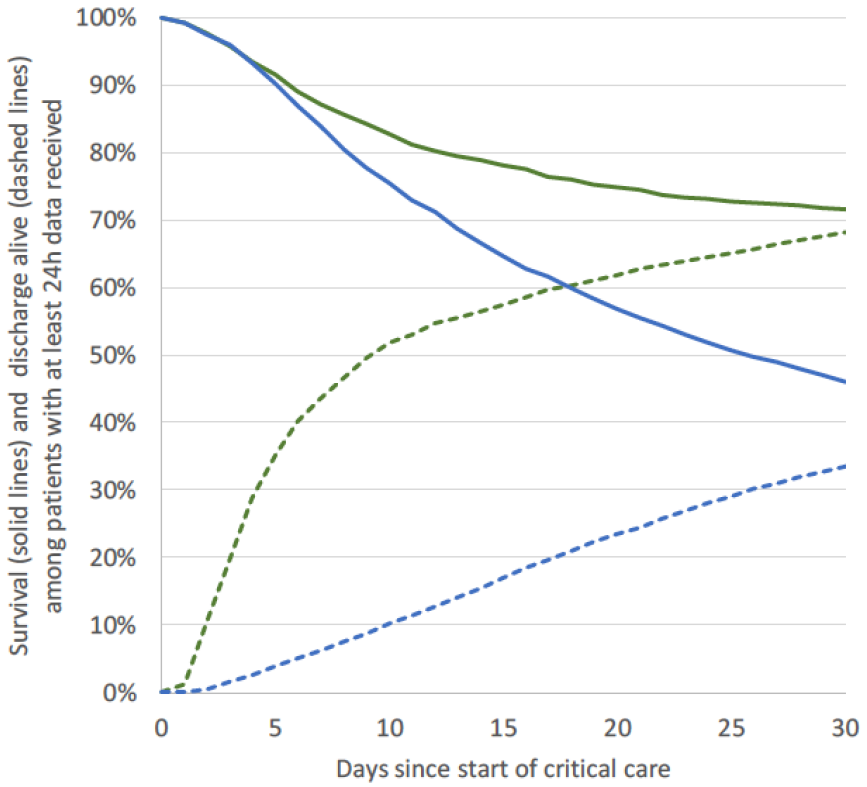
COVID-19 Compared to Non-COVID Viral Pneumonia

Characteristic	Patients with COVID-19 N = 7542	Non-COVID Viral PNA 2017-19 N=5782
Median Age (IQR)	60 (52 – 68) years	61 (48 – 71) years
Male Sex	**72%**	**54%**
Non-caucasian ethnicity	**41%**	**14%**
Very severe comorbidity	8%	24%
PaO2/FiO2 ratio < 200 mmHg	88%	77%
Median APACHE II (IQR)	14 (11 – 18)	17 (13 – 21)
Mechanical ventilation in 1st 24h	66%	43%
Death in ICU	**49%**	**22%**
Median ICU LOS in Survivors (IQR)	6 (3 – 13) days	6 (3 – 12) days
Median duration advanced resp support	9 (5 – 15) days	9 (4 – 17) days

COVID-19 Patients: Organ Support Received



Survival Dependent on Degree of Organ Support Required



Patients not receiving mechanical ventilation in the first 24h

Patients receiving mechanical ventilation in the first 24h

Survival > 70%

Survival < 50%

Other Factors Associated with Death: COVID-19 Compared to Non-COVID Viral Pneumonia

Characteristic	Patients with COVID-19 Who Died in Critical Care	Non-COVID Viral PNA 2017-19 Who Died in Critical Care
Age >= 70 years	67%	32%
Male sex	51%	24%
Any very severe comorbidities	57%	34%
Advanced resp support only	47%	19%
Adv resp & adv cardiovascular support	71%	41%
Adv resp, adv cardiovascular and any renal support	**83%**	**58%**

https://www.icnarc.org/Our-Audit/Audits/Cmp/Reports

COVID-19 Thrombotic Phenotype – Link To MODS?

Hamilton

Nick Cordero's leg amputation, one of many possible COVID-19 complications

The Canadian Press · Posted: Apr 23, 2020 9:42 AM ET | Last Updated: April 23

CORRESPONDENCE

COVID-19 CASES

Coagulopathy and Antiphospholipid Antibodies in Patients with Covid-19

CORRESPONDENCE

ST-Segment Elevation in Patients with Covid-19 — A Case Series

Photo by Brad Barket/Invision/AP, File
https://www.cbc.ca/news/canada/hamilton/cordero-amputations-complications-1.5542217

ORIGINAL

High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study

Check for updates

- **Propensity-matched cohort study from 4 ICUs** in France
  - Historical controls

- Matched 145 non-COVID ARDS pt, 77 COVID ARDS pt:
  - **Increased pulmonary emboli: 11.7% vs 2.1% (p = 0.01)**
  - Increased extracorporeal circuit clotting (CRRT Filters)

- **Mechanism increased thrombogenicity not clear**
  - **88% of tested patients has positive lupus anticoagulant**

COVID-19 Epidemiology & Outcomes: Take Home Points

- **Mortality rates** among patients admitted to ICU with COVID-19 are **highly variable**
  - Challenges include incomplete follow-up data and lack of information on 'cause of death'

- Mortality highest among those mechanically ventilated who also require advanced cardiovascular and renal support

COVID-19 Critical Care Literature Update: Role of corticosteroids

Chip Doig

OPEN

Fact Versus Science Fiction: Fighting Coronavirus Disease 2019 Requires the Wisdom to Know the Difference

Nicholas E. Ingraham, MD[1]; Christopher J. Tignanelli, MD[2,3]

Clinicaltrials.gov

- 25 ‘clinical trials’; 17 in COVID-P
- 1 completed (data to be shown)
- 12 recruiting
- 1 suspended
- 3 not yet recruiting
- Variability in populations studied (ARDS, requiring oxygen therapy, cytokine storm, etc)

Pharmacologic treatments for coronavirus disease 2019 (COVID-19). Sanders JM, Monogue ML, Jodlowski TZ et al. JAMA 2020 doi:10.1001/jama.2020.6019

Corticosteroids:

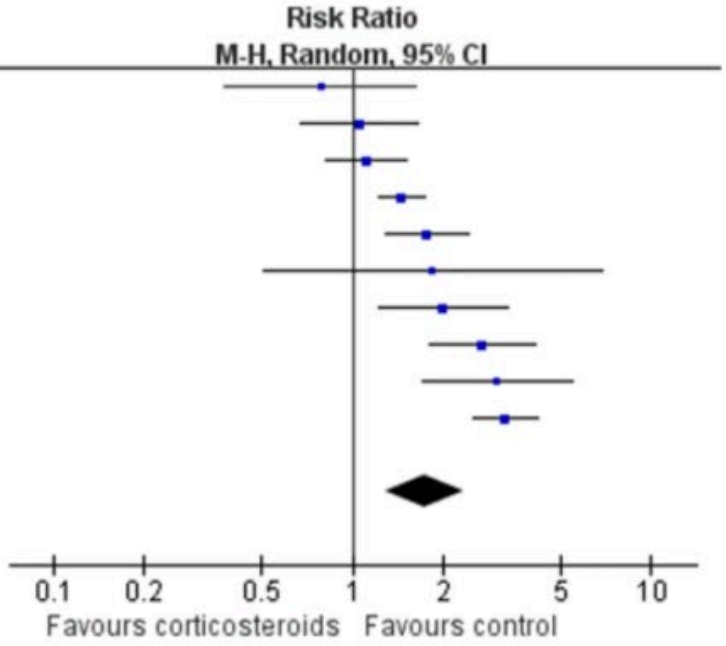
- Rationale is to decrease host inflammatory response which may lead to ALI/ARDS
- Risk is delayed viral clearance, and increased risk of secondary infections
- Observational data from SARS/MERS: no improved survival, delayed viral clearance blood/resp tract, and high rates of complications including avascular necrosis

The effect of corticosteroids on mortality of patients with influenza pneumonia: a systematic review and meta-analysis. Ni Y, Chen G, Sun J, et al. Crit Care 2019; doi:10.1186/s13054-019-2395-8

Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Perez-Padilla 2009	4	7	8	11	7.4%	0.79 [0.38, 1.64]
Diaz 2012	25	136	41	236	10.3%	1.06 [0.67, 1.66]
Rios 2011	38	75	47	103	11.8%	1.11 [0.82, 1.51]
Moreno 2018	166	604	234	1242	12.9%	1.46 [1.23, 1.74]
Lee 2014	50	264	87	817	11.7%	1.78 [1.29, 2.45]
Viasus 2011	3	37	7	160	3.7%	1.85 [0.50, 6.83]
Brun-Buisson 2011	28	83	21	125	9.9%	2.01 [1.23, 3.29]
Jung 2011	54	99	24	120	10.9%	2.73 [1.83, 4.07]
Cao 2016	81	204	11	84	9.0%	3.03 [1.70, 5.40]
Li 2017	232	1055	74	1086	12.4%	3.23 [2.52, 4.13]
Total (95% CI)		**2564**		**3984**	**100.0%**	**1.75 [1.30, 2.36]**
Total events	681		554			

Heterogeneity: $Tau^2 = 0.17$; $Chi^2 = 55.99$, $df = 9$ ($P < 0.00001$); $I^2 = 84\%$

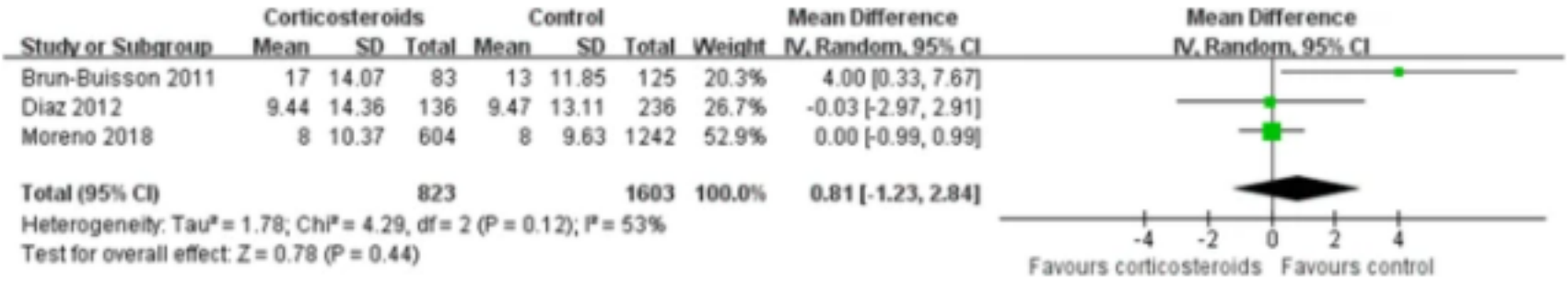
Test for overall effect: $Z = 3.71$ ($P = 0.0002$)



Effect of corticosteroids on mortality. CI, confidence interval; RR, risk ratio

The effect of corticosteroids on mortality of patients with influenza pneumonia: a systematic review and meta-analysis. Ni Y, Chen G, Sun J, et al. Crit Care 2019; doi:10.1186/s13054-019-2395-8

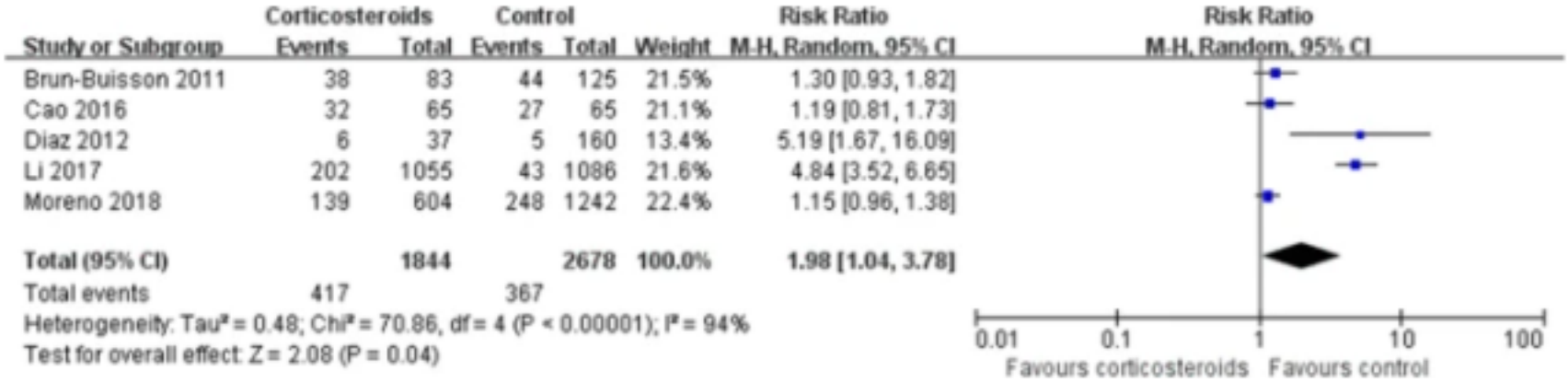
Fig. 4



Effect of corticosteroids on MV days. Diamonds indicate overall estimates from the meta-analysis; squares indicate point estimates of the result of each study; horizontal lines represent 95% CI. CI, confidence interval; MV, mechanical ventilation; MD, mean difference

The effect of corticosteroids on mortality of patients with influenza pneumonia: a systematic review and meta-analysis. Ni Y, Chen G, Sun J, et al. Crit Care 2019; doi:10.1186/s13054-019-2395-8

Fig. 6



Effect of corticosteroids on the rate of secondary infection. Diamonds indicate overall estimates from the meta-analysis; squares indicate point estimates of the result of each study; horizontal lines represent 95% CI. CI, confidence interval; RR, risk ratio

Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Russell CE, Millar JE, Baillie JK.
On the use of corticosteroids for 2019-nCoV pneumonia. Shang L, Zhao J, Hu Y, Du R, Cao B. Lancet 2020

Table

Summary of clinical evidence to date

	Outcomes of corticosteroid therapy*	Comment
MERS-CoV	Delayed clearance of viral RNA from respiratory tract[2]	Adjusted hazard ratio 0·4 (95% CI 0·2–0·7)
SARS-CoV	Delayed clearance of viral RNA from blood[5]	Significant difference but effect size not quantified
SARS-CoV	Complication: psychosis[6]	Associated with higher cumulative dose, 10 975 mg *vs* 6780 mg hydrocortisone equivalent
SARS-CoV	Complication: diabetes[7]	33 (35%) of 95 patients treated with corticosteroid developed corticosteroid-induced diabetes
SARS-CoV	Complication: avascular necrosis in survivors[8]	Among 40 patients who survived after corticosteroid treatment, 12 (30%) had avascular necrosis and 30 (75%) had osteoporosis
Influenza	Increased mortality[9]	Risk ratio for mortality 1·75 (95% CI 1·3–2·4) in a meta-analysis of 6548 patients from ten studies
RSV	No clinical benefit in children[10], [11]	No effect in largest randomised controlled trial of 600 children, of whom 305 (51%) had been treated with corticosteroids

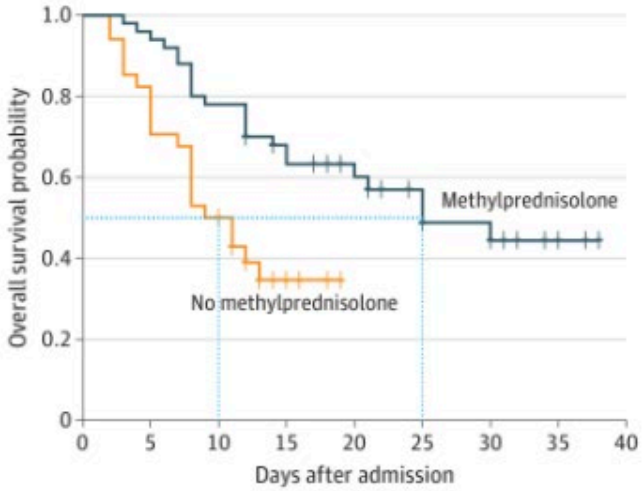
Risk factors associated with ARDS and death in patients with coronavirus disease 2019 pneumonia in Wuhan China.
Wu et al. JAMA Int Med 2020; doi:10.1001/jamainternmed.2020.0994

Methods:

- Retrospective cohort of 201 patients HOSPITALIZED with confirmed COVID-19 at Jinyintan Hospital, Wuhan
- Admitted Dec 25→Jan 26.
- All confirmed + by RT-PCR
- Broadly tested for other ILI and bacterial pathogens
- Outcome: development ARDS, mortality

Wu et al. JAMA Int Med 2020; doi:10.1001/jamainternmed.2020.0994
Controversial: corticosteroids not currently recommended.

Figure. Survival Curve in Patients With Acute Respiratory Distress Syndrome Who Did and Did Not Receive Methylprednisolone Treatment



No. at risk

No methylprednisolone	34	28	17	4	0	0	0	0	0
Methylprednisolone	50	48	39	29	20	14	11	4	0

Administration of methylprednisolone reduced the risk of death (hazard ratio, 0.38; 95% CI, 0.20-0.72; $P = .003$).

Early short course corticosteroids in hospitalized patients with COVID-19. Fadel R, et al. medRxiv doig:10.1101/2020.05.04/20074609
Pre print, not peer-reviewed!

- Quasi-experimental pre/post test study
- Moderate-severe adult patients with hypoxemia
- Multicentre health system in Michigan
- 0.5-1.0 mg/kg/d ÷ 2 doses methylprednisolone
- Composite end-point: transfer from ward to ICU, requirement for mechanical ventilation, mortality

Early short course corticosteroids in hospitalized patients with COVID-19. Fadel R, et al. medRxiv doig:10.1101/2020.05.04/20074609
Pre print, not peer-reviewed!

Results:

- N=213: 81 pre (control), 132 post (treatment)
- Composite outcome in 54.3% of control group compared to 34.9% of treatment group (reported effect in all endpoints); OR of composite outcome at 14 days 0.45 (0.25-0.81)
- Reduction in median hospital LOS: 8 vs 5 days

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- Reduction in median hospital LOS: 8 vs 5 days

Infectious Diseases Society of America Guidelines on the treatment and management of patients with COVID-19. Bhimraj A, et al. Clin Infec Dis 2020 (epub ahead of print) doi:10.1093/cid/ciaa478/5825667

- Evidence based rapid guidelines
- Multidisciplinary panel: clinicians/methodologists
- Systematic review + GRADE recommendations
- 7 treatment recommendations
- #5: patients who have been admitted to the hospital with ARDS due to COVID-19, … recommends the use of corticosteroids in the context of a clinical trial (Knowledge gap).

Remaining Recommendations: ✓ CCSCN guidelines

COVID-19 with mild ARDS	COVID-19 with Mod to Severe ARDS	Rescue/Adjunctive therapy
✓ **Do:** Vt 4-8 ml/kg and $P_{plat} < 30$ cm H_2O ✓	⚠ **CONSIDER:** Higher PEEP ✓	? **Uncertain:** Antivirals, chloroquine, anti-IL6
✓ **Do:** Investigate for bacterial infection ✓	⚠ **CONSIDER:** NMBA boluses to facilitate ventilation targets ✓	⚠ **CONSIDER:** if proning, high P_{plt}, asynchrony NMBA infusion for 24 h ✓
✓ **Do:** Target SPO2 92% - 96% ✓	⚠ **CONSIDER:** if PEEP responsive Traditional Recruitment maneuvers ✓	⚠ **CONSIDER:** Prone ventilation 12-16 h ✓
⚠ **CONSIDER:** Conservative fluid strategy ✓	⚠ **CONSIDER:** Prone ventilation 12-16 h ✓	⚠ **CONSIDER:** STOP if no quick response A trial of inhaled Nitric Oxide
⚠ **CONSIDER:** Empiric antibiotics ✓	⚠ **CONSIDER:** if proning, high P_{plt}, asynchrony NMBA infusion for 24 h ✓	⚠ **CONSIDER:** follow local criteria for ECMO V-V ECMO or referral to ECMO center ✓
? **Uncertain:** Systematic corticosteroids	⛔ **Don't do:** Staircase Recruitment maneuvers	
	⚠ **CONSIDER:** Short course of systemic corticosteroids ✓	
	? **Uncertain:** Antivirals, chloroquine, anti-IL6	

Primum non nocere!

Town Hall – Status Update

- Last COVID-19 town hall as part of this series on May 13 (next week)
- Regular DCCM grand rounds to resume May 20
  - Webinar format via Zoom
- Ongoing ability to incorporate pertinent COVID information into grand rounds as needed